Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

Produits thérapeutiques émergentes pour la COVID-19

Groupe de travail FPT sur les pénuries de médicaments

6 avril 2021

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH

Objectif

- Présenter au groupe de travail FPT sur les pénuries de médicaments une mise à jour sur les thérapies émergentes pour la COVID-19 :
  - *Essais cliniques en cours;*
  - *Résultats cliniques récemment rapportés.*
- Une attention particulière est accordée aux médicaments antiviraux et à certains médicaments actuellement à l'étude à Santé Canada

Produits thérapeutiques émergentes et autorisées pour la COVID-19

Médicaments Antiviraux

- **Remdesivir***
- **Favipiravir****
- **Molnupiravir**
- **PF-07321332**

Monoclonaux neutralisants

- Bamlanivimab en monothérapie*
- Bamlanivmab + Etesevimab**
- Casirivimab + Imdevimab**
- VIR-7831
- AZD-7442
- CT-P59

Médicaments immunomodulateurs

- Dexaméthasone/ Glucocorticoïdes
- Tocilizumab
- Sarilumab
- Anakinra
- Baricitinib
- Otilimab
- **Colchicine****
- **Leronlimab****
- Fumarate de diméthyle (DMF)

Autre

- Aspirine
- Ivermectine
- Fluvoxamine
- Oxyde nitrique

**Homologué par Santé Canada*
***En cours d'examen à Santé Canada*

Cibles pharmacologiques pour la COVID-19

Médicaments anti-inflammatoires à cibles multiples

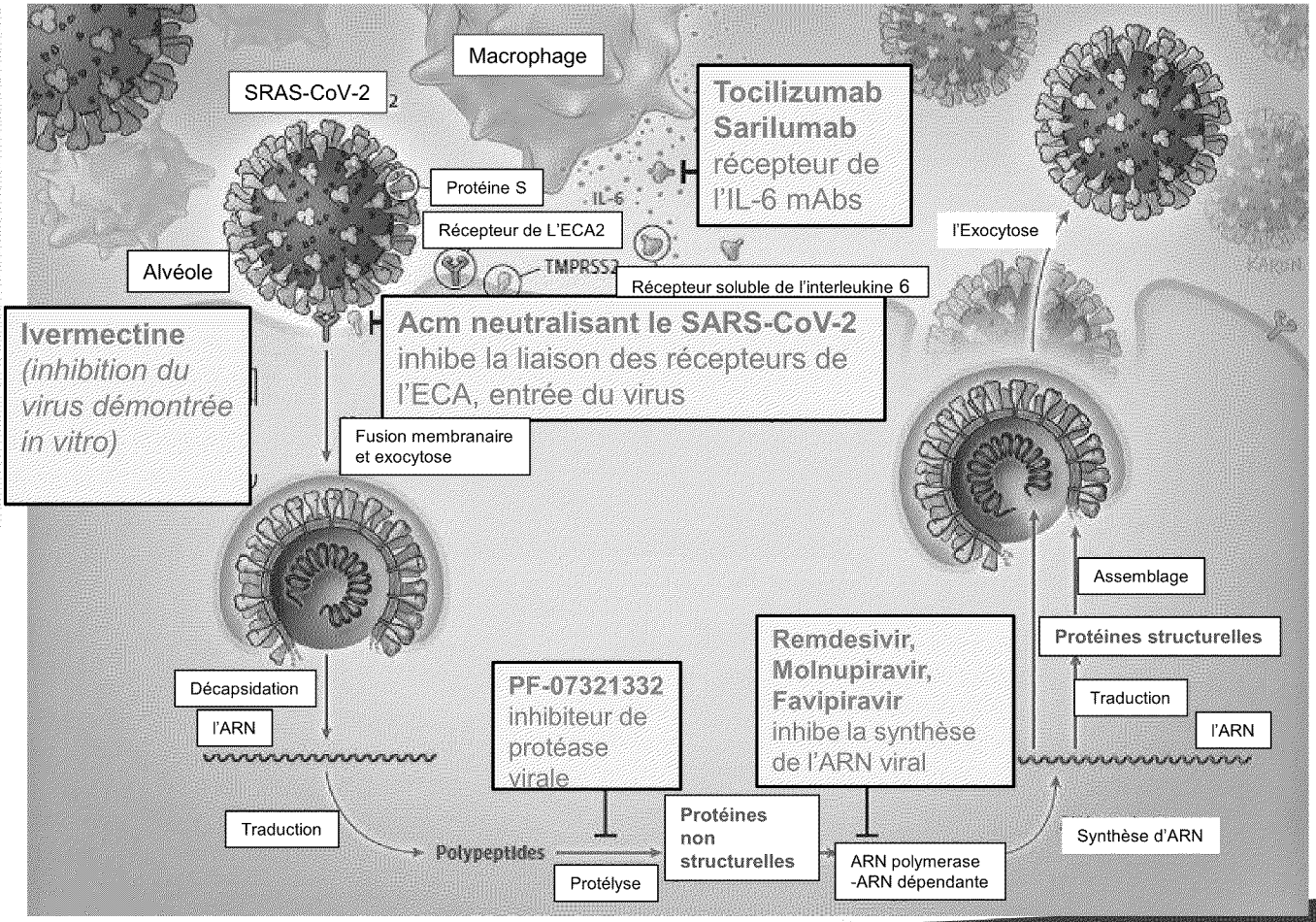
Dexaméthasone/ glucocorticoïdes de nombreux effets; antagoniste du NFkB

Colchicine, DMF de nombreux effets; inhibe l'inflammasome NLRP3

Autres thérapeutiques

Aspirine antiplaquettaire

Oxyde nitrique antiviral, immunomodulateur



Autres médicaments anti-inflammatoires ayant des cibles cellulaires spécifiques

Anakinra
Antagoniste de l'IL-1

Leronlimab
(*AcM* anti-CCR5)

Baricitinib
(inhibiteur de JAK1/2)

Otilimab
AcM anti-GM-CSF

Fluvoxamine
Active le récepteur sigma-1

AcM = anticorps monoclonal

Adapté de Sanders, JM, et coll. *Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19)*. Examen, JAMA, 2020, vol.18, nº 323, p.1824-1836

Médicaments antiviraux du SRAS-CoV-2

- Potentiels pour les thérapies combinées (par exemple le régime antiviral combiné du VIH);
- Ciblent la reproduction active du virus;
- Phase aiguë (avant ou début de la phase symptomatique);
- COVID de longue durée (excrétion virale prolongée).

Médicaments antiviraux autorisés et expérimentaux contre le SRAS-CoV-2

	Remdesivir *(Veklury®)*	Favipiravir *(Avigan®, Reeqonus®)*	Molnupiravir *(MK-4482)*	PF-07321332
Fabricant (Cible originale)	Gilead (Ebola; médicament expérimental)	Appili; Dr Reddy; Global Response Aid; FujiFilm (grippe pandémique).	Merck; Ridgeback Pharmaceuticals (grippe).	Pfizer (SRAS-CoV-1)
Cible	analogue de nucléotide.	enzyme virale (ARN polymérase ARN dépendante)	prodrogue d'analogue nucléosidique.	Protéase virale (3CL)
Mécanisme d' action	Inhibe la synthèse de l'ARN viral.	Inhibe la synthèse de l'ARN viral.	Inhibe la synthèse de l'ARN viral.	Inhibe la réplication viral
Administration	IV (forme inhalée dans les essais).	Oral	Oral	Oral
Statut	Autorisé par Santé Canada dans le cadre d'une ordonnance provisoire pour les adultes et les adolescents âgés de 12 ans et plus souffrant d'une COVID-19 grave et nécessitant un supplément d'O2.	Examen en cours par Santé Canada pour la COVID-19 légère à modérée chez les adultes	Essais de phase 2 et de phase 2 et 3 adaptatifs en cours, tant en milieu hospitalier qu'en milieu ambulatoire.	Début des essais de phas 1 en mars 2021
Essais en cours	Essai de phase 1/2 sous **par voie inhalée** (traitement ambulatoire	Autorisé en Russie, en Indonésie et en Inde pour la COVID-19.	Données de phase 2 positives pour la réduction de la charge virale.	

CM1

Slide 6

CM1 Données sur l'efficacité et l'innocuité de la phase 2 prévues au printemps 2021

Cheryl Marinsky, 2021-04-12

Favipiravir c. soins standard pour la gravité légère/modérée/non spécifiée de la COVID-19 : *Méta-analyse de réseau à partir de 7 essais contrôlés randomisés*

Résultats	Effets absolus anticipés (IC 95 %)		Risque relatif (IC 95 %)	Nombre de participants (études)	Certitude de la preuve (GRADE)	Commentaires
	Risque avec les soins standard/le placebo	Risque avec Favipiravir				
Conversion virale négative D7	668 per 1,000	**735 per 1,000** (641 to 848)	**RR 1.10** (0.96 to 1.27)	696 (6 RCTs) [b]	⨁⨁◯◯ LOW [c,d]	
Amélioration clinique D28	552 per 1,000	**563 per 1,000** (524 to 601)	**RR 1.02** (0.95 to 1.09)	579 (5 RCTs) [e]	⨁⨁◯◯ LOW [f,g]	
Amélioration clinique D60 ou plus - non signalé		-	-	-	-	Résultat non encore mesuré ou rapporté
Score de progression de l'OMS (niveau 7 ou supérieur) D28	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	370 (3 RCTs) [h]	⨁◯◯◯ VERY LOW [i,j]	Aucun événement dans les deux groupes
Score de progression de l'OMS (niveau 7 ou supérieur) D60 ou plus - non signalé	-	-	-	-	-	Résultat non encore mesuré ou rapporté
Mortalité toutes causes confondues D28	9 per 1,000	**3 per 1,000** (0 to 27)	**RR 0.33** (0.04 to 3.16)	470 (4 RCTs) [k]	⨁◯◯◯ VERY LOW [i,j]	
Mortalité toutes causes confondues D60 ou plus - non rapporté		-	-	-	-	Résultat non encore mesuré ou rapporté
Événements indésirables	287 per 1,000	**442 per 1,000** (250 to 789)	**RR 1.54** (0.87 to 2.75)	578 (4 RCTs) [m]	⨁◯◯◯ VERY LOW [n,o,p]	
Événements indésirables graves	21 per 1,000	**25 per 1,000** (10 to 62)	**RR 1.20** (0.48 to 3.00)	538 (4 RCTs) [q]	⨁◯◯◯ VERY LOW [l,n]	

Le risque dans le groupe d<intervention (et son intervalle de confiance à 95%) est fondé sur le risque présumé dans le groupe de comparaison et l'effet relatif de l'intervention (et son IC à 95%) RCT-ECR RR- Risque relatif (RR) CI-IC

+ Très faible **++ Faible** **+++ Modérée**

https://covid-nma.com/living_data

Remdesivir c. soins standard pour la COVID-19 légère/modérée/grave/critique : *Méta-analyse en réseau à partir de 5 essais contrôlés randomisés*

Résultats	Effets absolus anticipés (IC 95 %)		Risque relatif (IC 95 %)	Nombre de participants (études)	Certitude de la preuve (GRADE)	Commentaires
	Risque avec les soins standard /le placebo	Risque avec Remdesivir				
Conversion virale négative D3	292 per 1,000	**284 per 1,000** (178 to 450)	**RR 0.97** (0.61 to 1.54)	196 (1 RCT) [b]	⨁◯◯◯ VERY LOW [c,d,e]	
Conversion virale négative D7	492 per 1,000	**502 per 1,000** (374 to 679)	**RR 1.02** (0.76 to 1.38)	196 (1 RCT) [b]	⨁◯◯◯ VERY LOW [c,d,f]	
Amélioration clinique D7	345 per 1,000	**366 per 1,000** (307 to 439)	**RR 1.06** (0.89 to 1.27)	832 (2 RCTs) [g]	⨁⨁⨁◯ MODERATE [f]	
Amélioration clinique D14-D28	759 per 1,000	**805 per 1,000** (751 to 858)	**RR 1.06** (0.99 to 1.13)	832 (2 RCTs) [g]	⨁⨁⨁◯ MODERATE [h]	
Score de progression de l'OMS (niveau 6 ou supérieur) D7	451 per 1,000	**419 per 1,000** (243 to 717)	**RR 0.93** (0.54 to 1.59)	1298 (2 RCTs) [i]	⨁⨁◯◯ LOW [f,j]	
Score de progression de l'OMS (niveau 6 ou supérieur) D14-D28	193 per 1,000	**131 per 1,000** (106 to 164)	**RR 0.68** (0.55 to 0.85)	1894 (3 RCTs) [k]	⨁⨁⨁◯ MODERATE [l]	
Score de progression de l'OMS (niveau 7 ou supérieur) D7	359 per 1,000	**251 per 1,000** (212 to 294)	**RR 0.70** (0.59 to 0.82) ←	1298 (2 RCTs) [i]	⨁⨁⨁◯ MODERATE [h]	
Score de progression de l'OMS (niveau 7 ou supérieur) D14-D28	178 per 1,000	**124 per 1,000** (100 to 156)	**RR 0.70** (0.56 to 0.88) ←	1894 (3 RCTs) [k]	⨁⨁⨁⨁ HIGH	
Mortalité toutes causes confondues D7	63 per 1,000	**43 per 1,000** (18 to 104)	**RR 0.68** (0.28 to 1.64) ←	1298 (2 RCTs) [i]	⨁◯◯◯ VERY LOW [e,m]	
Mortalité toutes causes confondues D14-D28	112 per 1,000	**101 per 1,000** (82 to 125)	**RR 0.90** (0.73 to 1.11)	7345 (4 RCTs) [n]	⨁⨁⨁◯ MODERATE [f]	
Événements indésirables	583 per 1,000	**583 per 1,000** (507 to 671)	**RR 1.00** (0.87 to 1.15)	1894 (3 RCTs) [k]	⨁⨁⨁◯ MODERATE [l,o]	
Événements indésirables graves	252 per 1,000	**186 per 1,000** (156 to 221)	**RR 0.74** (0.62 to 0.88) ←	1894 (3 RCTs) [k]	⨁⨁⨁◯ MODERATE [o,p]	

Le risque dans le groupe d<intervention (et son intervalle de confiance à 95%) est fondé sur le risque présumé dans le groupe de comparaison et l'effet relatif de l'intervention (et son IC à 95%) RCT-ECR RR- Risque relatif (RR) CI-IC

+ Très faible **++ Faible** **+++ Modérée**

COLCHICINE -
EMPLOI NON CONFORME POUR LA COVID-19

Colchicine: Profil pharmaceutique et statut d'authorisation

- Autorisé par le Santé Canada pour le traitement de la goutte aiguë, la prophylaxie des crises de goutte récurrentes, et la prévention des crises aiguës de fièvre méditerranéenne familiale (FMF) chez les adultes; son utilisation n'est autorisée pour aucune indication chez les patients de moins de 16 ans.

- Commercialisé sous forme de comprimés de 0,6 mg par plusieurs fournisseurs.

- De nombreuses emplois courants non conforme à l'étiquette, notamment la prévention de la péricardite aiguë ou récurrente, le traitement du syndrome de Behçet, la prophylaxie et le traitement de la chondrocalcinose articulaire.

- Utilisation non-approuvée au Canada pour la prévention ou le traitement de la COVID-19.

- Santé Canada a reçu une soumission en vertu de l'ordonnance provisoire le 25 janvier 2021 pour des comprimés de colchicine, formulation de 0,5 mg (PendoPharm; PharmaScience) comme traitement contre la COVID-19 légère à modérée (examen en cours).

Colchicine:preuves clinique de premier ordre

Essai COLCORONA (prépublication; *non examinée pas les pairs*):

- Les investigateurs ont issu une prépublication de l'ECR COLCORONA multinationale, sans contact, en double aveugle le 27 janvier, 2021.
- L'essai a pris fin prématurément; les données cliniques préimprimées ont été analysées chez 4 488 adultes âgés de 40 ans et plus ayant reçu un diagnostic de COVID-19 probable ou confirmé dans les 24 heures précédant l'inscription, avec au moins un facteur de risque de complications liées à la COVID-19.
- Les facteurs de risque comprenaient l'âge (70 ans), l'obésité (IMC 30), les comorbidités cardiovasculaires, le diabète sucré, l'hypertension non contrôlée, la bicytopénie/pancytopénie, ainsi que les symptômes de la COVID-19 (fièvre 38,4 au cours des 48h précédentes et/ou combinaison d'un taux élevé de neutrophiles/d'un faible nombre de lymphocytes et/ou de dyspnée).
- Une dose de 0.5mg de colchicine administrée deux fois par jour pendant trois jours, puis une fois par jour pendant 27 jours (comprimés; PharmaScience, Québec; (n=2,235) ; ou placebo (n=2,253)), lancé dans les 48h suivant les résultats des tests / diagnostic positifs.

https://www.medrxiv.org/content/10.1101/2021.01.26.21250494v1

Colchicine: preuves clinique de premier ordre

Essai COLCORONA (prépublication; *non examinée pas les pairs*):

- L'essai n'a pas atteint son critère composite primaires de réduction des hospitalisations ou de la mortalité à 30 jours (4,7 % pour la colchicine contre 5,8 % pour le placebo).
- Aucune différence significative entre les deux groupes en ce qui concerne l'incidence des décès ou des hospitalisations, ni en ce qui concerne la ventilation mécanique, qui a été évaluée en tant que résultat secondaire.
- Dans une analyse de sous-groupe sur des patients confirmés par ACP (n=4159) : Incidence réduite des hospitalisations ou de la mortalité à 30 jours de la COVID-19, (4,6 % de colchicine [n=2075] contre 6,0 % de placebo [n=2084]; RC 0,75; IC à 95 % 0,57 à 0,99).
- Dans ce sous-groupe, le rapport de cotes pour la réduction des hospitalisations était de 0,75; (IC de 95 %, 0,57 à 0,99), mais aucune différence n'a été observée pour le décès seul (0,56 ; IC de 95 %, 0,19 à 1,66) ou la ventilation mécanique (0,50 ; IC de 95 %, 0,23 à 1,07).
- Des EI graves ont été signalés chez 4,9 % des participants du groupe colchicine [n=2 195] contre 6,3 % dans le groupe placebo [n=2 217] (p=0,05), notamment une pneumonie 2,9 % contre 4,1 % (p=0,02), une embolie pulmonaire 0,5 % contre 0,1 % (p=0,01) et une diarrhée 13,7 % contre 7,3 % (p<0,0001), respectivement.

https://www.medrxiv.org/content/10.1101/2021.01.26.21250494v1

Colchicine : Preuves cliniques de premier ordre

Essai RECOVERY (communiqué de presse; *non évalué par les pairs*) *:*

- Essai randomisé ouvert basé au Royaume-Uni chez des patients hospitalisés pour la COVID-19.
- Décision du Comité indépendant de surveillance de données, rendue le 4 mars, de fermer le volet de traitement à la colchicine en raison de la futilité
- Analyse préliminaire fondée sur 2 178 décès signalés parmi 11 162 patients randomisés (94 % également traités par un corticostéroïde).
- Aucune différence significative dans le critère principal de mortalité à 28 jours
  - 20 % colchicine contre 19 % soins habituels seuls; (p=0,63)
- Le suivi des patients est en cours; la publication de l'analyse finale est prévue prochainement.
  https://www.recoverytrial.net/news/recovery-trial-closes-recruitment-to-colchicine-treatment-for-patients-hospitalised-with-covid-19
- Preuves diverses de l'avantage clinique provenant de nombreux petits essais insuffisamment puissants chez les patients hospitalisés atteints de COVID-19

Colchicine pour le traitement de la COVID-19: L'OPINION D'EXPERTS

Le groupe de travail ad hoc sur la pharmacologie clinique de la COVID-19 (GTPC)**:** *10 Février, 2021*
Recommendation

Le Groupe de travail sur la pharmacologie clinique recommande que l'utilisation de la colchicine (d'un dose de 0.6mg) comme traitement pour les patients non hospitalisés atteints de COVID-19- pour un emploi non-conforme- soit limitée à des essais contrôlés aléatoires. Des preuves cliniques supplémentaires sont nécessaires pour déterminer si les bénéfices potentiels de la colchicine l'emportent sur les risques connus et potentiels. Cette orientation sera mise à jour au fur et à mesure que des preuves évaluées par des pairs apparaîtront, en particulier à partir d'essais cliniques bien étayés qui peuvent fournir des preuves supplémentaires des risques et des bénéfices dans des sous-groupes de patients spécifiques (comorbidités, populations âgées/pédiatriques, ethnicité ou sexe).

https://www.canada.ca/en/public-health/corporate/mandate/about-agency/external-advisory-bodies/list/covid-19-clinical-pharmacology-task-group/statement-colchicine.html

COVID-19 directives de traitement pour la colchicine dans les provinces et territoires

- Comité thérapeutique du BC COVID-19 : Le CTC ne recommande pas l'utilisation systématique de la colchicine à en ce moment. Chez les patients âgés de 40 ans ou plus atteints de COVID-19 confirmé par ACR, qui présentent au moins un facteur de risque (selon l'essai COLCORONA) et aucune contre-indication [spécifiée dans les directives], l'administration de colchicine à raison de 0,6 mg PO BID x 3 jours, puis 0,6 mg par jour x 27 jours peut être envisagée au cas par cas en discussion avec le patient en soulignant clairement l'incertitude quant au bénéfice du traitement, ainsi que les risques et les effets indésirables potentiels. Le consentement éclairé doit être obtenu et le traitement doit être initié dès que possible. La colchicine pour le traitement des patients gravement ou gravement malades atteints de COVID-19 n'est pas recommandée en dehors des essais cliniques approuvés.

- Groupe consultatif scientifique COVID-19 des services de santé de l'Alberta : Pour l'instant, la colchicine ne doit pas être prescrite ou administrée pour traiter la COVID-19. Les cliniciens et les chercheurs de l'Alberta devraient soutenir des essais cliniques de haute qualité en Alberta ou dans le cadre d'une étude multicentrique bien conçue pour aider à découvrir si la colchicine présente un avantage pour le traitement de la COVID-19.

- INESSS : L'état actuel des connaissances scientifiques et l'incertitude sur les avantages et les risques potentiels de l'administration de colchicine chez les personnes non hospitalisées ayant un diagnostic de COVID-19 confirmé ou non par un test RT-PCR, et qui répondent aux critères de sélection de l'étude COLCORONA (plus de 40 ans avec au moins un facteur de risque), ne permettent pas de soutenir l'utilisation de la colchicine pour cette population en dehors d'un protocole de recherche. SRAS-CoV-2 confirmé, traitement en milieu hospitalier.

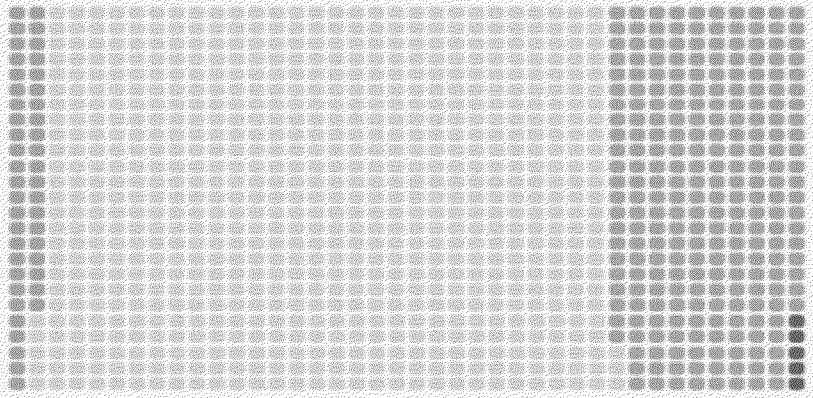
REPRÉSENTATION GRAPHIQUE DES EFFETS POTENTIELS DU TRAITEMENT

La figure ci-dessous illustre les effets potentiels de la colchicine sur les hospitalisations et les évènements indésirables chez des personnes qui correspondent aux critères de l'étude et qui ont un obtenu un test RT-PCR positif.

⚠ Les causes qui ont mené aux hospitalisations, la durée réelle du séjour au-delà des 24 heures prédéfinies et la nécessité d'un transfert aux soins intensifs sont non documentées dans la prépublication.

Traitement de 30 jours avec colchicine

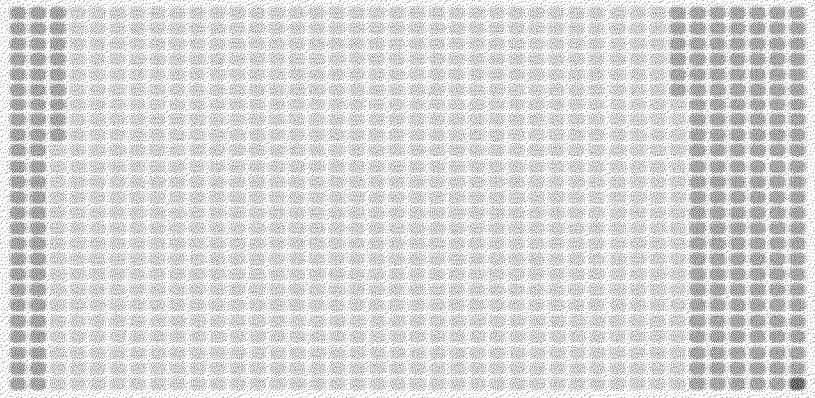
1000 personnes ayant résultat par RT-PCR positif pour la COVID-19
Non hospitalisées | 40 ans et plus | ≥ 1 Facteur de risque



- 45 auraient été hospitalisées en raison de la COVID-19
- 242 auraient subi des événements indésirables (surtout gastro-intestinal)
- 5 auraient subi une embolie pulmonaire

Traitement de 30 jours avec placébo

1000 personnes ayant résultat par RT-PCR positif pour la COVID-19
Non hospitalisées | 40 ans et plus | ≥ 1 Facteur de risque



- 59 auraient été hospitalisées en raison de la COVID-19
- 155 auraient subi des événements indésirables (surtout gastro-intestinal)
- 1 aurait subi une embolie pulmonaire

https://www.inesss.qc.ca/fileadmin/doc/INESSS/COVID-19/INESSS_COVID-19_Colcorona_outil_analyse_donnees.pdf

LERONLIMAB - *MÉDICAMENT EXPÉRIMENTAL POUR LES PATIENTS ATTEINTS DE COVID-19 CRITIQUE*

Leronlimab : Profil du médicament

- Anticorps monoclonal humanisé anti-CCR5 (récepteur de la chimiokine C-C de type 5); bloque le co-récepteur CCR5 présent sur les cellules T et d'autres cellules immunitaires.

- L'activation de CCR5 par l'intermédiaire de ligands immuno-stimulateurs (CCL5 (RANTES), CCL3 (MIP-1α) et CCL4 (MIP-1β)) entraîne une infiltration des cellules immunitaires.

- L'état hyper-inflammatoire caractérisé par la COVID-19 grave et critique peut être en partie attribuable à une infiltration accrue de cellules immunitaires.

Leronlimab : Statut de l'autorisation

- Non approuvé pour utilisation au Canada pour toute indication.

- Le 23 mars 2021, Santé Canada a reçu une demande dans le cadre de l'ordinance provisoire pour le leronlimab (CytoDyn, Inc.; Amarex) comme traitement de la COVID-19 légère à modérée (examen en cours).

- L'Administration des États-Unis chargée des aliments et des médicaments a accordé à **CytoDyn Inc.** le statut de médicament nouveau expérimental d'urgence (EIND) pour le leronlimab dans le cadre de la COVID-19.

Leronlimab : Preuves cliniques de premier ordre

- Un communiqué de presse portant sur une étude multicentre, randomisée, à double insu, contrôlée par placebo, de phase IIb/III, parrainée par une société pharmaceutique, à deux volets, randomisée, à double insu, contrôlée par placebo, chez des patients adultes hospitalisés atteints de la COVID-19 grave ou critique.

- Les patients ont été randomisés pour recevoir soit des doses hebdomadaires de 700 mg de leronlimab, soit un placebo, par voie sous-cutanée.

- Le critère de jugement principal est la mortalité toutes causes confondues à 28 jours.

- Les résultats basés sur 309 patients de la population en intention de traiter modifiée, rapportés dans un communiqué de presse le 30 mars 2021, ont indiqué une réduction du risque absolu de décès le 28^{e} jour de 6,5 % pour les patients ayant reçu le leronlimab par rapport au placebo, en plus des autres traitements de la COVID-19 (P = 0,0319).

- Aucune étude ou prépublication par les pairs n'a été effectuée sur des études contrôlées randomisées démontrant l'efficacité et l'innocuité clinique en tant que traitement pour la COVID-19

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From: Timmerman, Karen (PHAC/ASPC)

Sent: 2021-01-28 5:11 PM

To: Salvadori, Marina (PHAC/ASPC); Baclic, Oliver (PHAC/ASPC); Patel, Milan (PHAC/ASPC); Killikelly, April (PHAC/ASPC); Abraham, Natalia k (PHAC/ASPC); Chung, Yung-En (PHAC/ASPC); Lehman, Kelly (HC/SC); Frappier2, Fiona (HC/SC); Chigrinova, Mariya (HC/SC); Uhthoff, Peter (PHAC/ASPC); Beaulieu, Marc-Andre (PHAC/ASPC); Mitchelmore, Bradley (PHAC/ASPC); Blanchard, Bradley (PHAC/ASPC); Kamkar, Maryam (PHAC/ASPC); Forbes, Nicole (PHAC/ASPC); Murthy, Srinivas [CWBC; Lordkipanidze Marie; R.I.Hall@Dal.Ca; mrieder@uwo.ca; Collier, Abby; Goldhawk, Michael (PHAC/ASPC); m.piquette.miller@utoronto.ca; Sarwar, Elaha (PHAC/ASPC); Levesque2, Kaili (HC/SC); Carin, Kristi (HC/SC); Groeneweg, Sheryl (IC); Arancibia, Rodrigo (IC); Taha, Zaid (PHAC/ASPC); Courtemanche, Jocelyne (PHAC/ASPC); Arthur, Jacqueline (PHAC/ASPC); Siushansian, Jennifer (PHAC/ASPC); Lawuyi2, Niyi (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC); Krishnan, Ramya (PHAC/ASPC); Beique, Lizanne (PHAC/ASPC); Timmerman, Karen (PHAC/ASPC); Marinsky, Cheryl (PHAC/ASPC); Ha, Shalane (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC); PHAC.F Emerging Science Secretariat / Secrétariat des sciences émergentes F.ASPC; Garcia Carrasco, Alexandra (HC/SC); Farrah, Kelly (PHAC/ASPC); Jaahnavi Dave; Dave, Jaahnavi (PHAC/ASPC); Stephens-Rennie2, Ericka (HC/SC); Sigouin, Ryan (HC/SC)

Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)

Subject: Daily MCM Therapeutic Titles for Thursday January 28, 2021

Good afternoon,

Here are the Daily MCM Therapeutics Titles for Thursday January 28th, 2021:
Please note this email and any assessments contained within are intended for your situational awareness of emerging clinical evidence of COVID-19 therapeutics; it is not intended as a complete systematic review.

Colchicine

- **PREPRINT** Tardif et al. Efficacy of Colchicine in Non-Hospitalized Patients with COVID-19. medRxiv. January 27, 2021.
- DESCRIPTION: COLCORONA is a contactless, randomized, double-blind, placebo-controlled trial conducted in 6 countries from March 2020 to January 2021. Participants enrolled over a telephone assessment and drug was couriered to their home within 4h of enrollment
- ***Population***: Non-hospitalized patients diagnosed with COVID-19 disease and have at least one risk factor for severe disease (N=4,488); [Mean age 54.7 years; 53.9% women; and 19.9% had diabetes]
- Eligible patients were at least 40 years of age, received a diagnosis of COVID-19 within 24 hours of enrollment, not currently hospitalized or under consideration for hospitalization, and presented with at least one of high-risk criteria.

- ***High risk criteria:*** ≥70 years of age, BMI ≥30, diabetes, uncontrolled hypertension (systolic blood pressure ≥150 mm Hg), known respiratory disease, known heart failure, known coronary disease, fever of at least 38.4°C within the last 48 hours, dyspnea at the time of presentation, bicytopenia, pancytopenia, or the combination of high neutrophil and low lymphocyte counts.
- ***Exclusion criteria:*** Inflammatory bowel disease, chronic diarrhea/maladsorption, pre-existent progressive neuromuscular disease; estimated glomerular filtration rate less than 30 ml/minute/1.73 m2; severe liver disease; current treatment with colchicine; current chemotherapy for cancer; or a history of significant sensitivity to colchicine.
- ***Intervention***: 2,192 patients received colchicine (0.5mg twice daily for the first 3 days and then once daily for 27 days thereafter) so treatment would commence within 48h of COVID-19.
- ***Comparator***: 2,189 patients received a placebo
- ***Key Results:***
- Primary outcome***:*** composite of death or hospitalization due to COVID-19 infection within 30 days
    - Composite endpoint of death or hospitalization due to COVID-19 occurred in 4.7% (104/2,235) of patients in the colchicine group and 5.8% (131/2,253) of patients in the placebo group (OR 0.79 [95% CI 0.61 to 1.03; p=0.08]).
- Secondary outcomes:
    - Death occurred in 0.2% (5/2,235) of patients in the colchicine group and 0.4% (9/2,253) died in the placebo group (OR 0.56 [95% CI 0.19 to 1.67]).
    - Hospitalizations due to COVID-19 occurred in 4.5% (101/2,235) of patients in the colchicine group and 5.7% (128/2,253) in the placebo group (OR 0.79 [95% CI 0.60 to 1.03]).
    - Mechanical ventilation was required for 0.5% (11/2,235) of the patients in the colchicine group and 0.9% (21/2,253) in the placebo group (OR 0.53 [95% CI 0.25 to 1.09]).
- Pre-specified analysis of patients with RT-PCR confirmed COVID-19 (N=4,159):

  Primary outcomes:
    - The rate of death or hospitalization due to COVID-19 were 4.6% (96/2,075) in the colchicine group and 6.0% (126/2,084) in the placebo group (OR 0.75 [95% CI 0.57 to 0.99; p=0.04]).
    - Death occurred in 0.2% (5/2,075) of patients in the colchicine group and 0.4% (9/2,084) in the placebo group (OR 0.56 [95% CI, 0.19 to 1.66]).
    - Hospitalization due to COVID-19 occurred in 4.5% (93/2,075) patients in the colchicine group and 5.9% (123/2,084) in the placebo group (OR 0.75 [95% CI 0.57 to 0.99]).
    - Mechanical ventilation was required for 0.5% (10/2,075) of patients in the colchicine group and 1.0% (20/2,084) in the placebo group (OR 0.50 [95% CI 0.23 to 1.07]).

  Secondary outcomes:
    - The secondary efficacy endpoint of the need for mechanical ventilation occurred in 0.5% (11/2,235) of the patients in the colchicine group and 0.9% (21/2,253) in the placebo group (OR 0.50 [95% CI 0.23 to 1.07]).
- Treatment effect for the primary outcome in a pre-specified subgroup based on sex: The rate of death or hospitalization due to COVID-19 was maintained in men (0R 0.67; 95% CI 0.48-0.95) but no treatment effect was observed in women (OR 1.07; 95% CI 0.70-1.65).
- ***Safety Signals:***
    - The rate of serious adverse events were 4.9% in the colchicine group and 6.3% in the placebo group (p=0.05).
    - The number of pulmonary embolism and pneumonia SAE was higher in patients in the colchicine group compared to placebo (0.5% versus 0.1%).
    - The most common adverse events were gastrointestinal events. Diarrhea was reported in 13.7% and 7.3% of patients in the two trial groups (P<0.0001).

- SUMMARY + CONTEXT: **In this randomized, double-blind, placebo-controlled trial (COLCORONA) of 4,488 non-hospitalized patients with COVID-19 and at least one risk factor, colchicine treatment failed to meet statistical significance in the primary endpoint of composite of death or hospitalization due to COVID-19 infection within 30 days. In a pre-specified subgroup analysis in patients with PCR confirmed COVID-19 (N=4,159), colchicine treatment reduced the risk of death or hospitalization, as well as the risk of hospitalization alone, compared to placebo. The most common adverse events related to colchicine were gastrointestinal events and diarrhea.**
- Considerations:
  - The trial was stopped when 75% of the planned patients were recruited and had completed the 30-day follow-up. Reasons given for early termination were logistical issues related to maintaining the central study call centre and a perceived need to disseminate the study results rapidly.
  - The composite outcomes of death or hospitalizations show significance; however, when the outcomes were analyzed individually, no significant differences in the outcomes were observed, with the exception of hospitalization in the RT-PCR confirmed COVID-19 patients.
  - COVID-19 diagnosis was defined as positive PCR by naso-pharyngeal swab or by a clinical algorithm in a symptomatic patient without an obvious alternative cause, or by epidemiological link to a SARS-CoV-2 positive household member.

Ivermectin

- Chachar et al, 2020. Effectiveness of ivermectin in SARSCoV-2/COVID-19 patients. International Journal of Sciences, September 2020.
- *Taken from Abstract:*

Background: The first case of Infection with severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) were diagnosed in Wuhan, China in 2019. In the first half of 2020, this disease has already converted into a global pandemic. Objectives, to assess the efficacy of Ivermectin in mild cases of COVID-19 patients on the basis of predefined assessment criteria.
Methods: Study setting Fatima Memorial Hospital, Lahore open label randomized control trial. Duration of study, from 1st May, 2020 to 30th June, 2020. Sample size and technique: Sample size was 50 patients; 25 patients were kept in control group and 25 patients were kept in experimental group.
Results: There were total 50 patients, divided into two groups case and control group. The mean
age of the participants was 40.60 ± 17 and out of those 31 (62%) were male and 19 (38%) were females. Cough was observed more in case group (p= 0.049). Fever, myalgias and dyspnea were the commonest symptoms in both the groups (p= 1.000). Diarrhea and vomiting were more common in control group (p=0.0001, p= 0.042 respectively). On follow up at day 7, patients were stratified as asymptomatic and symptomatic. Amongst the case group, out of 25 patients, 16 (64%) patients were asymptomatic and rest of the 9 (36%) patients were symptomatic. In control group, out of 25 patients, 15 (60%) patients were asymptomatic and rest of the 10 (40%) patients was symptomatic p-value (0.500). Statistically there was no significant difference between case group who were given ivermectin along with symptomatic treatment and control group who were only given symptomatic treatment without ivermectin, being asymptomatic on day 7 at follow up. p-value (0.500)

Conclusions: Our study didn't show statistically any significant difference between case and control group. In Ivermectin's (case group) recovery was almost equal to control group who received only conventional symptomatic treatment, so this is the need of the day that we need to conduct more randomized controlled trials across our country involving major tertiary care health care facilities with larger sample size to assess its efficacy for validating the use of Ivermectin against SARS-CoV-2.

- SUMMARY + CONTEXT: **This open label randomized controlled trial in a single centre of 50 adult outpatients with mild COVID-19 disease compared the efficacy of ivermectin treatment + symptomatic care versus symptomatic care alone in symptom resolution. No difference was reported between groups on symptom resolution by day 7 follow-up.**

Note- As of October 23, 2020, clinical data on lopinavir/ritonavir and hydroxychloroquine/chloroquine are no longer included in this listing due to overwhelming evidence of little to no clinical benefit. However, these titles are still being retained in our cloud based database.
Feedback and discussion on this daily email is always welcome.

Have a good evening,

The MCM Daily Titles (Therapeutics) Team

(Yung-En Chung, Nicole Forbes, Ramya Krishnan, Shalane Ha, Cheryl Marinsky, Elaha Sarwar, and Karen Timmerman)

From: Siushansian, Jennifer (PHAC/ASPC)
Sent: 2021-02-04 5:05 PM
To: Sarwar, Elaha (PHAC/ASPC)
Cc: Forbes, Nicole (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC); Lawuyi2, Niyi (PHAC/ASPC); Arthur, Jacqueline (PHAC/ASPC); Dave, Jaahnavi (PHAC/ASPC); Cortés-Kaplan, Serena (PHAC/ASPC); Thomas, Sharon (PHAC/ASPC); Marinsky, Cheryl (PHAC/ASPC); Ha, Shalane (PHAC/ASPC); Timmerman, Karen (PHAC/ASPC)
Subject: RE: QF for Feb. 4

Thank you, Elaha. Have a lovely evening. Jennifer

From: Sarwar, Elaha (PHAC/ASPC) <elaha.sarwar@canada.ca>
Sent: 2021-02-04 4:59 PM
To: Siushansian, Jennifer (PHAC/ASPC) <jennifer.siushansian@canada.ca>
Cc: Forbes, Nicole (PHAC/ASPC) <nicole.forbes@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Dave, Jaahnavi (PHAC/ASPC) <jaahnavi.dave@canada.ca>; Cortés-Kaplan, Serena (PHAC/ASPC) <serena.cortes-kaplan@canada.ca>; Thomas, Sharon (PHAC/ASPC) <sharon.thomas@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Ha, Shalane (PHAC/ASPC) <shalane.ha@canada.ca>; Timmerman, Karen (PHAC/ASPC) <karen.timmerman@canada.ca>
Subject: QF for Feb. 4

Hi Jennifer,

Please see below QFs for today.

February 4, 2021: The NIH updated COVID-19 treatment guidelines on the use of tocilizumab and sarilumab.

NIH updated their guidelines following preprint of the REMAP-CAP trial, citing **insufficient data to recommend** either for or against the use of tocilizumab or sarilumab for the treatment of COVID-19 patients who are at high risk of ICU admission and mechanical ventilation, and that, consistent with previous recommendations from the NIH, these treatments should be used in the context of a clinical trial.

The guidelines notes that **some NIH Panel members would recommend** the use of tocilizumab, but not sarilumab, in addition to dexamethasone, to patients who meet the above criteria and are at risk of respiratory failure.

For patients who are not in the ICU or who are in the ICU but do not require mechanical ventilation the **Panel recommends against** the use of tocilizumab or sarilumab for the treatment of COVID-19, except in a clinical trial.

February 4, 2021: Merck & Co Inc. statement against the use of ivermectin for the treatment of COVID-19.

- The company announced that its analysis of existing and emerging preclinical and clinical data does not support the efficacy of its anti-parasite drug, ivermectin, for the treatment of COVID-19.
- The company also cites a concerning lack of safety data in the majority of studies evaluating ivermectin for COVID-19 and cautioned against the use of the drug beyond its indication as an anti-parasitic.
- Ivermectin is not approved for use in Canada or in the USA for the prevention or treatment of COVID-19.

Have a good evening,
Elaha

Bradley, Kevin (HC/SC)

From: Sarwar, Elaha (PHAC/ASPC) <elaha.sarwar@canada.ca> on behalf of COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-02-26 4:21 PM
To: Salvadori, Marina (PHAC/ASPC); Baclic, Oliver (PHAC/ASPC); Patel, Milan (PHAC/ASPC); Killikelly, April (PHAC/ASPC); Abraham, Natalia k (PHAC/ASPC); Chung, Yung-En (PHAC/ASPC); Lehman, Kelly (HC/SC); Frappier2, Fiona (HC/SC); Chigrinova, Mariya (HC/SC); Uhthoff, Peter (SAC/ISC); Beaulieu, Marc-Andre (PHAC/ASPC); Mitchelmore, Bradley (PHAC/ASPC); Blanchard, Bradley (PHAC/ASPC); Kamkar, Maryam (PHAC/ASPC); Forbes, Nicole (PHAC/ASPC); Murthy, Srinivas [CWBC; Lordkipanidze Marie; R.I.Hall@Dal.Ca; mrieder@uwo.ca; Collier, Abby; Goldhawk, Michael (PHAC/ASPC); m.piquette.miller@utoronto.ca; Sarwar, Elaha (PHAC/ASPC); Levesque2, Kaili (HC/SC); Carin, Kristi (AADNC/AANDC); Groeneweg, Sheryl (IC); Arancibia, Rodrigo (IC); Taha, Zaid (PHAC/ASPC); Courtemanche, Jocelyne (PHAC/ASPC); Arthur, Jacqueline (PHAC/ASPC); Siushansian, Jennifer (PHAC/ASPC); Lawuyi2, Niyi (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC); Krishnan, Ramya (PHAC/ASPC); Beique, Lizanne (PHAC/ASPC); Timmerman, Karen (PHAC/ASPC); Marinsky, Cheryl (PHAC/ASPC); Ha, Shalane (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC); PHAC.F Emerging Science Secretariat / Secrétariat des sciences émergentes F.ASPC; Garcia Carrasco, Alexandra (HC/SC); Farrah, Kelly (PHAC/ASPC); Jaahnavi Dave; Dave, Jaahnavi (PHAC/ASPC); Stephens-Rennie2, Ericka (HC/SC); Sigouin, Ryan (HC/SC); Cortés-Kaplan, Serena (PHAC/ASPC); Hanson Pastran, Sasha (HC/SC); Rajendra, Kanya (HC/SC)
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)
Subject: Daily MCM Therapeutics Titles for Friday February 26, 2021

Good afternoon,

Here are the Daily MCM Therapeutics Titles for Friday February 26, 2021:
Please note this email and any assessments contained within are intended for your situational awareness of emerging clinical evidence of COVID-19 therapeutics; it is not intended as a complete systematic review.

Interleukin-6 Inhibitors

- Gordon et al., Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 - Preliminary report. **New England Journal of Medicine.** February 25, 2021.
  Taken directly from the abstract:
  BACKGROUND: The efficacy of interleukin-6 receptor antagonists in critically ill patients with coronavirus disease 2019 (Covid-19) is unclear.
  METHODS: We evaluated tocilizumab and sarilumab in an ongoing international, multifactorial, adaptive platform trial. Adult patients with Covid-19, within 24 hours after starting organ support in the intensive care unit (ICU), were randomly assigned to receive tocilizumab (8 mg per kilogram of body weight), sarilumab (400 mg), or standard care (control). The primary outcome was respiratory and cardiovascular organ support–free days, on an ordinal scale combining in-hospital death (assigned a value of −1) and days free of organ support to day 21. The trial uses a Bayesian statistical model with predefined criteria for superiority, efficacy, equivalence, or futility. An odds ratio greater than 1 represented improved survival, more organ support–free days, or both.
  RESULTS: Both tocilizumab and sarilumab met the predefined criteria for efficacy. At that time, 353 patients had been assigned to tocilizumab, 48 to sarilumab, and 402 to control. The median number of organ support–free days was 10 (interquartile range, −1 to 16) in the tocilizumab group, 11 (interquartile range, 0 to 16) in the sarilumab group, and 0 (interquartile range, −1 to 15) in the control group. The median adjusted cumulative odds ratios were 1.64 (95% credible interval, 1.25 to 2.14) for tocilizumab and 1.76 (95% credible interval, 1.17 to 2.91) for sarilumab as compared with control, yielding posterior probabilities of superiority to control of more than 99.9% and of 99.5%, respectively. An analysis of 90-day survival showed improved survival in the pooled interleukin-6 receptor antagonist

groups, yielding a hazard ratio for the comparison with the control group of 1.61 (95% credible interval, 1.25 to 2.08) and a posterior probability of superiority of more than 99.9%. All secondary analyses supported efficacy of these interleukin-6 receptor antagonists.
CONCLUSIONS: In critically ill patients with Covid-19 receiving organ support in ICUs, treatment with the interleukin-6 receptor antagonists tocilizumab and sarilumab improved outcomes, including survival. (REMAP-CAP ClinicalTrials.gov number, **NCT02735707**).

- SUMMARY + CONTEXT: **This international, ongoing, adaptive, single-blinded randomized controlled trial showed that in critically ill patients with Covid-19 the IL-6 receptor antagonists, tocilizumab and sarilumab, are both effective compared with current standard of care, which included corticosteroids in the majority of patients (>80%). Specifically, tocilizumab and sarilumab compared to standard of care lead to reduced mortality and higher median organ-support-free days in this patient population, compared to the standard of care. Clinical benefits was consistent across primary and secondary outcomes, and across subgroups and secondary analyses. Some serious adverse events were reported in the tocilizumab group, but not in the sarilumab.**
  - This trial was previously summarized and reported in the daily titles as a preprint on January 7, 2021: **PREPRINT:** Gordon et al., Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 - Preliminary report. January 7, 2021.
  - No major updates to results were report between the preprint and this publication, except with additional information on the estimated interaction between interleukin-6 receptor antagonists and glucocorticoids being additive and slightly in the direction of synergistic, but with substantial variability in the estimate (Tables S5 and S6).
  - Methods section contained additional information on primary analysis being conducted by the statistical analysis committee
  - The results of the analysis reported by the statistical analysis committee and the international trial steering committee were consistent with the primary analysis.

Corticosteroids

- Ma et al., Efficacy and safety of systemic corticosteroids among severe COVID-19 patients: a systematic review and meta-analysis of randomized controlled trials. Signal Transduction and Targeted Therapy. February 21, 2021.
  Taken directly from Abstract:
  Background: The benefits and harms of corticosteroids for patients with severe coronavirus disease 2019 (COVID-19) remain unclear.
  Methods: We systematically searched PubMed, Embase, and Cochrane Central Register of Controlled Trials from December 31, 2019 to October 1, 2020 to identify randomized controlled trials (RCTs) that evaluated corticosteroids in severe COVID-19 patients. The primary outcome was all-cause mortality at the longest follow-up. Secondary outcomes included a composite disease progression (progression to intubation, ventilation, extracorporeal membrane oxygenation, ICU transfer, or death among those not ventilated at enrollment) and incidence of serious adverse events. A random-effects model was applied to calculate risk ratio (RR) with 95% confidence intervals (CIs). We used the Grading of Recommendations Assessment, Development, and Evaluation approach to evaluate the certainty of the evidence.
  Results: Seven RCTs involving 6250 patients were included, of which the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial comprised nearly 78% of all included subjects. Results showed that corticosteroids were associated with a decreased all-cause mortality (27.3 vs. 31.1%; RR: 0.85; 95% CI: 0.73–0.99; $P = 0.04$; low-certainty evidence). Trial sequential analysis suggested that more trials were still required to confirm the results. However, such survival benefit was absent if RECOVERY trial was excluded (RR: 0.83; 95% CI: 0.65–1.06; $P = 0.13$). Furthermore, corticosteroids decreased the occurrence of composite disease progression (30.6 vs. 33.3%; RR: 0.77; 95% CI: 0.64–0.92; $P = 0.005$), but not increased the incidence of serious adverse events (3.5 vs. 3.4%; RR: 1.16; 95% CI: 0.39–3.43; $P = 0.79$).
- SUMMARY + CONTEXT: **The findings from this systematic review and meta-analysis of randomized control trials (n=7) demonstrate that in hospitalized patients with severe COVID-19, corticosteroids treatment was associated with reduced mortality and disease progression, and no increase in serious adverse events. However, results only show survival benefit if RECOVERY trial, which account for 78% of patients, is included in pooled analysis. Based on AMSTAR-2 criteria, the overall confidence in the results from this study is rated as moderate. Therefore, the systematic review may provide an accurate summary of the results of the available studies that were included in the review.**

Ivermectin

- **PREPRINT**: Okumus et al, 2021. Evaluation of the Effectiveness and Safety of Adding Ivermectin to Treatment in Severe COVID-19 Patients. BMC Infectious Diseases. February 24,2021.
  Taken directly from Abstract:
  Background: An effective treatment option is not yet available for SARS-CoV2, which causes the COVID-19 pandemic and whose effects are felt more and more every day. Ivermectin is among the drugs whose effectiveness in treatment has been investigated. In this study; it was aimed to investigate the presence of gene mutations that alter ivermectin metabolism and cause toxic effects in patients with severe COVID-19 pneumonia, and to evaluate the effectiveness and safety of ivermectin use in the treatment of patients without mutation.
  Methods: Patients with severe COVID19 pneumonia were included in the study, which was planned as a prospective, randomized, controlled, single-blind phase 3 study. Two groups, the study group and the control group, took part in the study. Ivermectin 200 mcg/kg/day for five days in the form of a solution prepared for enteral use added to the reference treatment protocol -hydroxychloroquine + favipiravir + azithromycin- of patients included in the study group. Patients in the control group were given only reference treatment with 3 other drugs without ivermectin. The presence of mutations was investigated by performing sequence analysis in the mdr1/abcab1 gene with the Sanger method in patients included in the study group according to randomization. Patients with mutations were excluded from the study and ivermectin treatment was not continued. Patients were followed for 5 days after treatment. At the end of the treatment and follow-up period, clinical response and changes in laboratory parameters were evaluated.
  Results: A total of 66 patients, 36 in the study group and 30 in the control group were included in the study. Mutations affecting ivermectin metabolism was detected in genetic tests of six (16.7%) patients in the study group and they were excluded from the study. At the end of the 5-day follow-up period, the clinical improvement rate was higher in the study group [22/30 (73.3%)] compared to the control group [16/30 (53.3%)] (p=0.10). At the end of the study, mortality developed in 6 patients (20%) in the study group and in 9 (30%) patients in the control group (p=0.37). At the end of the follow-up period, the average peripheral capillary oxygen saturation (SpO2) values of the study and control groups were found to be 93.5% and 93.0%, respectively. Partial pressure of oxygen (PaO2)/FiO2 ratios were determined as 236.3 ± 85.7 and 220.8 ± 127.3 in the study and control groups, respectively. While the blood lymphocyte count was higher in the study group compared to the control group (1698±1438 and 1256±710, respectively) at the end of the follow-up period (p=0.24); reduction in serum C-reactive protein (CRP), ferritin and D-dimer levels was more pronounced in the study group (p=0.02, p=0.005 and p=0.03, respectively).
  Conclusions: According to the findings obtained, ivermectin can provide an increase in clinical recovery, improvement in prognostic laboratory parameters and a decrease in mortality rates even when used in patients with severe COVID-19. Consequently, ivermectin should be considered as an important alternative to the treatment of COVID-19 disease or as an additional option to existing protocols.
- SUMMARY + CONTEXT**: This prospective, randomized, controlled, single-blind multicenter Phase 3 clinical trial assessed the effectiveness of ivermectin treatment compared with standard of care (hydroxychloroquine + favipiravir + azithromycin) among 66 hospitalized, adult male patients with severe COVID-19 pneumonia. No statistically significant differences between groups on the rate of clinical improvement, mortality and SOFA scores at 5-day follow-up and/or by the end of the study was reported. Improved peripheral capillary oxygen saturation and reductions in various blood markers (C - reactive protein, ferritin and D-dimer) were reported for the ivermectin group vs the standard of care group by the end of the follow-up period.**

Notes:
As of January 28, 2021, systematic review and meta-analysis studies of low/very low quality (based on AMSTAR 2 criteria) and those on therapeutics that the CPTG has approved statements will be included in the daily titles as an abstract with a rapid critical appraisal.

As of October 23, 2020, clinical data on lopinavir/ritonavir and hydroxychloroquine/chloroquine are no longer included in this listing due to overwhelming evidence of little to no clinical benefit. However, these titles are still being retained in our cloud based database.
Feedback and discussion on this daily email is always welcome.

Have a good evening,

The MCM Daily Titles (Therapeutics) Team

(Yung-En Chung, Jaahnavi Dave, Nicole Forbes, Ramya Krishnan, Shalane Ha, Cheryl Marinsky, Elaha Sarwar, and Karen Timmerman)

Correspondence on Colchicine and Ivermectin and Vitamin D

Dear [redacted]

I am writing in response to your correspondence of April 21, 2021, addressed to Dr. Tam, alerting us to the use of Ivermectin, vitamin D, and Colchicine, to support Canada's response to COVID-19. The honourable Minister of Health, Patty Hajdu, has asked that I reply on her behalf. I sincerely regret the delay in responding.

The Government of Canada is closely tracking all potential therapeutic treatments, vaccines, diagnostic tests, medical devices, and disinfectants currently available and in development in Canada and abroad. The Public Health Agency of Canada (PHAC) conducts a thorough analysis and synthesis of the emerging evidence of promising therapeutics to treat COVID-19. This work informs decisions around procurement of therapeutics proven to be safe, effective, and authorized for COVID-19 indication by Health Canada.

Currently there is no clear evidence from any clinical trial to suggest that Vitamin D supplementation has any clinical benefit for the treatment or prevention of COVID-19, particularly in the Canadian context. Although some studies observed an association between vitamin D deficiency and higher COVID-19 incidence, this does not establish a causal link between low vitamin D levels and COVID-19 infection, nor does it serve as proof that supplementing with vitamin D could treat or prevent COVID-19.

Ivermectin is a broad-spectrum anti-parasitic agent authorized and approved by Health Canada for human and veterinary applications. Although ivermectin is used in humans to treat parasitic infections, Health Canada has **not** authorized its use for the treatment of COVID-19. The first of many steps in the authorization process includes the provision of promising results documented and obtained from high quality study designs and clinical trials demonstrating safety and efficacy followed by submission of an application by the manufacturer to Health Canada, which follows a well-defined channel to qualify for approval for a particular indication.

In laboratory studies ivermectin prevented the virus causing COVID-19 from replicating, raising the possibility that ivermectin may have a role in COVID-19 prophylaxis or treatment; however, many drugs that show promise in laboratory studies are not found to be effective in patients. To address the increased international attention on ivermectin as a potential treatment for COVID-19, the World Health Organization (WHO) convened an independent, international panel of clinical care experts from multiple specialties, patient partners and ethicists to review the evidence. Following a review of the existing data, the panel concluded that there was little proof of ivermectin's effectiveness on several important clinical measures such as reducing mortality, need for mechanical ventilation and time to clinical improvement. Consequently, on March 31st 2021, The WHO issued a statement on ivermectin advising against its use outside of clinical trials, stating the current evidence was inconclusive.

Colchicine is an anti-inflammatory drug authorized by Health Canada for the treatment of gout, and other inflammatory diseases, for short courses of treatment and is used off-label for other conditions at the discretion of the primary heath care provider. Use of this drug for therapeutic purposes is limited by side effects such as fatigue, nausea, vomiting, and diarrhea. Interest in this drug originates from its anti-inflammatory activity and potential use to prevent the "cytokine storm" characteristic of severe COVID-19. A review of available clinical trial results, evaluating the effectiveness of colchicine as a treatment for COVID-19 was independently conducted by

PHAC, the Canadian Agency for Drugs and Technologies in Health, l'Institut national d'excellence en santé et services sociaux and Alberta Health Services. All of whom concluded that there was no clear benefit to colchicine treatment and some concerning harms (e.g. a small number of patients treated with colchicine in the trials developed blood clots in the lungs, a serious complication that could lead to death). There are a number of ongoing clinical trials of colchicine, as these results become available; PHAC will assess if there is a benefit to treating COVID-19 patients with this repurposed drug. At this time, Canadian expert groups do not recommend prescribing colchicine to treat COVID-19.

In summary, currently there is no clear evidence to suggest that either ivermectin, colchicine, or Vitamin D supplementation provides clinical benefit for the treatment or prevention of COVID-19, particularly in the Canadian context. Health Canada, the regulator in Canada, will review clinical data once submitted from the manufacturer and determine the benefits and risks of potential therapeutics and provide regulatory approval for COVID-19 accordingly. PHAC is actively monitoring emerging evidence of clinical efficacy and safety on novel and repurposed therapeutics for COVID-19, including ivermectin, colchicine, and vitamin D; and makes recommendation based on findings from emerging high quality evidence on an ongoing basis.

For information, the following link provides an update from l'Institut national d'excellence en santé et services sociaux on colchicine:

https://www.inesss.qc.ca/en/covid-19/traitements-specifiques-a-la-covid-19/colchicine.html

For more information, the following link provides a statement from Merck and Co. Inc. issuing a statement against the use of ivermectin for the treatment of COVID-19:

https://www.merck.com/news/merck-statement-on-ivermectin-use-during-the-covid-19-pandemic/

For more information, the following link provides the World Health Organization's guidance on the use to ivermectin to treat COVID-19:

https://www.who.int/news-room/feature-stories/detail/who-advises-that-ivermectin-only-be-used-to-treat-covid-19-within-clinical-trials

Bradley, Kevin (HC/SC)

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-06-09 11:28 AM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)
Subject: FW: I-Mask+ Protocol for early treatment of Covid-19

Response to be sent to [redacted]

Dear [redacted]

On behalf of Ms. Ephrem, I am following up to provide you with the contact information for the Alberta Health Service's evidence report on ivermectin, DRAFT v3.1 Ivermectin (albertahealthservices.ca). You can submit your questions/comments to: scientificadvisorygroup@ahs.ca.

Best regards.

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>
Sent: 2021-06-04 5:47 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Subject: FW: I-Mask+ Protocol for early treatment of Covid-19

From: [redacted]
Sent: 2021-06-04 5:15 PM
To: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>
Subject: RE: I-Mask+ Protocol for early treatment of Covid-19

Thank you. I apologize for the email I just sent. I had not read this response yet.

Can you recommend what agency or person I might correspond with in Alberta? I have been told it was Health Canada's jurisdiction to recommend Covid 19 treatments so I would like to confirm. Thanks.

On Fri, Jun 4, 2021 at 2:59 PM, Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca> wrote:

Thank you [redacted] for your follow up questions. I would like to offer some points of clarification in my response.

One of the Public Health Agency of Canada's (PHAC) roles to support Canada's COVID-19 response is to acquire medications to treat COVID-19. This is to ensure that Canadians will have access to safe and effective treatments in the context of substantial global demand. PHAC monitors the emerging evidence around therapeutics to inform the decisions around procurement. Please note that PHAC does not issue recommendations as such, for or against the use of medications for COVID-19.

A manufacturer seeking market authorization will submit safety and efficacy data to Health Canada (HC). As the regulator, HC grants market authorization when it is satisfied that the benefits outweigh the potential risks. The list of applications received for drugs and vaccines for COVID-19 is available online.

The provinces and territories have primary responsibility for decisions around choice and use of therapeutics - including for COVID-19 – within their jurisdictions. In Canada, a health care professional's decision to prescribe or use a particular drug for a labelled or off-label indication is part of the practice of medicine, which falls under the jurisdiction of provincial and territorial professional regulatory authorities.

With best regards,

Bersabel

(She | Elle)

Bersabel Ephrem, BSc., MPA

Director General, Centre for Communicable Diseases and Infection Control

Infectious Disease Prevention and Control Branch

Public Health Agency of Canada

bersabel.ephrem@canada.ca / Tel: 613-948-6799 / Cell: 613-415-5897

Directrice générale, Centre de la lutte contre les maladies transmissibles et les infections

Direction générale de la prévention et du contrôle des maladies infectieuses

Agence de la santé publique du Canada

bersabel.ephrem@canada.ca / Tel: 613-948-6799 / Cell: 613-415-5897

From: [redacted]
Sent: 2021-06-04 10:57 AM
To: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>
Subject: RE: I-Mask+ Protocol for early treatment of Covid-19

Good morning

Thank you for your prompt response to my inquiry. If I may, I urge you to reconsider Canada's stance on this extremely important matter. Have you, personally, read the research studies? Have you been following new developments as more and more respected scientists and researchers become convinced of the efficacy of this treatment for Covid-19? I implore you and your committee to do your own research and that you be be willing to step out of the accepted norms. Would you consider even allowing it on a person by person basis with informed consent? I know many people who are considering self treatment with veterinary quality ivermectin which concerns me greatly. I believe that it's in the best interest of Canadian for Canada to reconsider.

Respectfully,

[redacted]

On Thu, Jun 3, 2021 at 3:23 PM, Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca> wrote:

> Dear [redacted]
>
> Thank you for your correspondence concerning the use of the I-Mask Protocol for early treatment and prophylaxis for COVID-19 to support Canada's response to COVID-19.
>
> The Public Health Agency of Canada (PHAC) conducts a thorough analysis of the emerging scientific evidence regarding promising therapeutics to treat COVID-19, and Health Canada (HC) formally reviews these drugs to assess their safety, efficacy and quality before authorizing their sale in Canada. Many drugs that show promise in laboratory studies are found to be ineffective in patients.
>
> I-MASK+ Protocol is a prevention and early outpatient treatment protocol for COVID-19. While it includes a number of medications and supplements, it is centred on ivermectin, a broad-spectrum anti-parasitic agent authorized and approved by HC for human and veterinary applications to treat parasitic infections. At this time, HC has not authorized its use for the treatment of COVID-19.
>
> Independent reviews of available clinical trial results that evaluate the effectiveness of ivermectin as a treatment for COVID-19 have been conducted by: the Canadian Agency for Drugs and Technologies in Health (CADTH); Alberta Health Services; British Columbia's COVID-19 Therapeutics Committee/COVID-19 Therapeutics Review and Advisory Working Group; and Ontario's COVID-19 Science Advisory table. These bodies of scientific experts all concluded that there is no clear benefit to ivermectin treatment among patients with COVID-19.
>
> On March 31, 2021, the World Health Organization (WHO) issued a statement on ivermectin advising against its use outside of clinical trials, stating the current evidence was inconclusive. Further, the manufacturer - Merck - has also issued a statement against the use of ivermectin for the treatment of COVID-19.

https://www.merck.com/news/merck-statement-on-ivermectin-use-during-the-covid-19-pandemic/

In summary, there is currently no robust evidence (i.e., from high quality, well-designed clinical trials) to suggest that the I-MASK+ Protocol provides clinical benefit for the treatment or prevention of COVID-19, particularly in the Canadian context. Please be assured that PHAC continues to monitor the emerging evidence of clinical efficacy and safety from high quality trials on novel and repurposed therapeutics for COVID-19. The provinces and territories have primary responsibility for decisions around choice and use of therapeutics - including for COVID-19 – within their jurisdictions.

Thank you for writing to the Public Health Agency of Canada. I hope this information is helpful.

With best regards,

Bersabel
(She | Elle)

Bersabel Ephrem, BSc., MPA
Director General, Centre for Communicable Diseases and Infection Control
Infectious Disease Prevention and Control Branch
Public Health Agency of Canada
bersabel.ephrem@canada.ca / Tel: 613-948-6799 / Cell: 613-415-5897

Directrice générale, Centre de la lutte contre les maladies transmissibles et les infections
Direction générale de la prévention et du contrôle des maladies infectieuses
Agence de la santé publique du Canada
bersabel.ephrem@canada.ca / Tel: 613-948-6799 / Cell: 613-415-5897

-----Original Message-----
From: McLean, Hollie (HC/SC) <hollie.mclean@canada.ca> On Behalf Of Levesque2, Kaili (HC/SC)
Sent: 2021-05-31 3:54 PM
To: [redacted]
Cc: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>; Levesque2, Kaili (HC/SC) <kaili.levesque2@canada.ca>; McLean, Hollie (HC/SC) <hollie.mclean@canada.ca>
Subject: RE: I-Mask+ Protocol for early treatment of Covid-19

H[redacted]

Thank you for your email. Note that I've recently assumed the role as Vice President, COVID-19 Vaccine Rollout at the Public Health Agency. I'm connecting you

with Bersabel Ephrem, the Director General responsible for the therapeutics file.

Thanks

Kaili

Kaili Levesque (she/her/elle)
613.818.0492

-----Original Message-----
From: [redacted]
Sent: 2021-05-31 12:13 PM
To: Levesque2, Kaili (HC/SC) <kaili.levesque2@canada.ca>
Subject: I-Mask+ Protocol for early treatment of Covid-19

Good morning Ms. Levesque:

I am writing to ask for your assistance. I have been following a growing body of research on the use of the I-Mask Protocol for early treatment and prophylaxis for Covid-19. Early in the pandemic, this protocol was not well understood and had only anecdotal evidence of its efficacy. Recently, however, I've been encouraged to see multiple studies showing good evidence of efficacy. I am puzzled as to why this treatment is not being studied in Canada as we are still in a situation across the country where people are being hospitalized for Covid-19. I am not a medical professional, but I wonder if it is not prudent and compassionate to open the door to other treatment possibilities which could prevent further deterioration of newly diagnosed victims of this virus? I do not know if you are the right person to send this email to, but I do know that you believe that we should be doing absolutely everything to try to treat this disease. My sincere hope is that you and your Task Force are seeking to include the use of existing medicines that we know are not harmful in and of themselves, such as Ivermectin, which is one of the components in the I-Mask Protocol. While we all look forward to the day when vaccinations take effect Canada-wide, in the meantime there are still many people who are falling ill and require medical treatment for this disease.

I respectfully submit to you this link to the growing body of knowledge and research studies around the I-Mask+ Protocol and I beg you to use your considerable influence to bring it to the attention of the Covid 19 Task Force and study it with all due diligence. If there is merit in this treatment, and your committee agrees to try it on a limited study basis, perhaps many Canadian lives could be saved and/or at the very least, saved from the longevity of hospitalizations for Covid 19 which they may be facing under the current treatment protocols. I believe that your committee has a moral and ethical obligation to fairly and diligently consider all possible treatments, irrespective of WHO or any other body who may be telling you otherwise. We are Canadians, first and foremost. We are responsible for one another.

Thank you so very much for your time. I ask you to please respectfully consider my request, and I very much look forward to your reply.

Sincerely,

[redacted]

https://covid19criticalcare.com/covid-19-protocols/i-mask-plus-protocol/

Bradley, Kevin (HC/SC)

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-06-16 11:41 AM
To: Gale-Rowe, Margaret (PHAC/ASPC); Djiometio, Joseph (PHAC/ASPC); Azad, Mina (PHAC/ASPC)
Cc: Crôteau, Adèle (PHAC/ASPC); Mitchell, Stephanie (PHAC/ASPC); Cassista, Caroline (PHAC/ASPC); Kolbe, Jane (IC); Marinsky, Cheryl (PHAC/ASPC); Cortés-Kaplan, Serena (PHAC/ASPC); Birdi, Harsimrat (PHAC/ASPC); Lawuyi2, Niyi (PHAC/ASPC)
Subject: COVID-19 Ontario Science Table webinar debrief: Treatment of outpatients with COVID-19.

As discussed at our division meeting, we didn't hear anything new at the Ontario webinar last night. It was designed to help primary care practitioners respond to questions from their patients about available treatments.

Ontario's science table does not recommend any current products available for outpatient use to treat COVID-19. They presented information on budesonide, dexamethasone, colchicine, vitamin D, ivermectin, bamlanivimab, hydroxychloroquine, and antibiotics.

Key take aways:
- no drugs or biologics recommended for outpatient use. Lack of strong evidence, weak studies.
- patient related outcomes very important when looking at clinical trial results (most trials so far are of poor quality)
    - critical appraisal lens very important when reviewing clinical trial results;
    - analysis of impact on vulnerable populations important as not all populations represented in clinical trials.
- for outpatients, emphasis should be placed on getting vaccinated, and other public health measures such as masking, physical distancing, hand washing, etc.

The Ontario science table did highlight a few drugs they are watching and I have asked Mina to take a look at the first 3 below:
- Camostat mesylate (protease inhibitor)
- Interferon beta (immune modulator)
- BMS-986414/BMS-986414
- Molnupiravir – we are already watching this one so good to see it on their list as well.

Mina, just looking for a quick summary of each so that we know a bit about them.

Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, Policy Development, AMR Division | Gestionnaire principale, elaboration de politiques, Division de la RAM
COVID-19 Therapeutics | thérapeutiques

Centre for Communicable Diseases and Infection Control | Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada | Agence de la santé publique du Canada
t. (613) 889-8455

Bradley, Kevin (HC/SC)

From: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-06-09 11:48 AM
To: [redacted]
Cc: blaine.calkins@parl.gc.ca
Subject: Response from the Public Health Agency of Canada

Dear [redacted]

On behalf of Ms. Ephrem, I am following up to provide you with the contact information for the Alberta Health Service's evidence report on ivermectin, DRAFT v3.1 Ivermectin (albertahealthservices.ca). You can submit your questions/comments to: scientificadvisorygroup@ahs.ca.

Best regards.

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC

From [redacted]
Sent: 2021-06-04 5:12 PM
To: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>
Cc: blaine.calkins@parl.gc.ca
Subject: Follow up request

Dear Mr. Ephrem,

As a final follow up, I am asking for your gracious indulgence. The link below will take you to a two hour interview with Dr.Peter McCullough from Dallas, Texas. Dr. McCullough has successfully submitted and published peer reviewed papers on the use of various protocols to treat outpatients with Covid-19, in The Lancet. Please make time in your busy schedule to listen to Dr. McCullough explain his perspective on the successful use of many existing drugs and neutraceuticals to treat early onset Covid 19 patients.

I am heartened and encouraged by your willingness to be open and to actively seek alternative treatments for Covid 19. May God grant you extraordinary insight, wisdom and courage.

I look forward to hearing from you and to your feedback on this interview.

I have copied my MP, Mr. Blaine Calkins on this correspondence. I hope you won't mind.

Kind Regards

[redacted]

ISSUE NOTE v2
Ivermectin; STROMECTOL® (Merck & Co.)
15 December 2021

Essential Facts

- **About the Product:** Ivermectin (Stromectol®, Mectizan®; Merck & Co.) is a broad-spectrum antiparasitic and belongs to a class of drugs called anthelmintics.
- **Method of administration:** Ivermectin is administered intravenously (I.V.) and orally in studies for the treatment of COVID-19. It is also being evaluated as a prophylaxis in oral tablet form.
- **Approved use in Canada**:
    - Ivermectin is not authorized for any COVID-19 indication in Canada.
    - Health Canada has authorized ivermectin for the treatment of parasitic infections in humans and animals. In humans, ivermectin is indicated for the treatment of intestinal strongyloidiasis and onchoceriasis, or rosacea.
- **Approved use for COVID-19 internationally**
    - In May 2020, the Peruvian Ministry of Health recommended ivermectin for the treatment of mild and severe COVID-19. The recommendation was removed in June 2020.
    - Ivermectin has not been authorized for the prevention or treatment of COVID-19 in any other jurisdiction worldwide.
- **Key benefits:** Orally administered. In small RCTs, ivermectin may reduce viral load in patients with mild-to-moderate COVID-19. However,
    - Ivermectin is generally well tolerated for its approved indications.
- **Key challenges:**
    - More robust clinical trials with larger sample sizes are needed to determine its efficacy for COVID-19. The majority of trials on ivermectin in COVID-19 were limited to small sample sizes and mixed evidence on clinical benefits.

Status of Agreements

- **Current procurement status**: Nil
- **Current distribution status**: Nil

Considerations (optional)

- In June 2020, the Pan American Health Organization (PAHO) released a statement for ivermectin to be used only in the context of clinical trials.
- On January 14 2021, the National Institutes of Health (NIH) issued a statement on the lack of clear benefit or harm in the use of ivermectin for the treatment of COVID-19 due to the insufficient evidence.
- On February 4 2021, Merck and Co. announced they do not support the safety and efficacy of ivermectin for the treatment of COVID-19 based on an analysis of the available data and emerging studies. Their analysis identified no scientific basis for ivermectin as a potential therapeutic from

pre-clinical studies; no meaningful evidence for clinical activity or clinical efficacy in patients with COVID-19 disease; and the lack of safety data in the majority of studies.

Positions

CPTG Position: The CPTG is monitoring emerging evidence of ivermectin as a treatment for COVID-19 and will conduct a detailed review once more evidence becomes available.

TTF Position: Nil

P/T Position: As of February 2021, the British Columbia COVID-19 Therapeutics Committee and the Alberta COVID-19 Scientific Advisory Group do not recommend ivermectin for the treatment or prophylaxis of COVID-19 outside of approved RCTs.

ANNEX

Key Findings (RCTs, Studies)

Ongoing RCTs:

- There are several ongoing randomized controlled trials (RCTs) evaluating the safety and efficacy of ivermectin for the prevention or treatment of COVID-19. The majority of trials are small with less than 100 participants.
    - NCT04527211: This RCT aims to determine the effectiveness and safety of ivermectin (200mcg/kg once a week for 7 days) as prophylactic treatment against SARS-CoV-2 infection in Columbian health workers with negative RT-PCR for SARS-CoV-2 infection (N=550). **Completion date: December 16, 2020.**
    - NCT04405843: The EPIC Trial is a Ph2/Ph3 RCT that aims to evaluate the efficacy of ivermectin treatment in adult patients with mild/moderate COVID-19 (N=476). **Completion date: December 21, 2020.**
    - NCT04529525: The IVERCORCOVID19 study is a single-center RCT that aims to evaluate the use of ivermectin in adults with mild/moderate COVID-19 disease (N=500) on incidence of hospitalizations. **Estimated completion date: January 31, 2021.**

Why is there no advise for use of Vitamin D3 for prevention of covid? It does prevent respiratory infections?
Why are ivermectin and HCQ not approved in Canada for use as prevention and treatment of covid? It's used in many countries with great success.

One of the Public Health Agency of Canada's (PHAC) roles to support Canada's COVID-19 response is to acquire medications to treat COVID-19. This is to ensure that Canadians will have access to safe and effective treatments in the context of substantial global demand. PHAC monitors the emerging evidence around therapeutics to inform the decisions around procurement.

Please note that PHAC does not issue recommendations as such, for or against the use of medications (including *vitamin D*) for COVID-19. Currently there is no clear evidence from any clinical trial to suggest that vitamin D supplementation has any clinical benefit for the treatment or prevention of COVID-19. Although some studies observed an association between vitamin D deficiency and higher COVID-19 incidence, this does not establish a causal link that vitamin D supplements could treat or prevent COVID-19.

Regarding your question about "approval" of ivermectin and HCQ for use as prevention and treatment of COVID: A manufacturer seeking market authorization (what you refer to as "*approval*") will submit safety and efficacy data to Health Canada (HC). As the regulator, HC grants market authorization when it is satisfied that the benefits outweigh the potential risks. The list of applications received for drugs and vaccines for COVID-19 is available online.

The provinces and territories have primary responsibility for decisions around choice and use of therapeutics - including for COVID-19 – within their jurisdictions. In Canada, a health care professional's decision to prescribe or use a particular drug for a labelled or off-label indication is part of the practice of medicine, which falls under the jurisdiction of provincial and territorial professional regulatory authorities.

Additional info from recent response, but I think the above is sufficient.

Ivermectin is a broad-spectrum anti-parasitic agent authorized and approved by Health Canada for human and veterinary applications to treat parasitic infections; Health Canada has not authorized its use for the treatment of COVID-19.

The World Health Organization (WHO) convened an independent, international panel of clinical care experts from multiple specialties, patient partners and ethicists to review the evidence. On March 31st 2021, the WHO issued a statement on ivermectin advising against its use outside of clinical trials, stating the current evidence was inconclusive. The manufacturer also issued the following statement against the use of ivermectin for the treatment of COVID-19:
https://www.merck.com/news/merck-statement-on-ivermectin-use-during-the-covid-19-pandemic/

Bradley, Kevin (HC/SC)

From: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-06-23 9:12 AM
To: Arthur, Jacqueline (PHAC/ASPC)
Cc: Lawuyi2, Niyi (PHAC/ASPC); Kolbe2, Jane (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC); COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)
Subject: RE: For Senior Manager review: draft input 21-110716-914 Correspondence Info COVID Therapies

Thanks. This is now with DGO.

Adele for…Single-Window / Guichet unique COVID-19 Therapeutics / thérapeutiques
Centre for Communicable Diseases and Infection Control / Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada / Agence de la santé publique du Canada

---

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-06-22 3:42 PM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Cc: Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Subject: RE: For Senior Manager review: draft input 21-110716-914 Correspondence Info COVID Therapies

I've tweaked our response based on Jane's input so use this version please.
Signed routing slip also attached.
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-06-22 12:37 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>

Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Subject: RE: For Senior Manager review: draft input 21-110716-914 Correspondence Info COVID Therapies

I have put everything on the template that was provided (see attached), which is to be used for multi-branch correspondence. I also have prepared the routing slip if you could put on your electronic signature Jackie. I will then route up through Laura.
-adele-

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-06-22 12:02 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: RE: For Senior Manager review: draft input 21-110716-914 Correspondence Info COVID Therapies

Thanks Margaret. It looks good.
Minor word smithing attached.
Adèle, please rout to DGO for approval.
Thanks,
J

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-06-22 11:37 AM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: For Senior Manager review: draft input 21-110716-914 Correspondence Info COVID Therapies

Proposed response (copied here and attached) drawn from recent responses.

Margaret

Why is there no advise for use of Vitamin D3 for prevention of covid? It does prevent respiratory infections?
Why are ivermectin and HCQ not approved in Canada for use as prevention and treatment of covid? It's used in many countries with great success.

One of the Public Health Agency of Canada's (PHAC) roles to support Canada's COVID-19 response is to acquire medications to treat COVID-19. This is to ensure that Canadians will have access to safe and effective treatments in the context of substantial global demand. PHAC monitors the emerging evidence around therapeutics to inform the decisions around procurement.

Please note that PHAC does not issue recommendations as such, for or against the use of medications (including *vitamin D*) for COVID-19. Currently there is no clear evidence from any clinical trial to suggest that vitamin D supplementation has any clinical benefit for the treatment or prevention of COVID-19. Although some studies observed an association between vitamin D deficiency and higher COVID-19 incidence, this does not establish a causal link that vitamin D supplements could treat or prevent COVID-19.

Regarding your question about "approval" of ivermectin and HCQ for use as prevention and treatment of COVID-19: A manufacturer seeking market authorization (what you refer to as "*approval*") will submit safety and efficacy data to Health Canada (HC). As the regulator, HC grants market authorization when it is satisfied that the benefits outweigh the potential risks. The list of applications received for drugs and vaccines for COVID-19 is available online.

The provinces and territories have primary responsibility for decisions around choice and use of therapeutics - including for COVID-19 – within their jurisdictions. In Canada, a health care professional's decision to prescribe or use a particular drug for a labelled or off-label indication is part of the practice of medicine, which falls under the jurisdiction of provincial and territorial professional regulatory authorities.

Additional info from recent response, but I think the above is sufficient.

Ivermectin is a broad-spectrum anti-parasitic agent authorized and approved by Health Canada for human and veterinary applications to treat parasitic infections; Health Canada has not authorized its use for the treatment of COVID-19.

The World Health Organization (WHO) convened an independent, international panel of clinical care experts from multiple specialties, patient partners and ethicists to review the evidence. On March 31st 2021, the WHO issued a statement on ivermectin advising against its use outside of clinical trials, stating the current evidence was inconclusive. The manufacturer also issued the following statement against the use of ivermectin for the treatment of COVID-19:
https://www.merck.com/news/merck-statement-on-ivermectin-use-during-the-covid-19-pandemic/

From: Gale-Rowe, Margaret (PHAC/ASPC)
Sent: 2021-06-21 8:17 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Kolbe2, Jane (PHAC/ASPC)

<jane.kolbe2@canada.ca>
Subject: RE: looping in Jane FW: For Action 21-110716-914 Correspondence Info Please COVID Therapies

Hi,

These are the only portions that I see us providing input for, There are many areas that the writer wants info on, but the others mainly concern public health measures and risks associated with vaccines.

1) We don't (CCDIC) provide guidance/recommendations for therapeutics (clinical management of COVID) though there is guidance on the PHAC website.
2) This is really under HC's jurisdiction though we could indicate that it is up to the manufacturer/sponsor to apply and submit data in support of a particular indication.

I will see what info we have provided in the past and send you a draft outline/response tomorrow.

Margaret

Why is there no advise for use of Vitamin D3 for prevention of covid? It does prevent respiratory infections?
Why are ivermectin and HCQ not approved in Canada for use as prevention and treatment of covid? It's used in many countries with great success.

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-06-21 2:59 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: looping in Jane FW: For Action 21-110716-914 Correspondence Info Please COVID Therapies
Importance: High

Sorry, Adèle reminded me to loop in Jane!
Jane, I've asked Margaret for her recommendation and you may also have some thoughts. It may be more appropriate for Health Canada…
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: Arthur, Jacqueline (PHAC/ASPC)
Sent: 2021-06-21 2:52 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>
Subject: FW: For Action 21-110716-914 Correspondence Info Please COVID Therapies
Importance: High

Margaret;
Could you have a look at the AR attached please and give me your recommendation and suggested response (if needed)?
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>
Sent: 2021-06-21 11:47 AM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Cc: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Apse, Krista (PHAC/ASPC) <krista.apse@canada.ca>; Shaikh, Shabana (PHAC/ASPC) <shabana.shaikh@canada.ca>
Subject: For Action 21-110716-914 Correspondence Info Please COVID Therapies

Hi,
Please review the new Incoming Correspondence attached. We are being asked to provide input only for the areas for which your section is responsible for. IDPB has the opinion that COVID Therapeutics may have some input. Please provide your Director approved input in the Mulit Branch template attached to me by **June 25, 2021** .
Thank you, Laura

Single Window, Centre for Communicable Diseases and Infection Control
Infectious Disease Programs Branch
Public Health Agency of Canada, Government of Canada
Laura Forsyth / Tél. : 613-864-9596
ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>

Guichet unique, Centre de la lutte contre les maladies transmissibles et les infections

Direction générale de la prévention et du contrôle des maladies infectieuses
Agence de la santé publique du Canada, Gouvernement du Canada
Laura Forsyth / Tél. : 613-864-9596
ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>

From: Nicky Hrycak <nicky.hrycak@phac-aspc.gc.ca>
Sent: 2021-06-21 9:42 AM
To: CIRID DGO / BDG CIMRI (PHAC/ASPC) <phac.cirid.dgo-bdg.cimri.aspc@canada.ca>; ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>; Duncan, Debbie (PHAC/ASPC) <debbie.duncan@canada.ca>; Carter, Luisa (PHAC/ASPC) <luisa.carter@canada.ca>
Subject: 21-110716 - 914 for / pour: Provide Input/Fournir des paragraphes

Health Canada Santé Canada

Canada

Audit Trail / Suivi de vérification
Branch Correspondence / Correspondance des directions générales

Subject / Sujet: 21-110716 - 914 for / pour: Provide Input/Fournir des paragraphes

21-110716 - 914

Send From / Envoyé de	Send To / Envoyé a	Date Sent / Date de l'envoi	Bring Forward / Rappel
PHAC-IDPCB-VPO Nicky Hrycak/HC-SC/GC/CA	**Organization/Organisme** PHAC-CIRID **Person/Personne** CIRID_DGO-CIMRI_BDG/GEN/HC-SC/GC/CA	2021-06-21	

Special Instructions / Instructions spéciales: Direct Reply
Document Status / Statut du dossier: Open/Ouvert
Action / Intervention: Provide Input/Fournir des paragraphes

Comment / Commentaires:
Correspondence - pls provide input only for the areas for which your centre is responsible. - CCDIC - therapeutics (mostly HC but sending in the event you have input), CIRID - PHM, OCSO - Vit D. Pls provide your input in the Mulit Branch template attached - due June 28. Thank you, Nicky

Here is the link to document / Voici le lien au document:

The documents provided to you may contain personal information.
If you have received these documents in error, notify the MECS-USER-SUPPORT group immediately.

Les documents qui vous sont fournis peuvent contenir des renseignements personnels.
Si vous avez reçu ces documents par erreur, avisez immédiatement le groupe courriel des MECS-USER-SUPPORT.

Created By / Créé par: Nicky Hrycak
Date Created / Créé le: 2021-06-21

Manuel, Suzzanne (PHAC/ASPC)

From: Web Mail / Courriel Web (PHAC/ASPC)
Sent: 2021-05-06 11:11 AM
To: Executive Correspondence (PHAC/ASPC)
Subject: 21-110716-914 [redacted]

Categories: Aida

Hello CU
Please see below FYA.
Webmail will close.

_____
Public Health Agency of Canada / l'Agence de la santé publique du Canada
phac.webmail-courrielweb.aspc@canada.ca
(RY)

From: Yorke, Rosa (PHAC/ASPC)
Sent: 2021-05-03 2:22 PM
To: Saghbini, Aida (PHAC/ASPC) <aida.saghbini@canada.ca>
Subject: AIDA: [redacted]

Hello Aida
I am not sure how to proceed and more precisely, I do not understand what IDPCB means as 'suggest that Corporate could turn this correspondence and treat as a multi branch'. Would this be webmail requesting input for the applicable programs ?

_____
Public Health Agency of Canada / l'Agence de la santé publique du Canada
phac.webmail-courrielweb.aspc@canada.ca
(RY)

From: idpcb / dgpcmi (PHAC/ASPC) <phac.idpcb-dgpcmi.aspc@canada.ca>
Sent: 2021-05-03 8:22 AM
To: Web Mail / Courriel Web (PHAC/ASPC) <phac.webmail-courrielweb.aspc@canada.ca>
Subject: FW: info please

Good morning. There are numerous areas that would need to be involved in providing input for this request, HC, VRAT, Stats Can, IDPB to name a few.

I would suggest that Corporate could change this into correspondence and treat as a multi branch where Corporate would request input from all pertinent areas and roll up the input. In the past I have seen the Director of Corporate sign correspondence. Perhaps they could be the signatory for this.

Pls let me know if you have any questions. Thank you, Nicky

Infectious Diseases Programs Branch
Public Health Agency of Canada

Direction générale des programmes des maladies infectieuses
Agence de la santé publique du Canada

From: Web Mail / Courriel Web (PHAC/ASPC) <phac.webmail-courrielweb.aspc@canada.ca>
Sent: 2021-05-02 7:38 AM
To: idpcb / dgpcmi (PHAC/ASPC) <phac.idpcb-dgpcmi.aspc@canada.ca>
Subject: FW: info please

FYA ?

Public Health Agency of Canada / l'Agence de la santé publique du Canada
phac.webmail-courrielweb.aspc@canada.ca
(RY)

From: COVID Alert / Alerte COVID (HC/SC) <hc.AlerteCOVIDAlert.sc@canada.ca>
Sent: 2021-04-30 10:48 AM
To: Web Mail / Courriel Web (PHAC/ASPC) <phac.webmail-courrielweb.aspc@canada.ca>
Subject: FW: info please

Good morning,

For direct reply please.

Thank you,
Gabrielle

From: Info SC, HC Info (HC/SC) <hcinfo.infosc@canada.ca>
Sent: 2021-04-26 3:40 PM
To: [redacted]
Subject: RE: info please

Thank you for contacting Health Canada.

Your recent enquiry has been redirected to the appropriate area for a response.

Sincerely,

Health Canada | Santé Canada
Ottawa, Canada K1A 0K9
info@hc-sc.gc.ca
Telephone | Téléphone 613-957-2991 / Toll free | Sans frais 1 866-225-0709 /
Facsimile | Télécopieur 613-941-5366 / Teletypewriter | Téléimprimeur 1 800-267-1245
Government of Canada | Gouvernement du Canada

From: [redacted]
Sent: 2021-04-20 7:29 PM

To: Info SC, HC Info (HC/SC) <hcinfo.infosc@canada.ca>
Subject: info please

Hello:

I was wondering if you could provide answers and links to the following questions:

Statistics on 2020 causes of death by month for Canada
Statistics on 2016-2019 causes of death by month for Canada
Statistics on monthly hospital admissions Canada 2016 to 2020

What are the conditions under which the covid vaccines are authorized for emergency use?
When does the emergency use of covid vaccines expire?
Why is there no advise for use of Vitamin D3 for prevention of covid? It does prevent respiratory infections?
Why are ivermectin and HCQ not approved in Canada for use as prevention and treatment of covid? It's used in many countries with great success.
Why are there still restrictions on people such as mask wearing and 'social distancing' which have zero effect on transmission as there's zero science behind such measures? Isolation and loneliness creates more harms and majority of people recover from covid quite fine and would recover better if therapeutics were used, such as ivermectin and HCQ, which have FDA and Health Canada approval?
Who is going to be responsible for deaths and injuries resulting from covid vaccines?
If people can't sue the drug companies, can they sue the pharmacists and/or health authorities administering experimental drugs?
What can be the long term adverse effects of these gene therapies injected for a virus that has very high recovery rate? If you don't know this, how can you promote this as 'safe' and how can you be telling people they save lives if:
1) you don't care about saving lives as lockdowns killed people
2) you don't care about saving lives as you're not allowing therapeutics which save people's lives and are used in other countries
3) majority of people recover from covid quite fine
4) natural immunity is long-lasting with no side effects of untested experimental injections
5) people who get covid and recover are helping others therefore locking people up prevents people from developing natural immunity
What type of informed consent are people being injected with this experimental gene therapy given? Are they advised of risk of injury and death following injection of this? Are they advised they're given experimental treatment which is more risky for majority of people than covid?
Why are there emergency orders? In real pandemics we would have around 20% of population at risk, hospitalized and dying, those are real pandemics when huge amount of population is at risk of dying.
Can you provide the link for vaccine adverse effects monitoring?
What % of vaccine injuries are usually reported (I gather it can be as low as 6% or less)?

thanks,

[redacted]

Docket #21
Note: ***Please note xxxx will also be providing*** *input.*

Subject: **xxxxx**

From: **xxxx**

Date:

The following paragraphs are suggested for inclusion in the above-mentioned docket*:*

Bradley, Kevin (HC/SC)

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-06-23 9:46 AM
To: Djiometio, Joseph (PHAC/ASPC); Azad, Mina (PHAC/ASPC)
Cc: Arthur, Jacqueline (PHAC/ASPC)
Subject: RE: Question re: ivermectin SR results: FYI ONLY: LOVE notifications

This isn't urgent but should be done.

Thanks in advance.

Margaret

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-06-23 9:40 AM
To: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Cc: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Subject: RE: Question re: ivermectin SR results: FYI ONLY: LOVE notifications

Thank you Mina
We can update the issue note only with important new publications.

Joe

From: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Sent: 2021-06-23 9:28 AM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Cc: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Subject: RE: Question re: ivermectin SR results: FYI ONLY: LOVE notifications

Hi Margaret,

Me and Serena provided some updates regarding Ivermectin and reviewed the publications that have become available since June 8th. We sent the summary to Joe. I've copy/pasted it here as well for your consideration. Bryant et al., was reviewed as well. We'll make sure to update the issue note today.

Best,
Mina

Two studies examining the efficacy of ivermectin in the treatment of covid-19 patients have been published since June 7th, 2021. Bryant et al. is kindly reviewed by Serena (please see below). Krolewiecki et al. did not include a large population size in their trial (n=45).

Although few observational studies and clinical trials have assessed ivermectin for the treatment and prevention of COVID-19 in humans, most had inadequate information and methodological limitations, according to another study (Lind et al.).

Bryant et al.:
A systematic review and meta-analysis of 24 randomized controlled trials assessed the efficacy of ivermectin treatment in reducing mortality, in several secondary outcomes such as time to PCR negativity, clinical recover, length of hospital stay..etc. All-cause mortality was assessed in 15 trials and found that ivermectin reduced the risk of mortality by 62% compared to no ivermectin treatment. For secondary outcomes, the evidence was less certain, rated low to very low certainty. They also assessed prophylaxis use of ivermectin, although only 3 studies were included in these analyses.

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-06-23 9:22 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Cc: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Subject: Question re: ivermectin SR results: FYI ONLY: LOVE notifications

Hi,

Could you please advise how the results of this study “align” with what is in our most recent version (June 8) of the issue sheet? As an aside, the issue sheet is entitled Feb. 23 so not sure if that should be revised/updated.

Thank you,

Margaret

- **Key benefits:** Orally administered. In small RCTs, ivermectin may reduce viral load in patients with mild-to-moderate COVID-19. However,
  - Ivermectin is generally well tolerated for its approved indications.
- **Key challenges:**
  - More robust clinical trials with larger sample sizes are needed to determine its efficacy for COVID-19. The majority of trials on ivermectin in COVID-19 were limited to small sample sizes and mixed evidence on clinical benefits.

Question: Ivermectin for COVID-19

Systematic reviews 1

1. Bryant A, Lawrie TA, Dowswell T, Fordham EJ, Mitchell S, Hill SR, Tham TC. Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines. American journal of therapeutics. 2021; | Epistemonikos | DOI

CONCLUSIONS:

Moderate-certainty evidence finds that large reductions in COVID-19 deaths are possible using ivermectin. Using ivermectin early in the clinical course may reduce numbers progressing to severe disease. The apparent safety and low cost suggest that ivermectin is likely to have a significant impact on the SARS-CoV-2 pandemic globally.

From: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-06-23 8:37 AM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Subject: FYI ONLY: LOVE notifications

For your information.

Adele for…Single-Window / Guichet unique COVID-19 Therapeutics / thérapeutiques
Centre for Communicable Diseases and Infection Control / Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada / Agence de la santé publique du Canada

---

From: no-reply@notifications.iloveevidence.com <no-reply@notifications.iloveevidence.com>
Sent: 2021-06-23 1:22 AM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Subject: LOVE notifications

Hi PHAC,

Your updates from 2021/06/22 to 2021/06/23

COVID-19

Question: Tocilizumab for COVID-19

Systematic reviews 1

1. Pinzon RT, Wijaya VO, Buana RB. Interleukin-6 (IL-6) inhibitors as therapeutic agents for coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Journal of infection and public health. 2021;14(8):1001-1009. | Epistemonikos | DOI

Primary studies 4

1. Lennie P.G. Derde, - The REMAP-CAP Investigators. Effectiveness of Tocilizumab, Sarilumab, and Anakinra for critically ill patients with COVID-19 The REMAP-CAP COVID-19 Immune Modulation Therapy Domain Randomized Clinical Trial. medRxiv. 2021; | Epistemonikos | DOI
2. Al-Baadani A, Eltayeb N, Alsufyani E, Albahrani S, Basheri S, Albayat H, Batubara E, Ballool S, Al Assiri A, Faqihi F, Musa AB, Robert AA, Alsherbeeni N, Elzein F. Efficacy of tocilizumab in patients with severe COVID-19: Survival and clinical outcomes. Journal of infection and public health. 2021;14(8):1021-1027. | Epistemonikos | DOI

3. Cardona-Pascual I, Berlana D, Martinez-Valle F, Campany-Herrero D, Montoro-Ronsano JB. Effect of tocilizumab versus standard of care in adults hospitalized with moderate-severe COVID-19 pneumonia. Medicina clinica. 2021; | Epistemonikos | DOI
4. Hamed DM, Belhoul KM, Al Maazmi NA, Ghayoor F, Moin M, Al Suwaidi M, Narainen M, Makki M, AbdulRahman M. Intravenous methylprednisolone with or without tocilizumab in patients with severe COVID-19 pneumonia requiring oxygen support: A prospective comparison. Journal of infection and public health. 2021;14(8):985-989. | Epistemonikos | DOI

Question: Remdesivir for COVID-19

Primary studies 2

1. Gazivoda VP, Ibrahim M, Kangas-Dick A, Sun A, Silver M, Wiesel O. Outcomes of Barotrauma in Critically Ill COVID-19 Patients With Severe Pneumonia. Journal of intensive care medicine. 2021;:8850666211023360. | Epistemonikos | DOI
2. Teoli D, Thompson V, Wright J, Ho I, Vlaminck B, Miller G, Feely M. Acute Pain Crisis Caused by Tramadol Remdesivir Drug-Drug Interaction. Journal of palliative medicine. 2021; | Epistemonikos | DOI

Question: Ivermectin for COVID-19

Systematic reviews 1

1. Bryant A, Lawrie TA, Dowswell T, Fordham EJ, Mitchell S, Hill SR, Tham TC. Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines. American journal of therapeutics. 2021; | Epistemonikos | DOI

Question: Otilimab for COVID-19

There are no new articles for this question

Question: Molnupiravir for COVID-19

There are no new articles for this question

Question: Anti-sars-cov-2 antibodies for COVID-19

There are no new articles for this question

Question: Colchicine for COVID-19

There are no new articles for this question

Question: Baricitinib for COVID-19

There are no new articles for this question

Question: Casirivimab and/or imdevimab for COVID-19

There are no new articles for this question

Question: Azd7442 for COVID-19

There are no new articles for this question

Question: Sarilumab for COVID-19

Systematic reviews 1

1. Pinzon RT, Wijaya VO, Buana RB. Interleukin-6 (IL-6) inhibitors as therapeutic agents for coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Journal of infection and public health. 2021;14(8):1001-1009. | Epistemonikos | DOI

Primary studies 1

1. Lennie P.G. Derde, - The REMAP-CAP Investigators. Effectiveness of Tocilizumab, Sarilumab, and Anakinra for critically ill patients with COVID-

19 The REMAP-CAP COVID-19 Immune Modulation Therapy Domain Randomized Clinical Trial. medRxiv. 2021; | Epistemonikos | DOI

Question: Antiviral drugs for COVID-19

Primary studies 3

1. Chen X, Lei L, Liu S, Han J, Li R, Men J, Li L, Wei L, Sheng Y, Yang L, Zhou B, Zhu L. Occurrence and risk assessment of pharmaceuticals and personal care products (PPCPs) against COVID-19 in lakes and WWTP-river-estuary system in Wuhan, China. The Science of the total environment. 2021;792:148352. | Epistemonikos | DOI
2. Gazivoda VP, Ibrahim M, Kangas-Dick A, Sun A, Silver M, Wiesel O. Outcomes of Barotrauma in Critically Ill COVID-19 Patients With Severe Pneumonia. Journal of intensive care medicine. 2021;:8850666211023360. | Epistemonikos | DOI
3. Teoli D, Thompson V, Wright J, Ho I, Vlaminck B, Miller G, Feely M. Acute Pain Crisis Caused by Tramadol Remdesivir Drug-Drug Interaction. Journal of palliative medicine. 2021; | Epistemonikos | DOI

Question: Anakinra for COVID-19

Primary studies 1

1. Lennie P.G. Derde, - The REMAP-CAP Investigators. Effectiveness of Tocilizumab, Sarilumab, and Anakinra for critically ill patients with COVID-19 The REMAP-CAP COVID-19 Immune Modulation Therapy Domain Randomized Clinical Trial. medRxiv. 2021; | Epistemonikos | DOI

As the identification of articles is a continuous process, including both automated and human tasks, this notification might not portray the most accurate list of evidence for this question. Go to the L·OVE platform to access it.

Bradley, Kevin (HC/SC)

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-06-25 10:47 AM
To: Arthur, Jacqueline (PHAC/ASPC); COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC); Kolbe2, Jane (PHAC/ASPC); Lawuyi2, Niyi (PHAC/ASPC); Djiometio, Joseph (PHAC/ASPC); Marinsky, Cheryl (PHAC/ASPC); Azad, Mina (PHAC/ASPC)
Subject: RE: Ivermectin and mAbs: FYI ONLY: LOVE notifications

Yes but it doesn't say "good evidence of no benefit," rather insufficient evidence of effect.
Having opened the can of worms, I will leave it to my learned colleagues to carry the torch…. ☺

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-06-25 10:13 AM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: Ivermectin and mAbs: FYI ONLY: LOVE notifications

Thanks Margaret. Not good news for REGN uptake.

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-06-25 9:21 AM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: Ivermectin and mAbs: FYI ONLY: LOVE notifications

DATA SYNTHESIS:

The collective search retrieved 3818 citations. Eight trials relating to 9 pharmacological interventions were identified. No evidence for nonpharmacological interventions was identified. Low certainty evidence of effectiveness in preventing severe disease was found for fluvoxamine (absolute difference: -8.7%; 95% CI.: -1.8% to -16.4%) and bamlanivimab plus etesevimab (absolute difference: -4.9%; 95% CI.: -0.8% to -8.9%). Both trials were limited by small sample sizes and short durations of follow-up. In addition, very low certainty evidence of effect was found for ivermectin plus doxycycline and sulodexide. Based on published data, insufficient evidence of effect was found for bamlanivimab (monotherapy), casirivimab plus imdevimab, ivermectin (monotherapy), nitazoxanide, and peginterferon lambda.

RELEVANCE TO PATIENT CARE AND CLINICAL PRACTI

From: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-06-25 8:52 AM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: FYI ONLY: LOVE notifications

For your information.

Adele for….Single-Window / Guichet unique COVID-19 Therapeutics / thérapeutiques
Centre for Communicable Diseases and Infection Control / Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada / Agence de la santé publique du Canada

---

From: no-reply@notifications.iloveevidence.com <no-reply@notifications.iloveevidence.com>
Sent: 2021-06-25 1:19 AM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Subject: LOVE notifications

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Hi PHAC,

Your updates from 2021/06/24 to 2021/06/25

COVID-19

Question: Tocilizumab for COVID-19

There are no new articles for this question

Question: Remdesivir for COVID-19

There are no new articles for this question

Question: Ivermectin for COVID-19

Systematic reviews 1

1. O Murchu E, Spillane S, Byrne P, O'Neill M, Harrington P, Ryan M. Interventions in an Ambulatory Setting to Prevent Progression to Severe Disease in Patients With COVID-19: A Systematic Review. The Annals of pharmacotherapy. 2021;:10600280211028242. | Epistemonikos | DOI

Question: Otilimab for COVID-19

There are no new articles for this question

Question: Molnupiravir for COVID-19

There are no new articles for this question

Question: Anti-sars-cov-2 antibodies for COVID-19

Systematic reviews 1

1. O Murchu E, Spillane S, Byrne P, O'Neill M, Harrington P, Ryan M. Interventions in an Ambulatory Setting to Prevent Progression to Severe Disease in Patients With COVID-19: A Systematic Review. The Annals of pharmacotherapy. 2021;:10600280211028242. | Epistemonikos | DOI

Primary studies 1

1. Prerna Arora, Nadine Krueger, Amy Kempf, Inga Nehlmeier, Anzhalika Sidarovich, Luise Graichen, Anna-Sophie Moldenhauer, Martin S. Winkler, Sebastian Schulz, Hans-Martin Jaeck, Metodi V. Stankov, Georg M.N. Behrens, Stefan Poehlmann, Markus Hoffmann. Increased lung cell entry of B.1.617.2 and evasion of antibodies induced by infection and BNT162b2 vaccination. bioRxiv. 2021; | Epistemonikos | DOI

Question: Colchicine for COVID-19

There are no new articles for this question

Question: Baricitinib for COVID-19

There are no new articles for this question

Question: Casirivimab and/or imdevimab for COVID-19

There are no new articles for this question

Question: Azd7442 for COVID-19

There are no new articles for this question

Question: Sarilumab for COVID-19

There are no new articles for this question

Question: Antiviral drugs for COVID-19

Systematic reviews 1

1. Diaz-Arocutipa C, Carvallo-Castañeda D, Luis-Ybañez O, Pariona M, Rivas-Lasarte M, Álvarez-García J. COVID-19 in heart transplant recipients during February - August 2020: A systematic review. Clinical transplantation. 2021; | Epistemonikos | DOI

Primary studies 6

1. Lennox JL, Dejesus E, Berger DS, Lazzarin A, Pollard RB, Ramalho Madruga JV, Zhao J, Wan H, Gilbert CL, Teppler H, Rodgers AJ, Barnard RJ, Miller MD, Dinubile MJ, Nguyen BY, Leavitt R, Sklar P, STARTMRK Investigators. Raltegravir versus Efavirenz regimens in treatment-naive HIV-1-infected patients: 96-week efficacy, durability, subgroup, safety, and metabolic analyses. Journal of acquired immune deficiency syndromes (1999). 2010;55(1):39-48. | Epistemonikos | DOI
2. Izzedine H, Hulot JS, Vittecoq D, Gallant JE, Staszewski S, Launay-Vacher V, Cheng A, Deray G, Study 903 Team. Long-term renal safety of tenofovir disoproxil fumarate in antiretroviral-naive HIV-1-infected patients. Data from a double-blind randomized active-controlled multicentre study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2005;20(4):743-6. | Epistemonikos | DOI
3. Campo R, DeJesus E, Bredeek UF, Henry K, Khanlou H, Logue K, Brinson C, Benson P, Dau L, Wang H, White K, Flaherty J, Fralich T, Guyer B, Piontkowsky D. SWIFT: prospective 48-week study to evaluate efficacy and safety of switching to emtricitabine/tenofovir from lamivudine/abacavir in virologically suppressed HIV-1 infected patients on a boosted protease inhibitor containing antiretroviral regimen. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2013;56(11):1637-45. | Epistemonikos | DOI
4. Delta: a randomised double-blind controlled trial comparing combinations of zidovudine plus didanosine or zalcitabine with zidovudine alone in HIV-infected individuals. Delta Coordinating Committee. Lancet. 1996;348(9023):283-91. | Epistemonikos
5. de Araujo ES, Dahari H, Cotler SJ, Layden TJ, Neumann AU, Melo CE, Barone AA. Pharmacodynamics of PEG-IFN-[alpha]-2a and HCV response as a function of IL28B polymorphism in HIV/HCV-coinfected patients.

Journal of acquired immune deficiency syndromes (1999). 2011;56(2):95-9. | Epistemonikos | DOI

6. Bonjoch A, Paredes R, Galvez J, Miralles C, Videla S, Martínez E, Miranda J, Muñoz-Moreno JA, De la Torre J, Prieto A, Vilades C, Clotet B, SimplifiHAART Study Group. Antiretroviral treatment simplification with 3 NRTIs or 2 NRTIs plus nevirapine in HIV-1-infected patients treated with successful first-line HAART. Journal of acquired immune deficiency syndromes (1999). 2005;39(3):313-6. | Epistemonikos

Question: Anakinra for COVID-19

There are no new articles for this question

Bradley, Kevin (HC/SC)

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-06-30 3:59 PM
To: Azad, Mina (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC)
Cc: Arthur, Jacqueline (PHAC/ASPC)
Subject: RE: Could we revise/remove the notes : Daily Therapeutics Titles for Wednesday, June 30th

Yes, Margaret you are correct

Joe

From: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Sent: 2021-06-30 3:57 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Cc: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Subject: RE: Could we revise/remove the notes : Daily Therapeutics Titles for Wednesday, June 30th

Hi Margaret,

I made a few changes. We are primarily focusing on abstracts at this point, and if a title comes up that is particularly intriguing to us (both in terms of quality and the importance of the therapeutic), we will consider it for a summary.
For ivermectin, we reviewed recent studies and were unable to come up with any promising results (Joe, am I correct? Could you please confirm that this is the case?)

Notes:
As of June 30, 2021, systematic review and meta-analysis studies of Moderate and high quality (based on AMSTAR 2 criteria) and those on therapeutics that the CPTG has approved statements will be included in the daily titles as an abstract with a rapid critical appraisal. The summary format will be provided only for the high-impact studies containing critical data on closely monitored therapeutics.

As of October 23, 2020, clinical data on lopinavir/ritonavir and hydroxychloroquine/chloroquine, and as of May 13th, 2021, clinical data on ivermectin, are no longer included in this listing due to overwhelming evidence of little to no clinical benefit. However, these titles are still being retained in our cloud-based database.

Feedback and discussion on this daily email are always welcome.

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-06-30 3:31 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: Could we revise/remove the notes : Daily Therapeutics Titles for Wednesday, June 30th

Some parts are out of date (reference to CPTG statements) and is it still accurate to say there's overwhelming evidence of no benefit to ivermectin?

Margaret

Notes:
As of January 28, 2021, systematic review and meta-analysis studies of low/very low quality (based on AMSTAR 2 criteria) and those on therapeutics that the CPTG has approved statements will be included in the daily titles as an abstract with a rapid critical appraisal.

As of October 23, 2020, clinical data on lopinavir/ritonavir and hydroxychloroquine/chloroquine, and as of May 13th, 2021, clinical data on ivermectin, are no longer included in this listing due to overwhelming evidence of little to no clinical benefit. However, these titles are still being retained in our cloud based database.

Feedback and discussion on this daily email is always welcome.

Medical Advisor - COVID Therapeutics Acquisitions
613-618-9266

Begin forwarded message:

> **From:** "Azad, Mina (PHAC/ASPC)" <mina.azad@canada.ca>
> **Date:** June 30, 2021 at 2:44:37 PM EDT
> **To:** "COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)" <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>, "Njoo, Howard (PHAC/ASPC)" <howard.njoo@canada.ca>, "Salvadori, Marina (PHAC/ASPC)" <marina.salvadori@canada.ca>, "Baclic, Oliver (PHAC/ASPC)" <oliver.baclic@canada.ca>, "Patel, Milan (PHAC/ASPC)" <milan.patel@canada.ca>, "Killikelly, April (PHAC/ASPC)" <april.killikelly@canada.ca>, "Abraham, Natalia k (PHAC/ASPC)" <nataliak.abraham@canada.ca>, "Chung, Yung-En (PHAC/ASPC)" <yung-en.chung@canada.ca>, "Lehman, Kelly (HC/SC)" <kelly.lehman@canada.ca>, "Frappier2, Fiona (HC/SC)" <fiona.frappier2@canada.ca>, "Chigrinova, Mariya (HC/SC)" <mariya.chigrinova@canada.ca>, "Uhthoff, Peter (SAC/ISC)" <peter.uhthoff@canada.ca>, "Beaulieu, Marc-Andre (PHAC/ASPC)" <marc-andre.beaulieu@canada.ca>, "Mitchelmore, Bradley (PHAC/ASPC)" <bradley.mitchelmore@canada.ca>, "Blanchard, Bradley (PHAC/ASPC)" <bradley.blanchard@canada.ca>, "Kamkar, Maryam (PHAC/ASPC)" <maryam.kamkar@canada.ca>, "Forbes, Nicole (PHAC/ASPC)" <nicole.forbes@canada.ca>, Srinivas.Murthy@cw.bc.ca, marie.lordkipanidze@umontreal.ca, R.I.Hall@dal.ca, mrieder@uwo.ca, Abby.Collier@ubc.ca, "Goldhawk, Michael (PHAC/ASPC)" <michael.goldhawk@canada.ca>, m.piquette.miller@utoronto.ca, "Levesque2, Kaili (HC/SC)" <kaili.levesque2@canada.ca>, "Groeneweg, Sheryl (IC)" <sheryl.groeneweg@canada.ca>, "Arancibia, Rodrigo (IC)" <rodrigo.arancibia@canada.ca>, "Taha, Zaid (PHAC/ASPC)" <zaid.taha@canada.ca>, "Courtemanche, Jocelyne (PHAC/ASPC)" <jocelyne.courtemanche@canada.ca>, "Arthur, Jacqueline (PHAC/ASPC)" <jacqueline.arthur@canada.ca>, "Lawuyi2, Niyi (PHAC/ASPC)" <niyi.lawuyi2@canada.ca>, "Gale-Rowe, Margaret (PHAC/ASPC)" <margaret.gale-rowe@canada.ca>, "Krishnan, Ramya (PHAC/ASPC)" <ramya.krishnan@canada.ca>,

"Beique, Lizanne (PHAC/ASPC)" <lizanne.beique@canada.ca>, "Marinsky, Cheryl (PHAC/ASPC)" <cheryl.marinsky@canada.ca>, "Ephrem, Bersabel (PHAC/ASPC)" <bersabel.ephrem@canada.ca>, "PHAC.F Emerging Science Secretariat / Secrétariat des sciences émergentes F.ASPC" <phac.emergingsciencesecretariat-secretariatdessciencesemergentes.aspc@canada.ca>, "Garcia Carrasco, Alexandra (HC/SC)" <alexandra.garciacarrasco@canada.ca>, "Farrah, Kelly (PHAC/ASPC)" <kelly.farrah@canada.ca>, "Jirovec, Anna (PHAC/ASPC)" <anna.jirovec@canada.ca>, "Stephens-Rennie2, Ericka (HC/SC)" <ericka.stephens-rennie2@canada.ca>, "Sigouin, Ryan (HC/SC)" <ryan.sigouin@canada.ca>, "Cortés-Kaplan, Serena (PHAC/ASPC)" <serena.cortes-kaplan@canada.ca>, "Hanson Pastran, Sasha (HC/SC)" <sasha.hansonpastran@canada.ca>, "Rajendra, Kanya (HC/SC)" <kanya.rajendra@canada.ca>, "Djiometio, Joseph (PHAC/ASPC)" <joseph.djiometio@canada.ca>, "Cassista, Caroline (PHAC/ASPC)" <caroline.cassista@canada.ca>, "Mitchell, Stephanie (PHAC/ASPC)" <stephanie.mitchell@canada.ca>, "Gaudreau, Marc-Andre (PHAC/ASPC)" <marc-andre.gaudreau@canada.ca>, "Birdi, Harsimrat (PHAC/ASPC)" <harsimrat.birdi@canada.ca>, "Azad, Mina (PHAC/ASPC)" <mina.azad@canada.ca>, "Kaur, Hargun (HC/SC)" <hargun.kaur@canada.ca>, "Beeharry, Yasnee (HC/SC)" <yasnee.beeharry@canada.ca>, "Montroy, Joshua" <joshua.montroy@phac-aspc.gc.ca>
Cc: "COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)" <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Subject: Daily Therapeutics Titles for Wednesday, June 30th

Notes:

As of January 28, 2021, systematic review and meta-analysis studies of low/very low quality (based on AMSTAR 2 criteria) and those on therapeutics that the CPTG has approved statements will be included in the daily titles as an abstract with a rapid critical appraisal.

As of October 23, 2020, clinical data on lopinavir/ritonavir and hydroxychloroquine/chloroquine, and as of May 13th, 2021, clinical data on ivermectin, are no longer included in this listing due to overwhelming evidence of little to no clinical benefit. However, these titles are still being retained in our cloud based database.

Feedback and discussion on this daily email is always welcome.

Bradley, Kevin (HC/SC)

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-06-30 5:43 PM
To: Ephrem, Bersabel (PHAC/ASPC); ccdic / siimd (PHAC/ASPC)
Cc: Hunt, Kelly (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC)
Subject: RE: FOR DG APPROVAL 21-110716-914 Correspondence Info Please COVID Therapies
Attachments: 21-110716-914_Input to multi from Therapeutics_June 22.2021v2 (002)_revised CLEAN.docx; 21-110716-914_Input to multi from Therapeutics_June 22.2021v2 (002)_revised tracked.docx

Your question is very valid so I have removed the subsequent sentences in the paragraph.
See revised attached.
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>
Sent: 2021-06-30 5:29 PM
To: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Cc: Hunt, Kelly (PHAC/ASPC) <kelly.hunt@canada.ca>
Subject: RE: FOR DG APPROVAL 21-110716-914 Correspondence Info Please COVID Therapies

I am good. But I have a quick question

From: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>
Sent: 2021-06-24 4:42 PM
To: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>
Cc: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>; Hunt, Kelly (PHAC/ASPC) <kelly.hunt@canada.ca>
Subject: FOR DG APPROVAL 21-110716-914 Correspondence Info Please COVID Therapies

Hi,

Please see a new Correspondence for DG Approval (PDF Incoming attached). We are being asked to provide input only for the areas for which your section is responsible for. IDPB-VPO has the opinion that COVID Therapeutics may have some input. Please see ED approved input in the Multi Branch template . Your DG approval is being requested by **June 28, 2021** .

Thanks Laura

Single Window, Centre for Communicable Diseases and Infection Control
Infectious Disease Programs Branch
Public Health Agency of Canada, Government of Canada
Laura Forsyth / Tél. : 613-864-9596
ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>

Guichet unique, Centre de la lutte contre les maladies transmissibles et les infections
Direction générale de la prévention et du contrôle des maladies infectieuses
Agence de la santé publique du Canada, Gouvernement du Canada
Laura Forsyth / Tél. : 613-864-9596
ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>

From: Adèle Crôteau <adele.croteau@phac-aspc.gc.ca>
Sent: 2021-06-23 9:13 AM
To: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>; Forsyth, Laura (PHAC/ASPC) <laura.forsyth@canada.ca>
Subject: 21-110716 - 914 for / pour: As Requested/Tel que demandé

Health Canada Santé Canada

Canada

Audit Trail / Suivi de vérification
Branch Correspondence / Correspondance des directions générales

Subject / Sujet: 21-110716 - 914 for / pour: As Requested/Tel que demandé

21-110716 - 914

Send From / Envoyé de	Send To / Envoyé a	Date Sent / Date de l'envoi	Bring Forward / Rappel

PHAC-IDPCB-CCDIC-DGO Adèle Crôteau/HC-SC/GC/CA	**Organization/Organisme** PHAC-IDPCB-CCDIC-SIIMD **Person/Personne** CCDIC-SIIMD/GEN/HC-SC/GC/CA	2021-06-23	

Special Instructions / Instructions spéciales: Direct Reply
Document Status / Statut du dossier: Open/Ouvert
Action / Intervention: As Requested/Tel que demandé

Comment / Commentaires:
Please find attached our input as requested. Ready for DG approval and then routing. (adele)

Here is the link to document / Voici le lien au document:

The documents provided to you may contain personal information.
If you have received these documents in error, notify the MECS-USER-SUPPORT group immediately.

Les documents qui vous sont fournis peuvent contenir des renseignements personnels.
Si vous avez reçu ces documents par erreur, avisez immédiatement le groupe courriel des MECS-USER-SUPPORT.

Created By / Créé par: Adèle Crôteau
Date Created / Créé le: 2021-06-23

Docket #21-110716-914
Note: ***Please note Health Canada will also be providing input.***

Subject: **Correspondent looking for info re data, vaccines, Vitamin D, etc.**

From: **IDPB-CCDIC-COVID-19 Therapeutics Team**

Date: **June 22, 2021**

The following paragraphs are suggested for inclusion in the above-mentioned docket:

We are providing input to the following questions taken from the incoming.

Why is there no advice for use of Vitamin D3 for prevention of Covid-19? It does prevent respiratory infections.
Why are ivermectin and Hydroxychloroquine not approved in Canada for use as prevention and treatment of Covid-19? It is used in many countries with great success.

One of the Public Health Agency of Canada's (PHAC) roles to support Canada's COVID-19 response is to acquire medications to treat COVID-19. This is to ensure that Canadians will have access to safe and effective treatments in the context of substantial global demand. PHAC monitors the emerging evidence around therapeutics to inform the decisions around procurement.

PHAC does not issue recommendations as such, for or against the use of medications (including *vitamin D*) for COVID-19.

Regarding the question about "approval" of ivermectin and hydroxychloroquine (HCQ) for use as prevention and treatment of COVID-19: Before drug products are authorized for sale in Canada, Health Canada (HC) reviews them to assess their safety, efficacy and quality. A manufacturer seeking market authorization must present scientific evidence of a product's safety, efficacy and quality to HC. As the regulator, HC grants market authorization when it is satisfied that the benefits outweigh the potential risks. The list of applications received for drugs and vaccines for COVID-19 is available at: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/applications.html.

Commented [JA1]: HC will need to review our suggested input.

The provinces and territories have primary responsibility for decisions around choice and use of therapeutics - including for COVID-19 – within their jurisdictions. In Canada, a health care professional's decision to prescribe or use a particular drug for a labelled or off-label indication is part of the practice of medicine, which falls under the jurisdiction of provincial and territorial professional regulatory authorities.

Bradley, Kevin (HC/SC)

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-07-20 2:59 PM
To: Djiometio, Joseph (PHAC/ASPC); Marinsky, Cheryl (PHAC/ASPC); Azad, Mina (PHAC/ASPC)
Cc: Arthur, Jacqueline (PHAC/ASPC); Kolbe2, Jane (PHAC/ASPC); Lawuyi2, Niyi (PHAC/ASPC)
Subject: RE: FYI Medscape Editorial FW: Ivermectin for COVID: How Do We Know What to Believe?

It's not novel but serves as a cautionary note to intended audience (primary care and public health) who are bombarded with contradictory "conclusions" about the effectiveness of COVID therapeutics…

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-07-20 3:56 PM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Cc: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>
Subject: RE: FYI Medscape Editorial FW: Ivermectin for COVID: How Do We Know What to Believe?

Hi
I don't see the novelty.
The authors stated that Many studies included were not peer reviewed and a wide range of doses were evaluated

---

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-07-20 2:47 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Cc: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>
Subject: RE: FYI Medscape Editorial FW: Ivermectin for COVID: How Do We Know What to Believe?

Thanks for sharing Margaret, I saw something similar in a critical appraisal thread that I follow. Similar conclusions though!

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-07-20 2:40 PM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Cc: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Lawuyi2, Niyi (PHAC/ASPC) <niyi.lawuyi2@canada.ca>
Subject: FYI Medscape Editorial FW: Ivermectin for COVID: How Do We Know What to Believe?

Hi,

You may or may not have seen this already via Medscape. It's a fairly quick read about a meta-analysis of trials looking at ivermectin to treat COVID.

Margaret

This transcript has been edited for clarity.
Welcome to *Impact Factor*, your weekly dose of commentary on a new medical study. I'm Dr F. Perry Wilson of the Yale School of Medicine.
This week, it's time we talk about ivermectin.
Since the first days of the COVID-19 pandemic, various existing drugs have been touted as near miracle cures for the disease. Often, the discussion of agents like hydroxychloroquine, lopinavir, and their ilk veered into the conspiratorial, squelching reasonable scientific discussion. Boosters would accuse detractors of hiding the truth of a safe and effective treatment at the behest of big pharma or the deep state. Detractors would accuse boosters of bad data analysis and wishful thinking.

Enter ivermectin and this meta-analysis of randomized trials by Andrew Hill and his colleagues in *Open Forum Infectious Diseases* that seems to show that the drug has pretty remarkable efficacy against COVID-19.

But before we dig in, let's put the mechanistic cards on the table.

Ivermectin is an antiparasitic agent that has been used to treat scabies, river blindness, and filariasis, among others. You may give it to your dog to prevent heartworm.
Discovered in 1975, the drug has been in worldwide use for nearly five decades and appears on the WHO list of essential medicines.
Ivermectin binds to certain chloride channels on nerve and muscle cells, paralyzing the creature exposed to it. These channels are present in worm and insect nervous systems, which is why the drug works.

Humans have the channels too, but only in our brains and spinal columns. Since ivermectin can't cross the blood-brain barrier, we are spared from its effects.
But you will note that SARS-CoV-2 has no muscles or nerves. So why the interest in this drug for this virus?
A lot of the enthusiasm comes from this study, by a group that has done nice work showing that the drug may have antiviral properties by affecting a protein called importin that a lot of viruses hijack for their own nefarious uses.
Researchers infected a cell culture with SARS-CoV-2 and added various concentrations of ivermectin. They then measured viral replication and found that the drug — in a petri dish, at least — could dramatically inhibit the ability of the virus to reproduce.
<< OLE Object: Picture (Device Independent Bitmap) >>
Caly L, et al. *Antiviral Res*. 2020;178:104787. https://doi.org/10.1016/j.antiviral.2020.104787

But there's a problem. The inhibitory concentration of the drug, around 2.5 micromolar, is not achievable in real live humans. In fact, standard ivermectin dosing achieves blood concentrations of about 25 nanomolar, 100-fold less than what was needed in vitro. Lung concentrations are a bit higher than blood concentrations but still 50-fold less than what is needed to inhibit the virus in cells in culture.

So, if ivermectin is going to work in humans with COVID-19, it has to be via some other mechanism — anti-inflammation or something. But as a starting point, biological plausibility here is not high.
But that never stopped us before. Multiple clinical trials at this point have evaluated the drug in COVID-19, and according to this meta-analysis at least, the results are compelling.

The authors combined data from 24 randomized trials of ivermectin — a total of 3328 patients — to examine a variety of outcomes ranging from resolution of symptoms to death. I'm going to focus on mortality because it's a pretty important endpoint, but the results for other outcomes are broadly similar.
Eleven trials with about 2000 patients total had death data available. Combining them gave a death rate of 3% in the ivermectin arm and 8.7% in the comparator arm, a statistically significant result.
<< OLE Object: Picture (Device Independent Bitmap) >>
Hill A, et al. *Open Forum Infect Dis*. 2021. https://doi.org/10.1093/ofid/ofab358
These forest plots can be a bit tough to read, but basically, each bar represents the effect of a single study and the diamond is the overall effect. Anything that crosses the line at 1 is not statistically significant. So, you have several studies trending toward significance that, when combined, give you that overall final result. This is how meta-analyses work.
But there is a bit of a problem here.
Remember that the data you get out of a meta-analysis are only as good as the data you put in. And there are some things to criticize about these data.
The authors aggregated data from studies that were peer-reviewed, those that were hosted on preprint servers, and those whose results they obtained through a network of researchers interested in ivermectin — even if the studies hadn't been published elsewhere. I broke down the mortality results by publication status here.
<< OLE Object: Picture (Device Independent Bitmap) >>
Hill A, et al. *Open Forum Infect Dis*. 2021. https://doi.org/10.1093/ofid/ofab358. Color-key modifications made by F. Perry Wilson, MD, MSCE.

I'm worried about a few things here. First, inclusion of completely unpublished studies is really problematic, since there is no way for anyone to vet the results. It's possible that those people running trials with promising data are even more likely to provide that to the meta-analyzers than those whose trials turned up nothing.
I do get why you might want to include preprints in your meta-analysis; peer-review is slow and the pandemic is happening fast. But peer review really does have a purpose. Some of these studies will probably never get published, and not because dark forces are conspiring against ivermectin; they just have some real problems.
One study driving the mortality benefit is this one, out of Iran, hosted on a preprint server.
It's a six-arm randomized trial of patients hospitalized with COVID-19. But it's weird. According to Table 1, 29% of them were PCR-negative for SARS-CoV-2. What's worse, this percentage is much higher in the two control groups (47%) compared with the ivermectin groups (20%). My math suggests that such a discrepancy would only occur 2 out of 10,000 times if randomization was, well, random.
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I'm not saying this is fake or anything, but this is exactly the sort of thing that peer review would pick up on and give the authors a chance to correct. And yet here, this trial is given equal weight to all the others.
The other trial that seems to drive these results, also not yet peer-reviewed, is the Elgazzar trial out of Egypt.
Here, ivermectin was compared with hydroxychloroquine in 400 individuals with COVID-19. The results were pretty stark, in terms of death. In the moderately ill group, there were no deaths in the ivermectin group, four in the hydroxychloroquine group. In the severely ill group, two deaths in the ivermectin group, 20 in the hydroxychloroquine group.
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Now, you'll note that hydroxychloroquine is not placebo, so there is some chance that what we are seeing is a sign that hydroxychloroquine is bad, not that ivermectin is good. But, inspired by the Iran paper, I went ahead and looked at Table 1 again. There were multiple statistically significant imbalances across baseline characteristics. Again, this is very unlikely if there wasn't some failure of randomization.

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Elgazzar A, et al. https://www.researchsquare.com/article/rs-100956/v3

All I'm doing is some peer review of a study that has not yet been peer-reviewed. I'm not saying it's wrong, but review would allow the authors to provide an explanation, or maybe even reanalyze their results. Mistakes get made all the time in research; it helps to have a critical eye.

Others have noted that if you remove the Iran and Elgazzar papers, the protective effect of ivermectin in this meta-analysis disappears:

Which doesn't mean ivermectin isn't useful. What it means is we still don't know. We don't have ironclad evidence. The meta-analysis authors note that there are multiple large clinical trials going on right now that should seal the deal one way or the other. But what do we do until then?

Well, the easy answer is to say just cut the Gordian knot and get vaccinated; then you won't even need ivermectin. But there are plenty of places around the world where vaccines are not available and ivermectin is.

So, here's my pitch. All of these trialists should, in the interest of public health, release not just their results but their analytic datasets in a de-identified format to a site like datadryad.org so the community can review them directly. Instead of trying to parse what the authors mean in this or that sentence in the manuscript, just share the data. We'll know right away if we should believe it or not. This is easy, transparent, and perfectly legal. All of us — ivermectin boosters or ivermectin detractors — should speak with one voice on this: We are in a public health emergency. Release the data so we can know, for sure, what to believe.

F. Perry Wilson, MD, MSCE, is an associate professor of medicine and director of Yale's Clinical and Translational Research Accelerator. His science communication work can be found in the Huffington Post, on NPR, and here on Medscape. He tweets @fperrywilson and hosts a repository of his communication work at www.methodsman.com.

https://www.medscape.com/viewarticle/954681?src=WNL_dne_210716_mscpedit&uac=8929DJ&impID=3507535&faf=1

Bradley, Kevin (HC/SC)

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Sent: 2021-07-26 1:33 PM
To: Azad, Mina (PHAC/ASPC); Djiometio, Joseph (PHAC/ASPC)
Subject: Previous response: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19
Attachments: 21-110593-856_FINAL sent reply_[redacted]pdf

Hi,

I know several people are working on this, but just sharing an earlier response we sent to someone who wrote about a treatment protocol. Some of the content might be useful, wrt our role etc.

I will see if I can find the word document as it is saved to our files as a pdf.

Margaret

From: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Sent: 2021-07-26 11:49 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Cc: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Hi Joe,

I also included some zinc information. I'm assuming you'll remove the majority of the details, so please accept my apologies for having too much text.
This is the version that includes all of the comments and changes. As soon as I receive new comments, I will create a clean version for you to share with Cheryl and Jane.
I've also copied Margaret here in case she's willing to share her valuable inputs ☺

Best,
Mina

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-07-23 1:53 PM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Thanks Joe, that sounds good!

Cheryl

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-07-23 1:51 PM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Mina will add ZINC's bullets and Samriti, hydrochloroquine bullets (Monday AM). My plan is to flip that to you Monday afternoon

Joe

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-07-23 1:36 PM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Thanks Joe, this looks good!

Cheryl

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-07-23 11:50 AM
To: Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Mina
Here is my comments

Joe

From: Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Sent: 2021-07-23 11:45 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Thanks everyone!

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-07-23 11:16 AM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Thank Cheryl
I will review make suggestions for summary

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-07-23 11:14 AM
To: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Hi Mina,

I just had a look at this doc., thank you for your prompt work!

Although I appreciate all the details that you have provided, the response that we will be crafting is limited to ¾ of page to one page. I would suggest summarizing this information in 2 bullets for our use. Briefly explaining the study parameters, findings and limitations- i.e. why this therapeutic is not suggested for use as a COVID-19 treatment. I suggest the same approach for zinc. I hope this helps. If you have any additional questions. Please reach out to me if you have any questions don't hesitate to ask ☺

Cheryl

From: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Sent: 2021-07-23 11:06 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Hello everyone,

I've attached a report for fluvoxamine. Although a paper was published in December 2020, it was not reviewed in our daily titles at the time. However, I was able to locate some information from a retrospective, observational cohort study in our daily title email from February 2021.

I was going to begin work on the other product (zinc), but I wanted to share this one with you first to ensure that I'm on the right track and that this is what you actually require. I would be grateful for your feedback.

Best,

Mina

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-07-23 9:25 AM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Yes.

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-07-23 9:24 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: RE: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

That is good news! We have a little breathing space ☺

From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-07-23 9:22 AM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Subject: FW: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

From: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-07-23 9:17 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Subject: EXTENSION GRANTED 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Just to let you know, our extension until July 30th was granted.

Adele for….Single-Window / Guichet unique COVID-19 Therapeutics / thérapeutiques
Centre for Communicable Diseases and Infection Control / Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada / Agence de la santé publique du Canada

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From: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Sent: 2021-07-22 2:04 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Subject: RE: FOR ACTION 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Ok. Thank you Jackie

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-07-22 2:03 PM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Subject: RE: FOR ACTION 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Just to clarify, I will send it to HC for input once we are comfortable from our perspective. Joe send me your draft by July 26th – hopefully we are granted the extension.
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Sent: 2021-07-22 1:46 PM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>
Cc: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Subject: FOR ACTION 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

Hi Jo,
Please see the incoming attached and prepare a draft reply in consultation with Health Canada. I hav requested an extension until July 30th and still waiting to hear back so will let you know. Right now, we would need this draft by July 26 at noon to allow enough time for Jackie to review and approve. If extension is granted, I will get back to you.

Please use template attached for drafting your reply.

_____
Adele for…Single-Window / Guichet unique COVID-19 Therapeutics / thérapeutiques
Centre for Communicable Diseases and Infection Control / Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada / Agence de la santé publique du Canada

From: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>
Sent: 2021-07-21 4:59 PM

To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC) <phac.covid-19therapeutics-therapeutiques.aspc@canada.ca>
Cc: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>; Poon Young, Celisse (PHAC/ASPC) <celisse.poonyoung@canada.ca>
Subject: FOR ACTION 21-107499-249 CPHO Correspondence A couple of suggestions for treating the novel COVID-19

HI, Please see new CPHO Correspondence attached. Your Director approved response is due to me by July 26, Cob

NOTE: , please advise if multi input would be needed from HC. Thanks Laura

Single Window, Centre for Communicable Diseases and Infection Control
Infectious Disease Programs Branch
Public Health Agency of Canada, Government of Canada
Laura Forsyth / Tél. : 613-864-9596
ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>

Guichet unique, Centre de la lutte contre les maladies transmissibles et les infections
Direction générale de la prévention et du contrôle des maladies infectieuses
Agence de la santé publique du Canada, Gouvernement du Canada
Laura Forsyth / Tél. : 613-864-9596
ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>

From: Ann McCurdy <ann.mccurdy@phac-aspc.gc.ca>
Sent: 2021-07-21 9:11 AM
To: ccdic / siimd (PHAC/ASPC) <phac.ccdic-siimd.aspc@canada.ca>
Subject: 21-107499 - 249 for / pour: Provide Input/Fournir des paragraphes

Health Canada Santé Canada

Canada

Audit Trail / Suivi de vérification
Branch Correspondence / Correspondance des directions générales

Subject / Sujet: 21-107499 - 249 for / pour: Provide Input/Fournir des paragraphes

21-107499 - 249

Send From / Envoyé de	Send To / Envoyé a	Date Sent / Date de l'envoi	Bring Forward / Rappel

PHAC-IDPCB-VPO Ann McCurdy/HC-SC/GC/CA	**Organization/Organisme** PHAC-IDPCB-CCDIC-SIIMD **Person/Personne** CCDIC-SIIMD/GEN/HC-SC/GC/CA	2021-07-21	

Special Instructions / Instructions spéciales: Branch direct reply
Document Status / Statut du dossier: Open/Ouvert
Action / Intervention: Provide Input/Fournir des paragraphes

Comment / Commentaires:
Correspondence, please provide input on template attached, please advise if muliti input would be needed from HC, due July 28, thank you

Here is the link to document / Voici le lien au document:

The documents provided to you may contain personal information.
If you have received these documents in error, notify the MECS-USER-SUPPORT group immediately.

Les documents qui vous sont fournis peuvent contenir des renseignements personnels.
Si vous avez reçu ces documents par erreur, avisez immédiatement le groupe courriel des MECS-USER-SUPPORT.

Created By / Créé par: Ann McCurdy
Date Created / Créé le: 2021-07-21

Crôteau, Adèle (PHAC/ASPC) MECS# 21-110593-856

From: Arthur, Jacqueline (PHAC/ASPC)
Sent: 2021-06-03 5:25 PM
To: COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)
Subject: FW: I-Mask+ Protocol for early treatment of Covid-19

For filing please, Bersabel's response to the I-Mask correspondence.
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

-----Original Message-----
From: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>
Sent: 2021-06-03 5:24 PM
To: [redacted]
Cc: McLean, Hollie (HC/SC) <hollie.mclean@canada.ca>; Levesque2, Kaili (HC/SC) <kaili.levesque2@canada.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Subject: RE: I-Mask+ Protocol for early treatment of Covid-19

Dear [redacted]

Thank you for your correspondence concerning the use of the I-Mask Protocol for early treatment and prophylaxis for COVID-19 to support Canada's response to COVID-19.

The Public Health Agency of Canada (PHAC) conducts a thorough analysis of the emerging scientific evidence regarding promising therapeutics to treat COVID-19, and Health Canada (HC) formally reviews these drugs to assess their safety, efficacy and quality before authorizing their sale in Canada. Many drugs that show promise in laboratory studies are found to be ineffective in patients.

I-MASK+ Protocol is a prevention and early outpatient treatment protocol for COVID-19. While it includes a number of medications and supplements, it is centred on ivermectin, a broad-spectrum anti-parasitic agent authorized and approved by HC for human and veterinary applications to treat parasitic infections. At this time, HC has not authorized its use for the treatment of COVID-19.

Independent reviews of available clinical trial results that evaluate the effectiveness of ivermectin as a treatment for COVID-19 have been conducted by: the Canadian Agency for Drugs and Technologies in Health (CADTH); Alberta Health Services; British Columbia's COVID-19 Therapeutics Committee/COVID-19 Therapeutics Review and Advisory Working Group; and Ontario's COVID-19 Science Advisory table. These bodies of scientific experts all concluded that there is no clear benefit to ivermectin treatment among patients with COVID-19.

On March 31, 2021, the World Health Organization (WHO) issued a statement on ivermectin advising against its use outside of clinical trials, stating the current evidence was inconclusive. Further, the manufacturer - Merck - has also issued a statement against the use of ivermectin for the treatment of COVID-19. https://www.merck.com/news/merck-statement-on-ivermectin-use-during-the-covid-19-pandemic/

In summary, there is currently no robust evidence (i.e., from high quality, well-designed clinical trials) to suggest that the I-MASK+ Protocol provides clinical benefit for the treatment or prevention of COVID-19, particularly in the Canadian context. Please be assured that PHAC continues to monitor the emerging evidence of clinical efficacy and safety from high quality trials on novel and repurposed therapeutics for COVID-19. The provinces and territories have primary responsibility for decisions around choice and use of therapeutics - including for COVID-19 – within their jurisdictions.

Thank you for writing to the Public Health Agency of Canada. I hope this information is helpful.

With best regards,

Bersabel
(She | Elle)

Bersabel Ephrem, BSc., MPA
Director General, Centre for Communicable Diseases and Infection Control Infectious Disease Prevention and Control Branch Public Health Agency of Canada bersabel.ephrem@canada.ca / Tel: 613-948-6799 / Cell: 613-415-5897

Directrice générale, Centre de la lutte contre les maladies transmissibles et les infections Direction générale de la prévention et du contrôle des maladies infectieuses Agence de la santé publique du Canada bersabel.ephrem@canada.ca / Tel: 613-948-6799 / Cell: 613-415-5897

-----Original Message-----
From: McLean, Hollie (HC/SC) <hollie.mclean@canada.ca> On Behalf Of Levesque2, Kaili (HC/SC)
Sent: 2021-05-31 3:54 PM
To: [redacted]
Cc: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@canada.ca>; Levesque2, Kaili (HC/SC) <kaili.levesque2@canada.ca>; McLean, Hollie (HC/SC) <hollie.mclean@canada.ca>
Subject: RE: I-Mask+ Protocol for early treatment of Covid-19

Hi [redacted]

Thank you for your email. Note that I've recently assumed the role as Vice President, COVID-19 Vaccine Rollout at the Public Health Agency. I'm connecting you with Bersabel Ephrem, the Director General responsible for the therapeutics file.

Thanks

Kaili

Kaili Levesque (she/her/elle)
613.818.0492

-----Original Message-----
From: [redacted]
Sent: 2021-05-31 12:13 PM

To: Levesque2, Kaili (HC/SC) <kaili.levesque2@canada.ca>
Subject: I-Mask+ Protocol for early treatment of Covid-19

Good morning Ms. Levesque:

I am writing to ask for your assistance. I have been following a growing body of research on the use of the I-Mask Protocol for early treatment and prophylaxis for Covid-19. Early in the pandemic, this protocol was not well understood and had only anecdotal evidence of its efficacy. Recently, however, I've been encouraged to see multiple studies showing good evidence of efficacy. I am puzzled as to why this treatment is not being studied in Canada as we are still in a situation across the country where people are being hospitalized for Covid-19. I am not a medical professional, but I wonder if it is not prudent and compassionate to open the door to other treatment possibilities which could prevent further deterioration of newly diagnosed victims of this virus? I do not know if you are the right person to send this email to, but I do know that you believe that we should be doing absolutely everything to try to treat this disease. My sincere hope is that you and your Task Force are seeking to include the use of existing medicines that we know are not harmful in and of themselves, such as Ivermectin, which is one of the components in the I-Mask Protocol. While we all look forward to the day when vaccinations take effect Canada-wide, in the meantime there are still many people who are falling ill and require medical treatment for this disease.

I respectfully submit to you this link to the growing body of knowledge and research studies around the I-Mask+ Protocol and I beg you to use your considerable influence to bring it to the attention of the Covid 19 Task Force and study it with all due diligence. If there is merit in this treatment, and your committee agrees to try it on a limited study basis, perhaps many Canadian lives could be saved and/or at the very least, saved from the longevity of hospitalizations for Covid 19 which they may be facing under the current treatment protocols. I believe that your committee has a moral and ethical obligation to fairly and diligently consider all possible treatments, irrespective of WHO or any other body who may be telling you otherwise. We are Canadians, first and foremost. We are responsible for one another.

Thank you so very much for your time. I ask you to please respectfully consider my request, and I very much look forward to your reply.

Sincerely,

[redacted]

https://covid19criticalcare.com/covid-19-protocols/i-mask-plus-protocol/

Bradley, Kevin (HC/SC)

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-07-28 9:50 AM
To: Arthur, Jacqueline (PHAC/ASPC); Djiometio, Joseph (PHAC/ASPC); Azad, Mina (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC)
Cc: Kolbe2, Jane (PHAC/ASPC)
Subject: RE: FYI Cochrane Review of Ivermectin

You are welcome!

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>
Sent: 2021-07-28 9:46 AM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>; Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Cc: Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: RE: FYI Cochrane Review of Ivermectin

Many thanks Cheryl. The issue sheet for ivermectin should be updated with this information. Joe, can you ensure it gets done please?
J

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager, AMR Division | Gestionnaire principale, Division de la RAM
COVID-19 Therapeutics | thérapeutiques
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-07-28 9:37 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Cc: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@canada.ca>; Kolbe2, Jane (PHAC/ASPC) <jane.kolbe2@canada.ca>
Subject: FYI Cochrane Review of Ivermectin

Hi everyone,

Just thought I would share the Cochrane review on Ivermectin just issued! Not surprisingly, ivermectin is not recommended for the treatment and prevention of COVID-19. Their confidence in the reviewed evidence was low, have a look at the explanation in the summary of findings table, very interesting. Here is a link to the full report:

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD015017.pub2/full

Thanks, please share with anyone else who might be interested!

Cheryl

Bradley, Kevin (HC/SC)

From: Marinsky, Cheryl (PHAC/ASPC)
Sent: 2021-08-10 10:13 AM
To: Azad, Mina (PHAC/ASPC)
Cc: Djiometio, Joseph (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC)
Subject: RE: Ivermectin Study Retraction

You are welcome. A lot going in the ivermectin research world at the moment among detractors and supporters!

From: Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>
Sent: 2021-08-10 10:12 AM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Cc: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Subject: RE: Ivermectin Study Retraction

Hi Cheryl,

Interesting! This is the second retraction of an Ivermectin article!!

Thank you so much for sharing them with us ☺

Best,
Mina

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@canada.ca>
Sent: 2021-08-10 9:59 AM
To: Djiometio, Joseph (PHAC/ASPC) <joseph.djiometio@canada.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@canada.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.gale-rowe@canada.ca>
Subject: Ivermectin Study Retraction

Hi everyone,

Not sure if you have seen this, came up in my alerts from last week that I am just getting through now!

There was a claim made that a study included in the following meta-analysis was retracted over concerns of scientific fraud:

Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection | Open Forum Infectious Diseases | Oxford Academic (oup.com)

A revised version of this study is underway.

Here is in interesting read from the same journal:

Ivermectin for the treatment of COVID-19 disease: Too good to pass up or too good to be true? | Open Forum Infectious Diseases | Oxford Academic (oup.com)

Thanks,

Cheryl

Bradley, Kevin (HC/SC)

From: Arthur, Jacqueline (PHAC/ASPC)
Sent: 2021-08-24 11:44 AM
To: Djiometio, Joseph (PHAC/ASPC)
Cc: Azad, Mina (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC); Kolbe, Jane (PHAC/ASPC); Marinsky, Cheryl (PHAC/ASPC); Cassista, Caroline (PHAC/ASPC)
Subject: FW: GPHIN Daily Report (24 August 2021)

Ivermectin info below Joe so please ensure the issue sheet is updated. Fyi for others.
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager | Gestionnaire principale
COVID-19 Therapeutics | thérapeutiques
Policy Development, AMR Division |Elaboration de politiques, Division de la RAM
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

From: Guerrero, Gerardo (PHAC/ASPC) <gerardo.guerrero@phac-aspc.gc.ca> **On Behalf Of** gphin / rmisp (PHAC/ASPC)
Sent: 2021-08-24 8:46 AM
To: gphin / rmisp (PHAC/ASPC) <gphin-rmisp@phac-aspc.gc.ca>
Subject: GPHIN Daily Report (24 August 2021)

Good morning,

Please find below the daily Summary and articles collected by GPHIN for your review and risk assessment.

GPHIN Daily Report
August 24, 2021

The Highlight of the Day

- **Burkina Faso:** The Ministry of Health announced on August 22, 2021 the detection of a suspected case of Ebola hemorrhagic fever at the Bogodogo University Hospital Center in Ouagadougou. According to officials, the 22-year-old patient arrived two days ago from Côte d'Ivoire. (AA, Africa Times)

Updates on COVID-19 (Media & Officials)

COVID-19 Variants

As of August 24, 2021:

- Countries with confirmed Alpha (B.1.1.7) variant: (171 countries)
- Countries with confirmed Beta (B.1.351) variant: (128 countries)
- Countries with confirmed Gamma (P.1) variant: (71 countries)
- Countries with Confirmed Delta (B.1.617.2) and Delta* (B.1.617 of unspecified lineage): **New** Egypt (138 countries)

***Please, note that countries may have reported directly to WHO and may not have been captured yet in our counts if no source was found. Both open source and WHO weekly Epi Update has been used to confirm the countries/ territories that have officially reported a variant. As of August 17, 2021, the WHO weekly Epi update has stated that the Alpha (B.1.1.7) variant has been reported in 190 countries, the Beta (B.1.351) variant in 138 countries and the Gamma (P.1) variant has been reported in 82 countries. As of August 10, Delta (B.1.617.2) has been detected in 148 countries. There have also been reports of Delta + (B.1.617 in 2 countries that did not identify the sub-lineage). No official source has yet been found for those countries that are not captured in our counts. Discrepancies between WHO and GPHIN's counts can also be attributed to geopolitics considerations, with WHO map not labelling Taiwan and Hong Kong SAR and therefore likely not including them in their list of countries. Variants of Interest (VOI) Eta (B.1.525) and Lambda (C.37) are being tracked on the spreadsheet.*

Immunization & Adverse events

- As of August 23, there were 52,441,903 doses of COVID-19 vaccine administered in Canada. For further information and breakdowns by province and territories, please view the link. (PHAC)
- As of August 23, 2021, 4,619,976,274 vaccine doses have been administered. For further information on country breakdown, please view the link. (WHO)
- **Canada:** Saskatchewan announced on Aug 20 that some 11-year-olds who turn 12 this year are allowed to get COVID-19 vaccination. This follows similar policy in Manitoba, British Columbia, Alberta and Ontario. Meanwhile, Health Canada has not approved any vaccines for children under 12. (National Post)
- **Cuba:** The Center for State Control of Medicines, Equipment and Medical Devices has granted emergency approval for its homegrown Soberana 2 vaccine which has an efficacy rate of 91.2%, and has already been used in areas with high rates of transmission. (Reuters)
- **United States:** On Aug 23, the U.S. FDA approved the first COVID-19 vaccine. The vaccine which has been known as the Pfizer-BioNTech COVID-19 Vaccine, and will now be marketed as Comirnaty, for the prevention of COVID-19 disease in individuals 16 years of age and older. The vaccine also continues to be available under emergency use authorization (EUA), including for individuals 12-15 years of age and for the administration of a third dose in certain immunocompromised individuals. (FDA)
- **South Africa**: Health Products Regulatory Authority received 1,473 reports of Covid-19 vaccine side-effects over a period of almost three months, but investigations showed no link between the drugs and people dying. The side-effect cases account for only 0.02% of the almost 7.1-million doses of vaccines administered in South Africa between the start of the nationwide vaccination roll-out on 17 May until 31 July. (Mail & Guardian)

Canada

- As of August 23, 2021 at 19:00 EST, there were 1,473,624 cases of COVID-19 recorded in Canada including 26,814 deaths. For further information and breakdowns by province and territories, please view the link. (PHAC)

- **Ontario**: Potentially 7,000 people need to get tested for COVID-19 after a basketball tournament, attended by teams from all over Ontario and other provinces, resulted in an outbreak. Durham Region Health Department is urging anyone who attended the 43rd Annual Jane and Finch Classic basketball tournament, which was held at Playground Global facility in Oshawa from Aug. 3 to 8, to get tested "immediately." (CTV)

International

- Globally, as of August 23, 2021, 5:09 pm CEST, there have been 211,730,035 confirmed cases of COVID-19, including 4,430,697 deaths. (WHO)
- **International:** FDA warns against the use of Ivermectin for use in treating or preventing COVID-19 in humans. The National Institutes of Health UK reviewed studies of the drug to treat COVID-19 patients and found insufficient evidence to recommend for or against use of the drug. (FDA, Daily Mail UK)
- **Niger:** A research, co-funded by European Union and ECOWAS Commission conducted in Niger, aimed at understanding the socio-economic impact of COVID-19 on free movement, migrant remittances and the well-being of migrant households, families, and communities in Niger has released their results. (Relief Web)
- **WHO:** On Aug 23th, WHO called for a two-month moratorium on administering booster shots of COVID-19 vaccines as a means of reducing global vaccine inequality and preventing the emergence of new coronavirus variants. Priority should be given to raising vaccination rates in countries where only 1 percent or 2 percent of the population has been inoculated (City News)

Studies Related to COVID -19

- **Canada:** The Wellesley Institute and Ontario Health released a report on race-based data collected between June 26, 2020, and April 21, 2021. The Institute found that racialized populations were much more likely to get COVID and to have negative impacts from COVID than the White population in Ontario. The Latino, Middle Eastern, Southeast Asian, South Asian and Black populations were five to seven times more likely to get COVID than the White population. Hospitalizations, ICU stays and deaths were also much higher. (*The Wellesley Institute*)
- **United States:**
    - Only 21 percent of patients with severe pneumonia caused by SARS-CoV-2 have a documented bacterial superinfection at the time of intubation, resulting in potential overuse of antibiotics, according to new research. (Outbreak News Today, *Journal of Respiratory and Critical Care Medicines*)
    - The majority of individuals who experience mild or moderate COVID-19 infection also experience long COVID-19, or persistent symptoms more than 30 days after they test positive, according to data from the longitudinal CoVHORT study at the University of Arizona Health Sciences. (Arizona,edu, *PLOS*)
- **China:** Inactivated COVID-19 vaccines developed by China curbed the spread of the Delta variant during a May outbreak in Guangzhou city in south China, a study has shown. Researchers from the Guangzhou Center for Disease Control and Prevention found that two shots of the vaccines provided an efficacy of 59 percent against COVID-19 caused by the Delta variant, 70.2 percent against moderate form of the disease, and 100 percent against severe cases. (ECNS, *Emerging Microbes and Infections*)

Domestic Events (Media & Officials)

- **Alberta:** Accidental opioid poisonings were increasingly reported in the emergency department at the Royal Alexandra Hospital in central Edmonton. Between January and May of this year, 624 Albertans died from accidental drug poisonings, a 41 per cent increase over the same time period in 2020. (Edmonton Journal)

- **Saskatchewan**: A study by University of Calgary showed higher rates of Kennedy's Disease among Indigenous people in Saskatchewan. The rate is 14.7 per 100,000 — way above the average rate of one to two per 100,000. Eighty-three per cent of the study's participants self-identified as Indigenous. (The Leader Post)

International Events (Media & Officials)

- **Hong Kong:** For the third time in a week, Hong Kong health officials report monitoring a human case of avian influenza A (H5N6) on the Chinese mainland. The latest case involves a 55-year-old man living in Liuzhou, Guangxi. He is a farmer and had contact with live poultry. He developed symptoms on August 17th and was admitted for treatment on the same day. The patient is in critical condition. (Outbreak News Today)

- **Sierra Leone:** Ebola booster vaccination kicks off following administration of the prime dose of Johnson & Johnson Ebola vaccine in May 2021 (Relief Web)

- **India:** There has been a spike in viral fever cases in rural areas of western UP. More than 70% of patients coming to the out-patient departments of government hospitals over the past week have complained of suffering from fever, cough, cold, dehydration and body ache. Health department has issued an alert at all the community health centres in the rural areas following the death of six people, including five children, in Mathura's Konh village in Farah due to a "mysterious" fever. The cause of death is still not clear but investigations are underway to test samples for malaria, dengue and COVID-19. (Times of India)

Research, policies, and guidelines (Media & Officials)

- **Study: Vaping damages blood vessels, much like cigarettes, study finds**
  Aerosol from vaping devices may impact human blood vessels to the same extent as smoke from cigarettes, according to an analysis presented on August 23rd. In experiments involving rats, the function of the endothelium, a layer of cells that help control blood clotting, blood pressure levels and immune function and keep blood vessels healthy was significantly impaired after a five-minute exposure to vaping aerosols, the data showed. (UPI)

Best Regards | Sincères salutations
The GPHIN Team / L'équipe du RMISP

Global Public Health Intelligence Network | Réseau mondial d'information en santé publique
Center for Emergency Preparedness | Centre des mesures d'urgence
Emergency Management Branch | Direction générale de la gestion des urgences
Public Health Agency of Canada | Agence de la santé publique du Canada
New GPHIN-RMISP@phac-aspc.gc.ca

Bradley, Kevin (HC/SC)

From: Apse, Krista (PHAC/ASPC)
Sent: 2021-08-31 10:19 AM
To: Ephrem, Bersabel (PHAC/ASPC)
Cc: Arthur, Jacqueline (PHAC/ASPC)
Subject: article

This one shows action on the part of a regulator, so provides a nice picture of the complexity of the environment…

https://www.theguardian.com/world/2021/aug/30/australian-imports-of-ivermectin-increase-10-fold-prompting-warning-from-tga

K.

Bradley, Kevin (HC/SC)

From: Gale-Rowe, Margaret (PHAC/ASPC)
Sent: 2021-09-01 5:58 PM
To: Arthur, Jacqueline (PHAC/ASPC); Kolbe, Jane (PHAC/ASPC)
Subject: RE: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

Thanks Jackie. There was a piece on the tv news as well, yesterday.

Margaret

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Sent: 2021-09-01 5:56 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>; Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@phac-aspc.gc.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: FW: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

Been wanting to share this but finally have time now ☺
J

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager | Gestionnaire principale
COVID-19 Therapeutics | thérapeutiques
Policy Development, AMR Division |Elaboration de politiques, Division de la RAM
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines
https://www.theglobeandmail.com/canada/article-the-ivermectin-mess-people-are-embracing-a-dangerous-livestock-drug/

Jackie

Bradley, Kevin (HC/SC)

From: Arthur, Jacqueline (PHAC/ASPC)
Sent: 2021-09-01 6:08 PM
To: Ephrem, Bersabel (PHAC/ASPC); Njoo, Howard (PHAC/ASPC)
Cc: Gaudreau, Marc-Andre (PHAC/ASPC); Ogouma, Eric (PHAC/ASPC); Kolbe, Jane (PHAC/ASPC); COVID-19 Therapeutics / Thérapeutiques (PHAC/ASPC)
Subject: Therapeutics Briefing deck for the President - final
Attachments: Therapeutics.Brief.President.Sept.2.2021.pptx

Importance: High

Attached, please find the final deck for Thursday's therapeutics briefing with the President.
Marc-André, I assume you will forward to the President's Office?
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager | Gestionnaire principale
COVID-19 Therapeutics | thérapeutiques
Policy Development, AMR Division |Elaboration de politiques, Division de la RAM
Centre for Communicable Diseases and Infection Control | Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada | Agence de la santé publique du Canada
t. (613) 889-8455

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

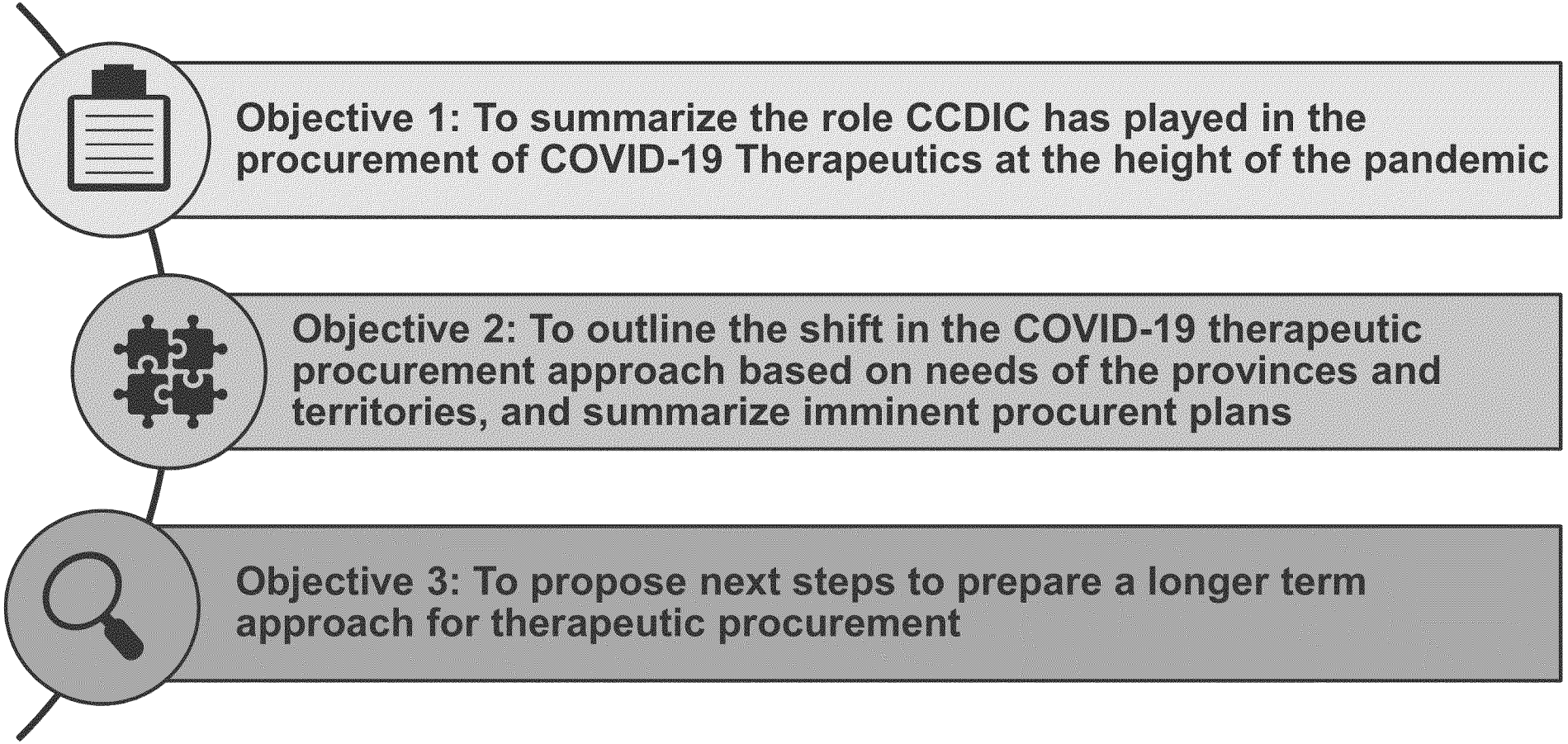
Update on COVID-19 Therapeutics and Next Steps

Briefing to the President

September 2, 2021

PROTECTING AND EMPOWERING CANADIANS
TO IMPROVE THEIR HEALTH

Objectives



The COVID-19 Therapeutics Procurement Landscape During the Height of the Pandemic

- Canada's ***health care system*** was at risk of being ***overwhelmed:***
  - Absence of safe and effective vaccines
  - Absence of prophylaxis to prevent and treat COVID-19
  - Shortage of novel therapeutics in development and fierce global competition for those that were
  - Uneven provincial and territorial capacity to urgently procure, and manage warehousing and logistics

- Therapeutic procurement is traditionally the ***responsibility of provinces and territories*** **(PTs)**, however during the unpresented global pandemic, the Government of Canada took responsibility for COVID-19 therapeutic procurement.
  - PHAC, with the support of Public Services and Procurement Canada (PSPC), assumed federal responsibility to urgently procure COVID-19 therapeutics to support timely access to (and equitable distribution of) critical COVID-19 therapies for the country.
    - PHAC received $200 million for the procurement of COVID-19 treatments through the Medical Countermeasures Wave 3a (MCM3a) budget. In September 2020, MCM3b secured an additional $300 million. (Approximately $338 million remains).

Governance

- Health Canada ***expedited the review of COVID-19 treatments*** while ensuring the products met safety, effectiveness and quality standards, and established the ***Critical Drug Reserve*** to help ensure that Canadians had access to the non-COVID-19 drugs they needed (divestment of the CDR is planned for March 31, 2022),

- The Deputy Minister Vaccine and Therapeutic Procurement Committee (DMPC) was established to integrate advice from different sources and make ***strategic decisions on the procurement of therapeutics***, vaccines and related supplies on behalf of Canada.

- PHAC's Infectious Diseases Programs Branch led the implementation of this ***new role*** to procure COVID-19 therapeutics that included identifying and building skills and expertise. *(see Appendix 1: Org Chart)*

- While PHAC made these products available free of charge for use by PTs, jurisdictions continued to execute their authorities to decide whether and how to use the novel COVID-19 therapeutics procured (i.e. adding new products to their formularies).

COVID-19 Therapeutic Procurements Completed to Date

Manufacturer	Type	Product Name	Number of Doses Procured	Remaining Doses	Source of External Advice (*see notes for details*)
Mint Pharmaceutical	Anti-malarial	Hydroxychloroquine Sulphate	[redacted]		N/A
Apotex	Anti-malarial	Hydroxychloroquine Sulphate			N/A
Gilead Sciences	Antiviral (Hospital use)	Remdesivir (Veklury)			COVID-19 Therapeutics Task Force (CTTF) recommendation COVID-19 Clinical Pharmacology Task Group (CPTG) limit use in clinical trials
Eli Lilly/AbCellera	Monoclonal Antibody (Outpatient use)	Bamlanivimab (LY-CoV555)			CTTF recommendation CPTG limit use in clinical trials
Hoffman La Roche	Monoclonal antibody (Hospital use)	Tocilizumab (Actemra)			CPTG and CTTF recommendations
Hoffman La Roche	Monoclonal Antibodies Cocktail (Outpatient use)	REGEN-COV			CTTF recommendation P/T clinical experts interest

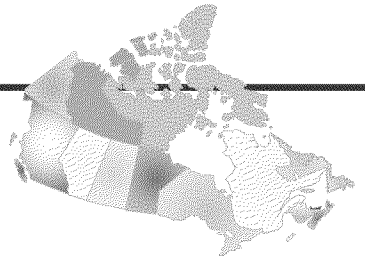
Provincial and Territorial Perspectives

Product Demand and Use

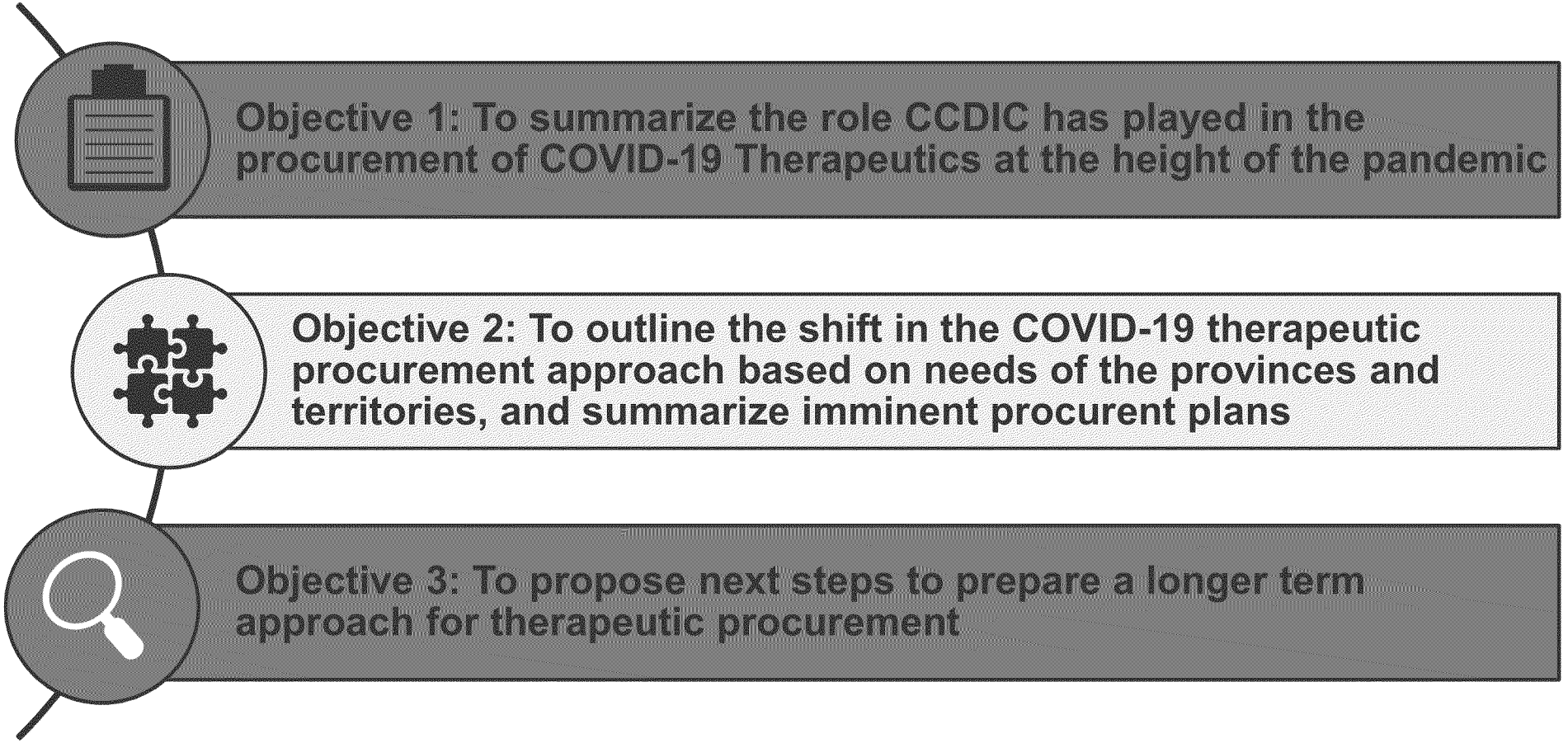
Tocilizumab	Distributed to PTs; used extensively
Bamlanivimab	Uptake has been limited; however, it has been used in some scenarios (immunocompromised patients)
Remdesivir	High demand by some PTs in the 3rd wave
REGN-COV	Several PTs have expressed interest and are requesting

Feedback From Provinces and Territories

- A desire for **early engagement** (prior to procurement) to assess the need for implementing new therapies in their jurisdiction.
- A need for **clinical guidance** from the Agency for Drugs and Technologies in Health (CADTH) and l'Institut national d'excellence en santé et services sociaux (INESSS).
- More **control** over what drugs enter into their Formulary.
- Concerns about future **costs** of novel COVID-19 drugs.



TACTICS



Section 2: Tactics - Fall 2021 COVID-19 Therapeutics Procurement Plans

Type of Drug & Mechanism of action	Immunomodulating drug (blocks the inflammatory cascade and improves survival in severe COVID-19)	Neutralizing monoclonal antibody (binds to and neutralizes the virus)	Broad spectrum antiviral (inhibits replication of SARS-CoV-2 to prevent disease progression and transmission) in mild or moderate COVID-19
Route of Administration	Intravenous (administered directly into a vein in a hospital setting that requires special equipment and trained personnel)	Intravenous (administered directly into a vein in a hospital setting that requires special equipment and trained personnel)	Oral (taken through the mouth in an “at home” setting)
Status in Canada	Off-label use for COVID-19 patients (authorized in Canada for the treatment of rheumatoid arthritis)	Authorized under the IO for the treatment of mild to moderate COVID-19	Submission to Health Canada anticipated in late 2021
International Regulatory Status	Authorized for treatment of rheumatoid arthritis, but not for treatment of COVID-19; use is “off-label”	May 26th 2021: FDA issued an EUA May 21, 2021 the EMA concluded that sotrovimab can be used to treat confirmed COVID-19	June 9th, 2021: U.S. government commits to purchase 1.7 million courses upon issuance of EUA by FDA
Key Product Benefits	- Similar to tocilizumab (purchased and used extensively) - Supplier of tocilizumab has been unable to meet demand, hence sarilumab would serve as a back-up	- Laboratory studies suggest superior performance against Variants of Concern (VOC) - Studies underway to determine if it can be provided through intramuscular injection, making it easy to administer in non-specialized settings (providing implementation benefit to PTs)	- There is no currently authorized oral antiviral for outpatient treatment of COVID-19 - Ease of administration makes it very suitable for use in the context of a pandemic

Fall 2021: COVID-19 Therapeutics Procurement Plans, con't:

- Additional quantity of ***tocilizumab*** (Hoffman La Roche) is being procured as part of current contract; used extensively by PTs.

- Continue to monitor the emerging evidence for COVID-19 treatments, including oral antivirals under development by ***Pfizer*** and monoclonal antibody by ***AstraZeneca*** . PHAC is in discussions with these companies for information exchange.

- Continue to monitor emerging scientific data from clinical trials as well as media to inform FPT discussions:
  - Casirivimab/imdevimab (REGN-COV) [HC authorized; PHAC procured]
    - Both the US and the UK have given emergency/conditional authorization for use for post-exposure prophylaxis, given intravenously (IV) or subcutaneously (SC)
  - Ivermectin [not authorized; not-procured]
    - High media interest due to US increasing use of veterinary drug; not supported by rigorous, scientific evidence.

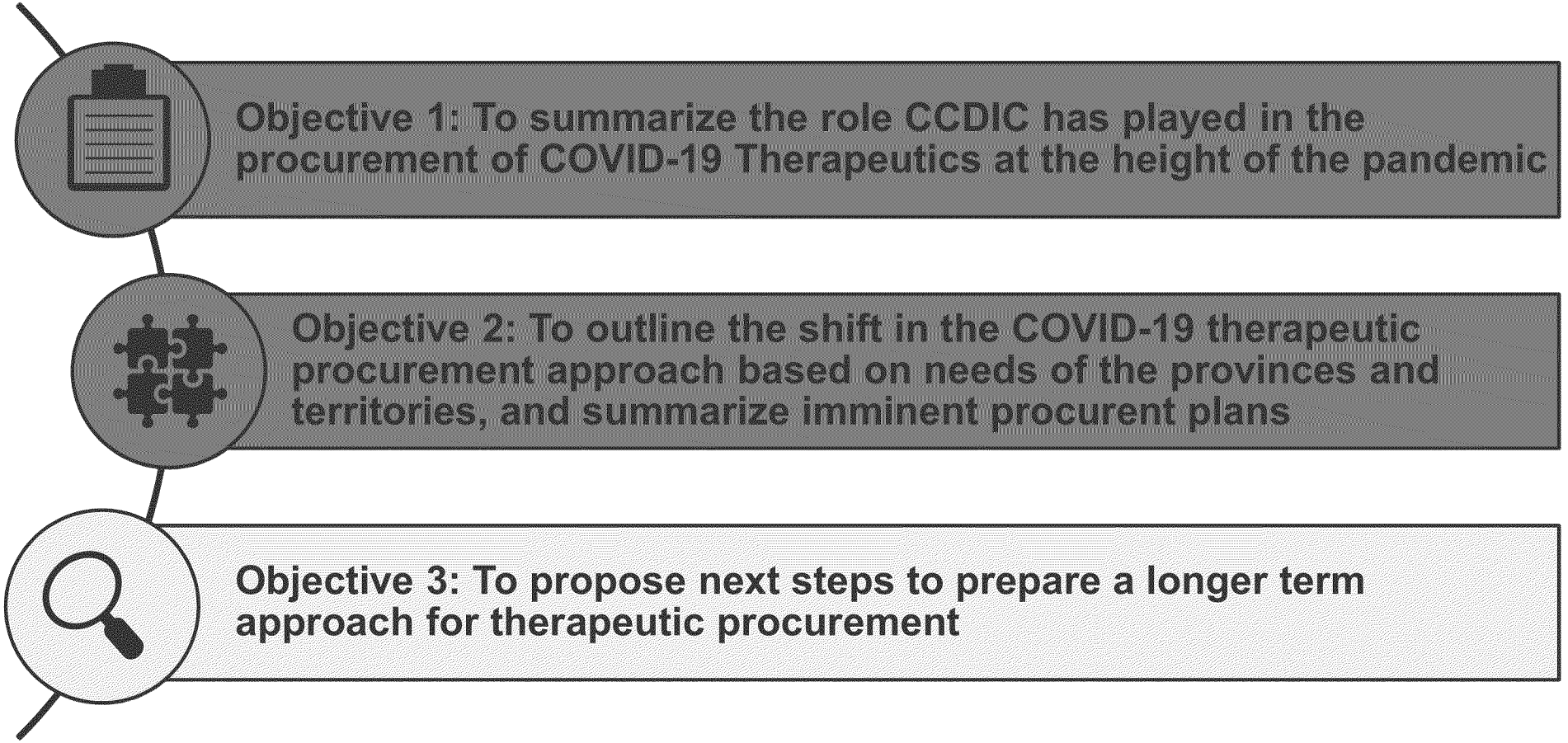
COVID-19 Lessons Learned at the Height of the Pandemic

- Federal procurement was initially ***more nimble*** than PT or FPT procurement, and ***removed barriers*** related to costs for PTs (if 100% covered by federal government). Drug companies ***preferred a single-window*** approach into the Canadian market in the context of a pandemic.
- Central buying power ensured that ***Canadians had equitable access*** to COVID-19 therapies, but required a high degree of ***interdepartmental coordination*** and ***collaboration.***
- The decision-making process to procure a COVID-19 therapeutic needs to be grounded in a consultative, science-based approach and is dependent on (*refer to Appendix 2: Decision-Making Process):*
  - A ***coherent approach*** among FPT governments with ***common understanding*** of roles and responsibilities;
  - Health Canada's independent ***regulatory review and authorization;***
  - The interest and needs of ***provinces and territories;***
  - Close collaboration with the FPT Drug Shortages tables responsible for PT procurement of drugs;
    - Input and advice through clinical expert discussions and feedback
  - ***Advice*** from CADTH and INESSS to guide PT decision-making about uptake and use of novel therapeutics.

Key Considerations in the Procurement Process and Engagement with Industry

- **Assessment of epidemiology and risk population:**
  - Does the new/repurposed therapeutic fill a treatment gap for COVID-19?
- **Impact of vaccines and alternative therapies:**
  - Does an alternative therapy already sufficiently address a COVID-19 treatment gap?
- **Urgency to act during global pandemic:**
  - Will Canada need to act quickly to secure access to the therapeutic so that it is available to clinicians and Canadians if needed?
- **PT interest and need:**
  - What is the evidence, feasibility and cost for implementation?
- **International partners actions/decisions:**
  - Has the therapy been authorized and implemented in similar healthcare systems?

NEXT STEPS



Therapeutics Procurement – COVID-19 and beyond

- Based on lessons learned, need to ***determine a FPT approach for decision-making*** in the acquisition and stockpiling of therapeutics in preparation for, and during future emergency situations.
  - With engagement of CADTH, INESSS and other key players

- Different branches/centres within PHAC (i.e., NESS, CIRID) and Health Canada (i.e., HPFB, SPB, ROEB) will need to be engaged to develop a coordinated approach for the future therapeutic procurement.

- A health portfolio-wide working group has been formed to explore options for moving forward on COVID-19 therapeutics (including divestment of inventory) for pandemic response by March 2022 .
  - Aligns with the Health Canada's Critical Drug Reserve set to end March 31, 2022
  - Considers changes to Health Canada's Interim Order as it extends beyond September 16, 2021.
  - Implications for PT formulary (costs) will need to be an important consideration.

- Further engagement of portfolio partners, provinces and territories, CADTH, INESSS and other government departments (e.g., PSPC, ISED) will help inform a transition approach for therapeutics procurement for COVID-19 and beyond.

Section 3: Next Steps

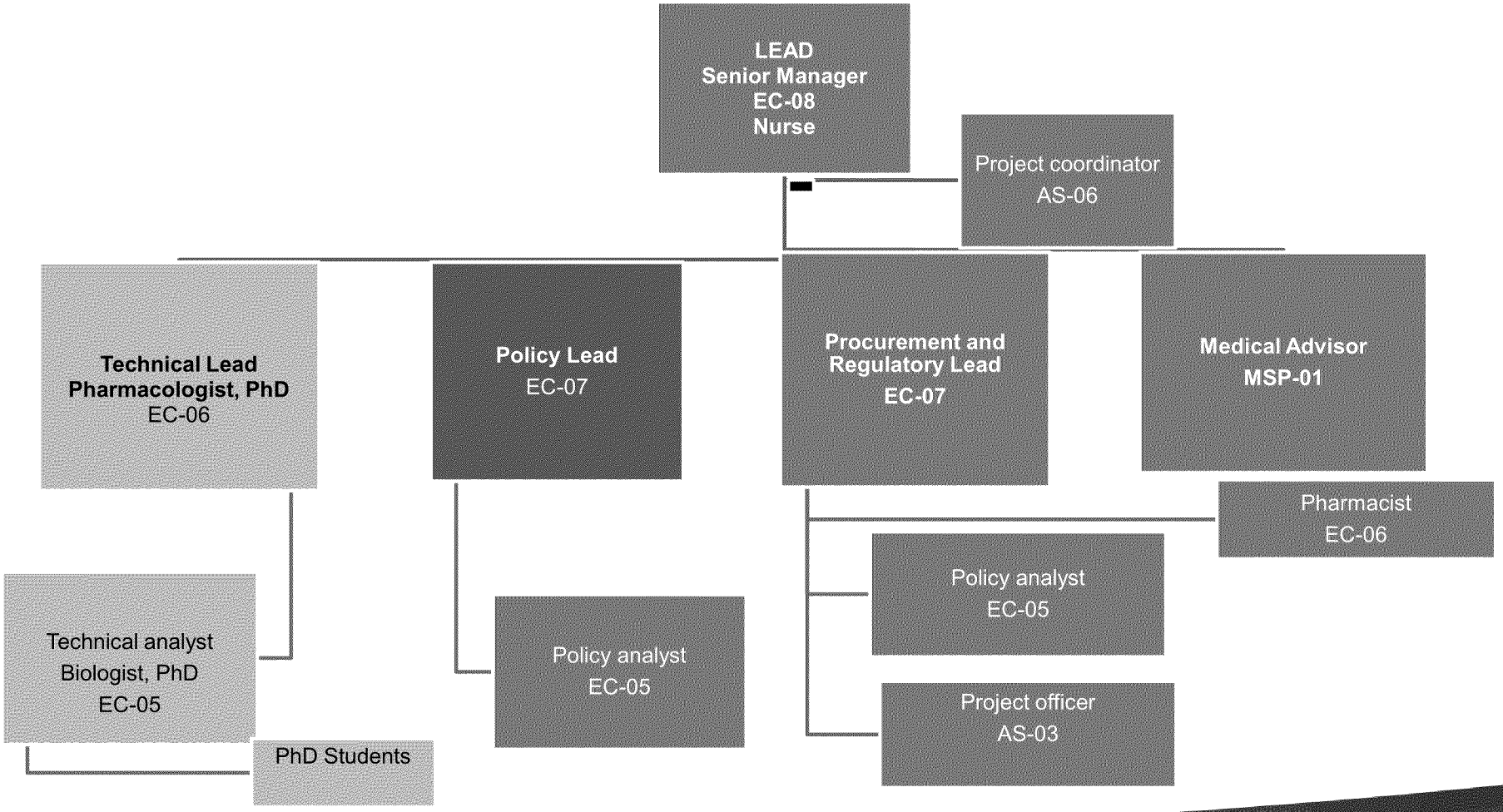
Next Steps: Longer Term Approach to Therapeutics – COVID-19 and beyond

- IDPB to come to Executive Committee in collaboration with the Emergency Preparedness and Response Branch and the Policy, Liaison and Coordination Branch (Vaccines) to discuss future PHAC role in therapeutics as well as the management of the COVID-19 therapeutics inventory.
- Bring forward a longer term approach to therapeutics procurement and use for discussion within the Health Portfolio.

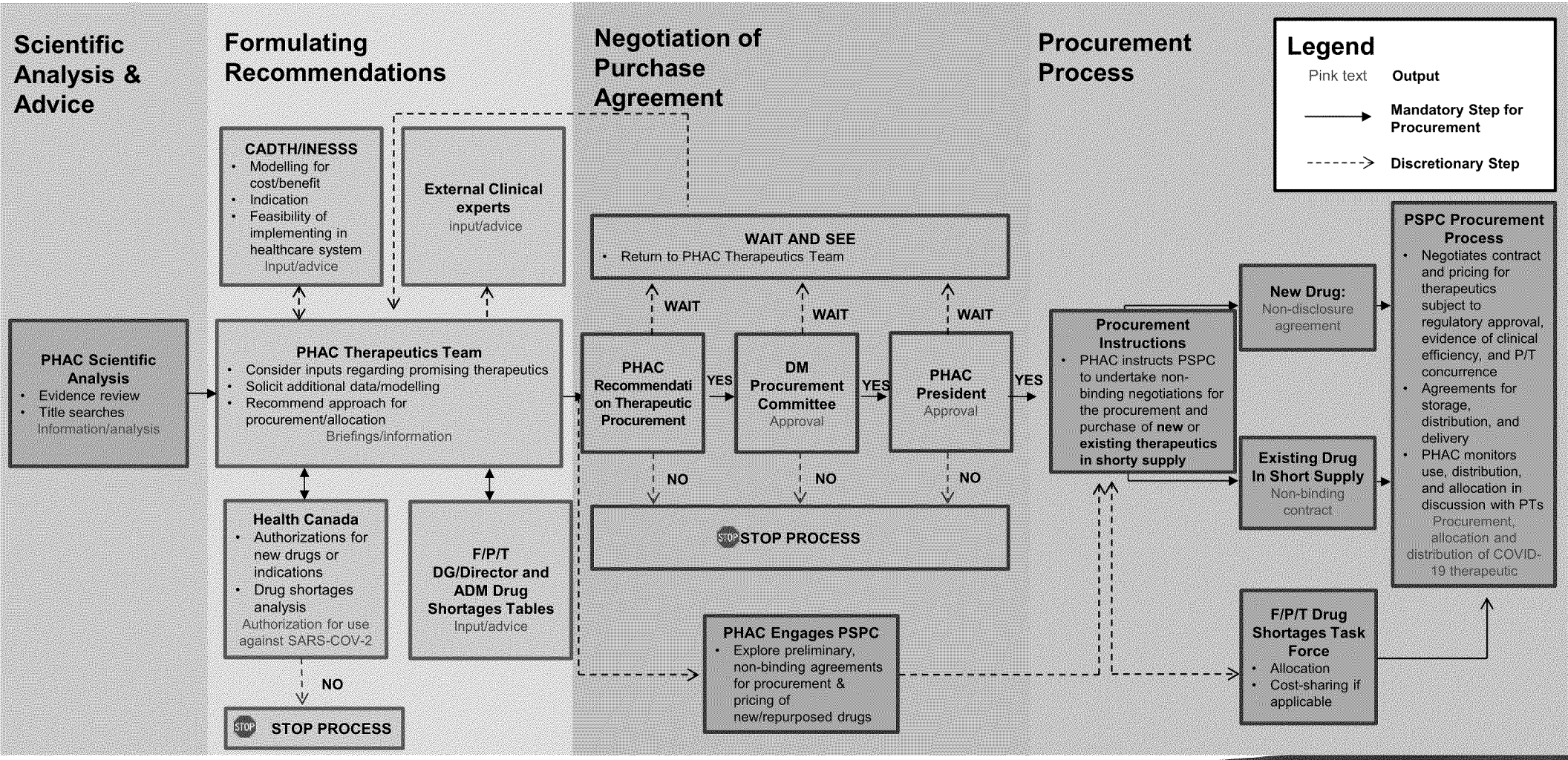
APPENDICES

Appendix 1

Org Chart: COVID-19 Therapeutics Team



APPENDIX 2 – Decision-Making Process for COVID-19 Therapeutic Procurement, May 2021



Bradley, Kevin (HC/SC)

From: Gale-Rowe, Margaret (PHAC/ASPC)
Sent: 2021-09-02 7:53 AM
To: Marinsky, Cheryl (PHAC/ASPC); Arthur, Jacqueline (PHAC/ASPC); Kolbe, Jane (PHAC/ASPC); Lawuyi, Niyi (PHAC/ASPC); Azad, Mina (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC)
Subject: RE: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

Not to rain on the parade, but there have been at least a couple of instances in the US of judges ORDERING a hospital to provide ivermectin to a patient. I read about that yesterday on Medscape. Horrifying to think of medical care being decided that way. No one on the hospital staff (physician) would administer it, so a physician who is sympathetic to the (ivermectin) cause was granted temporary privileges.

https://www.nbcnews.com/news/us-news/judge-orders-ohio-hospital-treat-covid-patient-ivermectin-n1278267

What a crazy, crazy place.

Margaret

From: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@phac-aspc.gc.ca>
Sent: 2021-09-02 7:16 AM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>; Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: RE: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

Thanks Jackie, saw this yesterday along with the warnings from both the FDA and Health Canada. Yes it is about time!

Cheryl

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Sent: 2021-09-01 5:56 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>; Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@phac-aspc.gc.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: FW: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

Been wanting to share this but finally have time now ☺
J

Jacqueline Arthur, BScN, RN
(she | elle)
Senior Manager | Gestionnaire principale
COVID-19 Therapeutics | thérapeutiques
Policy Development, AMR Division |Elaboration de politiques, Division de la RAM
CCDIC, PHAC | CLMTI, ASPC
t. (613) 889-8455

The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines
https://www.theglobeandmail.com/canada/article-the-ivermectin-mess-people-are-embracing-a-dangerous-livestock-drug/

Jackie

Bradley, Kevin (HC/SC)

From: Marinsky, Cheryl (PHAC/ASPC)
Sent: 2021-09-02 7:53 AM
To: Gale-Rowe, Margaret (PHAC/ASPC); Arthur, Jacqueline (PHAC/ASPC); Kolbe, Jane (PHAC/ASPC); Lawuyi, Niyi (PHAC/ASPC); Azad, Mina (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC)
Subject: RE: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

Wow! That is crazy…I have no words

From: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>
Sent: 2021-09-02 7:50 AM
To: Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@phac-aspc.gc.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>; Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>; Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Azad, Mina (PHAC/ASPC) <mina.azad@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: RE: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

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Sent: 2021-09-01 5:56 PM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>; Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Azad, Mina

(PHAC/ASPC) <mina.azad@phac-aspc.gc.ca>; Marinsky, Cheryl (PHAC/ASPC) <cheryl.marinsky@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: FW: The Globe and Mail: The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines

Been wanting to share this but finally have time now ☺
J

Jacqueline Arthur, BScN, RN
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Senior Manager | Gestionnaire principale
COVID-19 Therapeutics | thérapeutiques
Policy Development, AMR Division |Elaboration de politiques, Division de la RAM
CCDIC, PHAC | CLMTI, ASPC
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The ivermectin mess: People are embracing a dangerous livestock drug, while rejecting vaccines
https://www.theglobeandmail.com/canada/article-the-ivermectin-mess-people-are-embracing-a-dangerous-livestock-drug/

Jackie

Bradley, Kevin (HC/SC)

From: Lawuyi, Niyi (PHAC/ASPC)
Sent: 2021-09-03 10:32 AM
To: Fraser, Holly (HC/SC)
Subject: RE: Media article on treaments

I don't believe so, she expects it to go through the usually approval route. However, she just wanted it to proceed quickly, considering she reviewed and provided her feedback.

So please proceed with sending up for approvals.

Thanks,

Niyi

From: Fraser, Holly (HC/SC) <holly.fraser@hc-sc.gc.ca>
Sent: 2021-09-03 10:30 AM
To: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>
Subject: RE: Media article on treaments

Hi Niyi, is Bersabel planning to send it directly to VP and Pres/CPHO for approval? I can FYI the rest of the usual approval tree if that is the case.

From: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>
Sent: 2021-09-03 10:27 AM
To: Fraser, Holly (HC/SC) <holly.fraser@hc-sc.gc.ca>
Subject: RE: Media article on treaments

Hi Holly,

Thanks for the update.

Bersabel just replied with feedback. I would definitely make sure that we include Bersabel's proposed revision.

Margaret and Jane can look at it, but Bersabel mentioned that she wanted it to go up within the next few minutes.

Thanks,

Niyi

From: Fraser, Holly (HC/SC) <holly.fraser@hc-sc.gc.ca>
Sent: 2021-09-03 10:22 AM
To: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>
Subject: RE: Media article on treaments

Hi Niyi,

I've sent an updated draft of the MLs to the group just now, which will need to be approved by Margaret and Bersabel, then I can try to expedite the rest of the approvals for it and get a copy of the updated MLs to OCPHO.

I think Dr. Tam is doing a press conference today on modelling at noon, so she may be looking for the lines ASAP this morning. I will give her office the old approved MLs in the mean time and we will do our best to get them the updated ones this morning.

Holly

From: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>
Sent: 2021-09-03 10:10 AM
To: Fraser, Holly (HC/SC) <holly.fraser@hc-sc.gc.ca>
Subject: FW: Media article on treaments

Hi Holly,

I was wondering whether you have been informed the media preparation/update request from the President.

Can you please take a look at let us know if you have a particular plan for responding. Is CPAB aware or taking the lead on any of this? I was supposed to be off today, but I got called in to work on this. Just trying to catch-up on the exact request.

Thanks,

Niyi

From: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Sent: 2021-09-03 10:06 AM
To: Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-

aspc.gc.ca>; Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>
Subject: FW: Media article on treaments

FYA

From: Njoo, Howard (PHAC/ASPC) <howard.njoo@phac-aspc.gc.ca>
Sent: 2021-09-03 10:02 AM
To: Stewart, Iain (PHAC/ASPC) <iain.stewart@phac-aspc.gc.ca>; Tam, Dr.Theresa (PHAC/ASPC) <theresa.tam@phac-aspc.gc.ca>
Cc: Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>; Ponic, Pamela (PHAC/ASPC) <pamela.ponic@phac-aspc.gc.ca>; Rendall, Jennifer (PHAC/ASPC) <jennifer.rendall@phac-aspc.gc.ca>
Subject: RE: Media article on treaments

Yes, will do.

Howard Njoo MD, MHSc, FRCPC
(he | il)

Deputy Chief Public Health Officer and
Interim Vice-President
Infectious Disease Programs Branch
Public Health Agency of Canada

Sous-administrateur en chef de la santé publique et vice-président par intérim
Direction générale des programmes des maladies infectieuses
Agence de la santé publique du Canada

howard.njoo@phac-aspc.gc.ca
tel: 613-960-1940

From: Stewart, Iain (PHAC/ASPC) <iain.stewart@phac-aspc.gc.ca>
Sent: 2021-09-03 9:52 AM
To: Tam, Dr.Theresa (PHAC/ASPC) <theresa.tam@phac-aspc.gc.ca>
Cc: Njoo, Howard (PHAC/ASPC) <howard.njoo@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>; Ponic, Pamela (PHAC/ASPC) <pamela.ponic@phac-aspc.gc.ca>; Rendall, Jennifer (PHAC/ASPC) <jennifer.rendall@phac-aspc.gc.ca>
Subject: Re: Media article on treaments

But I think we need to take our discussion yesterday and turn it into an action plan to

- partner with CADTH as discussed now
- procure the new therapies now
- work with CADTH to provide use guidance in coming weeks

With milestones and target in use for Canadians date

Howard can you and Bersebel flesh this plan out so we

- can engage our partners?
- brief DM vaccines procurement committee (Simon's committee) week after next (sept 14) with a simple 1-page or so outline document we have pre discussed with HC regulator, PSPC?

Kaili can you work with Howard to get this on simon's agenda week after next?

Iain

Sent from my iPhone

On Sep 3, 2021, at 9:40 AM, Tam, Dr.Theresa (PHAC/ASPC) <theresa.tam@phac-aspc.gc.ca> wrote:

I am a media interest prediction machine ☺

So I think we are better set up to answer questions at media session given the discussion yesterday but it would be helpful to a few media lines asap

TT

published: 2021-09-03
received: 2021-09-03 00:28 (EST)
<image001.png>

National Post (NATIONAL)
CANADA | A1 / FRONT, **Words:** 1,399

The COVID super treatment Canadians can't get

The case for monoclonal antibody treatments

by: Sharon Kirkey

Florida and other American states seeing record-setting surges in COVID-19 cases are ordering truckloads of labmade antibodies Canadian doctors say are being underused in Canada.

Data suggest monoclonal antibody therapies, one of the formulations famously used to rid then-U.S.

President Donald Trump of COVID, can keep people with mild to moderate symptoms from ending up in hospital, or dead. Most recently, an early analysis of a Canadian-led study, a preprint not yet peer-reviewed, found a single dose of an antibody treatment developed by GlaxoSmithKline and Vir Biotechnology reduced the risk of COVID progressing from mild to serious illness in high-risk people by 85 per cent compared with a placebo.

"Importantly, in the test tube, this antibody retains activity against multiple variants," Dr. Anthony Fauci, U.S. President Joe Biden's top infectious diseases doctor told a recent White House briefing. GSK's antibody is a lab-engineered version of an antibody isolated from the blood of a survivor of the SARS outbreak two decades ago.

Vaccines offer the best hope of ultimately conquering COVID, but treatments are still needed to prevent severe disease in the infected, especially as the virus evolves. Ontario and other models are forecasting a "substantial" fall wave and while "we do not expect to see the same proportion of severely ill cases in the vaccinated," Ontario's COVID-19 science advisory table reported this week, not so for the unvaccinated. "Among the unvaccinated, we do expect to see a rapid increase in the number of seriously ill people needing hospital care as workplaces and education reopen in September."

Despite the pricey costs attached (typically $2,000 per dose) and logistical challenges (the drugs, for the most part, are administered via intravenous infusion) when given within five to 10 days of testing positive for COVID, monoclonal antibodies can slow the disease by blocking the virus, once inside the body, from invading new cells and replicating.

"These are valuable tools not being used in Canada, and should be," Dr. Andrew Morris, an infectious diseases specialist at Toronto's Mount Sinai Health System said on social media.

In Florida, state-run monoclonal antibody infusion clinics have been swamped with unvaccinated COVID patients seeking the free treatments.

In the U.S., the drugs have also been authorized as a "post-exposure" prophylaxis for close contacts of people infected with COVID who don't yet have symptoms, but who are at risk of getting infected, especially if they aren't fully vaccinated or might not have mounted a strong immune response to the vaccine.

But the prophylactic question hasn't been well studied. "Let's say you're at work and you find out that Bob down the hall is COVID positive and he's been talking to everybody at the coffee break," said infectious diseases specialist Dr. Donald Vinh, of McGill University Health Centre. Hypothetical Bob has symptoms, like sore throat and a fever. "In theory, you could say everybody who was talking to Bob is at high risk," Vinh said. "Those people might benefit from prophylaxis. But those studies are hard and expensive to do." It might make sense in principle, Vinh said, but the data are lacking.

GSK's sotrovimab was granted Health Canada authorization in July. The company is now "in active discussions with the federal government to secure supply of sotrovimab by early fall 2021," GSK said in an email to the National Post. The intent is that appropriate people will have access to it, with no out-of-pocket cost.

"Before somebody gets hospitalized with COVID, there isn't all that much," said Dr. Anil Gupta, a family doctor at William Osler Health System and lead investigator of the sotrovimab trial. By treating early, "we're preventing the cascade of events that includes viral replication and the body's inflammatory response. We're attacking before we get to that inflammatory response stage."

In the U.S. demand for sotrovimab has spiked almost 300 per cent over the past month, the Washington Post reported. Eli Lilly and Roche Canada also have been granted interim authorization for antibody cocktails.

The federal Liberals secured 26,000 doses of Lilly's bamlanivimab last November. Five months later, the government issued a "failure" warning that the drug may not be effective against certain variants. It's not known how many doses were used before the alert, but doctors say most of it sat on shelves, partly because there was no system to coordinate its use.

Bamlanivimab, Lilly said in an email this week, is not effective "against the variants currently at play in Canada." The company has another monoclonal combination currently under review by Health Canada that is effective at neutralizing Delta.

What hasn't proven effective against Delta are cow-sized doses of the dewormer ivermectin. In an Instagram video Wednesday, COVID-positive Joe Rogan said he threw "all kinds of meds" at the infection, including ivermectin, which conspiracy ideologues have been pushing as a "cure" for COVID. Health Canada issued an alert this week warning ivermectin, in livestock or human doses, has not been proven to treat COVID and that Canadians "should never consume health products intended for animals."

"Honestly, it's mind-boggling," Morris said in an interview. "In a variety of settings people have so-called 'drunk the Kool-Aid.'Ivermectin is the 2021 Kool-Aid."

Monoclonal antibodies aren't a magic bullet that will treat all. While the drugs seem well-tolerated, they can cause side effects like diarrhea and rash, though in fairly small numbers. What's more, bringing someone who has tested positive for COVID into a medical space that has adequate ventilation, personal protective equipment and skilled staff to infuse the drug and watch people for possible reactions requires a lot of infrastructure in an already stretched system, said Dr. Zain Chagla, an infectious diseases specialist and associate professor of medicine at McMaster University. "But the payoff is huge. There is probably a big cost benefit here, in preventing ventilator days and ICU days and hospitalization, to really scale this up as much as possible to mitigate the spread of the fourth wave, especially among people that are unvaccinated."

"This therapy is being used in the United States. It's being used in places in Europe," Chagla said. "It definitely can be done - I don't think there's anything to say we can't do this."

But with no national system, it's very possible that each province will land in different places in terms of who gets a monoclonal antibody and who doesn't, said Morris, a member of Ontario's COVID-19 science advisory table. "Across the provinces, they're looking at where and when to use them," he said.

"How do you figure out who's eligible and who is not? What are the criteria? How do you identify and notify them? We don't really have great systems in place for that."

Monoclonal antibodies shouldn't be seen as a substitute for vaccination, he and others stressed. "Are there going to be some people who avoid vaccination and just get this? I anticipate there will be. It's a shame," Morris said. "It's like the difference between quitting smoking and saying if I get lung cancer, I'll get an operation."

"The truth is that everyone who has forgone vaccination by now, the majority of them have no plans to get vaccinated in the near future. I'm not sure that they're banking on a monoclonal as a way to avoid future vaccination."

Still, experiences south of the border suggest some are unwisely putting their money on the treatments instead of the shots. "That is not a good thing," said Vinh.

Monoclonal antibodies have proven beneficial for high-risk people (including those with obesity, asthma, heart failure or chronic kidney disease and people over age 55) who have mild to moderate disease. "If you have more than that - you start requiring oxygen or hospitalization - not only is there no benefit in terms of survival from these monoclonal antibodies, there may even be a signal of increased risk of death, though it's hard to know if that's simply because those people were already too sick to begin with," Vinh said.

There's also a finite treatment window. The antibodies have to be given within 10 days after symptoms begin. "The thing about COVID is that it can progress rapidly," Vinh said. "You can literally go from sitting in your bed eating to, an hour or two later, requiring high amounts of oxygen. If you have to transport yourself to a setting where you have to wait in line and get triaged and get a monoclonal antibody, that window can close quickly."

Bradley, Kevin (HC/SC)

From: Ephrem, Bersabel (PHAC/ASPC)
Sent: 2021-09-08 12:12 PM
To: Kolbe, Jane (PHAC/ASPC); Arthur, Jacqueline (PHAC/ASPC)
Cc: Lawuyi, Niyi (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC)
Subject: RE: follow up from President briefing
Attachments: Meeting.Summary.Update.to.CPHO.Sept.2.2021.(v.1).docx

Thank you Jane. Captured the discussion quite well.

Please see attached some of my comments.

Can we have a summary table at the end with key actions, timeline and person responsible in leading the action?

Once you have that we can send it to Howard.

Thank you
bersabel

From: Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>
Sent: 2021-09-07 10:33 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Cc: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: RE: follow up from President briefing

Please find attached the Meeting record from the Sept 2, 2021 meeting between CPHO/President/VP/DG.

-jane

From: Kolbe, Jane (PHAC/ASPC)
Sent: 2021-09-07 2:24 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Cc: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: RE: follow up from President briefing

Yes. I will send this today.

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Sent: 2021-09-07 12:01 PM
To: Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>
Cc: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: follow up from President briefing

Hi Jane;
Bersabel has asked for the “to do” list we had discussed at our debrief last week after the President’s briefing. She wants to send it to Howard so could you circulate it by email for us to look at today please?
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
A/Executive Director | Directrice Exécutive par intérim
Strategic Issues and Integrated Management Division | Division des enjeux stratégiques et de la gestion intégrée
Centre for Communicable Diseases and Infection Control | Centre de la lutte contre les maladies transmissibles et les infections
Public Health Agency of Canada | Agence de la santé publique du Canada
t. (613) 889-8455

Meeting Summary
Therapeutics Briefing: CPHO
Sept 2, 2021
5:30 – 6:00 pm

Attendees: Dr. Theresa Tam, Ian Stewart, Howard Njoo, Bersabel Ephrem, Jacqueline Arthur, Pamela Ponic, Jennifer Rendall, Vicki Wiseman,

Observers: Jane Kolbe

Summary of Action Items:

- Document COVID-19 therapeutics procured
  - Create a shared folder with OCFO to house folders supporting decision-making
- Raising the profile of COVID-19 therapeutics
  - Raise awareness, and enhance communication (including with SAC, and PT Chief Medical Officers)
- International comparison
  - Provide President with the international comparison
- Partnership with CADTH/INESSS
  - Engage CADTH to seek their support for the development of clinical guidance as part of the procurement decision-making process

KEY DISCUSSION POINTS

- ~~CPHO noted that we have to focus more on treatments~~
- An overview of GoC measures taken, and achievements to date, including COVID-19 therapeutics procured to date.~~Howard noted that therapeutic procurement is traditionally the responsibility of provinces and territories (PTs)~~
- ~~PHAC, (with PSPC) assumed responsibility to procure COVID-19 therapeutics and received $500 million under through the Medical Countermeasures budget~~.
- There is a need to communicate more about the role of COVID-19 therapeutics and the Federal Government contribution in the procurement of COVID-19 Therapeutics therapeutics.
  - ~~o~~

Current State of COVID-19 Therapeutics Procurements

- Howard noted that therapeutic procurement is traditionally the responsibility of provinces and territories (PTs)
- PHAC, (with PSPC) assumed responsibility to procure COVID-19 therapeutics and received $500 million under through the Medical Countermeasures budget ~~Howard gave an overview of GoC measures taken, and achievements to date, including COVID-19 therapeutics procured to date.~~
- Lessons/learnings were integrated into future decision-making processes - continually strengthened the procurement decision-making process.
  - Hydroxychloroquine was used as an example of early decisions taken at the beginning of the pandemic.
  - Future procurement decisions were later, better informed by advisory groups, and made by the Deputy Minister Procurement Committee.

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- Discussion ensued regarding the role that the advisory groups that provided input to the decision-making. Specifically,
    - COVID-19 Therapeutics Task Force (CTTF)
    - COVID-19 Clinical Pharmacology Task Group (CPTG)
- Strengthening the process that documents procurement decisions requires attention and will enable PHAC to more expeditiously respond to an audit.
- CPHO – recognized that at the beginning, we needed to urgently invest, and now we need a different process.
    - Data from clinical trials are more informative at this stage of the pandemic, as opposed to early days
    - The UK was noted to be a useful jurisdiction to compare against in terms of procurements.

Action Item:

- *Document the decision-making process for the various COVID-19 therapeutics procured to date.*
- *Collect a complete record (Briefing Note, package, etc.).*
- *Work with the office of the Chief Financial Officer to ensure documents from IDPB and CFO documents are in a shared file.*

Shifting Needs of the PTs & Fall/2021 Procurement Plans

- Feedback from PTs was briefly discussed, including their desire for earlier engagement prior to procurement, a need for clinical guidance from CADTH and INESSS, more control over what drugs enter into their Formularies, and implementation costs and logistics.
- Howard noted our early thinking about the need to shift our procurement approach, collectively towards an FPT collective approach based on the needs of what PTs are telling us – and integrate this into our procurement plans.
- CPHO noted the important role that mAbs play – specifically in terms of having domestic capacity, "having mAb capacity is very important for an emerging pathogen".
- COVID-19 therapeutics currently under consideration for Fall/2021 procurement was discussed, including mAbs, and tocilizumab (as it was used extensively in previous waves)
    - The state of safety and efficacy data for oral antivirals was noted to be evolving.
    - PHAC is in the process of information exchanges with the drug makers, but until sufficient scientific data is available to assess safety and efficacy, procurement negotiations for oral anti-virals are premature.
- Ivermectin was discussed – The US FDA put out a tweet, and PHAC also issued a statement against the use of this drug for treatment of COVID-19

4th Wave Planning and the Role of COVID-19 Therapeutics

- CPHO noted that treatment is critical in the process of 4th wave/future wave planning.
    - She noted that treatment does not appear enough in 4th wave planning placemats, etc..
- CPHO brought this key consideration forward to DM – Health Canada
- Treatment must be a key aspect, as people will become ill and end up in the ICU
    - They can survive with an improvement in their treatment, or perhaps stay for a shorter time, which relieves the pressure on the health system
- There is a need to ensure we have a process, and if we don't, we have to make sure that we quickly have a plan to determine whether we have to procure any more
- We do not have a regularized process in for COVID-19 therapeutics as it exists for vaccine procurements (every-other day)

Commented [EB(1]: Don't recall this? When and what did she bring up to the DM?

Commented [EB(2]: I don't know if we can say that we do not have a regularized process. Do not have a long-standing and know process?

- Vaccine procurement was noted to differ from therapeutics in that it is less complex in that it does not require physician intervention, making bulk procurement of vaccines a more direct path
- The COVID-19 therapeutics landscape was noted to be more complex because of it requiring a physician prescription, and the role of formularies.

- How we communicate how we manage COVID has also been relatively silent in terms of therapeutics

Action Item:

- *CPHO signaled a desire for more regular executive involvement/communication – raising the profile of therapeutics*
  - *Governance work was noted to be important to the CPHO*
  - *CPHO interested in going to SAC to describe the role of therapeutics, and to more actively communicate PHAC's role in therapeutics*
  - *CPHO noted that COVID-19 therapeutics is not in the MTP process and tracker*

Discussion on Supply Issues of Specific COVID-19 Therapeutics

- Tocilizumab (was in high demand by PTs in wave 3) and sarilumab were noted to have excellent Clinical Trial results in terms of efficacy data
  - Both drugs are used for rheumatoid arthritis, high efficacy, and well established
  - PHAC was noted to be advancing contract negotiations to procure sarilumab as a result of the global shortage of tocilizumab, given it can be used as a back-up treatment in lieu of tocilizumab
- PSPC is in the process of advancing this negotiation with sarilumab

Action Item:

- *Send the Memo to President for the procurement of Sarilumab*
- *VP to check in with PHAC's – to ensure that funding is available for sarilumab*

Discussion on Next Steps:

- Howard introduced the need to take the lessons learned with COVID-19 procurement processes to date, and integrate this into longer term thinking
  - COVID-19 therapeutics is a complex process
  - Involving several Branches within PHAC
- Next steps would involve looking at a more fulsome FPT approach
- To build a sustainable model, beyond COVID-19 – for therapeutics in general for infectious diseases.
- Howard proposed the following process:
  - Commence internal discussions commence with VPs within PHAC to discuss the future role of therapeutic procurement within PHAC
  - Engage EC with a proposed approach for discussion
  - Roll out the discussion to the Health Portfolio
- The discussion of PHAC's public health role vs Health Canada's regulatory role regarding therapeutic procurement was also noted to be important to discern and articulate.
- Ian asked that we map out the needs/steps in the process of COVID-19 therapeutic procurement and perform an international comparison to visually demonstrate the public health role in therapeutics in other countries

Action Item:

- *Provide the President with the international comparison - mapping.*
- *Initiate engagement with PHAC VPs to discuss PHAC's future role in therapeutics with the view to developing a proposed approach for consideration at EC – with the eventual goal of consulting with the rest of the health portfolio partners to integrate their*
    - *Need a meeting of the minds of the VPs*

Discussion on the Use of FPT feedback to Inform procurement Decisions

- The Drug Shortages Table was noted to be a key existing mechanism that is being leveraged to inform PHAC's procurement recommendations.
- Current processes are ensuring that CCDIC is receiving PT endorsement before a procurement recommendation is rendered - to ascertain PT demand and likelihood of usage.
- CPHO noted that CCDIC has addressed the need for early engagement of PTs regarding COVID-19 therapeutic procurement recommendations.
- CPHO signaled her interest in ensuring broad awareness within PTs so that the Chief Medical Officers within the PTs are aware of the treatments procured and available
- CPHO also recognized that clinicians are needing clinical guidance – Either PHAC or HC to ensure that CADTH and INESS are engaged
    - Bersabel noted that we are pushing as far as we could to engage with CADTH to ensure that PTs have the guidance that they need. Conversations with CADTH are slow, but moving in the right direction.
    - CADTH may have resource limitations – which may influence the rate that they may be able to provide clinical guidance
- A request for top-up funding was requested prior to the writ dropping
    - 3 billion was given for vaccines, President advised that it could be repurposed for therapeutics, if necessary.
- CPHO – reiterated – the important role of therapeutics.
    - As we may see a variant of concern escaping the vaccine, and the vaccines being re-tooled, therapeutics plays a key role.

Action Item:

- *President suggested to consider partnering with CADTH to request that they provide guidance prior to PHAC doing large scale procurement*
- *CPHO would like to ascertain how many patients are being helped with the treatments that we have - to ensure that we are mapping out that what we have is aligned with the trajectory of the 4th wave modelling – with an assumption built in by clinicians who are indicating how they would be using the product.*

Bradley, Kevin (HC/SC)

From: Arthur, Jacqueline (PHAC/ASPC)
Sent: 2021-09-26 2:42 PM
To: Lawuyi, Niyi (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC)
Cc: Kolbe, Jane (PHAC/ASPC)
Subject: international comparison on therapeutics decision-making and "action items" from President briefing
Attachments: COVIDTHERA_InternationalScan_SummaryApril22.docx; RE: follow up from President briefing

Bersabel and Niyi;
As requested please find attached the Word document on international comparisons that was prepared by the OPSM and submitted in April 2021 to Roman Szumski, VP at the time. Also is the list prepared by Jane of the “action items” from the most recent President briefing – there may be a more recent version but I have been out of the loop so Jane please circulate any updates.
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
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COVID THERAPEUTICS[1] PROCUREMENT INTERNATIONAL SCAN					
Country	**How are potential COVID Therapeutics identified and prioritized?**	**How are decisions made to procure/not procure a COVID Therapeutic? Who is engaged as part of making these decisions?**	**Do you use an expert advisory group in the identification of promising therapies and in the selection of therapeutics for procurement purposes? If so how?**	**Who provides guidance on how the Therapeutic is to be used/implemented?**	**Any other general comments on your COVID Therapeutics processes**
Canada	• The Public Health Agency of Canada (PHAC) has a systematic process to monitor Registered Clinical Trials (RCTs) and other clinical studies • The most promising products then undergo assessment by internal and external experts (The Clinical Pharmacology Task Group (CPTG)). • The proposed new option would shift from the CPTG to a PT advisory table with membership from PT clinical/science tables and experts to identify and assess potential therapeutics as COVID-19 treatments.	• The Public Health Agency of Canada (PHAC), working with Public Services and Procurement Canada (PSPC) and Health Canada (HC), leads the procurement process to ensure Canadians have access to promising and effective COVID-19 treatments • At a minimum, the therapeutic being proposed for the negotiation of an Advanced Purchase Agreement (APA) or for procurement must be the subject of a submission for	• CPTG - An ad-hoc committee of external experts and representatives from the Canadian Agency for Drugs and Technologies (CADTH) and Institut national d'excellence en sante et sociaux (INESSS) mandated to provide PHAC with medical and scientific advice on an ad hoc basis relating to pharmaceutical products for treatment of COVID-19 in humans. • The proposed new option would shift from the CPTG to a PT advisory table with membership from PT clinical/science tables and experts to identify and assess potential therapeutics as COVID-19 treatments.	• The CPTG (ad-hoc) and the Institut national d'excellence en santé et services sociaux (INESSS) provided guidance on therapeutic use and implementation. • Some Provinces and Territories are issuing their own guidelines for the clinical management of patients with COVID-19. The Canadian Agency for Drugs and Technologies in Health (CADTH) convened an implementation panel for bamlanivimab at the request of the Federal Government. • Proposed option would support PTs sharing their	

[1] By COVID Therapeutic we are referring to products specifically intended to treat COVID-19 but not supportive medications (for example Salbutamol) or vaccines.

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		authorization by Health Canada.		clinical guidance across jurisdictions. CADTH and INESSS would also be asked to share their advice/reviews/guidance with PTs.	
United States	• Under the Federal COVID Response, the Research Team actively monitors the therapeutic landscape by assessing registered clinical trials, engaging with industry in preclinical work and surveying the peer-reviewed literature for promising compounds • Time to potential Emergency Use Authorization is the most important key attribute followed by (in no particular order) efficacy, safety profile, target population, ease of	• Procurement decisions are made by the Federal COVID Response leadership • The Department of Health and Human Services (HHS) through the Biomedical Advanced Research and Development Authority (BARDA) and the Department of Defence (DoD) through the Joint Program Executive Office (JPEO) solicit, review, negotiate and award	• The Research Team for the Federal COVID Response consists of product development experts from across the US government. Contributing agencies include the Food and Drug Administration (FDA), JPEO, BARDA and National Institute of Allergy and Infectious Diseases (NIAID). • The Research Team considers the candidate therapeutics and ranks them according to pre-specified criteria. The most promising therapeutics are forwarded for further interaction with the manufacturers.	• FDA establishes the conditions of use of the therapeutic when it achieves an EUA. • The National Institutes of Health (NIH) COVID-19 Treatment Guidelines; panel members include representation from health care and academic organizations, and professional societies including Infectious Diseases Society of America (IDSA), as well as federal agencies	

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	administration for intended use and manufacturing capacity.	funds for the purchase of COVID therapeutics		including NIH, CDC, and FDA. • The Infectious Diseases Society of America (ISDA) also issues Guidelines on the Treatment and Management of Patients with COVID-19.	
United Kingdom	• An independent COVID-19 Therapeutics Advisory Panel (UK C-TAP), chaired by Professor Patrick Chinnery, advises on what treatments should be proposed for testing through the government funded national platform trials RECOVERY+, REMAP-CAP, PRINCIPLE, PROTECT-V and AGILE. • UK Research and Innovation manage an open nominations portal and collate information on compounds based on the	• The Therapeutics Taskforce (TxT) in DHSC (Department for Health and Social Care) is responsible for ensuring that the population has access to promising and effective treatments. • The TxT works closely with the pharmaceutical industry, NHS and others in the supply	• RAPID C-19 is a multi-agency initiative including NIHR, NICE, MHRA, NHSE-I and representatives from the Devolved Administrations. By joining forces, the agencies aim to get treatments for COVID-19 to NHS patients quickly and safely. • RAPID C-19 uses horizon scanning from NIHR Innovation Observatory and produces briefings for the treatments that show the most promise. RAPID C-19 prioritises promising treatments for initial review based on the level of investigative activity, the number of	• NHS England and NHS Improvement makes sure the selected treatments can be delivered. This could include developing a commissioning policy or initiating an evidence review. This work is done together with the health services in Scotland, Wales and Northern Ireland	

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	evidence and data provided by academics, clinicians and industry experts as well as independently sources information. A core team of due-diligence mangers are responsible for validating the information and create briefings on potential compounds. • The final decision on which treatments are trialled lies with the Chief Investigators, who have ultimate responsibility for the delivery of the trials and Professor Chris Whitty, the Chief Medical Officer (CMO) for England and Chief Scientific Adviser for the Department of Health and Social Care. • The Therapeutics Taskforce also conducts horizon-	chain to help ensure patients can access the medicines they need, and precautions are in place to reduce the likelihood of future shortages.	participants in trials, the location of trials, trial phase and design, regulatory status and whether trials include special populations such as paediatric patients. • These treatments are considered by the RAPID C-19 oversight group and rapid action plans (RAP) are produced. A RAP is a shared vision and joint agency agreement on the approach to development, implementation and patient access. This includes the period between significant data emerging and a marketing authorisation being granted (if applicable). • The RAPID-C19 initiative has already enabled rapid patient access to therapeutics including dexamethasone and remdesivir. More detail on the specific therapeutics can be found online here: Overview | COVID-19 rapid guideline: managing COVID-19		

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	scanning activities to identify promising therapeutic candidates and encourages innovators to submit their compounds to the Covid Therapeutics Advisory Panel for consideration for UK trials.		| Guidance | NICE. Information on RAPID-C19 can be found here: Research to access pathway for investigational drugs for COVID-19 (RAPID-C19) | NICE • The UK C-TAP panel is composed of independent experts who recommend suitable candidates for national platform trials to the UK Chief Medical Officer and trial Chief Investigators.		
France	• **National Steering Committee for Therapeutic Trials and other research on COVID-19 (CAPNET)** - CAPNET is a consultative body composed of different experts of research involving the human person, whose mission is to regulate clinical and preclinical studies on Covid-19 in order to accelerate those that fall within the	• In the case of drug treatments, the molecules to be evaluated must meet the following conditions: 1) Data suggesting a therapeutic effect should be available 2) The proposed study/trial should not be redundant with existing ones to avoid a large	• The CAPNET is piloted by the Interministerial Research Task Force. This is a working group between the Ministry of Research, Higher Education and Innovation (**MESRI**) and the Ministry of Solidarity and Health (**MSS**). It comprises five representatives from three central administrations: the Directorate General for Research and Innovation (MESRI-DGRI), the Directorate General of Health (MSS-DGS) and the	• The European Medicines Agency (EMA), as well as the French National Drug Agency (Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) supported by the French Ministry for Solidarity and Health, are authorities to provide guidance on how the	

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	scope of national priorities and are the most promising. • CAPNET relies on scientific and methodological assessments carried out by the Scientific Council of REACTing, to issue a label of "National Research Priority" to studies with high potential impact. • The "National Research Priority" label allows exclusive access to an expedited process for evaluating the regulatory authorisation file, a specific valuation of the inclusions that will be carried out via the Research and Clinical Trials Information and Management System (SIGREC) and access to potential institutional funding.	number of trials already underway with this molecule.	Directorate General of Care Supply (MSS-DGOS). • Data suggesting a therapeutic effect for molecules are prioritized according to a methodology established by the REACTing Priority of Treatments Working Group, and validated by the REACTing COVID-19 Scientific Council. • REACTing is a multidisciplinary consortium of French research institutions. (https://reacting.inserm.fr/	Therapeutic is to be used and implemented.	

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Australia	• Australia is monitoring developments in relation to treatments for COVID-19. • The Australian Government has engaged an independent medical due diligence service to evaluate putative therapeutics for COVID-19 • Australia uses a bespoke decision-making framework tool to evaluate potential COVID-19 therapeutics.	• The COVID-19 Vaccines and Treatments for Australia – Science and Industry Technical Advisory Group provides advice to the Australian Government on the purchasing of COVID-19 treatments.	• The COVID-19 Vaccines and Treatments for Australia – Science and Industry Technical Advisory Group provides advice to the Australian Government on the purchasing of COVID-19 treatments.	• The National COVID-19 Clinical Evidence Taskforce, an independent body partially funded by the Australian Government, maintains the Australian guidelines for the clinical care of people with COVID-19.	• Therapeutics may be procured for inclusion in the National Medical Stockpile, a strategic reserve of drugs, vaccines, antidotes and personal protective equipment for use in national health emergencies. • Access by healthcare professionals to drugs in the National Medical Stockpile is evaluated against set inclusion and exclusion criteria that define eligible patients. • Prior to use in Australia, therapeutics must be approved

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					(registered) by the Therapeutic Goods Administration (TGA). • The Pharmaceutical Benefits Advisory Committee (PBAC) performs health technology assessment (HTA) processes and recommends to the Minister for Health medicines to be subsidised by the Australian Government under the Pharmaceutical Benefits Scheme (PBS).
Germany	Input still forthcoming.				

Bradley, Kevin (HC/SC)

From: Kolbe, Jane (PHAC/ASPC)
Sent: 2021-09-07 10:33 PM
To: Arthur, Jacqueline (PHAC/ASPC)
Cc: Lawuyi, Niyi (PHAC/ASPC); Gale-Rowe, Margaret (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC)
Subject: RE: follow up from President briefing
Attachments: Meeting.Summary.Update.to.CPHO.Sept.2.2021.(v.1).docx

Please find attached the Meeting record from the Sept 2, 2021 meeting between CPHO/President/VP/DG.

-jane

From: Kolbe, Jane (PHAC/ASPC)
Sent: 2021-09-07 2:24 PM
To: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Cc: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: RE: follow up from President briefing

Yes. I will send this today.

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Sent: 2021-09-07 12:01 PM
To: Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>
Cc: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Gale-Rowe, Margaret (PHAC/ASPC) <margaret.galerowe@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Subject: follow up from President briefing

Hi Jane;
Bersabel has asked for the “to do” list we had discussed at our debrief last week after the President’s briefing. She wants to send it to Howard so could you circulate it by email for us to look at today please?
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)

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Observers: Jane Kolbe

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- Howard noted that therapeutic procurement is traditionally the responsibility of provinces and territories (PTs)
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Current State of COVID-19 Therapeutics Procurements

- Howard gave an overview of GoC measures taken, and achievements to date, including COVID-19 therapeutics procured to date.
- Lessons/learnings were integrated into future decision-making processes - continually strengthened the procurement decision-making process.
  - Hydroxychloroquine was used as an example of early decisions taken at the beginning of the pandemic.
  - Future procurement decisions were later, better informed by advisory groups, and made by the Deputy Minister Procurement Committee.
- Discussion ensued regarding the role that the advisory groups that provided input to the decision-making. Specifically,
  - COVID-19 Therapeutics Task Force (CTTF)
  - COVID-19 Clinical Pharmacology Task Group (CPTG)
- Strengthening the process that documents procurement decisions requires attention and will enable PHAC to more expeditiously respond to an audit.

- CPHO – recognized that at the beginning, we needed to urgently invest, and now we need a different process.
    - Data from clinical trials are more informative at this stage of the pandemic, as opposed to early days
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- CPHO noted the important role that mAbs play – specifically in terms of having domestic capacity, "having mAb capacity is very important for an emerging pathogen".
- COVID-19 therapeutics currently under consideration for Fall/2021 procurement was discussed, including mAbs, and tocilizumab (as it was used extensively in previous waves)
    - The state of safety and efficacy data for oral antivirals was noted to be evolving.
    - PHAC is in the process of information exchanges with the drug makers, but until sufficient scientific data is available to assess safety and efficacy, procurement negotiations for oral anti-virals are premature.
- Ivermectin was discussed – The US FDA put out a tweet, and PHAC also issued a statement against the use of this drug for treatment of COVID-19

4th Wave Planning and the Role of COVID-19 Therapeutics

- CPHO noted that treatment is critical in the process of 4th wave/future wave planning.
    - She noted that treatment does not appear enough in 4th wave planning placemats, etc..
- CPHO brought this key consideration forward to DM – Health Canada
- Treatment must be a key aspect, as people will become ill and end up in the ICU
    - They can survive with an improvement in their treatment, or perhaps stay for a shorter time, which relieves the pressure on the health system
- There is a need to ensure we have a process, and if we don't, we have to make sure that we quickly have a plan to determine whether we have to procure any more
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    - Vaccine procurement was noted to differ from therapeutics in that it is less complex in that it does not require physician intervention, making bulk procurement of vaccines a more direct path
    - The COVID-19 therapeutics landscape was noted to be more complex because of it requiring a physician prescription, and the role of formularies.

- How we communicate how we manage COVID has also been relatively silent in terms of therapeutics

Action Item:

- *CPHO signaled a desire for more regular executive involvement/communication – raising the profile of therapeutics*
    - *Governance work was noted to be important to the CPHO*
    - *CPHO interested in going to SAC to describe the role of therapeutics, and to more actively communicate PHAC's role in therapeutics*
    - *CPHO noted that COVID-19 therapeutics is not in the MTP process and tracker*

Discussion on Supply Issues of Specific COVID-19 Therapeutics

- Tocilizumab (was in high demand by PTs in wave 3) and sarilumab were noted to have excellent Clinical Trial results in terms of efficacy data
    - Both drugs are used for rheumatoid arthritis, high efficacy, and well established
    - PHAC was noted to be advancing contract negotiations to procure sarilumab as a result of the global shortage of tocilizumab, given it can be used as a back-up treatment in lieu of tocilizumab
- PSPC is in the process of advancing this negotiation with sarilumab

Action Item:

- *Send the Memo to President for the procurement of Sarilumab*
- *VP to check in with PHAC's – to ensure that funding is available for sarilumab*

Discussion on Next Steps:

- Howard introduced the need to take the lessons learned with COVID-19 procurement processes to date, and integrate this into longer term thinking
    - COVID-19 therapeutics is a complex process
    - Involving several Branches within PHAC
- Next steps would involve looking at a more fulsome FPT approach
- To build a sustainable model, beyond COVID-19 – for therapeutics in general for infectious diseases.
- Howard proposed the following process:
    - Commence internal discussions commence with VPs within PHAC to discuss the future role of therapeutic procurement within PHAC
    - Engage EC with a proposed approach for discussion
    - Roll out the discussion to the Health Portfolio
- The discussion of PHAC's public health role vs Health Canada's regulatory role regarding therapeutic procurement was also noted to be important to discern and articulate.
- Ian asked that we map out the needs/steps in the process of COVID-19 therapeutic procurement and perform an international comparison to visually demonstrate the public health role in therapeutics in other countries

Action Item:

- *Provide the President with the international comparison - mapping.*
- *Initiate engagement with PHAC VPs to discuss PHAC's future role in therapeutics with the view to developing a proposed approach for consideration at EC – with the eventual goal of consulting with the rest of the health portfolio partners to integrate their*

- *Need a meeting of the minds of the VPs*

Discussion on the Use of FPT feedback to Inform procurement Decisions

- The Drug Shortages Table was noted to be a key existing mechanism that is being leveraged to inform PHAC's procurement recommendations.
- Current processes are ensuring that CCDIC is receiving PT endorsement before a procurement recommendation is rendered - to ascertain PT demand and likelihood of usage.
- CPHO noted that CCDIC has addressed the need for early engagement of PTs regarding COVID-19 therapeutic procurement recommendations.
- CPHO signaled her interest in ensuring broad awareness within PTs so that the Chief Medical Officers within the PTs are aware of the treatments procured and available
- CPHO also recognized that clinicians are needing clinical guidance – Either PHAC or HC to ensure that CADTH and INESS are engaged
    - Bersabel noted that we are pushing as far as we could to engage with CADTH to ensure that PTs have the guidance that they need. Conversations with CADTH are slow, but moving in the right direction.
    - CADTH may have resource limitations – which may influence the rate that they may be able to provide clinical guidance
- A request for top-up funding was requested prior to the writ dropping
    - 3 billion was given for vaccines, President advised that it could be repurposed for therapeutics, if necessary.
- CPHO – reiterated – the important role of therapeutics.
    - As we may see a variant of concern escaping the vaccine, and the vaccines being re-tooled, therapeutics plays a key role.

Action Item:

- *President suggested to consider partnering with CADTH to request that they provide guidance prior to PHAC doing large scale procurement*
- *CPHO would like to ascertain how many patients are being helped with the treatments that we have - to ensure that we are mapping out that what we have is aligned with the trajectory of the 4th wave modelling – with an assumption built in by clinicians who are indicating how they would be using the product.*

Bradley, Kevin (HC/SC)

From: Lawuyi, Niyi (PHAC/ASPC)
Sent: 2021-09-26 11:46 PM
To: Arthur, Jacqueline (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC)
Cc: Kolbe, Jane (PHAC/ASPC)
Subject: RE: international comparison on therapeutics decision-making and "action items" from President briefing
Attachments: List of Actions from Meeting Summary.docx; Meeting.Summary.Update.to.CPHO.Sept.2.2021.(v.5).docx

Hi Bersabel and Jackie,

Please find the most updated version of the Meeting Summary and the List of Actions as discussed.

Thanks,

Niyi

From: Arthur, Jacqueline (PHAC/ASPC) <jacqueline.arthur@phac-aspc.gc.ca>
Sent: 2021-09-26 2:42 PM
To: Lawuyi, Niyi (PHAC/ASPC) <niyi.lawuyi@phac-aspc.gc.ca>; Ephrem, Bersabel (PHAC/ASPC) <bersabel.ephrem@phac-aspc.gc.ca>
Cc: Kolbe, Jane (PHAC/ASPC) <jane.kolbe@phac-aspc.gc.ca>
Subject: international comparison on therapeutics decision-making and "action items" from President briefing

Bersabel and Niyi;
As requested please find attached the Word document on international comparisons that was prepared by the OPSM and submitted in April 2021 to Roman Szumski, VP at the time. Also is the list prepared by Jane of the “action items” from the most recent President briefing – there may be a more recent version but I have been out of the loop so Jane please circulate any updates.
Thanks,
Jackie

Jacqueline Arthur, BScN, RN
(she | elle)
A/Executive Director | Directrice Exécutive par intérim
Strategic Issues and Integrated Management Division | Division des enjeux stratégiques et de la gestion intégrée
Centre for Communicable Diseases and Infection Control | Centre de la lutte contre les maladies transmissibles et les infections

Public Health Agency of Canada | Agence de la santé publique du Canada
t. (613) 889-8455

Action Items

- Document the decision-making process for the various COVID-19 therapeutics procured to date.
    - Development of SOPs

- Create an inventory and collect a complete record of information and communication materials related to procurement (issue notes, briefing notes, memos, etc.).

- Work with the office of the Chief Financial Officer to ensure documents from IDPB and OCFO documents are in a shared file.

- Preparation of briefing materials to support increased regularity and frequency of meetings between Therapeutics, the CPHO and with executives to increase awareness, relevance and visibility of therapeutics
    - e.g. Therapeutics presence at SAC meetings and briefings with provincial Chief Medical officers to clarify and convey PHAC's role in therapeutics

- Continue work to improve governance of Therapeutics

- Preparation of documents and information materials that support inclusion of Therapeutics in medium term planning policy (MTP) for pandemic response and addition to MTP tracker

- Development of mechanisms/strategies that facilitate and expedite decision making related to the need to procure additional therapeutics and a policy process to fast track purchases

- Send the Memo to the President for the procurement of Sotrovimab and Sarilumab

- VP to check in with PHAC – to ensure that funding is available for Sarilumab

- Provide the President with a map comparing international public health approaches, actions and roles in therapeutics

- Initiate engagement with PHAC VPs to discuss and consider a future role for PHAC in Therapeutics and preparation of associated briefing materials for internal discussions and dissemination to health portfolio partners to solicit feedback

- Initiate discussions with CADTH to explore partnering with them to provide PHAC with guidance prior to large scale procurements

- Provide CPHO with metrics related to the number of patients treated with federally procured therapeutics.
    - Use these metrics to verify that aligns the trajectory of 4th wave modelling with assumptions that include how these products are being used by clinicians

Meeting Summary
Therapeutics Briefing: CPHO
September 2, 2021
5:30 – 6:00 pm

Attendees: Dr. Theresa Tam, Ian Stewart, Howard Njoo, Bersabel Ephrem, Jacqueline Arthur, Pamela Ponic, Jennifer Rendall, Vicki Wiseman,

Observers: Jane Kolbe

SUMMARY OF ACTION ITEMS

Document COVID-19 therapeutics procured

- *Collect a complete record (Briefing Note, contract, legal review, etc.).*
- *Work with the office of the Chief Financial Officer to ensure documents from IDPB and OCFO documents are in a shared file.*

Raise the profile of COVID-19 therapeutics

- Increase awareness of PHAC's role and actions in COVID-19 therapeutic procurement, and enhance communication (including with SAC, and PT Chief Medical Officers)
- *Ensure that PHAC is able to determine whether we have to procure any more therapeutics during the 4th wave, and has an enabling process to accomplish this.*

Procurements underway

- *Send the Memo to President for the procurement of Sotrovimab and Sarilumab*
- *VP to check in with PHAC – to ensure that funding is available for sarilumab*
- *Ascertain/quantify how many patients are being helped with the treatments procured to date*

Ascertaining PHAC's future role in therapeutic procurement

- *Provide the President with the international comparison regarding the roles and responsibilities of public health in therapeutic procurement - mapping.*
- *Initiate engagement with PHAC VPs to discuss PHAC's future role in therapeutics*

Partnership with CADTH/INESSS

- Engage CADTH to seek their support for the development of clinical guidance as part of the procurement decision-making process

Current State of COVID-19 Therapeutics Procurements

- An overview of GoC measures taken with respect to COVID-19 therapeutics procured was provided.
    - Howard noted that therapeutic procurement is traditionally the responsibility of provinces and territories (PTs).
    - PHAC, (with PSPC) assumed responsibility to procure COVID-19 therapeutics to respond to the pandemic - received $500 million under the Medical Countermeasures budget.
- Hydroxychloroquine was used as an example of early decisions taken at the height of the pandemic.
    - Lessons/learned were integrated into future decision-making processes with respect to procurement of emerging COVID-19 therapies.
        - Continuous learning –strengthened the procurement decision-making process, including the approval chain via Deputy Minister Procurement Committee.
- Discussion ensued regarding the role that external advisory groups have played in the procurement decision-making process. Specifically,
    - COVID-19 Therapeutics Task Force (CTTF)
    - COVID-19 Clinical Pharmacology Task Group (CPTG).
- Strengthening the process that documents procurement decisions was mentioned and requires attention to support PHAC in an expeditious response to an audit.
- CPHO – recognized that at the beginning, we needed to urgently invest, and now we need a different process.
    - Data from clinical trials are more informative at this stage of the pandemic versus early days.
    - The UK was noted to be a useful jurisdiction to compare with in terms of procurements and processes.
- CPHO expressed a desire to communicate more about PHAC's role in COVID-19 therapeutics procurement.

Action Item:

- *Document the decision-making process for the various COVID-19 therapeutics procured to date.*
- *Collect a complete record (Briefing Note, package, etc.).*
- *Work with the office of the Chief Financial Officer to ensure documents from IDPB and OCFO documents are in a shared file.*

Shifting Needs of the PTs & Fall/2021 Procurement Plans

- Feedback from PTs was briefly discussed, including their desire for earlier engagement prior to procurement, a need for clinical guidance from CADTH and INESSS, more control over what drugs enter into their Formularies, implementation costs, and logistics.
- Howard noted our early thinking about the need to shift the existing GoC procurement approach towards an FPT collective approach - based on the expressed needs of the PTs – and integrate this into our current and future procurement plans.
- CPHO noted the important role that mAbs play - specifically in terms of having domestic capacity, "having mAb capacity is very important for an emerging pathogen".
- COVID-19 therapeutics currently under consideration for Fall/2021 procurement was discussed, including mAbs. Tocilizumab was noted to have been extensively used by PTs in previous waves.
    - The state of safety and efficacy data for oral antivirals was noted to be evolving.
    - PHAC is in the process of information exchanges with the drug makers, but until sufficient scientific data is available to assess safety and efficacy, procurement negotiations for oral anti-virals are premature.
- Ivermectin was discussed – The US FDA put out a tweet, and PHAC and Health Canada issued a joint tweet against the use of this drug for treatment of COVID-19.

4th Wave Planning and the Role of COVID-19 Therapeutics

- CPHO noted that treatment is critical in the process of 4th wave/future wave planning.
    - She noted that treatment is not prominently featured in 4th wave planning.
        - CPHO identified the need for including treatment in 4th wave planning and communicated this to DM-HC (Steve), however it does not appear in the placemat.
- Treatment must be a key aspect, as people will become ill and end up in the ICU – they can survive with an improvement in their treatment, or perhaps stay for a shorter time, which also relieves the pressure on the health system.
- Given treatment as a key element of 4th wave planning, it is necessary to ensure the establishment of an enabling process that expedites procurement of additional therapeutics based on emerging needs.
- Regarding Executive briefings, it was noted that while vaccine procurement had frequent executive/Sr. Management touch-points (every other day) and a regularized process, a similar approach needs to be established for COVID-19 therapeutics.

- Vaccine procurement differs from therapeutics and is less complex since it does not require physician intervention, making bulk procurement of vaccines a more direct path.
- The COVID-19 therapeutics landscape was noted to be more complex because it requires a physician prescription, involves the role of formularies, and includes the enmeshed intra and inter-departmental nature of the procurement process/considerations for emerging COVID-19 therapies.

- How/what we communicate is also different from vaccine procurement communication – and we have been relatively silent in terms of measures taken in the space of COVID-19 therapeutic procurement.

Action Item:

- *CPHO signaled a desire for more regular executive involvement/communication – raising the profile of therapeutics*
  - *Governance work was noted to be important to the CPHO*
  - *CPHO interested in going to SAC, and Provincial Chief Medical Officers to more actively communicate PHAC's role in therapeutics*
  - *CPHO noted that COVID-19 therapeutics is not in the MTP process and tracker*
- *Ensuring that PHAC has the tools and enabling processes necessary to quickly determine the need to procure any additional therapeutics during the 4th wave*

Discussion on Supply Issues of Specific COVID-19 Therapeutics

- Tocilizumab (was in high demand by PTs in wave 3) and sarilumab were noted to have excellent efficacy data in clinical trial results.
  - Both drugs are used for rheumatoid arthritis, have high efficacy, and are well established.
  - There is a global shortage of tocilizumab, consequently it was reported that PHAC was advancing contract negotiations to procure sarilumab since it can be used as a back-up treatment in lieu of tocilizumab.
- PSPC is in the process of advancing this negotiation with sarilumab.

Action Item:

- *Send the Memo to the President for the procurement of sotrovimab and sarilumab*
- *VP to check in with PHAC – to ensure that funding is available for sarilumab*

Discussion on Next Steps:

- Howard introduced the need to take the lessons learned with COVID-19 procurement processes to date, and integrate this into longer-term thinking.
    - COVID-19 therapeutics is a complex process involving several Branches within PHAC.
    - Next steps would involve looking at a more fulsome FPT approach.
- To build a sustainable model, beyond COVID-19 for therapeutics in general, for infectious disease preparedness Howard proposed the following process:
    - Commence internal discourse with VPs within PHAC to examine and deliberate on a future role for therapeutic procurement within PHAC
    - Engage EC with a proposed approach for discussion
    - Roll out the discussion to the Health Portfolio
- A discussion drawing attention to PHAC's public health role vs Health Canada's regulatory role in the therapeutic procurement sphere/space was also mentioned along with the importance of discerning and articulating these distinct roles.
- Ian asked that we map out the requisite steps and needs in the COVID-19 therapeutic procurement process and perform an international comparison to visually demonstrate the public health role in therapeutics in other countries.

Action Item:

- *Provide the President with the international comparison - mapping.*
- *Initiate engagement with PHAC VPs to discuss PHAC's future role in therapeutics with the view to developing a proposed strategy for consideration at EC – with the eventual goal of consulting with all other health portfolio partners to integrate their feedback, predicated on a meeting of the minds of PHAC VPs*

Discussion on the Use of FPT feedback to Inform procurement Decisions

- The Drug Shortages Table was noted to be a key existing mechanism that is being leveraged to inform PHAC's procurement recommendations.
- Current processes are ensuring that CCDIC is receiving PT endorsement before a procurement recommendation is rendered - to ascertain PT demand and likelihood of usage.
- CPHO noted that CCDIC has addressed the need for early engagement of PTs regarding COVID-19 therapeutic procurement recommendations.
- CPHO signaled her interest in ensuring broad awareness within PTs so that the Chief Medical Officers within the PTs are aware of the treatments procured and available.
- CPHO also recognized that clinicians need clinical guidance – Either PHAC or HC to ensure that CADTH and INESS are engaged.
    - Bersabel noted that we are pushing as much as possible to engage with CADTH to ensure that PTs have the guidance that they need. Conversations with CADTH are slow, but moving in the right direction.
    - CADTH may have resource limitations – which may influence the rate that they may be able to provide clinical guidance.
- A request for top-up funding was provided prior to the writ dropping.
    - 3 billion was given for vaccines; President advised that it could be repurposed for therapeutics, if necessary.
- CPHO – reiterated – the important role of therapeutics.
    - As we may see a variant of concern escaping the vaccine and the vaccines being re-tooled, therapeutics have a key role to play.

Action Item:

- *President suggested consideration be given to partnering with CADTH to facilitate requests for guidance in advance of any large scale procurements on behalf of PHAC.*
- *CPHO would like to ascertain how many patients are being helped with the treatments that we have procured - to ensure that we are tracking how procured treatments to date align with 4th wave modelling trajectories and the inclusion of assumptions related to how clinicians would be using this product.*

Bradley, Kevin (HC/SC)

From: Rendall, Jennifer (PHAC/ASPC)
Sent: 2021-01-02 6:25 PM
To: Njoo, Howard (PHAC/ASPC); Szumski2, Roman (PHAC/ASPC); Ephrem, Bersabel (PHAC/ASPC); Levesque2, Kaili (HC/SC)
Cc: Ponic, Pamela (PHAC/ASPC); Currie, Andrea (PHAC/ASPC)
Subject: FW: Ivermectin

Hi Team,

Please see below correspondence into Dr. Tam.

Kaili can you please as your team/the HC team to do a roll up of what the TTF has done in this space?

Howard, Bersabel and Roman – can you please prepare advice for Dr. Tam and the President to consider in this area.

Thank you
Jen

From: Tam, Dr Theresa (PHAC/ASPC) <drtheresa.tam@canada.ca>
Sent: 2021-01-02 4:15 PM
To: Stewart, Iain (PHAC/ASPC) <iain.stewart@canada.ca>
Cc: Njoo, Howard (PHAC/ASPC) <howard.njoo@canada.ca>; Ponic, Pamela (PHAC/ASPC) <pamela.ponic@canada.ca>; Rendall, Jennifer (PHAC/ASPC) <jennifer.rendall@canada.ca>
Subject: Fwd: Ivermectin

There is an upsurge in emails on Ivermectin. Could we get the therapeutics task force to look at this?

Other research networks may also be able to review/summarize if this is not in line with what the therapeutic task force does.

TT
Sent from my iPad

Begin forwarded message:

From: [redacted]
Date: January 2, 2021 at 2:48:58 PM EST

To: "Tam, Dr Theresa (PHAC/ASPC)" <drtheresa.tam@canada.ca>
Subject: Ivermectin

Get Outlook for iOSI've compiled a list of the email addresses for the Federal Minister of Health, all Provincial Ministers of Health, Canada's Chief Public Health Officer (Dr. Tam), and all the Provincial Health Officers. I've also written a letter imploring them to introduce Ivermectin as the front-line treatment to stop Covid-19 and the never-ending pandemic and it's restrictions. I will be sending it to all of them, as often as I can.

I am posting my letter below to make it easier for others to do the same. Since they are refusing to openly acknowledge it, the only way to be sure they know is for us to flood them with our demands. They are, after all, public servants, and unless we no longer live in a democratic society then they are "our" public servants, not the other way around. As I say in my closing statement, they owe it to their constituents, those they are sworn to protect, and all Canadians, to do everything in their power to stop this pandemic. This is entirely within their power to change, and they are obligated by their oath of office to do so…

URGENT ATTENTION:

With the Covid-19 crisis showing no signs of slowing, and current treatment options proving to have little success in the elderly and those with pre-existing life-limiting conditions, the saving of those lives is of paramount importance.

Reducing the spread of the Cov-2 virus from person to person and limiting community spread is crucial for protecting those most susceptible to the virus's respiratory effects. The WHO and manufacturers of the vaccines that are being promoted and given to Canadians have stated that there is no data showing they will reduce infection or the transmission of Cov-2, and so one must ask, "Why is this the only option being used?"

There seems to be a tunnel-vision mindset that is blinding public health authorities from considering any other alternatives, operating with single mindedness, and ignoring any information that challenges this approach. This does not follow the principles of scientific methodology and excludes any hope of discovering a control mechanism to stop Cov-2 and the devastation it is reaping on our country's health, both physical and mental, and our economy, which is in ruins.

Seeing no mention of it in any national media, or in the public health messages being provided, it is obvious you are ignoring the latest clinical research on Covid-19, that being the work done by the doctors of the Front Line COVID-19 Critical Care Alliance (FLCCC) and their ground-breaking exploration in using Ivermectin as a phenomenally successful front-line treatment for Covid-19.

The doctors that make up the FLCCC are leaders in critical care with expertise in therapies directed at severe infections and have spent all of 2020 treating patients with an Ivermectin protocol, believing it to have vast potential as an off-label drug with anti-viral properties.

Their research, and the peer-reviewed empirical data derived from it, has proven Ivermectin to be immensely effective in both the prophylaxis and treatment of all phases of COVID-19. Here are the highlights of their findings:

1) Ivermectin inhibits the replication of many viruses, including SARS-CoV-2, influenza, and others;
2) Ivermectin has potent anti-inflammatory properties with multiple mechanisms of inhibition;
3) Ivermectin diminishes viral load and protects against organ damage in animal models;
4) Ivermectin prevents transmission of COVID-19 when taken either pre- or post-exposure;
5) Ivermectin hastens recovery and decreases hospitalization and mortality in patients with COVID-19;
6) Ivermectin leads to far lower case-fatality rates in regions with widespread use.

https://covid19criticalcare.com/wp-content/uploads/2020/11/FLCCC-Ivermectin-in-the-prophylaxis-and-treatment-of-COVID-19.pdf

Every day that this information is ignored more people die that could have been saved using the Ivermectin protocol. It could be an unknown soul dying alone, or a member of your own family. Every day, battle-weary health care workers are forced to watch helplessly in a vain attempt to save yet another casualty of Covid-19. Every day, more businesses are forced to close forever under the restrictive public health guidelines. With utmost urgency, I implore you to review the data and

make this a front-line treatment in the fight against Covid-19. You owe it to your constituents, those you are sworn to protect, and all Canadians, to do everything in your power to stop this pandemic. This is entirely within your power to change, and you are obligated by your oath of office to do so…

Most Sincerely,

[redacted]

Bradley, Kevin (HC/SC)

From: Lachapelle, Stephane (PHAC/ASPC) on behalf of Cidsc Secretariat (PHAC/ASPC)
Sent: 2021-08-27 3:31 PM
To: AHuang@gov.nu.ca; Andy_DelliPizzi@gov.nt.ca; annick.descormiers@msss.gouv.qc.ca; Archibald, Chris (PHAC/ASPC); [redacted] Cidsc Secretariat (PHAC/ASPC); [redacted] Fitzgerald-Husek, Alanna (PHAC/ASPC); Gaudreau, Marc-Andre (PHAC/ASPC); [redacted] Njoo, Howard (PHAC/ASPC); [redacted]
Subject: FW: TAC Weekly Evidence Tracker - August 23, 2021
Attachments: Weekly COVID-19 Evidence Review Tracker_23AUG2021.pdf

Dear TAC members,

Please see attached for the CSO approved Weekly COVID-19 Evidence Review Tracker for August 23, 2021.

This week's tracker includes two new non-PHAC reviews:

- McMaster Health Forum (funded by PHAC OCSO): What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? (Version 17)
- McMaster Health Forum/SPOR EA: Canadian provincial and territorial public health response to SARS-CoV-2 and variants of concern: A jurisdictional scan including select European countries

McMaster Health Forum (funded by PHAC OCSO) Canadian and Global Evidence Spotlights are also included for interest.

Thanks,

Mette

1. New Evidence Reviews and Findings[1]

[1] Findings presented in this tracker are subject to PHAC's final review before publication. Please note that PHAC-ESG reviews presented in Table 1 are approved for distribution to public health partners to inform timely decision-making, and that the linked documents are not for public distribution at this time.

https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-syntheses/covid-19-living-evidence-synthesis-6.17---what-is-the-efficacy-and-effectiveness-of-available-covid-19-vaccines-in-general-and-specifically-for-variants-of-concern.pdf?sfvrsn=b5aa1a72_5

https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-syntheses/covid-19-living-evidence-synthesis-6.17---what-is-the-efficacy-and-effectiveness-of-available-covid-19-vaccines-in-general-and-specifically-for-variants-of-concern.pdf?sfvrsn=b5aa1a72_5

https://www.mcmasterforum.org/docs/default-source/covidend/global-inventory-spotlight/covid-end_global-spotlight_8.2_2021-08-25.pdf?sfvrsn=311468e0_5

https://www.mcmasterforum.org/docs/default-source/covidend/canadian-inventory-spotlight/covid-end-in-canada_canadian-spotlight_2021-08-26.pdf?sfvrsn=d1ccc4f5_5

https://www.mcmasterforum.org/docs/default-source/covidend/global-inventory-spotlight/covid-end_global-spotlight_8.2_2021-08-25.pdf?sfvrsn=311468e0_5

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2021-47/issue-2-february-2021/mask-wearing-decrease-transmission-covid-19.html

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2020-46/issue-11-12-november-5-2020/covid-19-ethnicity.html

2. Previous PHAC Reviews[2]

[2] Links to PHAC-ESG reviews are provided for convenience, and are not to be distributed further. We invite you to request the updated product directly from the PHAC Evidence Secretariat where required.

https://www.medrxiv.org/content/10.1101/2021.06.03.21258317v1

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2021-47/issue-2-february-2021/mask-wearing-decrease-transmission-covid-19.html

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2020-46/issue-11-12-november-5-2020/covid-19-ethnicity.html

3. Previous non-PHAC Reviews[3]

[3] Note that links to external websites may link to the most updated information, or may not be currently active.

https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-syntheses/covid-19-living-evidence-synthesis-6.16---what-is-the-efficacy-and-effectiveness-of-available-covid-19-vaccines-in-general-and-specifically-for-variants-of-concern.pdf?sfvrsn=8450ac2c_5

https://www.mcmasterforum.org/networks/covid-end/resources-specific-to-canada/for-decision-makers/scan-evidence-products

https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-profiles/covid-19-living-evidence-profile-4.4_what-went-well-and-what-could-have-gone-better-in-the-covid-19-responses-as-well-as-what-will-need-to-go-well-in-future-given-any-available-foresight-work-being-conducted.pdf?sfvrsn=28d51398_7

https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-profiles/covid-19-living-evidence-profile-4.4-appendix_what-went-well-and-what-could-have-gone-better-in-the-covid-19-responses-as-well-as-what-will-need-to-go-well-in-future-given-any-available-foresight-work-being-conducted.pdf?sfvrsn=2037897e_9

https://www.mcmasterforum.org/find-evidence/products/project/covid-19-living-evidence-profile-4-what-went-well-and-what-could-have-gone-better-in-the-covid-19-response-as-well-as-what-will-need-to-go-well-in-the-future-given-any-available-foresight-work-being-conducted

https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-profiles/covid-19-living-evidence-profile-5.3_what-went-well-and-what-could-have-gone-better-in-the-covid-19-response-in-other-countries-as-well-as-what-will-need-to-go-well-in-future-given-any-available-foresight-work-being-conducted.pdf?sfvrsn=f73304e8_5

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Public Health Agency of Canada | Agence de la santé publique du Canada

Weekly COVID-19 Evidence Review – August 23, 2021

Version 66

Contents

1. New Evidence Reviews and Findings[1]

Summary information from recently released reviews produced by PHAC and public health partners. Knowledge mobilization by the Office of the Chief Science Officer. The full evidence reviews are accessible via the provided hyperlinks.

Title of review	Overview of the evidence	Key findings
MHF: What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? (Version 17) Full Review	This evidence product was funded by PHAC OCSO. This LES is updated weekly and includes 68 studies identified up to August 25, 2021. New studies this week include data on Alpha [B.1.1.7] (3), Delta [B.1.617.2] (3) and Beta [B.1.351] (1). A visual summary of the evidence is presented in Table 1, with details in Table 2. Full details are available in the review.	Additional details available in the full review. Pfizer: • Moderate certainty evidence that 2 doses of BNT162b2 [Pfizer] prevented infection (range of mean estimates (ROME): 70-97%), prevented severe disease (ROME: 92-98%), prevented death (ROME: 91-98%), and reduced transmission of Alpha to close contacts ROME: 65-80%). • Moderate certainty evidence that 2 doses of BNT162b2 prevented symptomatic infection from Beta (ROME: 84-88%). Moderna: • Moderate certainty evidence that 2 doses of mRNA-1273 [Moderna] prevented infection from Alpha (ROME: 86-100%) and low certainty evidence it prevented infection from Beta (96.4% – 1 Obs). We have low certainty evidence that it prevented severe, critical, or fatal disease from Alpha (combined with Beta) (95.7% – 1 Obs). • Moderate certainty evidence that 2 doses of mRNA-1273 prevented infection from Delta (ROME: 76-86%) and low certainty evidence that it prevented severe, critical, or fatal disease (ROME: 93-100%). AstraZeneca: • Moderate certainty evidence that 2 doses of ChAdOx1 [AstraZeneca] prevented infection from Alpha (ROME: 62-79%) and moderate certainty evidence that it provided limited protection from infection by Beta (10.4% - 1 RCT). Combinations of vaccines: • Low certainty evidence that 1 dose of ChAdOx1 [AstraZeneca] followed by 1 dose of BNT162b2 [Pfizer] or mRNA-1273 [Moderna] prevented infection by Alpha (88% – 1 Obs).

[1] Findings presented in this tracker are subject to PHAC's final review before publication. Please note that PHAC-ESG reviews presented in Table 1 are approved for distribution to public health partners to inform timely decision-making, and that the linked documents are not for public distribution at this time.

MHF/SPOR EA: Canadian provincial and territorial public health response to SARS-CoV-2 and variants of concern: A jurisdictional scan including select European countries Full Text	This jurisdictional scan compiles Canadian provincial and territorial public health guidance relating to COVID-19 and the VOC between August 8 and 18, 2021, as well as guidance from Belgium and Germany from the same time-period. This snapshot provides an overview of each region's vaccine rollout, proof of vaccination requirements, isolation and quarantine requirements, travel restrictions, and gathering limits, as well as whether or not any of this guidance has been influenced by VOC. Full details are available in the document.	• Very little guidance mentions VOC explicitly. It may be assumed that the prevalence of VOC in a region at any given time has an implicit impact on public health measures. • Vaccination is now available to everyone aged 12+ in every province and territory, and in Germany and Belgium. All provinces/territories are on the penultimate or final step of their reopening plans. • Some provinces/territories such as Manitoba and Nova Scotia have vaccination strategies/campaigns to support Indigenous populations. • Ontario is the only Canadian province offering third doses. Belgium and Germany are planning to offer third doses in the coming weeks. • Quebec will require proof of vaccination for non-essential activities starting in September, while Manitoba allows businesses to ask for proof at their own discretion. • Ontario requires long-term care workers to be vaccinated. No other province/territory requires proof for activities within the province. • No changes have been made to hand washing, masking, or physical distancing requirements due to VOC. • For confirmed COVID-19 cases, 10-14 days of isolation is required in most provinces/territories, while some consider length of isolation on a case-by-case basis. Alberta will be lifting this requirement in September. Belgium and Germany require 10 days of isolation. • 14 days of quarantine for close contacts is required in most provinces/territories and Germany and Belgium, with some exceptions for fully vaccinated individuals. Alberta no longer requires quarantine of close contacts. • No quarantine is required after entering Alberta, British Columbia, New Brunswick, Ontario, Quebec, Saskatchewan, or Yukon from within Canada. In all other provinces/territories and Belgium and Germany, exemptions from/modifications to quarantine apply to partially or fully vaccinated individuals. • Attendance limits on private and public gatherings vary widely between regions.

MHF: Evidence Spotlights
 	
Canadian Spotlight
 	
Global Spotlight
	This evidence product was funded by PHAC OCSO.
	
	Canadian and Global spotlights are each published twice a month, and horizon scans are published monthly.
		• Canadian spotlight 8.2: Key additions from the second half of August 2021:
		  ○ In the second half of August, contributing Canadian evidence-synthesis teams have shared with us 13 newly completed evidence syntheses which are listed in the table below. Two of these syntheses provide insights across all domains of the COVID-END taxonomy (public-health measures, clinical management, health-system arrangements, and economic and social response) and the remaining focus on public-health measures (n=8), and clinical management (n=3).
		• Global spotlight 8.2: Key additions from the second half of August 2021:
		  ○ There are two newly added syntheses and one update to a living evidence synthesis that is already included in the public-health measures part of the COVID-END inventory of 'best' evidence syntheses, six newly added syntheses and 20 updates to living evidence syntheses that are already included in the clinical management parts of the inventory, and one newly added synthesis in the health-system arrangements part of the inventory.

2. Previous PHAC Reviews[2]

Summary information from previously shared evidence products, beginning with the most recent reviews. The titles are hyperlinked to the original review at the time of distribution. Please note, if a review has been updated, only the most recent version of the review is included in this table with previous versions available upon request.

Review Date	Review Title	Accessible Content
August 13 2021	Evergreen Rapid Review on COVID-19 Vaccine Attitudes and Uptake in Canada – Update 9 *<Mise à jour 9 en traduction>*	Full Review *En traduction* Evidence Snapshot *En traduction*
August 10 2021	Living Summary of SARS-CoV-2 Variants of Interest: The C.37 (Lambda) Variant Profile, Highlights up to August 10, 2021 *<En traduction>*	Full Review *En traduction*
August 10 2021	VOC Comparison Table of Alpha, Beta, Gamma and Delta *<En traduction>*	Full Text *En traduction*
August 9 2021	Evidence Brief of SARS-CoV-2 Incubation Periods *<En traduction>*	Full Review *En traduction*
July 29 2021	Living Summary of SARS-CoV-2 Variants of Concern: The Delta variant (B.1.617.2) profile, Highlights up to July 29, 2021 Résumé évolutif à propos des variants préoccupants du SRAS-CoV-2 : Le profil du variant Delta (B.1.617.2), Faits saillants jusqu'au 29 juillet 2021 *<En traduction>*	Full Review *En traduction* Version précédente
July 14 2021	Evergreen Rapid Review on COVID-19 Vaccine Attitudes and Uptake – Update 8 Revue rapide et évolutive sur les attitudes à l'égard des vaccins et de l'adoption des vaccins contre la COVID-19, Mise à jour 8	Full Review Mise à jour 8 Evidence Snapshot Aperçu des éléments de preuve
July 1 2021	Living Summary of SARS-CoV-2 Variants of Concern: The Alpha Variant (B.1.1.7) profile, Highlights up to July 1, 2021 Résumé évolutif à propos des variants préoccupants du SRAS-CoV-2 : Le profil du variant Alpha (B.1.1.7), Faits saillants jusqu'au 1 juillet 2021 *<En traduction>*	Full Review *En traduction*

[2] Links to PHAC-ESG reviews are provided for convenience, and are not to be distributed further. We invite you to request the updated product directly from the PHAC Evidence Secretariat where required.

July 1 2021	Living Summary of SARS-CoV-2 Variants of Concern: The Beta Variant (B.1.351) profile, Highlights up to July 1, 2021 Résumé évolutif à propos des variants préoccupants du SRAS-CoV-2 : Le profil du variant Beta (B.1.351), Faits saillants jusqu'au 1 juillet 2021 *<En traduction>*	Full Review *En traduction*
July 1 2021	Living Summary of SARS-CoV-2 Variants of Concern: The Gamma variant (P.1) profile, Highlights up to July 1, 2021 Résumé évolutif à propos des variants préoccupants du SRAS-CoV-2 : Le profil du variant Gamma (P.1), Faits saillants jusqu'au 1 juillet 2021 *<En traduction>*	Full Review *En traduction*
June 23 2021	Evidence Brief of Ivermectin Synthèse en bref sur l'ivermectine	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
June 6 2021	Prevalence of long-term effects in individuals diagnosed with COVID-19: a living systematic review *(Preprint)*	Full Review
June 1 2021	Living Summary of SARS-CoV-2 Alpha, Beta and Gamma Variants of Concern; Highlights up to June 1, 2021 Résumé évolutif à propos des variants préoccupants Alpha, Beta et Gamma du SRAS-CoV-2, Faits saillants jusqu'au 1er juin 2021	Full Review Revue complète Version précédente
May 27 2021	Evidence Brief on the Therapeutic use of Vitamin D Supplementation for COVID-19 Synthèse en bref sur la supplémentation thérapeutique en vitamine D pour des cas de la COVID-19	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
May 14 2021	Evidence Brief on the Risk of COVID-19 Transmission in Flight, Update 2 Synthèse en bref sur le risque de transmission de COVID-19 en vol, Mise à jour 2	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
May 4 2021	Rapid Review on the Impact of School Closures and Re-openings on COVID-19 Transmission Examen rapide de l'impact des fermetures et réouvertures d'écoles sur la transmission de la COVID-19	Full Review Revue complète Evidence Snapshot

		Aperçu des éléments de preuve
April 21 2021	Rapid Review on Protective Immunity, Update 1 Revue rapide sur l'immunité protectrice, mise à jour 1	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
March 31 2021	Evidence Brief on viral load and the likelihood of transmission during the infectious period of SARS-CoV-2 Synthèse en bref sur la charge virale et la probabilité de transmission pendant la période infectieuse du SRAS-CoV-2	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
March 26 2021	Evidence Brief on SARS-CoV-2 Variants of Concern and Transmission in Children Synthèse en bref des données probantes sur les variantes préoccupantes du SRAS-CoV-2 et leur transmission chez les enfants	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
March 12 2021	Rapid Review on SARS-CoV-2 Aerosol Transmission, Update 2 Revue rapide sur la transmission par les aérosols du SRAS-CoV-2, Mise à jour 2	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
Feb 17 2021	Evidence Brief of COVID-19 Infectious Period in Immunosuppressed/Immunocompromised Individuals Synthèse en bref sur la période infectieuse de la COVID-19 chez les personnes immunodéprimées ou immunodéficientes	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
Feb 12 2021	Evidence Brief of SARS-CoV-2 Risks in Arenas Synthèse en bref sur les risques associés au SRAS-CoV-2 dans les arénas	Full Review Revue complète

		Evidence Snapshot Aperçu des éléments de preuve
Feb 10 2021	Evidence Brief of SARS-CoV-2 contract tracing Synthèse en bref sur la recherche des contacts pour le SRAS-CoV-2	Full Review Revue complète Evidence Snapshot Aperçu des éléments de preuve
Jan 28 2021	Rapid Review of Multisystem Inflammatory Syndrome in Children (MIS-C) Examen rapide du syndrome inflammatoire multisystémique chez les enfants (MIS-C)	Full Review Revue complète
Jan 26 2021	Evidence brief of maximum incubation period Synthèse en bref sur la période d'incubation maximale	Full Review Revue complète
Jan 20 2021	Evidence brief on adherence to isolation and quarantine recommendations during COVID-19 Synthèse en bref sur le respect des recommandations d'isolement et de quarantaine pendant la COVID-19	Full Review Revue complète
Jan 7 2021	Rapid review of vitamin D and zinc supplementation for therapeutic use on COVID-19 cases Sommaire des éléments de preuve sur la supplémentation thérapeutique en vitamine D or en zinc pour des cas de la COVID-19	Full Review Revue complète
Jan 5 2021	Rapid Review on the Characteristics of Effective Non-Medical Face Masks in Reducing the Risk of SARS-CoV-2 Transmission Revue rapide sur les caractéristiques des masques non médicaux ou des couvre-visages efficaces pour réduire le risque de transmission du SRAS-CoV-2	Full Review Revue complète
Dec 3 2020	Evidence brief of COVID-19 quarantine length reduction strategies and effectiveness, Update 1 Synthèse en bref sur les stratégies visant à réduire la durée de la quarantaine associée à la COVID-19 et leur efficacité, mise à jour 1	Full Review Revue complète
Dec 2 2020	Rapid review on the physiological effects of wearing face masks Revue rapide sur les effets physiologiques du port du couvre-visage	Full Review Revue complète
Dec 1 2020	Rapid review on the use of face masks to prevent COVID-19 in community settings, Update 1 Synthèse en bref sur le port du masque masques pour prévenir la COVID-19 en milieu communautaire, mise à jour 1	Full Review CCDR Abstract Revue complète

Nov 13 2020	Evidence on the clinical and epidemiological features of MIS-A associated with SARS-CoV-2 infection Sommaire des éléments de preuve sur le syndrome inflammatoire multisystémique chez l'adulte (MIS-A)	Full Review Revue complète
Oct 8 2020	Evidence brief of potential health risks of hard-surface disinfectants in environments shared by school-aged children Synthèse en bref sur les risques potentiels pour la santé de l'utilisation des désinfectants pour surfaces dures dans les environnements où se trouvent des enfants d'âge scolaire	Full Review Revue complète
Sept 22 2020	Evidence brief on ethnicity and COVID-19 Synthèse en bref sur l'origine ethnique et la COVID-19	Full Review CCDR Abstract Revue complète
Sept 11 2020	Rapid review on infectious period Revue rapide de la période infectieuse	Full Review Revue complète
Sept 9 2020	Evidence brief on SARS-COV-2 antibodies in patients that retest RT-PCR positive Synthèse en bref sur la présence des anticorps dirigés contre le SRAS-CoV-2 chez les patients ayant obtenu un nouveau résultat positif au test RT-PCR	Full Review Revue complète
Aug 25 2020	Evidence brief on the risk of COVID-19 outbreaks in the workplace (update) Revue rapide du risque d'éclosion de la COVID-19 sur le lieu de travail	Full Review Revue complète
Aug 20 2020	Rapid Review of COVID-19 hospitalizations and length of stay Examen rapide des hospitalisations liées à la COVID-19 et de la durée du séjour	Full Review Revue complète
Aug 20 2020	An evidence brief on SARS-CoV-2 transmission risks associated with playing non-professional sports Note d'information sur le risque lié à la COVID-19 et les sports non professionnels	Full Review Revue complète
Aug 18 2020	Evidence brief of size of gatherings and characteristics of high risk transmission events Note d'information sur la taille des rassemblements et les caractéristiques des événements à risque élevé de transmission	Full Review Revue complète
Aug 14 2020	COVID-19 summary of heating, ventilation, air conditioning (HVAC) systems and transmission of SARS-CoV-2 COVID-19 – Résumé en ce qui concerne les systèmes de chauffage, de ventilation, de climatisation (CVCA) et la transmission du virus SRAS-CoV-2	Full Review Revue complète
July 23 2020	Evidence brief on the determinants of individual adherence to public health interventions for COVID-19 Note d'information sur les déterminants de l'adhésion individuelle aux interventions de santé publique pour la COVID-19	Full Review Revue complète

July 22 2020	Evidence brief on age-dependent transmission Note d'information sur la transmission en fonction de l'âge	Full Review Revue complète
July 17 2020	Evidence brief of pregnancy and severity of COVID-19 Synthèse en bref des données probantes sur la grossesse et la gravité de la COVID-19	Full Review Revue complète
July 7 2020	COVID-19 summary of face shields to prevent transmission of SARS-CoV-2 COVID-19 – Résumé des études sur l'utilisation d'écrans faciaux pour prévenir la transmission du SRAS-CoV-2	Full Review Revue complète
July 5 2020	COVID-19 summary of SARS-CoV-2 transmission and singing/wind Instruments Résumé des connaissances relatives à la transmission du SRAS-CoV-2 par les instruments à vent et le chant	Full Review Revue complète
June 24 2020	Evidence brief on SARS-CoV-2 virus dispersion distance Synthèse en bref sur la distance de dispersion du virus SRAS-CoV-2	Full Review Revue complète
June 22 2020	Evidence brief on the infection risk from eye exposures to inform contact and droplet precautions Synthèse en bref sur le risque d'infection à la suite du contact oculaire pour orienter les précautions à prendre en cas de contact et d'exposition aux gouttelettes	Full Review Revue complète
June 19 2020	Evidence brief of de-escalation of social bubbles Synthèse en bref sur la désescalade des bulles sociales	Full Review Revue complète
June 11 2020	Evidence brief of aerosol generating procedures in dental care settings Résumé des éléments de preuve sur les procédures pouvant générer des aérosols dans le milieu des soins dentaires	Full Review Revue complète
June 4 2020	Evidence brief on infectiousness and symptom onset Synthèse en bref sur l'infectiosité et l'apparition des symptômes	Full Review Revue complète

3. Previous non-PHAC Reviews[3]

Release Date	Review Title	Accessible Content	Prepared By
20AUG2021	What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? (Version 16)	Full Review Archived Versions	McMaster Health Forum (funded by PHAC OCSO)
13AUG2021	What went well and what could have gone better in the COVID-19 response in Canada, as well as what will need to go well in future given any available foresight work being conducted? (Version 4)	Full Review Appendix Previous Versions	McMaster Health Forum (funded by PHAC OCSO)
13AUG2021	What went well and what could have gone better in the COVID-19 response in other countries, as well as what will need to go well in future given any available foresight work being conducted? (Version 3)	Full Review Appendix Previous Versions	McMaster Health Forum (funded by PHAC OCSO)
13AUG2021	Evidence Spotlights	Canadian Spotlight Global Spotlight Previous Horizon Scans Archived Versions	McMaster Health Forum (funded by PHAC OCSO)
13AUG2021	Living Rapid Review Update 3: What is known about the risk of transmission of COVID-19 within post-secondary institutions and the strategies to mitigate on-campus outbreaks?	Full Review	NCCMT
12AUG2021	Living Rapid Review Update 17: What is the specific role of daycares and schools in COVID-19 transmission?	Full Review	NCCMT
31JUL2021	Factors affecting COVID-19 vaccination acceptance and uptake among the general public: a living behavioural science evidence synthesis (Version 4)	Full Review Previous Version	McMaster Health Forum/Ottawa Hospital Research Institute (funded by PHAC OCSO)
30JUL2021	Public Health Implications of SARS-CoV-2 VOC	Full Review Supplementary Table	McMaster Health Forum/SPOR EA

[3] Note that links to external websites may link to the most updated information, or may not be currently active.

		Previous Version Public Health Measures Brief Health Systems Brief Jurisdictional Scan	
21JUL2021	Evidence to support safe return to clinical practice by oral health professionals in Canada during the COVID-19 pandemic: A report prepared for the Office of the Chief Dental Officer of Canada (July 2021 Update)	Full Review Previous Version	McGill University (for the Office of the Chief Dental Officer of Canada)
13JUL2021	How can we support crisis management and renewal in long-term care? (Version 4)	Full Review Appendix Summary: EN | FR Archived Versions	McMaster Health Forum (co-funded by PHAC OCSO)
28JUN2021	Rapid Review: What is known about parents' considerations for vaccine uptake for children and adolescents?	Full Review	NCCMT
28JUN2021	Surveillance of COVID-19 in a Vaccinated Population: A Rapid Literature Review	Full Review Rapid Review Brief Environmental Scan Brief	SPOR Evidence Alliance/McMaster Health Forum
25JUN2021	Rapid Review: What is the effectiveness, immunogenicity and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?	Full Review	NCCMT (requested by PHAC OCSO)
22JUN2021	Rapid Diagnostic Testing for COVID-19 in a Fully Vaccinated Population	Full Review Research Brief	SPOR Evidence Alliance/McMaster Health Forum
22JUN2021	Care Models for Long COVID: A Rapid Systematic Review	Full Review	SPOR Evidence Alliance/McMaster Health Forum
21JUN2021	Factors affecting healthcare worker COVID-19 vaccination acceptance and uptake: a living behavioural science evidence synthesis (Version 3)	Full Review Archived Version	McMaster Health Forum/Ottawa Hospital

			Research Institute (funded by PHAC OCSO)
21JUN2021	What is known about how schools (K-12) and post-secondary institutions (colleges and universities) adjust COVID-19 transmission-mitigation measures as infection rates change and vaccination rates increase? (Version 2)	Full Review Appendix Archived Versions	McMaster Health Forum (funded by PHAC OCSO)
16JUN2021	COVID-19 and indoor air: Risk mitigating measures and future-proofing	Full Review	NCCEH
10JUN2021	Masking during the COVID-19 pandemic – An update of the evidence	Full Text	NCCEH
02JUN2021	Rapid Review Update 2: What is the prevalence of household food insecurity in North America as a result of COVID-19 and associated public health measures?	Full Review	NCCMT
28MAY2021	COVID-19 living evidence profile: What is known about anticipated COVID-19 vaccine roll-out elements? (Version 7)	Full Review Appendix Archived Versions	McMaster Health Forum (co-funded by PHAC OCSO)
27MAY2021	Transmissibility of COVID-19 among vaccinated individuals, A Rapid Literature Review (Update 1)	Full Review Archived Version	SPOR Evidence Alliance/McMaster Health Forum
18MAY2021	Field Inquiry: Indoor CO2 Sensors for COVID-19 Risk Mitigation: Current Guidance and Limitations	Full Review	NCCEH
30APR2021	Rapid Review: What is known about reasons for vaccine confidence and uptake in populations experiencing inequities?	Full Review	NCCMT
31MAR2021	COVID-19 Impact on Intimate Partner Violence and Child Maltreatment: Summary of Evidence	Full Review	CADTH (at the request of PHAC)
24MAR2021	Contextualizing the risks of indirect COVID-19 transmission in multi-unit residential buildings	Full Summary	NCCEH
18MAR2021	COVID-19 Rapid Evidence Profile: When and in what order can COVID-19-related public-health measures be lifted (or stringency be reduced) as vaccination rates and seasonal temperatures increase?	Full Profile	McMaster Health Forum (funded by PHAC OCSO)
12MAR2021	Rapid Review Update 1: What are best practices for risk communication and strategies to mitigate risk behaviours?	Full Review	NCCMT

11MAR2021	Can people who are vaccinated develop asymptomatic COVID-19 infection and transmit the virus to other individuals and, if so, how large is the risk compared to unvaccinated people and those infected with SARS-CoV-2 variants? (Version 2)	Full Review Summary EN / FR Archived Versions	SPOR Evidence Alliance
09MAR2021	Rapid Review Update 2: What strategies mitigate risk of COVID-19 outbreaks and mortality in long-term care facilities?	Full Review	NCCMT
05MAR2021	Rapid Review Update 1: What is known about how long the virus can survive with potential for infection on surfaces found in community settings?	Full Review	NCCMT
01MAR2021	What are the transmission characteristics of SARS-CoV-2 variants of concern?	Full Review Summary –EN only	McMaster Health Forum/ SPOR Alliance (co-funded by PHAC OCSO)
22FEB2021	Field Inquiry: COVID-19 risks from handling the deceased	Full Review	NCCEH
01FEB2021	Rapid Review: What is known about the risk of transmission of COVID-19 during musical activities such as singing or playing a wind instrument, and how can these risks be mitigated?	Full Review	NCCMT
18JAN2021	Rapid Evidence Profile –What we know from both research and jurisdictional scans about whether to prioritize the vaccination of asymptomatic residents in long-term care homes during COVID outbreaks in the home?	Full Review	McMaster Health Forum
11JAN2020	COVID-19 Risks to mortuary workers	Full Review	NCCEH
11DEC2020	Rapid Review: What is the evidence for COVID-19 transmission in acute care settings?	Full Review	NCCMT
04DEC2020	Face shields in public: better than nothing, but not good enough	Full Review	NCCEH
16NOV2020	Environmental Surface and Air Sampling in the Context of the COVID-19 Pandemic	Full Review	NCCEH
18NOV2020	Outdoor Winter Dining during the COVID-19 Pandemic	Full Review	NCCEH
29OCT2020	What is known about whether vaccine injury-compensation programs and program elements affect vaccine acceptance and uptake and, where evaluations have been planned or conducted, how these programs are complemented by and timed in relation to other strategies to increase vaccine acceptance and uptake?	Full Review	COVID-END
09NOV2020	Rapid Review: What is the effect of the COVID-19 pandemic on the use and cessation of tobacco and vaping products?	Full Review	NCCMT

05NOV2020	What is known about anticipated COVID-19 vaccine-delivery program elements, and whether and how federated states are harmonizing these elements across constituent units of federations?	Full Review	COVID-END
04NOV2020	Rapid Review: What is known about the risk of COVID-19 transmission across different indoor settings in the community such as restaurants and gyms?	Full Review	NCCMT
26OCT2020	A Rapid Review of Disinfectant Chemical Exposures and Health Effects During COVID-19 Pandemic	Full Review	NCCEH
16OCT2020	High-humidity Environments and the Risk of COVID-19 Transmission	Full Review	NCCEH
16OCT2020	Rapid Review: What risk factors are associated with COVID-19 outbreaks and mortality in long-term care facilities and what strategies mitigate risk?	Full Review	NCCMT
16OCT2020	Rapid Review: What factors may help protect Indigenous peoples and communities in Canada and internationally from the COVID-19 pandemic and its impacts?	Full Review	NCCMT
08OCT2020	Rapid Review: What are best practices for risk communication and strategies to mitigate risk behaviours?	Full Review	NCCMT
28SEPT2020	Rapid Review Update 3: What is known on the potential for COVID-19 re-infection, including new transmission after recovery?	Full Review	NCCMT
25SEPT2020	Rapid Review: Food security: What is the impact of COVID-19 and related public health measures?	Full Review	NCCMT
21SEPT2020	Rapid Review Update 1: What is the effect of the COVID-19 pandemic on opioid and substance use and related harms?	Full Review	NCCMT
03SEPT2020	Rapid Review Update 1: Is there an increased risk of adverse maternal or fetal outcomes in women infected with COVID-19 during pregnancy?	Full Review	NCCMT
14AUG2020	Rapid Review: What is known about using wastewater surveillance to monitor the COVID-19 pandemic in the community? (Update)	Full Review	NCCMT
31JUL2020	Rapid Review: What factors increase the risk of COVID-19 outbreaks in congregate living settings? How do outcomes compare to outbreaks in community settings? (Update)	Full Review	NCCMT
26JUNE2020	What is known about best practices for infection prevention and control in inpatient psychiatric facilities?	Full Review	NCCMT

12JUN2020	Rapid review: what is known about the efficacy and cost-effectiveness of copper materials to reduce transmission of viruses?	Full Review	NCCMT
12JUN2020	Rapid review: what is the effectiveness of cohorting virus-positive residents to shared rooms in care facilities?	Full Review	NCCMT
08JUN2020	Are any jurisdictions using isolation periods other than 14 days in response to COVID-19? If yes, what is their rate of COVID-19 cases?	Full Review	NCCMT
08JUN2020	What is known about the duration from exposure to symptoms or diagnosis for COVID-19?	Full Review	NCCMT
29MAY2020	How have affected jurisdictions handled previously positive cases in the context of re-exposure/re-infection?	Full Review	NCCMT
29MAY2020	What serological tests are available, and what are the sensitivities and specificities?	Full Review	NCCMT
22MAY2020	Impact of COVID-19 on Indigenous communities in Canada	Full Review	NCCMT
22MAY2020	What is known about stigmatization related to COVID-19 in Canada	Full Review	NCCMT
15MAY2020	Role of indirect transmission in the pandemic	Full Review	NCCMT
15MAY2020	Evidence on potential for COVID re-infection	Full Review	NCCMT
15MAY2020	Impact of physical distancing on mental health	Full Review	NCCMT

Emerging Evidence on COVID-19

COVID-19 Summary of Face Shields to Prevent Transmission of SARS-CoV-2

Introduction

How effective are face shields at preventing SARS-CoV-2 virus transmission, with and without additional mask wearing?

This evidence brief summarizes the relevant research on face shields in preventing the transmission of respiratory droplets and aerosols from infected individuals to susceptible individuals, published until July 7, 2020. Eye protection and goggle use are not captured in this review.

Key Points

- Face shields are a form of personal protective equipment that has been used in healthcare settings (e.g., surgical/medical, dental, veterinary) to cover the face and mucosal membranes (eyes, nose, mouth) and prevent infectious particle exposure from aerosols and body fluid spatter. A face shield is often used when performing medical procedures that increase the risk of aerosols or patient body fluid splashes, sprays or splatter and is worn with other personal protective equipment (e.g., medical masks, respirators, medical gowns) (Roberge, 2016).
- All studies included in this review are experiments conducted under controlled conditions. With the exception of one study which used influenza (Lindsley et al., 2014), the studies in this review did not use virus contaminated fluids.
- Studies on face shield use by healthcare workers report a protective effect particularly from patient generated splatter during specific medical procedures when used in combination with other protective equipment such as a surgical mask (Table 1 and Table 2) (Mansour et al., 2009; Mostaghimi et al., 2020; Shoham et al., 2016). Face shields have also been designed for the patient to wear when undergoing an aerosol generating procedure to contain the aerosols and protect the health care workers doing the procedure from exposure (Anon, Denne, & Rees, 2020;)
- Two simulation studies reported on droplet inhalation and exposure when wearing face shields as the only protective equipment (Table 1). Both studies report 90% of the large droplets were blocked by a cough aimed at the middle of the face shield (Lindsley et al., 2014; Ronen et al., 2020), however the protective effects decreased when the direction of the cough was varied (higher/lower/side). Over time (30 minutes) inhalation of small droplets was only reduced by 23% by the face shield (Lindsley et al., 2014).
- Three studies simulated coughing in an individual wearing the face shield and reported the level of contamination resulting from respiratory particles released (Table 1 and Table 2). Two studies report

the release of droplets and aerosols from around the openings in the face shield (Anon et al., 2020; Viola et al., 2020), while the third reports that the face shield provided a good forward barrier as no droplets reached a simulator 60 cm away (Ronen et al., 2020).

- The design of the face mask is reported to be important. Face shields that wrap further around the face, fully shielding the cheek area, wrap under the chin and any enhancements that minimize bioaerosol leakage/entry around the edges of the mask were more protective (Viola et al., 2020; Anon et al., 2020; Mostaghimi et al., 2020).

Overview of the Evidence

Few studies examine and report on the protective effects of face shields with or without masks. All identified studies report findings from simulation studies conducted in controlled laboratory settings, and do not necessarily account for real-world parameters (e.g., height differences among individuals, temperatures, humidity, wind velocities etc.) or the infectious dose. None of the studies used SARS-CoV-2 in the simulation. Variation across studies in their design, how and what outcomes were measured and what face shields were used meant the findings are not directly comparable. Although the available body of evidence does support the use of face shields alongside medical masks in health care settings, results of face shields alone were less consistently protective.

CONTENTS

EFFECTIVENESS OF FACE SHIELDS

There were no studies identified that evaluated the efficacy of face shield use in the field to prevent respiratory infection transmission.

In health care settings, two simulation studies evaluating various medical procedures find face shields, usually worn with a medical mask, protect healthcare workers' faces from fluid splatters by providing a physical barrier, and some protection from the inhalation of small aerosols and droplet nuclei (Table 1) (Mansour et al., 2009; Shoham et al., 2016). One study found the combination of a face cover and face shield to be more effective than either alone (Mansour et al., 2009), while the other found a full face shield provided better protection than the combination of an eye shield and a surgical mask (Shoham et al., 2016).

Two studies reporting on the effectiveness of face shields used as the only protective equipment compared face shields to other face covers report face shields are effective barriers for the short term blockage of droplets (Lindsley et al., 2014; Ronen et al., 2020). The study by Ronan et al., describes the short term protective effects of a face shield blocking 90% of splatter from a cough 60 cm away directed at the center of

the face shield. A face mask in the same simulation blocked half the droplets. The protective effect of the face shield decreased significantly when the direction of the cough (higher/lower/side) was varied. (Ronen et al., 2020). Similarly, Lindsley et al., reported face shields reduce inhalation of large droplets by 90% and small droplets by over 60% immediately following a cough. However, the inhalation of smaller droplets was only reduced by 23% as the time since coughing (i.e. aerosol generation event) increased to 30 min. This increase in aerosol and small droplet inhalation risk is attributed to the formation of smaller droplet nuclei over time that can leak in from the face shield edges (Lindsley et al., 2014).

The three simulation studies evaluating the level of contamination by respiratory particles from an individual wearing a face shield reported a good forward barrier to projecting respiratory droplets (Ronen et al., 2020), however powerful backward and downward bioaerosol leakage jets were measured (Viola et al., 2020; Anon et al., 2020). Gross droplet splatter and contamination below the neck and chest area took place when a patient wearing a standard face shield underwent a simulated aerosol generating procedure, like flexible endoscopy (Anon et al., 2020). Observations of airflow and bioaerosol ejection while wearing different types of face shields find front airflow generated from breathing, loud speaking and coughing to be largely reduced, but substantial aerosol leakage to still take place. Powerful leakage jets of bioaerosols were identified near the wearer's brow region and in the downward direction (Viola et al., 2020). However, despite the leakage measured in two studies, the third reported a good forward barrier based on experimental results from a breathing simulator positioned 60 cm from a coughing simulator wearing a face shield that did not inhale or detect splatter droplets (Ronen et al., 2020). Thus, bioaerosols escape into the environment when an individual wears a face shield.

Table 1: Literature on face shield performance

Publication Title	Key Outcomes	Reference
Experimental and Simulation Studies		
Efficacy of Face Shields Against Cough Aerosol Droplets from a Cough Simulator	Simulation experiment (face shields only): Effectiveness of face shields in blocking the transmission of aerosols is measured using a breathing simulator intended to mimic a healthcare worker, and a cough aerosol simulator loaded with Influenza virus. The study finds more than a 90% reduction in larger aerosol (mean diameter of 8.5 µm) inhalation risk from face shield use, and an over 60% reduction in the risk of inhaling smaller aerosols (size of 3.4 µm) immediately after coughing. Face shields led to only a 23% reduction in smaller aerosol inhalation risk when the coughs generating the aerosols occurred within the previous 30 min, the increase in risk was due to smaller particles staying airborne longer and floating around the face shield to be inhaled.	(Lindsley et al., 2014)
Face Coverings, Aerosol Dispersion	Simulation and human experiment (face shield vs. surgical mask, homemade mask, and respirator)	(Viola et al., 2020)

and Mitigation of Virus Transmission Risk	Researchers use a background oriented schlieren technique to investigate airflow ejection by individual volunteers and manikins using different face coverings during breathing, coughing and aerosol generating procedures. Bioaerosol leakage with different face covers (i.e. homemade and surgical masks, filtering facepiece respirators (FFP1, FFP2), N95 respirators, and light and heavy weight face shields) was visualized. Overall, the study finds all face covers substantially reduced the front flow of bioaerosols. Only the tested FFP diminished backward and downward leakage jets, whereas the tested surgical masks, homemade masks, N95 respirators and face shields demonstrated backwards and downward jets to various degrees. Specific to face shields, bioaerosol containing airflow was found to leak through the seams and joints of the tested face shields and be minimally displaced horizontally (a distance of few centimetres). Face shields also generated upward (brow region), downward, sideway, and strong backward leakage jets. Backward jets occur when air escapes from the side of face covers and are projected backwards at high speed, potentially resulting in a significant displacement. Powerful downward leakage jets were noted for face shields that did not curve below the chin, which allowed for unobstructed air flow in and out.	
Examining the Protection Efficacy of Face Shields Against Cough Aerosol Droplets Using Water Sensitive Papers	Simulation experiment (face shield only vs. mask, respirator or no equipment) This simulation experiment reported on the effectiveness of face shields used as the only protective equipment, with the objective of this study informing use of face shields by the general population outside of a health care setting. The study used a cough simulator that was carefully tuned to replicate human cough in terms of droplet size distribution and outlet velocity. The tested personal protective equipment were placed on a manikin head simulating human breathing. An Aerodynamic Particle Sizer (APS) and water sensitive paper were used to analyze the concentration and size distribution of particles that reach the manikin head. The study reports face shields are as effective as face masks in successfully blocking respiratory droplets (3µm in diameter) from a cough, and blocked fine particles (0.3µm) better than medical masks in the short term. In other words, while the medical mask	(Ronen et al., 2020)

	reduced the number of inhaled particles by roughly a factor of two, the face shield provided superior protection by blocking more than 90% of the otherwise inhaled particles when a simulated cough was directly at the face shield. These blocking effects were reduced when contamination of areas beyond the middle of the face (i.e. cheeks and neck) were considered. Furthermore, in experiments where the vertical distance between the cough and breathing manikin simulators were varied, droplet deposits on the face was no different from droplets deposited over the shield, and blocking efficacy was as low as 45% in some instances. No respiratory contamination of the surroundings was noted when the cough simulator was covered by a face shield (simulating an infected person wearing the face shield).	
Eye Protection in Orthopaedic Surgery	Simulation Experiment (face shield with a mask): Mannequin heads outfitted with different personal protective equipment and sprayed with fluorescent dye sprays find face shields that cover the eyes worn in combination with facemasks to be effective barriers. This combination of personal protective equipment reduced contamination by macroscopic droplets and/or debris by 64% during simulated femoral osteotomies.	(Mansour et al., 2009)
Comparison of Protection Against Ocular Contamination with Disposable Eyewear Products	Poster Presentation - 2016 (Face shield vs. eye protection with a mask) A simulation study of manikin heads outfitted with eye shields or face shields, with and without face masks and N95 respirators. Using a Glogerm fluorescent dye system, eye contamination from micro droplet occurred with combination surgical mask and eye shield, but no face contamination (i.e. eyes, nose or mouth) occurred when a full face shield was used.	(Shoham et al., 2016)
Review Literature		
Face Shields for Infection Control: A Review	A literature review on face shields as a form of personal protective equipment for healthcare workers, and discusses various face shield designs. All outlined evidence predates the emergence of COVID-19.	(Roberge, 2016)
Facial Protection for Healthcare Workers During Pandemics: A Scoping Review	A scoping review of face protection for healthcare workers. The review identified one study on efficacy of face shields (Lindsley et al., 2014) and concluded that face shields should not be used by health care workers as the primary protection for preventing	(Godoy et al., 2020)

	transmission of respiratory diseases, but they can be used with other facial protection.	

NOVEL FACE SHIELD SYSTEMS

Alternative face shield systems are presented as physical barriers that provide better protection from patient generated body fluid splatter.

Table 2: Novel face shield systems

Publication Title	Key Outcomes	Reference
Patient-Worn Enhanced Protection Face Shield for Flexible Endoscopy	Simulation experiment (face shield vs. enhanced face shield) A simulation proof of concept study compares aerosolized dye exposure and contamination when a patient wears a standard face shield vs. face shield of enhanced design with a tab closure system (covering the space under the chin) during endoscopy procedures. The enhanced design is reported to have contained simulated respiratory splatter within the confines of the enclosed space around the patients face and prevented bioaerosol escape under the neck/chin area.	(Anon et al., 2020)
Rapid Prototyping and Clinical Testing of a Reusable Face Shield for Health Care Workers Responding to the COVID-19 Pandemic	Development/evaluation of enhanced face shields The clinical utility and user comfort of 3 face shield prototypes among healthcare workers are surveyed. The effectiveness of each design in preventing droplet splatter was not investigated.	(Mostaghimi et al., 2020)

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an Excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: (Face and Shield). An additional search was conducted in PubMed to identify older, non-COVID-19 research on face shields using: (face and shield and (virus or respiratory)).

Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review. This review contains research published up to July 7, 2020.

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References

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Emerging Evidence on COVID-19

COVID-19 Summary of SARS-CoV-2 Transmission and Singing/Wind Instruments

Introduction

What is the risk of SARS-CoV-2 virus transmission from singing or playing a wind instrument in a choir, orchestra and or practice setting with other people?

This evidence brief summarizes what is known on aerodynamic transmission of respiratory droplets and aerosols from activities that involve deep breathing and singing; the epidemiological evidence around music-related activities that resulted in transmission of SARS-CoV-2; and risk assessments, mitigation strategies or other decision analyses that may be relevant to creating music in groups. This evidence brief highlights specific literature on possible infection transmission linked to singing published until June 26, 2020.

Key Points

- The available evidence suggests the activity of singing in indoor settings can contribute to amplified infection transmission of SARS-CoV-2 if an infected person is participating. Epidemiological reports of COVID-19 clusters with high attack rates linked to choir practice in the US, Singapore, and the Netherlands, as well as a karaoke bar in South Korea provide evidence that transmission has occurred during activities that involve singing (Tables 2 and 3).
- Primary evidence on wind and brass instrument use and SARS-CoV-2 transmission could not be identified. However, one descriptive risk assessment and one grey literature study of wind instruments indicate more research should be done on the risk of SARS-CoV-2 transmission from wind instrument aerosols (Table 3). One protocol to study wind instruments and safe playing was identified (Miller, Vance, Hertzberg, & Toohey, 2020).
- No evidence on mitigation strategies for musicians was identified.
- Experimental evidence and modelled scenarios on droplet dispersion and aerosolization of SARS-CoV-2:
    - Infectious particles are commonly expelled into the surrounding air by an infected person (e.g., breathing, speaking, sneezing, singing and coughing) and these particles may transmit SARS-CoV-2 to another person when inhaled (Table 1).
    - Airborne SARS-CoV-2 particles can exist in the form of aerosols, droplets, droplet nuclei or other small particles containing viral RNA. One study reports SARS-CoV-2 virus can remain viable within aerosols for longer than three hours (van Doremalen et al., 2020).

- No simulation studies have examined particle generation during singing or wind instrument use, but studies do report on speaking and coughing. For example, 1000s of virus containing particles are estimated to be produced during a minute of loud speaking and remain airborne for longer than eight minutes (Table 1) (Stadnytskyi, Bax, Bax, & Anfinrud, 2020).
- Mathematical models informed by particle physics and aerodynamics predict respiratory and saliva particles can remain suspended in air for long enough to be inhaled by another individual, and has the potential to be dispersed some distance away from the infectious source (Vuorinen et al., 2020) (Guerrero, Brito, & Cornejo, 2020; Zhao, Qi, Luzzatto-Fegiz, Cui, & Zhu, 2020) (Feng, Marchal, Sperry, & Yi, 2020). According to mathematical models, droplet size, humidity, temperature, airflow and air turbulence all impact the movement and decay of virus containing airborne particles (Table 1).

Overview of the Evidence

The available empirical body of evidence on SARS-CoV-2 transmission during singing is linked to a few choir clusters from early in the SARS-CoV-2 outbreak. These studies are retrospective outbreak investigations that are considered to be at high risk of bias and low quality evidence.

Laboratory simulations and modelled scenarios also provide theoretical evidence to support increased transmission of SARS-CoV-2 from activities such as speaking loudly. These studies appear to have been conducted without obvious flaws in their methodology and are considered moderate to high quality evidence.

Major knowledge gaps were identified in examining the evidence underpinning the review question, additional research is needed to assess the transmission risk associated with singing or playing instruments in a group setting. There is a lack of experimental evidence that fully characterize the risk and the circumstances that lead to transmission. The risk of transmission events from singing and playing wind instruments in a choir, orchestra and/or practice setting with other people is unknown, but theoretical evidence and recorded clusters attributed to this activity indicate that there is a risk.

CONTENTS

SARS-COV-2 DROPLETS AND AEROSOLS

Six experiments and five models investigate aerosolization of SARS-CoV-2 and characterize some of the circumstances under which aerosolization or droplet dispersions occur. Infectious particles are commonly expelled into the surrounding air by an infected person (e.g., breathing, speaking, sneezing, singing or coughing) and these particles may transmit SARS-CoV-2 to another person when inhaled (Table 1). Risk of transmission likely depends on the characteristics of the environment, the activity, the distance from and duration of time spent with an infected person. Airborne SARS-CoV-2 particles can exist in the form of aerosols, droplets, droplet nuclei or other small particles containing viral RNA. van Doremalen provides primary evidence to support the viability of SARS-CoV-2 virus particles in aerosols. The study reports SARS-CoV-2 virus can remain viable within aerosols for longer than three hours (van Doremalen et al., 2020).

No simulation studies have examined particle generation during singing or wind instrument use, but studies reported on speaking and coughing. Simulations have successfully visualized thousands of minute respiratory droplets and aerosols that are generated during normal speech, and remain suspended in air for longer than eight minutes (Anfinrud, Bax, Stadnytskyi, & Bax, 2020; Chanpong, Tang, Rosenczweig, Lok, & Tang, 2020; Stadnytskyi et al., 2020). Additionally, 1,000s of virus containing particles are estimated to be produced during a minute of loud speaking, and remain airborne for longer than eight minutes (Stadnytskyi et al., 2020). Coughing also generated respiratory droplets and aerosol that traveled average distances of two and a half meters and a maximum of four meters, as well as substantial droplet splatter on nearby healthcare workers (Chanpong et al., 2020; Loh et al., 2020). As such it is likely singing can also lead to the dispersion of infectious particles.

Mathematical models informed by particle physics and aerodynamics predict respiratory and saliva particles can remain suspended in air for long enough to be inhaled by another individual. And have the potential to be dispersed some distance away from the infectious source (Vuorinen et al., 2020) (Guerrero et al., 2020; Zhao et al., 2020) (Feng et al., 2020). According to mathematical models, droplet size, humidity, temperature, air flow, and air turbulence all impact the movement and decay of virus containing airborne particles (Table 1).

Table 1: Primary literature on SARS-CoV-2 aerosol and droplets

Publication Title	Key Outcomes	Reference
Experimental and Simulation Studies		
Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1	The stability and decay of SARS-CoV-2 and SARS-CoV-1 in aerosols was estimated using a Bayesian regression model SARS-CoV-2 virus remained viable in aerosols up to three hours hrs (duration of the experiment), with a reduction in infectious titer from $10^{3.5}$ to $10^{2.7}$ $TCID_{50}$ per liter of air.	(van Doremalen et al., 2020)
The impact of high-flow nasal cannula (HFNC) on coughing	A simulation study using healthy volunteers (n=5) found cough-generated droplets spread a mean distance of 2.48 meters (1.03 standard deviation) at baseline, maximum of 3.90 meters.	(Loh et al., 2020)

distance: implications on its use during the novel coronavirus disease outbreak	When wearing well-fitting High Flow Nasal Cannula, mean cough generated droplet spread was 2.91 meters (1.09) with a maximum distance of 4.50 meters.	
Aerosol-generating procedures and simulated cough in dental anesthesia	Aerosol and droplet splatter was visualized using a Glo Germ system. Simulated cough was found to produce more extensive splatter than test aerosol generating dental procedures.	(Chanpong et al., 2020)
Could SARS-CoV-2 be transmitted via speech droplets?	A planar beam of laser light passing through a dust-free enclosure is used to detect saliva droplets emitted while speaking. The investigation provides visual evidence that infection transmission from droplets and aerosols is possible. Preliminary observations find thousands of respiratory and saliva droplets emitted while speaking are much smaller than those emitted during coughing, and simple phrases such as "stay healthy" can generate thousands of small droplets with the potential to transmit infection. Researchers state additional studies are necessary to assess the viral titre present in speech-induced droplets based on COVID-19 severity.	(Anfinrud et al., 2020)
The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission	Sensitive planar beam laser light scattering observations and aerodynamic particle sizer (APS) measurements are used to visualize droplet dispersion and decay. The experiments find droplets generated during normal speech to decay within 8-14 minutes in close stagnant environments (similar to indoor environments, particularly with poor ventilation), and the longest decay times were observed for droplets with a diameter ≥12 µm when exiting the mouth. The researchers estimate 1 minute of loud speaking can generate a minimum of 1,000 virion containing droplet nuclei that remain airborne for more than 8 minutes. The findings suggest air suspended virus containing particles could be inhaled by others.	(Stadnytskyi et al., 2020)
Mathematical Models		
Publication Title	**Key Outcomes**	**Reference**
COVID-19: Effects of weather conditions on the propagation	A comprehensive mathematical model was established to explore speech generated droplet evaporation, heat transfer and kinematics under different conditions (e.g., temperature, humidity and ventilation). Low temperature and high humidity	(Zhao et al., 2020)

of respiratory droplets	facilitate droplet transmission and dispersion, but supresses the formation of aerosols. On the other hand, high temperature and low humidity promotes rapid loss of respiratory droplet mass (from evaporation) and reduce droplet travel distance, but these conditions increase transmission risk from aerosol particles. The study concludes current social distancing recommendations may not be sufficient to diminish airborne transmission risks as droplets can travel distances up to 6 meters.	
COVID-19. Transport of respiratory droplets in a microclimatologic urban scenario	Examined the spread of respiratory droplets in outdoor environments by applying a computational model of a sneezing person in an urban scenario under a medium intensity climatological wind. The spread of respiratory droplets is characterized by the dynamics of droplet size: larger droplets (400 – 900 μm) are spread between two to five meters during 2.3 seconds while smaller droplets (100 – 200 μm) are transported between eight and eleven meters in 14.1 seconds when influenced by turbulent wind.	(Guerrero et al., 2020)
Influence of wind and relative humidity on the social distancing effectiveness to prevent COVID-19 airborne transmission: A numerical study	Air transmission of cough droplets with condensation and evaporation effects are modeled between 2 virtual humans under different environments and wind velocities. Micro-droplets follow airflow streamlines and can be deposited on virtual human bodies (including head regions) at greater than 3.05 meter (10 feet) distances. High Relative humidity (99.5%) also leads to larger droplet sizes and greater deposition of cough droplets on surfaces (due to hygroscopic growth effects). Suspended micro droplets could be transmitted between the 2 virtual humans in less than 5 seconds. The study concludes due to environmental wind, convection effects, and relative humidity on respiratory particles emitted by humans, the frequently recommended 1.83 meters (six feet) of social distancing may not be sufficient to prevent inter-person aerosol transmission.	(Feng et al., 2020)
Modelling aerosol transport and virus exposure with numerical simulations in relation to SARS-CoV-2 transmission	Available evidence on aerosol transport in air is combined with 0D-3D simulations in physics-based models and theoretical calculations. Monte Carlo simulations indicate droplets produced by speech and cough (diameter < 20 μm) can become airborne and linger in the air from 20 minutes up to 1 hour, and be inhaled by others. The exposure time to inhale 100 aerosols (assumed to be an adequate infectious dose) is variable based on	(Vuorinen et al., 2020)

by inhalation indoors	the situation and can range from one second, to 1 minute, to 1 hour. 3D computational fluid dynamic (CFD) simulations suggest aerosols (dp <20 µm) can be transported over 10 meter distances in generic environments, dependent on relative humidity and airflow. Finally the rapid drying of expelled mucus droplets would yield droplet nuclei and aerosols which could potentially carry airborne virus particles. Such droplets (initial particle diameter of 50 µm to 100 µm) could remain airborne for approximately 20 seconds to 3 minutes.	

COVID-19 CLUSTERS ATTRIBUTED TO SINGING

Five published articles were identified that document outbreaks of COVID-19 related to singing and/or playing instruments. One outbreak of Skagit Valley, WA choir COVID-19 cluster with a secondary attack rate of 53-87% (Hamner et al., 2020) and a mathematical model based estimation of emissions generated in this scenario (Miller et al., 2020) suggest infection transmission in this cluster primarily occurred from sharing an indoor space with a single infectious individual who was singing. Multiple case cluster summaries highlight singing class, karaoke, music concerts and choir practice clusters from Japan, and Singapore (Furuse et al., 2020; Dalton, Katelaris, & Wilson, 2020., Wei et al., 2020). Risk of transmission depends on the characteristics of the environment, the activity, the distance from and duration of time spent with an infected person (Waddell., 2020).

Table 2: Literature on epidemiological investigations that (partially) attribute singing to transmission

Publication Title	Key Outcomes	Reference
High SARS-CoV-2 attack rate following exposure at a choir practice — Skagit County, Washington, March 2020	A choir practice in Washington, US involving 61 singers, including the symptomatic index case, led to 32 confirmed and 20 probable secondary COVID-19 cases (attack rate = 53.3% to 86.7%); 3 patients were hospitalized, and 2 died. Authors conclude transmission was likely facilitated by close proximity (within 6 feet) during singing practice and augmented by the act of singing.	(Hamner et al., 2020)
Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale	Case study of the Skagit County choir outbreak that explores infection risk variability based on the rates of removal of respiratory aerosols by ventilation, deposition onto surfaces and viral decay. Due to the high secondary attack rate a common fomite and person to person transmission are assumed unlikely. Shared	(Shelly L. Miller et al., 2020)

superspreading event	indoor air at the practice site, and high emissions of respiratory aerosols during singing are assumed to be the dominant factors linked to infection transmission. Modeled airborne infection risk assessment infers an emission rate of E = 970 (± 390) quanta per hour in this scenario from the single infectious index case.	
Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020	Investigation of 7 COVID-19 clusters identified in Singapore find asymptomatic transmission to have occurred. In two independent clusters infection transmission is attributed to multiple women attending music class (Cluster B, Cluster F) with confirmed cases.	(Wei et al., 2020)
Clusters of Coronavirus disease in communities, Japan, January-April 2020	Investigation of 61 clusters of >5 cases in Japan Jan 15- Apr 4. 18 (30%) healthcare facilities; 10 (16%) care facilities of other types, such as nursing homes and day care centers; 10 (16%) restaurants or bars; 8 (13%) workplaces; 7 (11%) music-related events, such as live music concerts, chorus group rehearsals, and karaoke parties; 5 (8%) gymnasiums; 2 (3%) ceremonial functions; and 1 (2%) transportation-related incident in an airplane. The largest non–healthcare-related cluster was >30 persons who attended a live music concert, including performers, audience members, and event staff. Many COVID-19 clusters were associated with heavy breathing in close proximity, such as singing at karaoke parties, cheering at clubs, having conversations in bars, and exercising in gymnasiums.	(Furuse et al., 2020)
Open with care: minimising COVID-19 superspreading settings in Australia	Risk benefit evaluation Karaoke rooms and choir practice where singing is involved is viewed as possible amplification of transmission risk due to people congregated in closely and the action of singing. Churches and religious gathering outbreaks have been recorded in the USA, S. Korea and Singapore. Characteristics of religious gatherings may increase risk of transmission due to activities such as singing, hugging and handshakes during greetings and services, passing of sacramental objects, close seating arrangements and sharing of food and refreshments. The article warns, in the Australian context, lifting of restrictions should be done carefully. In conditions of very low community spread and high proportions of susceptible populations, these superspreading events may be very important sources of cases.	(Dalton, Katelaris, & Wilson, 2020)

GREY LITERATURE ON COVID-19 RISK AND SINGING AND WIND INSTRUMENTS

This table summarizes relevant grey literature. Two outbreaks, one in the Netherlands involving a large choir and orchestra and a second associated with a karaoke outbreak in South Korea. A risk assessment, an experiment and a protocol for future research on the risk of transmission due to playing wind instruments. As well as two previously conducted evidence summaries by Alberta (May 22) and Newfoundland (Jun 1), which also capture several guidance documents and position statements.

Table 3: Grey literature on infection transmission attributed to singing and wind instruments

Publication Title	Key Outcomes	Reference
Wind instrument aerosol in Covid Era - COVID-19 and horns, trumpets, trombones, euphoniums, tubas, recorders, flutes, oboes, clarinets, saxophones and bassoons	Risk Assessment This risk assessment provides an overview of the different activities involved in playing wind instruments that may result in aerosols or direct transmission. • There is no direct evidence, but indirect evidence suggests it may exceed normal background risk of transmission. • The authors describe common practices among musicians that have the potential to spread the virus. The practice of sharing or touching other musicians' reeds was described as high risk and there were no recommendations for disinfection of reeds. • The authors conclude there is insufficient evidence to properly assess the risk of SARS-CoV-2 transmission due to playing instruments with other people.	(Schwalje & Hoffman, 2020)
Aerosol generation from playing band instruments and risk of infectious disease transmission	This is a protocol for a study being conducted at University of Colorado. The goal of this project is to provide measurements and risk modelling estimates in a timely manner to better understand particle emissions from playing band instruments. Proposed four activities: 1. Flow imaging studies to qualitatively document the emission and particulate plume through photography and lasers 2. Chamber studies to measure particle generation rates from the following activities:	(Shelly L. Miller et al., 2020)

	a. 5 woodwinds – flute, clarinet, oboe, saxophone, bassoon b. 4 brass – french horn, trumpet, trombone, tuba c. The 4 vocal ranges – soprano, alto, tenor, bass d. Musical theatre – talking, monologue, singing, dancing (male and female actors) e. Elementary – male and female in grades 3-5 f. Aerobic simulation (marching band, show choir, dance, etc.) 3. Field rehearsal studies measuring concentrations in a rehearsal room with multiple players the University of Colorado Boulder (contingent upon IRB and campus approval) 4. Modelling of risk of transmission using the Wells-Riley Model	
Bamberg Symphony Orchestra: Scientists measure aerosol emissions	On-line publication (in German) Scientists at the Bamberg Symphony Orchestra use air currents to measure how many aerosols are emitted by a trombone, clarinet or horn. The emitted suspended matter is considered to represent the potential for air contaminated with SARS-CoV-2 to be expelled from the instrument if the musician was infected.	("Bamberg Symphony Orchestra: Scientists measure aerosol emissions," 2020)
(LEAD) Itaewon-tied cases rise to 153, karaoke facilities emerge as infection routes	Online newspaper article Infections in Seoul, South Korea linked to nightspots in the neighborhood of Itaewon, karaoke facilities are suspected infection transmission sites.	("(LEAD) Itaewon-tied cases rise to 153, karaoke facilities emerge as infection routes," 2020)
That one passion that did go on, with disastrous consequences.	Online newspaper article This outbreak involved 102 COVID-19 cases among 130 members of a choir and orchestra in Amsterdam, Netherlands. At the beginning of the outbreak, the group continued to practice despite members of the choir becoming ill. Based on the sequence of events and illnesses, there were potentially multiple transmission events.	(van der Lint, P., 2020)
COVID-19 quick response report: Choirs and COVID-19	Quick response report on the evidence with respect to choirs and COVID-19 up to June 3, 2020. The authors summarize many of the guidance documents, expert opinions and evidence on choirs and transmission of SARS-CoV-2.	(Williams, S and Navarro, P., 2020)

Singing as a risk for transmission of SARS-CoV-2 virus	Rapid review on the evidence and guidance around singing as a risk of transmission. It was last evaluated May 22, 2020. The review includes non-SARS-CoV-2 literature relevant to singing and the potential to spread pathogens. The report on choir related transmission events of influenza A, and tuberculosis.	(Kania-Richmond, A and Sharpe H., 2020)

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an Excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: sing, karaoke, choir, wind and instrument, music, singing, vocalize, religious, church. An additional search for grey literature was conducted using search strings (COVID-19 or SARS-CoV-2) AND (choir or music or (wind and instrument)) in google. Previously conducted reviews were sought from the NCCMT repository, CADTH, and SPOR evidence alliance.

Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review. This review contains research published up to June 26, 2020.

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Emerging Evidence on COVID-19

Evidence Brief of Aerosol Generating Procedures in Dental Care Settings

Introduction

What is the existing evidence of SARS-CoV-2 transmission in dental settings, and the infection transmission from Aerosol Generating Procedures (AGP) use in dental care?

AGP can increase risk of infection transmission from an infected patient to a healthcare worker due to close proximity and generation of aerosols in large volumes. This evidence brief summarizes the available literature and guidance on aerosol generating procedures (AGP) in dental care settings as they relate to SARS-CoV-2 transmission and can be used with the evidence summary on aerodynamics of SARS-COV-2 dated May 28, 2020, which summarizes the evidence on aerosolization of SARS-COV-2 - available through the PHAC emerging sciences secretariat.

Key Points

- No published reports of COVID-19 transmission, clusters, or outbreaks in dental care settings could be identified.
- SARS-COV-2 aerosolization:
    - Air samples collected from hospital care settings treating COVID-19 cases have demonstrated SARS-COV-2 RNA contamination, likely from aerosols and small respiratory droplets (Guo et al., 2020; Liu et al., 2020; Santarpia et al., 2020). SARS-CoV-2 is found to remain viable in aerosols for up to 4 hours, but neither the infectiousness or the infectious dose of these particles has been established (van Doremalen et al., 2020).
    - Dental procedures can induce gag reflexes leading to increased saliva secretion and coughing in patients. High speed dental instruments can create high volumes of aerosols containing water, saliva, blood, microorganisms and other debris (Ather, Patel, Ruparel, Diogenes, & Hargreaves, 2020; Jamal et al., 2020; Sales, Sales, & Da Hora Sales, 2020).
    - A recent publication by Workman et al., reports on cadaver simulations where aerosolization risks linked to endonasal procedures were assessed (Workman et al., 2020). The study concludes high-speed surgical drill procedures resulted in substantial aerosol contamination in all tested conditions. These findings may be extended to dental drills and procedures that are considered aerosol generating.

- Guidance Documents:
    - Published guidance indicates confirmed and suspected COVID-19 patients should NOT be treated in routine dental practice settings, and only be managed in negative-pressure infection isolation rooms (AIIR). (Ather et al., 2020; Jamal et al., 2020)
    - Reviews of multiple COVID-19 dental guidance documents indicate that some procedures and equipment used are associated with increased risk of aerosol generation and should be either avoided or modified during the COVID-19 pandemic (Table 1). Specific guidance linked to aerosol generating procedures and instruments from these publications are summarized below.
        - Intraoral Radiographs should be avoided and replaced with extraoral imaging such as panoramic radiography or cone-beam computed tomographic imaging when intraoral imaging is unavoidable (Ather et al., 2020; Jamal et al., 2020; Meng, Hua, & Bian, 2020).
        - Use of a rubber dam to minimize splatter generation is the standard of care for nonsurgical endodontic treatment. Recommendations suggest it may be advantageous to place the rubber dam so that it covers the nose (Ather et al., 2020; Jamal et al., 2020; Sales, Sales, & Da Hora Sales, 220). Also, when the rubber dam is applied, extra high-volume suction for aerosol and spatter is recommended along with regular suction (Peng et al., 2020).
        - Ultrasonic instruments such as triplex syringes, high-speed hand pieces, ultrasonic scalers, air abrasion devices, and intra-oral sandblasters are identified to be associated with increased aerosolization risk that should be avoided or the use minimized (Ather et al., 2020; Jamal et al., 2020; Meng et al., 2020; Sales et al., 220). If the use of such equipment is unavoidable, the application of high volume saliva ejectors are recommended alongside applicable instruments (Ather et al., 2020; Jamal et al., 2020; Meng et al., 2020).
        - To minimize the risk of dental aerosols, it is recommended that hand instruments, low-speed hand pieces, instruments without water spray and hand piece with an anti-retraction valve or other anti-reflex technology are used where possible (Ather et al., 2020; Jamal et al., 2020).
        - Peng et al., suggest the use of dental hand pieces without anti-retraction function should be prohibited during the epidemic period of COVID-19. Instead, anti-retraction dental hand piece with specially designed anti-retractive valves or other anti-reflux designs are strongly recommended as an extra preventive measure for cross-infection. It is important to note these recommendations are based on previous evidence from Hepatitis B infection transmission in dental care settings (Peng et al., 2020).

Overview of the Evidence

Currently, there is no published reports of COVID-19 clusters or outbreaks linked to dental care settings. No published simulation studies have specifically assessed droplet dispersion or aerosol generation of any dental procedures since the emergence of COVID-19. The designation of AGP in dental setting is largely based on evidence from medical procedure based simulations or national guidance from various dental associations. The available body of evidence from medical procedures is small, largely theoretical, and does not consider the infectiousness of SARS-CoV-2 aerosols specifically, yet the evidence does not appear to be of low quality.

Aerosol Generating Procedures (AGP) and COVID-19 transmission in dental care are understudied topics with substantial knowledge gaps. These areas would benefit from additional research and reporting that focus on COVID-19 pandemic experiences in dentistry.

CONTENTS

COVID-19 GUIDANCE FOR DENTAL CARE SETTINGS

Table 1: Five reviews describe aerosol generating dental procedures, the underpinning evidence and available guidance on minimizing aerosols from dental procedures.

Reference	Key Features
Ather et al., 2020	Provides a brief overview of the epidemiology, symptoms, and routes of transmission of COVID-19, as well as specific recommendations for dental practice during the current pandemic. These recommendations are informed by the emerging evidence on SARS-CoV-2 and past experiences from SARS-CoV transmission in healthcare settings.
Jamal et al., 2020	Reviews and summarizes COVID-19 guidance published by multiple national dental associations, including guidelines from American Dental Association, Scottish Dental Clinical Effectiveness Programme, New Zealand Dental Association and International federation of Endodontic Association - Indian Endodontic Society joint statement, and American Association of Endodontics.
Meng et al., 2020	Discusses aerosol producing procedures and techniques that were avoided at a Hospital of Stomatology in Wuhan, China during the emergence of the COVID-19 pandemic in early 2020.
Peng et al., 2020	Provides an overview of the available evidence on COVID-19 infection transmission routes, and details COVID-19 infection prevention and guidance for dental settings. The authors strongly advocate for prohibited use of dental hand pieces without anti-retraction function during the pandemic. The evidence against the use of hand pieces without anti-retraction function is from studies investigating cross infection risk from Hepatitis B virus (not a respiratory virus).
Sales et al., 2020	Examines the available literature and provides recommendations for dental care in light of the COVID-19 pandemic. Recommends the avoidance of high-speed instruments and the use of rubber dams to mitigate aerosol risk.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the emerging sciences group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: aerosol, dental

This review contains research published up to June 9, 2020.

EEach potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

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Emerging Evidence on COVID-19

Evidence Brief on Infection Risk from Eye Exposures to Inform Contact and Droplet Precautions

Introduction

This evidence brief summarizes the available evidence on whether the use of eye protection in addition to standard medical masks and respirators prevent infection transmission to Healthcare Workers (HCWs) caring for COVID-19 cases. Particularly pauci- or asymptomatic COVID-19 patients.

For the purposes of this review, COVID-19 is a respiratory infection that is primarily transmitted by droplets, and possibly aerosols, during close unprotected interactions [1]. Speaking, coughing, and sneezing by symptomatic patients can lead to infection transmission due to small virus-laden droplets (and possibly aerosols) being expelled into the healthcare environment [1-4]. Coughing is the most commonly reported symptom among COVID-19 cases in Canada [5].

Key Points

- No studies to date have specifically investigated or reported COVID-19 infection due to SARS-CoV-2 exposure of ocular surfaces due to interactions with asymptomatic and pre-symptomatic cases. Key evidence that support the use of eye protection by healthcare workers to minimize infection transmission of coronaviruses is outlined below (and in Table 1)
    - A systematic review and meta-analysis by Chu et al., examine the available evidence from observational studies on coronavirus (SARS-CoV-2, MERS-CoV, SARS) transmission risk from physical distancing, facemask and eye protection[13]. Based on the pooling of primary study data on SARS and MERS the reviewers conclude eye protection used in conjunction with surgical mask/ respirator further mitigates coronavirus infection transmission risk compared to face protection alone (risk difference and adjusted odds ratio between eye protection vs. no eye protection is estimated to be -10.6% 95% CI -12.5 to -7.7 and aOR 0·22, 95% CI 0·12 to 0·39 respectively).
    - ACE-2 receptors, a cellular receptor for SARS-CoV-2 virus attachment are found in human eye tissue. Numerous studies, including a systematic review, provide molecular biological evidence that SARS-CoV-2 can use optical tissues (i.e. the eye) as a portal of entry to infect human hosts [14-18].

- SARS-CoV-2 viral RNA has been identified from ocular swabs and during autopsy of COVID-19 cases with and without ocular manifestations [19].

- Exposure data from multiple hospitals during the SARS outbreak in Ontario, Canada provide observational data that reported eye protection reduced the incidence of SARS infections among responding healthcare workers [20].

- Available guidance for healthcare worker precautions indicate:

  - Infection prevention and control (IPAC) guidance recommend the use of contact AND droplet precautions (i.e. use of gloves, masks, face shields, and goggles) when healthcare workers 1) interact with symptomatic COVID-19 patients, or 2) are in proximity to any aerosol generating procedure - regardless of acute respiratory infection symptom presentation in the patient [6-8].

  - IPAC best practices specific to COVID-19 also recommend a point of care risk assessment be applied (based on the patient, the interaction, and the task) to determine additional precautions necessary for ALL patient and visitor at this time [6].

- Emerging evidence suggests the absolute risk of exposure of healthcare worker contact with a SARS-CoV-2 infected person increases with the prevalence in the community.

  - Serological testing of hospital workers in Italy revealed healthcare IgG positivity to be associated with the geographical prevalence of COVID-19 infections in the region [11].

  - COVID-19 outbreak data from Ontario's nursing homes also show associations between outbreaks and the incidence of COVID-19 infections in the surrounding health regions and nursing home bed-size [12].

Overview of the Evidence

A recent systematic review and meta-analysis presents the available evidence on eye protection and betacoronavirus (SARS, COVID-19/SARS-CoV-2, MERS) transmission, these estimates are considered to be of low certainty via the application of GRADE and do not include COVID-19 data. The review identified a single COVID-19 study [21] conducted in healthcare workers, however no SARS-COV-2 infections occurred among health care workers in either group.

Although observational study data on the protective effects of eye protection specific to COVID-19 transmission in healthcare is lacking, molecular biology data from other studies do provide evidence to support the plausibility of SARS-CoV-2 infection using the host eye as a portal of entry. The available evidence offers low certainty that the reported protective effects of wearing eye protection will not change with future research. There are knowledge gaps in the research that estimate infection transmission risks to healthcare workers, and under what circumstances that risk may be considered to increase or decrease.

CONTENTS

INFECTION VIA OCULAR EXPOSURE

COVID-19 is a respiratory infection that is primarily transmitted by droplets, and possibly aerosols, during close unprotected interactions [1]. Speaking, coughing, and sneezing by symptomatic patients can lead to infection transmission due to small virus-laden droplets (and possibly aerosols) being expelled into the healthcare environment [1-4]. Coughing is the most commonly reported symptom among COVID-19 cases in Canada [5].

Guidance for most high risk healthcare interactions during the ongoing pandemic would suggest droplet AND contact precautions. In instances where healthcare workers are required to interact with people of unknown COVID-19 status, IPAC best practices recommend a point of care risk assessment be applied as SARS-CoV-2 is a novel and emerging pathogen [6-8]. These risk assessments are intended to guide the use of appropriate additional precautions during potential COVID-19 patient interactions, and should be based on the patient, the specific interaction, and task to be performed by the healthcare worker. COVID-19 prevalence within the patient catchment areas should be considered when assessing transmission risk and use of additional precautions.

Table 1: Literature on infection transmission risk from ocular surface exposures.

Reference	Relevant Findings	Infection
Primary Literature		
Burke, RM et al [21]	The study reports on varied personal protection equipment (PPE) use among healthcare workers attending to the early travel related cluster of COVID-19 cases in the US. This is the only study (to date) to consider and provide data on selective personal protection equipment use among healthcare workers during COVID-19. Relative risk of COVID-19 infection based on eye protection vs. no eye protection can NOT be estimated as no secondary cases among healthcare workers were identified.	SARS-CoV-2
Ma, D et al [14] Lange, C et al [15] Zhang , L et al [16] Zhou, L et al [18]	Human eye tissue is found to express ACE-2 receptors, cellular receptors for SARS-CoV-2, thus confirming the ability of the virus to infect a host via the eye.	SARS-CoV-2
Raboud, J et al [20]	According to a multicenter investigation of a past SARS outbreak in Toronto, inconsistent goggle and eye protection when entering a patient room increased healthcare worker infection risk (n=624). A statistically significant association between eye protection and infection were identified, suggesting conjunctiva could have been a portal of pathogen entry.	SARS-CoV

Key Commentaries and Reviews		
Chu, D et al [13]	The review captures evidence available up to May 3rd, 2020 A systematic review and meta-analysis by Chu et al., examine the available evidence from observational studies on coronavirus (SARS-CoV-2, MERS-CoV, SARS) transmission risk based on eye protection. The review concludes eye protection alongside mask/respirator use is associated with a reduction in coronavirus infection transmission (Risk Difference of -10.6% (95% CI -12.5 to -7.7) and adjusted odds ratio 0·22, 95% CI 0·12 to 0·39 respectively with low certainty). SARS-CoV-2 are not considered in the eye protection risk estimates as this evidence does not presently exist. (Ref to Burk et al)	SARS-CoV-2 MERS-CoV SARS
Aiello, F et al [17]	A systematic review by Aiello summarizes the available information on the presence of SARS-CoV-2 in cornea, conjunctiva, lacrimal, sac and tears. The review confirms SARS-CoV-2 can be present and infect eye tissue, and therefore may use ocular structures as an additional transmission route.	SARS-CoV-2
Lu, C-W et al [22]	Commentary where authors refer to a media report (in Chinese) where infection transmission in a worker wearing an N95 mask but no eye protection was reported to have occurred.	SARS-CoV-2

Methods:

A daily scan of the literature (published and pre-published) is conducted by the emerging sciences group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a RefWorks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. An additional target keyword search was conducted on Pubmed to identify relevant citation not specific to COVID-19 and SARS-COV-2. Search terms used included: ocular, eye, ACE2, contact precautions, and droplet precautions,
Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

This review contains research published up to June 2nd, 2020.

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Emerging Evidence on COVID-19

Evidence Brief of De-escalation of Social Bubbles

Introduction

What evidence is available on the de-escalation of "household bubbles", is there suggestions for how we can decrease the network segmentation of communities to larger networks?

This review will examine the evidence on the concept of network segmentation. This has been implemented within the general public as "social bubbles". This concept refers to limitations on individual interactions with people outside of their closed network (e.g. immediate family). As we move to different phases of the epidemic, it is of interest to understand what impact increasing the social bubble size or segmented networks may have on the epidemic. This evidence brief includes literature up to June 15, 2020.

Key Points

- This evidence brief consists of four predictive models, three of which are recent preprints and have not undergone the peer-review process.
- One preprint was identified that directly models social bubbles and real world options using the UK as the case study. The study reports that single family bubbles are estimated to have reduced the number of cases by 17%. In their model they explore relaxing the single household bubble to different scenarios of multiple households using three different secondary attack rates and Ro as the outcome. Ro is shown to increase as restrictions are relaxed, but some of the limited options appear to have minimal increase in risk.
- Three social network models also provide some evidence to support that larger, but still closed and segmented networks offer a protective effect against introduction of SARS-CoV-2. The larger a segmented network and the more contacts outside of that network, the higher the risk of virus introduction.
- There are many studies that look at the impact of social distancing more generally and in combination with other interventions. They have not been summarized in this evidence brief, but are available upon request as they are collected within the Public Health Intervention evergreen review.
- One protocol for a systematic review on physical distancing interventions was also identified, but it will not be conducted until October 2020.

Overview of the Evidence

The concept of reducing transmission of SARS-CoV-2 by restricting close interactions to a very strict, small network (i.e.: a single family) is an effective intervention. Increasing the size of the network or de-escalation of the intervention is important to do carefully and not too quickly so control over the epidemic is maintained while slowly lifting restrictions. As there are few observations in the literature, the evidence is largely

contained in a few recent preprints that report on predictive models. These models are based on scenarios and are parameterized using observational data from the outbreak; caution should be exercised in using these findings, as the extent to which the results can be generalized to the local context is variable.

CONTENTS

SOCIAL BUBBLES

Four predictive models explored concepts of social bubbles using agent-based models and other network models to demonstrate the protective impact of having closed and limited contact networks during the COVID-19 epidemic (Block et al., 2020; Leng et al., 2020; Sneppen & Simonsen, 2020; St-Onge, Thibeault, Allard, Dube, & Hebert-Dufresne, 2020). One model directly explores a range of relaxing options for contact restrictions and explores the implications using Ro (Leng et al., 2020). These models explore and explain the concept of small-segmented community networks providing increased resistance to an introduction of the virus event into smaller networks. They also explore the activities that degrade the protection of a segmented network. This occurs when an individual from a closed network interacts with other networks and is particularly higher risk when the interaction is within a random gathering event where unknown people mix e.g. public transportation, commuting to a workplace outside of the segmented network, social places such as bars and restaurants, or sporting events. However, the extent that these estimates can be used is unknown as they were based on the epidemic dynamics in a specific place.

Table 1: Modelling studies on social bubbles or restricted social networks

Reference	Study Description	Relevant Outcomes
(Leng et al., 2020) *Preprint*	Individual-based model: Using the UK as a case study, a mathematical model was used to assess the effectiveness of various social bubble strategies as part of a gradual lockdown exit strategy. Using a base case where non-essential shops and schools are closed, the household attack rate is 20%, and R0=0.8, a number of social bubble strategies are simulated. Results demonstrate that in this base case scenario, social bubbles reduced cases and fatalities by 17% compared to an unclustered increase of contacts.	Keeping the secondary attack rate = 20% constant. The base scenario is single family bubbles Ro = 0.8 The following scenarios show how Ro would be expected to change with moderate relaxing of contact restrictions: 1. Allowing all households with primary school age children to pair up Ro= 0.85 2. Allowing all households with children of any age to pair up = 0.90 3. All single occupancy households to link up with other single occupancy households 0.85 4. All single occupancy households to

	Clustering contacts outside the household into exclusive social bubbles is an effective strategy of increasing contacts while limiting some of the associated increase in epidemic risk.	link up with any other household Ro=1.00 5. Scenarios 1 and 3 Ro=0.90 6. All households pair up Ro=1.11
(Block et al., 2020)	Stochastic Model: Adopting a social network approach, we evaluate the effectiveness of three distancing strategies designed to keep the curve flat and aid compliance in a post-lockdown world. We demonstrate that a strategic social network-based reduction of contact strongly enhances the effectiveness of social distancing measures while keeping risks lower.	3 scenarios for social distancing- "strengthening community and seeking similarity strategies". - Individuals choose their contact partners based on similarity of a predetermined individual characteristic. This facilitates forming small groups e.g. neighbourhood/ small organization. - Individuals consider who their contact partners interact and do not see people outside of a defined contact network. Build bubbles through repeat contacts. Individuals decide who they want to interact with. This can be used with work units as well. It is difficult for the virus to penetrate these micro-communities.
(St-Onge et al., 2020) *Preprint*	Canadian authors (Laval University) SIS/SIR models using a network science framework to look at the impact of having structures aka gatherings (groups/ classrooms/ sports teams etc.).	- They demonstrate that localized epidemics can collapse if the group or gathering size remains below a threshold. - The threshold for the mesoscopic localization regime, with a transmission rate $\beta = 0.07$ was 23 people and below.
(Sneppen & Simonsen, 2020) *Preprint*	This agent-based model explored the impact of super-spreading events. In the base model super-spreading events had little effect on the epidemic, however under various intervention strategies, limiting diffuse social contacts – random gathering events - in settings such as bars, transportation, restaurants, parties, concerts and lecture halls is far more effective than limiting the same amount of contact events in the home and work setting.	- Limiting random gathering events had a large impact on the risk of super spreading events in this model under scenarios where various intervention strategies are implemented.

ON-GOING RESEARCH PROTOCOL

One systematic review protocol was identified that will summarize the evidence on isolation, quarantine, and social distancing strategies.

Table 2: Research protocols

Reference	Study Description	
(Regmi & Lwin, 2020)	What has been the impact of social distancing measures for preventing coronavirus disease 2019 [COVID-19]?	Studies will be targeted from July to October 2020 and will be restricted to peer-reviewed articles in English.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Sciences Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: social AND (bubble or bubbles or network). Results were crosschecked with the evergreen review on Public Health Interventions. This review contains research published up to June 15, 2020
Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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Emerging Evidence on COVID-19

Evidence Brief on Infectiousness and Symptom Onset

Introduction

Case studies, case series, contact and cluster investigations, and large population studies have demonstrated that transmission from pre- and asymptomatic cases frequently occur. This review aimed to summarize the literature on whether there is a difference in risk of transmission from persons who are pre- and asymptomatic infected cases compared to symptomatic cases.

Key Points

- Literature from healthcare settings highlight that transmission of COVID-19 is complex and related to the situation, duration of exposure, and individual factors.
    - Potential asymptomatic transmission has been documented in healthcare settings among facility residents, healthcare workers, and visitors [9, 10]. One outbreak in a skilled nursing facility in Washington State found that over half of residents who had positive results were asymptomatic at time of testing and that viable virus was cultured from pre-symptomatic cases up to 6 days prior to symptom development [9].
    - Another study was unable to demonstrate that asymptomatic transmission occurred among close contacts and in healthcare settings [8]. This study had low power, which may not have been sufficient to estimate a risk of transmission.
- Asymptomatic transmission has been shown to occur and may be linked to time spent in close contact with an infected person and other attributes of the scenario under which transmission occurred.
    - In a meta-analysis of mild (n=8) and asymptomatic cases (n=36), high rates of transmission were observed in situations of close quarters such as meals/family events, talking while travelling in car, private meetings, and prayer service [1]. It is likely that in such situations, asymptomatic spread is facilitated via contact (contamination of hands and fomites) as well as droplet generation via talking and singing.
- The estimated viral load in aerosols emitted by patients while breathing normally was on average 0.34-11.5 copies/cm^3 while the corresponding numbers for patients exhibiting respiratory symptoms were much higher at 10,900-366,00 copies/cm^3 per cough [2]. An individual spending time in a room with a person breathing normally (i.e. not exhibiting respiratory symptoms) was still likely to inhale tens to hundreds of copies of the virus.

- The proportion of transmission events from pre- and asymptomatic individuals in epidemiological investigations are highly variable (range <10-73%) (Table 1). Predictive models estimate 40-80% of transmission events occur from pre- and asymptomatic individuals [3-5].

- Transmission probabilities for symptomatic and asymptomatic cases may be very similar:

    - An analysis reported no significant difference in transmission rates between symptomatic and asymptomatic patients (6.3/100 and 4.1/100, respectively) [6].

    - Similar SARS-CoV-2 upper respiratory viral loads have been reported among asymptomatic and symptomatic patients [7].

Overview of the Evidence

There are few studies that directly compare transmission potential and infectivity between cases exhibiting respiratory symptoms and cases not exhibiting respiratory symptoms. For the purposes of this review the majority of evidence on this topic has been extrapolated from studies comparing symptomatic and pre-symptomatic/asymptomatic cases in general as well as in the healthcare setting.

Evidence on this subject is mainly described via case reports and contact tracing studies, which are at high risk of bias and thus are considered of low quality. Many studies are pre-prints and have not undergone a peer-review process. Overall, the outcomes should be interpreted with caution.

There were no risk assessments or studies that estimated the risk of infection for healthcare workers from caring for pre- or asymptomatic patients compared to symptomatic patients.

Estimates are changing as new research becomes available and there are many knowledge gaps. New research addressing these gaps could significantly change our understanding of SARS-CoV-2 infectivity among symptomatic and asymptomatic cases. More evidence demonstrating cultivatable virus from asymptomatic, pre-symptomatic, and symptomatic infections is required to determine infectiousness at different stages with greater certainty.

CONTENTS

EVIDENCE OF PRE- AND ASYMPTOMATIC TRANSMISSION POTENTIAL

It is important to keep in mind that transmission between cases depends on context and multiple factors. Individuals exhibiting respiratory symptoms are much more likely to isolate than asymptomatic individuals, explaining the high rates of pre- and asymptomatic transmission reported in this literature. Transmission studies of pre- and asymptomatic cases have shown that pre- and asymptomatic transmission does occur at high proportions in this pandemic, both in the general population and within healthcare settings. Thus, cases not exhibiting obvious signs of infection, including droplet generating events such as coughing and sneezing, can still be highly infectious.

Table 1: Studies providing evidence related to infectivity and transmission potential of pre- and asymptomatic infections. An indicator of the quality of evidence is provided (low, moderate, high) based on the risk of bias in the study design and reporting.

Reference	Description	Quality
Pre-symptomatic transmission estimations		
Arons, MM et al [9]	Outbreak investigation of residents of a skilled nursing facility in Washington, US Apr 3, 2020 end date -48 (63%) of residents that participated in point-prevalence surveys tested positive. -24 were pre-syptomatic and 2 were asymptomatic. - Viable virus was isolated from specimens collected 6 days before to 9 days after onset of symptoms. -This indicates that pre- and asymptomatic infection was a major factor in the transmission of SARS-CoV-2 within the facility.	low
Du, Z et al [12]	Case review of publically available data in China 468 infector–infectee pairs identified via contact tracing Jan 21-Feb 8, 2020 -Fifty-nine of 468 infector-infectee pairs (12.6%) indicated that the infectee had symptoms earlier than the infector. -These negative serial intervals suggest that pre-symptomatic transmission likely occurred.	low
Chun, JY et al [13]	Case review of publically available data in South Korea 72 infector-infectee transmission pairs Jan 23-Mar 31, 2020 -The pre-symptomatic transmission proportion was 37% (16–52% 95%CI).	low
He, X et al [14]	Contact tracing study in Vietnam, Malaysia, Japan, China, Taiwan, USA, Singapore 77 infector–infectee transmission pairs Dec 18-Mar 5, 2020 -Estimated that 44% (25-69% 95%CI) of secondary cases were infected during the index cases' pre-symptomatic stage.	low
Pham, TQ et al [15]	Case review of publically available data in Vietnam 33 infector-infectee transmission pairs	low

	Apr 15 – May 1, 2020 - Serial intervals were calculated from infector-infectee pairs and used to estimate the proportion of pre-symptomatic transmission events -27.5% (15.7%-40.0% 95%CI) of transmissions occurred pre-symptomatically	
Wei, WE et al [16]	Contact tracing study of 243 cases and 7 clusters in Singapore Jan 23-March 16, 2020 - seven clusters of cases with probable pre-symptomatic transmission were identified. -The overall proportion of transmission from pre-symptomatic cases comprised 6.3% of overall transmission.	low
Xia, W et al [17]	Investigation of 50 clusters in China Symptom onset prior to Jan 25, 2020 -124 cases where the secondary case contact with the first generation case occurred before symptom onset. The infectious curve showed that in 73.0% of the infectees, their date of being infected was before symptom onset of their infectors, particularly in the last three days of the incubation period.	Moderate
Casey, M et al [18]	Secondary analysis of published data reporting serial interval or generation time originating from Hong Kong, Tianjin, Singapore, Mainland China excluding Hubei, mixed sources, Shenzhen, northern Italy and Wuhan Dec 1 – Apr 15, 2020 -Subtracted incubation period from serial interval or generation time to infer pre-symptomatic infectious period and to estimate the proportion of pre-symptomatic transmission -Pre-symptomatic transmission was estimated to be 56.1% based on serial interval estimates and 65.5% based on generation time estimates.	low
Prakash, MK et al [19]	Secondary analysis of published data 1251 individuals reported in the literature -Estimated that 68.4% (67.0-69.7% 95%CI) of infections are caused by pre-symptomatic infectors.	low
Nishiura, H et al [20]	Log-normal distributed Bayesian model built from case review of published research and investigation reports 28 infector-infectee pairs Feb 12, 2020 end date -Accounting for right truncation and analyzing all pairs, authors estimated a serial interval of 4.0 days (3.1-4.9 95%CI). -This interval is shorter than preliminary estimates of the incubation period of approximately 5 days. - This suggests that pre-symptomatic transmission may make up a substantial proportion of secondary transmission.	low
Asymptomatic transmission estimates		
McMichael, TM et al [10]	Outbreak investigation of residents, healthcare workers, and visitors of a long-term care facility in Washington, US Mar 18, 2020 end date -167 confirmed cases of Covid-19, including 101 residents, 50 health care personnel, and 16 visitors were found to be epidemiologically linked to the facility. -No symptoms were documented in 7 (6.9%) of residents.	low
Yin, G et al [6]	Re-analysis of case and contact data in Ningbo, China 157 symptomatic cases and 30 asymptomatic cases	low

	January 21st to March 6th 2020 -Transmission rates for the symptomatic and asymptomatic patients were 0.063 and 0.041 respectively (no significant difference). -Odds of transmitting to a healthy individual by a symptomatic patient is 1.2 times of that by an asymptomatic patient (not statistically significant)	
Danis, K et al [21]	Cluster investigation in the French Alps with exportation and spread to several countries in Europe. Pre-symptomatic index case and 15 contacts in chalet; 172 contacts identified overall of cases. January 25, 2020 onward -Attack rate from asymptomatic index case 12/15 (75%) over 4 days contact; 1/15 asymptomatic. Only one of the 172 subsequent contacts was positive. -Viral load in one symptomatic case similar to asymptomatic case.	low
Wang, R et al [22]	Retrospective study in China 125 patients confirmed by real-time RT-PCR. Jan 20 to Feb 18, 2020. -22.4% of cases reported no known exposure to ill individuals.	low
Wong, J et al [23]	Case review in travelers and returning residents to Brunei 53 symptomatic infector-infectee pairs. Mar 5 – Apr 24, 2020 -21 (39.6%) had a SI of ≤3 days and 6 (11.3%) had zero or negative SI values, suggesting potential infectivity when asymptomatic.	low
Zou, L et al [7]	Viral load study of 17 symptomatic patients and 1 asymptomatic patient in China Jan 7 –26, 2020 - Analyzed the viral load in nasal and throat swabs - The viral load detected in the asymptomatic patient was similar to that in the symptomatic patients. This suggests the transmission potential of asymptomatic or pauci- symptomatic patients.	low
Li, R et al [5]	Mathematical model that simulates the spatiotemporal dynamics of infections in China Jan 10 – Feb 8, 2020 -estimated 86% of all infections were undocumented prior to the Wuhan travel shutdown, and that per person, these undocumented infections (many of whom were likely not severely symptomatic) were 55% as contagious as documented infections and the source of infection for 79% of documented cases	low
Riediker, M et al [2]	A one-compartment model was used to estimate the virus load concentration for a perfectly mixed room of volume 50 m^3 with one patient as source - The cumulative total emission per breath from normal breathing patients was 0.34 copies/cm^3 (air) for an average patient, and 11.5 copies/cm^3 for high emitters. -Virus emissions from coughing patients were much higher with a cumulative total emission per cough of 19,400 copies/cm^3 for an average patient and 651,315 copies/cm^3 for high emitters. - A person spending time in a room with an average emitting patient breathing normally has a high probability of inhaling tens to hundreds of	low

	copies of the virus even when practicing distancing. The probability is higher in the presence of a high emitter or if the patient is a coughing high emitter. -Conclude that the high predicted virus concentrations may be why frequent community transmission from asymptomatic cases and high rates of infection in medical staff have been reported. -Authors recommend strict respiratory protection when being in a room with a patient, whether the patient is symptomatic or not.	
Aguirre-Duarte, N [24]	Systematic Review and narrative report of Cluster/contact investigations. Primary studies of the ability of asymptomatic carriers to infect others. 9 articles reported on 83 asymptomatic or pre-symptomatic persons. Published in indexed journals January 1 to March 31, 2020. -While no specific estimates reported, there is evidence that Asymptomatic and pre-symptomatic people can infect others with COVID-19.	Moderate
Prakash, MK [1]	This synthesis is not conducted using standard systematic review methodology although a through search was conducted. 20 situations that resulted in 418 infections across 32 instances from 44 individuals (8 had mild symptoms, 36 were asymptomatic). Situation (transmission rate): • Meals/ family events (15.7% to 66.7%) • Meetings (1 hour private meeting, 72.7% (43.6-98.0) • Open work space with people movement (78.7% (CI. 70.3-85.3%)) • Singing (e.g. 2 hour practice 86.7% (CI.76.2- 93.2%), (25)) • Prayer service (resulted in 1-7 secondary infections per infected individual) • Travelling in a car (closed environment) and talking had a high risk (100% (CI.20-100%)) • Public transportation, wearing a mask with no talking (~0%) • Hotels 53.3% (30.1-75.2%)/cruise ships 28.1% (27.3-29.0%) where space is shared for days • Direct interaction with an infected sales agent 25.0% (10.2-49.5%) • Nightclub, attack rate among direct contacts >50%, among patrons of the nightclub 6.27% (5.15-7.61%) (26) • Restaurant overall attack rate (9.9% (CI: 5.3-17.7%) vs. those in the flow of the air conditioner 45.0% (25.8- 65.8%)	Moderate

Methods:

A daily scan of the literature (published and pre-published) is conducted by the emerging sciences group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searches were done using a combination of the terms "outbreak", "hospital", "long-term care" and "nursing". Previous evidence summaries and briefs on asymptomatic infection, super-spreading events, and infectious period, were used to gather evidence related to respiratory symptoms and infectivity. This review contains research published up to May 29, 2020. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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Emerging Evidence on COVID-19

Evidence Brief on SARS-CoV-2 Virus Dispersion Distance

Introduction

What is the impact of physical distancing of 1 meter, 1.5 meters and 2 meters on SARS-CoV-2 virus transmission risk?

The complex physics and particle dynamics surrounding droplet and aerosol dispersion, as well as the limited evidence on infectious dose and virus viability within expelled particles, make it difficult to confidently quantify SARS-CoV-2 exposure risk based on distance. This evidence brief highlights specific literature on expelled droplet and aerosol particle dispersion distance published up to June 22, 2020.

Key Points

- The body of evidence suggest particle speed, evaporation, air flow, humidity, temperature, all play a role in the distances virus laden respiratory particles can travel after being released by an infectious individual. As such, the protective effects of physical distancing at different distances also depend on the conditions in which they are practiced.
- The available empirical and modeled evidence suggests in some circumstances respiratory droplets and aerosols expelled from infectious individuals may travel distances greater than 2 meters (Table 1), but face coverings are effective at limiting dispersion distances to less than 0.5 meters (Table 2).
- According to mathematical models and fluid dynamic analysis, droplet size, humidity, temperature, air flow, and air turbulence all impact the movement and decay of virus containing airborne particles (Table1).
    - Some models predict small droplets and aerosols can travel distances as far as ten meters when generated by coughs or sneezes, and frequently conclude social distance of two meters is not always sufficient to negate airborne SARS-CoV-2 transmission (Feng, Marchal, Sperry, & Yi, 2020; Guerrero, Brito, & Cornejo, 2020; Zhao, Qi, Luzzatto-Fegiz, Cui, & Zhu, 2020).
    - Low temperature and high humidity are found to facilitate respiratory droplet transmission and dispersion. High temperature and low humidity are found to promote the rapid loss of respiratory droplet mass (from evaporation) thereby reducing droplet travel distance (Feng et al., 2020; Zhao et al., 2020).

- A multidisciplinary research consortium applied evidence based Monte-Carlo models and 3D simulations to investigate the physics of SARS-CoV-2 aerosol dispersion (Vuorinen et al., 2020). The investigators use computer simulations to demonstrate SARS-CoV-2 aerosols can travel distances up to ten meters, and the inhalation of sufficient concentrations of aerosols (100 virus laden particles was assumed to be infectious) is possible within one second to one hour depending on the surrounding conditions.
- Results from an agent based model reported a decreasing risk of a transmission event within indoor settings (e.g. supermarket) when the distance between individuals are increase from 30 cm to 2 meters (Hernandez Mejia & Hernandez-Vargas, 2020).
- Speed of movement also impacts droplet travel distance. Computer fluid dynamic simulations find, although a distance of 1.5 meters may be sufficient when standing still, distances greater than 1.5 meters are necessary when two individuals are running or moving fast as inertia of expelled droplets also impacts droplet spread (Blocken, Malizia, van Druenen, & Marchal, 2020).

- Laboratory simulation studies report human and manikin generated cough droplets can travel distances between one to two meters, and a maximum of four meters in some simulations (Loh et al., 2020; Rodriguez-Palacios, Cominelli, Basson, Pizarro, & Ilic, 2020; Viola et al., 2020).
- Two simulation studies investigated the effects of face covers on expelled particle dispersion distance. Both studies find the inclusion of face covers, such as face shields, filtering face piece respirators, surgical face masks, and homemade masks, reduced the dispersion of expelled droplets to less than 0.5 meter, even when coughing.
- A recent systematic review by Chu et al., quantifies the relative risk of beta-corona virus infection based on distance (Chu et al., 2020). The authors report transmission of viruses to be lower with physical distancing of 1 m or more, compared with a distance of less than 1 m (n=10 736, pooled adjusted odds ratio [aOR] 0·18, 95% CI 0·09 to 0·38; risk difference [RD] −10·2%, 95% CI −11·5 to −7·5; moderate certainty); protection was increased as distance was lengthened (change in relative risk [RR] 2·02 per m; p interaction=0·041; moderate certainty). There appears to be some ambiguity in the measurement of physical distance for some of the evidence included in this review and as such is of low quality. Therefore, it may be premature to quantify the relative risk of SARS-CoV-2 infection based on incremental differences in physical distance, due to the lack of sufficient evidence.
- Presently there are no observational studies that estimate SARS-CoV-2 infection transmission risk based on varied distance from an infectious source.

Overview of the Evidence

Publications appearing in the emerging literature up to June 22, 2020 have informed this evidence brief. The available body of evidence is limited and largely based on simulations under controlled conditions. These studies are of good quality but the generalizability of these results to real world situations is unknown. For this reason additional research on transmission of SARS-CoV-2 under varying situations and distances may change the conclusions of this review.

CONTENTS

SARS-COV-2 DISPERSION DISTANCE

Table 1: Primary literature on droplet aerosol dispersion distance

Publication Title	Key Outcomes	Reference
Experimental Simulation Studies		
The impact of high-flow nasal cannula (HFNC) on coughing distance: implications on its use during the novel coronavirus disease outbreak	A simulation study using healthy volunteers (n=5) found cough-generated droplets spread a mean distance of 2.48 meters (1.03 standard deviation) at baseline, maximum of 3.90 meters. When wearing well-fitting High Flow Nasal Cannula, mean cough generated droplet spread was 2.91 meters (1.09) with a maximum distance of 4.50 meters.	(Loh et al., 2020)
Face Coverings, Aerosol Dispersion and Mitigation of Virus Transmission Risk	Researchers use a background oriented Schlieren technique to visualize airflow and investigate the effectiveness of different face covers in mitigating aerosol dispersion during breathing and coughing. The study reports a thermal plume containing respiratory particles were visible at distances less than 0.5 meters during normal breathing simulated by human subjects and manikins. Thermal plume were visible approximately 1.1 meter away from the source mouth during manikin generated coughing.	(Viola et al., 2020)
Textile Masks and Surface Covers- A Spray Simulation Method and a "Universal Droplet Reduction Model" Against Respiratory Pandemics	Dispersion distances of respiratory droplets when wearing face coverings made of common household materials was measured using a bacterial-suspension spray simulation (mimicking a sneeze). Most bacteria-carrying droplets landed within 1.2 meters of the source with a textile mask compared to droplet travel distances of greater than 1.8 meters when no barriers (meant to mimic no face covering) were in place.	(Rodriguez-Palacios et al., 2020)
Mathematical Models and Simulations		
Publication Title	**Key Outcomes**	**Reference**
Towards aerodynamically equivalent COVID19 1.5 m social distancing for walking and running	Computer Fluid Dynamics study informed by previous data on droplet dispersion around a runner takes into account the potential aerodynamic effects introduced by a person movements (e.g. walking fast, running and cycling) on droplet travel distance. The study investigates whether a leading infectious person standing still and moving nearby a second susceptible person at a distances of 1.5 meters or more can pose any infection transmission risk. Although particle exposure is negligible when two people are standing 1.5 meter apart, if	(Blocken et al., 2020)

	the individuals are running or walking fast even at 1.5 meters apart there is some risk of infectious particle exposure. The study results suggest the greatest exposure to the trailing person occurs if they are directly behind the leading person (positioned in the slipstream). Substantial droplet exposure risk reduction can be achieved by 1) avoiding to walk or run in the slipstream of the leading person, 2) keeping the 1.5 m distance in staggered or side by side arrangement, or 3) by keeping social distances greater than 1.5 meters when moving fast or running.	
When is SARS-CoV-2 in your shopping list?	The spread of COVID-19 in a commercial supermarket and the potential for contagions are estimated using agent based modeling. This method maps all desired characteristics of customers and staff (e.g. number infected vs. susceptible, simultaneous users) and the infectious agent, as well as possible interactions/trajectories in a hypothetical layout. The model analysis finds increasing the distance between individuals in a supermarket setting (tested distances were 30cm, 50cm, 1 meter, 1.5 meters, and 2 meters), as well as limiting the number of individuals within the supermarket improved the percentage of potential transmission events avoided in the simulations.	(Hernandez Mejia & Hernandez-Vargas, 2020)
COVID-19: Effects of weather conditions on the propagation of respiratory droplets	A comprehensive mathematical model is established to explore speech generated droplet evaporation, heat transfer and kinematics under different conditions (e.g. temperature, humidity and ventilation). Low temperature and high humidity facilitate droplet transmission and dispersion, but supresses the formation of aerosols. On the other hand, high temperature and low humidity promotes rapid loss of respiratory droplet mass (from evaporation) and reduce droplet travel distance but these conditions increases transmission risk from aerosol particles. The study concludes current social distancing recommendations may not be sufficient to diminish airborne transmission risks as droplets can travel distances up to 6 meters.	(Zhao et al., 2020)
COVID-19. Transport of respiratory droplets in a microclimatologic urban scenario	Examined the spread of respiratory droplets in outdoor environments by applying a computational model of a sneezing person in an urban scenario under a medium intensity climatological wind. The spread of respiratory droplets is characterized by the dynamics of droplet size: larger droplets (400 – 900µm) are spread between two to five meters during 2.3 seconds while smaller droplets (100 – 200µm) are transported between eight and eleven meters in 14.1 seconds when influenced by turbulent wind.	(Guerrero et al., 2020)
Influence of wind and relative	Air transmission of cough droplets with condensation and evaporation effects are modeled between two virtual humans under different	(Feng et al., 2020)

humidity on the social distancing effectiveness to prevent COVID-19 airborne transmission: A numerical study	environments and wind velocities. Micro-droplets follow airflow streamlines and can be deposited on virtual human bodies (including head regions) at greater than 3.05 meter (10 feet) distances. High relative humidity (99.5%) also leads to larger droplet sizes and greater deposition of cough droplets on surfaces (due to hygroscopic growth effects). Suspended microdroplets could be transmitted between the two virtual humans in less than 5 seconds. The study concludes due to environmental wind, convection effects, and relative humidity on respiratory particles emitted by humans, the frequently recommended 1.83 meters (six feet) of social distancing may not be sufficient to prevent inter-person aerosol transmission.	
Modelling aerosol transport and virus exposure with numerical simulations in relation to SARS-CoV-2 transmission by inhalation indoors	Available evidence on aerosol transport in air is combined with 0D-3D simulations in physics-based models and theoretical calculations. Monte Carlo simulations indicate droplets produced by speech and cough (diameter < 20 µm) can become airborne and linger in air from 20 minutes up to one hr, and be inhaled by others. The exposure time to inhale 100 aerosols (assumed to be an adequate infectious dose) is variable based on the situation and can range from one second, to one minute, to one hour. 3D computational fluid dynamic (CFD) simulations suggest aerosols (dp <20 µm) can be transported over 10 meter distances in generic environments, dependent on relative humidity and airflow. Finally the rapid drying of expelled mucus droplets would yield droplet nuclei and aerosols which could potentially carry airborne virus particles. Such droplets (initial particle diameter of 50µm to 100µm) could remain airborne for approximately 20 seconds to three minutes.	(Vuorinen et al., 2020)
Field Studies		
Publication Title	**Key Outcomes**	**Reference**
Aerosol and Surface Transmission Potential of SARS-CoV-2	Air and surface samples from isolation spaces housing individuals with COVID-19, in the United States, were collected and tested for SARS-CoV-2 viral RNA. High volume air samples, and low volume personal air samples were tested for SARS-CoV-2 presence by RT-PCR. 63.2% of air samples from patient isolation areas were positive for viral RNA, and 58.3% of air samples from hallways outside of patient isolation areas were also positive for the virus. The findings suggest viral aerosol particles can be produced by infected individuals even during the absence of cough, and travel distances greater than 6 feet (1.8 meters).	(Santarpia et al., 2020)

SARS-COV-2 DISPERSION DISTANCE AND FACE COVERING

Table 2: Primary literature on effectiveness of face covering and distance

Publication Title	Key Outcomes	Reference
Textile Masks and Surface Covers—A Spray Simulation Method and a "Universal Droplet Reduction Model" Against Respiratory Pandemics	Dispersion distances of respiratory droplets when wearing face coverings made of common household materials was measured using a bacterial-suspension spray simulation (mimicking a sneeze). Most bacteria-carrying droplets landed within 1.2 meters of the source, but some droplets did travel distances greater than 1.8 meters when no barriers (meant to mimic no face covering) were in place. All tested textiles reduced the number of droplets reaching surfaces, restricting their dispersion to <30 cm, when used as single layers. When used as double-layers, textiles were as effective as medical mask/surgical-cloth materials, reducing droplet dispersion to <10 cm, and the area of circumferential contamination to ~0.3%.	(Rodriguez-Palacios et al., 2020)
Face Coverings, Aerosol Dispersion and Mitigation of Virus Transmission Risk	Researchers use a background oriented Schlieren technique to visualize airflow and investigate the effectiveness of different face covers in mitigating aerosol dispersion during breathing and coughing. The study reports a thermal plume containing respiratory particles were visible at distances less than 0.5 meters during normal breathing generated by human subjects and manikins. Thermal plume were visible approximately 1.1 meter away from the source mouth during manikin generated coughing. All tested face covers (including surgical mask, homemade mask, filtering face piece respirators, and face shields) were found to reduce front flow of respiratory jets by more than 90%, and thermal plumes were visible at less than 0.5 meters for coughing. Several backward and downward leakage jets were also detected at distances less than 0.2 from the source for coughing.	(Viola et al., 2020)

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Sciences Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a RefWorks database and an Excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: distance.

Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review. This review contains research published up to June 22, 2020.

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Emerging Evidence on COVID-19

Evidence Brief on Adherence to Isolation and Quarantine Recommendations During COVID-19

Introduction

What is the evidence on the proportion of people that adhere to isolation and quarantine for COVID-19 and what drivers and barriers determine adherence?

Public health measures to control the spread of COVID-19 infections have included both isolation of people diagnosed with COVID-19 and quarantine of close contacts of cases and incoming travellers. Current Public Health Agency of Canada guidance recommends a mandatory 14 day quarantine for travellers entering Canada, suspect cases and/or known contact(s) of a confirmed COVID-19 case (1).

In a related evidence brief on quarantine strategies, December 2020 (available upon request), modeling studies show the benefits of quarantine in reducing transmission relies heavily on high adherence (2-4). This evidence review identifies and summarizes published and pre-published evidence on drivers and barriers, such as sociodemographic characteristics, knowledge and attitudes associated with adherence to COVID-19 isolation and quarantine recommendations. Studies up to January 15, 2021 were included.

Key Points

- A total of nine studies were identified, including seven observational studies reporting on COVID-19 infection isolation and/or quarantine adherence (Table 1), one study on intent to adhere to the recommendations (Table 2) and one rapid review summarising literature on factors associated with adherence to quarantine pre-COVID-19 (Table 3).
- Studies were from Europe (n=4), Asia (n=3) and the Middle East (n=1). The rapid review included three studies from Canada conducted during SARS.
- Adherence to COVID-19 isolation and quarantine were reported in four studies and ranged from 75% in a study from South Korea to 25% in a study from the UK (5, 6, 8, 10).
- Drivers of adherence to isolation and quarantine recommendations included increased quarantine and self-isolation adherence among adults of female gender, higher levels of education, being married or co-inhabiting with others and employment as a healthcare worker. Adherence by age group was variable from study to study.
- Individuals self-reporting symptoms, those with a confirmed COVID-19 test and those who received a COVID-19 diagnosis (suspect or confirmed) from a healthcare provider were more likely to comply

with isolation instructions compared with people told to quarantine due to their contacts with other COVID-19 cases and those who were not feeling ill themselves.

- Barriers to adherence were: lack of support from someone outside of the household, which is consistent with reported reasons for violation such as shopping for essential items and medication, and work demands. Support outside of the home was a driver of adherence during the SARS outbreak summarized in the rapid review (9).

- Higher perceptions of COVID-19 infection risk, infection transmission and confidence in effectiveness of isolation and quarantine were linked to improved adherence. These findings are consistent with the rapid review on adherence to quarantine due to other infections (9).

- Monetary compensation for lost wages, trust in public health regulations and worry about infection was linked to increased intent to adhere to quarantine. However, stricter sanctions, higher fines and penalties for violators of quarantine did not impact the degree of adherence with COVID-19 quarantine in a South Korean cohort.

- A study of quarantined children reported that increased adherence was attributed to female gender, older age of child, fewer children within the household, primary caregivers that were female and younger, as well as clear communications of quarantine instructions.

Overview of the Evidence

Nine articles were included in this review. There were seven published studies and one pre-print on adherence to isolation and quarantine during COVID-19, and one rapid review on adherence to quarantine for non-COVID-19 infections.

There were a number of limitations to the evidence. Most studies were conducted in Europe or Asia, therefore, the findings may not be reflective of the Canadian situation. Adherence is difficult to objectively measure and in most studies it was based on self-reports. This can lead to selection and social desirability biases. Some studies included efforts to adjust for selection bias and ensure representativeness of the study findings through random sampling, weighting of data to match the national populations and reporting adjusted effect estimates. However, not all of the studies reported efforts to adjust for selection biases.

The definitions of isolation and quarantine were not consistent across studies; the majority of studies did not distinguish between isolation and quarantine. This meant the identified barriers and drivers influencing isolation and quarantine adherence were often combined. Most studies examined a long list of potential risk factors that they may not have had appropriate power to include in an analysis without overfitting the regression model or they performed multiple comparisons where statistical adjustments such as a Bonferroni correction were needed. Such adjustments were not adopted by all included studies and may have led to spurious results. Carefully planned and executed analyses are needed to avoid this bias.

Important knowledge gaps within the available literature include the lack of Canadian data that consider local public health and infection transmission contexts. Data on the impact of multiple lockdowns and local infection prevalence are also lacking. Research in Canada, objective measures of adherence (over self-report) and measures of adherence over time would improve this body of research.

CONTENTS

COVID-19 ISOLATION AND QUARANTINE ADHERENCE

Seven studies that consider factors linked to quarantine and isolation adherence, are summarized in Table 1.

- Four cross-sectional surveys evaluated sociodemographics, knowledge and attitudes as drivers or barriers to adherence to isolation and quarantine of adults (n=3) and children (n=1) (7, 10-12).
- Adherence drivers included female gender, higher levels of education, being married or co-inhabiting with others, fewer children within a household and employment as a healthcare worker.
- Two longitudinal trend analysis studies with multiple survey cycles in Norway examined self-reported adherence to isolation and quarantine recommendations. One study found age to have an impact on quarantine adherence, while the other found gender, age and level of education to have a small impact on adherence (5, 6).
- Across studies individuals who had a positive test result or were diagnosed by a health care provider, those who perceived the infection to be more serious, or had received healthcare guidance on isolation were more likely to adhere to isolation and quarantine (5-7, 11, 12)
- The analysis of a South Korean cohort finds increased penalties for individuals who violated quarantine did not lead to better adherence (8).

Table 1: Studies Reporting on COVID-19 Isolation and Quarantine Adherence (n=7)

STUDY	METHOD	KEY OUTCOMES
Adults		
Ryu 2020 (8) Population-based Cohort South Korea Mar-Jun 2020	Public health data on the quarantined population (14 day quarantine) and quarantine violations was analysed via Poisson regression to measure the impact 1-strike out sanctions implemented April 5, 2020 with increased penalties (e.g. imprisonment, fines, deportation or electronic bracelets) for violators. Korean public health was "monitoring" quarantined individuals, but details are not provided.	High stake penalties, the "1-strike out" sanction, was not a driver of adherence as it did not have a significant effect (p=0.99) on the daily violation rate, among Koreans or foreigners. A median 36,561 (range, 8335-59,918) individuals were quarantined per day during the study period. Overall, adherence levels were high. The median number of daily violations was 6 (0-13), and the median rate of violation was 1.6/10,000 (0.0-8.0) quarantined individuals.
Carlsen (2020) (5) *Preprint* Longitudinal trend Study Norway Aug-Oct 2020	Participants from two prospective cohorts participated in a sub-study and submitted data every 14 days ~85000 responses per survey cycle) on illness, COVID-19 testing and quarantine. In the summer, testing became more accessible and the public health recommendation was to get tested if symptoms occurred and that confirmed or suspected cases should quarantine. This study analyzes self-reported adherence to isolation and quarantine from survey responders between Aug - Oct 2020. Response rates ranged from 55%-83%, across cohorts and survey cycles.	Illness was reported by 8.6-13% of people surveyed, 12%, 13% and 10% over the 4 survey cycles, 35-45% of men and 40% -45% women of respondents reported being tested in the past 14 days due to illness; and 4-5% of respondents reported being quarantined or isolated. Adherence to quarantine was higher in women. Among those that received a positive test result 79% were men and 91% women; suspect or confirmed diagnosis from a physician 65% men and 72% women; tested for SARS-CoV-2 53% of men and 59% of women; or reported illness in the last 14 days 26% men and 33% women. Norwegian county of residence, gender, older age and higher level of education were reported to have a small effect on increased odds of quarantine and self-isolation adherence.

		Adherence to recommendations for testing and quarantine was lower than expected in Norway despite high trust in government.
Steens (2020) (6) Longitudinal trend study Norway Apr – Jun 2020 (Multiple survey cycles)	An online survey was conducted among a representative sample (n=1400, 7% response rate) of adults to measure self-reported adherence to isolation and quarantine repeated every 3-6 weeks for 4 cycles. Response rates for cycle 2-4 ranged from 74% to 86%. The analysis was weighted by age and sex for representativeness. Isolation is required in Norway only for those with confirmed or probable COVID-19. Note: Participants were considered to have adhered to isolation/quarantine if they reported doing so for at least one day. This study also recruited additional people in each wave from their balanced internet population sample to try to balance dropouts which may bias the results.	1704 participants provided 4525 responses over the 4-cycle survey and the analysis was weighted to the national population. Participants reported 25% (95% CI 23-27) had received a quarantine request within 7 days of the survey and of these people 42% (37-48) adhered to quarantine. Adherence was higher for people with symptoms (75%, 95% CI 63-79) compared to those without (28%, 95% CI 23-34). 65% (60-70) of participants reported to have not adhered to a quarantine request. Adherence was highest among the 18-29 age group (72%; 95% CI 58-83), compared to those aged 30 or older. Reported adherence to quarantine/isolation declined over time, from 66% in April to 33% - 38% in May and June samples. Waning of adherence was particularly high in older age groups. In Norway, fines can be issued for violation of quarantine, but there is no active follow-up of cases. The authors suggest drivers were risk perception, knowledge, social norms and having symptoms; barriers were adverse financial consequences from adherence.
Carlucci (2020) (11) Cross-sectional Study Italy Mar 2020	Online survey of 3964 quarantined Italian adults, sampled at week 3 of national lockdown, on adherence to quarantine due to a COVID-19 infection. Sociodemographic, preventative behaviours including adherence to quarantine and risk perception factors were evaluated	Sociodemographic variables associated with higher adherence to quarantine: women ($p<0.001$), higher education (0.007), married/cohabitating ($p<0.001$), healthcare workers ($p<0.001$). Age: 50-59 ($p<0.001$) had higher adherence than 30-39, which was higher than 18-29

	in the survey and analyzed by analysis of variance.	($p<0.01$). Notably those over 60 were less likely to adhere to quarantine. Regional variation, higher adherence in southern Italy ($p<0.01$). Lower adherence was noted for single people, students. Higher risk perception and anxiety levels were associated with higher adherence to quarantine. Reasons for compliance included reducing spread (79.8%), transmission (75.7%), trust in government (40.2%). Reasons for going out during quarantine were: 23.9% receiving medical treatments or going to the pharmacy, 9.7% for essential necessities (e.g. groceries), 8.5% work demands, 5% to walk domestic animals and 1% assisting families.
Smith (2020) (7) Cross-sectional study UK May 2020	An online survey included 2240 adults from an established representative population sample. Quota sampling was used to ensure representativeness. The survey investigated factors associated with adherence to self-isolation and lockdown measures. Logistic regression was conducted with a Bonferroni correction to the results with $p<0.001$. Adjusted for gender, age, having a child in the household, being extremely clinically vulnerable, employment status, education, deprivation, social grade, rural or urban, living alone, marital status and region.	75.1% of the 217 individuals reporting symptoms in self or household reported having left their home at least once (i.e. not complying with self-isolation or quarantine) in the previous 24 hours. Adjusted analysis for not having left self-isolation or quarantine in the previous 24 hours included: - Females (OR_{adj} 0.32 (95% CI 0.14-0.76) - Report of symptoms in self OR_{adj} 0.23 (95% CI 0.09–0.61) - Increased worry of COVID OR_{adj} 0.61 (95% CI 0.37–0.98) - Received help from someone outside the household OR_{adj} 0.30 (95% CI 0.09-0.96) - Perception of high infection contraction risk OR_{adj} 0.40 (95% CI 0.16-0.99) - A sense of community with neighbours OR_{adj} 1.52 (95% CI 1.03-2.24)

		Perceptions of COVID-19 influenced higher adherence if responders thought they had COVID-19, were self isolating, possessed good knowledge of prevention, were worried about COVID-19 and had intentions to follow government advice.
Xu (2020) (10) Cross-sectional survey China Feb 2020	2956 community dwellers in China (≥16 years of age) completed a voluntary survey on compliance with mitigation measures which included home quarantine defined as leaving home <1 time over 3 days. The data was analysed via chi-square and logistic regression employing Bonferroni correction.	75.6% of respondents reported being compliant to home quarantine. Compliance with home quarantine was lower in men (OR =0.61 (0.51–0.73)). The age 31-40 group (OR=0.71 (0.54–0.93)) and 41–50 age group (OR=0.67 (0.46–0.97)) was found to be less compliant with home quarantine when compare to individuals less than or 20 years of age. No other indicators for compliance were identified within the study data.
Children and Adolescents		
Lou (2020) (12) Cross-sectional Study China Feb 2020	This study followed up on quarantine adherence 8 days after the children presented to a fever clinic (n=495). Data was collected by phone interviews. Multivariate logistic regression including gender and age of patients, gender and age of caregivers, education level of caregivers, place of residence, number of children in the family and whether a nurse explained the quarantine measures were taken as the independent variables.	Odds of quarantine compliance increased with female gender of the child and caregiver, higher age of children OR 0.25 (95% CI 0.19-0.32) and the explanation of quarantine measures by nurses OR 2.13 (95% CI 1.33-3.41). Children with elderly caregivers were OR 2.46 (95% CI 1.37-4.42) times more likely to report poor compliance, when compared to children with young adult caregivers.

COVID-19 ISOLATION AND QUARANTINE ADHERENCE INTENTION

- One survey conducted in Israel assessed the intention to adhere to COVID-19 quarantine in relation to the presence and absence of compensation for lost wages. Intention to comply with quarantine varied from 57% to 71% between February and March 2020 when wage compensation was not assumed. When monetary compensation was offered, intention increased to over 95% suggesting a lack of wages was a significant barrier to adherence to quarantine recommendations.

Table 2: Studies Reporting on COVID-19 Isolation and Quarantine Adherence Intention (n=1)

STUDY	METHOD	KEY OUTCOMES
Bodas 2020 (13) Cross-sectional Study Israel Feb-Mar 2020	Surveyed the intent to comply with medical official requested two-week self-quarantine. One question assumed compensation for lost wages by the state, and another question assumed no such compensation. The survey was administered in February (563 responders) and in March (511 responders). After pooling the two study samples, univariate and multivariate regression analyses identified factors associated with intention to comply with quarantine. Response rate of 25% for both time points.	When monetary compensation was assumed, 94% of respondents (in February) and 95.5% of responders (in March) reported they would comply with self-quarantine. When monetary compensation was NOT assumed, quarantine adherence was 57%, (in February) and 71.4% (in March). Assuming no monetary compensation, significant associations with the intent to adhere to quarantine in the multivariate analysis were: age OR_{adj} 1.01 (95% CI 1.01-1.03), religion OR_{adj} 0.48 (95% CI 0.33-0.70), worry over COVID-19 OR_{adj} 1.26 (95% CI 1.10-1.47) and trust in health regulations OR_{adj} 1.26 (95% CI 1.10-1.44).

PRE-COVID-19 RAPID REVIEW OF ISOLATION AND QUARANTINE ADHERENCE

- The review summarizes evidence from 14 studies that consider quarantine adherence following SARS, H1N1, Ebola and Mumps outbreaks, including three Canadian studies on quarantine adherence conducted during the SARS outbreak.

- The review highlights that perceived risk of disease and benefit of quarantine, but not knowledge of the disease were important drivers of adherence.
- Similarly cultural norm and societal acceptance of quarantine were important, this includes trust in government.
- Mainly Canadian research from SARS highlights that reasons for breaking quarantine include fear of lost wages and work, and the need to seek supplies or medical attention. These findings are consistent with other studies included in this evidence brief.

Table 3: Rapid Review of Factors Impacting Isolation and Quarantine Adherence during pre-COVID-19 Outbreaks (n=1)

STUDY	METHOD	KEY OUTCOMES
Webster 2020 (9) Rapid review Jan 2020	A rapid review of factors associated with adherence to quarantine during infectious disease outbreaks described in 14 studies. The infections were H1N1 (swine flu), Ebola, SARS and Mumps.	Adherence rates ranged from 0-92.8% and were conducted in healthcare workers, school staff, residents of cities, parents and individuals testing positive for infection. The quarantine periods were variable. Making quarantine mandatory or enforced by law increased adherence. Culture and societal norms are important, examples from the Ebola outbreaks show improved adherence when the head of a household favoured quarantine. In contrast, adherence was reduced when caretaking of the sick was of high cultural priority. Whereas studies from SARS show high adherence to quarantine when there was societal pressure or laws to do so. Drivers of adherence were: perceived high risk of disease, quarantine or isolation protocol and benefit of quarantine; however perceived knowledge of the disease was not. The studies in Canada during SARS highlight work and fear of lost wages as major drivers of non-adherence as well as the need to get supplies or seek medical attention. There was mixed evidence on length of quarantine and adherence.

		Trust in government was associated with adherence to quarantine.

Methods:

A daily scan of the literature (published and pre-published) related to COVID-19 is conducted by the Emerging Science Group, PHAC; and has been ongoing since the beginning of the outbreak. The literature is retrieved from Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the WHO COVID-19 literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. A search to retrieve relevant literature for this evidence summary was conducted in the Refworks database. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. The search algorithms used (isolation OR quarantine) AND (compliance OR adherence). 53 citations were screened for relevance and data was extracted from relevant articles into the review. This review contains research related to isolation and quarantine adherence published up to January 15, 2021.

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Preuve émergente sur la COVID-19

Synthèse en bref sur le respect des recommandations d'isolement et de quarantaine pendant la COVID-19

Introduction

Quelles sont les données probantes sur la proportion de personnes qui respectent l'isolement et la quarantaine en raison de la COVID-19 et quels facteurs et obstacles déterminent l'adhésion à ces mesures obligatoires?

Les mesures de santé publique visant à contrôler la propagation de l'infection par la COVID-19 incluent tant l'isolement des personnes ayant reçu un diagnostic de COVID-19 que la mise en quarantaine de celles qui ont eu des contacts étroits avec des cas et des voyageurs qui arrivent au pays. Les lignes directrices actuelles de l'Agence de la santé publique du Canada recommandent une quarantaine obligatoire de 14 jours pour les voyageurs qui entrent au Canada, les cas suspects ou tout contact connu d'un cas confirmé de COVID-19 (1).

Dans une synthèse en bref portant sur les stratégies de mise en quarantaine datant de décembre 2020 (disponible sur demande), les études de modélisation montrent que les avantages de la mise en quarantaine pour réduire la transmission dépendent fortement d'un niveau élevé de respect des mesures (2 à 4). Cette synthèse en bref vise donc à cerner et à résumer les données publiées et prépubliées sur les facteurs et les obstacles, comme les caractéristiques sociodémographiques, les connaissances et les attitudes associées au respect des recommandations sur l'isolement et la mise en quarantaine en raison de la COVID-19. Les études publiées et prépubliées jusqu'au 15 janvier 2021 ont été incluses dans la présente synthèse.

Points clés

- Au total, neuf études ont été recensées, dont sept études d'observation sur le respect de l'isolement de la quarantaine en raison d'une infection à la COVID-19 (tableau 1), une étude sur l'intention de respecter les recommandations (tableau 2) et une revue rapide résumant la documentation sur les facteurs associés au respect de la quarantaine avant la pandémie de COVID-19 (tableau 3).

- Les études ont été réalisées en Europe (n = 4), en Asie (n = 3) et au Moyen-Orient (n = 1). La revue rapide comprenait trois études canadiennes effectuées pendant la crise du SRAS.

- Le respect de l'isolement et de la quarantaine de la COVID-19 a été signalé dans quatre études et variait de 75 % dans une étude effectuée en Corée du Sud à 25 % dans une étude menée au Royaume-Uni (5, 6, 8, 10).

- Les facteurs de respect des recommandations en matière d'isolement et de quarantaine comprenaient une quarantaine prolongée et le respect de l'isolement chez des adultes de sexe féminin, ayant des

niveaux de scolarité plus élevés, être marié ou cohabitant avec d'autres personnes, et l'emploi dans le milieu de la santé. L'observance selon le groupe d'âge variait d'une étude à l'autre.

- Les personnes ayant déclaré elles-mêmes leurs symptômes, celles dont le test de dépistage de la COVID-19 a été confirmé et celles qui ont reçu un diagnostic de COVID-19 (soupçonné ou confirmé) d'un fournisseur de soins de santé, étaient plus susceptibles de se conformer aux instructions d'isolement que les personnes à qui on avait simplement dit de mettre en quarantaine en raison de leurs contacts avec d'autres cas de COVID-19 et celles qui ne se sentaient pas malades.

- Les exigences associées au travail ainsi que le manque de soutien d'une personne à l'extérieur du foyer, ce qui inclut le fait de devoir sortir pour aller acheter des fournitures essentielles et des médicaments, constituent les principaux obstacles au respect des mesures sanitaires et ont été mentionnés comme motifs de non-respect des mesures imposées. Le fait d'avoir du soutien à l'extérieur du foyer a été l'un des facteurs qui ont fait augmenter l'adhésion pendant l'éclosion du SRAS, comme cela est indiqué dans la revue rapide (9).

- Une plus grande perception du risque d'être infecté par la COVID-19, le niveau de transmission de l'infection et la confiance dans l'efficacité de l'isolement et de la mise en quarantaine ont tous été associés à une meilleure adhésion aux mesures. Ces différentes constatations concordent avec la revue rapide sur le respect de la quarantaine mise en œuvre pour faire face à d'autres infections (9).

- Le fait de recevoir un certain montant en compensation pour le salaire perdu, le fait d'avoir confiance en la réglementation sur la santé publique et le niveau d'inquiétude en raison de l'infection ont tous été associés à une plus grande intention de respecter la quarantaine. Une étude effectuée auprès d'une cohorte en Corée du Sud a révélé que des sanctions plus sévères, ainsi que des amendes et des pénalités plus élevées pour les contrevenants, n'avaient aucune incidence sur le degré de respect de la quarantaine en raison de la COVID-19.

- Une étude sur les enfants en quarantaine a révélé que l'augmentation du taux d'adhésion était attribuable au sexe (féminin), à l'âge de l'enfant (plus âgé), au fait qu'il y avait moins d'enfants dans un ménage, aux principaux fournisseurs de soins (plus jeunes et de sexe féminin), ainsi qu'à la communication claire des directives à propos de la quarantaine.

Vue d'ensemble des éléments de preuve

Cette revue comportait neuf articles, soit sept études publiées, une étude en préimpression sur le respect de l'isolement et de la quarantaine pendant la COVID-19, et une revue rapide sur le respect de la quarantaine pour les infections autres qu'associées à la COVID-19.

Les preuves obtenues comportaient cependant un certain nombre de limites. Par exemple, puisque la plupart des études ont été effectuées en Europe ou en Asie, les résultats ne reflètent peut-être pas la situation au

Canada. En outre, il est difficile de mesurer l'adhésion de façon objective et comme elle était autodéclarée dans bon nombre des études, cela peut créer des biais en raison de la sélection et de la désirabilité sociale. Certaines études ont également tenté de corriger ces biais de sélection afin de garantir la représentativité des résultats de l'étude en effectuant un échantillonnage aléatoire, en pondérant les données afin qu'elles correspondent aux populations nationales et en diffusant des estimations fondées sur des effets ajustés. Les études n'ont cependant pas toutes indiqué les efforts utilisés pour corriger ces biais.

Par exemple, les définitions de l'isolement et de la quarantaine n'étaient pas uniformes entre les études et la majorité d'entre elles ne faisaient aucune distinction entre l'isolement et la quarantaine. En un mot, les obstacles et les facteurs qui influencent l'isolement et le respect de la quarantaine ont souvent été combinés. La plupart des études ont cependant évalué une longue liste de facteurs de risque potentiels qu'elles n'avaient peut-être pas le pouvoir approprié d'inclure dans une analyse sans que cela ne dépasse le modèle de régression ou ont effectué de multiples comparaisons pour lesquelles des ajustements statistiques comme une correction de Bonferroni auraient été requis. De tels ajustements n'ont pas été utilisés dans toutes les études incluses et peuvent avoir entraîné de faux résultats. Des analyses soigneusement planifiées et exécutées sont donc nécessaires pour éviter un tel biais.

Parmi les lacunes importantes dans la documentation disponible, mentionnons le manque de données canadiennes qui tiennent compte des contextes locaux de la santé publique et de la transmission des infections. Il manque également des données sur l'incidence des confinements multiples et de la prévalence des infections à l'échelle locale. La recherche au Canada, les mesures objectives de l'adhésion (par l'entremise de l'auto-déclaration) et les mesures d'adhésion au fil du temps sont des éléments qui permettraient d'améliorer le corpus de recherche.

TABLE DES MATIÈRES

ISOLEMENT EN RAISON DE LA COVID-19 ET RESPECT DE LA QUARANTAINE

Le tableau 1 résume sept études qui tiennent compte des facteurs liés à la quarantaine et à l'isolement.

- Quatre enquêtes transversales ont évalué les caractéristiques sociodémographiques, les connaissances et les attitudes comme facteurs ou obstacles à l'isolement et à la mise en quarantaine des adultes (n = 3) et des enfants (n = 1) (7, 10 à 12).

- Les facteurs d'adhésion comprenaient le sexe féminin, des niveaux de scolarité plus élevés, le fait d'être marié ou de cohabiter avec d'autres personnes, le fait qu'il y ait moins d'enfants dans un ménage et le fait d'occuper un emploi dans le milieu de la santé.
- Deux études d'analyse des tendances longitudinales comportant de multiples cycles d'enquête en Norvège ont examiné l'adhésion autodéclarée aux recommandations en matière d'isolement et de quarantaine. Une étude a révélé que l'âge a un effet sur le respect de la quarantaine, alors que l'autre a constaté que le sexe, l'âge et le niveau de scolarité n'avaient que peu d'incidence sur l'adhésion (5, 6).
- Dans toutes les études, les personnes qui ont obtenu un résultat positif au test de dépistage ou celles qui ont été diagnostiquées par un fournisseur de soins de santé, celles qui ont perçu l'infection comme étant plus grave ou celles qui ont reçu des conseils de santé sur l'isolement étaient plus susceptibles de respecter les mesures sur l'isolement et la quarantaine (5 à 7, 11, 12)
- L'analyse d'une cohorte de la Corée du Sud révèle que l'imposition de peines plus sévères aux personnes qui ont contrevenu à la quarantaine n'a pas eu pour effet d'entraîner une meilleure adhésion (8).

Tableau 1 : Études portant sur l'isolement en raison de la COVID-19 et le respect de la quarantaine (n = 7)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
Adultes		
Ryu 2020 (8) Cohorte basée sur la population Corée du Sud Mars à juin 2020	Les données de santé publique sur la population en quarantaine (quarantaine de 14 jours) et les infractions à la quarantaine ont été analysées avec la régression de Poisson pour mesurer l'incidence des sanctions accrues imposées à compter du 5 avril 2020 aux contrevenants dès la première infraction (p. ex., emprisonnement, amendes, expulsion ou bracelets électroniques). La santé publique coréenne a indiqué que les personnes en quarantaine étaient « surveillées », mais aucun autre détail n'a été fourni.	Le fait d'imposer des sanctions ayant d'importants enjeux, comme lors de la première infraction, n'a pas été un facteur d'adhésion, puisque ces sanctions n'ont pas eu d'effet significatif (p = 0,99) sur le taux quotidien d'infraction, tant pour les Coréens que pour les étrangers. La médiane comportait 36 561 personnes (fourchette variant entre 8 335 et 59 918) mises en quarantaine chaque jour pendant la période de l'étude et dans l'ensemble, les niveaux d'adhésion étaient élevés. Le nombre médian d'infractions quotidiennes était de 6 (0 à 13) alors que le taux médian d'infractions était de 1,6/10 000 (0,0 à 8,0) pour les personnes en quarantaine.

Carlsen (2020) (5) *Prépublication* Étude de tendance longitudinale Norvège Août à octobre 2020	Les participants provenant de deux cohortes prospectives ont pris part à une sous-étude à laquelle ils ont soumis des données tous les 14 jours (environ 85 000 réponses par cycle d'enquête) sur la maladie, les tests de dépistage de COVID-19 et la quarantaine. Pendant l'été, les tests sont devenus plus accessibles, et la santé publique a recommandé aux gens de se soumettre à des tests s'ils avaient des symptômes, en plus de préciser que les cas confirmés ou soupçonnés devaient se mettre en quarantaine. Cette étude analyse donc le respect autodéclaré de l'isolement et de la quarantaine par les personnes qui ont répondu au sondage entre août et octobre 2020. Les taux de réponse ont varié de 55 % à 83 %, entre les cohortes et les cycles d'enquête.	Parmi les personnes interrogées, de 8,6 à 13 % ont dit avoir été malades, soit des taux de 12 %, de 13 % et de 10 % pendant les quatre cycles de l'enquête. De 35 à 45 % des hommes et de 40 à 45 % des femmes ont dit avoir subi un test de dépistage au cours des 14 derniers jours pour cause de maladie alors que 4 à 5 % des répondants ont dit s'être mis en quarantaine ou s'être isolés. Le respect de la quarantaine était plus élevé chez les femmes. Parmi les répondants qui ont reçu un résultat positif, 79 % étaient des hommes et 91 % des femmes. De ce nombre, 65 % des hommes et 72 % des femmes ont reçu un diagnostic de COVID-19 soupçonnée ou confirmée par un médecin, 53 % des hommes et 59 % des femmes ont subi un test de dépistage du SRAS-CoV-2 et 26 % des hommes et 33 % des femmes ont dit avoir été malade au cours des 14 derniers jours. Le comté de résidence, le sexe, être plus âgé et avoir un niveau de scolarité élevé n'ont eu que peu d'effet sur la probabilité accrue de respecter tant la mise en quarantaine que l'isolement. En fait, le respect des recommandations en ce qui concerne les tests et la quarantaine a été plus faible que prévu en Norvège, malgré la grande confiance que les Norvégiens accordent à leur gouvernement.
Steens (2020) (6) Étude de tendance longitudinale Norvège	Un sondage en ligne a été mené auprès d'un échantillon représentatif (n = 1 400, taux de réponse de 7 %) d'adultes afin de mesurer l'adhésion autodéclarée à l'isolement et à la quarantaine. Ce sondage a ensuite été répété toutes les 3 à 6 semaines pendant	1 704 participants ont ainsi fourni 4 525 réponses pendant les quatre cycles du sondage et l'analyse a été pondérée en fonction de la population nationale. Ainsi, 25 % (IC à 95 % : 23 à 27) des participants ont dit avoir reçu une demande de mise en quarantaine dans les 7 jours suivant le sondage et de ce nombre, 42 % (37 à 48) ont dit avoir

Avril et juin 2020 (de multiples cycles d'enquête)	4 cycles. Les taux de réponse pour les cycles 2 à 4 se situaient entre 74 % et 86 %. Pour des raisons de représentativité, l'analyse a ensuite été pondérée par âge et par sexe. En Norvège, l'isolement n'était requis que pour les personnes dont le diagnostic de COVID-19 est confirmé ou probable. Remarque : On considérait que les participants avaient respecté l'isolement ou la quarantaine s'ils avaient déclaré l'avoir fait pendant au moins une journée. Cette étude a également recruté des participants supplémentaires dans chacune des vagues de l'épidémie, des participants provenant d'un échantillon équilibré de population sur Internet, pour contrebalancer les participants qui ont abandonné en cours de route, une mesure qui peut cependant avoir faussé les résultats.	respecté la quarantaine. L'adhésion était plus élevée chez les personnes symptomatiques (75 %, IC à 95 % : 63 à 79) que chez celles qui n'en présentaient pas (28 %, IC à 95 % : 23 à 34). 65 % (60 à 70) des participants ont dit ne pas avoir respecté la demande de mise en quarantaine. L'adhésion était la plus élevée dans le groupe des 18 à 29 ans (72 %; IC à 95 % : 58 à 83) que chez les 30 ans et plus. Le respect de la quarantaine et de l'isolement a cependant diminué avec le temps, passant de 66 % en avril à un taux variant entre 33 % et 38 % en mai et en juin. Cette diminution de l'observance était particulièrement élevée chez les groupes plus âgés. En Norvège, des amendes pouvaient être imposées pour violation de la quarantaine, mais il n'y a eu aucun suivi actif des cas. Les auteurs ont notamment indiqué que la perception du risque, les connaissances, les normes sociales et les symptômes étaient des facteurs favorisant le respect alors que les conséquences financières négatives découlant de l'adhésion à la quarantaine et à l'isolement constituaient plutôt un obstacle.
Carlucci (2020) (11) Étude transversale Italie Mars 2020	Sondage en ligne effectué auprès de 3 964 adultes italiens en quarantaine. L'échantillonnage a été effectué pendant la troisième semaine du confinement national et portait sur le respect de la quarantaine en raison d'une infection à la COVID-19. Les comportements sociodémographiques et	Variables sociodémographiques associées à une plus grande adhésion à la quarantaine : femmes ($p < 0,001$), études supérieures (0,007), personnes mariées ou vivant en cohabitation ($p < 0,001$), travailleurs de la santé ($p < 0,001$). Age : les personnes âgées de 50 à 59 ans ($p < 0,001$) sont celles qui ont indiqué le plus haut taux de respect de la quarantaine ou de l'isolement, suivi des personnes de 30 à 39 ans et finalement des 18 à 29 ans ($p < 0,01$). Fait à

	préventifs, y compris le respect de la quarantaine et les facteurs de perception du risque, ont été évalués dans le sondage et analysés à l'aide d'une analyse de la variance.	noter, les personnes de plus de 60 ans sont celles qui étaient les moins susceptibles de respecter la quarantaine. Variation régionale : la plus forte adhésion au respect des mesures a eu lieu dans le sud de l'Italie ($p < 0,01$). On a cependant noté un niveau d'adhésion plus faible chez les personnes seules et les étudiants. Les niveaux plus élevés de perception du risque et d'anxiété étaient associés à une plus grande observance de la quarantaine. Les motifs ayant entraîné le respect des mesures incluaient la réduction de la propagation (79,8 %), la transmission (75,7 %) et la confiance dans le gouvernement (40,2 %). Quant aux raisons qui ont poussé les gens à sortir de la quarantaine, 23,9 % ont indiqué qu'ils l'ont fait parce qu'ils devaient recevoir des traitements médicaux ou se rendre à la pharmacie, 9,7 % ont dit être sortis pour acheter des biens essentiels (p. ex., épicerie), 8,5 % ont dû sortir en raison de leur travail, 5 % devaient aller promener leurs animaux domestiques alors que 1 % des participants ont dit être sortis de la quarantaine pour aller aider d'autres personnes.
Smith (2020) (7) Étude transversale Royaume-Uni Mai 2020	Un sondage en ligne a été mené auprès de 2 240 adultes provenant d'un échantillon représentatif établi de la population. L'échantillonnage par quota a été utilisé pour assurer la représentativité.	Parmi les 217 personnes ayant déclaré qu'elle-même ou un membre de leur famille avait eu des symptômes, 75,1 % ont dit être sorties de chez elles au moins une fois (c.-à-d. qu'elles n'ont pas respecté l'auto-isolement ou la quarantaine) au cours des 24 heures précédentes. L'analyse ajustée pour ne pas avoir quitté l'isolement volontaire ou la quarantaine au

	Le sondage a porté sur les facteurs associés au respect des mesures d'isolement et de confinement. La régression logistique a été effectuée en utilisant la correction de Bonferroni pour les résultats avec $p < 0,001$. Les données ont ainsi été ajustées en fonction du sexe, de l'âge, du fait d'avoir un enfant à la maison, du fait d'être extrêmement vulnérable sur le plan clinique, de la situation d'emploi, de l'éducation, de la privation, de la classe sociale, du fait de vivre dans un milieu rural ou urbain, du fait de vivre seul, de l'état matrimonial et de la région habitée.	cours des 24 heures précédentes incluait les éléments suivants : - Femmes : $RC_{ajusté}$ 0,32 (IC à 95 % : 0,14 à 0,76) - Personne ayant déclaré avoir des symptômes : $RC_{ajusté}$ 0,23 (IC à 95 % : 0,09 à 0,61) - Plus grande inquiétude par rapport à la COVID-19 : $RC_{ajusté}$ 0,61 (IC à 95 % : 0,37 à 0,98) - A reçu de l'aide d'une personne extérieure au ménage : $RC_{ajusté}$ 0,30 (IC à 95 % : 0,09 à 0,96) - Perception d'un risque élevé de contracter l'infection : $RC_{ajusté}$ 0,40 (IC à 95 % : 0,16 à 0,99) - Sentiment de communauté avec les voisins : $RC_{ajusté}$ 1,52 (IC à 95 % : 1,03 à 2,24) Les perceptions à l'égard de la COVID-19 favorisaient le respect des mesures lorsque les répondants croyaient avoir la COVID-19, s'étaient isolés, avaient une bonne connaissance des mesures de prévention, avaient des inquiétudes par rapport à la COVID-19 et avaient l'intention de suivre les conseils du gouvernement.
Xu (2020) (10) Enquête transversale Chine Février 2020	En Chine, 2 956 habitants d'une même communauté (âgés de 16 ans et plus) ont répondu à un sondage volontaire sur la conformité aux mesures d'atténuation, ce qui incluait la quarantaine à domicile (définie comme le fait de sortir une fois ou moins pendant une période de trois jours). Les données ont été analysées au moyen de la régression du chi carré et de la régression logistique utilisant la correction de Bonferroni.	75,6 % des répondants ont dit s'être conformés à la quarantaine à domicile. Le respect de la quarantaine à domicile était plus faible chez les hommes (RC = 0,61 (0,51 à 0,73)). Lorsqu'on les compare aux personnes de 20 ans et moins, le groupe des 31 à 40 ans (RC = 0,71 (0,54 à 0,93)) et celui des 41 à 50 ans (RC = 0,67 (0,46 à 0,97)) sont ceux qui ont le moins respecté la quarantaine à domicile.

		Aucun autre indicateur de conformité n'a été identifié dans les données de l'étude.
Enfants et adolescents		
Lou (2020) (12) Étude transversale Chine Février 2020	Cette étude a suivi l'adhésion à la quarantaine huit jours après que les enfants se soient présentés dans une clinique pour contagieux (n = 495). Lesdonnées ont été recueillies par des entrevues téléphoniques. La régression logistique multivariée a utilisé différentes variables indépendantes, soit le sexe et l'âge des patients, le sexe et l'âge des soignants, le niveau de scolarité des soignants, le lieu de résidence, le nombre d'enfants dans la famille et le fait qu'une infirmière ait ou non expliqué les mesures de quarantaine.	Les probabilités de conformité à la quarantaine ont augmenté lorsque tant l'enfant que le soignant étaient de sexe féminin, lorsque les enfants étaient plus âgés RC 0,25 (IC à 95 % : 0,19 à 0,32) et lorsque les mesures de quarantaine avaient été expliquées par les infirmières RC 2,13 (IC à 95 % : 1,33 à 3,41). Comparativement aux enfants dont les soignants étaient de jeunes adultes, les enfants dont les soignants étaient âgés étaient plus susceptibles de ne pas se conformer à la quarantaine (RC 2,46 (IC à 95 % : 1,37 à 4,42)).

INTENTION DE S'ISOLER EN RAISON DE LA COVID-19 ET DE RESPECTER LA QUARANTAINE

- Un sondage effectué en Israël a évalué l'intention de respecter la quarantaine en raison de la COVID-19 selon que les personnes recevaient ou non une compensation pour le salaire perdu. L'intention de respecter la quarantaine a varié entre 57 % et 71 % entre février et mars 2020 lorsqu'aucune compensation n'était présumée. Lorsqu'une compensation financière a été offerte, l'intention a augmenté à plus de 95 %, ce qui laisse sous-entendre que le fait de ne pas recevoir de salaire constituait un obstacle important au respect des recommandations en matière de quarantaine.

Tableau 2 : Études portant sur l'intention de s'isoler en raison de la COVID-19 et de respecter la quarantaine (n = 1)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
Bodas 2020 (13) Étude transversale Israël Février et mars 2020	Enquête qui a porté sur l'intention de se conformer à la demande officielle, émise par un médecin, de mise en quarantaine volontaire pendant deux semaines. Une des questions laissait entendre que l'État offrirait une compensation financière aux personnes alors que l'autre laissait présumer qu'elles ne recevraient rien. Le sondage a été réalisé en février (563 répondants) et en mars (511 répondants). Après avoir regroupé les deux échantillons de l'étude, les analyses de régression univariée et multivariée ont permis de déterminer les facteurs associés à l'intention de respecter la mise en quarantaine. Taux de réponse de 25 % pour les sondages.	Lorsque la question laissait entendre qu'une compensation financière serait versée, 94 % des répondants (en février) et 95,5 % des répondants (en mars) ont déclaré qu'ils se conformeraient aux mesures de quarantaine volontaire. À l'inverse, lorsque la question présumait qu'AUCUNE compensation ne serait versée, le taux d'adhésion à la quarantaine a atteint 57 % (en février) et 71,4 % (en mars). Si l'on présume qu'aucune compensation financière ne sera versée, on peut voir que les éléments suivants ont un lien important avec l'intention ou non de respecter la quarantaine dans l'analyse multivariée : âge $RC_{ajusté}$ 1,01 (IC à 95 % : 1,01 à 1,03), religion $RC_{ajusté}$ 0,48 (IC à 95 % : 0,33 à 0,70), inquiétude au sujet de la COVID-19 $RC_{ajusté}$ 1,26 (IC à 95 % : 1,10 à 1,47) et confiance dans les règlements sanitaires $RC_{ajusté}$ 1,26 (IC à 95 % : 1,10 à 1,44).

REVUE RAPIDE SUR LE RESPECT DE L'ISOLEMENT ET DE LA QUARANTAINE AVANT LA COVID-19

- La revue résume les données probantes tirées de 14 études qui ont tenu compte du respect de la quarantaine après les éclosions de SRAS, de grippe H1N1, d'Ebola et d'oreillons, ce qui inclut trois études canadiennes sur le respect de la quarantaine effectuées pendant l'éclosion de SRAS.
- La revue montre l'effet positif du risque perçu de maladie et des avantages de la quarantaine, mais démontre également que la connaissance de la maladie n'a qu'un petit rôle dans le taux d'adhésion.
- La norme culturelle et l'acceptation sociale de la quarantaine étaient également importantes, tout comme la confiance dans le gouvernement.
- La recherche principalement canadienne sur le SRAS démontre, quant à elle, que les motifs pour mettre fin à la quarantaine incluaient la crainte de perdre son salaire et son emploi, ainsi que la

nécessité de se procurer des fournitures ou d'obtenir des soins médicaux. Ces conclusions sont conformes à d'autres études incluses dans la présente synthèse en bref.

Tableau 3 : Revue rapide des facteurs qui ont eu une incidence sur le respect de l'isolement et de la quarantaine lors des éclosions antérieures à la COVID-19 (n = 1)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
Webster 2020 (9) Revue rapide Janvier 2020	Revue rapide portant sur 14 études sur les facteurs associés au respect de la quarantaine lors des éclosions de maladies infectieuses. Ces études portaient sur la grippe H1N1 (grippe porcine), Ebola, le SRAS et les oreillons.	Les taux d'adhésion variaient de 0 à 92,8 % et ont été observés chez les travailleurs de la santé, le personnel des écoles, les résidents des villes, les parents et les personnes ayant reçu un résultat positif au test de dépistage de l'infection. Les périodes de quarantaine étaient variables. Le fait de rendre la quarantaine obligatoire ou de s'assurer qu'elle tombe sous le coup de la loi a permis d'augmenter l'adhésion. La culture et les normes sociétales sont importantes et les différents exemples tirés des épidémies d'Ebola montrent une meilleure adhésion lorsque le chef de famille a dit qu'il favorisait la quarantaine. En revanche, l'adhésion était plus basse lorsque la prise en charge des malades était vue comme une priorité culturelle importante. Les études sur le SRAS montrent, quant à elles, une forte adhésion à la quarantaine en raison des pressions sociétales ou des lois à cet effet. Les facteurs d'adhésion incluaient la perception d'un risque élevé d'être malade, le protocole de mise en quarantaine ou d'isolement et les avantages de la quarantaine, mais la perception associée à la connaissance de la maladie ne faisait pas partie des facteurs ayant eu un effet positif. Les études effectuées au Canada pendant la crise du SRAS mettent en lumière la perte du salaire et de l'emploi comme facteurs principaux pour le non-respect, tout comme la nécessité d'obtenir des fournitures ou des soins médicaux.

		Les preuves en ce qui concerne la durée de la quarantaine et le respect des règles sont donc mitigées. La confiance dans le gouvernement a, quant à elle, été associée au respect de la quarantaine.

Méthodologie :

Une analyse quotidienne de la littérature (publiée et prépubliée) liée à la COVID-19 est effectuée par le Groupe des sciences émergentes de l'ASPC et se continue depuis le début de l'éclosion. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Une recherche visant à extraire la documentation pertinente pour inclusion dans cette synthèse a été effectuée dans la base de données Refworks. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Algorithmes de recherche utilisés : (isolation OU quarantine) ET (compliance OU adherence). 53 références potentiellement pertinentes ont été examinées pour confirmer qu'elles comportaient des données pertinentes, qui ont été extraites dans la revue. La présente revue contient des recherches relatives à l'isolement et au respect de la quarantaine publiées jusqu'au 15 janvier 2021.

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Emerging Evidence on COVID-19

Evidence Brief of Maximum Incubation Period

Introduction

What evidence exists that the incubation period of SARS-CoV-2 is greater than two weeks?

What policies are currently used for quarantine durations to account for longer incubation periods?

The incubation period determined by the World Health Organization (WHO), the European Centers for Disease Control (ECDC), US Centers for Disease Control and Prevention (CDC) and Public Health Agency of Canada ranges from 0-14.0 days, 0-14.0 days, 2.0-14.0 days, and 1.0-14.0 days, respectively. A comparison across coronaviruses in one review reported average incubation periods of SARS 4.6 days (95% CI: 3.8-5.8 d) and MERS 5.2 days (95% CI: 1.9-14.7 d) (1). This evidence brief focuses on the evidence up to January 25, 2020, on prolonged incubation periods beyond a 14-day quarantine period, and regions that have recently extended the quarantine period for some or all travellers.

Key Points

- The incubation period across all meta-analyses was an average or median of 5-7 days with the longest incubation period reported to be 32 days. There was some evidence the average incubation period may be longer for children and older adults compared to adults (Table 1). Over dispersion in the tail of incubation periods was noted, which may result in the mean and confidence intervals being skewed towards higher values due to a few very long incubation periods in the dataset. The reported range in upper percentiles across meta-analyses were:
    - 90th percentile: 9.7 days (95% CI: 8.1–11.6)
    - 95th percentile: 11.2 days (95% CI: 10.7–11.8) to 11.7 days (95% CI: 9.7–14.2)
    - 97.5th percentile: 11.5 days (95% CI: 8.2–15.6) to 19.2 days (95% CI: 17.4-21.4)
- Study point estimates ranged from 1%-6.7% and 0-1.4% of infected individuals would still be in their incubation periods at 14 days and 21 days, respectively.
- The Canadian model estimating incubation period over the pandemic up to November 2020 reported a mean of 6.89 days, a median of 6 days and 90th, 95th, 99th percentiles of 11, 12, 13.5 days. They also indicated results suggested a slight increase in the incubation period over time.
- As of January 25, 2021, four regions have increased the quarantine duration for travellers entering their borders (Table 2). No evidence was found for longer incubation periods of COVID-19 or a larger proportion of cases falling beyond the commonly accepted 14-day threshold (including the variants of concern) within the literature.

Overview of the Evidence

Eleven reviews were included, mainly systematic reviews and meta-analysis, which summarized studies that measured incubation periods. In addition, eleven primary research studies presented evidence of incubation periods beyond 14 days. The final paper is a quantitative model on incubation period developed using Canadian data (Table 1).

Most incubation period data comes from public health contact tracing investigations mainly from studies done in Asia. Contact tracing investigations were at high risk of bias due to their retrospective nature. The data may also be affected by the fact that people do not know with certainty that they were exposed at a certain time or place. The systematic reviews were not evaluated by AMSTAR-2 due to the speed that this brief was developed, however the quality of individual reviews is highly variable ranging from few systematic review attributes to well conducted systematic reviews. The systematic reviews and meta-analyses overlap in the studies included. The quantitative model uses Canadian data to estimate the incubation period in the Canadian context. This model would be sensitive to the quality of the data used to develop the model.

As noted above, most of the data used to estimate incubation period were from studies conducted in Asia and are largely from early in the pandemic. Knowledge gaps include few recent studies and limited global representation of data on incubation period.

Other related evidence reviews are available on SARS-CoV-2 infectious period (2) and the efficacy of various quarantine strategies (3) by request.

CONTENTS

INCUBATION PERIODS

Table 1: Evidence of Incubation Period Beyond 14 Days (n=23)

STUDY	METHODS	KEY OUTCOMES
Reviews (n=11)		
Public Health Ontario (2020) (4) Rapid review NA	Search included references found in Nov 2020; and 16 meta-analyses were included. PHO compiled 4 systematic reviews and meta-analysis studies	Range of median incubation periods (tail-end analysis) reported across included meta-analyses: • 50th percentile: 5.1 days (95% CI: 4.5–5.8) to 5.4 days (95% CI: 5.0–5.7)

Nov 2020	(Quesada, 2020; McAloon, 2020; Li, 2020; Lauer, 2020) for tail-end analysis of the pooled estimates of the median incubation period.	• 75th percentile: 6.7 days (95% CI: 5.7–7.9) to 8.5 days (95% CI: 7.9–9.1) • 90th percentile: 9.7 days (95% CI: 8.1–11.6) • 95th percentile: 11.2 days (95% CI: 10.7–11.8) to 11.7 days (95% CI: 9.7–14.2) • 97.5th percentile: 11.5 days (95% CI: 8.2–15.6) to 16.5 days (95% CI: 14.8–18.3) Mean incubation period ranged from 4.2 to 6.7 days across all studies.
Quesada (2021) (5) Systematic review and meta-analysis NA Mar 2020	Systematic review was conducted with a search up to March 21, 2020. The meta-analysis included 7 studies.	The mean incubation period ranged from 5.6 (95% CI: 5.2 to 6.0) to 6.7 days (95% CI: 6.0 to 7.4), high heterogeneity (I^2 83.0%, p <0.001), depending on the statistical model used. A meta-regression of the 95th percentile data including mean age explained observed heterogeneity. Where for each 10 year increase in age, there was a 1 day increase in incubation period. Where the 95th percentile by mean age was 10.5, 11.5 and 12,5 days for 40, 50 and 60 year old, respectively.
McAloon (2020) (6) Rapid review and meta-analysis NA Apr 2020	Rapid review and meta-analysis with search conducted April 8, 2020. 24 studies were included for review, 9 of them were analysed.	Mean incubation period was 5.8 days (95% CI: 5.0 to 6.7) days with uncertainty in tail of the distribution. Median incubation period of 5.1 (95% CI: 4.5 to 5.8) days. The 95th percentile was 11.7 (95% CI: 9.7 to 14.2) days.
Li (2020) (7) Preprint Systematic review NA May 2020	Systematic review search conducted May 30, 2020, 64 studies were included, 30 studies were analysed, 12 of which included incubations greater than 14 days.	Incubation period 4.9 days (95% CI: 4.6-5.2) and a 97.5th percentile of 19.2 days (95% CI: 17.4-21.4).
Lauer (2020) (8) Meta-analysis	Pooled analysis of 181 cases reported Jan 4 – Feb 24, 2020 outside of Hubei province.	Median incubation period 5.1 days (95% CI: 4.5 to 5.8 days).

NA Jan – Feb 2020		97.5% of symptomatic cases developed symptoms within 11.5 days (CI: 8.2 to 15.6 days). Authors report that these estimates indicate that from 10,000 cases, 101 would develop symptoms after 14 days.
Daley (2020) (9) Preprint Systematic Review NA Jul 2020	Systematic review, search conducted July 18, 2020 and included 21 studies reporting incubation period.	Across studies the mean 5.9 days and median 5.6 days were in agreement.
Khalili (2020) (10) Systematic review and meta-analysis NA Mar 2020	A systematic review was conducted up to March 11, 2020, 18 studies were included in the meta-analysis of incubation period, only 2 were from outside China.	The pooled mean incubation period was 5.68 (99% CI: 4.78- 6.59) days, I^2= 98.4%.
Wang (2020) (1) Review NA Mar 2020	Narrative review of SARS, MERS, and SARS-CoV-2.	Average incubation period: • SARS : 4.6 d (95% CI: 3.8-5.8 d), • MERS : 5.2 d (95% CI: 1.9-14.7 d), • SARS-CoV-2: 6.4 d (range, 0-24.0 d)/ median 4 days (IQR 2-7) (Guan 2020)
Lin (2020) (11) Systematic Review NA Jun 2020	Search date was Feb 21, 2020. 8 studies were included in the meta-analysis of incubation period.	The median incubation 5.90 days (IQR 4.78–6.25) across 9 studies.
Wei (2020) (12) Preprint Systematic review NA Apr 2020	56 studies in the meta-analysis (4095 observations).	Median incubation period of 5.8 days (95% CI: 5.3 - 6.2, I^2 = 96.1%, P < 0.0001) and mean 6.9 days. Incubation period was longer for asymptomatic cases (median, 7.7; 95% CI: 6.3–9.4, P = 0.0408) and children (median, 7.3 d; 95% CI: 6.2–8.6, P = 0.0219). An estimated 6.7% (95% CI: 2.4–11.2%) and 1.4% (95% CI: 0.1–3.6%) of infected

		people had incubation periods over 14 d and 21 d respectively. The 97.5th percentile was 18 days incubation period for symptomatic cases, 14 days for asymptomatic and 25 days for children.
Bikbov (2021) (13) Letter to the Editor NA Jul 2020	Letter to the Editor, the authors summarize as a narrative synthesis the evidence of COVID-19 incubation period beyond 14-days (Koff, 2020; Guan, 2020; Tan, 2020; Jiang, 2020; Bai, 2020; Qiu, 2020; Bi, 2020).	The author's strongly advocate the need for open access data, specifically concerning incubation period of COVID-19 infection.
Primary Literature (n=11)		
Koff (2020) (14) Case Report USA Oct 2020	A case report of a patient who developed COVID-19 in California.	Patient with a confirmed incubation period of at least 21 days.
Guan (2020) (15) Case Series China Feb 2020	The study reported clinical data for 1099 patients.	The preprint mentioned 1 individual with an incubation period of 24 days, but this was labelled as a double exposure when WHO objected the data. The accepted article does not use this 24 day length in quantifying the incubation period and does not provide an upper limit.
Tan (2020) (16) Preprint Case Series China Jan-Feb 2020	A cohort of 67 patients admitted to hospital in China from Jan 26 – Feb 5, 2020. Cases confirmed by observation of corona viral particles by transmission electron microscopy.	Median incubation period of 6.0 days (range 1-15 days). The study notes a longer incubation period is observed in children. 1/67 (1.5%) were observed to have an incubation period greater than 14 days (15 days reported).
Jiang (2020) (17) Preprint Case Series China Jan 2020	Data from 136 patients who travelled to Hubei from Jan 5 - 31, 2020 and returned to their respective 21 cities after 48 hours or less in Hubei.	Cases 15-64 years old had a median incubation period of 7.0 days (95% CI, 6.1-8.1 days). Cases in the 65-86 year old range had a median incubation period of 10.9 days (95% CI, 8.9-13.6 days). A maximum of 17 days was observed (within the 65-86 year cohort).

Bai (2020) (18) Case Series China Jan-Feb 2020	This case series follows a familial cluster of 5 symptomatic patients and 1 asymptomatic family member.	The asymptomatic case had a reported incubation period of 19 days from initial contact with family members on January 10, 2020 to a positive RT-PCR test on Jan 28 (negative tests reported Jan 26, Feb 5, and Feb 8). It should be noted that this period is from first potential exposure, and may reflect a longer period than clinically experienced.
Qiu (2020) (19) Contact tracing investigations China Jan-Feb 2020	Results of contact investigations of 104 cases of COVID-19 in Hunan province, all were confirmed by RT-PCR.	The median incubation period was 6 (range, 1-32) days, which of 8/104 patients had incubation periods longer than 14 days: 18-32 days.
Bi (2020) (20) Contact tracing investigations China Jan-Feb 2020	Results of contact investigations of 391 cases of COVID-19 in Shenzhen province, all were confirmed by RT-PCR. 183 cases were considered to have well defined timelines for exposure and symptom onset.	Median incubation period reported as 4.8 days (95% CI: 4.2-5.4 days). 95% of symptomatic cases developed symptoms within 14 days (95% CI: 12.2-15.9 days)
Li (2021) (21) Preprint Case series China NR	787 cases from outside Wuhan were identified from a database in China. Gamma distribution best fit the data, thus a long tail.	The mean incubation period is 7.8 (7.4-8.5) days. Percentiles: 50th, 7.0 (6.7~7.3) days 75th 10.0 (9.7~10.4) days 97.5th 17.9 (17.1~18.7) days
Liu (2020) (22) Retrospective Cohort China Jan-Mar 2020	Until the end of March 2020, 93 patients were identified in Jilin province China. This study details the epidemiology and clinical results of the 93 RT-PCR confirmed COVID-19 cases.	The mean period of incubation for 87 patients was 10.4 days (range 2-25 days). The authors acknowledge this is longer than many other reports.
Leung (2020) (23) Case series China	A Google search for cases in China was conducted up to Feb 12, 2020. 175 cases with exposure data that included travel to Wuhan or known contact with	The Weibull distribution provided the best fit of the incubation period data and there was a dichotomy by whether the person had travelled to Hubei (mean 1.8 days, variance 0.7) or was not a traveller,

Jan-Feb 2020	infected person/place were included.	meaning local exposure, (mean 7.2 days, variance 16.2). This study found incubation period length at the 95% confidence interval was between 14.6-17.1 days, which is longer than current quarantine interventions.
Zhu (2020) (24) Preprint Contact tracing investigations China Feb-Apr 2020	Analysis of 670 COVID-19 cases imported into China that underwent quarantine and RT-PCR testing.	Median incubation period was 3 days (IQR 1-6 days.) The 95th percentile 11.6 days. (Table 3 lists incubation periods of 19 studies and the 95th percentile crosses 14 days in most estimates).
Model (n=1)		
Paul (2020) (25) Preprint Model Canada Nov 2020	SEIR model of the Canadian epidemic was developed to estimate the incubation period up to Nov 2020.	Estimates include a mean incubation period of 6.89 days, a median of 6 days and 90th percentile of 11 days, 95th percentile of 12 days and 99th percentile of 13.5 days. The model predicts a peak incubation period at 6 days with a second smaller peak at 10 days. This model also detected a slight increase over time in incubation period.

NR = not reported, NA = Not applicable

QUARANTINE POLICIES BEYOND 14 DAYS

Early in the COVID-19 pandemic, a maximum incubation period of 14 days was established by WHO and accepted as a standard quarantine or isolation period for travelers, cases and contacts by many countries and regions. At this point in the pandemic a few countries have eliminated or have very little local transmission of SARS-CoV-2, while other countries are reporting their highest case counts. There are also new variants of concern that have been identified and may be more transmissible than the original SARS-CoV-2. As such, countries with well controlled SARS-CoV-2 situations have amended their policies on quarantine duration as a precaution (Table 2). The table below describes the current quarantine requirements from countries with extended quarantine as of January 25, 2021.

Table 2: Government Quarantine Policies (n=4)

POLICY	KEY OUTCOMES
Australia	Hotel quarantine is required for those entering Australia, minimum 14 days, to a maximum of 24 days.

National Policy, Hotel Quarantine FAQ Posted Jan 22, 2021 (Accessed Jan 25, 2021)	Testing is conducted on days 2 and 12. Quarantine ends after 14 days for those with negative test results and no symptoms. A positive test, symptoms or close contact with a case restarts the 14 day count. Those refusing testing are quarantined the full 24 days.
Beijing, China Entry/exit requirements, listed by Government of Canada Posted Jan 21, 2021 (Accessed Jan 25, 2021)	Nationally, China requires a 14 day quarantine in a government designated facility. This procedure may vary by port of entry or final destination. International travellers entering Beijing will be subject to: • 21 days of quarantine in a local government designated facility; you may be allowed to self-isolate at home for the last 7 days. • An additional 7 days of health monitoring. International travellers entering Beijing via any other Chinese city will be subject to: • 21 days of self-isolation at the international point-of-entry, before they can continue to Beijing. • An additional 7 days of health monitoring upon arrival to Beijing.
Hong Kong Quarantine Extension, Press Release Posted Dec 25, 2020 (Accessed Jan 25, 2021)	Those arriving in Hong Kong who have been anywhere other than China in the past 21 days are subject to a 21 day quarantine in a designated hotel. Further, anyone who has spent more than 2 hours in the United Kingdom or South Africa in the past 21 days are not allowed entry to Hong Kong.
Singapore Quarantine Requirements Posted Jan 25, 2021 (Accessed Jan 26, 2021)	Singapore requires a 14 days quarantine for all travelers entering the country. Quarantine is spent at a designated facility. Recently, the quarantine for travellers from the United Kingdom and South Africa has been increased to a mandatory 21 days. The first 14 days are spent at a designated facility, with an addition 7 days at their place of residence.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ,

Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these repositories to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: (incubation period AND (prolonged OR review). This review contains research published up to January 25, 2021.

A Google search and search of targeted government websites was conducted to find publicly available reports, protocols and clinical data pertinent to the evidence questions. Search terms used included: COVID-19 AND incubation period; quarantine AND increase; quarantine AND length; variant AND quarantine. Searches were conducted and websites accessed on January 25, 2021.

Each potentially relevant reference was examined to confirm it had relevant data, and relevant citations were explored for further detail; relevant data was extracted into the review.

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Emerging Evidence on COVID-19

Evidence Brief of SARS-CoV-2 Incubation Periods

Introduction

What is the incubation period for SARS-CoV-2 and has it changed with variants of concern (VOC)?

The incubation period is defined as the time between exposure to an infectious pathogen and symptom onset. The incubation period of SARS-CoV-2 determined by the World Health Organization (WHO) and the European Centers for Disease Control (ECDC) is 0-14.0 days, the US Centers for Disease Control and Prevention (CDC) is 2.0-14.0 days and the Public Health Agency of Canada is 1.0-14.0 days. A comparison across what was known on incubation periods for other coronaviruses reported the average incubation periods of SARS was 4.6 days (95% CI: 3.8-5.8 d) and MERS was 5.2 days (95% CI: 1.9-14.7 d) (1). This review summarizes the incubation period of the original SARS-CoV-2 variants prior to the emergence of variants of concern (VOC) from several systematic reviews that included studies from the first 12 months of the pandemic (Table 2) and more recent research that has focused on establishing the incubation period of the VOCs (Table 1).

SARS-CoV-2 VOCs are circulating variants that have been flagged by national or global public health organizations. There are currently four VOCs: B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma) and B.1.617.2 (Delta). VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or are associated with diagnostic detection failures (2-4). Canada has established a national definition for VOCs (3). In May 2021, the WHO released a naming system for VOCs and variants of interest (VOIs) using Greek letters to improve the ease of communication on variants and potential stigma related to places where variants were first identified. This naming system has been adopted in this report (2).

This evidence brief focuses on the evidence up to August 17th, 2021 on incubation periods for SARS-CoV-2 and whether there is evidence that the incubation period for any VOC is different than previously circulating variants. In this summary, "original variant" refers to any variant that was not designated as a VOC or VOI.

Key Points

Incubation period for the original SARS-CoV-2 variants (prior to VOCs):

- The incubation period of SARS-CoV-2 based on a range of estimates from meta-analyses of studies conducted in 2020 prior to the emergence of VOCs estimated pooled mean incubation periods of 4.9-6.9 days (9 meta-analyses) and pooled median incubation periods of 4.8-5.9 days (8 meta-analyses) (Table 2).

- The largest meta-analysis included 99 studies with a range of 2.33-17.60 days incubation period reported across studies and the pooled mean incubation period 6.38 days (95%CI 5.79-6.97) and median 5.41 days (95%CI 4.74- 6.07) had high between study heterogeneity (5).
- In most meta-analyses the incubation period mean estimate is longer than the median estimate because there appears to be a few cases in each dataset with very long incubation periods, which causes a right skew in the data, also known as over dispersion in the tail of incubation periods. Long incubation periods are well documented particularly for immunocompromised populations, which have been covered in previous reviews and can be requested here.
- Two reviews reported evidence of a longer incubation period in children compared to adults: median, 7.3 days in children vs. 5.8 days in adults (6), median 10 days vs. 7 days, respectively (7).
- The majority (up to 90%) of the studies included in the meta-analyses were from China and represented data collected in the first half of 2020 (8, 9). The incubation period estimated prior to the end of January 2020 was shorter than after January 2020 in these studies, which is hypothesized to represent a bias in the data as cases were increasing exponentially (9).
- The Canadian model estimating incubation period over the pandemic up to November 2020 reported a mean of 6.89 days, a median of 6 days and 90th, 95th, 99th percentiles of 11, 12, 13.5 days. The results suggested a slight increase in the incubation period over time (10).

Incubation period for VOCs:

- Four studies were found on the incubation period for VOCs; one that looked at Alpha, two that looked at Delta, and one that looked at both Alpha and Delta (Table 1). No studies reporting on the incubation period for Beta or Gamma were found.
- The two studies included in this summary on Alpha incubation period found it could be shorter than original strains by 2 days. The first study is a small retrospective cohort study in Japan that reported incubation period of Alpha was shorter compared to other strains (mean: 3.53 days vs. 5.71 days / median 3.0 days vs. 5.0 days) (11). The other was a surveillance report from England that reported the median incubation period for Alpha was 4 days and no mean incubation period was provided (12). Both results indicate that Alpha incubation period may be shorter, however there is low confidence in these estimates, which are likely to change as additional research is published.
- The three studies on Delta incubation period included two contact tracing investigations from Guangdong, China. All results indicated that Delta incubation period may be shorter, however the difference may not be significant and there is low confidence in these estimates, which are likely to change as additional research is published. The first study reported the mean incubation period was 5.8 days (95%CI 5.2-6.4) and the latent period was 4.0 days (95%CI 3.5-4.4) (13). The latent period is defined as the time from acquiring infection to infectiousness onset. The other study estimated time to first positive PCR test, latent period rather than incubation period, in quarantined cases with Delta compared to a sample of cases from the initial epidemic wave in 2020: median 4 days (IQR 3-5) vs. 6

days (IQR 5-8), respectively (11). The third estimate was a surveillance report from England that reported the median incubation period for Delta was 4 days (12).

Overview of the Evidence

Thirteen reviews on incubation periods prior to the emergence of VOCs were included in this review including systematic reviews and meta-analysis (n=9), meta-analyses (n=2), a rapid review (n=1), and a scoping review (n=1). In addition, one recently published primary research study and one quantitative model using Canadian data were included for information on pre-VOC incubation period estimates as they were not included in the 13 reviews (Table 2). Studies reporting on incubation period for any VOC were reported in four studies or reports (Table 1).

Most incubation period data comes from public health contact tracing investigations mainly from studies done in Asia. One study reported contact tracing surveillance data for VOCs in the UK. Contact tracing investigations are at high risk of bias due to their retrospective nature. The data may also be affected by the fact that people do not know with certainty when or where they were exposed. The systematic reviews were not evaluated by the AMSTAR-2, a tool for evaluating systematic reviews, however the methods synopsis indicates the missing steps of each systematic review. The quality of the reviews was highly variable in both conduct and reporting across reviews. The systematic reviews and meta-analyses that are included in this brief overlap with the studies that were included. The quantitative model uses Canadian data to estimate the incubation period in the Canadian context. This model would be sensitive to the quality of the data used to develop the model.

The evidence for the non-VOC incubation period is abundant but not conclusive and the evidence for the VOC incubation period is sparce. This has resulted in large knowledge gaps on all SARS-CoV-2 viruses. Additional cohort studies are needed to assess early signals that the incubation period for original variants have evolved over time and to establish incubation periods for all the VOCs including pediatric studies to assess the early signal that children exposed to VOCs have a longer incubation period than adults.

CONTENTS

VOC INCUBATION PERIODS

Table 1: Evidence of Incubation Period for VOCs (n=4): Alpha (n=2), Delta (n=3)

STUDY	METHODS	KEY OUTCOMES
Primary Literature on Alpha and Delta		
Homma (2021) (11) Retrospective cohort study Japan Mar 2020-2021	A small retrospective cohort that included 30 Alpha cases from March 2021 and compared them to other SARS-CoV-2 strains from Mar 2020-Jan 2021.	• The reported incubation period of Alpha was shorter compared to other strains: mean 3.53 vs 5.71 days/ median 3.0 vs 5.0 days, respectively. • The incubation period for Alpha in close-contact environments was 0.62 times shorter than other strains (95% CI: 0.47, 0.82) after adjusting for age and sex.
Li (2021) (14) Preprint Outbreak investigation China June 2021	A study from China reported a shorter time interval between exposure and first PCR positive test in quarantined cases involved in an outbreak of Delta across the province of Guangdong (n=34) compared to cases caused by 19A/19B genetic strains during the early 2020 epidemic (n=29).	• Shorter time interval between exposure and first PCR positive test (latent period) in quarantined cases infected with Delta was a median 4 days (IQR 3-5) compared to a sample of traced cases from the initial epidemic wave in 2020, 6 days (IQR 5-8).
Kang (2021) (13) Preprint Outbreak investigation China May - June 2021	The transmission and epidemiological characteristics of the outbreak in Southern China is described. Analysis includes 167 cases of Delta in Guangdong.	• Mean estimate of the incubation period from 95 symptomatic cases was 5.8 days (95%CI 5.2-6.4) • The 95th percentile for Delta incubation cases was 11.5 days (95%CI 10.1-13.0) • Latent period was mean 4.0 days, (95%CI 3.5-4.4) • In this study, 73.9% of transmission occurred before symptom onset with peak infectiousness estimated at 2.1 days (95%CI 1.5-2.7) before symptom onset.
Public Health England (2021) (12) Report Surveillance data analysis UK	Contact tracing surveillance data from the UK between March 29 and June 9, 2021.	• For both household and non-household contacts the median incubation period was 4 days (estimated IQR from graph 2–7 days) for Delta and Alpha.

Mar - May 2021		

CI = Confidence interval, IQR= Interquartile range, PCR= Polymerase Chain Reaction

ORIGINAL VARIANTS (NON-VOC) INCUBATION PERIODS

Table 2: Estimates of Incubation Period for the original variants prior to the emergence of VOCs from Systematic Reviews (n=9), Meta-analyses (n=2), Rapid Reviews (n=1) and Scoping Reviews (n=1) and select primary research not included in the syntheses (n=2)

STUDY	METHODS	KEY OUTCOMES
Reviews (n=13)		
Song (2021) (7) Systematic review NA Jun 2021	This systematic review conducted a search up to 10 March 2021 on COVID-19 family clusters. Eighteen studies (published Jan-May 2020) involving 34 children and 98 adults from 28 families were included. Incubation period was reported in 31 children and 72 adults. No risk of bias assessment conducted.	• The median (IQR) incubation period was longer in children 10 days (1–30) compared to adults 7 days (1–29) (p=0.045).
Elias (2021) (5) Short communication Meta-analysis Jan 2021	A systematic search was carried out on studies published from 1 January 2020 to 10 January 2021 reporting the SARS-CoV-2 incubation period. No studies on VOCs were identified. There is no systematic review protocol or risk of bias assessment reported. The meta-analysis included 99 studies, of which 23 (23.2%) were cohort studies, 61 (61.6%) were case series, and 15 (15.2%) were modeling studies. Results of meta-analysis available here.	• The mean incubation period was 6.38 days (95%CI 5.79-6.97, I^2=100%, 99 studies), range 2.33-17.60 days. • The median incubation period was estimated at 5.41 days (95%CI 4.74-6.07, I^2=95%, 99 studies). • In the meta-regression, study design only explained 10% of the between study heterogeneity, the finding was the incubation period for cohort studies and predictive models was shorter than case series (p<0.01).
Li (2021) (15) Scoping review NA Apr 2021	This scoping review conducted a search up to 10 December 2020. There were 1920 confirmed cases included. Individual patient analysis was conducted by transforming case data to be double interval-censored, which was considered	• The median incubation period was 4.8 days (4.6–5.0), with the 95th and 99th percentile of the distribution being 15.1 days (95%CI 14.4–15.7) and 22.9 days (95%CI 21.7–24.3).

	to be best for obtaining a precise estimate. An accelerated failure time model was used to estimate the time to event distribution. This scoping review included a search, inclusion/exclusion criteria and data extraction and analysis. Thus, other than the omission of a risk of bias assessment resembles a systematic review more than a scoping review.	
Dhouib (2021) (8) Systematic review and meta-analysis NA Apr 2021	This systematic review was conducted with a search from December 2019 to December 1, 2020. Forty-two studies were included and consisted of 9 strong, 19 moderate, and 14 weak quality studies. The meta-analysis included 10 studies on mean incubation period. This systematic review has a registered protocol CRD42020196347, included a risk of bias and SIGN assessment of the certainty of the evidence. Random effects meta-analysis was conducted.	• The median incubation period ranged from 2-12 days with an IQR lower bound of 2 days and higher bound of 14 days (n=17 studies). The 95th percentile range was 10.3-16 days and the 99th percentile was up to 24 days. • The mean incubation period ranged between 3.9-9.0 days (n=9 studies). The total incubation period ranged from 0-26 days. • The pooled mean incubation period was 6.2 days (95% CI 5.4-7.0, I^2=77.1%, p < 0.001, 10 studies). Note included studies were from China (8), Singapore (1) and Argentina (1). Subgroup analysis revealed that heterogeneity was explained by study quality and method of calculation. • One study reported the mean incubation period for children was 8 days (range 1-13).
Xin (2021) (9) Systematic review and meta-analysis NA Apr 2021	This systematic review included a search conducted from 1 February 2020 and 25 September 2020. The meta-analysis included 31 studies that reported mean incubation period and 41 studies that reported median incubation period. The search strategy is presented, articles were evaluated with the	• 62/72 studies were using data from China. The pooled median of the point estimates of the mean incubation period was 6.3 days (range: 1.8–9.1 days). • The pooled estimate of mean incubation periods before the epidemic peak in China (January 2020) was 5.2 days (9 studies; 95%CI 4.8–5.7; I^2 = 56.5%), significantly lower than the

	STROBE checklist for quality and a random effects meta-analyses and meta-regression were conducted.	pooled estimate for studies conducted after the peak (March 2020) (18 studies; 7.2 days, 95%CI, 6.6–7.8; I^2 = 89.5%). • The pooled median of the point estimates of the median incubation period were 5.4 days (range, 2.0–17.6 days). The median value is lower than the mean due to the right skew in the data. • The 95th percentile of the incubation period was 11.0 days (5 studies; 95%CI 9.9–12.0; I^2=0.0%) before peak and 14.6 days (7 studies; 95%CI 13.7–15.5; I^2=66.9%) after peak of the outbreak in China. • Analysis of incubation period data from China in Jan-May 2020 suggests that when cases were rising exponentially there was a bias towards shorter estimates.
Daley (2020) (16) Preprint Systematic Review NA Jul 2020	The systematic review search was conducted 18 July 2020 and included 21 studies reporting incubation period. There is no protocol, a brief search description, no risk of bias assessment and the statistical analysis was averaging.	• Across studies the mean 5.9 days and median 5.6 days were in agreement.
Alene (2021) (17) Systematic review and meta-analysis NA Mar 2021	This systematic review was conducted on studies published up to 30 June 2020. Search, screening and data extractions details provided. Risk of bias was assessed using the Ottawa-Newcastle Scale. Random effects meta-analysis included 14 studies on mean incubation period.	• The mean incubation period of COVID-19 ranged from 4.8-9 days. • The weighted pooled mean incubation period of COVID-19 was 6.5 days (95%CI 5.9–7.1, I^2=97%, 14 studies, 1453 observations). • 71.4% of the studies were assessed to be of good quality.
Wei (2020) (6) Preprint	The systematic review search was conducted up to 26 April 2020.	• Median incubation period of 5.8 days (95%CI 5.3-6.2, I^2=96.1%, p<0.0001) and mean 6.9 days.

Systematic review and meta-analysis NA Apr 2020	56 studies were included in the meta-analysis (4095 observations). Methods for the search, selection, data extraction and quality assessment (AHRQ) of studies are described. Random effects meta-analysis was conducted. Bayesian meta-analysis was also employed to better simulate the distribution of the incubation period. Meta-regression was used to explore heterogeneity.	• Incubation period was longer for asymptomatic cases (median, 7.7 days; 95%CI 6.3–9.4, p=0.0408) and children (median, 7.3 days; 95%CI 6.2–8.6, p =0.0219). • A linear relationship between age and median incubation period was detected with a 16% increase for every 10 years age. • An estimated 6.7% (95%CI 2.4–11.2%) and 1.4% (95%CI 0.1–3.6%) of infected people had incubation periods over 14 days and 21 days, respectively. • The 97.5th percentile was 18 days incubation period for symptomatic cases, 14 days for asymptomatic and 25 days for children.
McAloon (2020) (18) Rapid review and meta-analysis NA Apr 2020	Rapid review and meta-analysis included a search conducted 8 April 2020. 24 studies were included for review, 9 of them were analyzed. The search, selection criteria, data extraction details and quality assessment using the Ottawa-Newcastle scale was described. Random effects meta-analysis was conducted.	• Mean incubation period was 5.8 days (95%CI 5.0-6.7) with uncertainty in the tail of the distribution. • Median incubation period of 5.1 days (95%CI 4.5-5.8). • The 95th percentile was 11.7 days (95%CI 9.7-14.2).
Quesada (2021) (19) Systematic review and meta-analysis NA Mar 2020	This systematic review was conducted with a search up to 21 March 2020. The meta-analysis included 7 studies. Search, selection strategies and meta-analysis methods are reported. Quality assessment was not done.	• The mean incubation period ranged from 5.6 (95%CI 5.2-6.0) to 6.7 days (95%CI 6.0-7.4), high heterogeneity (I^2 83.0%, p<0.001), depending on the statistical model used. • A meta-regression of the 95th percentile data including mean age explained observed heterogeneity. For each 10 year increase in age, there was a 1 day increase in incubation period. Where the 95th percentile by mean age was 10.5, 11.5 and 12.5 days for 40, 50 and 60 year old, respectively.

Khalili (2020) (20) Systematic review and meta-analysis NA Mar 2020	A systematic review was conducted up to 11 March 2020. 18 studies were included in the meta-analysis of incubation period, only 2 were from outside China. Search, selection strategies and meta-analysis methods are reported. Quality assessment was not done.	• The pooled mean incubation period was 5.68 (99% CI: 4.78-6.59) days, I^2= 98.4%.
Lauer (2020) (21) Meta-analysis NA Jan – Feb 2020	Pooled analysis of 181 cases reported Jan 4 – Feb 24, 2020 outside of Hubei province. The analysis in this paper is individual patient data meta-analysis. However the data was scraped from many different sources.	• Median incubation period was 5.1 days (95%CI 4.5-5.8 days). • 97.5% of symptomatic cases developed symptoms within 11.5 days (95%CI 8.2-15.6 days). • Authors reported that these estimates indicate that from 10,000 cases, 101 would develop symptoms after 14 days.
Lin (2020) (22) Systematic Review NA Jun 2020	Search date was Feb 21, 2020. 8 mathematical or statistical models that estimated incubation period were included. The search strategy, selection criteria and data extraction are described. The ISPOR-SMDM Modelling Good Research Practices Task Force tool was used to evaluate the models. Estimates are descriptively summarized.	• The median incubation was 5.90 days (IQR 4.78–6.25) across 9 studies.
Primary Literature (n=1)		
Huang (2021) (23) Preprint Retrospective cohort China NR	787 cases from outside Wuhan with sufficient information about exposure and symptom onset were identified from a national database of cases during 2020 in China. An interval-censored data estimation methods was used to study the data and factors that may explain the variability in incubation period. A gamma	The mean incubation period was 7.8 (7.4-8.5) days. Percentiles: 50th (median), 7.0 (6.7~7.3) days 75th 10.0 (9.7~10.4) days 97.5th 17.9 (17.1~18.7) days Factors that may explain heterogeneity in incubation period estimates were analysed and the findings indicate longer incubation periods were associated with

	distribution best fit the data which was right skewed.	females, older people and those with mild disease.
Model (n=1)		
Paul (2021) (10) Model Canada Nov 2020	SEIR model of the Canadian epidemic was developed to estimate the incubation period up to Nov 2020.	Estimates include a mean incubation period of 6.74 days (95%CI 6.35-7.13), a median of 6 days and 90th percentile of 11.64 days (95%CI 11.22-12.17), 95th percentile of 12 days and 99th percentile of 13.5 days. The model predicts a peak incubation period at 6 days with a second smaller peak at 10 days. This model also detected a slight increase over time in incubation period.

CI = Confidence interval NR = Not reported, NA = country not applicable, IQR = Interquartile range,

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these repositories to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: (incubation period AND (review OR "variant of concern terms")). This review contains research published up to August 17, 2021.

A Google search and search of targeted government websites was conducted to find publicly available reports, protocols and clinical data pertinent to the evidence questions. Search terms used included: COVID-19 AND incubation period. Searches were conducted and websites accessed on August 17, 2021.

Each potentially relevant reference was examined to confirm it had relevant data, and relevant citations were explored for further detail; relevant data was extracted into the review.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur la période d'incubation maximale

Introduction

Existe-t-il des preuves qui montrent que la période d'incubation du SRAS-CoV-2 peut durer plus de deux semaines?

Les politiques actuelles qui portent sur les périodes de quarantaine ont-elles prévu des périodes d'incubation plus longues?

L'Organisation mondiale de la santé (OMS), les European Centers for Disease Control (ECDC), les Centers for Disease Control and Prevention (CDC) des États-Unis et l'Agence de la santé publique du Canada ont déterminé que la période d'incubation du SRAS-CoV-2 variait de 0 à 14,0 jours, de 0 à 14,0 jours, de 2,0 à 14,0 jours et de 1,0 à 14,0 jours, respectivement. Une étude comprenant une comparaison entre différents coronavirus a, quant à elle, révélé des périodes d'incubation moyennes de 4,6 jours pour le SRAS (IC à 95 % : 3,8 à 5,8 jours) et de 5,2 jours pour le SRMO (IC à 95 % : 1,9 à 14,714,7 jours) (1). La présente synthèse en bref se fonde donc sur les données probantes recueillies jusqu'au 25 janvier 2020 à propos des périodes d'incubation qui se sont prolongées au-delà de la quarantaine de 14 jours et des régions qui ont récemment décidé d'allonger cette période de quarantaine pour certains voyageurs ou pour tous les voyageurs.

Points clés

- Toutes les méta-analyses examinées ont mentionné une période d'incubation moyenne ou médiane de 5 à 7 jours, à l'exception d'une méta-analyse qui a mentionné une période beaucoup plus longue (32 jours). Certains éléments de preuve indiquent que la période d'incubation moyenne peut cependant être plus longue chez les enfants et les adultes plus âgés que chez les adultes (tableau 1). Certaines études ont également mentionné qu'une surdispersion s'était produite pendant l'extrémité supérieure de la fourchette de la période d'incubation, ce qui peut faire augmenter la moyenne et les intervalles de confiance en raison de quelques très longues périodes d'incubation indiquées dans l'ensemble de données. Les méta-analyses ont indiqué les tranches de centiles supérieurs suivantes :
    - 90^{e} centile : 9,7 jours (IC de 95 % : 8,1 à 11,6)
    - 95^{e} centile : 11,2 jours (IC de 95 % : 10,7 à 11,8) à 11,7 jours (IC à 95 % : 9,7 à 14,2)
    - 97,5^{e} centile : 11,5 jours (IC de 95 % : 8,2 à 15,6) à 19,2 jours (IC à 95 % : 17,4 à 21,4)
- Les estimations ponctuelles présentées dans l'étude indiquaient qu'entre 1 et 6,7 % des personnes infectées seraient encore en période d'incubation au 14^{e} et qu'entre 0 et 1,4 % le seraient encore au 21^{e} jour.

- Le modèle canadien utilisé pour estimer la période d'incubation créé pendant la pandémie en fonction des données disponibles jusqu'en novembre 2020 a cependant donné une moyenne de 6,89 jours, une médiane de 6 jours et des 90^{e}, 95^{e} et 99^{e} centiles de 11, de 12 et de 13,5 jours pour la période d'incubation. Les résultats obtenus suggéraient également une période d'incubation qui s'allongeait légèrement avec le temps.
- Quatre régions ont décidé de prolonger, à compter du 25 janvier 2021, la durée de la quarantaine pour les voyageurs qui traversent leurs frontières (tableau 2). Aucun des documents consultés n'incluait de preuve sur des périodes d'incubation plus longues pour la COVID-19 ou sur un plus grand nombre de cas ayant dépassé le seuil communément accepté de 14 jours (ce qui inclut les différentes variantes préoccupantes).

Vue d'ensemble des éléments de preuve

Onze études ont été incluses dans cette synthèse, principalement des revues systématiques et des méta-analyses qui résumaient différentes études ayant mesuré les périodes d'incubation. Onze autres études de recherche originale comprenant des preuves sur les périodes d'incubation de plus de 14 jours ont également été incluses dans la synthèse. Le document final est donc un modèle quantitatif sur la période d'incubation élaboré à partir de données canadiennes (tableau 1).

La plupart des données sur la période d'incubation proviennent d'enquêtes de santé publique axées sur la recherche des contacts effectuées principalement en Asie. Les enquêtes avec recherche des contacts présentent un risque élevé de biais en raison de leur nature rétrospective. Les données peuvent aussi être biaisées du fait que les gens ne savent pas avec certitude à quel endroit et à quel moment ils ont été exposés. Les revues systématiques n'ont pas été évaluées avec AMSTAR-2 en raison de la rapidité avec laquelle ce dossier a été élaboré, mais la qualité des différentes études est très variable, allant de quelques attributs d'examen systématique à des revues systématiques bien effectuées. Les revues systématiques et les méta-analyses se chevauchent dans les études incluses dans la présente synthèse. Quant au modèle quantitatif, il utilise des données canadiennes pour estimer la période d'incubation dans le contexte canadien. Ce modèle serait sensible à la qualité des données utilisées pour le développer.

Comme il a été mentionné précédemment, la plupart des données utilisées pour estimer la période d'incubation provenaient d'études effectuées en Asie, en grande partie au début de la pandémie. Il y a donc des lacunes en matière de connaissances du fait qu'il n'y a que peu d'études récentes et une représentation mondiale limitée des données sur la période d'incubation.

D'autres revues connexes sur les données probantes sont disponibles à la demande. Elles portent notamment sur la période infectieuse du SRAS-CoV-2 (2) et sur l'efficacité de diverses stratégies de quarantaine (3).

TABLE DES MATIÈRES

PÉRIODES D'INCUBATION

Tableau 1 : Preuve d'une période d'incubation supérieure à 14 jours (n = 23)

ANNÉE	MÉTHODES	PRINCIPAUX RÉSULTATS
Revues (n = 11)		
Santé publique Ontario (2020) (4) Revue rapide Sans objet Novembre 2020	La recherche comprenait des références trouvées en novembre 2020, ainsi que 16 méta-analyses. Santé publique Ontario a compilé quatre examens et méta-analyses (Quesada, 2020; McAloon, 2020; Li, 2020; Lauer, 2020) pour l'extrémité supérieure de la distribution des estimations regroupées de la période médiane d'incubation.	Fourchette de la période d'incubation médiane (analyse de l'extrémité de la période) déclarée dans les méta-analyses examinées : • 50e centile : de 5,1 jours (IC de 95 % : 4,5 à 5,8) à 5,4 jours (IC de 95 % : 5,0 à 5,7) • 75e centile : de 6,7 jours (IC de 95 % : 5,7 à 7,9) à 8,5 jours (IC de 95 % : 7,9 à 9,1) • 90e centile : 9,7 jours (IC de 95 % : 8,1 à 11,6) • 95e centile : de 11,2 jours (IC de 95 % : 10,7 à 11,8) à 11,7 jours (IC de 95 % : 9,7 à 14,2) • 97,5e centile : de 11,5 jours (IC de 95 % : 8,2 à 15,6) à 16,5 jours (IC de 95 % : 14,8 à 18,3) La période moyenne d'incubation varie de 4,2 à 6,7 jours pour l'ensemble des études.
Quesada (2021) (5) Revue systématique et méta-analyse Sans objet Mars 2020	Revue systématique avec recherche jusqu'au 21 mars 2020. La méta-analyse comprenait 7 études.	La période moyenne d'incubation variait de de 5,6 (IC à 95 %) : 5,2 à 6,0) à 6,7 jours (IC à 95 % : 6,0 à 7,4), une hétérogénéité élevée (I^2 83,0%, p < 0,001) selon le modèle statistique utilisé. Une métarégression des données du 95e centile, y compris l'âge moyen, explique l'hétérogénéité observée. Pour chaque augmentation de 10 ans dans l'âge, la période d'incubation a augmenté d'une journée. Le 95e centile selon l'âge moyen était de 10,5, de 11,5 et de 12,5

		jours pour les gens de 40, de 50 et de 60 ans, respectivement.
McAloon (2020) (6) Examen rapide et méta-analyse Sans objet Avril 2020	Revue rapide et méta-analyse avec recherches effectuées le 8 avril 2020. 24 études ont été incluses dans la revue, dont 9 ont été analysées.	La période moyenne d'incubation était de 5,8 jours (IC à 95 % : 5,0 à 6,7) jours avec une incertitude dans l'extrémité de la distribution. La période d'incubation médiane est de 5,1 (IC à 95 % : 4,5 à 5,8) jours. Le 95^{e} centile était de 11,7 (IC à 95 % : 9,7 à 14,2) jours.
Li (2020) (7) Prépublication Revue systématique Sans objet Mai 2020	Recherche des revues systématiques effectuée le 30 mai 2020 ayant permis d'inclure 64 études. 30 de ces études ont été analysées, dont 12 comportaient une incubation ayant duré plus de 14 jours.	La période d'incubation est de 4,9 jours (IC à 95 % : 4,6 à 5,2) et un 97,5^{e} centile de 19,2 jours (IC à 95 % : 17,4 à 21,4).
Lauer (2020) (8) Méta-analyse Sans objet Janvier et février 2020	Analyse combinée comprenant 181 cas signalés entre le 4 janvier et le 24 février 2020 à l'extérieur de la province du Hubei.	La période médiane d'incubation est de 5,1 jours (IC à 95 % : 4,5 à 5,8 jours). 97,5 % des cas symptomatiques ont présenté des symptômes dans les 11,5 jours (IC : 8,2 à 15,6 jours). Les auteurs signalent que ces estimations présument que, sur 10 000 cas, 101 développeraient des symptômes après 14 jours.
Daley (2020) (9) Prépublication Revue systématique Sans objet Juillet 2020	Revue systématique avec recherche effectuée le 18 juillet 2020 comprenant 21 études mentionnant la période d'incubation.	Dans l'ensemble des études, la moyenne de 5,9 jours et la médiane de 5,6 jours correspondaient.
Khalili (2020) (10) Revue systématique et méta-analyse Sans objet Mars 2020	Revue systématique effectuée jusqu'au 11 mars 2020 comprenant 18 études qui ont été incluses dans la méta-analyse de la période d'incubation, seules 2 études provenaient de l'extérieur de la Chine.	La période moyenne d'incubation combinée était de 5,68 (IC de 99 % : 4,78 à 6,59) jours, I^2= 98,4 %.

Wang (2020) (1) Revue Sans objet Mars 2020	Revue narrative portant sur le SRAS, le SRMO et le SARS-CoV-2.	Période moyenne d'incubation : • SRAS : 4,6 jours (IC à 95 % : 3,8 à 5,8 jours), • SRMO : 5,2 jours (IC à 95 % : 1,9 à 14,7 jours), • SARS-CoV-2 : 6,4 jours (fourchette, 0 à 24,0 jours)/médiane de 4 jours (EI 2 à 7) (Guan 2020)
Lin (2020) (11) Revue systématique Sans objet Juin 2020	Recherche effectuée le 21 février 2020. La méta-analyse de la période d'incubation comprenait 8 études.	L'incubation médiane est de 5,90 jours (EI 4,78 à 6,25) dans 9 études.
Wei (2020) (12) Prépublication Revue systématique Sans objet Avril 2020	Méta-analyse ayant porté sur 56 études (4 095 observations).	La période médiane d'incubation est de 5,8 jours (IC à 95 % : 5,3 à 6,2, I^2 = 96,1%, P < 0,0001) alors que la moyenne est de 6,9 jours. La période d'incubation était plus longue chez les cas asymptomatiques (médiane de 7,7 jours; IC à 95 % : 6,3 à 9,4, P = 0,0408) et les enfants (médiane de 7,3 jours; IC à 95 % : 6,2 à 8,6, P = 0,0219). On estime que 6,7 % (IC à 95 % : 2,4 à 11,2 %) et 1,4 % (IC à 95 % : 0,1 à 3,6 %) des personnes infectées ont eu des périodes d'incubation de 14 et de 21 jours respectivement. Le 97,5^{e} centile était de 18 jours d'incubation pour les cas symptomatiques, de 14 jours pour les cas asymptomatiques et de 25 jours pour les enfants.
Bikbov (2021) (13) Lettre à l'éditeur Sans objet Juillet 2020	Dans leur lettre à l'éditeur, les auteurs résument, sous forme de synthèse narrative, les preuves associées à une période d'incubation qui dépasse 14 jours pour la COVID-19 (Koff, 2020; Guan, 2020; Tan, 2020; Jiang, 2020; Bai, 2020; Qiu, 2020; Bi, 2020).	L'auteur défend fermement le besoin d'avoir des données en libre accès, particulièrement en ce qui concerne la période d'incubation de l'infection à COVID-19.
Littérature primaire (n = 11)		

Koff (2020) (14) Exposé de cas É.-U. Octobre 2020	Exposé de cas sur un patient de Californie qui a eu la COVID-19.	Patient ayant eu une période d'incubation confirmée d'au moins 21 jours.
Guan (2020) (15) Série de cas Chine Février 2020	Étude qui présente des données cliniques sur 1 099 patients.	La page préenregistrée mentionnait une période d'incubation de 24 jours pour une personne, mais cette mention a plutôt été indiquée comme une double exposition lorsque l'OMS s'est opposée aux données présentées. L'article accepté n'utilise donc pas cette durée de 24 jours pour quantifier la période d'incubation et ne fournit aucune limite supérieure.
Tan (2020) (16) Prépublication Série de cas Chine Entre janvier et février 2020	Cohorte de 67 patients admis dans un hôpital en Chine, entre le 26 janvier et le 5 février 2020. Les cas ont été confirmés par l'observation des particules virales du coronavirus par microscope électronique à transmission.	La période d'incubation médiane est de 6,0 jours (fourchette de 1 à 15 jours). L'étude mentionne qu'une période d'incubation plus longue a été observée chez les enfants. Un seul patient sur les 67 (1,5 %) a été indiqué comme ayant eu une période d'incubation de plus de 14 jours (durée indiquée de 15 jours).
Jiang (2020) (17) Prépublication Série de cas Chine Janvier 2020	Données sur 136 patients qui se sont rendus à Hubei entre le 5 et le 31 janvier 2020, avant de retourner dans leurs 21 villes respectives après un séjour de 48 heures ou moins à Hubei.	Les patients âgés de 15 à 64 ans ont eu une période médiane d'incubation de 7,0 jours (IC à 95 %, 6,1 à 8,1 jours). Les patients âgés de 65 à 86 ans ont eu une période médiane d'incubation de 10,9 jours (IC à 95 %, 8,9 à 13,6 jours). Un maximum de 17 jours a cependant été observé (dans la cohorte des 65 à 86 ans).
Bai (2020) (18) Série de cas Chine Entre janvier et février 2020	Cette série de cas suit un groupe familial de cinq patients symptomatiques et d'une personne asymptomatique.	Le cas asymptomatique a eu une période d'incubation indiquée de 19 jours entre le premier contact avec les membres de la famille le 10 janvier 2020 et un test RT-PCR positif le 28 janvier (tests négatifs déclarés les 26 janvier, 5 février et 8 février). Il faut savoir que cette période a été calculée à partir de la première exposition potentielle et peut donc refléter une période plus longue que celle qui a été indiquée en clinique.

Qiu (2020) (19) Enquête sur la recherche des contacts Chine Entre janvier et février 2020	Les résultats des recherches de contacts effectuées sur 104 personnes atteintes de la COVID-19 dans la province du Hunan ont tous été confirmés par RT-PCR.	La période d'incubation médiane était de 6 (fourchette de 1 à 32) jours. Des 104 patients, 8 ont eu des périodes d'incubation de plus de 14 jours, soit entre 18 à 32 jours.
Bi (2020) (20) Enquête sur la recherche des contacts Chine Entre janvier et février 2020	Les résultats des recherches de contacts effectuées sur 391 personnes atteintes de la COVID-19 dans la province de Shenzhen ont tous été confirmés par RT-PCR. 183 cas ont été jugés avoir des cadres bien définis pour l'exposition et l'apparition des symptômes.	La période médiane d'incubation indiquée était de 4,8 jours (IC à 95 %) : 4,2 à 5,4 jours). 95 % des cas symptomatiques ont développé des symptômes dans les 14 jours (IC à 95 % : 12,2 à 15,9 jours)
Li (2021) (21) Prépublication Série de cas Chine Non déclaré	787 cas à l'extérieur de Wuhan ont été identifiés à l'aide d'une base de données de Chine. La distribution gamma correspond le mieux aux données, ce qui veut dire une longue extrémité.	La période moyenne d'incubation est de 7,8 (7,4 à 8,5) jours. Percentiles : 50^{e}, 7,0 (6,7 à 7,3) jours 75^{e}, 10,0 (9,7 à 10,4) jours 97,5^{e}, 17,9 (17,1 à 18,7) jours
Liu (2020) (22) Cohorte rétrospective Chine Janvier à mars 2020	Jusqu'à la fin du mois de mars 2020, 93 patients ont été identifiés dans la province du Jilin, en Chine. Cette étude décrit en détail l'épidémiologie et les résultats cliniques des 93 cas de COVID-19 confirmés par RT-PCR.	La période moyenne d'incubation pour 87 patients était de 10,4 jours (entre 2 et 25 jours). Les auteurs reconnaissent que cette période d'incubation est plus longue que ce qui est indiqué dans de nombreux autres rapports.
Leung (2020) (23) Série de cas Chine Entre janvier et février 2020	Recherche effectuée sur Google jusqu'au 12 février 2020 pour des cas en Chine. 175 cas dont les données d'exposition comprennent des déplacements à Wuhan ou des contacts connus avec une personne ou dans un endroit infectés ont été inclus.	La distribution de Weibull a la meilleure correspondance avec les données sur la période d'incubation. On a cependant vu une dichotomie selon que la personne s'était rendue à Hubei (moyenne de 1,8 jour, variance de 0,7) ou n'avait pas voyagé, ce qui signifie qu'elle avait subi une exposition locale (moyenne de 7,2 jours, variance de 16,2). Cette étude a révélé que la durée de la période d'incubation avec l'intervalle de confiance de 95 % se situait entre 14,6 et

		17,1 jours, ce qui est plus long que les quarantaines actuelles.
Zhu (2020) (24) Prépublication Enquête sur la recherche des contacts Chine Février à avril 2020	Analyse de 670 cas de COVID-19 importés en Chine qui ont été en quarantaine et ont passé des tests RT-PCR.	La période médiane d'incubation était de 3 jours (EI 1 à 6 jours). Le 95e centile était de 11,6 jours. (Le tableau 3 dresse la liste des périodes d'incubation présentées dans 19 études et le 95e centile passe à 14 jours dans la plupart des estimations).
Modèle (n = 1)		
Paul (2020) (25) Prépublication Modèle Canada Novembre 2020	Le modèle susceptible-exposé-infectieux-retiré (modèle SEIR) de l'épidémie canadienne a été développé afin d'estimer la période d'incubation jusqu'en novembre 2020.	Les estimations comprennent une période d'incubation moyenne de 6,89 jours, une médiane de 6 jours et un 90e centile de 11 jours, un 95e centile de 12 jours et un 99e centile de 13,5 jours. Le modèle prédit une pointe dans la période d'incubation à 6 jours et une deuxième plus petite à 10 jours. Il a également détecté une légère augmentation au fil du temps pendant la période d'incubation.

NR = non déclaré, NA = sans objet

POLITIQUES DE QUARANTAINE DE PLUS DE 14 JOURS

Au début de la pandémie de COVID-19, une période d'incubation maximale de 14 jours a été établie par l'OMS et acceptée comme période standard de quarantaine ou d'isolement pour les voyageurs, les cas et les contacts par de nombreux pays et régions. À ce stade-ci de la pandémie, alors quelques pays ont réussi à éliminer la transmission locale du SRAS-CoV-2 ou n'en ont eu que très peu, d'autres continuent de déclarer les nombres de cas les plus élevés à ce jour. De nouvelles variantes préoccupantes ont également été identifiées et pourraient se révéler encore plus transmissibles que le SRAS-CoV-2 original. Par conséquent, les pays dans lesquels la situation associée au SRAS-CoV-2 est bien contrôlée ont décidé de modifier leurs politiques sur la durée de la quarantaine à titre préventif (tableau 2). Le tableau ci-dessous décrit les exigences actuelles en matière de quarantaine des pays dans lesquels la quarantaine a été prolongée en date du 25 janvier 2021.

Tableau 2 : Politiques gouvernementales de quarantaine (n = 4)

POLITIQUE	PRINCIPAUX RÉSULTATS
Australie Politique nationale, FAQ sur la quarantaine dans les hôtels Publiée le 22 janvier 2021 (document consulté le 25 janvier 2021)	La quarantaine à l'hôtel est obligatoire pour toute personne qui entre en Australie. Durée : minimum de 14 jours et maximum de 24 jours. Les tests sont effectués les jours 2 et 12. La quarantaine prend fin au bout de 14 jours pour les personnes dont les résultats des tests de dépistage sont négatifs et qui ne présentent aucun symptôme. Un test positif, des symptômes ou un contact étroit avec un cas sont tous des éléments qui redémarrent le décompte des 14 jours. Ceux qui refusent les tests sont mis en quarantaine pendant 24 jours.
Beijing, Chine Exigences d'entrée et de sortie, indiquées par le gouvernement du Canada Publié le 21 janvier 2021 (document consulté le 25 janvier 2021)	À l'échelle nationale, la Chine exige une quarantaine de 14 jours dans un établissement désigné par le gouvernement. Cette procédure peut varier selon le point d'entrée ou la destination finale. Les voyageurs internationaux qui entrent à Beijing sont assujettis à ce qui suit : • 21 jours de quarantaine dans un établissement désigné par l'administration locale; ils peuvent être autorisés à s'isoler à la maison pendant les 7 derniers jours. • Sept jours supplémentaires pendant lesquels l'état de santé est surveillé. Les voyageurs internationaux qui arrivent à Beijing en provenance de n'importe quelle autre ville chinoise sont assujettis à ce qui suit : • 21 jours d'auto-isolement au point d'entrée international, avant qu'ils puissent se rendre à Beijing. • Lors de leur arrivée à Beijing, sept jours supplémentaires pendant lesquels leur état de santé sera surveillé.
Hong Kong Prolongation de la quarantaine, Communiqué de presse Publié le 25 décembre 2020 (document consulté le 25 janvier 2021)	Les personnes qui arrivent à Hong Kong en provenance d'un pays autre que la Chine pendant les 21 derniers jours sont soumises à une quarantaine de 21 jours dans un hôtel désigné. De plus, quiconque a passé plus de deux heures au Royaume-Uni ou en Afrique du Sud au cours des 21 derniers jours n'est pas autorisé à entrer à Hong Kong.
Singapour	Singapour exige une quarantaine de 14 jours pour tous les voyageurs qui arrivent au pays. La quarantaine doit être effectuée dans un établissement désigné.

Exigences en matière de quarantaine Publiées le 22 janvier 2021 (document consulté le 26 janvier 2021)	La durée de la quarantaine pour les voyageurs en provenance du Royaume-Uni et de l'Afrique du Sud a récemment été augmentée, ce qui fait qu'ils doivent désormais effectuer une quarantaine obligatoire de 21 jours. Les 14 premiers jours doivent être passés dans un établissement désigné, avec 7 jours supplémentaires au lieu de résidence des voyageurs.

Méthodologie :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces systèmes d'archivage pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient : (incubation period ET (prolonged OU review). Cette synthèse contient des recherches publiées jusqu'au 25 janvier 2021.

Une recherche sur Google et sur des sites web gouvernementaux ciblés a été effectuée pour trouver des rapports, des protocoles et des données cliniques accessibles au public et pertinents pour les questions de preuve. Les termes de recherche utilisés comprenaient : COVID-19 ET incubation period; quarantine ET increase; quarantine ET length; variant ET quarantine. Les recherches ont été effectuées et les sites web consultés le 25 janvier 2021.

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les citations pertinentes ont été explorées plus en détail, alors que les données pertinentes ont été extraites dans la revue.

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Emerging Evidence on COVID-19

COVID-19 Summary of Heating, Ventilation, Air Conditioning (HVAC) Systems and Transmission of SARS-CoV-2

Introduction

What is the impact of Heating, Ventilation, Air Conditioning (HVAC) systems on SARS-CoV-2 virus transmission?

This evidence brief summarizes relevant literature up to August 13, 2020 on the potential role of HVAC systems in the transmission of SARS-CoV-2. Evidence from other related respiratory infections (i.e. SARS, MERS-CoV) was also identified to improve our understanding of the possible role of HVAC systems in transmission of similar viruses.

Key Points

- SARS-CoV-2 RNA contamination in air samples and HVAC system surfaces (e.g. air grates and filters) from healthcare settings indicate it may be possible for SARS-CoV-2 to spread through the HVAC system (Table 1). The viability of isolated viral RNA has not been confirmed by cell culture in the majority of studies, with the exception of two studies that collected viable virus from air samples in COVID-19 patients' rooms.
    - Lednicky and colleagues demonstrate viable SARS-CoV-2 can be found in air 2 to 4.8 meters away from patients in hospital care settings, using virus culture (RT-qPCR) (Lednicky et al., 2020). Moreover, the authors suggest virus particles becoming inactivated during sample collection to be the reason for studies failing to culture viable SARS-CoV-2 in air samples.
    - Air samples from a hospital setting treating SARS-CoV-2 patients were contaminated with viral RNA. Minor indications of cytopathic effects and viral replication were observed in an air and surface sample (Santarpia et al., 2020).
- A single study reports on the presence of SARS-CoV-2 RNA downstream of air filters in a hospital ventilation system, however the viability of the isolated virus was not evaluated (Table 1). As such, the potential for SARS-CoV-2 infection from air circulated through a ventilation system remains unestablished.
- A small number of SARS-CoV-2 clusters has been attributed to air conditioning units and air recirculation (Table 2) at a dine-in restaurant (Lu et al., 2020), bus ride to a worship event, and a professional workshop (Shen et al., 2020). Strong air jets created by air conditioning units and the recirculation of indoor air are considered likely modes transmitting infectious respiratory particles

from the index case to other susceptible individuals nearby (Yuguo Li et al., 2020). Other investigations into SARS-CoV-2 outbreak in a cruise ship have failed to implicate the HVAC system in infection transmission (Almilaji & Thomas, 2020; Xu et al., 2020).

- Transmission of other coronavirus infections (i.e. MERS and SARS) predating SARS-CoV-2 point to an association between poor ventilation (i.e. insufficient movement and clearance of contaminated indoor air) and infection transmission, this association likely extends to SARS-CoV-2 (Table 4).
- Expert statements and guidance documents advocate for HVAC testing and certification to ensure properly functioning systems to minimize air contaminants in indoor settings based on local standards.
- Commentaries and reviews that consider the body of evidence on the topic, and mathematical models, consistently report that increasing the flow of outside fresh air into built environments (e.g. open windows) and reducing occupancy within enclosed indoor settings, where feasible and appropriate, to be simple strategies that can mitigate SARS-CoV-2 transmission in indoor settings (Dai & Zhao, 2020; Dietz et al., 2020; Morawska & Cao, 2020).

Overview of the Evidence

Various investigations have aimed to evaluate the evidence connecting HVAC systems and indoor air to infection transmission, both before and following the emergence of COVID-19. The variability of studies in their design, experimental settings (healthcare vs. non healthcare), examined viral pathogens, and HVAC systems do not allow direct comparison of the literature.

Nine surveys of environmental contamination in hospitals with COVID-19 patients provide a snapshot of virus laden surfaces (Table 1). These studies are of moderate risk of bias as they are point in time observational surveys that confirm the presence of viral RNA, but many do not confirm the infectiousness of identified viral particles. Four outbreaks where HVAC systems were investigated as a source of infection transmission have been described in various retrospective epidemiological investigations (Table 2). These epidemiological investigations are at high risk of bias, as demonstrated by the conflicting reports about the Diamond Princess cruise ship where different analytical approaches and assumptions led to different conclusions. Mathematical models and computer simulations were parameterized using observational data from a small number of outbreaks to explore scenarios of how HVAC systems can impact SARS-CoV-2, MERS, and SARS transmission (Table 2 and Table 4). Caution should be exercised when interpreting these findings, as the extent to which the results can be generalized is variable.

There are several knowledge gaps in the current COVID-19 literature. The available evidence has not directly established infectious SARS-CoV-2 particles can travel through an HVAC system or system generated air flow to cause infection when reintroduced to a susceptible population of individuals. Evidence on the optimal number of air changes per hour required in non-healthcare settings, ideal ventilation system configurations, and the role of HEPA filters in mitigating SARS-CoV-2 transmission is limited.

CONTENTS

LITERATURE ON INFECTION TRANSMISSION AND HVAC SYSTEMS

There are no studies that specifically quantify SARS-CoV-2 transmission risk due to HVAC systems or indoor ventilation. Nine studies conducting environmental sampling identified SARS-CoV-2 viral RNA in air samples and on surfaces of HVAC system components (e.g. pre and post air re-circulation filters, air dampers, air grates) in healthcare settings treating COVID-19 cases; virus viability and infectiousness was not established in the majority of studies (Table 1). Thus, dispersion of viable SARS-CoV-2 by a HVAC system has not been demonstrated.

A single cluster of COVID-19 cases from three unrelated families are reported to be associated with air circulation and uni-directional air streams generated by a ductless air conditioning unit in a Chinese restaurant (Lu et al., 2020). In this cluster, the index case from Family A dined upwind of Families B and C, who did not have any other connections or exposures to Family A. Staff and other patrons were not affected. Air re-circulation in enclosed environments linked to air conditioning units, indoor ventilation and fans are reported to have played a role in two unrelated SARS-CoV-2 outbreaks, from a religious worship event and a professional workshop(Shen et al., 2020). Moreover, the HVAC system on-board the Diamond Princess cruise ship that had a large COVID-19 outbreak was also investigated for evidence of its contribution to SARS-CoV-2 spread. One study took into account the lock-down, quarantine period, and incubation period and provides evidence that the quarantine of passengers in cabins stopped transmission on board the ship and no transmission could be attributed to ventilation (Xu et al., 2020). A second study that analysed the same data suggests transmission via circulating air may have occurred, but failed to account for the incubation period (Almilaji & Thomas, 2020).

Investigations of clusters of coronaviruses that predate the emergence of COVID-19 have been linked to poor indoor ventilation and HVAC systems being non-functional (Haselbach et al., 2009; Y Li, Huang, Yu, Wong, & Qian, 2005; Satheesan, Mui, & Wong, 2020; Wong et al., 2004). Multiple investigations into a MERS-CoV cluster within a patient isolation unit attribute high air flow near an infected patient, imbalanced supply and exhaust airflow rates, and a malfunctioning exhaust and air supply to infection spread to healthcare workers (Y Li et al., 2005; Wong et al., 2004). A US study of acute respiratory infections occurring in several army barracks of different designs attributed the HVAC configurations (i.e. the number of individuals that come in contact with and share recirculated air in an HVAC system) to increased infection rates, however they failed to rule out direct transmission (Haselbach et al., 2009). Although this literature is not specific to SARS-CoV-2, it does provide evidence that poor ventilation and non-functional HVAC systems are associated with respiratory infection transmission in indoor settings.

The American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE), a leading US authority on HVAC system design, operation and maintenance, published a position statement on COVID-19,

in April 2020. The position statement advocates for properly functioning HVAC systems as these systems are designed to reduce contaminants in indoor air and as a result minimize airborne transmission of pathogens such as SARS-CoV-2. This statement has been adopted by other organizations, including the Center for Disease Control and Prevention, in back to work and business re-opening guidance.

Table 1: Literature on SARS-CoV-2 contamination of air and air vents in healthcare settings

Reference	Publication Title	Key Outcomes
Environmental Surveys		
(Lednicky et al., 2020) *preprint*	Viable SARS-CoV-2 in the Air of a Hospital Room with COVID-19 Patients.	Air samples were collected from a designated SARS-CoV-2 hospital ward housing infected patients, in Florida, USA. VIV AS and BioSpot air samplers that preserved virus viability were used for sample collection. Viable virus was isolated from air samples collected 2-4.8 meters away from infected patients, thus supporting viable SARS-CoV-2 virus dispersion within airborne aerosols in healthcare settings. Genomic sequencing establishes a relationship between viral RNA isolated from air samples and an infected patient occupying the ward. Finally, viable virus was only isolated from air samples collected without a HEPA filter cover on inlet tubes, based on cytopathic effects on Vero E6 cells. Isolated virus concentrations in air samples ranged from 2-74 $TCID_{50}$ units/L of air.
(Horve et al., 2020) *preprint*	Identification of SARS-CoV-2 RNA in Healthcare Heating, Ventilation, and Air Conditioning Units.	Surfaces of air handling units in a healthcare facility treating COVID-19 patients in Oregon, USA were tested for the presence of viral RNA within HVAC systems. The presence of viral RNA was confirmed by RT-PCR. 25% of sampled surfaces from multiple air handlers were contaminated with SARS-CoV-2 RNA; positive samples were identified on pre-filters (35%), supply air dampers (20.8%), and final filters (16.67%). Recovered viral gene copies decreased from the pre-filter to final filter surfaces.

		The supply air dampers and air sampled in this study represent re-circulated air that is mixed with outside air pre and post HVAC filtration. Samples were found to be contaminated with viral RNA, which is concerning. Since no attempt was made to culture the virus, further research is needed to further investigate the implications of this study; typical filtration systems in healthcare settings may not completely eliminate the passage of viral particles.
(Cheng et al., 2020)	Air and Environmental Sampling for SARS-CoV-2 Around Hospitalized Patients with Coronavirus Disease 2019 (COVID-19).	Air samples near asymptomatic and symptomatic COVID-19 patients (n=6) with and without surgical masks in an airborne infection isolation room (AIIR), in Hong Kong and China, were tested for SARS-CoV-2 contamination. All collected air samples were negative for SARS-CoV-2 RNA.
(Chia et al., 2020)	Detection of Air and Surface Contamination by SARS-CoV-2 in Hospital Rooms of Infected Patients.	Environmental surface and air samples from airborne infection isolation rooms (AIIR) housing COVID-19 patients in Singapore were tested for SARS-CoV-2 RNA. Among the contaminated surface samples, the floors followed by air exhaust vents were the most contaminated. 66% (n=2/3) of the air samples collected from AIIR environments were SARS-CoV-2 RNA positive. The authors suggest the presence of SARS-CoV-2 in the air is likely highest during the first week of illness when respiratory viral load is high. The infectiousness of the recovered viral particles were not assessed.
(Liu et al., 2020)	Aerodynamic Analysis of SARS-CoV-2 in Two Wuhan Hospitals.	SARS-CoV-2 RNA concentrations in aerosol samples, the size and deposition of airborne SARS-CoV-2 aerosols from Wuhan, China hospital settings was quantified. Sampled environments included patient care, public and staff areas within or near a hospital, and field hospital settings. In patient care areas SARS-CoV-2 concentrations from air samples were very low to undetectable, suggesting the negative pressure isolation room and high rate of air exchange was effective.

		In the field hospital setting, the greatest SARS-CoV-2 suspended aerosols were identified in a temporary patient toilet room (1 m^2 area) with low ventilation. In public areas low to undetectable SARS-CoV-2 suspended aerosol concentrations were identified for the majority of sampled public areas. However, virus concentrations were detected in two public sites, a department store entrance and an outdoor site near the hospital. Results suggest high traffic flow and crowding may play a role in the presence of SARS-CoV-2 detection in air samples. Healthcare worker staff areas had the highest SARS-CoV-2 concentrations and aerosol size distributions. Samples from the field hospital staff personal protective equipment removal and changing rooms demonstrated the greatest virus concentrations and aerosol size distribution. The authors hypothesize the observed high concentrations are due to resuspension of virus containing aerosols from healthcare worker PPE surfaces and apparel. The infectiousness of recovered viral particles was not established.
(Guo et al., 2020)	Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020.	35% of air samples collected from hospital ICU and general wards in Wuhan, China tested positive for SARS-CoV2 virus particles. Positive samples were identified near air outlets (35.7%), patient rooms (44.4%) and physician offices (12.5%). Virus-laden samples were most often identified downstream from COVID-19 patients. In the ICU ward space, patient care and treatment areas were positive for SARS-CoV-2 virus aerosols, and positive samples were identified up to 4 meters from a COVID-19 patient. In the general ward's space, areas positive for SARS-CoV-2 were within 2.5 meters upstream of the patient. No SARS-CoV-2 virus aerosols were identified in patient corridor areas.

		The infectiousness of recovered viral particles was not established.
(Ong et al., 2020)	Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient.	Survey of air samples collected from negative pressure airborne infection isolation rooms (AIIR), containing anterooms and bathrooms, in the dedicated SARS-CoV-2 outbreak center in Singapore, housing three symptomatic confirmed cases of COVID-19. Although some environmental samples were found to be SARS-CoV-2 contaminated, no air samples were positive for SARS-CoV-2 virus. The infectiousness of recovered viral particles was not established.
(Santarpia et al., 2020) *preprint*	Aerosol and Surface Transmission Potential of SARS-CoV-2.	Air and surface samples from isolation spaces housing COVID-19 cases at the University of Nebraska, United States were collected and tested for SARS-CoV-2 viral RNA by RT-PCR. 63.2% of air samples from patient isolation areas were positive for viral RNA, particularly under the patient's bed and window ledges at the edge of the room. Based on airflow modelling, the authors suggest turbulent eddies (i.e. swirling of a fluid and the reverse current created when the fluid is in a turbulent flow) that form under the patient's bed, and dominate airflow carrying respiratory/viral particles away from the patient toward the edges of the rooms led to the observed contamination. 58.3% of air samples collected in hallways outside of patient isolation areas also contained the virus. The surface of an air grate was found to be contaminated with SARS-CoV-2; the highest viral load observed was recovered from this study surface (1.75 copies/µL). The study findings suggest viral aerosol particles can be produced by infected individuals even during the absence of

		cough, with the virus travelling distances greater than 6 feet (1.8 meters). Cultivation of the isolated viral RNA could not be confirmed via Vero E6 cell assay due to low concentrations of recovered virus. However, minor indications of cytopathic effects and viral replication were observed in an air and surface sample.
(Zhou et al., 2020)	Investigating SARS-CoV-2 Surface and Air Contamination in an Acute Healthcare Setting During the Peak of the COVID-19 Pandemic in London.	Levels of SARS-CoV-2 surface and air contamination in a London, UK hospital at the peak of the COVID-19 pandemic was investigated. Environmental surface swabs from clinical and public areas of the hospital were collected. Viral RNA was detected by RT-PCR in 52.3% of the collected surface samples (most often in COVID-19 patient care areas), and 38.7% of the air samples collected. Contaminated samples were more frequent in areas occupied by a COVID-19 patient. The reclaimed virus could not be cultured in Vero E6 cell lines, as the recovered viral load was less than 30 Ct.
Mathematical Models		
(Dai & Zhao, 2020) *preprint*	Association of Infected Probability of COVID-19 with Ventilation Rates in Confined Spaces: a Wells-Riley Equation Based Investigation.	The Wells-Riley mathematical equation is applied to determine associations between infection probability and indoor ventilation rates. The authors report that less than 1% of the susceptible unmasked population would be infected in confined indoor spaces if the following ventilation rates and exposure periods are applied (100-350 m^3/h and 1200-4000 m^3/h for 15 minutes and 3 hours). If both the infected and susceptible individuals wear masks, the ventilation rate can be reduced to 50-180 m^3/h and 600-2000 m^3/h correspondingly. The authors state former rates would be easier to be achieved by normal ventilation models in typical office, classrooms, buses and aircraft cabin settings.
Commentaries		
(Melikov, Ai, & Markov, 2020)	Intermittent Occupancy Combined with Ventilation: An Efficient Strategy for the	Due to inherent limitations of most mechanical ventilation systems the fresh air flow supply cannot be increased to eliminate infection risk from expiratory airborne aerosols in indoor settings. As such, authors propose a source control

	Reduction of Airborne Transmission Indoors.	strategy based on intermittent breaks for room occupants (i.e. all occupants leaving the room periodically) and minimized room occupancy rates to maximize the effectiveness of indoor ventilation systems reducing airborne infectious pathogens.
(Morawska & Cao, 2020)	Airborne Transmission of SARS-CoV-2: The World Should Face the Reality.	Based on the available evidence, the authors conclude SARS-CoV-2 can likely be transmitted via airborne route. Therefore, all possible precautions against airborne transmission in indoor scenarios should be taken. Precautions include increased ventilation rate, using natural ventilation, avoiding air recirculation, avoiding staying in another person's direct air flow, and minimizing the number of people sharing the same environment. Of significance is maximizing natural ventilation in buildings that are or can be naturally ventilated ensuring that the ventilation rate is sufficiently high.
(Dietz et al., 2020)	2019 Novel Coronavirus (COVID-19) Pandemic: Built Environment Considerations To Reduce Transmission.	A review of the available evidence on the build environment that can be applied to the current COVID-19 pandemic. SARS-CoV-2 has been observed in aerosolized particles and droplets in a range of sizes, including 0.25 to 0.5 µm, which require high efficacy filtration for removal from shared indoor air. Residential and commercial ventilation systems with minimum efficiency reporting values (MERV) of 8 can only capture 70 to 85% of particles ranging from 3.0 to 10.0 µm (not sufficient for SARS-CoV-2 aerosols). Ventilation systems of MERV 13 or higher and HEPA filters commonly used in healthcare settings would effectively remove particle matter in the 0.25 to 0.5 µm size range. However, authors point to limitations within healthcare HVAC systems and filters arising from gaps at the edges of filters. Overall, the authors note that although higher ventilation rates, outdoor air fractions and higher grade filters can reduce and dilute air contaminants (i.e. infectious particles) within indoor air, the risk of airborne infection transmission is never fully eliminated.

Table 2: COVID-19 clusters primarily attributed to indoor ventilation

Reference	Publication Title	Key Outcomes
(Lu et al., 2020)	COVID-19 Outbreak Associated with Air Conditioning in Restaurant, Guangzhou, China.	Indoor ventilation air flow and droplet transmission at distances less than one meter are considered to be the primary modes of transmission for a cluster (n=10) attributed to an air conditioning unit at a dine-in restaurant. The only interaction for multiple cases in the cluster (Family B and Family C) with the index case (Family A) was sitting at neighbouring tables. In the table arrangement, the air outlet and the return air inlet for the central air conditioner were located above table of Family C, and all three tables were in line with the airflow for the same air conditioning unit. Droplet and aerosol infection transmission linked to air conditioning air flow is considered the mode of transmission between the three families.
(Yuguo Li et al., 2020) *preprint*	Evidence for Probable Aerosol Transmission of SARS-CoV-2 in a Poorly Ventilated Restaurant.	A thorough follow-up analysis of the restaurant outbreak by computer simulations and aerodynamic analysis concludes transmission to be consistent with a viral spread from poor ventilation, air flow zones created by the air condition unit, and index case exhaled virus-laden respiratory particles.
(Almilaji & Thomas, 2020) *preprint*	Air Recirculation Role in the Infection with COVID-19, Lessons Learned from Diamond Princess Cruise Ship.	Based on the analysis of clinical data from cruise ship passengers, symptomatic infections diagnosed after the initiation of quarantine was the same in cabins with and without an infected person. The authors' conclude airborne transmission of SARS-CoV-2 through the ventilation system of the cruise ship could explain infection rates observed during the quarantine period.
(Xu et al., 2020) *preprint*	Transmission Routes of COVID-19 Virus in the Diamond Princess Cruise Ship.	Analysis of passenger and COVID-19 case data (n=343) from the Diamond Princess cruise ship cluster, considered the HVAC and sewage systems of the ship and the epidemiological risk factors of each case and close contact to explore the most plausible modes of transmission. Based on the analyses the authors conclude the cruise ship's air condition (HVAC) system did not play a role in long-range airborne transmission of COVID-19 on the ship and that most passenger cases were likely exposed prior to the ship being quarantined.

(Shen et al., 2020) *preprint*	Airborne Transmission of COVID-19: Epidemiologic Evidence from Two Outbreak Investigation.	Airborne transmission by aerosols is assumed to be enhanced by fans and air conditioning units (re-circulating air) in shared transportation and indoor spaces and to have contributed to two independent COVID-19 outbreaks. One involving bus riders to and from a worship event (n=172), and another involving a three day conference workshop (n=30) where attendees shared indoor meeting space. In the worship, event outbreak COVID-19 infection risk among Bus #2 passengers was 41.5 (95% CI: 2.6–669.5) times higher compared to Bus #1 passengers and 11.4 (95% CI: 5.1–25.4) times higher compared to all other individuals attending the worship event. The overall attack rate from the conference outbreak was 48.3%.

Table 3: Grey literature on COVID-19 transmission and HVAC systems

Reference	Organization	Key statements
(ASHRAE, 2020) Accessed here	American Society of Heating, Refrigerating, and Air-Conditioning Engineers	ASHRAE Position Document on Infectious Aerosols released in April 2020. Transmission of SARS-CoV-2 through the air is sufficiently likely and airborne exposure to the virus should be controlled. Changes to building operations, including the operation of heating, ventilating and air conditioning systems can reduce airborne exposures. Ventilation and filtration provided by HVAC systems can reduce airborne concentration of SARS-CoV-2 and thus the risk of transmission through the air.
(CSA Group, 2020) Accessed here	CSA Group	HVAC equipment (intended for healthcare settings) testing and certification standards for manufacturers. Standard CSA Z317.2:19: Special requirements for HVAC systems in health care facilities Standard CAN/CSA-Z317.13-17: Infection control during construction, renovation, and maintenance of health care facilities, among others.

(CDC, 2020) Accessed here	Center for Disease Control and Prevention	Expert guidance on preparations and reopening businesses reference ASHRAE statement on HVAC systems, and HVAC start up guide. The guidance alludes to ensuring HVAC systems are operating properly. Increasing circulation of outdoor air by opening windows and doors after assessing the risks of outdoor air to occupants. Additional recommendations outlined in the documents include: increasing airflow supply to occupied spaces, disabling demand-control ventilation controls that reduce air supply based on temperature or occupancy, using natural ventilation, improving central air filtration, running the ventilation system during unoccupied times, generating clean-to-less-clean air movement, considering using portable high-efficiency particulate air (HEPA) fan/filtration systems, ensuring exhaust fans in restroom facilities are functional and operating, and considering using ultraviolet germicidal irradiation as a supplement.
(ECDC, 2020) Accessed here	European Center for Disease Prevention and Control	Guidance on heating, ventilation and air-conditioning systems in the context of COVID-19. The document covers maintenance, avoidance of recirculation, fan direction, and air exchange rate.
(AHS, 2020) Accessed here	Alberta Health Services	Rapid Evidence Report Outlines the available evidence and grey literature on COVID-19 transmission and HVAC systems in healthcare and non-healthcare settings, up to May 11, 2020. The key findings from the evidence review state HVAC system factors may contribute to pathogen transmission, especially when HVAC systems are not operating properly. The exact potential of HVAC systems to contribute to SARS-CoV-2 infection transmission could not be assessed due to limited evidence on viable virus in air samples, variability in HVAC systems, and complexities in transmission modalities. The Reviewer Committee recommend a committee with the necessary expertise be established to explore the role of

		HVAC systems in the transmission of viral pathogens including SARS CoV-2.

Table 4: Other Infection transmission (not SARS-CoV-2) and HVAC systems

Reference	Publication Title	Key Outcomes
(Wong et al., 2004)	Cluster of SARS Among Medical Students Exposed to Single Patient, Hong Kong.	SARS outbreak at a Hong Kong hospital isolation ward, among healthcare workers is described. Epidemiological data of exposed healthcare workers, an inspection of the ventilation system, and computational fluid dynamic analysis find index patient's cubicle had the highest supply flow rate, while the adjacent exhaust grille had the lowest flow rate among all four functional exhaust grilles in the ward. The authors discuss the possibility of aerosol transmission from the index patient via the ventilation system.
(Y Li et al., 2005)	Role of Air Distribution in SARS Transmission During the Largest Nosocomial Outbreak in Hong Kong.	A second retrospective analysis of in-patient cases and healthcare worker cases from the above SARS hospital outbreak is detailed. On-site inspections, measurements of the ventilation design and air distribution, and computational fluid dynamics simulations conclude airflow rate imbalances and non-functional HVAC system components (e.g. supply diffusers and exhaust grilles) to have contributed to infection transmission. The analysis revealed the need for improved ventilation and air-conditioning systems in the isolation ward to effectively reduce the risk of infection spread between patients and health care workers.
(Satheesan et al., 2020)	A Numerical Study of Ventilation Strategies for Infection Risk Mitigation in General Inpatient Wards.	Simulations are applied to examine the transport mechanisms and deposition patterns of MERS-CoV within a general ward. The authors concluded that air change and exhaust airflow rates had significant impacts on airflow and particle distribution.

		Within the mechanically vented space, exhaust grilles near a patient (ideally above each patient's bed), and high exhaust airflow rates are recommended to reduce transmission.
(Haselbach et al., 2009)	Airborne Transmission via HVAC of Acute Respiratory Infections in Military Facilities? Review of a Basic Training Cohort Study.	Examination of acute respiratory infections among military recruits living in military barracks, while considering HVAC system configurations and the sum of occupants from multiple zones that share return air mixed within the same HVAC system and redistributed as supply (termed contact population). The study found significant risk of airborne ARI transmission through HVAC systems. Higher rates of infection were found in the systems with both higher HVAC contact populations and less access to windows allowing for outside ventilation and air supply.
(Sundell et al., 2011)	Ventilation Rates and Health: Multidisciplinary Review of the Scientific Literature.	A multidisciplinary review team explore the evidence (published up to 2005) linking ventilation rate to multiple health endpoints. The evidence show biological plausibility for an association of health outcomes with ventilation rates, but does not provide clear evidence on particular agent(s) or infectious loads.
(Y. Li et al., 2007)	Role of Ventilation in Airborne Transmission of Infectious Agents in the Built Environment - a Multidisciplinary Systematic Review.	Review of literature published between 1960 and 2005 identified ten articles linking infection transmission to HVAC systems. The reviewers conclude there is strong and sufficient evidence to demonstrate an association between ventilation, air movements in buildings and the transmission/spread of infectious diseases such as measles, tuberculosis, chickenpox, influenza, smallpox and SARS. However, there was insufficient data to specify and quantify the minimum ventilation requirements in hospitals, schools, offices, homes and isolation rooms in relation to spread of infectious diseases via the airborne route.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an Excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms included in this review were (indoor and air), ventilation, HVAC, air conditioning. Each potentially relevant reference was examined to confirm it relevance data and relevant data was extracted. This review contains COVID-19 research published up to August 13, 2020. Relevant literature predating COVID-19 was identified by examining the reference lists of the relevant reviews and papers included in this summary.

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Preuve émergente sur la COVID-19

COVID-19 – Résumé en ce qui concerne les systèmes de chauffage, de ventilation, de climatisation (CVCA) et la transmission du virus SRAS-CoV-2

Introduction

Quelles répercussions les systèmes de chauffage, de ventilation et de climatisation (CVCA) ont-ils sur la transmission du virus SRAS-CoV-2?

Cette synthèse en bref résume la documentation pertinente disponible jusqu'au 13 août 2020 à propos du rôle que peuvent jouer les systèmes de CVCA dans la transmission du SRAS-CoV-2. Des données probantes associées à d'autres infections respiratoires connexes (c.-à-d. SRAS, MERS-CoV) ont également été incluses afin d'obtenir une meilleure compréhension du rôle que les systèmes de CVCA peuvent possiblement jouer dans la transmission de virus semblables.

Points clés

- La contamination des échantillons d'air et de surface du système de CVCA (p. ex., grilles d'air et filtres) par l'ARN du SRAS-CoV-2 dans les établissements de soins de santé indique qu'il est possible que ce système puisse permettre au virus de se propager (Tableau 1). La viabilité de l'ARN viral isolé n'a cependant pu être confirmée par la culture cellulaire dans la majorité des études, sauf dans deux études dans lesquelles des virus viables présents dans les échantillons d'air provenant des chambres de patients atteints de la COVID-19 ont pu être recueillis.
    - À l'aide d'une culture de virus (RT-qPCR), Lednicky et ses collaborateurs ont pu démontrer la présence dans l'air, d'un virus SRAS-CoV-2 viable, à une distance de 2 à 4,8 mètres des patients dans un milieu hospitalier (Lednicky et al., 2020). Les auteurs ont également suggéré que le fait que les particules de virus s'inactivent pendant le prélèvement d'échantillons explique pour quelle raison les études n'ont pas réussi à cultiver de virus SRAS-CoV-2 viable dans les échantillons d'air.
    - Des échantillons d'air prélevés dans un contexte hospitalier où étaient traités des patients atteints du SRAS-CoV-2 ont été contaminés par de l'ARN viral. Des indications mineures d'effet cytopathologiques et de réplication virale ont également pu être observées dans un échantillon d'air et de surface (Santarpia et al., 2020).
- Une seule étude a cependant fait état de la présence d'ARN du SRAS-CoV-2 en aval des filtres à air dans le système de ventilation d'un hôpital, mais la viabilité du virus isolé n'a pu être évaluée

(Tableau 1). Le risque d'infection au SRAS-CoV-2 en raison de l'air qui circule dans un système de ventilation n'a donc pas encore été établi.

- Un petit nombre de grappes de SRAS-CoV-2 ont cependant été attribuées à des unités de climatisation et de recirculation d'air (Tableau 2) dans un restaurant (Lu et al., 2020), dans un trajet d'autobus à destination d'un événement religieux et dans un atelier professionnel (Shen et al., 2020). Les puissants jets d'air créés par les climatiseurs et la recirculation de l'air intérieur sont jugés être des modes probables de transmission de particules respiratoires infectieuses d'un cas index vers d'autres personnes vulnérables se trouvant à proximité (Yuguo Li et al., 2020). D'autres enquêtes sur la flambée de SRAS-CoV-2 à bord d'un navire de croisière n'ont cependant pas permis de mettre en cause le système de CVCA dans la transmission de l'infection (Almilaji & Thomas, 2020; Xu et al., 2020).
- Puisqu'un lien entre une mauvaise ventilation (c.-à-d. niveau insuffisant de déplacement d'air et d'élimination de l'air intérieur contaminé) et la transmission de l'infection a été établi pour la transmission d'autres infections par coronavirus (c.-à-d. MERS et SRAS) antérieures au SRAS-CoV-2, il devrait en être de même pour le SRAS-CoV-2 (Tableau 4).
- Les déclarations d'experts et les documents d'orientation préconisent la mise à l'essai et la certification du système de CVCA afin d'en assurer le bon fonctionnement et de réduire au minimum, conformément aux normes locales, la présence de contaminants atmosphériques dans les environnements intérieurs.
- Les commentaires et revues qui tiennent compte de l'ensemble des données probantes sur le sujet ainsi que les modèles mathématiques indiquent constamment que l'apport d'air frais en provenance de l'extérieur dans les environnements bâtis (p. ex., par des fenêtres ouvertes) et la réduction de l'occupation dans les environnements intérieurs fermés, lorsque cela est possible et approprié, sont deux stratégies simples qui peuvent permettre d'atténuer la transmission du SRAS-CoV-2 à l'intérieur (Dai & Zhao, 2020; Dietz et al., 2020; Morawska & Cao, 2020).

Vue d'ensemble des éléments de preuve

Diverses enquêtes visaient à évaluer les données probantes qui établissent un lien entre les systèmes de CVCA/l'air intérieur et la transmission des infections, tant avant qu'après l'émergence de la COVID-19. La variabilité dans la conception des études, dans les milieux expérimentaux (établissements de soins de santé c. environnements non médicaux), dans les pathogènes viraux examinés et dans les systèmes de CVCA ne permet cependant pas d'effectuer de comparaison directe de la documentation disponible.

Neuf enquêtes sur la contamination de l'environnement dans les hôpitaux où se trouvaient des patients atteints de la COVID-19 ont permis de déceler des surfaces contaminées de virus (Tableau 1). Ces études présentent cependant un risque modéré de biais, puisqu'il s'agit d'observations ponctuelles qui, même si elles confirment la présence d'ARN viral, n'ont pu confirmer l'infectiosité de ces particules virales. Quatre éclosions dans lesquelles les systèmes de CVC ont été étudiés comme source de transmission d'infection ont

été décrites dans différentes études épidémiologiques rétrospectives (Tableau 2). Ces études épidémiologiques présentent un risque élevé de biais, comme le démontrent les rapports contradictoires à propos du navire de croisière Diamond Princess dans lesquels différentes approches et hypothèses analytiques ont mené à des conclusions différentes. Des modèles mathématiques et des simulations informatiques ont été paramétrés avec des données d'observation provenant d'un petit nombre d'éclosions pour explorer différents scénarios sur la façon dont les systèmes de CVC peuvent avoir une incidence sur le SRAS-CoV-2, le MERS et la transmission du SRAS (Tableaux 2 et 4). Il faut cependant faire preuve de prudence dans l'interprétation de ces constatations puisque la mesure dans laquelle les résultats peuvent être généralisés est variable.

Plusieurs lacunes ont également été notées dans la documentation actuelle sur la COVID-19. Les données probantes disponibles n'ont pas permis d'établir directement que les particules infectieuses du SRAS-CoV-2 aient pu se déplacer dans un système de CVCA ou dans le débit d'air généré par le système et entraîner une infection lorsqu'elles sont réintroduites dans une population de personnes vulnérables. Les données probantes sur le nombre optimal de changements d'air par heure requis dans des environnements non médicaux, sur les configurations idéales du système de ventilation et sur le rôle des filtres HEPA dans l'atténuation de la transmission du SRAS-CoV-2 sont cependant limitées.

CONTENU

DOCUMENTATION SUR LA TRANSMISSION DES INFECTIONS ET LES SYSTÈMES DE CVCA

Aucune étude ne quantifie spécifiquement le risque de transmission du SRAS-CoV-2 lié aux systèmes de CVCA ou à la ventilation intérieure. Neuf études ayant effectué un échantillonnage environnemental ont identifié l'ARN viral du SRAS-CoV-2 dans des échantillons d'air et sur les surfaces des composants du système de CVCA (p. ex., filtres de recirculation d'air avant et après, registres d'air, grilles d'air) dans des établissements de soins de santé où des patients atteints de COVID-19 étaient traités, mais la viabilité du virus et l'infectiosité n'ont pu être établies dans la majorité des études (Tableau 1). Par conséquent, la dispersion par un système de CVCA du virus viable du SRAS-CoV-2 viable n'a pas été démontrée.

Une seule grappe de cas de COVID-19 ayant touché les membres de trois familles non apparentées a été associée à la circulation d'air et aux courants d'air unidirectionnels générés par une unité de climatisation sans conduit dans un restaurant chinois (Lu et al., 2020). Dans cette grappe, le cas index de la famille A a mangé en amont des membres des familles B et C. Aucun autre lien ni exposition n'a pu être établi entre ces familles et la famille A et aucun autre membre du personnel ni aucun autre client du restaurant n'a été infecté

par le virus. La recirculation de l'air dans les environnements clos associée aux climatiseurs, à la ventilation intérieure et aux ventilateurs a joué un rôle dans deux éclosions non liées de SRAS-CoV-2 à la suite d'un événement à caractère religieux et d'un atelier professionnel (Shen et al., 2020). De plus, le système de CVCA à bord du navire de croisière Diamond Princess où l'on a dénombré une importante éclosion de COVID-19 a également fait l'objet d'une enquête afin d'avoir des preuves en ce qui concerne sa contribution à la propagation du SRAS-CoV-2. Une étude ayant cependant tenu compte du confinement, de la période de quarantaine et de la période d'incubation a fourni la preuve que la mise en quarantaine des passagers dans les cabines avait arrêté la transmission à bord du navire et qu'aucune transmission ne pouvait donc être attribuée à la ventilation (Xu et al., 2020). Une seconde étude qui a analysé les mêmes données a, quant à elle, suggéré que la transmission par l'air circulant aurait pu se produire, mais n'a pas tenu compte de la période d'incubation (Almilaji & Thomas, 2020).

Les enquêtes sur les grappes de coronavirus qui existaient avant l'apparition de la COVID-19 ont été associées à une mauvaise ventilation à l'intérieur et à des systèmes de CVC non fonctionnels (Haselbach et al., 2009; Y Li, Huang, Yu, Wong, & Qian, 2005; Satheesan, Mui, & Wong, 2020; Wong et al., 2004). De multiples enquêtes sur une grappe de cas de MERS-CoV dans une unité d'isolement ont attribué le fait que l'infection se soit propagée aux travailleurs de la santé à un débit d'air élevé près d'un patient infecté, à des débits d'air déséquilibrés en ce qui concerne l'alimentation en air et l'élimination de l'air vicié, ainsi qu'au mauvais fonctionnement du système d'échappement et de l'alimentation en air (Y Li et al., 2005; Wong et al., 2004). Une étude américaine sur les infections respiratoires aiguës qui se sont déclarées dans plusieurs casernes de l'armée de terre a cependant attribué l'augmentation des taux d'infection aux différentes configurations du système de CVCA (c.-à-d. le nombre de personnes qui entrent en contact avec l'air recirculé et respirent le même air provenant d'un système de CVCA). Elle n'a cependant pas pu exclure la transmission directe (Haselbach et al., 2009). Bien que cette documentation ne porte pas spécifiquement sur le SRAS-CoV-2, elle fournit des preuves indiquant qu'une mauvaise ventilation et des systèmes de CVCA non fonctionnels sont associés à la transmission des infections respiratoires dans les environnements intérieurs.

L'American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE), une autorité américaine de premier plan en matière de conception, d'exploitation et d'entretien des systèmes de CVCA, a publié un énoncé de position en avril 2020 sur la COVID-19. Elle y préconise notamment le bon fonctionnement des systèmes de CVCA, puisque ces systèmes sont conçus pour réduire les contaminants dans l'air intérieur et, par conséquent, minimiser la transmission aérienne de pathogènes comme le SRAS-CoV-2. Cet énoncé de déclaration a été adopté par d'autres organisations, y compris le Center for Disease Control and Prevention, dans le cadre des directives en ce qui concerne le retour au travail et la réouverture des entreprises.

Tableau 1 : Documentation sur la contamination de l'air par le SRAS-CoV-2 et les éventsdans les établissements de soins de santé

Référence	Titre de la publication	Principaux résultats
Études de l'environnement		
(Lednicky et al., 2020) *prépublication*	Un cas de SRAS-CoV-2 viable dans l'air d'une chambre d'hôpital où se trouvaient des patients atteints de COVID-19.	Des échantillons d'air ont été prélevés dans un hôpital désigné où étaient traités des patients infectés au SRAS-CoV-2 en Floride, aux États-Unis. Des échantillonneurs d'air VIV AS et BioSpot qui ont pu préserver la viabilité du virus ont été utilisés pour le prélèvement de ces échantillons. Un virus viable a ainsi pu être isolé dans des échantillons d'air prélevés à des distances variant entre 2 et 4,8 mètres des patients infectés, ce qui indique la dispersion d'un virus SRAS-CoV-2 viable dans les aérosols en suspension dans l'air dans les établissements de soins de santé. Le séquençage génomique a établi une relation entre l'ARN viral isolé des échantillons d'air et un patient infecté qui se trouvait dans le service. Ce virus viable n'a cependant pu être isolé qu'à partir d'échantillons d'air prélevés dans des tubes d'admission sans couvercle de filtre HEPA en fonction des effets cytopathiques sur les cellules Vero E6. Les concentrations de virus isolés dans les échantillons d'air variaient de 2 à 74 unités $TCID_{50}$/L d'air.
(Horve et al., 2020) *prépublication*	Identification de l'ARN du SRAS-CoV-2 dans les unités de chauffage, de ventilation et de conditionnement d'air des établissements de soins de santé.	Les surfaces des unités de traitement de l'air d'un établissement de soins de santé où étaient traités des patients atteints de la COVID-19 en Oregon, aux États-Unis, ont été testées pour y déceler la présence d'ARN viral dans les systèmes de CVCA. Le RT-PCR a confirmé la présence d'ARN viral. Ainsi, 25 % des surfaces échantillonnées provenant de plusieurs unités de traitement de l'air étaient contaminées par l'ARN du SRAS-CoV-2. Des échantillons positifs ont ainsi pu être obtenus sur des préfiltres (35 %), des registres d'air d'alimentation (20,8 %) et des filtres finaux (16,67 %). Le

		nombre de copies de gènes viraux récupérés a cependant diminué entre la surface du préfiltre et celle du filtre final. Les registres d'air d'alimentation et l'air échantillonné dans le cadre de cette étude comprenaient de l'air recirculé mélangé à de l'air provenant de l'extérieur avant et après le filtrage par le système CVCA. Les échantillons étaient cependant contaminés par de l'ARN viral, ce qui est préoccupant. Comme aucune tentative de culture du virus n'a été faite, d'autres recherches seront nécessaires pour étudier plus à fond les répercussions de cette étude puisque les systèmes de filtration typiques dans les établissements de soins de santé pourraient ne pas pouvoir éliminer complètement le passage des particules virales.
(Cheng et al., 2020)	Prélèvement d'échantillons d'air et d'échantillon sur le terrain pour déceler la présence du SRAS-CoV-2 près de patients hospitalisés et atteints de la maladie au coronavirus 2019 (COVID-19).	Des échantillons d'air prélevés près de patients asymptomatiques et symptomatiques atteints de COVID-19 (n=6) portant ou non un masque chirurgical dans une chambre d'isolement des infections aéroportées à Hong Kong et en Chine ont été analysés pour déterminer s'ils étaient contaminés par le SRAS-CoV-2. Tous les échantillons d'air prélevés étaient négatifs pour l'ARN du SRAS-CoV-2.
(Chia et al., 2020)	Détection de la contamination de l'air et des surfaces par le SRAS-CoV-2 dans les chambres d'hôpital des patients infectés.	Des échantillons de surface et d'air prélevés dans des chambres d'isolement des infections aéroportées où se trouvaient des patients atteints de la COVID-19 à Singapour ont été analysés afin de détecter la présence de l'ARN du SRAS-CoV-2. Parmi les échantillons de surface contaminés, les planchers étaient les plus contaminés, suivis des évents d'évacuation. 66 % (n=2/3) des échantillons d'air prélevés dans des chambres d'isolement des infections aéroportées étaient positifs pour l'ARN du SRAS-CoV-2. Les auteurs suggèrent que la présence du SRAS-CoV-2 dans l'air est plus importante pendant la première semaine de maladie, alors que la charge virale respiratoire est élevée.

		L'infection des particules virales récupérées n'a cependant pas été évaluée.
(Liu et al., 2020)	Analyse aérodynamique du SRAS-CoV-2 dans deux hôpitaux de Wuhan	Les concentrations d'ARN du SRAS-CoV-2 dans les échantillons d'aérosols, ainsi que la taille et le dépôt des aérosols du SRAS-CoV-2 en suspension dans l'air provenant d'hôpitaux de Wuhan, en Chine, ont été quantifiés. Les environnements échantillonnés comprennent les services de soins aux patients, les espaces publics et les espaces réservés au personnel au sein ou à proximité d'un hôpital, et les environnements des hôpitaux de campagne. Dans les espaces de soins aux patients, les concentrations de SRAS-CoV-2 provenant d'échantillons d'air étaient très faibles à indétectables, ce qui indique que la chambre d'isolement à pression négative et le taux élevé d'échange d'air étaient efficaces. Dans le cadre de l'hôpital de campagne, les plus fortes concentrations de SRAS-CoV-2 dans les aérosols en suspension ont été identifiées dans la salle de toilette temporairement mal ventilée d'un patient (1 m^2). Dans les zones publiques, des concentrations faibles à indétectables de SRAS-CoV-2 dans les aérosols en suspension ont été identifiées dans la majorité des espaces publics échantillonnés. Cependant, les concentrations de virus ont été détectées dans deux sites publics, à l'entrée d'un grand magasin et sur un site extérieur près d'un hôpital. Les résultats indiquent qu'une circulation élevé et un grand nombre de personnes peuvent tous deux jouer un rôle dans la détection du SRAS-CoV-2 dans les échantillons d'air. Les secteurs où se trouvaient des travailleurs de la santé affichaient les concentrations les plus élevées de SRAS-CoV-2 et les plus grandes distributions de la taille des aérosols. Les échantillons prélevés sur l'équipement de protection individuelle que portait les membres du personnel des

		hôpitaux de campagne et dans les vestiaires de ces hôpitaux ont montré les plus fortes concentrations de virus et la plus grande distribution de la taille des aérosols. Les auteurs ont émis l'hypothèse que ces concentrations élevées observées étaient attribuables à la remise en suspension du virus contenant des aérosols provenant des surfaces de l'EPI et des vêtements que portaient les travailleurs de la santé. L'infection des particules virales récupérées n'a cependant pas été établie.
(Guo et al., 2020)	Distribution en aérosol et en surface du coronavirus 2 du syndrome respiratoire aigu sévère dans les services hospitaliers, Wuhan, Chine, 2020	35 % des échantillons d'air prélevés dans les services de soins intensifs des hôpitaux et les services généraux de Wuhan, en Chine, et testés pour détecter des particules du virus SRAS-CoV-2 se sont révélés positifs. Des échantillons positifs ont été identifiés près des sorties d'air (35,7 %), des chambres des patients (44,4 %) et des bureaux des médecins (12,5 %). Les échantillons chargés de virus ont été le plus souvent identifiés en aval des patients souffrant de la COVID-19. Dans l'espace des unités de soins intensifs, les zones de soins et de traitement des patients, des aérosols du virus SRAS-CoV-2 ont été trouvés et des échantillons positifs ont également été identifiés jusqu'à 4 mètres des patients atteints de COVID-19. Dans les espaces de soins généraux, les zones testées positives au SRAS-CoV-2 se trouvaient à moins de 2,5 mètres en amont d'un patient. Aucun aérosol du virus SRAS-CoV-2 n'a été identifié dans les couloirs fréquentés par les patients. L'infection des particules virales récupérées n'a cependant pas été établie.
(Ong et al., 2020)	Contamination de l'air, des surfaces environnementales et des équipements de	Enquête sur des échantillons d'air prélevés dans des chambres d'isolement des infections aéroportées à pression négative qui comprennent des antichambres et des salles de bain, dans le centre spécialisé d'éclosion du SRAS-CoV-2 à

	protection individuelle par le coronavirus 2 du syndrome respiratoire aigu sévère (SRAS-CoV-2) chez un patient symptomatique	Singapour, où se trouvent trois cas symptomatiques confirmés de COVID-19. Bien que certains échantillons environnementaux aient été contaminés par le SRAS-CoV-2, aucun échantillon d'air n'a révélé la présence du virus du SRAS-CoV-2. L'infection des particules virales récupérées n'a cependant pas été établie.
(Santarpia et al., 2020) *prépublication*	Potentiel de transmission du SRAS-CoV-2 par les aérosols et les surfaces	Des échantillons d'air et de surface provenant d'espaces isolés abritant des cas de COVID-19 à l'Université du Nebraska aux États-Unis ont été recueillis et testés par RT-PCR pour détecter la présence de l'ARN viral du SRAS-CoV-2. 63,2 % des échantillons d'air prélevés dans les espaces isolés pour les patients étaient positifs pour l'ARN viral, en particulier sous le lit du patient et sur les rebords des fenêtres à l'extrémité de la pièce. Selon la modélisation du débit d'air, les auteurs suggèrent que des tourbillons turbulents (c.-à-d. des tourbillons d'un fluide et le courant inverse qui est créé lorsque le fluide se trouve dans un flux turbulent) qui se forment sous le lit du patient et le flux d'air dominant transportent les particules respiratoires/virales loin du patient, vers les extrémités de la pièce. Ce serait donc ce qui a permis d'obtenir la contamination observée. Le virus se trouvait également dans 58,3 % des échantillons d'air prélevés dans les couloirs à l'extérieur des espaces isolés pour les patients. L'étude a également permis de récupérer la charge virale la plus élevée (1,75 copie/µL) observée de la surface contaminée d'une grille d'aération. Les conclusions de l'étude suggèrent que les particules d'aérosol viral peuvent être produites par les personnes infectées même en l'absence de toux, puisque le virus peut parcourir des distances supérieures à 1,8 mètre.

		La culture de l'ARN viral isolé n'a pu être confirmée par un essai sur les cellules Vero E6 en raison des faibles concentrations du virus récupéré. Toutefois, des indications mineures d'effet cytopathologiques et de réplication virale ont pu être observées dans un échantillon d'air et de surface.
(Zhou et al., 2020)	Enquête sur la contamination de la surface et de l'air par le SRAS-CoV-2 dans un service de soins actifs au plus fort de la pandémie de COVID-19 à Londres	Les niveaux de contamination de surface et d'air du SRAS-CoV-2 dans un hôpital de Londres, au Royaume-Uni, au plus fort de la pandémie de COVID-19 ont été évalués. Des écouvillons de surface ont été utilisés pour effectuer des prélèvements dans les zones cliniques et publiques de l'hôpital. L'ARN viral a été détecté par RT-PCR dans 52,3 % des échantillons de surface prélevés (le plus souvent dans les espaces de soins aux patients atteints de la COVID-19) et dans 38,7 % des échantillons d'air prélevés. Les échantillons contaminés étaient plus nombreux dans les espaces occupés par des patients atteints de la COVID-19. Le virus récupéré n'a pas pu être cultivé dans les lignées cellulaires Vero E6, puisque la charge virale récupérée était inférieure à 30 Ct.
Modèles mathématiques		
(Dai & Zhao, 2020) *prépublication*	Lien entre la probabilité d'infection à la COVID-19 et les taux de ventilation dans les espaces confinés : une enquête fondée sur l'équation de Wells-Riley	L'équation mathématique de Wells-Riley a été utilisée pour déterminer le lien entre la probabilité d'infection et les taux de ventilation intérieure. Les auteurs indiquent que si les taux de ventilation et les périodes d'exposition suivants étaient appliqués (valeur variant entre 100 et 350 m^3/h et 1 200 et 4 000 m^3/h pendant 15 minutes et 3 heures), moins de 1 % de la population vulnérable ne portant pas de masque serait infectée dans des espaces intérieurs confinés. Par contre, si les personnes infectées et les personnes vulnérables portent un masque, le débit de ventilation pourra alors être réduit à une valeur variant entre 50 et 180 m^3/h et entre 600 et 2 000 m3/h. Les auteurs affirment que les anciens taux seraient plus faciles à atteindre grâce aux modèles de ventilation normalement utilisés dans les

		bureaux, les salles de classe, les autobus et les cabines d'aéronefs.
Commentaires		
(Melikov, Ai, & Markov, 2020)	Occupation intermittente combinée à la ventilation : une stratégie efficace pour réduire la transmission aéroportée à l'intérieur	En raison des limites inhérentes à la plupart des systèmes de ventilation mécanique, il n'est pas possible d'augmenter l'alimentation en air frais pour éliminer le risque d'infection par les aérosols en suspension dans l'air expiatoire en milieu intérieur. Par conséquent, les auteurs proposent une stratégie de contrôle à la source fondée sur des pauses intermittentes pour les occupants (c.-à-d. que tous les occupants quittent périodiquement la pièce) et sur des taux d'occupation de la pièce réduits afin de maximiser l'efficacité des systèmes de ventilation intérieure qui réduisent les pathogènes infectieux en suspension dans l'air.
(Morawska & Cao, 2020)	Transmission aérienne du SRAS-CoV-2 : le monde devrait faire face à la réalité.	Selon les preuves disponibles, les auteurs concluent que le virus SRAS-CoV-2 peut probablement être transmis par voie aérienne. Par conséquent, il faut donc prendre toutes les précautions possibles contre la transmission par voie aérienne dans les scénarios intérieurs. Les précautions comprennent augmenter le débit de ventilation, utiliser une ventilation naturelle, éviter la recirculation de l'air, éviter de rester dans le flux d'air direct d'une autre personne et réduire le nombre de personnes qui se trouvent dans le même environnement. Il est important de maximiser la ventilation naturelle dans les bâtiments qui sont ou peuvent être ventilés naturellement en s'assurant d'obtenir un débit de ventilation suffisamment élevé.
(Dietz et al., 2020)	Pandémie du nouveau coronavirus de 2019 : considérations en ce qui concerne l'environnement bâti pour réduire la transmission	Un examen des données probantes disponibles sur l'environnement bâti qui peuvent être appliquées à la pandémie actuelle de COVID-19. Le SRAS-CoV-2 a été observé dans des particules et des gouttelettes aérosolisées d'une gamme de tailles, y compris de 0,25 à 0,5 µm, qui nécessitent une filtration haute efficacité pour les éliminer de l'air intérieur partagé. Les systèmes de ventilation résidentiels et commerciaux ayant des valeurs minimales d'efficacité (VEEM) de 8 peuvent seulement capter de 70 à 85 % des particules de 3,0 à

		10,0 µm (ce qui n'est pas suffisant pour les aérosols du virus SRAS-CoV-2). Les systèmes de ventilation des filtres VEEM 13 ou supérieurs et HEPA couramment utilisés dans les établissements de soins de santé élimineraient efficacement les particules de 0,25 à 0,5 µm. Toutefois, les auteurs indiquent des limites dans les systèmes et filtres de CVCA dans les établissements de soins de santé en raison des espaces dans les bordures des filtres. Dans l'ensemble, les auteurs font remarquer que, bien que des taux de ventilation plus élevés, de l'air extérieur et des filtres de qualité supérieure puissent réduire et diluer les contaminants atmosphériques (c.-à-d. les particules infectieuses) dans l'air intérieur, ces éléments ne permettent toutefois jamais d'éliminer complètement le risque de transmission des infections par voie aérienne.

Tableau 2 Les grappes d'infection à la COVID-19 sont principalement attribuées à la ventilation intérieure

Référence	Titre de la publication	Principaux résultats
(Lu et al., 2020)	Foyer de COVID-19 liée à la climatisation d'un restaurant, Guangzhou, Chine	Le débit d'air de la ventilation intérieure et la transmission de gouttelettes à des distances inférieures à 1 mètre sont vus comme les principaux modes de transmission pour une grappe (n=10) attribuée à un système de climatisation utilisé dans un restaurant lors d'un repas. La seule interaction entre les cas multiples de cette grappe (famille B et famille C) et le cas index (famille A) était le fait d'avoir été assis à des tables voisines. En raison de la façon dont les tables étaient disposées, la sortie d'air et l'entrée d'air de retour du climatiseur central étaient situées au-dessus de la table de la famille C, et les trois tables étaient alignées avec le flux d'air diffusé par le même appareil de climatisation. La transmission de l'infection par les gouttelettes et les aérosols en raison de la circulation de l'air conditionné est

		donc vue comme le mode de transmission qui a infecté les membres de ces trois familles.
(Yuguo Li et al., 2020) *prépublication*	Preuve de la transmission probable du SRAS-CoV-2 par aérosol dans un restaurant mal ventilé	Une analyse de suivi approfondie de l'éclosion dans le restaurant par des simulations informatiques et une analyse aérodynamique a permis de conclure que la transmission était conforme à une propagation virale associée à une mauvaise ventilation, aux zones de débit d'air créées par l'unité de traitement de l'air et aux particules respiratoires chargées de virus qu'expirait le cas index.
(Almilaji & Thomas, 2020) *prépublication*	Rôle de la recirculation de l'air dans l'infection à la COVID-19, leçons tirées du bateau de croisière Diamond Princess.	D'après l'analyse des données cliniques des passagers de ce navire de croisière, les infections symptomatiques diagnostiquées après le début de la quarantaine étaient les mêmes dans les cabines, qu'elles aient ou non inclus une personne infectée. Les auteurs concluent que la transmission aéroportée du SRAS-CoV-2 par le système de ventilation du navire de croisière pourrait expliquer les taux d'infection observés pendant la période de quarantaine.
(Xu et al., 2020) *prépublication*	Itinéraires de transmission du virus de la COVID-19 à bord du navire de croisière Diamond Princess	L'analyse des données sur les passagers et les cas de COVID-19 (n=343) du groupe de navires de croisière Diamond Princess a tenu compte des systèmes de CVCA et d'égouts du navire et des facteurs de risque épidémiologiques de chaque cas et d'un contact étroit pour explorer les modes de transmission les plus plausibles. D'après les analyses, les auteurs ont conclu que le système de CVCA du navire de croisière n'a pas joué un rôle dans la transmission aéroportée sur longue distance du virus de la COVID-19 à bord du navire et que la plupart des passagers ont probablement été exposés avant que le navire ne soit mis en quarantaine.
(Shen et al., 2020) *prépublication*	Transmission aérienne de COVID-19 : preuves épidémiologiques issues de l'enquête sur deux foyers	On suppose que la transmission aéroportée par aérosols a été favorisée par les ventilateurs et les unités de climatisation (recirculation d'air) dans les espaces de transport et dans les espaces intérieurs communs et qu'elle a contribué à deux éclosions indépendantes de COVID-19. La première a touché les passagers d'un autobus qui se rendaient dans un lieu de culte et en revenaient (n=172) et la deuxième visait plutôt un

		atelier-conférence de trois jours (n=30) dans lequel les participants ont partagé un espace de réunion intérieur. En ce qui concerne la première éclosion, le risque d'infection par la COVID-19 chez les passagers de l'autobus nº 2 était 41,5 fois plus élevé (IC à 95 %, de 2,6 à 669,5) que pour les passagers de l'autobus nº 1 et de 11,4 fois plus élevé (IC à 95 %, de 5,1 à 25,4) que pour toutes les autres personnes ayant pris part à cet événement. Le taux d'attaque global à la suite de l'éclosion dans le cadre de la conférence était de 48,3 %.

Tableau 3 Littérature grise sur la transmission de la COVID-19 et les systèmes de CVCA

Référence	Organisation	Déclarations clés
(ASHRAE, 2020) Accéder ici	American Society of Heating, Refrigerating, and Air-Conditioning Engineers	Document de position de l'ASHRAE sur les aérosols infectieux publié en avril 2020. La transmission du SRAS-CoV-2 par l'air est assez probable et l'exposition au virus par voie aéroportée devrait être contrôlée. Les changements apportés au fonctionnement de l'immeuble, y compris le fonctionnement des systèmes de chauffage, de ventilation et de climatisation, peuvent réduire l'exposition par voie aéroportée. La ventilation et la filtration fournies par les systèmes de CVCA peuvent réduire la concentration atmosphérique de SRAS-CoV-2 et donc le risque de transmission dans l'air.
(CSA Group, 2020) Accéder ici	Groupe CSA	Normes d'essai et de certification de l'équipement de CVCA (destiné aux établissements de soins de santé) pour les fabricants. Norme CSA Z317.2:19 : Systèmes de chauffage, de ventilation et de conditionnement d'air (CVCA) dans les établissements de soins de santé : exigences particulières

		Norme CAN/CSA-Z317.13-17 : Lutte contre l'infection pendant les travaux de construction, de rénovation et d'entretien dans les établissements de santé
(CDC, 2020) Accéder ici	Center for Disease Control and Prevention	Les conseils d'experts en ce qui concerne les préparatifs des entreprises et la réouverture de ces dernières font référence à l'énoncé de déclaration de l'ASHRAE sur les systèmes de CVC et au guide de démarrage du système de CVC. Les lignes directrices font allusion au fait de s'assurer que les systèmes de CVCA fonctionnent correctement. Accroître la circulation de l'air provenant de l'extérieur en ouvrant les fenêtres et les portes après avoir évalué les risques de l'air extérieur pour les occupants. Parmi les autres recommandations énoncées dans les documents, mentionnons augmenter l'approvisionnement en air dans les espaces occupés, désactiver les contrôles de la ventilation de contrôle de la demande qui réduisent l'approvisionnement en air selon la température ou l'occupation, utiliser une ventilation naturelle, améliorer la filtration centrale de l'air, faire fonctionner le système de ventilation pendant les périodes inoccupées, générer des mouvements d'air propre à moins propre, penser à utiliser des systèmes portatifs de ventilation et de filtration à haute efficacité des particules d'air (HEPA), s'assurer que les ventilateurs d'évacuation des toilettes sont fonctionnels et en état de fonctionner; et envisager d'utiliser l'irradiation germicide aux ultraviolets comme supplément.
(ECDC, 2020) Accéder ici	Centre européen de prévention et de contrôle des maladies	Conseils sur les systèmes de chauffage, de ventilation et de climatisation dans le contexte de la COVID-19. Le document traite de l'entretien, de l'évitement de la recirculation, de la direction du ventilateur et du taux d'échange d'air.
(AHS, 2020) Accéder ici	Services de santé de l'Alberta	Rapid Evidence Report Décrit les données probantes et la littérature grise sur la transmission de la COVID-19 et les systèmes de CVCA dans les milieux de soins de santé et les milieux non médicaux disponibles jusqu'au 11 mai 2020. Les principales

		constatations découlant de l'examen des données probantes indiquent que les facteurs associés au système de CVCA peuvent contribuer à la transmission d'agents pathogènes, surtout lorsque ces deniers ne fonctionnent pas correctement. Le potentiel exact dans lequel les systèmes de CVCA peuvent contribuer à la transmission de l'infection par le SRAS-CoV-2 n'a pas pu être évalué en raison du peu de données probantes sur les virus viables dans les échantillons d'air, de la variabilité des systèmes de CVCA et de la complexité des modalités de transmission. Le Comité d'examen recommande la création d'un comité possédant l'expertise nécessaire pour explorer le rôle des systèmes de CVCA dans la transmission des pathogènes viraux, y compris le CoV-2 du SRAS.

Tableau 4 Transmission d'autres infections (excluant le SRAS-CoV-2) et systèmes de CVCA

Référence	Titre de la publication	Principaux résultats
(Wong et al., 2004)	Grappe de cas du SRAS chez des étudiants en médecine ayant été exposés à un seul patient, Hong Kong.	Description de l'éclosion de SRAS dans une unité d'isolement d'un hôpital de Hong Kong, chez les travailleurs de la santé. Des données épidémiologiques sur les travailleurs de la santé exposés, une inspection du système de ventilation et une analyse dynamique des fluides de calcul ont révélé que la chambre du patient avait le débit d'approvisionnement le plus élevé alors que la grille d'échappement adjacente présentait le débit le plus faible parmi les quatre grilles d'échappement fonctionnelles de l'unité. Les auteurs discutent de la possibilité de transmission d'aérosols du patient index par l'entremise du système de ventilation.
(Y Li et al., 2005)	Rôle de la distribution de l'air dans la transmission du SRAS lors de la plus grande épidémie nosocomiale à Hong Kong	Une deuxième analyse rétrospective des cas de patients hospitalisés et des cas de travailleurs de la santé associés à l'éclosion de SRAS mentionnée ci-dessus est présentée plus en détail.

		Les inspections sur place, les mesures de la conception de la ventilation et de la distribution de l'air, ainsi que les simulations de la dynamique des fluides par calcul concluent que les déséquilibres dans le débit d'air et les composants non fonctionnels du système de CVCA (p. ex., diffuseurs d'alimentation et grilles d'échappement) ont contribué à la transmission de l'infection. L'analyse a révélé la nécessité d'améliorer les systèmes de ventilation et de climatisation dans l'unité d'isolement afin de réduire efficacement le risque de propagation de l'infection entre les patients et les travailleurs de la santé.
(Satheesan et al., 2020)	Une étude numérique des stratégies de ventilation visant à atténuer les risques d'infection dans les services d'hospitalisation générale	Des simulations ont été appliquées pour examiner les mécanismes de transport et les modèles de dépôt du MERS-CoV dans une unité générale. Les auteurs ont conclu que les taux de changement d'air et de débit d'air d'extraction avaient des répercussions importantes sur le débit d'air et la distribution des particules. Dans l'espace ventilé mécaniquement, des grilles d'échappement près d'un patient (idéalement au-dessus du lit de chaque patient) et des débits d'air d'extraction élevés sont recommandés pour réduire la transmission.
(Haselbach et al., 2009)	Transmission aéroportée des infections respiratoires aiguës dans les installations militaires en raison du système de CVCA? Examen d'une étude de cohorte sur la formation de base.	Examen des infections aiguës des voies respiratoires chez les nouveaux militaires qui vivaient dans les casernes militaires qui tient compte de la configuration des systèmes de CVCA et du nombre d'occupants de plusieurs zones qui se partagent l'air de retour mélangé dans le même système de CVCA et redistribué comme air d'approvisionnement (population de contact). L'étude a révélé un risque important de transmission aérienne des particules aéroportées par les systèmes de CVCA. Des taux d'infection plus élevés ont été observés dans les systèmes où les populations avaient un plus grand contact avec le système de CVCA et où l'accès aux fenêtres était

		réduit, empêchant la ventilation extérieure et l'alimentation en air.
(Sundell et al., 2011)	Taux de ventilation et santé : revue pluridisciplinaire de la documentation scientifique.	Une équipe d'examen multidisciplinaire a exploré les données probantes (publiées jusqu'en 2005) établissant un lien entre le taux de ventilation et de multiples effets sur la santé. Les données probantes démontrent la plausibilité biologique d'un lien entre les résultats pour la santé et les taux de ventilation, mais ne fournissent pas de preuves claires sur aucun agent ou aucune charge infectieuse particuliers.
(Y. Li et al., 2007)	Rôle de la ventilation dans la transmission aéroportée d'agents infectieux dans l'environnement bâti - étude systématique multidisciplinaire.	L'examen de la documentation publiée entre 1960 et 2005 a permis de trouver dix articles établissant un lien entre la transmission des infections et les systèmes de CVCA. Les examinateurs ont conclu qu'il existe des preuves solides et suffisantes démontrant un lien entre la ventilation, les mouvements de l'air dans les bâtiments et la transmission ou la propagation de maladies infectieuses comme la rougeole, la tuberculose, la varicelle, la grippe, la variole et le SRAS. Il n'y avait toutefois pas suffisamment de données pour préciser et quantifier les exigences minimales en matière de ventilation dans les hôpitaux, les écoles, les bureaux, les maisons et les salles d'isolement en ce qui a trait à la propagation des maladies infectieuses par voie aérienne.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont menées par Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont recoupées avec la littérature de la liste de littérature COVID de l'OMS, et les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche inclus dans cette revue étaient (indoor et air), ventilation, HVAC, air conditioning. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes ont été extraites. Cette revue contient des recherches

publiées sur la COVID-19 jusqu'au 13 août 2020. La documentation pertinente antérieure à la COVID-19 a été établie en examinant les listes de référence des revues et des documents pertinents inclus dans la présente synthèse.

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Nouveaux éléments de preuve sur la COVID-19

COVID-19 – Résumé des études sur l'utilisation d'écrans faciaux pour prévenir la transmission du SRAS-CoV-2

Introduction

Quelle est l'efficacité des écrans faciaux pour prévenir la transmission du virus SRAS-CoV-2, en combinaison avec le masque et sans masque?

Cette note d'information résume les recherches pertinentes sur les écrans faciaux utilisés dans la prévention de la transmission par gouttelettes et par aérosols de personnes infectées aux personnes vulnérables, publiées avant le 7 juillet 2020. La protection des yeux et l'utilisation de lunettes de protection ne sont pas prises en compte dans cette revue.

Points clés

- Les écrans faciaux sont une forme d'équipement de protection individuelle utilisée dans les établissements de santé (p. ex. soins chirurgicaux/médicaux, dentaires, vétérinaires) pour couvrir le visage et les muqueuses (yeux, nez, bouche) et prévenir l'exposition aux particules infectieuses provenant d'aérosols et de projections de liquides organiques. Un écran facial est souvent utilisé lors de procédures médicales au cours desquelles le risque d'aérosols ou de projections de liquides organiques provenant du patient est accru. Il est porté avec d'autres équipements de protection individuelle (p. ex. masques médicaux, respirateurs, blouses médicales) (Roberge, 2016).
- Toutes les études incluses dans cette revue sont des expériences menées dans des conditions contrôlées. À l'exception d'une étude qui a utilisé des liquides contaminés par la grippe (Lindsley et al., 2014), les études de cette revue n'ont pas utilisé de liquides contaminés par des virus.
- Les études sur l'utilisation des écrans faciaux par les travailleurs de la santé font état d'un effet protecteur, notamment contre les projections de liquides organiques produites par les patients lors de procédures médicales particulières, lorsqu'ils sont utilisés en combinaison avec d'autres équipements de protection tels qu'un masque chirurgical (tableau 1 et tableau 2) (Mansour et al., 2009; Mostaghimi et al., 2020; Shoham et al., 2016). Des écrans faciaux ont également été conçus pour que le patient puisse les porter lorsqu'il subit une procédure générant des aérosols afin de contenir ces derniers et de protéger les travailleurs de la santé qui effectuent la procédure contre l'exposition (Anon, Denne et Rees, 2020).
- Deux études de simulation recensées portent sur l'inhalation de gouttelettes et l'exposition dans des situations où l'écran facial est le seul équipement de protection porté (tableau 1). Les deux études indiquent que 90 % des grosses gouttelettes générées par une toux dirigée vers le milieu de l'écran facial ont été bloquées (Lindsley et al., 2014; Ronen et al., 2020). Cependant, les effets protecteurs

diminuent lorsque la direction de la toux varie (plus haut/plus bas/côté). Au fil du temps (30 minutes), l'inhalation de petites gouttelettes n'a été réduite que de 23 % par l'écran facial (Lindsley et al., 2014).

- Trois études ont simulé la toux chez une personne portant l'écran facial et ont rapporté le niveau de contamination résultant des particules respiratoires projetées (tableau 1 et tableau 2). Deux études font état de la libération de gouttelettes et d'aérosols par les ouvertures de l'écran facial (Anon et al., 2020; Viola et al., 2020), tandis qu'une troisième indique que le masque facial constituait une bonne barrière vers l'avant, car aucune gouttelette n'a atteint un simulateur situé à 60 cm (Ronen et al., 2020).
- La conception du masque facial serait importante. Les écrans faciaux qui s'enroulent davantage autour du visage, protégeant entièrement la zone des joues, et qui s'enroulent sous le menton, ainsi que toute amélioration qui réduit au minimum les fuites/entrées de bioaérosols autour des bords du masque, offraient une meilleure protection (Viola et al., 2020; Anon et al., 2020; Mostaghimi et al., 2020).

Vue d'ensemble des éléments de preuve

Peu d'études examinent et rapportent les effets protecteurs des écrans faciaux portés en combinaison avec un masque ou sans masque. Toutes les études recensées font état de résultats d'études de simulation menées dans des laboratoires contrôlés et ne tiennent pas nécessairement compte des paramètres du monde réel (par exemple, les différences de taille entre les personnes, les températures, l'humidité, la vitesse du vent, etc.) ni de la dose infectieuse. Aucune des études n'a utilisé le SARS-CoV-2 dans la simulation. Les différences entre les études en ce qui concerne leur conception, la manière dont les résultats ont été mesurés et les écrans utilisés font en sorte que les résultats ne sont pas directement comparables. Bien que l'ensemble des preuves disponibles soutiennent l'utilisation d'écrans faciaux parallèlement aux masques médicaux dans les établissements de soins de santé, les résultats des études sur le port d'écrans faciaux seuls ont révélé de manière moins systématique un effet protecteur.

CONTENU

EFFICACITÉ DES ÉCRANS FACIAUX

Parmi les études recensées, aucune n'a évalué l'efficacité de l'utilisation d'un écran facial sur le terrain pour prévenir la transmission d'infections respiratoires.

Dans les établissements de soins de santé, deux études de simulation évaluant diverses procédures médicales ont montré que les écrans faciaux, généralement portés avec un masque médical, protègent le visage des

travailleurs de la santé contre les projections de liquides en fournissant une barrière physique, ainsi qu'une certaine protection contre l'inhalation de petits aérosols et de noyaux de gouttelettes (tableau 1) (Mansour et al., 2009; Shoham et al., 2016). Une étude a montré que la combinaison d'un couvre-visage et d'un écran facial est plus efficace que l'un ou l'autre utilisé seul (Mansour et al., 2009), tandis que dans une autre étude, on a constaté qu'un écran facial complet offrait une meilleure protection que la combinaison d'un écran oculaire et d'un masque chirurgical (Shoham et al., 2016).

Deux études portant sur l'efficacité des écrans faciaux utilisés comme seul équipement de protection, dans le cadre desquelles on a comparé les écrans faciaux et les autres couvre-visage, ont révélé que les écrans faciaux sont des barrières efficaces pour le blocage à court terme des gouttelettes (Lindsley et al., 2014; Ronen et al., 2020). L'étude de Ronan et coll. décrit les effets protecteurs à court terme d'un écran facial bloquant 90 % des projections générées par une toux à 60 cm de distance, dirigées vers le centre de l'écran facial. Dans la même simulation, un masque facial a bloqué la moitié des gouttelettes. L'effet protecteur de l'écran facial diminue de manière significative lorsque la direction de la toux (plus haut/plus bas/côté) est modifiée (Ronen et al., 2020). De même, Lindsley et coll. ont rapporté que les écrans faciaux réduisent de 90 % l'inhalation de grosses gouttelettes et de plus de 60 % l'inhalation de petites gouttelettes immédiatement après une toux. Cependant, l'inhalation de gouttelettes plus petites n'a été réduite que de 23 %, car le temps écoulé depuis la toux (c'est-à-dire l'événement de génération d'aérosols) a été augmenté à 30 minutes. Cette augmentation du risque d'inhalation d'aérosols et de petites gouttelettes est attribuée à la formation, au fil du temps, de noyaux de gouttelettes plus petites qui peuvent s'infiltrer par les bords de l'écran facial (Lindsley et al., 2014).

Les trois études de simulation évaluant le niveau de contamination par les particules respiratoires d'une personne portant un écran facial ont fait état d'une bonne barrière vers l'avant pour la projection de gouttelettes respiratoires (Ronen et al., 2020). Cependant, de puissantes projections de bioaérosols fuyant vers l'arrière et vers le bas ont été mesurées (Viola et al., 2020; Anon et al., 2020). La projection de grosses gouttelettes et la contamination sous le cou et au niveau de la poitrine ont eu lieu lorsqu'un patient portant un écran facial standard a subi une procédure simulant la production d'aérosols, comme l'endoscopie souple (Anon et al., 2020). L'observation du flux d'air et de l'éjection de bioaérosols lorsque l'on porte différents types d'écrans faciaux montre que le flux d'air frontal généré par la respiration, la parole forte et la toux est largement réduit, mais qu'il y a toujours des fuites importantes d'aérosols. De puissantes projections de bioaérosols fuyant de l'écran facial ont été observées près de la région du front du porteur et vers le bas.(Viola et al., 2020). Cependant, malgré les fuites mesurées dans deux études, la troisième étude a fait état d'une bonne barrière vers l'avant. Cette constatation est fondée sur les résultats expérimentaux obtenus au moyen d'un simulateur de respiration placé à 60 cm d'un simulateur de toux avec écran facial, sur lequel on n'a observé aucune inhalation ni présence de projections de gouttelettes(Ronen et al., 2020). Par conséquent, les bioaérosols s'échappent dans l'environnement lorsqu'un individu porte un écran facial.

Tableau 1 : Littérature sur l'efficacité des écrans faciaux

Titre de la publication	Principaux résultats	Référence

Études expérimentales et de simulation		
Efficacy of Face Shields Against Cough Aerosol Droplets from a Cough Simulator	Expérience de simulation (écrans faciaux uniquement) : L'efficacité des écrans faciaux pour bloquer la transmission des aérosols est mesurée à l'aide d'un simulateur de respiration destiné à imiter un travailleur de la santé, et d'un simulateur d'aérosols projetés lors d'une toux qui contiennent le virus de la grippe. L'étude révèle une réduction de plus de 90 % du risque d'inhalation des grands aérosols (diamètre moyen de 8,5 µm) avec utilisation d'un écran facial, et une réduction de plus de 60 % du risque d'inhalation des petits aérosols (taille de 3,4 µm) immédiatement après la toux. Les écrans faciaux n'ont entraîné qu'une réduction de 23 % du risque d'inhalation des petits aérosols lorsque la toux générant les aérosols s'est produite dans les 30 minutes précédentes. L'augmentation du risque est due au fait que les petites particules restent en suspension plus longtemps, flottent autour de l'écran facial et peuvent ensuite être inhalées.	(Lindsley et al., 2014)
Face Coverings, Aerosol Dispersion and Mitigation of Virus Transmission Risk	Expérience de simulation et étude menée sur des humains (comparaison entre l'écran facial et le masque chirurgical, le masque fait maison et le respirateur) Les chercheurs utilisent la technique schlieren pour étudier l'éjection de flux d'air par des volontaires individuels et des mannequins utilisant différents couvre-visage pendant la respiration, la toux et les procédures générant des aérosols. Les fuites de bioaérosols observées avec différents masques faciaux (c.-à-d. masques faits maison et masques chirurgicaux, respirateurs filtrants [FFP1, FFP2], respirateurs N95 et écrans faciaux légers et robustes) ont été visualisées. Dans l'ensemble, l'étude révèle que tous les dispositifs de protection du visage ont réduit considérablement le flux frontal des bioaérosols. Seul le FFP testé a permis de diminuer les projections fuyant vers l'arrière et vers le bas, alors que les masques chirurgicaux testés, les masques faits maison, les respirateurs N95 et les écrans faciaux ont montré des projections fuyant vers l'arrière et vers le bas à des degrés divers. En ce qui concerne les écrans faciaux précisément, on a constaté que les bioaérosols contenant un flux d'air fuyaient par les coutures et les joints des écrans faciaux testés et qu'ils se déplaçaient horizontalement de façon minimale (sur une distance	(Viola et al., 2020)

	de quelques centimètres). Les écrans faciaux ont également généré des projections fuyant vers le haut (région des sourcils), vers le bas, sur les côtés et vers l'arrière. Les projections vers l'arrière se produisent lorsque l'air s'échappe par les côtés des couvre-visage et sont projetées vers l'arrière à grande vitesse, ce qui peut entraîner un déplacement important. De puissantes projections fuyant vers le bas ont été observées pour les écrans faciaux qui ne se courbent pas sous le menton, ce qui permet une circulation d'air sans entrave à l'entrée et à la sortie.	
Examining the Protection Efficacy of Face Shields Against Cough Aerosol Droplets Using Water Sensitive Papers	Expérience de simulation (comparaison entre le port d'un écran facial uniquement et le port du masque, du respirateur ou d'aucun équipement) Cette expérience de simulation a fait état de l'efficacité des écrans faciaux utilisés comme seul équipement de protection. L'objectif de cette étude est d'informer sur l'utilisation des écrans faciaux par la population générale en dehors d'un établissement de soins de santé. Pour mener cette étude, on a utilisé un simulateur de toux qui a été soigneusement réglé pour reproduire la toux humaine en termes de répartition de la taille des gouttelettes et de vitesse de sortie. Les équipements de protection individuelle testés ont été placés sur une tête de mannequin simulant la respiration humaine. Un granulomètre aérodynamique et du papier hydrosensible ont été utilisés pour analyser la concentration et la répartition de la taille des particules qui atteignent la tête du mannequin. L'étude indique que les écrans faciaux sont aussi efficaces que les masques faciaux pour bloquer les gouttelettes respiratoires (3 µm de diamètre) générées par une toux, et qu'ils sont plus efficaces pour bloquer les particules fines (0,3µm) que les masques médicaux, à court terme. En d'autres termes, alors que le masque médical réduisait le nombre de particules inhalées selon un facteur d'environ deux, l'écran facial offrait une protection supérieure en bloquant plus de 90 % des particules autrement inhalées lorsqu'une toux simulée était dirigée directement sur l'écran facial. Ces effets de blocage ont été réduits lorsque la contamination des zones situées au-delà du milieu du visage (c.-à-d. les joues et le cou) a été prise en compte. De plus, dans les expériences où la distance verticale entre les simulateurs de toux et de respiration était variable, les	(Ronen et al., 2020)

	dépôts de gouttelettes sur le visage n'étaient pas différents de ceux qui se déposaient sur l'écran, et l'efficacité de blocage n'était que de 45 % dans certains cas. Aucune contamination respiratoire des environs n'a été constatée lorsque le simulateur de toux était recouvert d'un écran facial (simulant une personne infectée portant l'écran facial).	
Eye Protection in Orthopaedic Surgery	Expérience de simulation (écran facial avec un masque) : Des têtes de mannequins portant de différents équipements de protection individuelle et vaporisées avec des jets de colorants fluorescents ont révélé que les écrans faciaux qui couvrent les yeux et qui sont portés en combinaison avec un masque facial sont des barrières efficaces. Cette combinaison d'équipements de protection individuelle a permis de réduire de 64 % la contamination par gouttelettes et/ou débris macroscopiques lors d'ostéotomies fémorales simulées.	(Mansour et al., 2009)
Comparison of Protection Against Ocular Contamination with Disposable Eyewear Products	Présentation sur affiche – 2016 (comparaison entre l'écran facial et la protection des yeux avec un masque) Une étude de simulation menée sur des têtes de mannequins portant un écran oculaire ou facial, avec ou sans masque facial et respirateur N95. Au moyen d'un système de colorant fluorescent Glo Germ, on a observé que la contamination des yeux par des micro-gouttelettes s'est produite lorsque le masque chirurgical était porté en combinaison avec un écran oculaire, mais qu'aucune contamination du visage (c.-à-d. des yeux, du nez ou de la bouche) n'a eu lieu lorsqu'un écran facial complet a été utilisé.	(Shoham et al., 2016)
Revue de la littérature		
Face Shields for Infection Control: A Review	Une revue de la littérature sur les écrans faciaux comme forme d'équipement de protection individuelle pour les travailleurs de la santé; on y aborde les différents modèles d'écrans faciaux. Toutes les preuves décrites sont antérieures à l'émergence de la COVID-19.	(Roberge, 2016)
Facial Protection for Healthcare Workers During Pandemics: A Scoping Review	Un examen de la portée de la protection faciale chez les travailleurs de la santé. L'examen a permis d'isoler une étude sur l'efficacité des écrans faciaux (Lindsley et al., 2014) et a conclu que les écrans faciaux ne devraient pas être utilisés par les travailleurs de la santé comme principale protection pour prévenir la transmission des maladies respiratoires, mais qu'ils	(Godoy et coll., 2020)

	peuvent être utilisés en combinaison avec d'autres types de protection faciale.	

NOUVEAUX SYSTÈMES D'ÉCRAN FACIAL

D'autres options de systèmes de protection faciale sont présentées comme des barrières physiques qui offrent une meilleure protection contre les projections de liquides organiques générées par le patient.

Tableau 2 : Nouveaux systèmes d'écran facial

Titre de la publication	Principaux résultats	Référence
Patient-Worn Enhanced Protection Face Shield for Flexible Endoscopy	Expérience de simulation (comparaison entre l'écran facial et l'écran facial amélioré) Une étude de validation de principe par simulation compare l'exposition à des colorants en aérosol et la contamination lorsqu'un patient porte un écran facial standard par rapport à un écran facial de conception améliorée avec un système de fermeture à languette (couvrant l'espace sous le menton) pendant les procédures d'endoscopie. La conception améliorée aurait permis de contenir les projections respiratoires simulées dans les limites de l'espace clos autour du visage des patients et d'empêcher que des bioaérosols s'échappent sous la zone du cou/menton.	(Anon et al., 2020)
Rapid Prototyping and Clinical Testing of a Reusable Face Shield for Health Care Workers Responding to the COVID-19 Pandemic	Création/évaluation d'écrans faciaux améliorés L'utilité clinique et le confort d'utilisation de 3 prototypes d'écran faciaux chez les travailleurs de la santé sont étudiés. L'efficacité de chaque concept pour prévenir les projections de gouttelettes n'a pas été étudiée.	(Mostaghimi et al., 2020)

Méthodologies

Une recension quotidienne de la littérature (publiée et prépubliée) est effectuée par le Groupe des sciences émergentes de l'ASPC. Cette recension a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver de la littérature pertinente sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont mises en correspondance avec les publications figurant sur la liste de littérature de l'OMS au sujet de la COVID, et

les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de la recension sont conservés dans une base de données Refworks et une liste Excel qui peut être consultée. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour y relever des citations pertinentes sur la COVID-19 et le SARS-CoV-2. Les termes de recherche utilisés comprennent : (visage et écran). Une recherche supplémentaire a été menée dans PubMed pour obtenir les recherches plus anciennes, non liées à la COVID-19, sur l'utilisation des écrans faciaux : (visage et écran et [virus ou respiratoire]).

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, lesquelles ont été extraites et incluses dans la recension de la littérature. Cette revue contient des recherches publiées avant le 7 juillet 2020.

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Nouveaux éléments de preuve sur la COVID-19

Résumé des connaissances relatives à la transmission du SRAS-CoV-2 par les instruments à vent et le chant

Introduction

Quel est le risque de transmission du virus du SRAS-CoV-2 par le chant ou l'utilisation d'un instrument à vent dans une chorale, un orchestre ou lors de répétitions avec d'autres personnes?

Cette note de synthèse résume les connaissances relatives à la transmission aérodynamique des gouttelettes et aérosols respiratoires provenant d'activités impliquant de respirer profondément et de chanter, les données probantes épidémiologiques se rapportant aux activités liées à la musique qui ont entraîné la transmission du SRAS-CoV-2 et les évaluations des risques, les stratégies d'atténuation ou autres analyses décisionnelles qui peuvent être pertinentes concernant la création de musique en groupe. Cette synthèse met en évidence la littérature spécifique portant sur la possibilité de transmission d'infections par le chant, publiée au 26 juin 2020.

Points clés

- Les données probantes disponibles suggèrent que le chant, pratiqué dans un espace intérieur, peut contribuer à amplifier la transmission de l'infection par le SRAS-CoV-2, si une personne infectée y participe. Les rapports épidémiologiques portant sur des grappes de cas de COVID-19 présentant des taux d'atteinte élevés et associées à la pratique de la chorale aux États-Unis, à Singapour et aux Pays-Bas, ainsi que du karaoké dans un bar en Corée du Sud, fournissent des données probantes selon lesquelles la transmission s'est produite au cours d'activités impliquant le chant (tableaux 2 et 3).
- Il n'a pas été possible d'identifier des données probantes primaires relatives à l'utilisation d'instruments à vent et de cuivres ni son incidence sur la transmission du SRAS-CoV-2. Toutefois, une évaluation descriptive des risques et une étude de la littérature grise portant sur les instruments à vent indiquent qu'il faudrait faire davantage de recherches sur le risque de transmission du SRAS-CoV-2 par les aérosols produits par les instruments à vent (Tableau 3). Un protocole d'étude des instruments à vent et de la sécurité liée à leur utilisation a été identifié (Miller, Vance, Hertzberg, & Toohey, 2020).
- Aucune donnée probante relative à des stratégies d'atténuation s'appliquant aux musiciens n'a été identifiée.
- Données probantes expérimentales et scénarios modélisés relatifs à la dispersion des gouttelettes et à l'aérosolisation du SRAS-CoV-2:

- Les particules infectieuses sont généralement expulsées dans l'air ambiant par une personne infectée (par exemple, en respirant, en parlant, en éternuant, en chantant et en toussant) et ces particules peuvent transmettre le SRAS-CoV-2 à une autre personne lorsqu'elles sont inhalées (Tableau 1).
- Les particules de SRAS-CoV-2 en suspension dans l'air peuvent exister sous forme d'aérosols, de gouttelettes, de noyaux de gouttelettes ou d'autres petites particules contenant de l'ARN viral. Selon une étude, le virus du SRAS-CoV-2 peut rester viable dans des aérosols pendant plus de trois heures (van Doremalen et al., 2020).
- Aucune étude de simulation n'a examiné la production de particules pendant le chant ou l'utilisation d'instruments à vent, mais des études font état de la parole et de la toux. Par exemple, on estime que des milliers de particules contenant des virus sont produites pendant une minute de conversation à haute voix et restent en suspension dans l'air pendant plus de huit minutes (Tableau 1) (Stadnytskyi, Bax, Bax, & Anfinrud, 2020).
- Les modèles mathématiques fondés sur la physique des particules et l'aérodynamique prédisent que les particules respiratoires et salivaires peuvent rester en suspension dans l'air suffisamment longtemps pour être inhalées par un autre individu, et qu'elles peuvent être dispersées à une certaine distance de la source infectieuse (Vuorinen et al., 2020) (Guerrero, Brito, & Cornejo, 2020; Zhao, Qi, Luzzatto-Fegiz, Cui, & Zhu, 2020) (Feng, Marchal, Sperry, & Yi, 2020). Selon les modèles mathématiques, la taille des gouttelettes, l'humidité, la température, le flux d'air et les turbulences de l'air ont tous un impact sur le mouvement et la décomposition des virus contenant des particules en suspension dans l'air (Tableau 1).

Vue d'ensemble des éléments de preuve

L'ensemble des données probantes empiriques disponibles sur la transmission du SRAS-CoV-2 pendant le chant provient de quelques grappes de cas apparues dans des chorales dès le début de l'épidémie de SRAS-CoV-2. Ces études constituent des enquêtes réalisées rétrospectivement sur les éclosions et il convient de considérer qu'elles présentent un risque de biais élevé et offrent des données probantes de mauvaise qualité.

Les simulations en laboratoire et les scénarios modélisés fournissent également des données probantes théoriques à l'appui de l'hypothèse de transmission accrue du SRAS-CoV-2 par des activités telles que le fait de parler fort. Ces études semblent avoir été menées sans lacune manifeste dans la méthodologie utilisée et sont considérées comme des données probantes de qualité moyenne à élevée.

Des lacunes majeures dans les connaissances ont été identifiées lors de l'analyse des données probantes qui sous-tendent l'examen; des recherches supplémentaires sont nécessaires afin d'évaluer le risque de

transmission associé au fait de chanter ou de jouer d'un instrument dans un contexte de groupe. Le manque de données probantes expérimentales caractérise de manière complète le risque et les circonstances qui conduisent à la transmission. Le risque de transmission lié au fait de chanter et de jouer des instruments à vent dans une chorale, un orchestre et/ou dans le cadre d'une pratique avec d'autres personnes est inconnu, mais des données probantes théoriques et des grappes attestées, attribuées à cette activité, indiquent qu'il existe un risque.

TABLE DES MATIÈRES

GOUTTELETTES ET AÉROSOLS CONTENANT DU SRAS-COV-2

Six expériences et cinq modèles étudient l'aérosolisation du SRAS-CoV-2 et définissent certaines des circonstances dans lesquelles se produisent l'aérosolisation ou la dispersion des gouttelettes. Les particules infectieuses sont généralement expulsées dans l'air ambiant par une personne infectée (par exemple, en respirant, en parlant, en éternuant, en chantant ou en toussant) et ces particules peuvent transmettre le SRAS-CoV-2 à une autre personne, lorsqu'elles sont inhalées (Tableau 1). Le risque de transmission dépend vraisemblablement des caractéristiques de l'environnement, de l'activité, de la distance et du temps passé avec une personne infectée. Les particules de SRAS-CoV-2 en suspension dans l'air peuvent exister sous forme d'aérosols, de gouttelettes, de noyaux de gouttelettes ou d'autres petites particules contenant de l'ARN viral. L'étude de van Doremalen fournit les données probantes primaires relatives à la viabilité des particules du virus SRAS-CoV-2 sous forme d'aérosols. L'étude indique que le virus du SRAS-CoV-2 peut rester viable dans les aérosols pendant plus de trois heures (van Doremalen et al., 2020).

Aucune étude de simulation n'a examiné la production de particules pendant le chant ou l'utilisation d'instruments à vent, mais des études ont fait état de la parole et de la toux. Les simulations ont permis de visualiser avec succès des milliers de gouttelettes et aérosols respiratoires minuscules qui sont émis lorsque l'on parle normalement et restent en suspension dans l'air pendant plus de huit minutes (Anfinrud, Bax, Stadnytskyi, & Bax, 2020; Chanpong, Tang, Rosenczweig, Lok, & Tang, 2020; Stadnytskyi et al., 2020). En outre, on estime que des milliers de particules contenant des virus sont produites pendant une minute de conversation à haute voix et restent en suspension dans l'air pendant plus de huit minutes (Stadnytskyi et al., 2020). La toux génère également des gouttelettes respiratoires et des aérosols qui parcourent des distances moyennes comprises entre deux mètres et demi et quatre mètres maximum, ainsi que des projections importantes de gouttelettes sur les travailleurs de la santé se trouvant à proximité (Chanpong et al., 2020; Loh et al., 2020). En tant que tel, il est probable que le chant entraîne également la dispersion de particules infectieuses.

Les modèles mathématiques fondés sur la physique des particules et l'aérodynamique prédisent que les particules respiratoires et salivaires peuvent rester en suspension dans l'air suffisamment longtemps pour être inhalées par un autre individu et peuvent potentiellement être dispersées à une certaine distance de la source infectieuse (Vuorinen et al., 2020) (Guerrero et al., 2020; Zhao et al., 2020) (Feng et al., 2020). Selon les modèles mathématiques, la taille des gouttelettes, l'humidité, la température, le flux d'air et les turbulences de l'air ont tous un impact sur le mouvement et la décomposition des virus contenant des particules en suspension dans l'air (Tableau 1).

Tableau 1 : Littérature primaire relative aux aérosols et gouttelettes contenant du SRAS-CoV-2

Titre de la publication	Principaux résultats	Référence
Études expérimentales et de simulation		
Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1	La stabilité et la décomposition du SRAS-CoV-2 et du SRAS-CoV-1 contenus dans les aérosols ont été estimées à l'aide d'un modèle de régression bayésien Le virus du SRAS-CoV-2 est resté viable en aérosols jusqu'à trois heures (durée de l'expérience), avec une réduction du titre infectieux de $10^{3.5}$ à $10^{2.7}$ $TCID_{50}$ par litre d'air.	(van Doremalen et al., 2020)
The impact of high-flow nasal cannula (HFNC) on coughing distance: implications on its use during the novel coronavirus disease outbreak	Une étude de simulation impliquant des volontaires sains (n=5) a révélé que les gouttelettes produites par la toux se répandaient sur une distance moyenne de 2,48 mètres (1,03 écart-type) au départ, et sur une distance maximale de 3,90 mètres. Lorsque l'on porte une canule nasale à haut débit bien ajustée, la dispersion moyenne des gouttelettes générées par la toux est de 2,91 mètres (1,09) avec une distance maximale de 4,50 mètres.	(Loh et al., 2020)
Aerosol-generating procedures and simulated cough in dental anesthesia	La projection d'aérosols et de gouttelettes a été visualisée à l'aide d'un système Glo Germ. On a constaté que la simulation de la toux produisait des projections plus importantes que les procédures dentaires d'essai générant des aérosols.	(Chanpong et al., 2020)
Could SARS-CoV-2 be transmitted via speech droplets?	Un faisceau plan de lumière laser traversant une enceinte sans poussière est utilisé pour détecter les gouttelettes de salive émises en parlant. L'étude apporte la preuve visuelle que la transmission de l'infection par les gouttelettes et les aérosols est possible. Les observations préliminaires démontrent que les milliers de gouttelettes respiratoires et de salive émises en parlant sont beaucoup plus petites que celles émises en toussant, et des phrases simples comme « Bonne santé! » peuvent générer des milliers de petites gouttelettes susceptibles de transmettre une infection. Les chercheurs affirment que des études supplémentaires sont nécessaires afin d'évaluer le titrage viral présent dans les gouttelettes induites par la parole en fonction de la gravité de la COVID-19.	(Anfinrud et al., 2020)

The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission	Les observations par diffusion d'un faisceau laser planaire sensible et les mesures d'un spectromètre aérodynamique (APS) sont utilisées afin de visualiser la dispersion et la désintégration des gouttelettes. Les expériences ont révélé que les gouttelettes émises en parlant normalement se désintègrent en 8 à 14 minutes dans des milieux clos où l'air est stagnant (tels que les espaces fermés, en particulier mal ventilés) et les durées de désintégration les plus longues observées concernaient les gouttelettes ayant un diamètre de 12 µm ou plus au moment de leur émission. Les chercheurs estiment qu'une minute de parole à voix haute peut générer un minimum de 1 000 virions contenant des noyaux de gouttelettes qui restent en suspension dans l'air pendant plus de 8 minutes. Les résultats suggèrent que les particules en suspension dans l'air chargées de virus pourraient être inhalées par d'autres personnes.	(Stadnytskyi et al., 2020)
Modèles mathématiques		
Titre de la publication	**Principaux résultats**	**Référence**
COVID-19 : Effects of weather conditions on the propagation of respiratory droplets	Un modèle mathématique complet a été établi afin d'explorer l'évaporation des gouttelettes générées par la parole, le transfert de chaleur et la cinématique dans différentes conditions (par exemple, la température, l'humidité et la ventilation). Une température basse et une humidité élevée favorisent la transmission et la dispersion des gouttelettes, mais suppriment la formation d'aérosols. D'autre part, une température élevée et une faible humidité favorisent la perte rapide de la masse des gouttelettes respiratoires (par évaporation) et réduisent la distance de parcours des gouttelettes, mais ces conditions augmentent le risque de transmission des particules d'aérosol. L'étude conclut que les recommandations actuelles en matière de distanciation sociale pourraient ne pas suffire à diminuer les risques de transmission par voie aérienne, car les gouttelettes peuvent parcourir des distances allant jusqu'à 6 mètres.	(Zhao et al., 2020)
COVID-19. Transport of respiratory droplets	Examen de la propagation des gouttelettes respiratoires dans les environnements extérieurs en appliquant le modèle de calcul d'une personne qui éternue en milieu urbain sous un vent	(Guerrero et al., 2020)

in a microclimatologic urban scenario	climatologique d'intensité moyenne. La propagation des gouttelettes respiratoires est caractérisée par la dynamique de la taille des gouttelettes : les gouttelettes les plus grosses (400 - 900 µm) se propagent entre deux et cinq mètres en 2,3 secondes, tandis que des gouttelettes plus petites (100 - 200 µm) sont transportées entre huit et onze mètres en 14,1 secondes sous l'action d'un vent turbulent.	
Influence of wind and relative humidity on the social distancing effectiveness to prevent COVID-19 airborne transmission: A numerical study	La transmission aérienne des gouttelettes de toux avec des effets de condensation et d'évaporation est modélisée à partir de l'observation de 2 personnes virtuelles soumises à différents environnements et vitesses de vent. Les microgouttelettes suivent les courants d'air et peuvent être déposées sur des corps humains virtuels (y compris la région de la tête) à des distances supérieures à 3,05 mètres. Une humidité relative élevée (99,5 %) entraîne également des gouttelettes plus grosses et un dépôt plus important de gouttelettes de toux sur les surfaces (en raison des effets de croissance hygroscopique). Des microgouttelettes en suspension peuvent se transmettre d'une personne virtuelle à l'autre en moins de 5 secondes. L'étude conclut que compte tenu des effets du vent ambiant, de la convection et de l'humidité relative sur les particules respiratoires émises par l'homme, la distance sociale fréquemment recommandée de 1,83 mètre pourrait ne pas être suffisante pour prévenir la transmission d'aérosols entre les personnes.	(Feng et al., 2020)
Modelling aerosol transport and virus exposure with numerical simulations in relation to SARS-CoV-2 transmission by inhalation indoors	Les données probantes disponibles sur le transport des aérosols dans l'air sont combinées à des simulations 0D-3D dans des modèles basés sur la physique et des calculs théoriques. Les simulations de Monte Carlo indiquent que les gouttelettes produites par la parole et la toux (diamètre inférieur à 20 µm) peuvent rester en suspension dans l'air, y rester de 20 minutes à 1 heure et être inhalées par d'autres personnes. La durée d'exposition conduisant à inhaler 100 aérosols (dose infectieuse présumée suffisante) est variable en fonction de la situation et peut varier d'une seconde, à une minute, voire à une heure. Les simulations 3D de la dynamique des fluides numériques (CFD) suggèrent que les aérosols (dp < 20 µm) peuvent être transportés sur des distances pouvant atteindre 10 mètres dans	(Vuorinen et al., 2020)

	des environnements génériques, en fonction de l'humidité relative et du débit d'air. Enfin, le séchage rapide des gouttelettes de mucus expulsées produirait des noyaux de gouttelettes et des aérosols qui susceptibles de transporter des particules de virus en suspension dans l'air. Ces gouttelettes (diamètre initial des particules de 50 µm à 100 µm) pourraient rester en suspension dans l'air pendant environ 20 secondes à 3 minutes.	

LES GRAPPES DE CAS DE COVID-19 ATTRIBUÉES AU CHANT

Cinq articles publiés décrivant les éclosions de cas de COVID-19 liées au chant et/ou à l'utilisation d'instruments ont été identifiés. Une éclosion de cas de COVID-19 apparue dans la chorale de Skagit Valley, WA, avec un taux d'atteinte secondaire de 53 à 87 % (Hamner et al., 2020), et une estimation des émissions générées dans ce scénario basée sur un modèle mathématique (Miller et al., 2020) suggèrent que la transmission des infections dans cette grappe est principalement due au partage d'un espace fermé dans lequel un seul individu infectieux chantait. Plusieurs résumés relatifs à l'apparition de grappes de cas mettent en exergue les pratiques liées aux cours de chant, au karaoké, aux concerts de musique et aux chorales au Japon et à Singapour (Furuse et al., 2020 ; Dalton, Katelaris, & Wilson, 2020, Wei et al., 2020). Le risque de transmission dépend des caractéristiques propres à l'environnement, l'activité, la distance et le temps passé avec une personne infectée (Waddell., 2020).

Tableau 2 : Littérature relative aux enquêtes épidémiologiques qui attribuent (partiellement) la transmission au chant

Titre de la publication	Principaux résultats	Référence
High SARS-CoV-2 attack rate following exposure at a choir practice — Skagit County, Washington, March 2020	Un groupe de chorale à Washington, aux États-Unis, impliquant 61 chanteurs, y compris le cas de référence symptomatique, a donné lieu à 32 cas confirmés et 20 cas secondaires probables de COVID-19 (taux d'atteinte de 53,3 % à 86,7 %); 3 patients ont été hospitalisés et 2 sont décédés. Les auteurs concluent que la transmission a vraisemblablement été facilitée par la proximité physique (moins de 1,80 m) pendant la pratique du chant et augmentée par l'activité de chant.	(Hamner et al., 2020)
Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley	Étude de cas de l'éclosion associée à la chorale du comté de Skagit qui explore la variabilité du risque d'infection en fonction des taux d'élimination des aérosols respiratoires grâce à la	(Shelly L. Miller et al., 2020)

Chorale superspreading event	ventilation, au dépôt sur les surfaces et à la décomposition virale. En raison du taux élevé d'atteintes secondaires, on suppose que l'hypothèse d'un vecteur passif commun ou d'une transmission de personne à personne est peu probable. On estime que l'exposition commune à l'air intérieur sur le lieu des répétitions et les fortes émissions d'aérosols respiratoires pendant le chant sont les principaux facteurs liés à la transmission de l'infection. L'évaluation modélisée du risque d'infection par particules en suspension infère, dans le scénario présent, un taux d'émission de E = 970 (± 390) quanta par heure, à partir du cas de référence infectieux unique.	
Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020	L'étude portant sur 7 grappes de cas COVID-19 identifiées à Singapour a révélé qu'une transmission asymptomatique s'était produite. Dans deux grappes indépendantes, la transmission de l'infection est attribuée à plusieurs femmes ayant assisté à un cours de musique (grappe B, grappe F) dont les cas ont été confirmés.	(Wei et al., 2020)
Clusters of coronavirus disease in communities, Japan, January-April 2020	Étude sur 61 grappes de plus de 5 cas au Japon, du 15 janvier au 4 avril. 18 établissements de soins de santé (30 %); 10 établissements de soins d'autres types, tels que des maisons de soins infirmiers et des centres de jour (16 %); 10 restaurants ou bars (16 %); 8 lieux de travail (13 %); 7 événements liés à la musique, tels que des concerts de musique en direct, des répétitions de chorales et des soirées karaoké (11 %); 5 gymnases (8 %); 2 cérémonies (3 %); et 1 incident lié au transport en avion (2 %). La plus grande grappe de cas non liée aux soins de santé était composée de plus de 30 personnes ayant participé à un concert de musique en direct, y compris les artistes, les membres du public et le personnel de l'événement. De nombreuses grappes de cas de COVID-19 ont été liées à l'exposition à des situations impliquant une forte respiration associée à une proximité physique, comme le chant lors de soirées karaoké, les acclamations des clubs, les conversations dans les bars et l'exercice physique dans des gymnases.	(Furuse et al., 2020)
Open with care: minimising COVID-	Évaluation des risques et des avantages	(Dalton, Katelaris, & Wilson, 2020)

19 superspreading settings in Australia	Les salles de karaoké et les groupes de chorale, impliquant le chant, sont considérés comme des sources vraisemblables d'amplification du risque de transmission en raison du rapprochement physique des personnes rassemblées et de l'action même de chanter. Des éclosions associées à des églises et à des rassemblements religieux ont été enregistrées aux États-Unis, en Corée du Sud et à Singapour. Les caractéristiques propres aux rassemblements religieux peuvent augmenter le risque de transmission en raison d'activités telles que le chant, les accolades et les poignées de main à l'occasion des salutations et des offices religieux, la transmission d'objets sacramentels, la disposition des sièges à proximité les uns des autres et le partage de nourriture et de rafraîchissements. L'article avertit que, dans le contexte australien, la levée des restrictions doit être faite avec précaution. Dans des conditions de très faible propagation communautaire et de fortes proportions de populations sensibles, ces événements de super propagation peuvent constituer des sources très importantes de cas.	

LITTÉRATURE GRISE SUR LE RISQUE DE COVID-19 ASSOCIÉ AUX INSTRUMENTS À VENT ET AU CHANT

Le tableau suivant résume la littérature grise pertinente. Deux éclosions, l'une aux Pays-Bas impliquant une grande chorale et un orchestre et l'autre associée à une éclosion apparue dans un karaoké en Corée du Sud. Une évaluation des risques, une expérience et un protocole à l'appui des futures recherches sur le risque de transmission lié à l'utilisation des instruments à vent. Ainsi que deux notes de synthèse précédemment réalisées par l'Alberta (22 mai) et Terre-Neuve (1er juin), qui reprennent elles-mêmes plusieurs documents d'orientation et déclarations de position.

Tableau 3 : Littérature grise sur la transmission de l'infection attribuée au chant et aux instruments à vent

Titre de la publication	Principaux résultats	Référence
Wind instrument aerosol in COVID	Évaluation des risques	(Schwalje & Hoffman, 2020)

Era - COVID-19 and horns, trumpets, trombones, euphoniums, tubas, recorders, flutes, oboes, clarinets, saxophones and bassoons	Cette évaluation des risques donne un aperçu des différentes activités liées à la pratique des instruments à vent pouvant entraîner la formation d'aérosols ou une transmission directe. • Il n'existe aucune donnée probante directe, mais les données probantes indirectes suggèrent qu'il peut y avoir un risque de transmission supérieur au risque de fond normal. • Les auteurs décrivent des pratiques courantes, parmi les musiciens, qui ont le potentiel de propager le virus. La pratique consistant à partager ou à toucher les anches d'autres musiciens a été décrite comme étant à haut risque et il n'y avait pas de recommandations relatives à la désinfection des anches. • Les auteurs concluent qu'il n'y a pas suffisamment de données probantes permettant d'évaluer correctement le risque de transmission du SRAS-CoV-2 lié au fait de jouer d'un instrument avec d'autres personnes.	
Aerosol generation from playing band instruments and risk of infectious disease transmission	Il s'agit d'un protocole pour une étude menée à l'université du Colorado. L'objectif de ce projet est de fournir des mesures et des estimations de modélisation des risques en temps utile afin de mieux comprendre les émissions de particules provenant des instruments de musique. Quatre actions sont proposées : 1. Études d'imagerie des flux afin de documenter qualitativement l'émission et le panache de particules par la photographie et les lasers 2. Études en laboratoire d'essai afin de mesurer les taux de génération de particules provenant des activités suivantes : a. 5 bois : flûte, clarinette, hautbois, saxophone, basson b. 4 cuivres : cor, trompette, trombone, tuba c. 4 gammes vocales : soprano, alto, ténor, basse d. Comédie musicale : paroles, monologue, chant, danse (acteurs et actrices) e. Élémentaire - garçons et filles de la troisième à la cinquième année f. Simulation aérobie (fanfare, spectacle de chorale, danse, etc.)	(Shelly L. Miller et al., 2020)

	3. Études sur le terrain relatives aux répétitions mesurant les concentrations dans une salle de répétition comptant plusieurs musiciens et située à l'Université du Colorado à Boulder (sous réserve de l'approbation de l'IRB et du campus) 4. Modélisation du risque de transmission à l'aide du modèle Wells-Riley	
Bamberg Symphony Orchestra: Scientists measure aerosol emissions	Publication en ligne (en allemand) Les scientifiques présents auprès de l'Orchestre symphonique de Bamberg utilisent les flux d'air pour mesurer le nombre d'aérosols émis par un trombone, une clarinette ou un cor. On considère que les matières en suspension émises représentent l'air potentiellement contaminé par le SRAS-CoV-2 qui serait expulsé par l'instrument si le musicien était infecté.	("Bamberg Symphony Orchestra: Scientists measure aerosol emissions," 2020)
(LEAD) Itaewon-tied cases rise to 153, karaoke facilities emerge as infection routes	Article de journal en ligne Infections à Séoul, en Corée du Sud, liées à des boîtes de nuit dans le quartier d'Itaewon : les installations de karaoké sont des sites de transmission d'infections présumés.	("(LEAD) Itaewon-tied cases rise to 153, karaoke facilities emerge as infection routes," 2020)
That one passion that did go on, with disastrous consequences.	Article de journal en ligne L'éclosion dont il est question ici a impliqué 102 cas de COVID-19 parmi 130 membres d'une chorale et d'un orchestre à Amsterdam, aux Pays-Bas. Au début de l'éclosion, le groupe a continué à pratiquer bien que des membres de la chorale commençaient à tomber malades. D'après la séquence des événements et des maladies, plusieurs événements de transmission se sont potentiellement croisés.	(van der Lint, P., 2020)
COVID-19 quick response report: choirs and COVID-19	Rapport de réponse rapide sur les données probantes concernant les chorales et la COVID-19 disponibles au 3 juin2020. Les auteurs résument un grand nombre de documents d'orientation, d'avis d'experts et de données probantes portant sur les chorales et la transmission du SRAS-CoV-2.	(Williams, S et Navarro, P., 2020)
Singing as a risk for transmission of SARS-CoV-2 virus	Examen rapide des données et des orientations concernant le chant comme risque de transmission. La dernière évaluation date du 22 mai 2020.	(Kania-Richmond, A et Sharpe H., 2020)

	L'examen comprend des documents qui ne sont pas liés au SRAS-CoV-2 mais relatifs au chant et au potentiel de propagation des agents pathogènes. Rapport sur les événements de transmission de la grippe A et de la tuberculose liés aux chorales.	

Méthodologies

Une analyse quotidienne de la littérature (publiée et pré-publiée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse compile la littérature disponible sur le COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature COVID-19 pertinente sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont croisées avec la littérature de la liste de l'OMS relative à la littérature COVID, et les centres d'information COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel qui peut être consultée. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes se rapportant à la COVID-19 et au SRAS-CoV-2. Les termes de recherche utilisés sont les suivants : chanter, karaoké, chorale, vent et instrument, musique, chant, vocaliser, religieux, église. Une recherche supplémentaire de littérature grise a été effectuée à l'aide de chaînes de recherche (COVID-19 ou SRAS-CoV-2) ET (chorale ou musique ou (vent et instrument)) dans Google. Les examens effectués précédemment sont issus des Référentiels du CCNMO, ACMTSet SPOR evidence alliance.

Chaque référence potentiellement pertinente a été examinée afin de confirmer qu'elle comportait des données pertinentes, puis ces données ont été extraites aux fins de l'élaboration de l'examen. Le présent examen contient les recherches publiées au 26 juin 2020.

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Emerging Evidence on COVID-19

Evidence Brief of Potential Health Risks of Hard-Surface Disinfectants in Environments Shared by School-aged Children

Introduction

What evidence exists to inform the potential health risks (contact exposure, inhalation toxicity, poisoning) of increased use of hard-surface disinfectants in environments (e.g. school/ home/ recreation) shared by school-aged children during the COVID-19 pandemic?

Schools are re-opening with more frequent sanitation and hygiene requirements in an effort to mitigate the spread of SARS-CoV-2, the virus that causes the COVID-19 disease, between students and staff. In addition, many public facilities, businesses and homes have adopted enhanced sanitation procedures, which includes increased use of hard-surface disinfectants to reduce the risk of spread of the virus. Hard-surface disinfectants are known to have some associated health risks and their increased use may pose additional health risks to school-aged children.

Hard-surface disinfectants are intended for use as disinfectants on hard, non-porous surfaces and contain active ingredients permitted by Health Canada. Enveloped viruses such as coronaviruses are readily inactivated by many disinfectants (Rai, 2020). A list of approved products (n=526) effective against SARS-CoV-2 is available on Health Canada's website (Health Canada, 2020). Common categories of active ingredients for hard-surface disinfectants include quaternary ammonium compounds, phenolic, idophor, chlorine releasing compounds, and peroxygen (Health Canada, 2015). A general overview of each category is provided in the appendix table. Each of these classes of active ingredients have warnings about the proper use of each chemical.

Disinfectants are regulated as drugs in Canada and although the *Food and Drugs Act* and the Food and Drug Regulations do not specify acute toxicity hazard classification criteria for disinfectant drugs, manufacturers are recommended to consider referencing the Consumer Chemicals and Containers Regulations, 2001 for products intended for non-commercial uses (domestic) by consumers (Canada, 2020a); or Hazardous Products Regulations, 2015 for products intended for use in workplaces or commercial use (Canada, 2020b). When Health Canada approves a disinfectant, precautionary statements to ensure their appropriate use are included on the product labels. These statements describe recommended actions that can be taken to minimize, mitigate and/or prevent adverse reactions from occurring. They are displayed prominently on the labelling of disinfectants to ensure the safe use and handling of the product by the end users in accordance with the label directions. The precautionary statements are relevant to the potential acute toxicity exposure

hazards of the product. In determining the appropriate precautionary statements, Health Canada takes into consideration all the ingredients in the formulation including inert or non-medicinal ingredients. Health Canada ensures that the overall risk benefit of using a product is positive and that potential risks can be mitigated by appropriate labelling.

Contact, inhalation or ingestion of disinfectants can lead to immediate irritation or poisoning. These compounds could cause contact burns or sensitivities to skin and eyes, are harmful if ingested and have inhalation risks during handling and application (CDC, 2020 and Health Canada, 2020). Some disinfectants may leave chemical residues which can become airborne and inhaled; to use safely, these products need to be rinsed off after use. Of particular interest are disinfectant by-products, such as those from chlorine containing compounds like household bleach that may form volatile organic compounds (VOCs) if accidentally mixed with other cleaning products or when it comes into contact with organic matter on a dirty surface (Odabasi, 2014). Some categories of disinfectants have been associated with respiratory issues including asthma due to long term occupational exposure (Appendix table). Measures to address these risks include: using soap and water to clean all visibly dirty surfaces before disinfecting, not mixing disinfectants with other products, opening windows to increase ventilation, wearing gloves when disinfecting, and allowing surfaces to air dry completely before using and staying out of a freshly disinfected area for 20-30 minutes after cleaning (Bello, 2010). Long-term exposure toxicology data is incomplete for many disinfectants, and is generally supported by animal studies. While some have limited adult human data, few have data on children, see the appendix table for a summary for each category of disinfectant.

This review focuses on health risks associated with hard-surface disinfectant use around school-age children both before and during the COVID-19 pandemic. It includes literature published up to October 5, 2020 (Methods are at the end of the document).

Key Points

There is limited evidence on the health risks of hard surface disinfectant use in school-aged children, this review demonstrates that

- Compared with previous years, reports on calls to poison control centres in both the United States (USA) and Canada have documented an increase in calls during the COVID-19 pandemic related to disinfectants and cleaners, with exposures frequently involving children (Table 1).
- People using disinfectants may lack knowledge of their safe use and potential harms based on a consumer survey in the USA (Table 1).
- Studies of children that reside in homes with high disinfectant use have a higher frequency of skin and respiratory effects as well as sensitization to disinfectants (Table 2).

- Some cross-sectional studies have shown an association between the frequency of disinfectant use around children and health effects such as asthma and wheezing in young children (Table 2).
- Chloroform (one of the VOCs that can form when bleach comes into contact with other products or organic matter) has been found at unacceptable concentrations in several early childhood education centres; most of these centres reported using bleach regularly (Table 2).
- Overall, there remains considerable knowledge gaps in the literature on both the short and long term effects that may be experienced by children as a result of the increased use of hard-surface disinfectants.

Overview of the Evidence

Publications that directly report on the potential health risks of increased use of hard-surface disinfectants in environments shared by school-aged children are scarce. We examined not only literature reviews and information about calls to poison control centres during the pandemic (Table 1), but also included available evidence on the health impacts on children from the use of hard-surface disinfectants prior to the COVID-19 pandemic (Table 2). Sixteen relevant publications on exposure to hard-surface disinfectants informed this review. These included epidemiological studies (cohort and cross sectional), reports from poison control, a consumer knowledge survey, risk assessments, literature reviews and commentaries. The overall body of research is very small, of low quality and is insufficient to provide conclusive evidence on the health risks of disinfectant use is school-age children. Additional research in this area is needed.

Excluded from this review were studies that focused on adult or occupational exposure, as well as animal studies, as their exposure levels may differ from school-aged children. General features of disinfectant categories and links to additional information on each category is provided in the appendix table.

CONTENTS

HARD-SURFACE DISINFECTANTS EXPOSURE DURING THE COVID-19 PANDEMIC

Seven studies on the effect of exposure to hard-surface disinfectants in children during the COVID-19 pandemic are summarized in Table 1. This includes two reports from poison control centres, one consumer knowledge survey, one risk assessment, one literature review and two relevant commentaries.

Poison control centres in both the USA and Canada have reported a rise in calls related to disinfectants and general household cleaning products in 2020 compared to previous years (Chang, 2020; Yasseen, 2020). In the Canadian study that tracked calls on cleaners and disinfectants, 42% of calls were related to bleaches and 21% to disinfectants (Yasseen, 2020). The increase was seen in all age groups, but the majority were for adults, not children. In the USA study, bleaches accounted for the largest percentage increase in calls followed by non-alcohol disinfectants. Calls due to exposures among children aged ≤5 years consistently represented a large percentage of total calls from 2018 to 2020 (range = 39.9–47.3%) (Chang, 2020).

A survey conducted in May 2020 found sixty percent of respondents reported cleaning or disinfecting their home more frequently since the pandemic started compared to the preceding months (Gharpure, 2020). It also reported that respondents had limited knowledge of how to safely prepare their cleaning products and disinfectant solutions and 25% of respondents reported experiencing at least one adverse health effect that they believed had resulted from using these products (Gharpure, 2020).

A risk assessment found three-year-old children had the highest potential exposure to disinfected surfaces compared to any other age group due to the higher likelihood of hand contact and mouthing activities (Li, 2020). This risk assessment looked at several chemicals, but not all were hard-surface disinfectants. They also assumed that disinfectants were used at full strength without dilution, the individual was exposed via direct hand contact, and that disinfectants were not wiped off after surface application, which may not be representative of how such disinfectants were actually used by consumers.

Reviews of approved disinfectants which contain quaternary ammonium, sodium hypochlorite or hydrogen peroxide and their use during the COVID-19 pandemic highlight the majority of hard-surface disinfectants used against SARS-CoV-2 (Samara, 2020, Rai, 2020). The literature review identified that residues from some hard-surface disinfectants can contribute to poor air quality, and there is evidence of higher cancer rates attributed to regular use of some of these disinfectants in adults from occupational exposure (Rai, 2020). In some high exposure occupations, studies have shown an association with increased risk of chronic obstructive pulmonary disease, asthma and eye irritation (Rai, 2020; Samara, 2020). Similar data was not identified for children and although 5% percent of childhood cancer and 30% of childhood asthma are related to chemical exposures, the proportion that may be attributed to hard-surface disinfectant use is unknown (Rai, 2020).

Table 1: Studies and reviews on the health risks of hard-surface disinfectants use for school-aged children (n=7)

Study	Method	Key Outcomes
Poison Control Calls		
Chang, 2020 Before/after study USA Jan– Mar 2018, 2019 and 2020	The National Poison Data System calls were analysed for the number of exposures reported for January–March 2020 compared with the same 3-month period in 2018 and 2019.	During January–March 2020, poison centres received 45,550 exposure calls related to cleaners (28,158) and disinfectants (17,392), representing overall increases of 20.4% and 16.4% from 2019 and 2018, respectively. The increase in calls was seen across all age groups but exposures among children aged ≤5 years represented 39.9%–47.3% of calls in the three time periods. Inhalation accounted for the largest percentage increase in calls from 2019 to 2020. The largest increase in calls possibly related to hard-surface disinfectants (2019 vs 2020) were for bleach (62.1%) and non-alcohol disinfectants (36.7%).
Yasseen, 2020 Before/after study Canada Jan – Jun 2019 and 2020	Five Canadian Poison Control Center exposure reports for Jan – June 2020 were compared with the same 6-month period in 2019.	There was a 35% rise in total number of exposures to cleaning products/ disinfectants/ hand sanitizers in 2020 compared to 2019. Of 8187 calls reporting exposures between January and June in 2019 and 2020, those possibly related to hard-surface disinfectants were: 42% for bleach, 21% disinfectants, 12% chlorine gas, and 2% chloramine gas (the latter are bi-products of mixing bleach with other disinfectants or cleaners, see appendix). In the 2020 period, the number of calls peaked in March and generally decreased after April 2020. Exposure calls were predominately among those aged 19+ for both years. The results do not suggest that there was a large increase among those aged <19 years between 2019 and 2020.
Knowledge Survey		
Gharpure, 2020 Opt-in adult internet survey on household cleaning USA May, 2020	The survey included questions to assess knowledge and practices regarding household cleaning and disinfection during the COVID-19 pandemic.	Included 502 adults (18+) 60% reported more frequent home cleaning/ disinfection use compared with preceding months. Limited knowledge of safe preparation of cleaning and disinfectant solutions was reported across several questions. 39% of respondents reported high-risk practices not recommended by CDC including: 1) Applying bleach to food (19%)

		2) Use of household cleaners and disinfectants on hands (18%) 3) Misting the body with cleaners and disinfectants (10%) 4) Inhaling vapors (6%) 5) Drinking or gargling diluted bleach solutions (4%), soapy water (4%), or other cleaner/ disinfectant solutions (4%). 25% reported at least one adverse health effect that they believed resulted from using cleaners or disinfectants. These were more common (33% vs. 25%) in respondents who reported a high risk practice.
Risk Assessment		
Li, 2020 Risk assessment and quantitative exposure model of 22 disinfecting chemicals which have been highlighted to kill SARS-CoV-2 USA and Canada[1] September, 2020[1]	Risk assessment use PROTEX an indoor fate and chemical exposure model. Three exposure routes (mouthing-mediated oral ingestion, inhalation, and dermal absorption) were investigated. The application scenario relevant to this review was disinfection of indoor surfaces and objects (surface application). Three age groups were modelled: 3, 14, and 24 year olds.	<u>Exposure risk assessment</u> Three-year-old children had highest overall exposure, especially to disinfected surfaces, due to higher frequency of hand contact and mouthing activity. Surface disinfectant exposure risk, especially for young children were noted. Mouthing-mediated ingestion dominates the exposure to non-volatile disinfectants whose residues can stay on surfaces until removed by normal cleaning (e.g. quaternary ammonium compounds). For older age groups this exposure was through dermal absorption and was also noted for phenolic chemicals. For disinfectants like triethylene glycol (low toxicity) that are aerosolized to disinfect and clean the air, exposure was mainly due to inhalation. Although this risk assessment looked at 22 chemicals, many were not hard-surface disinfectants.
literature reviews		
Rai, 2020 Literature review Jun 2020	Studies on the potential harmful effect of disinfectants and safe alternatives were summarized in the context of COVID-19.	5% of childhood cancer and 30% of childhood asthma are related to chemical exposures, it is unknown if any of these are attributed to hard-surface disinfectants. The majority of products recommended by the EPA for use against COVID-19 contain the active ingredients from quaternary ammonium compounds (Quats).

		Many of these are linked with an increased risk of chronic obstructive pulmonary disease (COPD), asthma, and eye irritation when used regularly (occupational exposure). Quats have been shown to possibly cause fertility issues in animal studies. When not rinsed properly after use, biodegradable disinfectants will leave an active chemical residue on the surface applied. Disturbance of the residue can cause it to be airborne, which may cause irritation for some people. Thorough rinsing and general cleaning removes the residue.
Commentaries		
Rivera, 2020 Commentary USA[1] Jan – May 2020	Using Google Trends, evaluated search interests for the purchase and consumption of disinfectants and for poison control centres after the USA president implied injecting disinfectants may be a potential treatment for COVID-19. Confidence intervals for each trend were calculated by averaging multiple samples collected daily over a 3-week period.	The relative search fraction (RSF) values from January-February, 2020 for purchasing, drinking, or injecting disinfectants were minimal (<1). A day after Trump's comment, RSF for drinking disinfectants was 32.3 and injecting disinfectants was 100. RSF for poison control centres peaked a day later (RSF=11·05), indicating an increase in interest or possibly for information or assistance following off-label use of disinfectants.
Samara, 2020 Commentary United Arab Emirates[1] 2020[1]	Safety of disinfectants is presented for some of the most widely used natural and synthetic surface disinfectants approved by the Environmental Protection Agency for the prevention of SARS-CoV-2 and reviews associated health effects.	Hard-surface disinfectants can cause irritation of the skin and eyes, irritation to the respiratory tract, and asthma in some individuals. The use of bleach can result in the formation of VOCs in the indoor air, and high concentrations of VOCs are reported 30 minutes after application. This indicates that the use of bleach may be an important source of VOC inhalation exposure. An ideal disinfectant should have a low toxicity profile with short and long term exposure e.g. Quaternary ammonium compounds and peracetic acid: (see appendix table).

[1] The country was based on author location or the date was based on date of publication.

GENERAL EXPOSURE TO HARD-SURFACE DISINFECTANTS

While there are no recent studies on how the increased exposure to hard-surface disinfectants during the pandemic will affect the health and safety of school-aged children, studies conducted prior to the COVID-19 pandemic can provide additional information on the effects of exposure to hard-surface disinfectants among children.

The biologic monitoring study of 34 early childhood education centres in California reported that chloroform, a VOC related to chlorine bleach use, exceeded the acceptable cancer risk levels in 38% of facilities (Hoang, 2016).

Two exposure assessment studies found that bleach is commonly used in daycare centers in the USA. A survey in fourteen childcare facilities in Washington, DC reported on the use of chlorine bleach (92.8%) in their facilities for sanitation purposes and chloroform was detected in all facilities (Quirós-Alcalá, 2016). The most common sanitized surfaces were tables, bathrooms, chairs along with beds, changing tables and children's toys. Bleach has been reported to be an airway irritant if inhaled and can release VOCs (e.g. chloroform) when it reacts with organic material, which is a known carcinogen. The third risk assessment measured and modelled the quantity of VOCs produced during normal indoor cleaning tasks. The results suggest that there is potential for exposure to above-average levels of VOCs to anyone who enters the room up to 20 minutes after cleaning sinks, mirrors, or toilets with disinfectants containing quaternary ammonium compounds or sodium hydroxide (Bello, 2010). Increasing ventilation and decreasing time in a newly cleaned room would reduce exposure to VOCs. Three epidemiologic studies have been published. A prospective cohort study from Germany of youth ages 19-24 showed the use of disinfection products was associated with an increase in asthma and atopic dermatitis. Self-reported exposure to household disinfectants and high use of disinfectants was associated with a two-fold increased odds of asthma incidence compared to those who reported no use (Weinmann, 2017). Youth who reported low or medium use of disinfectants were also more likely to report remittent asthma (Weinmann, 2017). In a cross-sectional study of 4-year olds in several European countries, households with high use of disinfectant room sprays were associated with increased atopic dermatitis and itchy rashes, but not asthma (Krauss-Etschmann, 2009). A weakness of this study was general disinfectant use was not recorded (Krauss-Etschmann, 2009). A cross-sectional study from Sweden found that use of chlorine bleach in the home had a protective association with developing asthma and sensitization to indoor allergens, but did not specify whether children were present during cleaning (Nickmilder, 2007).

Three literature reviews summarized the evidence on the potential risk to children which is mostly cross-sectional studies of cleaning/disinfection products and the VOCs associated with those products (Holm, 2019; Mendell, 2007; Slaughter, 2019). The most common categories of disinfectants reported across studies included bleach, quaternary ammonium compounds and peroxides, chosen for their broader range of disinfection across pathogens (Holme 2019). Indoor cleaning activities were associated with allergies, asthma and other respiratory issues in infants and young children (Mendell, 2017). Most of these studies did not

specify the products being used, and often multiple types of products were used, so separating out the impact of one product over another was not possible.

Table 2: Reports on health risks of hard-surface disinfectants from pre-pandemic literature (n=9)

Study	Method	Key Outcomes
Exposure / Risk Assessments		
Hoang, 2017 Biological monitoring study USA May 2010 - May 2011	38 VOCs were measured in single-day air samples collected in 2010-2011 from 34 ECE facilities serving California children and evaluated "No Significant Risk Levels" (NSRLs) defined as the daily dose posing a one in 100 000 excess risk of cancer over a lifetime.	Chloroform - a VOC associated with the use of chlorine bleach - was identified in some samples. Other VOCs were not associated with hard-surface disinfectants, however they maybe VOCs produced by fragrances that are added to a cleaning or disinfection product. The 95th percentile dose estimates for chloroform exceeded the age-specific NSRL in all four age groups assessed. Findings: VOC levels in ECE facilities resemble those in school and home environments and, if reflective of long-term averages, child dose estimates exceeded age-adjusted NSRL benchmarks for benzene, chloroform, ethylbenzene, and naphthalene in 71%, 38%, 56%, and 97% of facilities, respectively. In bivariate analysis: Levels of VOCs were similar in facilities that reported use/purchase of low-toxicity cleaners compared with those using traditional cleaners. However, some VOCs were significantly higher in facilities with higher mopping frequency, suggesting VOC emissions from floor cleaners.
Bello, 2010 Exposure assessment study USA[1] 2010[1]	Sink, mirror, and toilet bowl cleaning tasks were simulated for 20 minutes in a large ventilated bathroom and a small unventilated bathroom using a general purpose, a glass, and a bathroom cleaner. Airborne total volatile organic compounds generated during the tasks were measured.	The household cleaners used contained Quaternary Ammonium Compound or sodium hydroxide. Exposures above the background level were present for approximately 20 minutes after the tasks ended. The highest concentration of ammonia occurred while mirrors were being cleaned. Results suggest that there is potential exposure to anyone who is cleaning the room or who enters the room shortly after cleaning.
Quirós-Alcalá, 2016	Childcare center directors were initially contacted via email and letters. A	Chloroform (a VOC that may originate from products containing chlorine bleach) was detected in every

Exposure assessment study Washington, DC. Fall of 2012 and 2013	questionnaire was administered to childcare center directors. They also collected information on the number of children with asthma at each facility and whether any children experienced asthma attacks or wheezing episodes in the three months prior. To characterize VOCs within the facilities, they collected between two and five 10-h air samples and real-time particulate matter instrument samples at 1 min intervals.	facility. It is important to note that there may be other sources of chloroform. 92.9% of center respondents stated that chlorine bleach was used for sanitizing in the facility. The most commonly reported surfaces sanitized were tables, bathrooms, and chairs, however, respondents also reported the use of chlorine bleach to sanitize beds, changing tables, and children's toys. The indoor pollutants from using chlorine bleach are known respiratory irritants. The authors recommend looking at bleach-free alternatives for disinfection to avoid introducing other hazards into the childcare setting.
Epidemiological Studies		
Weinmann, 2017 Prospective cohort study Germany 2007-2009	2051 young adults between the ages of 19-24 years living in two major German cities took part in a study to self report their exposure to household sprays and disinfectants. Associations with clean product exposure and asthma or wheezing were investigated.	In this sample 83.8% of respondents did not report using disinfectants. No information on what disinfectants were used were collected. Asthma was reported in 5.4% of the sample: - High use of disinfectants was seen to be associated with two-fold increase odds of asthma compared to those with no use (OR 2.79, 95% CI 1.14 to 6.83). - Low and medium disinfectant use was associated with remittent asthma (OR 2.39, 95% CI 1.29 to 4.47). Wheezing in the last 12 months (not related to cold) 17.1%. There was no clear association between exposures and wheezing identified. No causal inferences can be drawn from this data, additional exposure assessments are warranted.
Krauss-Etschmann, 2009 Cross sectional study of 4 year olds (106 Spanish, 45 German, and 25 Hungarian infants).	Children at the age of 4 years underwent a medical and neurophysiologic examination. During this visit, parents completed a standardized questionnaire, which included questions about allergies and asthma in childhood and lifestyle	No information on room disinfectant used was provided. Use was categorized as daily, weekly, occasional or never. Application of room disinfectants was not associated with higher effect estimates for asthma but significantly increased effect estimates for atopic dermatitis and itchy rash. No data on the type of disinfectant was reported.

Spain, Germany and Hungary 2009[1]	related factors. Descriptive categorical data were analyzed with χ^2 analysis. The likelihood of allergic symptoms in relation to household room spray application was assessed in bivariate analyses.	
Nickmilder, 2007 Cross sectional study Sweden Mar-May 2002	The study evaluated the extent that regular house cleaning products with bleach influence the risk of allergies and respiratory diseases. A group of 234 schoolchildren aged 10–13 years old among whom 78 children were living in a house cleaned with bleach at least once per week. Parents of children were asked to complete a questionnaire that included a total of 38 questions.	Children living in houses regularly cleaned with chlorine bleach: - Lower risk of developing asthma, which was significant if both physician diagnosed and screening test positive children were included in the analysis. - They were less likely to be sensitized to indoor allergens including house dust mites (significant). - They were less likely to report wheezing (not significant).
Literature reviews		
Mendell, 2007 Literature review of epidemiologic studies USA[1] Up to mid 2004	Assessed the association between indoor residential chemical emissions, materials or emission-related activities and respiratory or allergic effects in children and infants.	Types of indoor residential materials and coatings, as well as renovation or cleaning activities, were associated with health effects related to asthma or allergy in infants or children. Use of many chemical-based cleaning products (women used more than one, however 87.4% were disinfectants, 84.8% were bleach) by mothers was measured by questionnaire and total chemical burden (TCB) in one study (Sherrif 2005). High TCB was associated with a significant dose–response increase in persistent wheeze in young children (adjusted OR 2.3 (95% CI 1.2 to 4.4) and late-onset wheeze in young children (adjusted OR 2.0 (95% CI 0.8 to 5.2)). No single product was implicated in children wheezing. These findings could be impacted by numerous confounders and conclusions about a causal relationship cannot be inferred from the studies presented.

Slaughter, 2019 Literature review New Zealand[1] Jan 1950 to Jun 2018	Review of hypochlorite poisoning.	Sodium hypochlorite is used as a bleaching and disinfecting agent and is commonly found in household bleach. 110 citations were deemed relevant. Estimates of greater than 40 mL or 5 mL/kg in children of dilute solutions have been suggested as amounts likely to cause corrosive or systemic poisoning. This review describes multiple case reports/series of children ingesting bleach. Common effects included minor gastrointestinal features, such as nausea, vomiting, and superficial burns in the mouth/esophagus. Brief skin exposure to household bleach normally causes minimal effects. Prolonged or extensive exposure may cause skin irritation or hypersensitivity.
Holm, 2019 Literature review USA[1] 2018[1]	Summarized findings from: (1) Environmental Protection Agency registration data on the efficacy of hospital-grade disinfectants (n= 1907 products, 529 of which were included). (2) A review of the research on the toxicities/health risks of common disinfectants in childcare settings.	Bleach is the most common disinfectant used in childcare settings. A bi-product of bleach is the VOC chloroform. Without optimal ventilation rates, some studies have reported chloroform levels above those considered safe for managing cancer risk. Similar findings were reported for formaldehyde which can be a bi-product of improper mixing of cleaning and disinfectant chemicals. Data on the effects of cleaning products on children are limited. Cross-sectional studies have indicated that homes cleaned with bleach were not more likely to have asthma whereas others have found an increased risk with use of sprays and disinfectants in the home. A relationship between use of cleaning sprays and wheezing has been reported across a couple studies in infants and young children. Classes of disinfectants with at least one product that had wide pathogen coverage included bleach, peroxides, quaternary ammonia compounds, and combination products that included quaternary ammonia compounds. Health Risks: Bleach: airway irritant if inhaled and can release VOCs e.g. chloroform when it reacts with organic material, which is a known carcinogen. Skin and eye irritation is common, poisonings have been reported and long-

		term exposure in adults has resulted in respiratory effects, asthma. Quaternary ammonium compounds: Increased risk of asthma and allergic sensitization has been reported. Some have been shown to be mutagenic and reduce fertility rates in animal models. Carcinogenicity has not been shown. Peroxides: Acute toxicity includes poisoning and eye irritation. No other toxicity data have been published. All disinfectants are less effective in the presence of organic material.

Abbreviations: ECE: Early Childhood Education, VOC: Volatile Organic Compounds
[1] The country was based on author location or the date was based on date of publication.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Sciences Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Additional searches for supporting evidence published prior to the COVID-19 pandemic was conducted by keyword searches of PubMed, using a snowball technique and reviewing reference lists. Search terms used included: Disinfect*, Chemical, Safety, Risk, Child*. This review contains research published up to October 5, 2020. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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APPENDIX

Appendix table of common categories of hard-surface disinfectants that comprise the active ingredients in disinfectants used in a range of settings: home, public, hospital [1]

Category (Examples)	Properties and Uses	Potential health impacts: longer term[2]	Safety measures[3]
Chlorine and Chlorine compounds Includes "household bleach" (sodium hypochlorite)- aqueous solution of 5.25%-6.25%, solid calcium hypochlorite. Other compounds designed to hold chlorine longer: demand-release chlorine dioxide, sodium dichloroisocyanurate, and chloramine-T.	Does not leave a residue, inexpensive, fast acting. Rapidly inactivated by organic material. Diluted and applied to surface. Do not mix with: - Ammonia or household cleaning agents as it produces toxic chlorine gas - Formaldehyde and hypochlorite solutions as it produces a carcinogen bis(chloromethyl) ether	Low incidence of serious toxicity. Household bleach (5.25-6.15%) can produce ocular irritation or oropharyngeal, esophageal, and gastric burns. Associated with asthma and other respiratory issues. Chloramines create "organic chloramines" as they attach to organic materials are known as VOCs, studies have shown they increase during household cleaning and some are known carcinogens (Odabasi, 2014). However no adverse effects are expected from normal exposure and proper use.	Diluted household bleach solutions: Use bleach containing 5.25%–8.25% sodium hypochlorite. Do not use a bleach product if the percentage is not in this range or is not specified. Ensure proper ventilation during and after application. Check to ensure the product is not past its expiration date. Never mix household bleach with ammonia or any other cleanser. This can cause fumes that may be very dangerous to breathe in. Prepare a bleach solution by mixing: 5 tablespoons (1/3rd cup) of 5.25–8.25% bleach per gallon of room temperature water or 4 teaspoons of 5.25–8.25% bleach per quart of room temperature water. Bleach solutions will be effective for disinfection up to 24 hours.

Quaternary Ammonium Compound Includes approximately 300 product registrations. Group 1 is hydroxyalkyl substituted quats, Group II non-halogenatred benzyl substituted. Group III is the di and tri-chlorobenzyl substituted quats Group IV are quats with unusual substitutions. (e.g. alkyl dimethyl benzyl ammonium chloride, alkyl didecyl dimethyl ammonium chloride, and dialkyl dimethyl ammonium chloride; twin-chain or dialkyl quaternaries e.g. didecyl dimethyl ammonium bromide and dioctyl dimethyl ammonium bromide).	Non-volatile, leaves residue. Generally approved for disinfection of surfaces and are okay on use of equipment that touches skin. They can be applied as a liquid spray or in a wipe.	No long term health impacts reported: Not dermal sensitizers, not developmental or reproductive toxicants and not carcinogenic or genotoxic (Luz, 2020). Some cases of occupational asthma (e.g. among cleaners) has been reported with exposure to benzalkonium chloride.	Follow the label instructions for use of any disinfectant. Health Canada considers the overall risk benefit prior to approval, ensuring that potential risks can be mitigated by appropriate labelling.
Hydrogen peroxide: Peroxygen, several liquid disinfectants contain hydrogen peroxide. Concentrations range from 6-25% in a premixed -ready to use- chemical. Common combination: 7.5% hydrogen peroxide and 0.85% phosphoric acid.	Leaves residue. Generally approved for disinfection of surfaces. Found in disinfectants at 3-9%. They can be applied as a liquid spray or in a wipe. Is unstable and readily decomposes.	The data on carcinogenicity is inconclusive. Can cause respiratory effects.	Follow the label instructions for use of any disinfectant. Health Canada considers the overall risk benefit prior to approval, ensuring that potential risks can be mitigated by appropriate labelling.
Phenol and phenol derivatives The newer versions-phonolic (chloroxylenol, thymol, O-phenylphenol, triclosan, ortho-phenylphenol ortho-benzyl-para-chlorophenol	Leaves a residue. Generally approved for dis-infection of surfaces. They can be applied as a liquid spray or in a wipe.	Residues can be irritating to skin and dermal absorption is the main route of exposure. Has been linked to hyperbilirubinemia in infants in nurseries using this on bassinettes.	Follow the label instructions for use of any disinfectant. Health Canada considers the overall risk benefit prior to approval, ensuring that potential risks can be mitigated by appropriate labelling.

Peracetic Acid: Peracetic or peroxyacetic	No harmful decomposition products, enhances removal of organic material, leaves no residue, strong pungent odor. They can be applied as a liquid spray. Remains active at low temperatures and in the presence of organic matter. It is unstable when diluted, so should be mixed just prior to use. Can be used in "non-rinse" applications.	Considered a chemical of low concern, low dermal adsorption and no long term health concerns are listed.	Follow the label instructions for use of any disinfectant. Health Canada considers the overall risk benefit prior to approval, ensuring that potential risks can be mitigated by appropriate labelling.
Ortho-phthalaldehyde (OPA or 1,2-benzenedicarboxaldehyde)	Is not a known irritant, no odor, does not require exposure monitoring. Stable at a range of pH from 3-9.	Causes skin staining as it turns proteins gray. Has also been associated with anaphylaxis. Long term exposure is associated with asthma.	Follow the label instructions for use of any disinfectant. Health Canada considers the overall risk benefit prior to approval, ensuring that potential risks can be mitigated by appropriate labelling.
Idophors povidone-iodine aka polybinylpyrrolidone with iodine is most common	Can be used as a surface disinfectant (but better known as an antiseptic). Explodes if mixed with hydrogen peroxide.	Can cause hypothyroidism if ingested in large quantities. Fetus and neonates are particularly sensitive.	Follow the label instructions for use of any disinfectant. Health Canada considers the overall risk benefit prior to approval, ensuring that potential risks can be mitigated by appropriate labelling.

VOC=Volatile organic compounds (VOCs) are compounds that have a high vapor pressure and low water solubility and are emitted as gases from certain solids or liquids. VOCs are released by a wide array of products including paints, cleaning supplies, pesticides, new materials, printers, markers etc. VOCs are higher indoors than outdoors.

[1] Sources: https://www.cdc.gov/infectioncontrol/guidelines/disinfection/index.html, https://pubchem.ncbi.nlm.nih.gov/ and https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/cleaning-disinfection.html

[2]Health impacts related to improper use are not listed: e.g. none of these are safe to ingest, most cause skin irritation and damage to the eye if the product comes in contact with these surfaces. Many of the spray products and bleach also have inhalation warnings during their use.

[3] General safety precautions when using disinfectants: wear skin protection and consider eye protection for potential splash hazards, ensure adequate ventilation, use no more than the amount recommended on the label, use water at room temperature for dilution (unless stated otherwise on the label), avoid mixing chemical products.

Preuve émergente sur la COVID-19

Synthèse en bref sur les risques potentiels pour la santé de l'utilisation des désinfectants pour surfaces dures dans les environnements où se trouvent des enfants d'âge scolaire

Introduction

Quelles preuves existe-t-il en ce qui concerne les risques potentiels pour la santé (exposition par contact, toxicité par inhalation, empoisonnement) découlant de l'utilisation accrue des désinfectants pour surfaces dures dans les environnements (p. ex., école, maison, loisirs) où se trouvent des enfants d'âge scolaire pendant la pandémie de COVID-19?

Les écoles rouvrent et doivent se conformer à des exigences plus strictes en ce qui concerne l'hygiène et la fréquence d'assainissement pour atténuer la propagation du SRAS-CoV-2, le virus qui cause la COVID-19, parmi les élèves et les membres du personnel. De plus, de nombreux établissements publics, entreprises et résidences ont également adopté des procédures d'assainissement plus strictes, qui incluent l'utilisation accrue de désinfectants pour surfaces dures afin de réduire le risque de propagation du virus. On sait que les désinfectants pour surfaces dures présentent certains risques pour la santé, et leur utilisation accrue pourrait entraîner des risques supplémentaires pour la santé des enfants d'âge scolaire.

Les désinfectants pour surfaces dures qui sont conçus pour être utilisés comme désinfectants pour surfaces dures non poreuses contiennent des ingrédients actifs autorisés par Santé Canada. Les virus enveloppés comme les coronavirus sont facilement inactivés par de nombreux désinfectants (Rai, 2020). Une liste de produits approuvés (n = 526), efficaces contre le SRAS-CoV-2, figure sur le site web de Santé Canada (Santé Canada, 2020). Les composés d'ammonium quaternaire, les phénoliques, les idophores, les composés dégageant du chlore et le peroxygène font partie de certaines catégories courantes d'ingrédients actifs que l'on retrouve dans les désinfectants pour surfaces dures (Santé Canada, 2015). Le tableau en annexe donne un aperçu général de chacune des catégories. Chacune de ces catégories d'ingrédients actifs comporte des mises en garde quant à l'utilisation appropriée de chacun des produits chimiques.

Les désinfectants sont réglementés comme des médicaments au Canada et, bien que la *Loi sur les aliments et drogues* et le Règlement sur les aliments et drogues ne précisent pas les critères de classification pour les dangers de toxicité aiguë pour les désinfectants assimilés aux drogues, l'on recommande aux fabricants de penser à faire référence au Règlement sur les produits chimiques et contenants destinés aux consommateurs

de 2001 lorsque ces produits sont conçus pour des utilisations non commerciales (domestiques) par des consommateurs (Canada, 2020a) ou au Règlement sur les produits dangereux de 2015 lorsque ces produits seront utilisés dans les lieux de travail ou à des fins commerciales (Canada, 2020b). Lorsque Santé Canada approuve un désinfectant, des mises en garde visant à garantir son utilisation appropriée sont incluses sur les étiquettes des produits. Ces mises en garde décrivent les mesures recommandées qui peuvent être prises pour minimiser, atténuer et/ou prévenir les effets indésirables. Elles sont indiquées et mises en évidence sur les étiquettes afin de garantir une utilisation et une manipulation sécuritaires du produit par les utilisateurs finaux lorsque ces derniers les utilisent de la façon indiquée sur l'étiquette. Ces mises en garde sont également pertinentes en ce qui concerne les dangers potentiels d'exposition à la toxicité aiguë du produit. Pour déterminer les mises en garde appropriées, Santé Canada tient compte de tous les ingrédients présents dans la préparation, y compris les ingrédients inertes ou non médicinaux. Santé Canada s'assure également que les risques-avantages globaux associés à l'utilisation d'un produit sont positifs et que les risques potentiels peuvent être atténués par un étiquetage approprié.

Tout contact avec les désinfectants, ou toute inhalation ou ingestion de ces derniers, peut entraîner une irritation ou un empoisonnement immédiat. Les composés que l'on retrouve dans ces produits peuvent également causer des brûlures par contact, augmenter la sensibilité au niveau de la peau et des yeux, être nocifs s'ils sont ingérés et présenter des risques en cas d'inhalation tant pendant la manipulation qu'au moment de l'utilisation (CDC, 2020 et Santé Canada, 2020). Certains désinfectants peuvent aussi laisser des résidus chimiques qui pourront ensuite se retrouver dans l'air et être inhalés. Pour assurer une utilisation sûre, il faudrait donc rincer les surfaces après avoir utilisé des désinfectants. Les sous-produits des désinfectants, comme ceux qui proviennent de composés contenant du chlore, comme l'eau de Javel d'usage courant, présentent un intérêt particulier, car ils peuvent former des composés organiques volatils (COV) s'ils sont accidentellement mélangés à d'autres produits de nettoyage ou s'ils entrent en contact avec des matières organiques sur une surface sale (Odabasi, 2014). Certaines catégories de désinfectants également ont été associées à des problèmes respiratoires, y compris à l'asthme, en raison d'une exposition professionnelle prolongée (voir le tableau en annexe). Les mesures qui visent à contrer ces risques incluent notamment l'utilisation du savon et de l'eau, avant le désinfectant, pour retirer la saleté visible des surfaces, éviter de mélanger les désinfectants à d'autres produits, ouvrir les fenêtres pour augmenter la ventilation, porter des gants pendant la désinfection, laisser les surfaces sécher complètement à l'air avant de les utiliser et éviter de s'approcher d'une zone qui vient d'être désinfectée pendant 20 à 30 minutes (Bello, 2010). Les données toxicologiques sur l'exposition à long terme sont incomplètes pour bon nombre de désinfectants et sont généralement appuyées par des études sur les animaux. Bien que certaines études comprennent des données limitées sur les adultes, peu d'entre elles comportent des données sur les enfants (voir le tableau en annexe pour un résumé de chacune des catégories de désinfectants).

Cette synthèse porte donc sur les risques pour la santé associés à l'utilisation de désinfectants pour surfaces dures près des enfants d'âge scolaire, tant avant la pandémie de COVID-19 que pendant celle-ci. Elle

comprend la documentation publiée jusqu'au 5 octobre 2020 (la méthodologie utilisée est présentée à la fin du document).

Principaux points

Bien qu'il n'existe que peu de données probantes sur les risques pour la santé associés à l'utilisation de désinfectants pour surfaces dures auprès des enfants d'âge scolaire, la présente synthèse démontre ce qui suit :

- Comparativement aux années précédentes, les rapports sur les appels qu'ont reçus les centres antipoison aux États-Unis (É.-U.) et au Canada ont fait état d'une augmentation du nombre d'appels pendant la pandémie de COVID-19, en lien avec les désinfectants et les nettoyants, en raison d'expositions souvent liées aux enfants (tableau 1).
- Selon une enquête effectuée auprès des consommateurs aux États-Unis, les personnes qui utilisent des désinfectants manqueraient peut-être de connaissances sur l'utilisation sécuritaire et les risques potentiels qui y sont associés (tableau 1).
- Les études effectuées sur les enfants qui vivent dans des foyers qui utilisent un grand nombre de produits désinfectants montrent qu'ils présentent une fréquence beaucoup plus élevée d'effets cutanés et d'effets respiratoires, en plus d'une plus grande sensibilisation aux désinfectants (tableau 2).
- Certaines études transversales ont montré un lien entre la fréquence d'utilisation des désinfectants près des enfants et les effets sur la santé comme l'asthme et la respiration sifflante chez les jeunes enfants (tableau 2).
- Le chloroforme (un des COV qui peut se former lorsqu'un agent de blanchiment entre en contact avec d'autres produits ou matières organiques) a été trouvé dans des concentrations inacceptables dans plusieurs centres de la petite enfance et la plupart de ces centres ont indiqué utiliser régulièrement de tels agents de blanchiment (tableau 2).
- Dans l'ensemble, il subsiste cependant de grandes lacunes dans la documentation en ce qui concerne les effets à court et à long terme que l'utilisation accrue de désinfectants pour surfaces dures peut avoir sur les enfants.

Vue d'ensemble des éléments de preuve

Les publications qui font directement état des risques potentiels pour la santé découlant de l'utilisation accrue des désinfectants pour surfaces dures dans des environnements où se trouvent des enfants d'âge scolaire sont rares. Nous avons examiné non seulement la revue de la littérature et l'information sur les appels

reçus par les centres antipoison pendant la pandémie (tableau 1), mais avons également inclus les données disponibles sur les effets sur la santé des enfants en raison de l'utilisation de désinfectants pour surfaces dures avant la pandémie de COVID-19 (tableau 2). Seize publications pertinentes sur l'exposition aux désinfectants pour surfaces dures ont orienté cette synthèse. Elles comprenaient notamment des études épidémiologiques (cohortes et études transversales), des rapports publiés par les centres antipoison, un sondage sur les connaissances des consommateurs, des évaluations des risques, des revues de la littérature et des commentaires. Le corpus de recherche global est cependant très petit, de piètre qualité et est insuffisant pour fournir des preuves concluantes sur les risques pour la santé découlant de l'utilisation de désinfectants autour des enfants d'âge scolaire. Des recherches supplémentaires seront donc nécessaires à ce sujet.

Différentes études ont cependant été exclues de cet examen, soit celles qui portaient sur l'exposition des adultes ou sur l'exposition professionnelle aux désinfectants, ainsi que les études sur les animaux, puisque leurs niveaux d'exposition peuvent différer de ceux des enfants d'âge scolaire. Les caractéristiques générales des catégories de désinfectants et les liens vers des renseignements supplémentaires sur chacune des catégories sont présentés dans le tableau en annexe.

TABLE DES MATIÈRES

EXPOSITION À DES DÉSINFECTANTS POUR SURFACES DURES PENDANT LA PANDÉMIE DE COVID-19

Sept études sur l'effet de l'exposition aux désinfectants pour surfaces dures chez les enfants pendant la pandémie de COVID-19 sont résumées dans le tableau 1. Cela inclut notamment deux rapports publiés par des centres antipoison, un sondage sur les connaissances des consommateurs, une évaluation des risques, une revue de la littérature et deux commentaires pertinents.

Les centres antipoison des États-Unis et du Canada ont signalé une augmentation du nombre d'appels relatifs aux désinfectants et aux produits d'entretien ménager généraux en 2020 comparativement aux années précédentes (Chang, 2020; Yasseen, 2020). Dans l'étude canadienne qui a fait le suivi des appels portant sur les produits de nettoyage et les désinfectants, 42 % des appels étaient liés à des agents de blanchiment et 21 % à des désinfectants (Yasseen, 2020). L'augmentation a été observée dans tous les groupes d'âge, mais la majorité des appels portaient sur des adultes plutôt que sur des enfants. Dans l'étude menée aux États-Unis, les agents de blanchiment, suivis des désinfectants sans alcool, ont été à l'origine de la plus forte

augmentation en pourcentage du nombre d'appels. Entre 2018 et 2020, les appels attribuables à l'exposition des enfants de ≤ 5 ans à ces produits ont représenté de façon consistante un pourcentage élevé du nombre total d'appels (intervalle = de 39,9 à 47,3 %) (Chang, 2020).

Un sondage réalisé en mai 2020 a révélé que 60 % des répondants ont déclaré nettoyer ou désinfecter leur maison plus fréquemment depuis le début de la pandémie comparativement aux mois précédents (Gharpure, 2020). Il a également indiqué que les répondants avaient une connaissance limitée sur la façon de préparer leurs produits de nettoyage et solutions désinfectantes de façon sécuritaire. En outre, 25 % d'entre eux ont ajouté que selon eux, l'utilisation de ces produits aurait contribué à au moins un effet néfaste sur leur santé (Gharpure, 2020).

Une évaluation des risques a révélé que les enfants de trois ans étaient ceux qui présentaient la plus grande possibilité d'exposition potentielle à des surfaces désinfectées comparativement à tout autre groupe d'âge puisqu'ils sont plus susceptibles de toucher ces surfaces et qu'ils se mettent souvent les doigts dans la bouche (Li, 2020). Bien que cette évaluation des risques ait porté sur plusieurs produits chimiques, elle ne comportait pas uniquement des désinfectants pour surfaces dures. L'évaluation des risques a également présumé que les désinfectants étaient utilisés à concentration intégrale sans dilution, que la personne y était exposée par contact direct avec la main et que les désinfectants n'avaient pas été essuyés après l'application sur la surface, ce qui peut ne pas être représentatif de la façon dont ces désinfectants étaient véritablement utilisés par les consommateurs.

Les examens des désinfectants approuvés qui contenaient de l'ammonium quaternaire, de l'hypochlorite de sodium ou du peroxyde d'hydrogène et leur utilisation pendant la pandémie de COVID-19 incluent la majorité des désinfectants pour surfaces dures qui ont été utilisées contre le SRAS-CoV-2 (Samara, 2020, Rai, 2020). La revue de la littérature a révélé que les résidus de certains désinfectants pour surfaces dures peuvent contribuer à la mauvaise qualité de l'air. Elle présente également des éléments de preuve qui montrent des taux de cancer plus élevés attribuables à l'utilisation régulière de certains de ces désinfectants chez les adultes qui y ont été exposés en milieu de travail (Rai, 2020). Dans certaines professions dans lesquelles les travailleurs étaient fortement exposés à ces produits, des études ont montré un lien entre ces produits et un risque accru de maladie pulmonaire obstructive chronique, d'asthme et d'irritation oculaire (Rai, 2020; Samara, 2020). Bien qu'aucune donnée semblable n'a pu être obtenue pour les enfants et que 5 % des cancers chez les enfants et 30 % de l'asthme chez les enfants soient liés à une exposition à des produits chimiques, la proportion pouvant être attribuée à l'utilisation des désinfectants pour surfaces dures est cependant inconnue (Rai, 2020).

Tableau 1 : Études et analyses des risques pour la santé découlant de l'utilisation de désinfectants pour surfaces dures chez les enfants d'âge scolaire (n = 7)

Année	Méthode	Principaux résultats
Appels aux centres antipoison		
Chang, 2020 Avant/après l'étude États-Unis De janvier à mars 2018, 2019 et 2020	Les appels au Système national de données sur les poisons (National Poison Data System) ont été analysés afin de déterminer le nombre d'expositions signalées pour la période de janvier à mars 2020 comparativement à la même période de trois mois en 2018 et en 2019.	Ainsi, de janvier à mars 2020, les centres antipoison ont reçu 45 550 appels pour une exposition liée à des produits nettoyants (28 158) et à des désinfectants (17 392), ce qui représente des augmentations globales de 20,4 % et de 16,4 % par rapport à 2019 et 2018, respectivement. L'augmentation des appels a été observée dans tous les groupes d'âge, mais l'exposition chez les enfants de ≤5 ans a représenté entre 39,9 % et 47,3 % des appels durant les trois périodes mentionnées L'inhalation est l'élément qui a vu la plus forte augmentation en pourcentage dans le nombre des appels entre 2019 et 2020. La plus forte augmentation du nombre d'appels possiblement liée aux désinfectants pour surfaces dures (2019 comparativement à 2020) portait sur des agents de blanchiment (62,1 %) et les désinfectants sans alcool (36,7 %).
Yasseen, 2020 Avant/après l'étude Canada De janvier à juin 2019 et 2020	Cinq rapports d'exposition provenant des centres antipoison canadiens entre janvier et juin 2020 ont été comparés à la même période de six mois en 2019.	Le nombre total d'expositions aux produits de nettoyage/désinfectants/désinfectants pour les mains a augmenté de 35 % en 2020 par rapport à 2019. Parmi les 8 187 appels signalant des expositions reçus entre janvier et juin 2019 et janvier et juin 2020, ceux qui pourraient être liés aux désinfectants pour surfaces dures étaient les suivants : 42 % concernaient des agents de blanchiment, 21 % des désinfectants, 12 % du chlore gazeux et 2 % de la chloramine gazeuse (ces derniers sont des sous-produits provenant du mélange d'un agent de blanchiment avec d'autres désinfectants ou nettoyants, voir l'annexe). Pendant la période examinée en 2020, le nombre d'appels a atteint un pic en mars pour ensuite diminuer de manière générale après avril 2020. Le plus grand nombre d'appels signalant une exposition portait principalement sur des personnes âgées de plus de 19 ans et plus pour les deux années. Les résultats ne donnent pas à penser qu'il y ait eu une forte augmentation chez les personnes âgées de moins de 19 ans entre 2019 et 2020.
Sondage sur les connaissances		

Gharpure, 2020 Sondage volontaire sur Internet destinée aux adultes et portant sur l'entretien ménager États-Unis Mai 2020	L'étude comprenait des questions visant à évaluer les connaissances et les pratiques relatives à l'entretien ménager et à la désinfection utilisées par les ménages pendant la pandémie de COVID-19.	Cette étude comprenait 502 adultes (âgés de 18 ans et plus). 60 % ont déclaré avoir utilisé plus souvent des produits de nettoyage et de désinfection à la maison comparativement aux mois précédents. Plusieurs questions ont cependant révélé une connaissance limitée sur la façon sécuritaire de préparer les solutions de nettoyage et de désinfection. 39 % des répondants ont déclaré avoir eu recours à des pratiques à risque élevé non recommandées par le CDC, y compris : 1) Mettre de l'eau de Javel sur les aliments (19 %); 2) Appliquer des nettoyants et des désinfectants ménagers sur leurs mains (18 %); 3) Vaporiser des produits nettoyants et désinfectants sur leur corps (10 %); 4) Inhaler des vapeurs (6 %); 5) Avoir bu des solutions d'eau de Javel diluée (4 %), de l'eau savonneuse (4 %) ou d'autres solutions nettoyantes ou désinfectantes (4 %) ou s'être gargarisé avec de telles solutions. En outre, 25 % des répondants ont dit avoir ressenti au moins un effet indésirable sur la santé découlant, à leur avis, de l'utilisation de nettoyants ou de désinfectants. Ces cas étaient plus fréquents (33 % comparativement à 25 %) chez les répondants qui ont dit avoir eu recours à une pratique à risque élevé.
Évaluation du risque		
Li, 2020 Évaluation des risques et modèle d'exposition quantitative relatifs à 22 produits chimiques désinfectants qui ont été indiqués comme étant capables de tuer le SRAS-CoV-2	L'évaluation des risques utilise le modèle PROTEX qui évalue le devenir et l'exposition chimique à l'intérieur. Trois voies d'exposition ont été étudiées dans cette évaluation, soit ingestion orale par la bouche, inhalation et absorption cutanée. Le scénario d'application utilisé	<u>Évaluation du risque d'exposition</u> Les enfants de trois ans présentaient la plus forte exposition globale, tout particulièrement aux surfaces désinfectées, en raison du plus grand nombre de contacts entre leurs mains et la surface, puisqu'ils mettent souvent leurs doigts dans leur bouche. Le risque d'exposition aux désinfectants de surface, en particulier chez les jeunes enfants, a été mentionné. L'ingestion par la bouche est le principal mode d'exposition aux désinfectants non volatils dont les résidus peuvent rester sur les surfaces jusqu'à ce qu'ils aient été éliminés par un nettoyage normal (p. ex., les composés d'ammonium quaternaire). Pour les groupes d'âge plus âgés, cette

États-Unis et Canada[1] Septembre 2020[1]	dans cette évaluation portait sur la désinfection des surfaces intérieures et des objets (application de surface). Trois groupes d'âge ont été modélisés : 3, 14 et 24 ans.	exposition s'est plutôt produite par l'absorption cutanée et a également été mentionnée à propos des produits chimiques phénoliques. En ce qui concerne les désinfectants comme le triéthylèneglycol (faible toxicité) qui sont aérosolisés pour désinfecter et nettoyer l'air, l'exposition s'était principalement produite par l'inhalation. Bien que cette évaluation des risques ait porté sur 22 produits chimiques, bon nombre d'entre eux n'étaient pas des désinfectants pour surfaces dures.
Revues de la littérature		
Rai, 2020 Revue de la littérature Juin 2020	Les études sur les effets potentiellement nocifs des désinfectants et des solutions alternatives sécuritaires ont été résumées dans le contexte de la COVID-19.	On sait que 5 % des cas de cancer chez les enfants et 30 % des cas d'asthme chez les enfants sont liés à des expositions à des produits chimiques. On ne sait cependant pas si l'une de ces maladies est attribuée à des désinfectants pour surfaces dures. La majorité des produits que recommande l'EPA contre la COVID-19 contiennent des ingrédients actifs tirés des composés d'ammonium quaternaire (Quats). Bon nombre de ces composés sont associés à un risque accru de maladie pulmonaire obstructive chronique (MPOC), d'asthme et d'irritation oculaire lorsqu'ils sont utilisés de façon régulière (exposition professionnelle). Il a été démontré que les quats pouvaient également entraîner des problèmes de fertilité dans les études sur les animaux. Lorsque les surfaces ne sont pas rincées correctement après l'utilisation, les désinfectants biodégradables vont laisser un résidu chimique actif sur la surface. Toute perturbation du résidu peut ensuite en entraîner la propagation dans l'air, ce qui peut alors causer une irritation chez certaines personnes. Un rinçage complet et un nettoyage général permettent cependant d'éliminer les résidus.
Commentaires		
Rivera, 2020 Commentaires É.-U.[1] Janvier à mai 2020	L'étude a évalué, avec Google Trends, l'intérêt d'effectuer une recherche sur les achats et la consommation de désinfectants, et sur les appels aux centres antipoison, après que le	Les valeurs des fractions de recherche relatives obtenues entre janvier et février 2020 en ce qui concerne l'achat, la consommation ou l'injection de désinfectants étaient minimes (< 1). La journée qui a suivi le commentaire de Donald Trump sur l'injection de désinfectants, la fraction de recherche relative pour la consommation de désinfectants a atteint 32,3 alors qu'elle était de 100 pour l'injection de désinfectants.

	président des États-Unis ait laissé entendre que de s'injecter des désinfectants pourrait être un traitement possible pour la COVID-19. Les intervalles de confiance pour chacune des tendances ont été calculés en faisant la moyenne de plusieurs échantillons recueillis quotidiennement pendant une période de trois semaines.	La fraction de recherche relative pour les centres antipoison a atteint un sommet une journée plus tard (fraction de recherche relative = 11,05), ce qui indique une augmentation de l'intérêt ou peut-être des demandes d'information ou d'aide après un usage hors indication des désinfectants.
Samara, 2020 Commentaires Émirats arabes unis[1] 2020[1]	L'étude indique la sécurité d'emploi de certains des désinfectants pour surfaces naturels et synthétiques les plus utilisés et approuvés par l'Environmental Protection Agency pour la prévention du SRAS-CoV-2 et examine les effets connexes de ces produits sur la santé.	Les désinfectants pour surfaces dures peuvent causer une irritation de la peau et des yeux, une irritation des voies respiratoires et de l'asthme chez certaines personnes. L'utilisation d'un agent de blanchiment peut entraîner la formation de COV dans l'air intérieur, et des concentrations élevées de COV ont été signalées 30 minutes après l'application de ce produit, ce qui démontre que l'utilisation de l'eau de Javel peut être une source importante d'exposition aux COV par inhalation. Le désinfectant idéal devrait avoir un profil de toxicité faible lié à une exposition à court et à long terme, p. ex., composés d'ammonium quaternaire et acide peracétique : (voir le tableau en annexe).

[1] Le pays indiqué est lié à l'endroit où se trouvait l'auteur ou la date est fondée sur la date de publication.

EXPOSITION GÉNÉRALE AUX DÉSINFECTANTS POUR SURFACES DURES

Bien qu'il n'y ait aucune étude récente sur l'effet que l'exposition accrue aux désinfectants pour surfaces dures pendant la pandémie aura sur la santé et la sécurité des enfants d'âge scolaire, les études menées avant la pandémie de COVID-19 peuvent fournir des renseignements supplémentaires sur les effets de l'exposition aux désinfectants pour surfaces dures chez les enfants.

L'étude de surveillance biologique réalisée dans 34 centres de la petite enfance en Californie a révélé que dans 38 % des établissements, le chloroforme, un COV découlant de l'utilisation d'un agent de blanchiment avec chlore, dépassait les niveaux acceptables en ce qui concerne les risques de cancer. (Hoang, 2016).

Deux études d'évaluation de l'exposition ont révélé que l'eau de Javel est couramment utilisée dans les garderies aux États-Unis. Une enquête menée dans quatorze garderies de Washington (D.C.) a fait état de l'utilisation d'eau de Javel avec chlore (92,8 %) dans les établissements à des fins d'assainissement et de la présence de chloroforme dans tous les établissements (Quirós-Alcalá, 2016). Les surfaces les plus couramment désinfectées étaient les tables, salles de bain, chaises, lits, tables à langer et jouets des enfants. L'eau de Javel a été signalée comme étant un irritant des voies respiratoires si elle est inhalée, sans oublier qu'elle peut libérer des COV (p. ex., du chloroforme), qui sont des cancérogènes connus, lorsqu'elle réagit avec des matières organiques. La troisième évaluation des risques a permis de mesurer et de modéliser la quantité de COV produits pendant un nettoyage normal à l'intérieur. Les résultats laissent entendre qu'il existe un risque d'exposition à des niveaux de COV supérieurs à la moyenne pour toute personne qui entre dans la pièce jusqu'à 20 minutes après le nettoyage des éviers, des miroirs ou des toilettes avec des désinfectants contenant des composés d'ammonium quaternaire ou de l'hydroxyde de sodium (Bello, 2010). Augmenter la ventilation et réduire le temps passé dans une pièce qui vient d'être nettoyée réduiraient cependant l'exposition aux COV. Trois études épidémiologiques ont été publiées. Une étude de cohorte prospective effectuée en Allemagne chez des jeunes âgés de 19 à 24 ans a montré que l'utilisation de produits de désinfection était associée à une augmentation de l'asthme et de la dermatite atopique. L'exposition autodéclarée à des désinfectants ménagers et la forte utilisation de désinfectants ont été associées à une probabilité deux fois plus élevée d'incidence d'asthme que chez les personnes qui ont déclaré ne pas en avoir utilisé (Weinmann, 2017). Les jeunes qui ont déclaré une utilisation faible ou moyenne des désinfectants étaient également plus susceptibles d'indiquer qu'ils souffraient d'une forme récurrente d'asthme (Weinmann, 2017). Dans une étude transversale portant sur des enfants de quatre ans provenant de plusieurs pays d'Europe, un lien a été établi entre la forte utilisation de désinfectants en spray dans les pièces et une augmentation de la dermatite atopique et des éruptions cutanées avec démangeaisons, mais pas avec l'asthme (Krauss-Etschmann, 2009). Cette étude comportait cependant une faiblesse, puisque l'utilisation générale des désinfectants n'a pas été consignée (Krauss-Etschmann, 2009). Une étude transversale menée en Suède a révélé que l'utilisation d'eau de Javel chlorée à la maison avait une association protectrice avec le développement de l'asthme et la sensibilisation aux allergènes intérieurs, mais ne précisait cependant pas si les enfants étaient présents pendant le nettoyage (Nickmilder, 2007).

Trois revues de la littérature ont résumé les données probantes sur le risque potentiel pour les enfants. Elles comprennent principalement des études transversales des produits de nettoyage et de désinfection et des COV associés à ces produits (Holm, 2019; Mendell, 2007; Slaughter, 2019). Les catégories les plus courantes de désinfectants mentionnées dans les études comprenaient l'agent de blanchiment (eau de Javel), les composés d'ammonium quaternaire et les peroxydes, choisis en fonction de leur gamme élargie de désinfection pour différents pathogènes (Holme, 2019). Les activités de nettoyage à l'intérieur étaient

associées à des allergies, à de l'asthme et à d'autres problèmes respiratoires chez les nourrissons et les jeunes enfants (Mendell, 2017). La plupart de ces études ne précisaient cependant pas les produits utilisés, et souvent, plusieurs types de produits étaient utilisés, de sorte qu'il n'était pas possible de séparer les effets des différents produits.

Tableau 2 : Rapports sur les risques pour la santé associés à l'utilisation des désinfectants pour surfaces dures tirés de la littérature publiée avant la pandémie (n = 9)

Année	Méthode	Principaux résultats
Évaluations de l'exposition / des risques		
Hoang, 2017 Surveillance biologique États-Unis Mai 2010 à mai 2011	L'étude a permis de mesurer 38 COV dans des échantillons d'air prélevés en une seule journée en 2010 et 2011 dans 34 CPE où se trouvaient des enfants californiens. Elle a également établi la « concentration sans risque » comme la dose quotidienne qui représente un risque supplémentaire de cancer au cours d'une vie de un sur 100 000.	Le chloroforme, un COV associé à l'utilisation de l'eau de javel, a été identifié dans certains échantillons. Même si d'autres COV n'étaient pas associés à des désinfectants pour surfaces dures, ils peuvent cependant être produits par des parfums ajoutés à un produit de nettoyage ou de désinfection. Les estimations du 95^{e} percentile de la dose de chloroforme dépassaient la concentration sans risque spécifique à l'âge pour les quatre groupes d'âge évalués. Constatations: Les concentrations de COV dans les CPE ressemblent à celles observées dans les milieux scolaires et domestiques et, si elles reflètent les moyennes à long terme, les estimations des doses qu'ont reçu les enfants dépassaient les valeurs de référence des concentrations sans risque rajustées selon l'âge pour le benzène, le chloroforme, l'éthylbenzène et le naphtalène dans 71 %, 38 %, 56 % et 97 % des établissements, respectivement. Dans une analyse bivariée : Les niveaux de COV étaient semblables dans les établissements qui ont déclaré utiliser ou acheter des nettoyants à faible toxicité comparativement à ceux qui utilisent des nettoyants traditionnels. Toutefois, les niveaux de certains COV étaient beaucoup plus élevés dans les établissements où la fréquence de passage de la vadrouille était plus élevée, ce qui suggère des émissions de COV provenant des produits de nettoyage pour plancher.
Bello, 2010	Les tâches de nettoyage de l'évier, du miroir et de la toilette ont été simulées	Les nettoyants domestiques utilisés contenaient des composés d'ammonium quaternaire ou de l'hydroxyde de sodium.

Étude sur l'évaluation de l'exposition É.-U.[1] 2010[1]	pendant 20 minutes dans une grande salle de bain ventilée et dans une petite salle de bain non ventilée. Les produits utilisés étaient un nettoyant tout usage, un nettoyant pour le verre et un nettoyant pour salle de bain. Les composés organiques volatils totaux libérés dans l'air pendant ces tâches ont ensuite été mesurés.	Les expositions supérieures au niveau naturel ont été présentées pendant environ 20 minutes après la fin du nettoyage. La plus forte concentration d'ammoniac s'est produite pendant le nettoyage des miroirs. Les résultats indiquent donc qu'il y a une possibilité d'exposition pour toute personne qui nettoie la pièce ou entre dans la pièce peu après le nettoyage.
Quirós-Alcalá, 2016 Étude sur l'évaluation de l'exposition Washington (D.C.) Automne 2012 et 2013	Les directeurs des CPE ont d'abord été contactés par courriel et par lettre. Un questionnaire leur a été envoyé. Les directeurs ont également recueilli de l'information sur le nombre d'enfants atteints d'asthme dans chaque établissement et sur le fait de savoir si des enfants avaient eu des crises d'asthme ou des épisodes de respiration sifflante au cours des trois mois précédents. Pour pouvoir caractériser les COV dans les établissements, ils ont prélevé entre deux et cinq échantillons d'air sur 10 heures et des échantillons prélevés en temps réel par des instruments de mesure des particules à des intervalles d'une minute.	Du chloroforme (un COV qui peut provenir de produits contenant de l'eau de Javel chlorée) a été détecté dans chaque établissement. Il est important de noter qu'il peut y avoir d'autres sources de chloroforme. 92,9 % des répondants du CPE ont déclaré que l'eau de Javel chlorée était utilisée pour aseptiser l'établissement. Les surfaces désinfectées les plus fréquemment indiquées étaient les tables, les salles de bain et les chaises, mais les répondants ont aussi dit utiliser l'eau de Javel chlorée pour aseptiser les lits, les tables à langer et les jouets des enfants. Les polluants intérieurs provenant de l'eau de Javel chlorée sont des irritants respiratoires connus. Les auteurs recommandent de penser à utiliser des solutions de rechange sans eau de Javel pour la désinfection afin d'éviter d'introduire d'autres dangers dans les milieux de garde des enfants.
Études épidémiologiques		
Weinmann, 2017 Étude de cohorte prospective Allemagne 2007-2009	L'étude a évalué 2 051 jeunes adultes âgés de 19 à 24 ans qui habitaient dans deux grandes villes allemandes et ont participé à une étude dans laquelle ils autodéclaraient leur	Dans cet échantillon, 83,8 % des répondants n'ont pas déclaré qu'ils utilisaient des désinfectants. Aucune information sur les désinfectants utilisés n'a été recueillie. L'asthme a été signalé dans 5,4 % de l'échantillon :

	exposition aux vaporisateurs et aux désinfectants ménagers. Les liens entre l'exposition à des produits propres et l'asthme ou la respiration sifflante ont été étudiés.	- Une forte utilisation de désinfectants a été associée à une probabilité deux fois plus élevée d'asthme que chez les personnes qui n'utilisaient pas ces produits (RC 2,79, IC à 95 % : de 1,14 à 6,83). - Une utilisation de désinfectants de faible à moyenne a été associée à un asthme récurrent (RC 2,39, IC à 95 % : de 1,29 à 4,47). Respiration sifflante au cours des 12 derniers mois (sans lien avec le rhume) 17,1 %. Aucun lien clair n'a été établi entre les expositions et la respiration sifflante. Aucune inférence causale ne peut être tirée de ces données et d'autres évaluations de l'exposition sont donc justifiées.
Krauss-Etschmann, 2009 Étude transversale chez des enfants de 4 ans (106 Espagnols, 45 Allemands et 25 Hongrois). Espagne, Allemagne et Hongrie 2009[1]	Les enfants de quatre ans ont subi un examen médical et neurophysiologique. Pendant cette visite, les parents ont répondu à un questionnaire normalisé qui comprenait des questions sur les allergies et l'asthme dans l'enfance et les facteurs liés au mode de vie. Les données catégoriques descriptives ont fait l'objet d'une analyse χ^2. La probabilité de symptômes allergiques liés à l'utilisation de vaporisateurs dans la pièce a été évaluée dans les analyses bivariées.	Aucune information sur le désinfectant utilisé dans les pièces n'a été fournie. L'utilisation a été classée comme quotidienne, hebdomadaire, occasionnelle ou jamais. L'utilisation de désinfectants dans la pièce n'a pas été associée à des estimations d'effets plus élevés pour l'asthme, mais à des estimations d'effets beaucoup plus élevées pour la dermatite atopique et les éruptions cutanées accompagnées de démangeaisons. Aucune donnée sur le type de désinfectant n'a été indiquée.
Nickmilder, 2007 Étude transversale Suède Mars à mai 2002	L'étude a évalué la mesure dans laquelle les produits d'entretien ménager ordinaires avec javellisant influent sur le risque d'allergies et de maladies respiratoires. Un groupe de 234 écoliers âgés de 10 à 13 ans dont 78 vivaient dans une maison nettoyée avec un	Les enfants qui vivaient dans des maisons nettoyées régulièrement avec de l'eau de Javel chlorée : - avaient un risque plus faible de développer de l'asthme, ce qui était significatif si l'analyse tenait compte à la fois du diagnostic du médecin et du dépistage chez les enfants positifs; - étaient moins susceptibles d'être sensibilisés aux allergènes intérieurs, y compris aux acariens (important);

	agent de blanchiment au moins une fois par semaine. On a demandé aux parents d'enfants de remplir un questionnaire comportant un total de 38 questions.	- étaient moins susceptibles d'indiquer une respiration sifflante (non important).
Revues de la littérature		
Mendell, 2007 Revue de la littérature des études épidémiologiques É.-U.[1] Jusqu'au milieu de l'année 2004	L'étude a évalué le lien entre les émissions de produits chimiques, les émissions provenant des matériaux ou des activités liées aux émissions dans les résidences et les effets sur la respiration ou les allergies chez les enfants et les nourrissons.	Les types de matériaux et de revêtements utilisés dans les résidences, ainsi que les activités de rénovation ou de nettoyage, étaient associés aux effets sur la santé associés à l'asthme ou aux allergies chez les nourrissons ou les enfants. L'utilisation de nombreux produits nettoyants à base de produits chimiques (les femmes en utilisaient plus d'un, mais 87,4 % étaient des désinfectants et 84,8 % utilisaient de l'eau de Javel) par les mères a été mesurée par un questionnaire et la charge totale des produits chimiques dans une étude (Sherrif, 2005). Une charge totale des produits chimiques élevée était associée à une augmentation significative de la dose-réponse pour la respiration sifflante persistante chez les jeunes enfants (RR corrigé de 2,3 (IC à 95 %, de 1,2 à 4,4) et pour la respiration sifflante tardive chez les jeunes enfants (RR corrigé de 2,0 (IC à 95 %, de 0,8 à 5,2)). Aucun produit n'a été lié à la respiration sifflante chez les enfants. Ces résultats pourraient être influencés par de nombreux facteurs de confusion, et les études présentées ne permettent pas de tirer de conclusions sur une relation causale.
Slaughter, 2019 Analyse documentaire Nouvelle-Zélande[1] Janvier 1950 à juin 2018	Examen de l'intoxication à l'hypochlorite.	L'hypochlorite de sodium est un agent de blanchiment et de désinfection qu'on trouve couramment dans l'eau de Javel domestique. 110 citations ont été jugées pertinentes. Des estimations supérieures à 40 ml ou à 5 ml/kg de solutions diluées ont été suggérées comme quantités susceptibles de causer un empoisonnement corrosif ou systémique chez les enfants. Cet examen décrit plusieurs rapports de cas/séries d'enfants qui ont ingéré de l'eau de Javel. Les effets

		courants comprenaient des problèmes gastro-intestinaux mineurs, comme des nausées, des vomissements et des brûlures superficielles dans la bouche et l'œsophage. Une brève exposition de la peau à l'eau de Javel domestique entraîne normalement des effets minimes alors qu'une exposition longue ou prolongée peut causer une irritation cutanée ou une hypersensibilité.
Holm, 2019 Analyse documentaire É.-U.[1] 2018[1]	Résumé des conclusions à partir de: (1) Données d'enregistrement de l'Environmental Protection Agency sur l'efficacité des désinfectants approuvés pour une utilisation en milieu hospitalier (n = 1 907 produits, dont 529 étaient inclus). (2) Un examen de la recherche sur les toxicités et les risques pour la santé associés aux désinfectants couramment utilisés dans les établissements de garde d'enfants.	L'eau de Javel est le désinfectant le plus couramment utilisé dans les garderies. Le chloroforme, un COV, est un sous-produit de l'eau de Javel. En l'absence d'un taux de ventilation optimal, certaines études ont fait état de niveaux de chloroforme supérieurs à ceux jugés sécuritaires pour la gestion du risque de cancer. Des résultats semblables ont été indiqués pour le formaldéhyde, qui peut être un sous-produit d'un mauvais mélange de produits chimiques de nettoyage et de désinfectants. Les données sur les effets des produits de nettoyage sur les enfants sont limitées. Des études transversales ont indiqué que les enfants qui vivaient dans des maisons nettoyées avec de l'eau de Javel n'étaient pas plus susceptibles de souffrir d'asthme, tandis que d'autres ont constaté un risque accru associé à l'utilisation de vaporisateurs et de désinfectants dans la maison. Un lien entre l'utilisation de nettoyants en vaporisateur et la respiration sifflante a été signalé dans le cadre de deux études sur des nourrissons et de jeunes enfants. Les catégories de désinfectants contenant au moins un produit couvrant un vaste éventail de pathogènes comprenaient l'eau de Javel, les peroxydes, les composés d'ammoniac quaternaires et les produits combinés comprenant des composés d'ammoniac quaternaire. Risques pour la santé : Eau de Javel : irritant des voies respiratoires si elle était inhalée, elle peut libérer des COV, p. ex., du chloroforme lorsqu'elle réagit avec des matières organiques, qui sont des cancérogènes connus. L'irritation de la peau et des yeux est courante, des empoisonnements ont été signalés et une exposition

		à long terme chez les adultes a entraîné des effets respiratoires et de l'asthme. Composés d'ammonium quaternaire : risque accru d'asthme et de sensibilisation allergique indiqué. Des études ont démontré que certains de ces composés étaient mutagènes et réduisaient les taux de fécondité dans les modèles animaux. La cancérogénicité n'a pas été démontrée. Peroxydes : toxicité aiguë comprenant l'empoisonnement et l'irritation des yeux. Aucune autre donnée sur la toxicité n'a été publiée. Tous les désinfectants sont moins efficaces en présence de matières organiques.

Abréviations : CPE : Centre de la petite enfance, COV : Composés organiques volatils
[1] Le pays indiqué est lié à l'endroit où se trouvait l'auteur ou la date est fondée sur la date de publication.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe de science émergente de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont menées par Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont recoupées avec la littérature de la liste de littérature COVID de l'OMS, et les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Afin de repérer des éléments de preuve publiés avant la pandémie de COVID-19, des recherches supplémentaires par mot-clé ciblé ont été effectuées dans Pubmed, en utilisant une méthode en boule de neige et en révisant des listes de référence. Les termes de recherche utilisés comprenaient : désinfecter*, chimique, sécurité, risque, enfant*. Cette synthèse contient des recherches publiées jusqu'au 5 octobre 2020. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites dans l'examen.

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ANNEXE

Tableau en annexe des catégories courantes de désinfectants pour surfaces dures qui comprennent les ingrédients actifs des désinfectants utilisés dans divers milieux (domicile, public, hôpital)[1]

Catégorie (exemples)	Propriétés et utilisations	Répercussions possibles sur la santé : à plus long terme[2]	Mesures de sécurité[3]
Chlore et composés chlorés Comprend l'« eau de Javel domestique » (hypochlorite de sodium), une solution aqueuse comprenant de 5,25 % à 6,25 % d'hypochlorite de calcium solide. Autres composés conçus pour retenir le chlore plus longtemps. Comprennent le dioxyde de chlore à libération sous forme de demande, le dichloroisocyanurate de sodium et la chloramine-T.	Aucun résidu, peu coûteux, à action rapide. Rendu rapidement inactif par les matières organiques. Dilué et appliqué en surface. Ne pas mélanger avec : - Ammoniac ou produits d'entretien ménager, car le mélange produit du chlore gazeux toxique. - Solutions de formaldéhyde et d'hypochlorite, car le mélange produit un oxyde de bis(chlorométhyle) cancérogène.	Une faible incidence de toxicité grave. L'eau de Javel domestique (5,25 à 6,15 %) peut causer une irritation oculaire ou des brûlures oropharyngées, œsophagiennes et gastriques. A été associée à l'asthme et à d'autres problèmes respiratoires. Les chloramines créent des « chloramines organiques » puisqu'elles s'attachent à des matières organiques et forment des composés connus sous le nom de COV. Les études ont montré que les COV augmentent pendant le nettoyage domestique. Certains sont des cancérogènes connus (Odabasi, 2014). Aucun effet nocif n'est prévu en cas d'exposition normale et d'utilisation appropriée.	Solutions diluées d'eau de Javel domestique : Utiliser de l'eau de Javel contenant de 5,25 % à 8,25 % d'hypochlorite de sodium. Ne pas utiliser de produit javellisant si le pourcentage n'est pas dans cette fourchette ou n'est pas précisé. Assurer une ventilation adéquate tant pendant qu'après l'utilisation. S'assurer que le produit n'a pas dépassé sa date de péremption. Ne jamais mélanger l'eau de Javel domestique à de l'ammoniac ou à un autre produit nettoyant, car cela pourrait causer des émanations dont l'inhalation peut être très dangereuse. Préparer une solution d'eau de Javel en

			mélangeant : 5 cuillères à soupe (1/3 tasse) d'eau de Javel à 5,25 à 8,25 % par gallon d'eau à température ambiante ou 4 cuillères à thé d'eau de Javel à 5,25 à 8,25 % par pinte d'eau à température ambiante. Les solutions d'eau de Javel sont efficaces pour désinfecter pendant un maximum de 24 heures.
Composé d'ammonium quaternaire Comprend environ 300 homologations de produits. Le groupe I est composé de Quats hydroxyalkylés substitués. Le groupe II comprend, quant à lui, le benzyle non halogéné. Le groupe III comprend les Quats di et tri-chlorobenzyl substitués alors que le groupe IV se compose de Quats avec des substitutions inhabituelles (p. ex., chlorure d'alkyldiméthylbenzylammonium chlorure d'alkyldidécyldiméthylammonium, et chlorure de diméthylammonium dialkyle; quaternaires à deux chaînes ou dialkyles, p. ex., bromure de didécyldiméthylammonium et bromure de dioctyldiméthylammonium).	Non volatile, laisse des résidus. Est généralement approuvé pour la désinfection des surfaces et peut être utilisé sur l'équipement qui entrera en contact avec la peau. Peut être utilisé sous forme liquide ou sur une lingette.	Aucun effet à long terme sur la santé n'a été signalé : non sensibilisant au niveau de la peau, non toxique pour le développement ou la reproduction et non cancérogène ou génotoxique (Luz, 2020). Certains cas d'asthme professionnel (p. ex., chez les nettoyeurs) ont été signalés à la suite d'une exposition au chlorure de benzalkonium.	Suivre les instructions indiquées sur l'étiquette en ce qui concerne l'utilisation de tout désinfectant. Santé Canada tient compte des risques-avantages globaux associés au risque avant l'approbation, en s'assurant que les risques potentiels puissent être atténués par un étiquetage approprié.

Peroxyde d'hydrogène : Peroxygène, plusieurs désinfectants liquides contiennent du peroxyde d'hydrogène dont les concentrations varient de 6 à 25 % dans un produit chimique prémélangé prêt à l'emploi. Combinaison commune : 7,5 % de peroxyde d'hydrogène et 0,85 % d'acide phosphorique.	Laisse des résidus. Généralement approuvé pour la désinfection des surfaces. Présent dans les désinfectants, dans une teneur variant entre 3 et 9 %. Peut être utilisé sous forme liquide ou sur une lingette. Est instable et se décompose facilement.	Les données sur la cancérogénicité ne sont pas concluantes. Peut avoir des effets respiratoires.	Suivre les instructions indiquées sur l'étiquette en ce qui concerne l'utilisation de tout désinfectant. Santé Canada tient compte des risques-avantages globaux associés au risque avant l'approbation, en s'assurant que les risques potentiels puissent être atténués par un étiquetage approprié.
Phénol et dérivés du phénol Des versions plus récentes ont été créées, soit phénolique (chloroxylenol, thymol, O-Phenylphénol, triclosan, ortho-Phenylphénol ortho-benzyl-para-chlorophénol.	Laisse un résidu. Généralement approuvé pour la désinfection des surfaces. Peut être utilisé sous forme liquide ou sur une lingette.	Les résidus peuvent irriter la peau et l'absorption cutanée est la principale voie d'exposition. Un lien a été établi avec l'hyperbilirubinémie chez les nourrissons dans les pouponnières qui l'utilisent pour nettoyer les lits de bébé.	Suivre les instructions indiquées sur l'étiquette en ce qui concerne l'utilisation de tout désinfectant. Santé Canada tient compte des risques-avantages globaux associés au risque avant l'approbation, en s'assurant que les risques potentiels puissent être atténués par un étiquetage approprié.
Acide peracétique: Péracétique ou peroxyacétique	Aucun produit de décomposition nocif, augmente le pouvoir d'élimination des matières organiques, ne laisse aucun résidu, forte odeur piquante. Peut être utilisé sous forme de vaporisation liquide. Reste actif à basse température et en	Considéré comme un produit chimique peu préoccupant, à faible adsorption cutanée et aucun risque à long terme pour la santé n'a été répertorié.	Suivre les instructions indiquées sur l'étiquette en ce qui concerne l'utilisation de tout désinfectant. Santé Canada tient compte des risques-avantages globaux associés au risque avant l'approbation, en s'assurant que les risques potentiels puissent être atténués

	présence de matières organiques. Est instable lorsqu'il est dilué et doit donc être mélangé juste avant d'être utilisé. N'exige aucun rinçage.		par un étiquetage approprié.
Ortho-phtalaldéhyde (OPA ou 1,2-benzène-dicarboxaldéhyde)	N'est pas un irritant connu, sans odeur, ne nécessite pas de surveillance de l'exposition. Stable à un pH compris entre 3 et 9.	Provoque des taches sur la peau lorsqu'il transforme les protéines qui deviennent grises. A aussi été associé à l'anaphylaxie. Exposition à long terme associée à l'asthme.	Suivre les instructions indiquées sur l'étiquette en ce qui concerne l'utilisation de tout désinfectant. Santé Canada tient compte des risques-avantages globaux associés au risque avant l'approbation, en s'assurant que les risques potentiels puissent être atténués par un étiquetage approprié.
Idophores La povidone-iodine, aussi appelée polybinylpyrrolidone avec iode, est la forme la plus courante.	Peuvent être utilisés comme désinfectant de surface (mieux connu en tant qu'antiseptique). Explosent s'ils sont mélangés avec du peroxyde d'hydrogène.	Peuvent entraîner une hypothyroïdie s'ils sont ingérés en grandes quantités. Les fœtus et les nouveau-nés y sont particulièrement sensibles.	Suivre les instructions indiquées sur l'étiquette en ce qui concerne l'utilisation de tout désinfectant. Santé Canada tient compte des risques-avantages globaux associés au risque avant l'approbation, en s'assurant que les risques potentiels puissent être atténués par un étiquetage approprié.

VOC = Les composés organiques volatils (COV) sont des composés qui ont une pression de vapeur élevée, une faible solubilité dans l'eau et sont émis sous forme de gaz par certains solides ou liquides. Les COV sont libérés par un large éventail de produits, notamment les peintures, les produits de nettoyage, les pesticides, les nouveaux matériaux, les imprimantes, les marqueurs, etc. Les COV sont plus élevés à l'intérieur qu'à l'extérieur.

[1] Sources : https://www.cdc.gov/infectioncontrol/guidelines/disinfection/index.html, https://pubchem.ncbi.nlm.nih.gov/ et https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/cleaning-disinfection.html

[2]Les effets sur la santé qui découlent d'une mauvaise utilisation ne sont pas indiqués. Ainsi, de ces produits ne peut être ingéré sans danger, la plupart provoquent une irritation de la peau et des lésions oculaires si le produit entre en contact avec ces surfaces. L'eau de Javel, tout comme un grand nombre de produits en spray, comporte également des avertissements en cas d'inhalation lors de l'utilisation.

[3] Précautions générales de sécurité à respecter au moment d'utiliser les désinfectants : protéger la peau et penser à porter une protection des yeux pour éviter de recevoir des éclaboussures, assurer une ventilation adéquate, ne pas utiliser plus que la quantité recommandée sur l'étiquette, utiliser de l'eau à température ambiante pour la dilution (sauf indication contraire sur l'étiquette) et éviter de mélanger différents produits chimiques.

Emerging Evidence on COVID-19

Evidence Brief of SARS-CoV-2 Contact Tracing

Introduction

What evidence exists for the strategic use of effective and efficient COVID-19 contact tracing during the pandemic?

Contact tracing is one of several public health measures (PHMs) being used to control the spread of COVID-19. When a case is identified, contact tracing may be initiated by local public health authorities to identify individuals who have potentially been exposed to the case and assess their risk of exposure. Currently in Canada, close (i.e., high risk) contacts of COVID-19 cases are required to quarantine (i.e., self-isolate) away from others for 14 days (1). It is an important, but resource-intensive activity, and during periods of high COVID-19 transmission local public health has not always had the capacity for complete contact tracing. Thus, tools or strategies to improve efficiencies in contract tracing and tools to assess tipping points in the public health capacity to perform effective contact tracing are needed. This brief highlights studies and systematic reviews on strategies for effective and efficient contact tracing during COVID-19 available up to February 10, 2021. For the purpose of this evidence brief, contact tracing is defined as the identification of people recently exposed to an infected individual in order to quarantine them with or without testing to prevent further transmission. In this review isolation refers to confirmed cases isolating to prevent transmission within or outside of their household and quarantine refers to isolation of potentially exposed contacts from the community while they complete their incubation period.

Key Points

- The ability of public health to undertake comprehensive contact tracing depends on many factors including the transmission rate in the community, the capacity of public health to undertake contact tracing, and the ability to identify infected individuals and their contacts (2). Strategies to improve contact tracing in the context of the COVID-19 pandemic were summarized in seven rapid or systematic reviews with studies up to December 2020; and two empirical and fourteen modeling studies posted November 2020 through February 10, 2021.
- People who are infected with SARS-CoV-2 can transmit the virus before developing symptoms (presymptomatic) and when they are asymptomatic, which means that contact tracing will miss infected individuals if only symptomatic cases are targeted.
    - Contact tracing strategies that relied on identifying symptomatic cases for initiating contact tracing and quarantine of contacts were shown in included models to miss a proportion of cases and thus failed to control the COVID-19 epidemic (3).

- Modeling studies showed that mass testing strategies to identify cases and conducting forward contact tracing were more effective in identifying cases and thus at controlling the spread of COVID-19 compared to contact tracing of symptomatic cases only (3-5); however, mass testing is very resource intensive in the short-term and has higher associated costs (6). For example mass testing of identified high risk populations (various healthcare workers, essential business employees, teachers and students) and contact tracing for cases in Canada was estimated to be up to $820 million per month in additional costs compared to the 70 million contact tracing activities were costing in July 2020 (7).
- Contact tracing is effective at reducing transmission of variants of concern (8).

- Minimizing the time to identify a case and notify the high risk contacts of the case is an important factor in contact tracing to minimize the potential infectious days a person is not in quarantine or isolation.
    - Several included reviews and studies suggest that timely identification of cases (within 3 days of symptom onset) and quarantine of most of the high risk contacts (~60-90% contacts needed to be traced across studies) as quickly as possible was required for a test and contact-trace strategy to be effective (5, 9-11).
- Models show that the effectiveness of contact tracing in controlling the epidemic is reduced when the prevalence of cases (and number of potential contacts) in the community exceeds public health resources.
    - The local context will determine the maximum number of cases that can be handled per day. Exceeding that capacity will result in less effective contact tracing because some cases will not be traced or there will be delays in tracing cases leading to longer time to initiate quarantine or failure to quarantine of people exposed, which may lead to more transmission (2).
- Contact tracing is one of several PHMs used to control COVID-19 which work synergistically to control the epidemic. Studies have shown that as transmission decreases and restrictive PHMs (e.g., lockdowns, closures and restricted movement) are lifted, a strong contact tracing system with sufficient capacity is needed to avoid a resurgence (5% chance of resurgence vs. <50% chance if sufficient contact tracing capacity is not in place) (12).
- Increasing efficiency and effectiveness of contact tracing using new tools and strategies was evaluated in several reviews and studies.
    - Bidirectional contact tracing (contact tracing as early as 6 days prior to symptoms) more than doubles the reduction to R_e when compared with only forward tracing (contacts of the case from 1-2 days prior to symptoms until isolation). (8, 13). However the latter requires more public health capacity.

- Bidirectional contact tracing to identify the primary case of a cluster was found to be 2-3 times more effective against the spread of SARS-CoV-2 when compared to forward contact tracing alone (23).
- Efficiency of contact tracing is improved by the use of electronic data management tools which can double the number of contacts traced and is less prone to error and data loss (14).
- Contact tracing apps have been studied and evaluated in the context of COVID-19 quickly to reach more potentially exposed individuals. As these are a new technology, most models estimated a low uptake of the apps (e.g., 50%), which resulted in a reduced R_e by 18-26% compared to public health contact tracing that resulted in a 35-53% reduction in R_e (14). Higher proportions of population uptake of automated contact-tracing apps (estimates from 56% up to 100%) resulted in improved performance of contact tracing (13, 15, 16).
- A single empirical study reported a significant decrease in R_e (from 1.3 to 0.5) after regional testing of the United Kingdom's contact tracing app that had high uptake by the majority of the population. Version 1, reported in the study, was a Bluetooth enabled proximity contact tracing app which identified probable cases with self-reported symptomatic status (17).

Overview of the Evidence

Twenty-three articles were included in this evidence brief. Systematic and rapid reviews concerning contact tracing to mitigate spread of COVID-19 accounted for seven of the cited articles (three of them in pre-print status). In addition, 16 recent articles (published in Fall 2020/Winter 2021) presented evidence on effective contact tracing strategies, two with epidemiological evidence and 14 based on modelling studies (6 of the models are pre-prints).

AMSTAR-2 tool was used to evaluate the rapid and systematic reviews (n=7) in Table 1 (18). Overall quality of the review is categorized as high, medium, low or very low quality depending on how many AMSTAR criteria were not met.

The empirical evidence (n=2) is based on observational studies aimed to evaluate contact tracing strategies, or changes in current strategies. The observational studies were at risk of many biases. Caution should be used in the interpretation of the predictive models (n=13) as they may be sensitive to the assumptions of the model and are best used to compare different scenarios, as they may not reflect a real situation or be generalizable. Most of the evidence on this topic is from predictive models.

The limitations of the evidence include a lack of empirical evidence and high reliance on the findings of modelling studies or reviews based on pre-pandemic experience.

CONTENTS

REVIEWS OF CONTACT TRACING STUDIES

Table 1: Rapid and Systematic Reviews on Contact Tracing of COVID-19 Cases (n=7)

STUDY	METHOD	KEY OUTCOMES
Overall contact tracing strategies		
Mbwogge (2020) (4) Preprint Rapid Review United Kingdom Dec 2020 AMSTAR-moderate	A rapid review included 35 articles with evidence available up to December 22, 2020 on whether mass testing and tracing would be more effective than current testing and tracing in the UK. Results were synthesized by vote counting, considering the direction of effect and degree of bias in reported outcomes.	Across 13 of the studies mass testing was more effective than symptom-based testing in 76.9% (95% CI: 46.2-95.0) of the studies, thus would improve the suppression of COVID-19 beyond the current symptom based test and trace protocol in the UK. Mass testing improves detection of asymptomatic COVID-19 cases that are not detected in a symptom-based test scheme. Across 22 studies 40.7% (95%CI: 38.8-42.5%) of cases detected would be asymptomatic and would be expected to identify 28% (95%CI: 25.9-30.2%) of asymptomatic cases in the general population and 96.6% (95%CI: 82.2-99.9%) of asymptomatic cases among long term care staff.
Girum (2020) (19) Systematic Review Ethiopia Jun 2020 AMSTAR-moderate	The review identified 22 observational (n=9) and modelling (n=13) studies providing evidence of COVID-19 prevention through contact tracing, screening, quarantine and isolation. Studies up to June 2, 2020 were included in the review. 3 studies assessed all prevention strategies, and 5 specifically assessed contact tracing effects.	Contact tracing studies: • Isolating only symptomatic patients may not contain the epidemic. • Intimate contacts have transmission rates of 40-60%, indicating household contacts of cases should quarantine. • Outbreaks may not be contained, unless high levels of tracing and quarantine are introduced. • If R_o is 2.5, more than 70% of contacts must be traced for outbreak control (20). • Using a contact trace and quarantine strategy reduces transmission 50-60% compared to mass testing or self-isolation alone 2-30% (5) (listed in Table 2).

Juneau (2020) (9) Preprint Systematic Review Quebec, Canada Jul 2020 AMSTAR- low	The review identified 32 observational (n=14) and modelling (n=18) studies concerning the effectiveness of contact tracing for COVID-19 control. All methods of contact tracing were included in the review (i.e. mobile apps, etc.). Studies were excluded if they did not consider community transmission settings or if they were not peer reviewed. The search dates are not provided in the preprint article.	Overall, the review asserts that a case must be isolated within 2-3 days of symptom onset; as well as at least 80% of their contacts quarantined, to result in no tertiary cases. Less efficient tracing and quarantine systems may slow the spread of SARS-CoV-2, but will be unable to stop the epidemic. Delays of ≥ 4 days or quarantine of less than 60% of contacts will be ineffective at controlling the epidemic.
Chung (2020) (16) Preprint Rapid Review United Kingdom May 2020 AMSTAR- very low	A rapid review of efficacy and policy of contact tracing, testing and isolation (TTI) for COVID-19 control identified 48 relevant studies. The search included publications as of May 28, 2020.	The evidence is synthesized into a suggested public health intervention strategy for Taiwan. • Public health interventions provide significant control in the absence of herd immunity for COVID-19, including contact tracing. • Test turn around of <24 hours is documented in multiple studies and is needed for quick case confirmation. • Mass testing of specific groups (i.e. healthcare workers) facilitates detection of additional cases and their contacts. • Digital tools to facilitate timely contact tracing are successfully utilized by many regions; including: cell phone based mobility, location, and apps for location, symptoms tracking and QR scans upon entry and exit of community locations. It is noted that 60-75% app usage is necessary for it to be effective against COVID-19 spread.
Digital Technology and Contact Tracing		
Anglemyer (2020) (14) Rapid review	This Cochrane rapid review conducted up to May 5, 2020 (pre-pandemic to early in pandemic) aimed to assess the benefits,	Gen pop apps: This review included 6 cohort and 6 modelling studies. Two modelling studies indicated compared to isolation alone, manual contact tracing resulted in a 35-53% reduction in R_e while digital contact tracing only reduced R_e by 18-26% across the models, the

New Zealand May 2020 AMSTAR- high	harms and acceptability of personal digital tracing solutions for identifying contacts of an identified positive case of an infectious disease.	latter assumed only 50% of the population used the app. Threats associated with privacy breaches, particularly from wearable devices were considered a possible threat. Public Health data collection apps: Having a data collection application for electronic contact tracing investigations identified 2x more contacts than paper forms during an Ebola outbreak. Another cohort reported reduced times to complete contact tracing with electronic data management system (plus they were less prone to error and data loss.) 2 cohorts reported digital systems save time and are simpler to use. Cost and internet access were barriers.
Braithwaite (2020) (15) Systematic Review United Kingdom Apr 2020 AMSTAR - medium	This systematic review on automated contact tracing, including by automating the processing of test results or symptom reports and by use of smartphone capabilities (eg, Bluetooth) to identify and notify contacts instantaneously who are at risk of infection, included articles published up to April 14-30, 2020 (pre-pandemic and early pandemic). 15 studies were included.	• No empirical evidence of the effectiveness of automated contact tracing (regarding contacts identified or transmission reduction) was identified. Four of seven included modelling studies suggested that controlling COVID-19 requires a high population uptake of automated contact-tracing apps (estimates from 56% to 95%), typically alongside other control measures. • Studies of partly automated contact tracing generally reported more complete contact identification and follow-up compared with manual systems. Automated contact tracing could potentially reduce transmission with sufficient population uptake. However, concerns regarding privacy and equity should be considered. • Automation of contact-tracing may improve the speed of quarantining contacts, which would lead to a bigger impact. Cohorts from Ebola demonstrated 69% contacts vs 39% contacts were visited and speed was reduced by 0.5- 5 hours across studies. • Resource requirements for test-based release from quarantine in the UK estimated 30-50 tests per positive case and 100000-200000 tests per day in the UK.
Qualitative Analysis of Knowledge, Attitudes and Behaviours		
Megnin-Viggars (2020) (21) Rapid review United Kingdom Jul 2020	This rapid systematic review on barriers and facilitators to engagement with contact tracing includes research up to July 15, 2020. Eleven studies were included, 6 on COVID-19, 5 on Ebola	Four themes were identified as facilitators to the uptake of, and engagement with, contact tracing: collective responsibility; personal benefit; co-production of contact tracing systems; and the perception of the system as efficient, rigorous and reliable. Participants reported that their intentions to use a contact tracing app was strongly influenced by a sense of collective responsibility (3 studies), and their desire to

AMSTAR - high	and 1 on other infectious diseases.	help reduce the deaths of others, particularly those who are vulnerable (2 studies). Many indicated it was a means to ending the pandemic and embraced their role (2 studies) even when participants had some concerns over using a contact tracing app they viewed it as the "only way out" and this collective responsibility was prioritised over personal doubts (1 study). Five themes were identified as barriers to the uptake of, and engagement with, contact tracing: privacy concerns; mistrust and/or apprehension; unmet need for more information and support; fear of stigmatization; and mode-specific challenges.

EFFECTIVENESS OF CONTACT TRACING

Table 2: Epidemiological and Modeling Studies Published Fall 2020/Winter2021 on Effective Contact Tracing Strategies (n=16)

STUDY	METHOD	KEY OUTCOMES
Epidemiological Evidence (n=2)		
Carroll (2020) (3) Contact Tracing Evaluation Ireland May – Aug 2020	The study monitors and evaluates the testing and contact tracing system in Ireland. Contacts of laboratory confirmed COVID-19 cases identified May 19 – August 2, 2020 were included (n=7272).	4586 of the 7272 contacts were tested at least once during the study period. • The attack rate of contacts was 7% (95% CI: 6.3 – 7.8%). • Symptomatic contacts testing positive on 'Day 0' was 14.6% • Asymptomatic contacts testing positive on 'Day 0' was 5.2% Symptom based criteria for contact testing at the time of identification misses >66% of secondary cases and their contacts.
Kendall (2020) (17) Contact Tracing Evaluation United Kingdom May – Jun 2020	The study assesses the impact of the test and trace system applied on the Isle of Wight, England as of May 2020. The system was introduced to Isle of Wight before being expanded to the entire UK. Version 1 of the NHS contact tracing app was implemented, which used Bluetooth to detect physically close contacts and allowed users to input cough or fever symptoms if	A significant decrease in R_e was observed after implementation of the system (from 1.3 to 0.5).

	experienced. Once symptoms were indicated, historical contacts would be notified of potential exposure and provided infection control guidance (this did not include direction to isolate or quarantine at the time).	
Modeling Analyses (n=13)		
Aleman (2021) (22) Preprint Model Canada May 2020	An agent-based model is employed to evaluate PHMs, including contact tracing, in Newfoundland on COVID-19 prevention. The model is age-stratified and considers spatial movement and comorbidities of individuals. Travel volumes of low, medium and high are modeled for comparison.	Stringent contact tracing minimized transmission of COVID-19 by 4-74x compared to no contact tracing. The model also shows that cases of COVID-19 would have overwhelmed with the contact tracing capabilities in Newfoundland without additional PHMs to control the epidemic.
Campbell (2020) (7) Economic Model Canada July 2020	5 populations were identified for strategic testing within Canada: • contacts of COVID-19 cases • acute care hospital employees • community health care workers; and both staff and residents of long-term care homes; • essential business employees with high levels of interpersonal or public contact (excluding healthcare); and • students and staff in primary and secondary schools. The testing rates of July 8-17, 2020 were used as a baseline, to compare the increased testing necessary for scenarios of strategically testing the populations identified. Testing costs considered: • direct test costs; • laboratory capacity; and • human resources for sampling, administrative scheduling/recording and contact tracing.	5 strategies were modelled and compared to the baseline (which had a monthly cost of $69.8 million): 1. Systematic tracing and testing of contacts – all provinces have lab capacity, administrative requirements increase 1.2 times and cost increase of $11.1 million per month above baseline. 2. Acute care hospital employee testing – cost of $29 million per month. 3. CHW and LTC testing – cost of $12.8 million per month. 4. Essential employees with high contacts - $321.7 million per month. 5. Students and school staff testing - $816 million per month. Lab capacity and staffing increases were all necessary in strategies 2-5. Epidemiological impacts of contact tracing were not directly modelled, and no cost-benefit analysis provided. It is hypothesized these testing costs and associated contact tracing will

		reduce downstream healthcare costs, due to transmission prevention.
Bradshaw (2021) (13) Model United States Jan 2021	A Bayesian model is used to demonstrate the effects on the COVID-19 pandemic when implementing bidirectional contact tracing, as opposed to the more common forward tracing being used in most strategies. 'Forward tracing' is informing recently exposed individuals; while bidirectional tracing additionally identifies the potential infector to allow for notification to them and their others that were potentially exposed.	Implementing bidirectional contact tracing in the model scenarios more than doubles the reduction to R_e when compared with only forward tracing. Increasing the window of contacts to be notified from 2 days presymptomatic to 6 days provided the greatest decrease in R_e. This can be replaced by smartphone exposure notification applications, but only if uptake of the app is near 100%.
Endo (2020) (23) Model United Kingdom 2021	A branching process model is used to simulate the effect of combining backward and forward contact tracing in the PHMs for COVID-19. Index cases are identified though symptom-based surveillance in both scenarios. With forward tracing subsequent exposures since the index may have been infectious are identified and quarantined. Backwards tracing identifies the primary case (infector of the index) and traces all of the primary case's exposures forwards for quarantine. The model is intended to simulate potential case detections and compare the effect on the COVID-19 cases in a community. The probability of identifying the primary case with backward tracking was set at 50 and 80% for different scenarios. The probability of identifying descendant cases from a confirmed case was varied from 0-100%; and the probability of an index case being identified by symptom surveillance was explored at 10%, 20% and 50%.	Backward tracing identifies a much larger proportion of cases, and therefore creates greater control over the spread of COVID-19 when implemented. The model found that the addition of backward tracing to the PHMs was 2-3 times more effective than forward tracing alone. The model assumes that secondary cases (from the index) were quarantined prior to becoming infectious and therefore did not result in any tertiary cases. This may under estimate the effects of backward contact tracing measures.
Bracis (2020) (24) Model	An age stratified model projects COVID-19 cases and deaths during and after a reopening period for King County, WA. Various scenarios of public	Lockdown fit a rate pC_PI of ~35% and maintaining <45% pC_PI was necessary to have reasonable control

USA Mar-Nov 2020	health interventions are presented, including variations of pre-COVID physical interaction (pC_PI) rates, testing practices, isolation and contact tracing.	of the epidemic with the testing practices as of May, 2020. The model indicated that increased testing, isolation and tracing would permit 60% pC_PI while still maintaining reasonable control. • Enhanced testing is more than 50% of symptomatic infections identified. • Contact tracing of at least 50% of contacts identifies at least 5% of asymptomatic and pre-symptomatic cases. • Random mass testing will increase identified rates of all cases 0.5 percentage points (assumes 4.5% of population tested daily).
Aleta (2020) (11) Model United States Aug 2020	Agent based model of SARS-CoV-2 transmission in Boston, MA. The model is used to analyze unmitigated spread of SARS-CoV-2, as well as with two different lockdown and release strategies; both with various levels of case detection and tracing effectiveness. Only testing, tracing and quarantine are considered, all other public health interventions are excluded from the main analyses.	The study compares scenarios that range from i) only household contacts of cases are quarantined to ii) 40% of case contacts are traced and quarantined, as well as the contacts' household members. Quarantine of the contact and their household provides a reduction in transmission sufficient to flatten the epidemic curve and prevent a second wave. The model shows that enhanced testing and contact tracing can control the COVID-19 epidemic to within healthcare capacity, even while relaxing physical distancing interventions.
Kucharski (2020) (5) Model United Kingdom Oct 2020	A quantitative model of individual-level transmission was used to simulate the effects of testing, isolation, tracing and contact reduction in household, work, school and other settings. Social contacts were modelled with data from 40,162 participants in the UK via a contact tracing app on smartphones.	In general, a large proportion of cases need to be isolated and their contacts quarantined to control the COVID-19 epidemic in the simulations. A combination of case isolation and contract tracing was found to be more effective than mass testing. Mean transmission reductions are presented for scenarios of various interventions:

		• 2% - mass testing of 5% of a population per week. • 29% - isolation of cases within their household. • 35% - isolation of cases outside of their household. • 64% - isolation of cases with quarantine of their household and manual tracing of all contacts. • 47% - isolation of cases with quarantine of their household and app-based contact tracing (assumes app use of 53%).
Ashcroft (2020) (25) Preprint Model Switzerland Dec 2020	A theoretical model is created to analyze the effectiveness of test-trace-isolate-quarantine (TTIQ) strategies to control COVID-19. Empirical distributions are used to study how the probability of detecting cases, fraction of contacts quarantined and the delay of these events effect the timing of SARS-CoV-2 transmission. The model predicts the number of secondary cases and if necessary tertiary cases that result from the index case given the circumstances.	Introducing contact tracing and contact quarantine to the mitigations is analyzed and it is found that the fraction of index cases identified and isolated has the largest effect on controlling the epidemic: • R_e = 1.5 cannot be controlled with 30% of index cases isolated, even if 100% of their contacts quarantine. Most to least effective efforts within the TTIQ Strategies: • Increase fraction of index cases identified and isolated. • Reduce time from symptom onset to isolation of index case. • Reduce time to quarantine secondary cases. • Increase the fraction of secondary cases identified and quarantined. • Extending the lookback window to identify contacts. As the R_e of the epidemic increases, it becomes increasingly difficult to flatten the epidemic curve with testing and isolation.
Bradshaw (2021) (8) Preprint	A Bayesian model presented in an earlier publication (13) is used to assess the effectiveness of various strategies of	The model R_e estimated at 1.2 to 2.0 for variant transmission, accounting for interventions already in place to reduce COVID-19 spread.

Model Germany Jan 2021	contact tracing against the B.1.1.7, P.1 and B.1.351 variants of SARS-CoV-2.	• Isolation of symptomatic cases at low compliance rates, with no contact tracing reduces R_e by 0.2-0.3; and if R_e is then ≥ 1.4, even 50% of exposures being identified successfully could move R_e below 1. • Contact tracing of 60-70% of the exposed, up to 2 days before index symptom onset produces a R_e reduction of 0.1 above isolation alone; and implementing bidirectional tracing of up to 6 days before symptom onset with 45-55% contacts successfully traced provides a similar level of mitigation. • A reduction of 0.1 or 0.2 to R_e results in case reductions over 2 months of 37-43% and 61-66%, respectively.

Stuart (2021) (10)
Preprint
 	
Model
 	
South Wales, Australia
Oct – Dec 2020
	A stochastic model is created to analyze various levels of testing, tracing and mask utilization and the resulting vulnerability to resurgences of COVID-19 in a low transmission community.	• Testing and tracing rates have a larger relative impact, particularly when there is inconsistency in community mask wearing.
		• Testing 90% of symptomatic individuals and 90% of their contacts controlled the epidemic.
		• Reducing testing rates of symptomatic individuals resulted in many times more infections (numbers for Oct 1 – Dec 31, and reflect scenario of high mask use):
		  • 90% -> ~180 cases
		  • 80% -> 2-3x increase
		  • 65% -> 8-12x increase
		  • 50% -> 30-50x increase

Amaku (2021) (26) Preprint Model Brazil Feb 2021	This quantitative model aims to evaluate the impact of contact tracing symptomatic (assumed) cases, in the absence of testing, in Sao Paulo, Brazil. Symptomatic individuals are not confirmed by testing, but isolated and traced contacts are also isolated.	The model baseline assumes no contact tracing strategy. A scenario of 5000 symptomatic individuals isolated per day, and 80% of isolated contacts are COVID-19 infections, reduces cases and deaths in the population by 80% after 60 days.

	The proportion of isolated contacts with this strategy who are actual COVID-19 infections is varied through scenarios.	A scenario of 5000 symptomatic individuals isolated per day, and 20% of isolated contacts are COVID-19 infections, reduces cases and deaths in the population by 40% and 50%, respectively after 60 days. In areas with high transmission between contacts and low availability of tests, the symptomatic contact tracing strategy can significantly impact COVID-19 spread.
Amaku (2020) (6) Model Brazil Nov 2020	A modified SEIR model is used to simulate the COVID-19 epidemic in Sao Paulo, Brazil from March through December 2020. Epidemiological data through July 18, 2020 was used to fit the model. Public health interventions reached at most a 59% reduction in contacts per individual in late March, and by August this was only 41%. Sao Paulo attempted to control the epidemic primarily through high testing rates.	Model scenarios with start dates of April, May, June, July or August 1 were run to the end of Dec 2020 to assess the effect of 1) mass testing of individuals; and 2) testing symptomatic individuals and if positive, testing of their contacts. • Mass testing (1) and strategic testing (2) were predicted to reduce cases by 90% compared to predicted case levels at the end of 2020. Mass testing would have an estimated cost of 2.25 billion USD; while strategic testing costs would be 150 million USD.
Contreras (2021) (27) Model Chile Jan 2021	A model of COVID-19 transmission in a community is used to study a test-trace-and-isolate (TTI) strategy.	The model identifies 2 tipping points between controlled and uncontrolled COVID-19 in the population: • 'Hidden' infection chains due to asymptomatic, presymptomatic, avoiders and undetected cases becomes too high; or • New infections exceed the capacity for tracing. A scenario of the hidden R_e run at 1.8 provides a stable system, but instability is introduced with an increase of the hidden R_e to 2.0. When the workload of tracing causes delays to exceed the generation time (4 days in this model) contact tracing is no longer effective.

		TTI alone cannot contain the COVID-19 epidemic due to these tipping points, and in the absence of herd immunity additional public health interventions must also be employed.
Yin (2021) (12) Preprint Model China Jan – May 2020	A quantitative model of individual-level transmission simulates the effects of testing delays, tracing and mask use in megacity populations. Spread of COVID-19 was simulated in a population of 11.2 million in Shenzhen City, China using mobile phone tracking data. The likelihood of a sporadic cases causing a COVID-19 resurgence once the city reopens, applying various public health intervention scenarios.	If the city reopens in the absence of a contact tracing system, there is less than a 50% chance of mitigating resurgence due to sporadic cases. Reopening with household contact tracing, 100% masking compliance and testing within 28 hours of symptom onset reduced the probability of a resurgence of cases to 5%. The same level of mitigation (5% resurgence) is achieved with mask compliance of 80% and testing of 40%, if tracing is expanded to include work/school contacts. This relationship holds for equivalent mitigation with decreased masking and testing, as long as contact tracing efforts are increased accordingly.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included:
[(test AND (trace OR tracing OR contact)) OR (contact tracing AND review) OR mass testing OR active test] [TITLE]. Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review. Relevant systematic reviews and rapid reviews were identified and summarized and new research from Fall 2020 and Winter 2021 were also identified to update the review results. A cross analysis of studies in the reviews was not conducted. This review contains research published up to February 10, 2021.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur la recherche des contacts pour le SRAS-CoV-2

Introduction

Quelles données probantes existent sur l'utilisation stratégique d'une recherche efficace et efficiente des contacts pendant la pandémie la COVID-19?

La recherche des contacts est l'une des nombreuses mesures de santé publique qui ont été utilisées pour contrôler la propagation de COVID-19. Dès qu'un cas d'infection est trouvé, les autorités locales de santé publique peuvent alors entreprendre la recherche des contacts pour déterminer toutes les personnes qui pourraient avoir été exposées à un cas et ainsi évaluer leur risque d'exposition. À l'heure actuelle, au Canada, les personnes ayant des contacts rapprochés (c.-à-d. à risque élevé) avec des cas de COVID-19 doivent être mises en quarantaine (c.-à-d. en isolement volontaire) et rester à l'écart des autres pendant 14 jours (1). Il s'agit d'un élément important, mais qui exige de nombreuses ressources, et pendant les périodes de transmission élevée de la COVID-19, la santé publique locale n'a pas toujours eu la capacité d'effectuer une recherche exhaustive des contacts. Il faut donc avoir et utiliser des outils ou des stratégies conçus pour permettre d'améliorer l'efficacité de la recherche de contacts. Il faut également avoir des outils pour évaluer les points de bascule dans la capacité de la santé publique à effectuer une recherche efficace des contacts. Cette synthèse en bref met donc en lumière les études et revues systématiques disponibles jusqu'au 10 février 2021 et portant sur des stratégies de recherche efficace et efficiente des contacts pendant la pandémie de COVID-19. Aux fins de la présente synthèse en bref, la recherche des contacts est définie comme la détermination des personnes qui ont récemment été exposées à une personne infectée pour ensuite mettre cette personne en quarantaine pour éviter la transmission, que des tests de dépistage soient effectués ou non. Dans le cadre de cette synthèse, « isolement » désigne tout isolement des cas confirmés afin de prévenir la transmission à l'intérieur ou à l'extérieur du ménage, alors que « quarantaine » désigne l'isolement de toute personne ayant potentiellement été exposée dans la collectivité avant la fin de sa période d'incubation.

Principaux points

- La capacité de la santé publique à effectuer une recherche exhaustive des contacts dépend de nombreux facteurs, notamment du taux de transmission dans la collectivité, de la capacité de la santé publique à effectuer une recherche des contacts et de sa capacité à déterminer les personnes infectées et leurs contacts (2). Les stratégies qui visent à améliorer la recherche des contacts dans le contexte de la pandémie de COVID-19 ont été résumées dans sept revues rapides ou systématiques incluant des études effectuées jusqu'en décembre 2020, deux études empiriques et quatorze études de modélisation publiées entre novembre 2020 et le 10 février 2021.

- Les personnes infectées par le SRAS-CoV-2 peuvent transmettre le virus avant qu'elles ne développent des symptômes (présymptomatiques) ainsi que lorsqu'elles sont asymptomatiques, ce qui signifie que si seuls les cas symptomatiques sont ciblés, la recherche des contacts ne permettra pas de détecter toutes les personnes infectées.
    - Parmi les modèles évalués, il a été déterminé que ceux dont les stratégies de recherche des contacts s'appuyaient uniquement sur la détermination des cas symptomatiques pour entamer la recherche et la mise en quarantaine des contacts ne tenaient pas compte d'un certain nombre de cas et ne pouvaient donc pas permettre de contrôler l'épidémie de COVID-19 (3).
    - Les études de modélisation ont montré que les stratégies qui utilisaient le dépistage de masse pour déterminer les cas et effectuer la recherche de traçage des contacts en aval étaient plus efficaces pour déterminer les cas et contrôler la propagation de la COVID-19 que la seule recherche des contacts effectuée auprès des cas symptomatiques (3-5). Toutefois, le dépistage de masse exige beaucoup de ressources à court terme et entraîne donc des coûts plus élevés (6). L'on a ainsi estimé qu'effectuer du dépistage de masse sur des populations à haut risque précises (différents travailleurs de la santé, employés d'entreprise essentiels, enseignants et étudiants) et la recherche des contacts pour les cas au Canada entraîneraient des coûts supplémentaires pouvant atteindre 820 millions de dollars par mois comparativement au montant de 70 millions associé aux activités de recherche des contacts effectuées en juillet 2020 (7).
    - La recherche des contacts est efficace pour réduire la transmission des variants préoccupants (8).
- Le fait de réduire au minimum le temps nécessaire pour déterminer un cas et en aviser les contacts à risque élevé est un élément important de la recherche des contacts qui permettra de réduire au minimum les jours d'infection potentiels pendant lesquels une personne n'est pas en quarantaine ou isolée.
    - Plusieurs des revues et des études incluses dans la présente synthèse en bref laissent entendre que la détermination des cas en temps opportun (dans les trois jours qui suivent l'apparition des symptômes) et la mise en quarantaine de la plupart des contacts à risque élevé (environ 60 à 90 % des contacts devaient être retracés d'une étude à l'autre) devait être effectuée le plus rapidement possible pour que la stratégie avec test de dépistage et recherche des contacts soit efficace (5, 9 à 11).
- Les modèles montrent que l'efficacité de la recherche des contacts dans le contrôle de l'épidémie diminue lorsque la prévalence des cas (et le nombre de contacts potentiels) dans la collectivité dépasse les ressources de santé publique disponibles.

- Le contexte local déterminera le nombre maximal de cas pouvant être traités par jour. Si cette capacité est dépassée, la recherche des contacts sera alors moins efficace, car certains cas ne pourront pas être retracés ou il y aura des retards dans la recherche, ce qui repoussera le début de la mise en quarantaine ou empêchera la mise en quarantaine de personnes exposées, ce qui, en retour, pourrait faire augmenter la transmission (2).

- La recherche des contacts est l'une des nombreuses mesures de santé publique utilisées pour contrôler la COVID-19 qui fonctionnent en synergie pour contrôler l'épidémie. Des études ont montré qu'à mesure que la transmission diminue et que les mesures de santé publique restrictives (p. ex., confinement, fermetures et déplacements restreints) sont levées, un système de recherche des contacts solide et suffisamment puissant est nécessaire pour éviter une résurgence (5 % de probabilité de résurgence par rapport à moins de 50 % si la capacité de recherche des contacts n'est pas suffisante) (12).
- L'amélioration de l'efficience et de l'efficacité de la recherche des contacts à l'aide de nouveaux outils et stratégies a été évaluée dans plusieurs revues et études.
    - La recherche bidirectionnelle des contacts (recherche des contacts jusqu'à 6 jours avant les symptômes) fait plus que doubler la réduction du R_e (taux d'exposition) lorsqu'on le compare avec la recherche de traçage des contacts en aval seulement (contacts du cas déterminés jusqu'à un ou deux jours avant l'apparition des symptômes puis jusqu'à l'isolement). (8, 13). Ce type de recherche exige cependant une plus grande capacité au niveau de la santé publique.
    - On a cependant constaté que la recherche de traçage bidirectionnelle utilisée pour déterminer le cas primaire dans une grappe était de 2 à 3 fois plus efficace contre la propagation du SRAS-CoV-2 que la recherche de traçage des contacts en aval utilisée seule (23).
    - L'efficacité de la recherche des contacts est améliorée par l'utilisation d'outils électroniques de gestion des données qui peuvent doubler le nombre de contacts suivis, en plus d'être moins sujets aux erreurs et aux pertes de données (14).
    - Les applications de recherche des contacts ont été étudiées et évaluées rapidement dans le contexte de la COVID-19 afin d'atteindre un plus grand nombre de personnes potentiellement exposées. Comme il s'agit d'une nouvelle technologie, la plupart des modèles ont estimé une faible utilisation des applications (p. ex., 50 %), ce qui a entraîné une réduction du R_e de 18 à 26 % comparativement à la recherche des contacts effectuée par la santé publique, ce qui a entraîné une réduction de 35 à 53 % du R_e (14). Des proportions plus élevées d'adoption par la population d'applications automatisées de recherche des contacts (estimations variant entre 56 % et 100 %) ont permis d'améliorer le rendement de la recherche des contacts (13, 15, 16).
    - Une seule étude empirique a fait état d'une diminution importante du R_e (qui est passé de 1,3 à 0,5) après des essais régionaux effectués avec l'application de recherche des contacts au Royaume-Uni, une application qui fut utilisée par la majorité de la population. La version 1,

mentionnée dans l'étude, était une application de recherche de contacts de proximité avec Bluetooth qui déterminait les cas probables en fonction d'un état symptomatique autodéclaré (17).

Vue d'ensemble des éléments de preuve

Vingt-trois articles ont été inclus dans cette synthèse. Les revues systématiques et les revues rapides qui portaient sur la recherche des contacts comme moyen pour atténuer la propagation de la COVID-19 représentant sept des articles cités (trois d'entre eux étant en préimpression). De plus, 16 articles récents (publiés à l'automne 2020 et à l'hiver 2021) présentaient des données probantes sur des stratégies efficaces de recherche des contacts, dont deux contaient des données épidémiologiques et 14 étaient fondés sur des études de modélisation (6 des modèles sont en préimpression).

L'outil AMSTAR-2 a été utilisé pour évaluer les revues rapides et les revues systématiques (n = 7) indiquées dans le tableau 1 (18). La qualité globale de l'examen est classée comme étant élevée, moyenne, faible ou très faible, selon le nombre de critères de l'AMSTAR qui n'ont pas été respectés.

Les données empiriques (n = 2) sont fondées sur des études d'observation visant à évaluer les stratégies de recherche des contacts ou les changements dans les stratégies actuelles. Les études d'observation risquaient de comporter de nombreux biais. Il faut faire preuve de prudence dans l'interprétation des modèles prédictifs (n = 13), car ils peuvent être sensibles aux hypothèses du modèle et sont plus adaptés pour comparer différents scénarios puisqu'ils pourraient ne pas refléter une situation réelle ou ne pas pouvoir être généralisés. La plupart des données probantes sur ce sujet proviennent de modèles prédictifs.

Les limites de la preuve comprennent un manque de preuves empiriques et une forte dépendance aux conclusions d'études de modélisation ou d'examens fondés sur l'expérience prépandémique.

TABLE DES MATIÈRES

EXAMENS DES ÉTUDES SUR LA RECHERCHE DES CONTACTS

Tableau 1 : Revues systématiques et revues rapides sur la recherche des contacts dans les cas de COVID-19 (n = 7)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
Stratégies globales de recherche des contacts		
Mbwogge (2020) (4) Prépublication Revue rapide Royaume-Uni Décembre 2020 AMSTAR – niveau modéré	La revue rapide comprenait 35 articles contenant les données probantes disponibles jusqu'au 22 décembre 2020 sur la question de savoir si le dépistage de masse et la recherche des contacts seraient plus efficaces que la méthode avec tests de dépistage et recherche des contacts actuellement utilisée au Royaume-Uni. Les résultats ont été synthétisés en comptant les votes, en tenant compte de la direction de l'effet et du degré de biais dans les résultats déclarés.	Selon 13 des études, le dépistage de masse était plus efficace que le test basé sur les symptômes dans 76,9 % des études (IC à 95 % : 46,2 à 95,0), ce qui donnerait un résultat pour la réduction de la COVID-19 supérieur à celui obtenu avec le protocole avec test basé sur les symptômes et la recherche des contacts actuellement utilisé au Royaume-Uni. Le dépistage de masse améliore la détection des cas asymptomatiques de COVID-19 qui ne sont pas détectés lors d'un test basé sur les symptômes. Dans 22 études, 40,7 % (IC à 95 % : 38,8 à 42,5 %) des cas détectés seraient asymptomatiques, ce qui veut dire qu'on s'attendrait à avoir 28 % (IC à 95 % : 25,9 à 30,2 %) de cas asymptomatiques dans la population en général et à avoir 96,6 % (IC à 95 % : 82,2 à 99,9 %) de cas asymptomatiques parmi le personnel fournissant des soins de longue durée.
Girum (2020) (19) Revue systématique Éthiopie Juin 2020 AMSTAR – niveau modéré	La revue incluait 22 études d'observation (n = 9) et de modélisation (n = 13) qui ont fourni des preuves de prévention de la COVID-19 grâce au dépistage, à la recherche de contacts, à la quarantaine et à l'isolement. Les études réalisées jusqu'au 2 juin 2020 ont été incluses dans cette revue. Trois études ont évalué toutes les stratégies de prévention alors que cinq	Étude de recherche des contacts : • Isoler uniquement les patients symptomatiques pourrait ne pas permettre de contenir l'épidémie. • Les personnes qui ont des contacts intimes ont des taux de transmission de 40 à 60 %, ce qui indique que les membres des familles qui ont été en contact avec des cas devraient être mis en quarantaine. • Les éclosions pourraient ne pas pouvoir être contenues, à moins que des niveaux élevés de recherche et de quarantaine ne soient utilisés. • Si le R_o est de 2,5, plus de 70 % des contacts doivent être inclus dans la recherche pour ainsi pouvoir lutter contre l'éclosion (20). • L'utilisation d'une stratégie de recherche des contacts et de mise en quarantaine réduit la transmission de 50 à

	ont porté spécifiquement sur les effets de la recherche des contacts.	60 % comparativement au dépistage de masse ou à la quarantaine volontaire qui ne l'a réduite que de 2 à 30 % (5) (comme cela est indiqué dans le tableau 2).
Juneau (2020) (9) Prépublication Revue systématique Québec, Canada Juillet 2020 AMSTAR – niveau faible	La revue a permis de relever 32 études d'observation (n = 14) et de modélisation (n = 18) portant sur l'efficacité de la recherche des contacts dans le contrôle de la COVID-19. Toutes les méthodes de recherche des contacts ont été incluses dans l'examen (c.-à-d., applications mobiles, etc.). Les études étaient exclues si elles ne tenaient pas compte des milieux de transmission communautaire ou si elles n'avaient pas été examinées par des pairs. Les dates de la recherche ne sont pas fournies dans l'article en préimpression.	Dans l'ensemble, la revue affirme qu'un cas doit être isolé dans les 2 à 3 jours qui suivent l'apparition des symptômes, et qu'au moins 80 % de leurs contacts doivent être mis en quarantaine pour qu'il n'y ait pas de cas tertiaires. Des systèmes de recherche des contacts et de quarantaine moins efficaces pourraient ralentir la propagation du SRAS-CoV-2, mais ne pourront pas enrayer l'épidémie. Des retards de quatre jours ou plus ou la mise en quarantaine de moins de 60 % des contacts seront inefficaces pour contrôler l'épidémie.
Chung (2020) (16) Prépublication Revue rapide Royaume-Uni Mai 2020 AMSTAR – niveau très faible	Une revue rapide portant sur l'efficacité et la politique de recherche des contacts, de tests de dépistage et d'isolement pour le contrôle de la COVID-19 a permis de relever 48 études pertinentes. La recherche a porté sur les publications disponibles jusqu'au 28 mai 2020.	Les données probantes sont résumées dans une stratégie d'intervention en santé publique suggérée pour Taïwan. • Les interventions en santé publique, incluant la recherche des contacts, permettent d'obtenir un niveau significatif de contrôle en l'absence d'immunité collective pour la COVID-19. • Un délai d'exécution des tests inférieur à 24 heures est documenté dans plusieurs études et jugé nécessaire pour obtenir la confirmation rapide d'un cas. • Le dépistage de masse dans des groupes particuliers (c.-à-d., les travailleurs de la santé) facilite la détection de cas supplémentaires et de leurs contacts. • De nombreuses régions utilisent avec succès des outils numériques pour faciliter la recherche rapide des contacts, ce qui inclut le suivi de la mobilité avec les

		téléphones cellulaires, l'emplacement et les applications de détermination de l'emplacement, le suivi des symptômes et les balayages de codes QR à l'entrée et à la sortie des lieux communautaires. Il est à noter qu'il faut que l'application soit utilisée par 60 à 75 % des gens pour qu'elle soit efficace contre la propagation de la COVID-19.
Technologie numérique et recherche des contacts		
Anglemyer (2020) (14) Revue rapide Nouvelle-Zélande Mai 2020 AMSTAR – niveau élevé	Cette revue rapide Cochrane effectuée jusqu'au 5 mai 2020 (avant la pandémie ou au début de la pandémie) visait à évaluer les avantages, les préjudices et l'acceptabilité des solutions de dépistage numérique personnel pour identifier les contacts d'un cas positif à une maladie infectieuse.	Applications pour la population en général : Cette revue comprenait six études de cohorte et six études de modélisation. Deux études de modélisation ont indiqué que, comparativement à l'isolement seul, la recherche manuelle des contacts a entraîné une réduction de 35 à 53 % du R_e, tandis que la recherche numérique des contacts n'a réduit le R_e que de 18 à 26 % dans l'ensemble des modèles (sachant que ces derniers ont présumé que l'application n'était utilisée que par 50 % de la population). Les menaces associées aux atteintes à la vie privée, en particulier pour les appareils portables, étaient vues comme une menace possible. Applications de collecte de données sur la santé publique : Pendant une éclosion d'Ebola, le fait d'avoir une application de collecte de données pour effectuer des enquêtes de recherche électronique des contacts a permis d'identifier deux fois plus de contacts que les formulaires papier. Une autre cohorte a mentionné une réduction du temps requis pour effectuer la recherche des contacts avec un système électronique de gestion des données (sans oublier que ce système était également moins sujet aux erreurs et aux pertes de données). Deux cohortes ont indiqué que les systèmes numériques permettaient de gagner du temps et étaient plus faciles à utiliser. Le coût et l'accès à Internet constituaient des obstacles.
Braithwaite (2020) (15) Revue systématique Royaume-Uni	Cette revue systématique qui porte sur la recherche automatisée des contacts, y compris le fait d'automatiser le traitement des résultats des tests ou la déclaration des symptômes et l'utilisation des	• Aucune preuve empirique de l'efficacité de la recherche automatisée des contacts (en ce qui concerne les contacts identifiés ou la réduction de la transmission) n'a été trouvée. Quatre des sept études de modélisation incluses laissaient entendre que le contrôle de la COVID-19 exigeait qu'une grande partie de la population adopte les applications automatisées de recherche des contacts (estimations variant entre 56 %

Avril 2020 AMSTAR – niveau moyen	fonctionnalités des téléphones intelligents (p. ex., Bluetooth) pour déterminer les contacts et aviser instantanément les personnes à risque d'être infectées, comprend des articles publiés jusqu'à la période du 14 au 30 avril 2020 (avant la pandémie et au début de la pandémie). Elle comprenait 15 études.	et 95 %) habituellement utilisées en parallèle avec d'autres mesures de contrôle. • Les études sur la recherche partiellement automatisée des contacts ont généralement révélé une détermination et un suivi plus complets des contacts comparativement aux systèmes manuels. La recherche automatisée des contacts pourrait réduire la transmission si une partie importante de la population y participait. Il faut toutefois tenir compte des préoccupations relatives à la protection des renseignements personnels et à l'équité. • L'automatisation de la recherche des contacts pourrait accélérer la mise en quarantaine des contacts, ce qui entraînerait des répercussions plus importantes. Les cohortes d'Ebola ont démontré un niveau de visite des contacts de 69 % comparativement à 39 % et une réduction de la vitesse variant entre 0,5 et 5 heures dans l'ensemble des études. • L'on estime les besoins en ressources pour une quarantaine basée sur un test de dépistage au Royaume-Uni à un chiffre variant entre 30 et 50 tests par cas positif et par tranche de 10 000 à 20 000 tests faits chaque jour au Royaume-Uni.
Analyse qualitative des connaissances, des attitudes et des comportements		
Megnin-Viggars (2020) (21) Revue rapide Royaume-Uni Juillet 2020 AMSTAR – niveau élevé	Cette revue systématique rapide qui porte sur les obstacles et les facteurs qui augmentent la participation à la recherche des contacts comprend des recherches publiées jusqu'au 15 juillet 2020. Elle comprend onze études, soit six sur la COVID-19, cinq sur le virus Ebola et une sur une autre maladie infectieuse.	Quatre thèmes ont été retenus comme facteurs facilitant l'adoption et l'engagement à l'égard de la recherche des contacts, soit la responsabilité collective, les avantages personnels, la coproduction des systèmes de recherche des contacts et la perception que le système est efficace, rigoureux et fiable. Les participants ont déclaré que leur intention d'utiliser l'application de recherche des contacts était fortement influencée par un sentiment de responsabilité collective (trois études) et leur désir d'aider à réduire le nombre de décès des autres personnes, en particulier celles qui sont vulnérables (deux études). Bon nombre d'entre eux ont indiqué qu'il s'agissait d'un moyen de mettre fin à la pandémie et ont assumé leurs responsabilités à cet égard (deux études), même lorsque les participants avaient certaines préoccupations quant à l'utilisation d'une application de recherche des contacts, ils jugeaient qu'elle était la « seule façon de s'en sortir » et que cette

		responsabilité collective devait être prioritaire par rapport aux doutes personnels (une étude). Cinq thèmes ont été cernés comme étant des obstacles à l'adoption et à la participation à la recherche des contacts, soit les préoccupations relatives à la protection de la vie privée, la méfiance ou l'appréhension, le besoin non satisfait d'obtenir plus d'information et de soutien, la peur de la stigmatisation et les défis propres au moyen utilisé.

EFFICACITÉ DE LA RECHERCHE DES CONTACTS

Tableau 2 : Études épidémiologiques et de modélisation publiées à l'automne 2020/hiver 2021 sur les stratégies efficaces de recherche des contacts (n = 16)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
Preuves épidémiologiques (n = 2)		
Carroll (2020) (3) Évaluation de la recherche des contacts Irlande Mai à août 2020	L'étude a surveillé et évalué le système de dépistage et de recherche des contacts en Irlande. Les contacts du laboratoire ont confirmé les cas de COVID-19 identifiés entre le 19 mai et le 2 août 2020 (n = 7 272).	De ces 7 272 contacts, 4 586 ont été testés au moins une fois pendant la durée de l'étude. • Le taux d'attaque des contacts était de 7 % (IC à 95 % : 6,3 à 7,8 %). • On a obtenu 14,6 % de contacts symptomatiques positifs au « jour 0 ». • Le test effectué sur les contacts asymptomatiques au « jour 0 » indiquait un résultat de 5,2 %. Les critères basés sur les symptômes pour la recherche des contacts lors de l'identification n'ont pas permis de détecter plus de 66 % des cas secondaires et de leurs contacts.
Kendall (2020) (17) Évaluation de la recherche des contacts Royaume-Uni	L'étude évalue l'impact du système de test de dépistage et de recherche des contacts utilisés à l'île de Wight, en Angleterre, en mai 2020. Le système a d'abord été utilisé à l'île de Wight avant d'être étendu à tout le Royaume-Uni. La version 1 de l'application de recherche des contacts	Une diminution importante du R_e a été observée après la mise en œuvre du système (passant de 1,3 à 0,5).

Mai et juin 2020	du NHS a été mise en œuvre. Elle utilisait la fonctionnalité Bluetooth pour détecter les contacts physiques étroits entre les gens et permettait aux utilisateurs d'entrer leurs symptômes, soit la toux ou la fièvre, le cas échéant. Une fois les symptômes entrés, les contacts historiques étaient alors avisés de l'exposition potentielle et l'application donnait des conseils sur la prévention des infections (n'incluait cependant pas la directive visant à s'isoler ou à se mettre en quarantaine).	
Analyses de modélisation (n = 13)		
Aleman (2021) (22) Préimpression Modèle Canada Mai 2020	Un modèle basé sur les agents a été utilisé pour évaluer les mesures de santé publique sur la prévention de la COVID-19, ce qui incluait la recherche des contacts, à Terre-Neuve-et-Labrador. Le modèle est stratifié selon l'âge et tient compte des mouvements spatiaux et des comorbidités des personnes. Des volumes de déplacements bas, moyens et élevés ont été modélisés à des fins de comparaison.	La recherche rigoureuse des contacts a réduit la transmission de la COVID-19 de 4 à 74 fois comparativement à la non-utilisation de cette recherche. Le modèle montre également si Terre-Neuve-et-Labrador n'avait pas ajouté de mesures de santé publique pour contrôler l'épidémie, la recherche des contacts aurait dépassé les capacités de la province.
Campbell (2020) (7) Modèle économique Canada Juillet 2020	Cinq populations ont été sélectionnées à des fins de tests stratégiques au Canada : • les contacts des cas de COVID-19; • les employés des hôpitaux de soins actifs; • les travailleurs des soins de santé communautaires, ainsi que le personnel et les résidents des maisons de soins de longue durée; • les employés essentiels des entreprises ayant un niveau élevé de contacts interpersonnels ou avec le public (à l'exclusion des soins de santé);	Cinq stratégies ont été modélisées et comparées à la base de référence (dont le coût mensuel était de 69,8 millions de dollars) : 1. Recherche et analyse systématiques des contacts – toutes les provinces ont la capacité de laboratoire requise, les exigences administratives augmentent de 1,2 fois et les coûts augmentent de 11,1 millions de dollars par mois par rapport au niveau de référence. 2. Tests de dépistage auprès d'employés d'hôpitaux de soins

	• les élèves et le personnel des écoles primaires et secondaires. Les taux de test obtenus entre le 8 et le 17 juillet 2020 ont été utilisés comme base de référence pour comparer l'augmentation des tests requise dans les scénarios dans lesquels les populations sélectionnées feraient l'objet d'un test de dépistage stratégique. Coûts des tests pris en compte : • coûts directs des tests; • capacité du laboratoire; • ressources humaines requises pour l'échantillonnage, l'établissement et l'enregistrement des calendriers administratifs et la recherche des contacts.	actifs – coût de 29 millions de dollars par mois. 3. Test des travailleurs des soins de santé communautaires, ainsi que du personnel et des résidents des maisons de soins de longue durée – 29 millions de dollars par mois. 4. Tests effectués chez les employés essentiels ayant un grand nombre de contacts – 321,7 millions de dollars par mois. 5. Tests effectués chez les étudiants et les membres du personnel des écoles – 816 millions de dollars par mois. La capacité de laboratoire et l'augmentation du personnel étaient toutes requises pour les stratégies 2 à 5. Les répercussions épidémiologiques de la recherche des contacts n'ont pas été modélisées directement, et aucune analyse coûts-avantages n'a été fournie. On a émis l'hypothèse que les coûts des tests et la recherche connexe des contacts réduiraient les coûts des soins de santé en aval, en raison de la prévention de la transmission.
Bradshaw (2021) (13) Modèle États-Unis Janvier 2021	Un modèle bayésien a été utilisé pour démontrer les effets sur la pandémie de COVID-19 de la mise en œuvre de la recherche de contacts bidirectionnelle, par opposition à certains types de recherche de traçage en aval plus courants, utilisés dans la plupart des stratégies. La « recherche de traçage des contacts en aval » informe les personnes récemment exposées, alors que la recherche bidirectionnelle permet également de déterminer l'agent	La mise en œuvre de la recherche bidirectionnelle des contacts dans les scénarios du modèle a fait plus que doubler la réduction de R_e par rapport à la recherche de traçage des contacts en aval seulement. Le fait d'augmenter de 2 jours dans les cas présymptomatiques à 6 jours la période pendant laquelle les contacts sont avisés a permis d'obtenir la plus grande diminution de R_e. Cette façon de faire peut être remplacée par des applications d'avis d'exposition

	infectieux potentiel et l'indique à ces personnes et aux autres personnes ayant potentiellement été exposées.	conçues pour les téléphones intelligents, mais cette façon de faire ne fonctionnera que si l'application est adoptée par presque 100 % de la population.
Endo (2020) (23) Modèle Royaume-Uni 2021	Un modèle avec processus de ramification est utilisé pour simuler l'effet que la combinaison de la recherche de traçage des contacts en amont et en aval peut avoir sur les mesures de santé publique en ce qui concerne la COVID-19. Dans les deux scénarios, les cas index sont déterminés par la surveillance basée sur les symptômes. Dans le cas des expositions avec recherche de traçage des contacts en aval, puisque le cas index peut avoir été infectieux, il est alors identifié et mis en quarantaine. La recherche de traçage des contacts en amont permet de déterminer le cas primaire (infecteur du cas index) et de retracer toutes les expositions du cas primaire en avant pour ensuite savoir qui doit se mettre en quarantaine. Le modèle vise à simuler les détections de cas possibles et à en comparer l'effet sur les cas de COVID-19 dans une collectivité. La probabilité de pouvoir déterminer le cas primaire avec la recherche de traçage des contacts en aval a été établie à 50 et à 80 % pour différents scénarios. La probabilité d'identifier les cas en amont d'un cas confirmé variait de 0 à 100 %, alors que la probabilité qu'un cas index puisse être déterminé par la surveillance des symptômes n'a atteint que 10 %, 20 % et 50 %.	La recherche de traçage des contacts en amont permet de repérer une proportion beaucoup plus grande de cas et, par conséquent, d'exercer un plus grand contrôle sur la propagation de la COVID-19 lorsqu'elle est mise en œuvre. Le modèle a révélé que l'ajout de la recherche de traçage des contacts en amont aux mesures de santé publique était de 2 à 3 fois plus efficace que la seule recherche de traçage des contacts en aval. Le modèle suppose que les cas secondaires (découlant du cas index) ont été mis en quarantaine avant de devenir infectieux et n'ont donc pas créé de cas tertiaires, ce qui pourrait donc sous-estimer les effets des mesures de recherche de traçage des contacts en amont.
Bracis (2020) (24) Modèle	Un modèle stratifié selon l'âge a été utilisé pour effectuer des prédictions du nombre de cas et de décès associés à la COVID-19 pendant et après une période de réouverture dans le comté de King, à Washington. Divers scénarios	Un taux fixe pC_PI a été établi à environ 35 % pendant le confinement et il a fallu maintenir un taux pC_PI inférieur à 45 % pour avoir un contrôle raisonnable sur l'épidémie avec les

ÉTATS-UNIS De mars à novembre 2020	d'interventions en santé publique y sont présentés, ce qui inclut les variations des taux d'interaction physique (pC_PI) avant la maladie de Lyme, les pratiques associées aux tests de dépistage, l'isolement et la recherche des contacts.	pratiques de dépistage en date de mai 2020. Le modèle indiquait qu'une augmentation du nombre de tests de dépistage, de l'isolement et de la recherche des contacts permettrait d'atteindre un taux de pC_PI de 60 % tout en conservant un contrôle raisonnable. • Les tests de dépistage améliorés ont permis de détecter plus de 50 % des infections symptomatiques. • La recherche d'au moins 50 % des contacts a permis d'identifier au moins 5 % des cas asymptomatiques et présymptomatiques. • Les tests de dépistage de masse aléatoires permettront d'augmenter les taux déterminés de tous les cas de 0,5 point de pourcentage (en supposant que 4,5 % de la population soit testée quotidiennement).
Aleta (2020) (11) Modèle États-Unis Août 2020	Modèle de transmission du SRAS-CoV-2 basé sur un agent effectué à Boston au Massachusetts. Le modèle est utilisé pour analyser la propagation non atténuée du SRAS-CoV-2, ainsi que deux stratégies de confinement et de sortie du confinement différentes, toutes deux avec divers niveaux de recherche des cas et d'efficacité du dépistage. Seuls les tests, la recherche des contacts et la quarantaine sont pris en compte. Toutes les autres interventions en santé publique ont été exclues des principales analyses.	L'étude compare différents scénarios qui vont de i) seuls les contacts du ménage de l'un des cas sont mis en quarantaine, à ii) 40 % des contacts du cas ont fait l'objet d'une recherche et ont été mis en quarantaine, tout comme les membres du ménage des contacts. La mise en quarantaine du contact et des membres de son ménage permet une réduction de la transmission suffisante pour aplanir la courbe de l'épidémie et prévenir une seconde vague. Le modèle montre qu'une amélioration dans les tests de dépistage et dans la recherche des contacts peut permettre de contrôler l'épidémie de COVID-19, en fonction du respect des capacités limites pour les soins de santé, même en réduisant

		les interventions avec distanciation physique.
Kucharski (2020) (5) Modèle Royaume-Uni Octobre 2020	Un modèle quantitatif de transmission au niveau individuel a été utilisé pour simuler les effets des tests de dépistage, de l'isolement, de la recherche des contacts et de la réduction des contacts dans les ménages, le travail, l'école et d'autres milieux. Les contacts sociaux ont été modélisés à partir des données fournies par 40 162 participants au Royaume-Uni grâce à une application de recherche de contacts sur les téléphones intelligents.	De façon générale, une grande proportion des cas doivent être isolés et leurs contacts mis en quarantaine pour contrôler l'épidémie de COVID-19 dans les simulations. On a constaté qu'une combinaison d'isolement des cas et de recherche des contacts était plus efficace que les tests de dépistage de masse. Les réductions moyennes de la transmission sont présentées pour les scénarios associés à différentes interventions : • 2 % – dépistage de masse de 5 % de la population par semaine. • 29 % – isolement des cas dans le ménage. • 35 % – isolement des cas à l'extérieur du ménage. • 64 % – isolement des cas avec mise en quarantaine du ménage et recherche manuelle de tous les contacts. • 47 % – isolement des cas avec mise en quarantaine du ménage et recherche des contacts à l'aide de l'application (suppose une utilisation des applications de 53 %).
Ashcroft (2020) (25) Prépublication Modèle Suisse Décembre 2020	Un modèle théorique a été créé pour analyser l'efficacité des stratégies avec recherche des contacts, tests de dépistage, isolement et quarantaine pour contrôler la COVID-19. Les distributions empiriques sont utilisées pour étudier la façon dont la probabilité de détection des cas, la fraction des contacts mis en quarantaine et le retard dans ces événements influent sur le moment où le SRAS-CoV-2 est transmis.	On a analysé l'ajout de la recherche des contacts et de la mise en quarantaine aux mesures d'atténuation, ce qui a permis de constater que la fraction des cas index déterminés et isolés est l'élément qui a l'effet le plus important sur le contrôle de l'épidémie : • R_e = 1,5 ne peut pas être contrôlé lorsque 30 % des cas index sont

	Le modèle prédit le nombre de cas secondaires et, au besoin, tertiaires qui découlent du cas index selon les circonstances.	isolés, même si 100 % de leurs contacts ont été mis en quarantaine. Liste des efforts, des plus efficaces aux moins efficaces dans le cadre des stratégies avec recherche des contacts, tests de dépistage, isolement et quarantaine : • Augmenter la fraction des cas index déterminés et isolés. • Réduire le temps entre l'apparition des symptômes et l'isolement du cas index. • Réduire le temps requis avant de mettre les cas secondaires en quarantaine. • Augmenter la fraction des cas secondaires déterminés et mis en quarantaine. • Prolonger la fenêtre de recherche pour déterminer les contacts. Au fur et à mesure que le R_e de l'épidémie augmente, il devient de plus en plus difficile d'aplanir la courbe de l'épidémie par les tests de dépistage et l'isolement.
Bradshaw (2021) (8) Prépublication Modèle Allemagne Janvier 2021	Un modèle bayésien présenté dans une publication antérieure (13) est utilisé pour évaluer l'efficacité de diverses stratégies de recherche des contacts par rapport aux variants B.1.1.7, P.1 et B.1.351 du SRAS-CoV-2.	Le modèle R_e a estimé la transmission des variants entre 1,2 et 2,0, en tenant compte des interventions déjà en place pour réduire la propagation de la COVID-19. • L'isolement des cas symptomatiques avec faibles taux de conformité, sans recherche des contacts, réduit le R_e de 0,2 à 0,3, ce qui donne un R_e de 1,4, même 50 % des expositions identifiées avec succès pousser le R_e a descendre sous 1. • La recherche des contacts chez 60 à 70 % des personnes exposées, jusqu'à deux jours avant l'apparition des symptômes chez le cas index, entraîne une réduction du R_e de

		0,1 pour l'isolement seulement, alors que la mise en œuvre de la recherche bidirectionnelle effectuée jusqu'à 6 jours avant l'apparition des symptômes avec une recherche de contacts variant entre 45 et 55 % a permis d'atteindre un niveau d'atténuation similaire. • Une réduction de 0,1 ou de 0,2 du R_e entraîne une réduction du nombre de cas sur deux mois de 37 à 43 % et de 61 à 66 %, respectivement.

Stuart (2021) (10)
Prépublication
 	
Modèle
 	
Galles du Sud, Australie
Octobre à décembre 2020
	Un modèle stochastique a été créé pour analyser différents niveaux d'utilisation des tests de dépistage, de la recherche des contacts et du port du couvre-visage et la vulnérabilité qui en résulte à la résurgence de la COVID-19 dans une collectivité où le niveau de transmission est faible.	• Les taux de tests de dépistage et de recherche des contacts ont une incidence relative plus importante, particulièrement lorsqu'il y a une incohérence dans le port du couvre-visage dans la collectivité.
		• Le dépistage de 90 % des personnes symptomatiques et de 90 % de leurs contacts a permis de contrôler l'épidémie.
		• La réduction des taux de dépistage chez les personnes symptomatiques a entraîné un nombre beaucoup plus grand d'infections (données pour la période du 1er octobre au 31 décembre, et reflète le scénario avec port élevé du couvre-visage) :
		  • 90 % -> ~180 cas
		  • 80 % -> de 2 à 3 fois plus
		  • 65 % -> de 8 à 12 fois plus
		  • 50 % -> de 30 à 50 fois plus

Amaku (2021) (26) Préimpression Modèle Brésil Février 2021	Ce modèle quantitatif vise à évaluer les répercussions de la recherche des contacts sur les cas symptomatiques (présumés) en l'absence de tests, à Sao Paulo, au Brésil. La proportion de personnes symptomatiques n'a pas été confirmée par des tests, mais ces dernières ont	Le modèle de référence suppose une stratégie sans recherche de contacts. Un scénario avec 5 000 personnes symptomatiques isolées par jour, dans lequel 80 % des contacts isolés sont infectés par la COVID-19, a permis de

	plutôt été isolées, tout comme leurs contacts trouvés par la recherche des contacts. La proportion de contacts isolés en raison de cette stratégie qui ont véritablement été infectés par la COVID-19 varie selon les scénarios.	réduire de 80 % les cas et les décès dans la population après 60 jours. Un scénario avec 5 000 personnes symptomatiques isolées par jour, dans lequel 20 % des contacts isolés sont infectés par la COVID-19, a permis de réduire de 40 % les cas et les décès dans la population, puis de 50 % après 60 jours. Dans les régions où la transmission est élevée entre les contacts et où peu de tests de dépistage sont disponibles, la stratégie de recherche des contacts symptomatiques peut avoir une incidence importante sur la propagation de la COVID-19.
Amaku (2020) (6) Modèle Brésil Novembre 2020	Un modèle susceptible-exposé-infectieux-retiré (modèle SEIR) modifié est utilisé pour simuler l'épidémie de COVID-19 à Sao Paulo, au Brésil, de mars à décembre 2020. Les données épidémiologiques disponibles jusqu'au 18 juillet 2020 ont été utilisées pour s'adapter au modèle. Les interventions en santé publique ont atteint une réduction maximale de 59 % des contacts par personne à la fin de mars, alors qu'en août, cette réduction n'a atteint que 41 %. Sao Paulo a tenté de contrôler l'épidémie principalement grâce à des taux de dépistage élevés.	Les scénarios des modèles débutant en avril, en mai, en juin, en juillet ou en août ont été exécutés jusqu'à la fin de décembre 2020 pour évaluer l'effet 1) des tests de dépistage de masse sur les personnes; et 2) des tests effectués sur les personnes symptomatiques qui, s'ils étaient positifs, entraînaient l'exécution de tests de dépistage sur leurs contacts. • Les tests de dépistage de masse (1) et les tests de dépistage stratégiques (2) devraient réduire les cas de 90 % par rapport aux niveaux prévus à la fin de 2020. Le coût des tests de masse était estimé à 2,25 milliards de dollars, tandis que le coût associé aux tests stratégiques atteindrait 150 millions de dollars.
Contreras (2021) (27) Modèle Chili	Un modèle de transmission de la COVID-19 dans une collectivité est utilisé pour étudier une stratégie de dépistage, de recherche de contacts et d'isolement.	Le modèle détermine 2 points de bascule entre la COVID-19 contrôlée et non contrôlée dans la population : • les chaînes d'infection « cachées » découlant de cas asymptomatiques,

Janvier 2021		présymptomatiques, évités et non détectés deviennent trop hautes; • les nouvelles infections qui dépassent la capacité de dépistage. Un scénario avec R_e caché effectué à un niveau de 1,8 donne un système stable, mais l'instabilité est introduite lorsque le R_e caché passe à 2,0. Lorsque la charge de travail de la recherche des contacts entraîne des retards supérieurs au temps de génération (4 jours dans ce modèle), la recherche des contacts n'est plus efficace. En raison de ces points de bascule, la stratégie avec tests de dépistage, recherche de contacts et isolement ne peut contenir à elle seule l'épidémie de COVID-19, et en l'absence d'immunité collective, il faut également utiliser des interventions supplémentaires en santé publique.
Yin (2021) (12) Prépublication Modèle Chine Janvier à mai 2020	Un modèle quantitatif de transmission au niveau individuel simule les effets des retards dans le dépistage, la recherche des contacts et le port de couvre-visage dans les populations des mégavilles. La propagation de la COVID-19 a été simulée dans une population de 11,2 millions d'habitants à Shenzhen City, en Chine, à l'aide de données de suivi avec téléphone mobile. La probabilité d'un cas sporadique causant une résurgence de la COVID-19 après la réouverture de la ville a exigé la mise en œuvre de différents scénarios d'intervention en santé publique.	Si la ville rouvre sans qu'un système de recherche des contacts n'ait été mis en œuvre, il y a moins de 50 % de chance que la résurgence soit atténuée en raison des cas sporadiques. Rouvrir la ville une fois que la recherche des contacts des ménages a été effectuée, que tout le monde porte un couvre-visage et après avoir obligé l'exécution de tests de dépistage dans les 28 heures suivant l'apparition des symptômes, a cependant réduit la probabilité d'une résurgence des cas à 5 %. Le même niveau d'atténuation (résurgence de 5 %) est obtenu lorsque 80 % des personnes portent un couvre-vidage et que 40 % des personnes se font test, si la recherche

		des contacts est élargie pour inclure les contacts au travail ou à l'école. Cette relation permet d'obtenir une atténuation équivalente avec une diminution du port du couvre-visage et des tests de dépistage, dans la mesure où les efforts de recherche des contacts augmentent en conséquence.

Méthodologie :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient :
[(test ET (trace OU tracing OU contact)) OU (contact tracing ET review) OU mass testing OU active test] [TITRE]. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue. Les revues systématiques et les revues rapides pertinentes ont été identifiées et résumées et de nouvelles recherches datant de l'automne 2020 et de l'hiver 2021 ont également été sélectionnées pour mettre à jour les résultats de la revue. Une analyse croisée des études figurant dans les examens n'a pas été effectuée. Cette synthèse contient des recherches publiées jusqu'au 10 février 2021.

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Emerging Evidence on COVID-19

Evidence Brief on Ethnicity and COVID-19

Introduction

This evidence brief aims to summarize the literature on associations of ethnicity with risk of COVID-19 infection, severity, and mortality in Canada and globally.

This evidence brief contains literature up to September 7, 2020. Ethnicity in the included studies is mostly defined by the census bureaus of the included countries and is a self-reported variable based on the individual's identification with a social/cultural group from a predefined list. For consistency in this document the main categories of reported ethnicities will be referred to as Black, White, Asian, and Hispanic. Others or more specific minority ethnic group categories e.g. East Asian, South Asian, indigenous people and Pacific Islanders were also reported and are specified in the summary tables. Please see the Appendix for a table of acronyms and additional definitions.

This review summarizes observational studies (including cohort, cross-sectional, case control and case series) analysing individual-level data where examination of ethnicity was an objective of the study rather than just a potential confounder that was used in the multivariate model. Ecological studies, studies that use aggregate data, were excluded from summarization because these studies may suffer from a high risk of bias and the results cannot be extrapolated to the individual level. In an effort to collect all the available Canadian studies and reports, grey literature and ecological studies on the Canadian population were included in this review.

Key Points

- Regarding ethnicity and COVID-19, two systematic reviews with literature up to May 15 and June 15, sixty-seven individual studies published since May 15 and four of five Canadian studies or reports were identified in the grey literature and are included in this review. There were 34 studies that assessed COVID-19 risk of infection, 31 on severity of disease and 22 studies on mortality (Table 1 & 2). Most of the research came from the USA and UK. There were two studies from France and one study from Brazil. Studies from Canada included a prepublication of an ecological study and two cross-sectional surveys and two relevant surveillance reports were identified in the grey literature (Table 3).
- This is the second version of this review. The first included a systematic review that summarized studies to May 15 and primary research published May 15 -30. This update added studies published between June 1 and Sept 7 including an additional systematic review with studies up to June 15. Analysis of studies captured in the tables and the new systematic review identified 15 studies which are marked with an asterisk (Tables 1 & 2).

Risk of Infection

- One systematic review included risk of infection and concluded across studies Blacks, Asians and Hispanics were more likely to test positive for COVID-19 compared to Whites (D. Pan, 2020).

- Twenty-nine studies examined risk of infection among different ethnic groups from people tested by RT-PCR for active infection (Table 1) and four seroprevalence studies measured risk of exposure (Table 2). Multivariable analyses with age, sex, comorbidities and socioeconomic variables attenuated associations with specific ethnicities, but in many studies the association was still significant:
    - Among twenty studies from the USA, compared to Whites, a higher risk of infection among Blacks (six adjusted and three univariate results) and Hispanics (six adjusted and six univariate results) were reported and conflicting data on Asians (two adjusted, and one univariate association and two no association results). One USA study reported a higher risk of infection among American Indians and Alaskan natives (Hatcher, 2020).
    - Fourteen studies from the UK, compared to Whites, consistently identify Black (nine adjusted results), South Asian (four adjusted results), Asian (three adjusted results) and more generally BAME groups (one adjusted and two univariate and one no association result) at higher risk of infection, whereas the results for other ethnicities were rarely reported.

COVID-19 Severity Outcomes

- Outcomes of COVID-19 severity (hospitalization, ICU admission and mechanical ventilation) were reported in two systematic reviews and thirty one studies reported associations for different ethnicities compared to Whites (Table 1).
    - For hospitalization: The systematic review reports meta-analyses of univariate associations compared to Whites for Blacks (overall countries) and for Asians (UK only), with a significantly higher magnitude association from UK studies and the adjusted analyses (age, sex and comorbidities) reported no association. Across individual studies from the USA, Blacks were found to have higher risk of hospitalization; for Asians and Hispanics there were mixed results. Mixed results from two USA studies reported on the proportion of American Indians, Alaskan Natives hospitalized (Alvarez Retamales, 2020; Karaca-Mandic, 2020). No association with Pacific Islander hospitalizations was reported in two studies (Alvarez Retamales, 2020; McPadden, 2020). In the UK, Blacks and South Asians had a higher risk of hospitalization; for Asians, mixed ethnicity or BAME groups the findings were inconsistent.
    - For ICU admission: The systematic review findings reported Asian and BAME ethnicities in UK studies were over-represented in the ICU, however the meta-analyses reported no association in adjusted analysis for Blacks, Hispanics and Asians (USA only). New studies in the USA had conflicting results for Blacks and Hispanics. In the UK, Blacks, South Asians and BAME had higher risk of admission.
    - For mechanical ventilation: Eighteen studies in the systematic review reported no association for Blacks and Hispanics, however Asians (four studies) had an association with ventilation that persisted with age and sex adjusted analysis. Few recent studies looked at the risk of ventilation by ethnicity; one from the USA reported no association for Blacks and Hispanics

and a study from the UK indicated Blacks and Asians were at increased risk compared to Whites.

- Multisystem Inflammatory Syndrome in Children (MIS-C) and ethnicity was reported in three studies one prospective cohort (ISARIC study, (Swann, 2020)) and two small case series from the UK and France (Riphagen, 2020; Toubiana, 2020). Across these studies a disproportionate number of MIS-C cases occurred in non-White ethnicities. No further analysis was conducted in these studies.

COVID-19 Mortality

- The systematic reviews reported no association with Blacks or Asians, and a protective association identified for Hispanics in univariate analyses, however the association did not persist in models adjusted for age, sex and comorbidities. An association with Asians who required mechanical ventilation due to COVID-19 was reported (4 studies). It is important to note there was high heterogeneity across studies and both reviews describe approximately 50% of studies reporting an association and the others report no association.
- In the USA and the UK twenty-two studies analysed mortality among hospitalized patients and did not report an association with ethnicity. However, when considering a population level denominator, certain ethnic groups were more likely to acquire COVID-19 disease, so proportionally they represent a higher than expected number of COVID-19 deaths. In UK studies that identified an association across all COVID-19 cases, there was an increased risk of mortality among BAME, Blacks, South Asians and Asians compared to Whites (Table 1).

Canadian studies

Despite an additional grey literature search, limited Canadian evidence was identified. Available Canadian data suggest non-White ethnicities, with the exception of East Asians, are disproportionately infected with COVID-19. The analyses largely did not adjust for comorbidities or socio-economic factors that attenuated results in other studies in this review. No Canadian data on ethnicity and hospitalizations, severity or mortality was identified.

- A cross-sectional survey designed to compare COVID-19 impacts on Black Canadians to a representative "national" sample reported a higher likelihood of COVID-19 among Black Canadians individually and among people they know. Black Canadians had a higher frequency of risk factors such as taking public transportation and having a job that requires face-to-face interactions with people. They also had a higher frequency of severe financial impacts associated with the pandemic. These data are consistent with similar studies published in the USA (Table 1).
- Toronto Public Health dashboard shows that a higher proportion of COVID-19 cases than the representation in the community was seen for Black, Hispanic, Southeast Asian, South Asian/ Indo-Caribbean and Middle Eastern ethnic groups.
- The ecological study analysed population data on number of COVID-19 cases and deaths in Canada by population level demographic information including proportion Black, proportion foreign-born,

proportion over 65 years, population density and median income. Findings from their multivariable analysis include:

- 1% increase in the proportion Black in a health unit was associated with double the case count. A 1% increase in the proportion foreign-born residents was associated with a 3% increase in the case count.
- A 1% increase in the proportion of Black residents in the health region was associated with 2.1x increase in COVID-19 death rates.

Overview of the Evidence

Seventy-four studies, including two systematic reviews published up to September 7, 2020 were included in this review. Two systematic reviews were evaluated using the AMSTAR tool, they were of moderate to high quality. One ecological study from Canada was included to allow for awareness of Canadian research, ecological studies use aggregated data for analysis, they have a high risk of bias and ecological fallacy and their findings are cannot be extrapolated to the individual level.

This review focused on studies with datasets at the individual level, this included a range of observational study designs: moderate-high quality large prospective cohorts, moderate to low quality retrospective cohorts and cross-sectional studies and low quality retrospective case series.

This literature has evolved quickly, the more recent large cohort studies have sufficient power to control for many potential confounding variables. These studies provide better estimates of the association than studies reporting crude or minimally adjusted estimates. The large cohort studies are in moderate agreement across studies and offer some confidence that future research will not change the conclusions of this review. Knowledge gaps remain on this topic, such as why some ethnic groups may be at a higher risk of infection given that confounding variables such as socio-economic factors and co-morbidities do not entirely account for this association. Potential genetic factors, related to comorbidities, ACE2 activity, pro-inflammatory cytokine response or other differences in immune system function that may be associated with the immune profile of high risk ethnic groups have been suggested, but not been explained in the literature (Tal, 2020).

CONTENTS

ETHNICITY AND COVID-19 RISK OF INFECTION, SEVERITY OF DISEASE AND MORTALITY

Two systematic reviews and sixty-one observational studies are included in the table below and report on the risk of COVID-19, hospitalizations, severe disease, ICU admission, ventilation, acute kidney injury or mortality.

The systematic reviews include studies published up to May 15 and June 15 (D. Pan, 2020; Raharja, 2020). Only 15 studies overlap the results in Table 1 and the systematic review (Raharja, 2020), the systematic review included ecological studies (results not summarized), as well as studies that did not focus on the association between ethnicity and COVID-19 were included in their meta-analyses.

Most of the research on ethnicity has come from the USA and UK, with two studies from France and Canada, and one study from Brazil (Table 1). Increasingly studies have focused on exploring why ethnicity may be associated with the risk of COVID-19 infection, severity or mortality. Potentially confounding or mediating variables included in multivariable models are age, sex, comorbidities, and socioeconomic factors. The actual variables used for socio-economic factors varied from study to study e.g. income, neighbourhood status, and other composite indices and in some studies they were more complex measures of societal factors that result in barriers to access to medical care, health seeking behaviors or other disparities. The variability in the risk factors tested in the models, and differences in the final model across studies makes direct comparison of results difficult, as seen in the meta-analyses that frequently had high between study heterogeneity. It is also notable that in studies that control for age, sex, comorbidities and socio-economic factors in their analysis, some ethnic groups are still at higher risk of COVID-19 disease.

Table 1 below lists the studies on COVID-19 infection, severity and mortality by country. A summary of their contents is briefly listed below.

- Risk of infection or likelihood of testing positive was assessed in the USA (n=18 studies), UK (n=11) and France (n=1) and one systematic review.
    - Black, Asian and Hispanic ethnicity were shown to have a higher likelihood of testing positive in one systematic review (D. Pan, 2020).
    - Sixteen studies examined testing data in the USA and analysed the probability of testing positive. There was a range of analyses and outcomes were often adjusted for a range of individual, health and socio-economic factors. Despite this, significantly more test positives (in the magnitude of 1.5-3.5 times higher risk) compared to Whites were reported for Blacks in nine studies, Hispanics in eleven studies, Asians in two studies, Native American/Alaskan in one study (Table 1).
    - Eleven studies examined testing data in the UK and reported higher probability of testing positive compared to Whites among BAME groups (3/4 studies), Blacks (seven studies), South Asians (two studies) and Asian (one study).
    - One survey of US and UK populations reported an adjusted (sex, comorbidities, BMI, smoking) higher risk of being COVID-19 positive among Black and Hispanics, not Asian or other

ethnicities compared to Whites in the USA. In the UK, different ethnicity categories were used; higher risk was reported in Black, South Asian, Chinese, Middle Eastern and Other, not East Asian or Hispanic (Lo, 2020).

- One study in France of kidney transplant recipients reported that non-white ethnicity was associated with higher odds of COVID-19 disease after adjusting for age, sex and comorbidities (Elias, 2020).

- Risk of severe disease was measured as hospitalizations, ICU admission or mechanical ventilation was reported, and across studies, mixed results were often identified. The summaries listed below have been grouped by the denominator for the sampling frame, the entire population, the number of positive COVID-19 cases or hospitalized for COVID-19, as this was considered a potential source of heterogeneity. The analysis, univariate vs. adjusted results is also a source of heterogeneity across studies as estimates adjusted for comorbidities or socio-economic factors usually resulted in the association with ethnicity attenuated towards the null.
  - For hospitalization: The systematic review reported an association with Blacks (RR: 1.68 [95%CI: 1.28-2.20], I^2=98, k=13) in univariate analysis and subgrouping by country RR UK 5.47 [95%CI: 2.51; 12.06] vs. RR USA 1.36 [95%CI: 1.08; 1.72] showed higher magnitude in the association among UK studies. In studies that adjusted for age, sex and comorbidities no association was reported. No association with Hispanics (RR: 1.00 [95%CI: 0.95-1.06], I^2=0, k=8) in the univariate analysis, but there was an association in the adjusted analysis. No association with Asians was determined overall or in adjusted analyses. However, when sub-grouped by country an association with Asians was seen in UK studies: RR UK: 2.95 [95%CI: 1.55-5.53] vs. RR USA: 0.90 [95%CI: 0.82-1.66]. No association with ICU admission and mechanical ventilation was identified in adjusted meta-analyses, except for UK studies that identified an increased risk among Asians and over-representation of BAME groups.
  - Eight USA studies provided analysis of ethnicity by severity in a population. Hospitalizations compared to Whites were higher for Blacks (n=4/4 studies), Hispanics (n=3/4), Native American/Alaskans (n=1/2), Pacific Islanders (0/2) and other ethnicities (n=1/1). Whereas in one study lower than expected hospitalization was reported for Asian ethnicity. More severe outcomes were reported for Blacks (n=2/2), Hispanic (n=2/2) and Asians (n=2/2) compared to Whites. ICU admittance was significantly more common in Blacks (n=2/3) and Hispanics (n=1/2) and ventilation was reported to be more common for Black and Hispanics in one study.
  - Ten USA studies looked at hospitalization and risk of ICU among confirmed cases of COVID-19. Hospitalizations occurs significantly more among Blacks (n=5/7 studies), Hispanics (n=3/5), Asian (n=1/2), mixed ethnicity and overall (n=1 each). There was no association with ethnicity and risk of ICU admittance among the hospitalized COVID-19 cases.

  - Two UK studies noted higher hospitalization rates for children of BAME groups compared to Whites and similarly a second study reported higher risk of hospitalization among Black and mixed ethnicity groups, but not for Asians.
  - Eight UK studies report on hospitalizations and ICU admittance among confirmed cases of COVID-19. The UK results found no association among BAME groups (n=2/2 studies) and high risk associations with Blacks (n=2/2), S. Asians (n=2/2) and Asians (n=1/1). ICU admission were also associated with BAME groups (n=4/4), South Asian (n=2/3) and Blacks (n=2/2). Higher odds of mechanical ventilation was reported for Blacks and Asians in one study.

- MIS-C, multisystem inflammatory syndrome in children, and a potential association with ethnicity was reported in three studies, two from the UK and one from France. Across these studies, higher frequency of non-white ethnicities diagnosed with MIS-C was reported; this difference was significant in the largest study.
- Mortality was reported similar to severity where the denominators were either the general population or a hospitalized population of COVID-19 cases.
  - The systematic reviews report no association with mortality for Blacks and Hispanics in adjusted analyses, and a higher risk among Asians who were mechanically ventilated compared to Whites with significant heterogeneity between studies and a notable higher mortality risk among different ethnic groups from the UK studies (Raharja, 2020).
  - Seven USA studies reported an analysis of mortality among hospitalized COVID-19 cases and ethnicity. One reported higher odds among Blacks, one reported lower odds among Hispanics and most reported no associations with Blacks (n=5), Hispanics (n=4) or all minority ethnic groups (n=1).
  - One study in the US reported mortality across all positive COVID-19 cases and found no association with Black ethnicity.
  - Seven UK studies report an analysis of mortality among hospitalized COVID-19 cases and ethnicity. An association with higher risk of mortality was reported for South Asians (n=2/3 studies), Blacks (n=1/4), Asians (n=2) and no association was reported for East Asians (n=1), Mixed ethnicity (n=2) and BAME groups (n=1).
  - Six UK studies report COVID-19 mortality across the general population. Higher associations were noted for Blacks (n=3/4 studies), South Asians (n=2/2), mixed ethnicity (n=1/2), BAME (n=1/1) and Asians (n=1/2), where the studies for Asians and mixed ethnicity were conflicting results reporting both protective and higher risk associations compared to Whites across two studies each.
  - A single study from Brazil reported an association with higher mortality among mixed and Black ethnicities.

Table 1: The association of ethnicity and risk of COVID-19 infection, severity and mortality in systematic reviews (n=2) and observational studies (n=61)

Reference	Study information	Key Outcomes
Susceptibility, Clinical Severity and Mortality associated with COVID-19		
Systematic Review		
(Raharja, 2020) preprint new	A systematic review and meta-analysis on the association between ethnicity and poor outcomes. (AMSTAR – high quality) Data up to June 15, 2020. 72 articles (13 ecological) from the USA (54), UK (15), Brazil (1) and Israel (1) were included, although the data from the later two are not presented in the results. Outcomes included mortality, hospitalization, ICU, respiratory and kidney failure. Analysis results focus on Black, Asian and Hispanic as there were very few studies for other native ethnic groups or studies outside the USA and UK. Random effects meta-analysis was conducted on quantitative outcomes in 45 studies. Studies not included in the meta-analyses were descriptively summarized. Their results are also noted if an association was identified and/or is different than the meta-analysis.	The evidence does not confirm ethnicity is an independent risk factor for poor outcomes in COVID-19 patients. Meta-analyses generally had high heterogeneity (I^2 > 60%) and where examined, adjusted analyses for age, sex and comorbidities attenuated univariate associations. Significant associations are shown below, other results of analysis are available in the paper. Hospitalization (20 studies): Compared to Whites, - Associated with Blacks (RR: 1.68 [95%CI: 1.28-2.20], I^2=98, k=13) in univariate analysis (RR UK 5.47 [95%CI: 2.51; 12.06] vs. RR USA 1.36 [95%CI: 1.08; 1.72] was significantly different). Studies that adjusted for age, sex and comorbidities report no association. - No association with Hispanics (RR: 1.00 [95%CI: 0.95-1.06], I^2=0, k=8) in the univariate analysis, but was significant in the adjusted analysis. - No association with Asians was determined overall or in adjusted analyses. However, when sub-grouped by country an association was seen in UK studies: RR UK: 2.95 [95%CI: 1.55-5.53] vs. RR USA: 0.90 [95%CI: 0.82-1.66]. ICU (18 studies): Compared to White ethnicity, - A univariate association with Blacks (RR: 1.51 [95%CI: 1.11-2.04], I^2=94, k=10) was observed, however there

		was no association after adjusted for age, sex and comorbidities. - The unadjusted and adjusted association with ICU admission not significant for Asian or Hispanic in the US. The UK studies reported an increased risk of ICU in Asians. - 5 UK studies not included in the meta-analysis, reported over-representation of BAME communities in ICU cohorts. 2 USA studies did not find an association with Blacks. Mortality (51 studies): Compared to Whites, - A protective association with overall mortality was observed across the unadjusted data: Hispanics (RR: 0.69 [95%CI: 0.57-0.84], I^2=76, k=11), however the association did not persist in models adjusted for age, sex and comorbidities. - Asians who were mechanically ventilated cases were at higher risk of mortality in four studies (RR: 1.39 [95%CI: 1.07-1.80], I^2=14, k=4). - No other associations with mortality was found in the meta-analysis conducted on overall mortality, hospitalized cases, ICU cases, mechanical ventilation cases or acute kidney injury cases and Black, Asian or Hispanic ethnicity. Mechanical Ventilation (18 studies): Compared to Whites, - An association with Asians (RR: 1.39 [95%CI: 1.07-1.80], I^2=14, k=4) was seen in the univariate and age/sex adjusted analysis.

		- No association with risk of ventilation was observed for Blacks or Hispanics, even in adjusted analysis (age, sex and comorbidities). Acute Kidney Injury (AKI) (8 studies): Compared to Whites, - No association with AKI was observed for Asians. - An association was reported for Blacks (RR: 1.35 [95%CI: 1.04-1.76], I^2= 92%, k=5) in the univariate analysis that did not persist in adjusted (age, sex and comorbidity) analysis.
(D. Pan, 2020)	A systematic review of ethnicity and clinical outcomes of COVID-19. (AMSTAR rating – medium quality: registered protocol may or may not have been done *a priori*, studies included for each outcome is not clearly reported and no discussion of heterogeneity). Data up to May 15, 2020 162 studies (80 in preprint) Supplementary files 2-6 describe each of the studies included in this SR. Searches included primary literature, clinical trials, preprints and grey literature. Analysis was descriptive and does not report the results of individual studies, number of studies or which studies contribute to each outcome. Few studies that examined ethnicity were published as of May 15, 2020.	Compared to Whites, several studies reported Blacks, Asians and Hispanics are more likely to: 1. Test positive for COVID-19 Mixed evidence was identified for 1. Hospitalization 2. Intubation 3. ICU 4. Mortality - Ethnicity and risk of infection with SARS-CoV-2: in one published study (S. de Lusignan, 2020b) Blacks were more likely to test positive and similarly in preprints higher susceptibility was reported in 14 studies for Blacks, 3 for Asians and 3 for Hispanics compared to Whites. - Hospitalization, intubation and ICU rates by ethnicity were conflicting across studies. A large cohort in the UK report higher proportion of non-white patients admitted to the ICU. - Mortality: 8 studies found no association with mortality, and others recorded an association for

		Blacks (n=6), Asian (n=3) compared to Whites. Grey literature in the US and UK are reporting higher mortality in non-White ethnicities (mainly Black and Asian).
United States (USA)		
(Petrilli, 2020)	USA, New York, multi-center health network, prospective cohort, case data up to Apr 8, follow-up to May 5. N=5279 admitted to hospital for COVID-19 COVID-19 positive tests n=5279 Hospitalizations n=2741 Hospice or death n=665 Ventilation n=647	- Risk of hospitalization among COVID-19 positive cases was significantly higher in Hispanic aOR 1.63 (95%CI 1.35-1.97) and other/mixed aOR 1.6 (95%CI 1.21 – 2.11) compared to Whites. Multivariable logistic regression adjusted for age, sex, smoking, week of outbreak and BMI.
(Goldfarb, 2020)	Single medical center, prospective cohort of pregnant women. Mar 6- May 4, 2020. 65 Hispanic (represent 18% of the population) and 127 non-Hispanic women presented with COVID-19 symptoms – not everyone was tested. No statistical analysis was performed due to sample size. Ethnicity was not shown to be a factor in this disparity which may be explained by socio-economic factors.	- Hispanic women were more likely to test positive (72%) 39/54 vs. 27% (22/82) for non-Hispanic women ($p<0.001$). This mirrored the increasing number of cases in the Hispanic population vs. non-Hispanic population in the general public after social distancing interventions were introduced. - Of those that tested positive, a similar proportion were admitted to hospital. 13/39 Hispanic and 8/22 non-Hispanic women. Of these, 5 Hispanic and 1 non-Hispanic case were admitted to ICU. No deaths.
(Bandi, 2020)	USA, Chicago, prospective cohort single hospital, pediatric COVID-19 cases. All children tested for SARS-CoV-2 were enrolled Mar 12- Apr 20, 2020. N=474 children examined, 5.2% (25) were COVID-19 positive. (n=5 children were hospitalized.) Proportion in sample: White 25.1%	- Compared to Whites, Blacks had a significantly higher positive test rate (6.8% vs. 1.7%, p=0.046). - Blacks had a higher adjusted odds aOR 3.1 (95%CI 1.23-5.34) of a positive test, adjusted age and sex. - Hispanics were similar by not significant.

	Black 43.2% Hispanic 24.7% Asian 1.5%	- Hospitalizations: 80% (20/25) were Black, which is higher than expected, but this outcome was not further analysed by the author.
(Lo, 2020) preprint new	Longitudinal survey targeting the general population in the USA and UK using an app that prompts input from users daily. Data collected March 24- May 25, 2020. All self reported. Respondents: USA = 179 873, UK= 2 234 728 Multivariable model by country: Adjusted for sex, history of diabetes, heart disease, lung disease, kidney disease, and current smoker status (each yes/no), and body mass index (17-18.4, 18.5-24.9, 25-29.9, and ≥30 kg/m2). Multivariable model combined USA and UK: also adjusted for isolation, frontline healthcare worker, community exposure to COVID-19, population density, income, and education.	- Risk of reporting a positive COVID-19 test (Odds Ratio and 95%CI): o USA: Black 2.49 (1.68-3.69), Hispanic 1.66 (1.18-2.34), Asian 1.42 (0.86-2.35) Other 1.32 (0.67-2.61). o UK: Black 1.97 (1.47-2.64), Hispanic 1.71 (0.89-3.27), South Asian 1.68 (1.43-1.97), Chinese 1.79 (1.08-2.96), East Asian 1.02 (0.55-1.87), Middle Eastern 2.10 (1.52-1.87), Other 2.10 (1.52-2.91) o USA and UK data combined compared to Whites: Blacks 1.17 (1.10-1.25), Hispanic 1.11 (1.00-1.23), Asian 1.06 (1.03-1.10), Other 1.21 (1.17-1.25) - Risk Factors: Black and Hispanic participants were more likely to be obese and have diabetes. - All ethnic minorities reported lower social isolation, were over-represented by front line health care workers and reported a higher likelihood of contact with a case of COVID-19.
(Martinez, 2020) new	Longitudinal study of the general population serviced by Johns Hopkins Health System (5 hospitals and 30 clinics) from March 11- May 25, 2020. Data represents 32 727 people tested by RT-PCR for SARS-CoV-2 (over time this increased from only high risk to all symptomatic individuals).	- The positivity rate was significantly different ($p<0.001$) across groups compared to the Hispanic ethnicity 42.6% (95% CI, 41.1%-44.1%), Whites (8.8% [95% CI, 8.4%-9.2%]), Blacks (17.6% [95% CI, 16.6%-18.3%]), or other ethnicity (17.2% [95% CI, 16.2%-18.3%]). It is unclear whether high positivity in Hispanics is due to

	Statistics: proportion positive and hospitalized was analysed by ethnic category using omnibus ANOVA with a correction for multiple comparisons.	higher prevalence of disease or lower rates of using healthcare. - Hospitalizations was lower for Hispanics (29.1% [95% CI, 27.0%-31.2%]) than Whites (40.1% [95% CI, 37.6%-42.5%]) or Blacks (41.7% [95% CI, 39.5%-43.8%]).
(Lee, 2020) preprint new	USA, retrospective cohort analysis of patient records from 12 Midwest hospitals and 60 clinics between March 4, and August 19, 2020. The primary outcome was COVID-19 severity using hospitalization within 45 days of diagnosis. 5,577 COVID-19 patients were included and 866 (n=15.5%) were hospitalized within 45 days of diagnosis. Of those hospitalized, 43.9% (n=381) were White 19.9% (n=172) were Black 18.6% (n=161) were Asian 11.8% (n=102) were Hispanic Model was adjusted for age, gender, comorbidity, relationship status, and rurality/ urbanity.	Independent of neighborhood deprivation, minority race/ethnicity of patients was associated with increased COVID-19 disease severity. - Hispanic (OR 3.8, 95% CI 2.72–5.30) - Asians (OR 2.39, 95% CI 1.74–3.29) - Blacks (OR 1.50, 95% CI 1.15–1.94)
(Hatcher, 2020) new	USA, retrospective cohort analysis of COVID-19 among the American Indian and Alaska Native (AI/AN) populations from 23 states (n=345,093). Findings on incidence of SARS-CoV-2 infection reported between January 22 and July 3, 2020 show a 3.5 times increased incidence of COVID-19 among AI/AN persons.	Cumulative incidence of COVID-19: - AI/AN persons: 594 (95%CI 203–1,740 per 100,000 AI/AN population) - White 169 (95% CI 137–209) per 100,000 white population - AI/AN had significantly higher relative risk of getting COVID-19 RR 3.5, 95%CI 1.2–10.1 compared to Whites.

(McCarty, 2020) new	USA, retrospective cohort analysis of 9 Massachusetts hospitals including 379 COVID-19 patients. Association of race/ethnicity of patients and hospitalization outcomes (i.e. in-hospital mortality, ICU admission, or mechanical ventilation).	- On multivariable analysis controlling for age, gender, obesity, cardiopulmonary comorbidities, hypertension, and diabetes, no significant differences in in-hospital mortality, ICU admission, or mechanical ventilation by race/ethnicity were found.
(Karaca-Mandic, 2020) new	USA, retrospective cohort examined the racial/ethnic prevalence of cumulative COVID-19 hospitalizations in 12 states between April 30 and June 24, 2020. The proportion of hospitalizations by ethnicity was compared to the proportion of each ethnicity in the population. Ethnicities reported on: Hispanic, White, Black, Asian, American Indian/ Alaskan Native. Data are descriptive and not adjusted.	Hospitalizations: Whites had a substantially smaller proportion hospitalized compared to their share of state population in all 12 states. - The percentage of hospitalizations among Black patients exceeded the percentage of their representative proportion of the state population in all 12 states. - Hispanic hospitalizations exceeded their representative proportion in 10 states, this was very pronounced in Virginia, Utah, and Rhode Island. - Asians hospitalized for COVID-19 were approximately equivalent or lower than their proportion in the population. - American Indians and Alaskan Native populations were reported in 8 states with large disparities in Arizona and Utah.
(Gottlieb, 2020) new	USA, retrospective case-control study conducted at Rush University Medical Center in Chicago, Illinois between March 4 and June 21, 2020, explored risk factors associated with hospitalization.	- Hispanic ethnicity was a risk factor for hospital admission (OR = 1.52, 95% CI = 1.18 to 1.92).
(Rozenfeld, 2020) new	USA, retrospective cohort study conducted between February 28 and April 27, 2020, to characterize risk factors in 34,503 patients in the Providence Health System.	Risk of SARS-CoV-2 infection compared to White patients: - Asian (OR 1.43; 95% CI 1.18–1.72, p = 0.0002) - Black (OR 1.51; 95% CI 1.25–1.83, p < 0.0001) - Hispanic (OR 2.07; 95% CI 1.77–2.41, p < 0.0001)

(McPadden, 2020) preprint new	USA, retrospective cohort study conducted at the Yale New Haven Health (YNHH) on 7,995 patients with SARS-CoV-2 between March 1 and April 30, 2020. The study assessed hospitalization and in-hospital mortality.	Race/ ethnicity with increased risk of hospitalization: - Asian (OR 1.58, 95%CI=1.02-2.41) - Black (OR 1.43, 95%CI 1.14-1.78) - Hispanic (OR 1.81, 95%CI 1.50-2.18) In the discharged population, age-adjusted, in-hospital mortality was similar among all racial and ethnic groups. In-hospital, age adjusted mortality rates: - White = 4.3% - Black = 3.3% - Hispanic = 3.4% - Asian = 4.6% - Hawaiian = 4.0% - Pacific Islander = 3.1%
(Emeruwa, 2020) new	USA, New York retrospective cohort study of women (n=100) delivering at two New York-Presbyterian–affiliated hospitals in Manhattan from March 13 through April 23, 2020. The SARS-CoV-2 infection rate per racial–ethnic group of women delivering was analyzed.	- There was a significantly higher SARS-CoV-2 infection rate among Hispanic women compared with non-Hispanic White women (18.1% vs 9.4%, P< 0.01). - The rate of positive SARS-CoV-2 infection results in non-Hispanic Black women (12.7%) was not significantly different.
(Mendy, 2020) preprint new	Retrospective cohort of hospitalized cases at the University of Cincinnati health system (4 hospitals) March 13 to May 31, 2020. N=689 cases (RT-PCR positive) Logistic regression modeling adjusted for covariates: age, sex, ethnicity, smoking, comorbidities.	- Hospitalizations (31.3% total): Adjusted analyses Black OR 2.23 (95%CI 1.41-3.53) and Hispanic OR 1.91 (95%CI 1.11-3.29) compared to Whites - Severe COVID-19: Adjusted analyses Black OR 3.15 (95%CI 1.71-5.79) and Hispanic OR 2.78 (95%CI 1.29-5.96) compared to Whites - ICU (13.2% total): Adjusted analyses Black OR 3.32 (95%CI 1.56-7.07) and Hispanic OR 3.44 (95CI 1.42-8.34) compared to Whites

		- Deaths: adjusted analysis Blacks OR 3.44 (95%CI 1.32-9.00)
(Kalyanaraman Marcello, 2020)* preprint new	Retrospective cohort, New York's public hospital system data, New York City, March 5- April 9 with follow-up to April 16, 2020. 22254 patients tested in the hospital catchment area, 13442 positive SARS-CoV-2. Black and Hispanics comprised approximately a third of the COVID-19 cases, which is an over-representation of these ethnicities compared to the NYC population. Descriptive analysis, Chi-square test used. No multivariable analysis was conducted.	- Positive Test 13442/22254 (61%). 26% Black, and 34% Hispanic. Both had significantly higher proportion of positive tests than Whites P<0.001. The higher proportion may be due to Blacks and Hispanics were more likely to present for testing at the ER rather than outpatient clinics. - Hospitalization 6248/13442 (46%). 31% Black, and 34% Hispanic. A significantly higher proportion of Blacks were hospitalized P<0.001, no association for Hispanic. - Deaths 1724/6248 (28%). 29% Black, and 31% Hispanic.
(Price-Haywood, 2020)	Retrospective cohort, Louisiana, USA, Ochsner Health system, March 1- April 11. N=3481 positive COVID-19 tests in the catchment area The population serviced by this hospital are 31% Black and 65% White. Analysis: - Multivariable logistic regression (hospitalization) adjusted by age, sex, comorbidity index score, low-income residence, public health insurance. -Survival analysis (mortality), adjusted by age, sex and comorbidity index score.	- The racial profile of positive COVID-19 tests 70.4% Black, 29.6% White. - Hospitalization (N=1382) 76.9% Black. Blacks had a higher odds OR 1.96 (95%CI 1.62-2.37) of being hospitalized. - ICU (N=474) 80.2% Black. - Mechanical Ventilation (N=364) 81.6% Black. - Death (N=326) 70.6% Black. In the survival analysis, Black race was not independently associated with mortality (HR= 1.14, 95%CI 0.88-1.49).
(Azar, 2020)*	Multihospital, retrospective cohort. San Francisco USA, patients Jan 1- Apr 8, 2020	- Hospitalization of Black 52.5% (n = 32) vs. 25.7% (n = 110) of White patients.

	Overall data: n=14036 tested for COVID-19 n=1025 COVID-19 n= 256 hospitalized n= 110 ICU	- Black case hospitalization odds was 2.7 (OR) times higher compared to White cases, multivariable model adjusted for age, gender, and sociodemographic variables. Note: Black cases were more likely to be captured at the ER in severe condition rather than in a non-ambulatory setting, which may explain this association. - ICU admittance was higher for Black cases 24.6% vs. the White cases 10.7%. - Black cases with COVID-19 lived in ZIP codes with lower income compared to all other racial and ethnic groups (p<0.001). - There was no significant difference in mortality across ethnic groups.
(Rentsch, 2020)* preprint	USA, 6 million US veterans, Feb 8- May 4. Retrospective cohort. N= 5630 COVID-19 cases from 62098 tested. Ethnicity: Whites 74%, Black 19%, Hispanic 7%. Estimates were adjusted by demographic, medical and high risk behaviours, socio economic variables.	- Tests per 1000 were higher for Blacks 16.4 (95%CI 16.2 - 16.7) and Hispanic 12.2 (95%CI 11.9 - 12.5) vs. White 9.0 (95%CI 8.9 - 9.1) - Compared to Whites, Blacks were more likely to test positive aOR 1.96 (95%CI 1.81-2.12) as were Hispanics aOR 1.73 (95%CI 1.53 – 1.96). - There was no significant difference in 30 day mortality by ethnic group among the COVID-19 cases.
(Gu, 2020)* preprint new	Retrospective cohort, Michigan USA, March 10- April 22, 2020. N= 5698 tested patients (randomly selected unmatched controls n=7211 and frequency matched controls by race, age and sex n=13351) logistic regression, adjusted for age, sex and socioeconomic characteristics.	- Risk factors for testing positive: Black test positive rate (42.6%) was significantly higher than Whites (13.7%, P<0.001) - Hospitalized Blacks 52.2% vs. Whites 39%, p<0.001 and OR 1.66 (95% CI, 1.09-2.52) - ICU Black 27% vs. Whites 14.8% p<0.001 and OR 1.52 (95%CI 0.92-2.52)

		- Mortality Blacks 5.3% vs. Whites 3.0%, p<0.12 and OR 1.17 (95%CI 0.4-3.45)
(Joseph, 2020) new	USA, single institution retrospective cohort study to study whether non-White COVID-19 patients present with increased severity on admission chest X-ray than White patients, between March 27-April 10 2020, total n=326 (210 non-White; 116 White)	- Non-White patients hospitalized with COVID-19 infection were more likely to present with higher severity of disease on admission chest X-ray than White/Non-Hispanic patients (adjusted average difference 1.6, 95% CI 0.5–2.7, p<0.01).
(Antwi-Amoabeng, 2020) preprint	Single Center, retrospective cohort study Nevada USA, n=172 COVID-19 patients Mar 12- May 8 Hispanic vs. non-Hispanic Overall outcomes: - 121 hospitalized - 28 ICU 18 died	- Significantly more Hispanics were COVID-19 cases (50.6%) than would be expected, they represent 25.7% of the population. - Mortality significantly higher in non-Hispanic group (15.3% vs. 5.8%), p=0.048. *Analysis accounting for the Hispanic group being significantly younger, fewer comorbidities, more likely to be uninsured and live in low income communities compared to the non-Hispanic group was not conducted.
(Kim, 2020)*	US COVID-NET (surveillance across 14 states): 2491 hospitalized cases March 1- May2. N=16318 COVID-19 cases n= 2491 COVID-19 cases with complete records that were discharged as of May 3, 2020 were analysed. Of these 47% White, 30% Black and 12% Hispanic. n= 798 ICU n= 420 died n=246/462 died of those receiving mechanical ventilation Multivariable logistic regression controlling for age, sex, and underlying conditions, smoking, treatment with ACE inhibitors.	Among hospitalized cases of COVID-19, ethnicity was not associated with admission to the ICU or mortality.

(Bui, 2020) new	USA, Utah outbreak investigations March 6 and June 5, 2020. Racial and ethnic composition of workplace outbreak-associated cases were compared with the overall racial and ethnic composition in each sector in Utah.	Although 24% of Utah's workforce in all 15 affected sectors identified as Hispanic or a race other than White (non-White), 73% (970 of 1,335) of workplace outbreak-associated COVID-19 cases were in persons who identified as Hispanic or non-White.
(Chamie, 2020) new	A cross-sectional study was conducted in a 16 square block area of San Francisco's Mission District April 25-28. Serology and RT-PCR testing was conducted on residents that volunteered. N=3953 tested, 40% Hispanic, 41% White, 9% Asian/Pacific Islander, 2% Black, and 7% other/mixed	- 83/3953 were RT-PCR positive, 95% of the positive individuals were Hispanic. - Prevalence among residents/workers for Hispanics: 3.9% (2.0-6.4)/10.4% (7.0-14.8) compared to other ethnicities: 0.2% (0.0-0.4) / 0.0% (0.0-2.0). - Recent infection was most likely to be identified in a Hispanic 10.1 (2.81-64.6) compared to others. - Positive Hispanics in this study were more likely to be male, work in a frontline service job, have a low income (50k) and report a COVID-19 contact.
(Ko, 2020) new	USA, cross-sectional study examined factors associated with COVID-19 hospitalizations by assessing data from 70 counties participating in the Coronavirus Disease 2019-Associated Hospitalized Surveillance Network (COVID-NET) and a population-based sample of non-hospitalized adults residing in the COVID-NET catchment area.	Risk of hospitalization by ethnicity compared to Whites: - Blacks (aRR: 4.7; 95%CI: 3.8, 5.9) - Other ethnicities (aRR: 3.5; 95%: 2.8, 4.3)
(A. Pan, 2020) preprint new	USA, Houston cross-sectional analysis conducted between March 3 and July 18, 2020, evaluated hospitalization and mortality outcomes for Blacks vs. Whites and Hispanics vs. Whites in the Greater Houston Metropolitan Area.	In a fully adjusted model, statistically significant higher likelihood of hospitalization - Blacks aOR 1·42 (95%CI 1·24–1·63) - Hispanics aOR 1·61 (95%CI 1·46–1·78) There was no association with mortality.
(Vahidy, 2020) new	USA, cross-sectional study on data being contemporaneously collected since March 5, 2020 by the Houston Methodist Hospital system on association of ethnicity and susceptibility of SARS-CoV-2 infection.	In the fully adjusted model compared to Whites, there was a higher likelihood of infection among: - Black; aOR, CI: 1.84, 1.49-2.27) - Hispanic; aOR, CI: 1.70, 1.35-2.14)

		- Asians; aOR, CI: 1.46, 1.09-1.95)
(Goyal, 2020) new	USA, cross-sectional study of 1000 children tested between March 21 and April 28, 2020 to assess association between patient ethnicity and SARS-CoV-2 infection rates.	In comparison to Whites (7.3%), minority children had higher rates of SARS-CoV-2 infection (Black: (30.0%; adjusted OR 2.3 [95% CI 1.2, 4.4]; Hispanic: 46.4%; adjusted OR 6.3 [95% CI 3.3, 11.9]).
(Alvarez Retamales, 2020) preprint new	USA, observational cross-sectional, nationwide hospital admission data taken from CDC COVID-NET on June 11, 2020 to investigate the discrepancy in hospitalization rate by race/ethnicity, 21,221 hospitalized COVID-19 patients compared to population of 328,239,523.	Significant differences in the ethnic proportion of COVID-19 cohort vs the population respectively: - White: 38% vs 60.4% - Hispanic: 19% vs 18.3% - Black: 36% vs 13.4% - Asian/Pacific Islander: 5% vs 6% - American Indian/Alaska Native: 1.6% vs 1.3% The discrepancy is greatest for Whites and Blacks: with Whites being disproportionately underrepresented and Blacks being disproportionately overrepresented in the COVID-19 cohort compared to total population.
(Gross, 2020)	USA, 28 states: Cross-sectional study up to April 21, 2020. Data from CDC was extracted by state, 28 states and NYC have racial data. Analysis adjusted for age (standardised mortality by age across race groups in each state) and meta-regression analysis was conducted to assess the association of state-level racial disparities.	- Risk of death in Black compared to the White population was aRR 3.57 (95%CI 2.84-4.48). Pennsylvania was the only state where Black risk of COVID-19 death was lower than White. - Hispanic aRR 1.88 (95%CI 1.61-2.19) times higher risk of death than white population. 12 states reported a significantly higher risk of COVID-19 deaths among Hispanic populations.
United Kingdom (UK)		
(Leeds, 2020) new	UK, NHS Trust hospital healthcare workers prospective cohort study. A staff testing programme was conducted in	- Age, sex, occupation and ethnicity are not associated with increased risk of contracting SARS-CoV-2.

	April and examined the characteristics of 991 affected healthcare workers.	
(Harrison, 2020) preprint new	Prospective cohort, England Scotland and Wales. 260 hospitals, February 6th - May 8th. N=30693 suspected and confirmed COVID-19 cases Analysis: hierarchical regression models / Cox Proportional Hazards regression, adjusted for age, sex, location	- Compared to Whites, critical care admission was more common in South Asian OR 1.28 (95%CI 1.09 - 1.52), Black OR 1.36 (95%CI 1.14 - 1.62) and other ethnic minority OR 1.29 (95%CI 1.13-1.47). - Mortality compared to Whites: South Asian HR 1.19 (95%CI 1.05 - 1.36), East Asian HR 1.00 (95%CI 0.74 - 1.35), Black HR 1.05 (95%CI 0.91 - 1.26), Other Ethnic Minority HR 0.99 (95%CI 0.89 - 1.10). - Diabetes had a significant mediation effect (17.8%, 8.9-65.7) of South Asian ethnicity on mortality.
(Williamson, 2020) new	UK NHS patient notification system, OPENSafely, for 24 million registered adults (40% population), prospective cohort. N= 12 718 279 people with ethnicity data from the general population in this cohort. Data Feb 1- May 6 was analysed (multivariable Cox proportional hazards model) for the outcome death of confirmed COVID-19 cases (n= 10 926). Adjusted by age, sex, BMI, smoking status, comorbidities, asthma, cancer, socio-economic indices, ethnicity.	- Mortality due to COVID-19: Compared to Whites, hazard ratio for black ethnicity aHR 1.48 (95%CI 1.29-1.69), South Asian ethnicity aHR 1.45 (95%CI 1.32-1.58), mixed ethnicity aHR 1.43 (95%CI 1.11-1.84) in the population. - Higher risk of death was associated with male, older age, deprivation, uncontrolled diabetes, severe asthma and other medical conditions. - Controlled for socio-economic and medical factors, ethnicity remained a strong predictor of mortality within the population.
(Razieh, 2020) new	Prospective cohort, UK Biobank Study (N= 502 543). COVID data March 16 - June 14. N=5623 tested, 1087 positive Logistic regression looking at BMI and ethnicity. Analysis adjusted for: age at test, sex, social deprivation (Townsend score), smoking status, cancer illnesses (number) and non-	- Greater risk of COVID-19 in Blacks relative to Whites was only apparent at higher BMI values (Figure 1). For example, at a BMI value of 25 kg/m2, there was no difference in risk (OR = 0.96; 95% CI: 0.61, 1.52), whereas at a BMI of 30 or 35 kg/m2, the odds of

	cancer illnesses (number), systolic blood pressure, HDL-cholesterol, total cholesterol and HbA1c	COVID-19 were 1.75 (1.24, 2.48) and 2.56 (1.63, 4.03) higher in Blacks, respectively.
(McQueenie, 2020) new	UK Biobank, prospective cohort of 502,503 participants COVID-19 Data: March 16 and May 18.	- Non-White ethnicities with multi-morbidity had nearly three times the risk [RR 2.81 (2.09-3.78)] of having COVID-19 infection compared to those of White ethnicity.
(Woolford, 2020) new	UK Biobank, prospective cohort analysis of adults admitted (n=470) with COVID-19 to Royal Oldham Hospital, UK to explore factors predicting death. COVID-19 Data: March 16- June 1 logistic regression model	Association of mortality by ethnicity compared to White - Asian [OR = 0.37, (95%CI: 0.18-0.76), p<0.01)] - Other ethnicity [OR=0.29, (95%CI: 0.10-0.88), p=0.03] - Black had no significant association with death from COVID-19 [OR = 1.18, {95%CI: 0.31-4.45), p=0.81]
(Chadeau-Hyam, 2020) new	Prospective cohort, UK, Biobank study. Test-negative case-control design modelling the risk of testing positive conditional on being tested. Data up to May 18 N=4509 tests (1325 positive COVID-19 cases) Statistics: multivariable and penalized logistic regression models Adjusted for age, sex, education, home ownership, number in household, income, healthcare worker, unemployed, smoker, obesity, comorbidities.	Risk factors for testing positive or negative: Black vs White ethnicity (OR 1.05 [1.02–1.08])
(Lassale, 2020) new	Prospective cohort, UK, Biobank study. N=340966 (640 COVID-19 cases March 16- April 26) Logistic regression to estimate risk of COVID-19 hospitalization. Adjusted for age, sex, neighbourhood deprivation, household crowding, smoking BMI, inflammation, glycated haemoglobin and mental illness.	Hospitalization compared to White: - Black OR 2.66 (95%CI 1.82, 3.91) - Asian OR 1.43 (95%CI 0.91, 2.26) - Other non-white group OR 1.41 (95%CI 0.87, 2.31) After controlling for measured factors, clear ethnic differences in risk of COVID-19 hospitalization remained. The largest attenuating factors were for socioeconomic factors.

(Raisi-Estabragh, 2020)	UK biobank (prospective cohort of >500 000 participants, recruited in 2006-2010 at age 40-69) Data Mar 16 – May 18, 2020 N= 4510 tested for COVID, 1326 positive. Analysis is restricted to within the tested cohort, the tested people in the UK are considered those with severe disease at this time.	- Multivariate logistic regression for COVID-19 positivity, non-Whites had a higher odds OR 1.59 (95%CI 1.26-1.99) compared to Whites. Adjusted for sex, ethnicity, BMI, Townsend score, and household size.
(Niedzwiedz, 2020)	UK biobank (prospective cohort of 392116 participants in England, recruited in 2006-2010 at age 40-69) Mar 16-May 3. Logistic regression model adjusted for: Initial adjustment= age, sex and assessment centre Full adjustment= Above adjustments + healthcare worker status, socioeconomic variables, lifestyle variables, medical conditions	- Compared to Whites a positive test was more likely for Blacks aRR 2.05 (95%CI 1.39–3.03, full adjustment) and south Asians aRR 2.42 (95%CI 1.75–3.36, initial adjustment). - In defined ethnic groups for risk of testing positive (initial adjustment): - Pakistani RR 3.24 (95%CI 1.73–6.07)> other south Asians RR 3.00 (95%CI 1.64-5.49)> Indian RR 1.98 (95%CI 1.26-3.09) for testing positive compared to Whites. - Black Caribbean RR 3.51 (95%CI 2.39-5.15) and Black Africans RR 3.11 (95%CI 1.97-4.91) were similar.
(Kolin, 2020) preprint	UK Biobank, (prospective cohort of >500 000 participants, recruited in 2006-2010 at age 40-69) review of the first 669 cases of COVID-19, Mar 16-data pull date not provided. Adjusted for age, sex, body-mass index, Townsend deprivation score, and history of diabetes, angina, or myocardial infarction,	Compared to White participants - Blacks aRR 3.14 (95%CI 2.28-4.31) were at a higher risk of COVID-19. - Asians s were also at higher risk of COVID-19 aRR 2.03 (95%CI 1.40-2.95). *Denominator is the Biobank cohort/population.
(Patel, 2020)	UK Biobank, (prospective cohort of 418,794 participants, recruited in 2006-2010 at age 40-69) Dates are not specified.	Both Blacks aOR 3.1 (95%CI 2.0–4.8) and Asianss2.0 (95%CI 1.2-3.1) were at increased risk of hospitalisation due to COVID-19 positive test as compared to White participants.

	Regression adjusted for age, sex and socioeconomic factors.	*Denominator is the Biobank cohort/population.
(Harman, 2020)*	Small single center cohort of children admitted with COVID-19. Prospectively identified from King's College Hospital, London, UK, between Feb 25, and April 28, 2020.	- Hospitalization: 9/12 (75%) were from Black, Asian, and minority ethnic background vs. the 39% that these ethnic backgrounds represent in the inner London area.
(Sapey, 2020) new	UK, University Hospitals Birmingham NHS Foundation Trust (UHB) retrospective cohort study on SARS-CoV-2 patients (n=2217) admitted between March 10 and April 17, 2020. South Asian ethnicity defined as Pakistani, Bangladeshi and Indian. Cox regression analysis adjusted for age, sex, deprivation and comorbidities.	- Severe disease on presentation among South Asian patients 34/137 (24.8%) vs White patients 54/483 (11.2%) p <0.0001. - ICU admissions of South Asian patients 86/410 (21.0%) vs White patients 133/1540 (8.6%), p <0.001. - Mortality comparted to Whites was aHR 1.4 (95%CI: 1.2-1.8) for South Asians. - There was no significant difference noted in survival for Blacks compared to Whites.
(Russell, 2020)* new	UK, London's Guy's Cancer Center conducted a retrospective cohort study to assess 156 cancer patients with COVID-19 diagnosis between February 29 and May 12, 2020 and their clinical characteristics associated with COVID-19 death.	- Among cancer patients with a COVID-19 diagnosis, Asians as compared to White (OR 3.73 (95%CI 1.28-10.91) had a positive statistically significant association with COVID-19 death.
(Martin, 2020) new	UK, Leicester retrospective study on COVID-19 patients at University Hospitals of Leicester NHS Trust between March 1 and April 28, 2020, and assessed factors associated with SARS-CoV-2 PCR positivity before/after lockdown.	After adjustment, compared to Whites, the odds of testing positive for other ethnicities was: - South Asian (aOR 2.44 95%CI 2.01, 2.97) - Black (aOR 2.56 95%CI 1.71, 3.84) - Other (aOR 2.53 95%CI 1.74, 3.70)
(Perez-Guzman, 2020)* new	UK, London NHS Trust retrospective cohort study assessing factors associated with mortality in 614 patients admitted between February 25 and April 5 in three large London hospitals. Patient population ethnicities:	- When adjusting for age, sex and comorbidities Black patients were at higher odds of death compared to Whites (aOR 1.69, 95%CI 1.00-2.86). - This association was stronger when further adjusting for admission severity (aOR 1.85 95% CI 1.06-3.24).

	- BAME = 40% (244) - White = 38% (235) - Unknown ethnicity = 22% (135) Analysis: logistic regression	
(Ayoubkhani, 2020) preprint new	UK, England and Wales retrospective cohort study assessing deaths occurring between March 2 and May 15, 2020, and association of deaths with ethnic minority groups. Analysis: Cox proportional hazards model.	- The fully adjusted model for females, only Black females were associated with mortality (aHR 1.29 [95% CI: 1.18 to 1.42]). - For males, COVID-19 mortality risk remained elevated for the Black (1.76 [1.29 [95% CI: 1.63 to 1.90]), Bangladeshi/Pakistani (1.35 [1.29 [95% CI: 1.21 to 1.49]) and Indian (1.30 [1.29 [95% CI: 1.19 to 1.43]) groups.
(Zakeri, 2020) preprint new	UK, South London (King's College Hospital Trust), case-control + retrospective cohort study to examine relationship between ethnicity and hospital admission and in-hospital mortality for severe COVID-19 between March 1-June 2, 2020, 872 cases, 3488 controls. Of the cases, - 48.1% were Black - 33.7% were White - 12.6% were Mixed/other - 5.6% were Asian	- Compared to Whites, admission risk was higher in Black (OR 2.28 [95%CI: 1.87-2.79]) and mixed/other patients (OR 2.66 [95%CI: 2.01-3.52]) Asians were not at higher risk of admission (OR 1.04 [95%CI: 0.72-1.48]). - In hospital mortality was not associated with Black (HR 0.84 [95%CI: 0.63-1.11]) and mixed/other ethnicities (HR 0.69 [95%CI: 0.43-1.10]). Asians had higher risk of in-hospital mortality (HR 1.54 [95%CI: 0.98-2.41]).
(Swann, 2020) preprint new	UK, multi-hospital retrospective cohort (260) in England, Wales, and Scotland from January 17-July 3, 2020, to investigate admission to ICU, mortality and multisystem inflammatory syndrome in children and adolescents (MIS-C) admitted with SARS-CoV-2 infection, n=651	- Critical care admission was associated with age younger than 1 month, age 10-14 years, and Black ethnicity. Blacks were significantly associated with admission to critical care aOR 2.82 (95% CI 1.41 to 5.57) as was other ethnicities aOR 1.91 (95%CI 1.07-3.34), and no association was identified for South Asians compared to Whites. - 11% cases were classified as MIS-C more likely to be of non-White ethnicity (64% (29/45) vs. 42% (148/355); P=0.004).

(Kakkar, 2020)* new	Retrospective cohort of adults tested (n=3018) for COVID-19 at Sheffield Teaching Hospitals, UK, January 3 - April 25, 2020. BAME 19% of Sheffield population Descriptive analysis, chi-square.	BAME vs. Whites - Test positive 95/296 vs 631/2424, p=0.026 - Hospitalized 86/95 vs. 599/631, p0.083 (not significant) - ICU 20/86 vs. 43/599 p<0.00001 - Significantly fewer tests were done on BAME population compared to their proportion in society and BAME people tested were significantly younger than Whites.
(Galloway, 2020)* new	Retrospective cohort, London UK, 2 hospitals March 1-April 17, 2020. N=1157 COVID-19 hospital admissions with positive RT-PCR for SARS-CoV-2. Analysis: Competing risks regression models, adjusted for age and sex.	- Admission to Critical Care compared to Whites: BAME ethnicity HR 1.53 (95%CI 1.12, 2.09) - Mortality compared to Whites: BAME ethnicity HR 1.19 (95%CI 0.89, 1.58) There was an association with ethnicity and more severe disease, but not mortality among hospitalized cases.
(Apea, 2020)* preprint new	Retrospective cohort, 5 hospitals, London UK, January 1-May 13. N=1996 SARS-CoV-2 cases Analysis: Logistic regression modelling of ethnicity on ICU treatment using mechanical ventilation was carried out adjusted for age and sex. Cox proportional hazards model adjusted for age and sex	Racial profile of cases 35.2% White, 27.0% Asian, 17.0% Black. - ICU admission was significant p<0.001 where 11% White, 20.1% Asian and 18.5% Black group were admitted to ICU. - Mechanical ventilation, age/sex adjusted odds compared to Whites across hospitalized cases: Asian OR 1.54 (95%CI 1.06-2.23), Black OR 1.80 (95%CI 1.20-2.71) - Mortality (30 day) Asian HR 1.49 (95%CI 1.19-1.86), Black HR 1.30 (95%CI 1.02-1.63) compared to Whites, controlling for comorbidities widened the confidence interval for ethnicity, Black p=0.09. - Mortality (90 day) Asian HR 1.46 (95%CI 1.18-1.81) compared to Whites

(Fletcher, 2020) preprint	UK, Single center retrospective cohort study. 2756 patients admitted to the Chelsea and Westminster Hospital NHS Foundation Trust, Jan 1- Apr 23. multivariable logistic regression model Note: self-reported ethnicity, many observations were unspecified leading to underpowered estimates.	- Presentation at a clinic with symptomatic COVID-19 was higher in Asians aOR 1.63 (95%CI 1.00-2.69) and other 1.70 (95%CI 1.21-2.39) compared to Whites (adjusted by age, sex and some blood biomarkers). The adjusted comparison for Black was similar, but not significant. - No association with admission to ICU and ethnicity was observed in this study. - Mortality was associated with Asians aOR 2.24 (95%CI 1.23-4.50), and similar among Blacks, but not significant.
(S. de Lusignan, 2020a) preprint	UK, Retrospective medical chart review – cross sectional study, Oxford RCGP research and surveillance centre network, Jan 28-Apr 4, 2020. COVID-19 positive cases n=587, negative test n=3215. Ethnic distribution: White n=2497 (65·7%) Asian n=152 (4·0%) Black n=58 (1·5%) Mixed, other n=81 (2·1%) Missing n=1014 (26·7%) Multivariate logistic regression.	- Compared with Whites (15.5%), the adjusted odds of a positive test were greater in Blacks (62.1%) aOR 4.75 (95%CI 2.65–8.51), adjusted by age, sex, socioeconomic deprivation, household size, urban/rural, smoking, BMI, hypertension, chronic kidney disease, diabetes, chronic heart disease.
(Wright, 2020) new	Cross-sectional data of hospital patients tested for COVID-19 March 18- April 27 in Bradford, UK. Chi-square tests.	- Mortality rates in COVID-19 cases compared to negative patients. No significant difference in mortality among White (25.4%) compared to South Asian (18.1%) in hospitalized COVID-19 cases (P=0.122). However, South Asians were significantly younger than Whites.

(Hull, 2020) preprint	UK, east London general practice dataset. Cross-sectional study of 1.2 million people in 157 practices that included n=8985 COVID-19 cases Feb 14- Apr 30, 2020. Adjusted model: age, sex, social deprivation, clinical predictors.	- The odds of SARS-COV-2 infection, fully adjusted for other variables were: South Asian aOR 1.93 (95%CI 1.83-2.04) and Black aOR 1.47 (95%CI 1.38-1.57).
(Cook, 2020)	UK, NHS staff: Cross-sectional data on health care worker deaths up to April 22, 2020 was analysed. 106 cases, 98 had patient facing roles. HCW deaths were 0.51-0.58% of deaths. No statistical analysis.	- The proportion of BAME deaths (verses their proportion in a profession) - Nurse 71% (20%) - Healthcare support worker 56% (17%) - Doctor / Dentist 94% (44%) - Other staff 29% (-)
(Riphagen, 2020)	London, UK: A small case series of children with a multisystem inflammatory syndrome that is now well recognised. 8 children were identified over 10 days mid-April 2020 in a single pediatric hospital.	- 6/8 children with this inflammatory condition were of Black ethnicity. No analysis or investigation on this potential association was undertaken in this small study.
Other countries		
(Toubiana, 2020)	Paris, France, prospective observational study of multisystem inflammatory syndrome in Children Apr 27-May 11 (follow up to May 15). 21 children median age 7.9 years (3.7-16.6)	- 57% (12/21) were Black, 3/21 were Asian. There was insufficient data in this study to explore the association, however the proportions were higher than would generally be expected based on the population demographics and what is known about Kawasaki disease in children.
(Elias, 2020) new	Paris, France, prospective cohort study of kidney transplant patients (n=1216) under active follow-up in two referral transplant centers between March 1 and April 30, 2020.	- Non-White ethnicity was independently associated with higher risk of developing COVID-19 disease: aOR= 2.17; [95% CI], 1.23 to 3.78; p=0.007)
(Baqui, 2020)*	Brazil, cross-sectional study of hospital mortality (country wide). Data from Feb 27 – May 4, 2020. N= 6882 cases with known outcomes.	- Hospital mortality was higher in mixed ethnicity aHR 1.47 (95%CI 1.33-1.58) and Blacks aHR 1.32 (95%CI 1.15-1.52) compared to Whites. Mixed ethnicity was the most influential risk factor on mortality after age.

	Racially classifies the Brazilian population in five categories (percentages as of 2010 of Brazilian population): branco (white) (47.5%), pardo (mixed ethnic) (43.4%), preto (black) (7.5%), amarelo (yellow) (1.1%) and indígena (0.4%). Cox regression analysis adjusted by age, sex, ethnic group, and comorbidities (fixed effects), with state (random effect)	

*= study is also included in (Raharja, 2020). New= Study has been published since June 1, 2020 when the first version of this review was completed. Preprint = refers to papers that have not undergone the peer-review process. BAME = Black, Asian and minority ethnic, OR= odds ratio, HR= Hazard Ratio, RR= risk ratio, 95%CI = confidence interval, I^2= measure of heterogeneity in a meta-analysis, k= number of studies.

ETHNICITY AND EXPOSURE TO COVID-19 (SEROLOGY STUDIES)

Seroprevalence and other serological investigations and associations with ethnicity were reported in five studies. Four seroprevalence studies conducted in USA on the general population, healthcare workers and pregnant women reported that there were significantly higher proportion of people seropositive among certain ethnicities: Blacks (n=3/4 studies), Hispanic (n=3), Asian (n=1/2) (Table 2). One UK study examined the dynamics of IgG antibodies to SARS-CoV-2 during acute and convalescent phases of SARS-CoV-2 infection and found that there was a difference in the magnitude of the ELISA results that may indicate during infection COVID-19 cases of non-White ethnicity may have higher viral loads (Staines, 2020). This finding requires further research to understand the significance of the difference noted in this study. Registered trials described in the systematic review included seroprevalence studies that will add to the body of information (D. Pan, 2020).

Table 2: Serology based studies on cumulative incidence and the dynamics of antibodies against SARS-COV-2 (n=5)

Reference	Study Description	Key Outcome
(Ebinger, 2020)* preprint new	USA, seroprevalence survey in a large diverse healthcare employee cohort of 6,062 adults employed in Los Angeles County. Date: May-June 2020	- The main factors significantly associated with greater odds of seropositive status were Hispanic (OR 1.80 [95% CI 1.31, 2.46], P<0.001), and Black (1.72[1.03, 2.89], P=0.04), compared to Whites.

	Analysis: multivariable-adjusted analyses of pre-existing characteristics e.g. ethnicity, age, sex, asthma, hypertension	
(Flannery, 2020) new	USA, Pennsylvania prospective cohort study conducted serological testing of 1293 parturient women at two centers in Philadelphia between April 4 and June 3, 2020, and assessed for differences among race/ethnicities among the women.	Seroprevalence rates by race/ethnicity: - Black (9.7%; 95% CI, 7.3-12.5%) - Hispanic (10.4%; 95% CI, 5.7-17.1%) - White (2.0%; 95% CI, 0.9 to 3.8%) - Asian (0.9%; 95% CI, 0.0 to 5.1%)
(Biggs, 2020) new	USA, cross-sectional study in 2 Atlanta counties between April 28 and May 3, 2020 assessing SARS-CoV-2 seroprevalence in 696 persons.	Total weighted seroprevalence rate = 2.5% (95% CI: 1.4-4.5) - Black 5.2% (95% CI: 2.9-9.1), p<0.01 compared to other ethnicities.
(Rosenberg, 2020)	New York State seroprevalence survey n=15101 adults, Apr 19-28, 2020. Estimated cumulative incidence using a post-stratification weighting to standardize to the New York population and adjustments by the antibody test characteristics.	Cumulative incidence varied significantly by ethnicity: - Hispanic 29.2% (95%CI 27.2-31.2%) - Black 20.2% (95%CI 18.1-22.3%) - Asian 12.4% (95%CI 9.4-15.4%) - Compared to Whites 8.1% (95%CI 7.4-8.7%), p<0.0001)
(Staines, 2020) preprint	Single center prospective cohort Mar 29 – May 22, London UK. 177/1785 COVID-19 cases are included. Test: COVID-19 IgG ELISA assay developed by Mologic (Bedford, UK) and manufactured by Omega (Omega Diagnostics, Cambridge UK) - 2-8% of the cases did not seroconvert.	- Non-White ethnicity was associated with a higher normalized optical density value from the ELISA than White ethnicity, mean value 1.06 vs. 0.85, p 0.035 (unpaired t-test) - Author suggests this finding may be associated with higher viral loads

*= study is also included in (Raharja, 2020). New= Study has been published since June 1, 2020 when the first version of this review was completed. Preprint = refers to papers that have not undergone the peer-review process. OR= odds ratio, 95%CI = confidence interval.

ETHNICITY AND COVID-19 IN CANADA

Limited Canadian research was identified despite a grey literature search; a preprint ecological study, two unpublished reports of surveys conducted in Canada, Indigenous Service Canada surveillance reports and Toronto Public Health's COVID-19 dashboard had relevant results addressing ethnicity and COVID-19 in Canada (Table 3). The search also identified provinces (Ontario / British Columbia) and/or health units (Toronto) collecting or planning to start collecting ethnicity data on COVID-19 cases. As of September 2020, only Toronto Public Health had an available report.

The available Canadian data suggests non-White ethnicities, with the exception of East Asians, are disproportionately infected with COVID-19 which is in agreement with other studies on risk of COVID-19 infection from other countries in this review. These studies also highlight inequalities in the social determinants of health that may be related to increased risk of COVID-19 such as housing, education, income, occupation and access to healthcare.

- A cross-sectional survey designed to compare COVID-19 impacts on Black Canadians to a representative "national" sample reported a higher likelihood of COVID-19 among Black Canadians individually and in their social circle. Canadian Blacks had a higher frequency of risk factors such as taking public transportation and having a job that requires face-to-face interactions with people. Higher frequency of severe financial impacts associated with the pandemic. These data are consistent with similar studies published in the USA (Table 1).
- Toronto Public Health dashboard shows that a higher proportion of COVID-19 cases than the representation in the community was seen for Black, Hispanic, Southeast Asian, South Asian/ Indo-Caribbean and Middle Eastern ethnic groups.
- The ecological study analysed population data on number of COVID-19 cases and deaths in Canada by population level demographic information including proportion Black, proportion foreign-born, proportion over 65 years, population density and median income. Findings from their multivariable negative binomial model include:
    - Double the case count was associated with a 1% increase in proportion Black and 3% increase in case count was associated with 1% increase in foreign born population.
    - 2.1 increase in the rate of COIVD-19 deaths was associated with a 1% increase in proportion Black in the population.

COVID-19 data focusing on Canada's indigenous population was only identified on the Indigenous Services Canada webpage and provincial webpages for Alberta, British Columbia, and Manitoba {{85811;}}. Analysis conducted at the end of July indicated that indigenous populations in Canada has reported on-reserve COVID-19 rates that were a quarter of the rate in the general population and a case fatality rate approximately one fifth that in the general population {{85811;}}. To date commentaries and news articles in CMAJ have reported successful public health

mitigation efforts by indigenous communities across Canada {{65290;}}. Indigenous populations are also more likely to live in remote communities which may protect a closed community from COVID-19, however if these communities are affected by COVID-19, they have more limited access to healthcare and are more likely be in poor socioeconomic condition (Statistics Canada, 2020). No Canadian data on ethnicity and hospitalizations, severity or mortality was identified. However publications on the relationship between ethnicity and medical conditions or socioeconomic factors identified as risk factors for severe COVID-19 disease may be useful indicators of what could be expected until COVID-19 data is available. The search identified two publications that suggested compared to Whites; Black immigrants, Indigenous people and South Asian immigrants were significantly more likely to have one or more medical conditions that have been associated with a higher risk of severe COVID-19 (Lin, 2020).

Table 3: Details of observational studies and reports conducted in Canada on the association of ethnicity and risk of COVID-19 infection (n=5)

Reference	Study information	Key Outcomes
Susceptibility, Clinical Severity and Mortality associated with COVID-19		
Canada		
(Nur, 2020) new unpublished report	An online survey (cross-sectional) was conducted June 17-30, 2020. The sample strategy was weighted by age, gender, region, ethnicity and place of birth to target a representative sample of 1500 Canadians and 400 Black Canadians (Black). N=2322 adult Canadians	COVID-19 outcomes: - Blacks were more likely to report COVID-19 symptoms and treatment (10% vs. 7% national). - Blacks were more likely have had (10% vs. 7% national) or to know someone who has had COVID-19 symptoms (28% vs. 17% national). - Commuters had higher results: they were more likely to have had (16% Black vs 12% national) and to know someone who has had COVID-19 symptoms (34% vs. 18%). - Blacks were 3x more likely to know someone who died of COVID-19 (21% vs. 8% national). Risk Factors for COVID-19 - Blacks were more likely to commute to work using public transit (25% vs. 12% national), (This has been

		shown to be an indicator for higher COVID-19 risk in other studies.). - Blacks were more likely to report frequent face-to-face requirements of their job (61% vs. 50% national). Impacts of COVID-19 - Minimal financial impact was reported in 45% of both Black and national respondents. - Black men age 45+ were more likely to report significant negative financial impact 38% vs. 22% national. - Financial confidence was lower among Black households (67% vs. 72% national).
Requested a copy of the report, not available on line. new	BC COVID-19 population survey (N=394000). (Information from news articles, Aug 14, 2020)	- Data indicate that Hispanics, West and South Asians, and Blacks were disproportionately affected by the pandemic and financially having difficulty due to lost work. - Ethnicity and access to health care was identified, where Japanese, Korean, multi-ethnic and South Asians reported difficulties.
(Toronto Public Health, 2020) new	Toronto COVID-19 by Ethno-Racial Identity and Income by Proportions surveillance dashboard. Data May 20 to August 16, 2020 24% of the ethnicity data is missing. Excludes cases in long-term care facilities. Results are descriptive and only include observations with ethnicity data.	83% of COVID-19 cases identified with an ethnic minority group compared to 52% of Toronto's population. The list below is % COVID-19 vs. % of population. - White 17% vs. 48% - Black 22% vs. 9% - Hispanic 10% vs. 3% - Southeast Asian 16% vs. 7% - South Asian or Indo-Caribbean 20% vs. 13% - Middle Eastern 11% vs. 4% - East Asian 4% vs. 13%

(Choi, 2020) preprint	Canada wide, ecological study with data up to May 5, 2020. Data sources included PHAC data, STATsCan data and crowd sourced data to compare COVID-19 cases and deaths by health unit data analysing proportion black, proportion foreign born, percent over 65 years, population density and median income as predictors. Analysis for cases and deaths respectively were conducted in a negative binomial multivariable (for over dispersed count data) model with the above predictors.	- COVID-19 infection multivariate model estimated that a 1% increase in the proportion of Black residents in a health region was associated with the doubling of COVID-19 infection rates. And a 1% increase in share of foreign-born residents was association with a 3% rise in COVID-19 infection rates. - A 1% increase in the proportion of Black residents in the health region was associated with 2.1x increase in COVID-19 death rates. An increase of 1% in the proportion of residents 65 and older were associated with a 26% increase in deaths.
{{85811;}} Surveillance report new	Surveillance Data: as of September 20, 2020 there had been 408 cases of COVID-19 in Indigenous communities' on-reserve.	As of July 31, 2020: - The percentage of Indigenous individuals living on reserve reported positive for COVID-19 is currently one-quarter the rate of the general Canadian population - The COVID-19 case fatality rate for Indigenous Peoples living on reserve is about one-fifth that of the fatality rate in the general Canadian population

New= Study has been published since June 1, 2020 when the first version of this review was completed. Preprint = refers to papers that have not undergone the peer-review process.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: racial, ethnic, ethnicity. This review contains research published up to September 7, 2020.
An augmented search for Canadian literature on ethnicity was also conducted using the indicated search terms with COVID-19 AND Canada or provinces as key terms in google and on official websites. 464 citations were captured by the search, studies were screened out for not being relevant, not primary research or systematic reviews, and not an included study design. Seventy-three studies that analyzed an association with ethnicity are included in this review. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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APPENDIX:

Within the studies captured in this review ethnicity is self reported based upon a person's self-identification with one or more social groups within a list of predefined options. There were variations in the lists between countries and between studies. The table below captures the main categories of ethnicity or ethno-racial classifications and definitions used by the US and UK. In some studies there was additional granularity or classification options, those are also noted below.

Definitions:

Ethnicity: The social group a person belongs to, and either identifies with or is identified with by others, as a result of a mix of cultural and other factors including language, diet, religion, ancestry, and physical features traditionally associated with race (see race). Increasingly, the concept is being used synonymously with race but the trend is pragmatic rather than scientific.

Ethno-racial classifications refers to the administrative categorization of people along ethnic and racial lines for the purposes of statistics. This term was used by Toronto Public Health.

Ethnic Category used in the Review	Acronyms and definitions of the category.
White	Non-Hispanic White, USA definition: people with origins in Europe, the Middle East or North Africa. UK definition: British, Irish or other white background
Black	Non- Hispanic Black, African American, Black British, Black Caribbean, African, Afro-Caribbean, Haitian. USA definitions: person that have origins in any of the black racial groups of Africa. UK definition: Caribbean, African, Any other black background
Hispanic	Latino, Latinx, Latin American. Note: the US census bureau uses "Hispanic" for both Hispanic and Latinx referring to anyone born in or with ancestors from Latin America. USA definition: person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.
Indigenous	First Nations, Inuit and Metis (Canada), American Indian and Alaska Native (USA). By definition Indigenous people refers to the original populations of North and South America.
Pacific Islander	Native Hawaiian. Refers to a person having origins Hawaii, Guam, Samoa, or other Pacific Islands.
Asian	A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. UK definition: Indian, Pakistani, Bangladeshi, any other Asian background
Chinese	UK definition: Chinese or any other
Mixed	UK definition: white and black Caribbean, White and Black African, White and Asian, or any other mixed background
BAME	Black Asian and minority ethnic group is a term used in many UK-based studies to denote non-White ethnicity.
Racialized communities	Refers to visible minorities and usually encompasses all people that are non-Caucasian in race or non-white in color. In Canada this may or may not include indigenous people depending on the individual report/study.
East Asians	A racialized classification for people descended from east Asian countries: China, Taiwan, Japan, Mongolia, North Korea and South Korea.

South Asian	A person whose ancestry is in the countries of the Indian subcontinent, including India, Pakistan, Bangladesh, and Sri Lanka. Indo-Caribbean was also grouped with South Asian, these are people of Indian descent that live in the Caribbean.
Southeast Asian	This is a group of mixed cultures from 11 countries Brunei, Burma (Myanmar), Cambodia, Timor-Leste, Indonesia, Laos, Malaysia, the Philippines, Singapore, Thailand and Vietnam.
Middle Eastern	Arab, Western Asian people of Middle Eastern and North African descent

Notes: Capitalization is in line with the ASA style guide for sociology research papers. United States Census Bureau definitions of ethnicity or race indicate that these are a social construct of race/ethnicity rather than a biologically based segregation. United Kingdom Census Bureau ethnicity categories.

Preuve émergente sur la COVID-19

Synthèse en bref sur l'origine ethnique et la COVID-19

Introduction

Cette synthèse en bref vise à résumer la documentation disponible sur les liens entre l'origine ethnique, le risque d'infection par la COVID-19, la gravité de l'infection et le taux de mortalité qui en découle, tant au Canada qu'à l'échelle mondiale.

Cette synthèse en bref comprend la littérature disponible jusqu'au 7 septembre 2020. L'origine ethnique mentionnée dans les études incluses dans la présente synthèse a été principalement définie par les bureaux de recensement des pays visés par les études. Elle constitue donc une variable autodéclarée, établie d'après la façon dont une personne s'identifie à un groupe social ou culturel indiqué dans une liste prédéfinie. Par souci d'uniformité, les principales catégories d'ethnies déclarées et utilisées dans la présente synthèse sont Noir, Blanc, Asiatique et Hispanique. D'autres catégories ou des catégories de groupes ethniques minoritaires plus spécifiques, p. ex., les Asiatiques de l'Est, les Asiatiques du Sud, les Autochtones et les habitants des îles du Pacifique, ont également été déclarées et sont précisées dans les tableaux sommaires. Veuillez consulter l'annexe pour voir le tableau des acronymes et certaines définitions supplémentaires.

La présente synthèse résume différentes études d'observation (y compris les études de cohortes, les études transversales, les études cas-témoins et les séries de cas) ayant analysé des données au niveau individuel lorsque l'examen de l'origine ethnique était l'un des objectifs de l'étude plutôt qu'une simple variable confusionnelle pouvant être utilisée dans le modèle multivarié. Les études écologiques qui utilisent des données agrégées ont été exclues de cette synthèse puisqu'elles peuvent présenter un risque élevé de biais et qu'il est impossible d'extrapoler les résultats au niveau individuel. Cependant, pour s'assurer de recueillir l'ensemble des études et des rapports canadiens disponibles, la littérature grise ainsi que les études écologiques sur la population canadienne ont été incluses dans la présente synthèse.

Points clés

- Pour établir le lien entre l'origine ethnique et la COVID-19, deux revues systématiques contenant la documentation disponible jusqu'au 15 mai et jusqu'au 15 juin, ainsi que soixante-sept études individuelles publiées depuis le 15 mai et quatre des cinq études ou rapports canadiens recensés dans la littérature grise ont été inclus dans la présente synthèse. De ces études, 34 ont évalué le risque d'infection au coronavirus (la COVID-19), alors que 31 portaient plutôt sur la gravité de la maladie et 22 sur la mortalité (tableaux 1 et 2). Bon nombre des recherches ont été menées aux États-Unis et au Royaume-Uni. Deux études provenant de la France et une du Brésil ont également été incluses. Les études canadiennes comprenaient une étude écologique déjà prépubliée et deux enquêtes transversales. Deux rapports de surveillance pertinents ont également été recensés dans la littérature grise (tableau 3).

- Cette synthèse en est à sa deuxième version. La première comprenait une revue systématique résumant les études diffusées jusqu'au 15 mai et des recherches originales publiées entre le 15 et le 30 mai. La présente mise à jour comprend, quant à elle, les études publiées entre le 1er juin et le 7 septembre, ce qui inclut une revue systématique supplémentaire des études publiées jusqu'au 15 juin. L'analyse des études indiquées dans les tableaux et la nouvelle revue systématique ont permis d'identifier 15 études qui sont marquées d'un astérisque (tableaux 1 et 2).

Risque d'infection

- Une revue systématique portant sur le risque d'infection a conclu que les Noirs, les Asiatiques et les Hispaniques étaient plus susceptibles que les Blancs d'obtenir un résultat positif au test de dépistage de la COVID-19 (D. Pan, 2020).
- Vingt-neuf études ont examiné le risque d'infection dans différents groupes ethniques de personnes ayant subi le test RT-PCR en raison d'une infection active (tableau 1) alors que quatre études de séroprévalence ont mesuré le risque d'exposition (tableau 2). Bien que les analyses multivariables qui incluaient l'âge, le sexe, les comorbidités et les variables socioéconomiques aient atténué les liens avec certaines ethnies en particulier, ce lien était cependant encore significatif dans de nombreuses études.
    - Parmi les 20 études réalisées aux États-Unis, un certain nombre ont indiqué un risque plus élevé d'infection chez les Noirs (six résultats corrigés et trois résultats univariés) et les Hispaniques (six résultats corrigés et six résultats univariés) que chez les Blancs, et ces études comportaient des données contradictoires sur les Asiatiques (deux résultats corrigés, un résultat avec lien univarié et deux résultats non liés). Une étude menée aux États-Unis a également révélé un risque plus élevé d'infection chez les Amérindiens et les Autochtones de l'Alaska (Hatcher, 2020).
    - Quatorze études effectuées au Royaume-Uni indiquaient systématiquement que les Noirs (neuf résultats corrigés), les Asiatiques du Sud (quatre résultats corrigés), les Asiatiques (trois résultats corrigés) et, de façon plus générale, les groupes de MECNA (Minorités Ethniques et Communautés Noire et Asiatique; un résultat corrigé, deux résultats univariés et un résultat non lié) présentaient un risque plus élevé d'infection comparativement aux Blancs, alors que les résultats pour d'autres ethnies étaient rarement déclarés.

COVID-19 Résultats relatifs à la gravité

- Les résultats en ce qui concerne la gravité de l'infection par COVID-19 (hospitalisation, admission aux soins intensifs (USI) et mise sous ventilation mécanique) figuraient dans deux revues systématiques alors que 31 études ont plutôt établi des liens entre le taux d'infection de différentes ethnies et celui des Blancs (tableau 1).
    - Hospitalisation : La revue systématique présente des méta-analyses portant sur des associations univariées qui comparent les Blancs aux Noirs (pour l'ensemble des pays) et aux Asiatiques (Royaume-Uni seulement) ainsi qu'un lien d'une ampleur significativement plus

importante pour les études britanniques et les analyses corrigées (âge, sexe et comorbidités) mentionnaient qu'il n'y avait aucune association. Les études individuelles menées aux États-Unis ont indiqué que les Noirs présentaient un risque plus élevé d'hospitalisation alors que les résultats étaient mitigés pour les Asiatiques et les Hispaniques. Deux études américaines ont, quant à elles, indiqué des résultats mitigés quant à la proportion d'Amérindiens et d'Autochtones de l'Alaska hospitalisés (Alvarez Retamales, 2020 ; Karaca-Mandic, 2020) alors que deux autres études (Alvarez Retamales, 2020 ; McPadden, 2020) n'ont révélé aucun lien avec les niveaux d'hospitalisation des habitants de l'île du Pacifique. Au Royaume-Uni, les Noirs et les Asiatiques du Sud présentaient un risque plus élevé d'hospitalisation alors que les résultats étaient incohérents pour les Asiatiques, les groupes d'ethnicité mixte ou les MECNA.

  - Admission à l'USI : Les résultats de la revue systématique indiquaient que dans les études britanniques les Asiatiques et les membres des groupes MECNA étaient surreprésentées dans les USI, alors que les méta-analyses ne rapportaient aucune association selon les analyses corrigées effectuées pour les Noirs, les Hispaniques et les Asiatiques (États-Unis seulement). De nouvelles études menées aux États-Unis ont cependant donné des résultats contradictoires pour les Noirs et les Hispaniques. Selon les études effectuées au Royaume-Uni, les Noirs, les Asiatiques du Sud et MECNA présentaient un risque plus élevé d'admission à l'USI.
  - Ventilation mécanique : Dix-huit études évaluées dans le cadre de la revue systématique n'ont indiqué aucun lien à cet égard pour les Noirs et les Hispaniques. Un lien a cependant été établi entre les Asiatiques (selon quatre études) et la ventilation, lien qui a persisté après correction de l'analyse en fonction de l'âge et du sexe. Peu d'études récentes ont tenté d'établir un lien entre l'origine ethnique et le risque de devoir utiliser la ventilation. Selon une étude américaine, aucun lien ne peut être établi ce risque et les Noirs et les Hispaniques alors qu'une étude du Royaume-Uni a indiqué que les Noirs et les Asiatiques présentaient un risque accru comparativement aux Blancs.

- Le syndrome inflammatoire multisystémique de l'enfant (SIME) et l'origine ethnique ont, quant à eux, été indiqués dans trois études, soit une cohorte prospective (étude ISARIC, (Swann, 2020)) et deux séries de cas avec des échantillons d'étude de petite taille provenant du Royaume-Uni et de la France (Riphagen, 2020 ; Toubiana, 2020). Dans l'ensemble de ces études, un nombre disproportionné de cas de SIME se sont produits dans des groupes ethniques non blancs. Aucune autre analyse n'a cependant été effectuée dans le cadre de ces études.

Taux de mortalité lié à la COVID-19

- Les revues systématiques n'ont indiqué aucun lien avec les Noirs ou les Asiatiques, même si une association protectrice a été mentionnée dans les analyses univariées pour les Hispaniques. Cette association a cependant disparu une fois les modèles corrigés en fonction de l'âge, du sexe et des comorbidités. Un lien avec des Asiatiques qui ont dû être mis sous ventilation mécanique en raison de la COVID-19 a cependant été mentionné (quatre études). Il ne faut pas oublier le haut niveau

d'hétérogénéité entre les études et le fait que les deux revues décrivent environ 50 % des études ayant établi un lien alors que les autres n'en ont déclaré aucun.

- Aux États-Unis et au Royaume-Uni, 22 études ont analysé le taux de mortalité chez les patients hospitalisés, mais aucune n'a établi de lien avec l'origine ethnique. Toutefois, lorsque l'on tient compte d'un dénominateur au niveau de la population, on peut voir que certains groupes ethniques étaient plus susceptibles de contracter la COVID-19, ce qui explique pourquoi le nombre de décès liés à l'infection au coronavirus dans ces populations est proportionnellement plus élevé que prévu. Les études britanniques effectuées sur tous les cas de COVID-19 ayant indiqué un tel lien montrent cependant un risque accru de mortalité chez les MECNA, les Noirs, les Asiatiques du Sud et les Asiatiques comparativement aux Blancs (tableau 1).

Études canadiennes

En dépit des recherches supplémentaires effectuées dans la littérature grise, nous n'avons relevé qu'un nombre limité de données canadiennes. Elles indiquent cependant que les groupes ethniques non blancs, à l'exception des Asiatiques de l'Est, ont été infectés de manière disproportionnée par la COVID-19. Dans l'ensemble, les analyses n'ont pas été corrigées en fonction de comorbidités ou de facteurs socioéconomiques ayant eu pour effet d'atténuer les résultats d'autres études incluses dans la présente synthèse. Aucune donnée canadienne sur l'origine ethnique et les hospitalisations, la gravité ou la mortalité n'a été relevée.

- Une enquête transversale conçue pour comparer les répercussions de la COVID-19 sur les Canadiens noirs à un échantillon « national » représentatif a cependant révélé une plus grande susceptibilité à la COVID-19 chez les Canadiens noirs tant au niveau individuel que parmi les personnes qu'ils connaissent. La fréquence de certains facteurs de risque liés à l'utilisation des transports en commun et au fait d'occuper un emploi exigeant des interactions en personne était plus élevée chez les Canadiens noirs. Ils étaient également plus à risque de subir de graves conséquences financières en raison de la pandémie. Ces données concordent donc avec d'autres données tirées d'études similaires publiées aux États-Unis (tableau 1).
- Le tableau de bord créé par le Bureau de santé publique de Toronto montre une proportion plus élevée de cas de COVID-19 dans les groupes ethniques composés de Noirs, d'Hispaniques, d'Asiatiques du Sud-Est, d'Asiatiques du Sud-Est/Indo-Caribéens et de Moyen-Orientaux par rapport à leur représentation dans la communauté.
- L'étude écologique a analysé les données de la population sur le nombre de cas et de décès liés à la COVID-19 au Canada en fonction de l'information démographique au niveau de la population, incluant la proportion de Noirs, la proportion de personnes nées à l'étranger, la proportion de personnes âgées de plus de 65 ans, la densité de la population et le revenu médian. Cette analyse multivariée a ainsi permis d'obtenir les résultats suivants :
    - chaque augmentation de 1 % de la proportion de Noirs dans une unité sanitaire était associée au double du nombre de cas. Chaque augmentation de 1 % de la proportion

de résidents nés à l'étranger était associée à une augmentation de 3 % du nombre de cas.

- Chaque augmentation de 1 % de la proportion de résidents noirs dans une région sanitaire était liée à une augmentation de 2,1 fois du taux de mortalité lié à la COVID-19.

Vue d'ensemble des éléments de preuve

Soixante-quatorze études, dont deux revues systématiques publiées avant le 7 septembre 2020, ont été incluses dans cette synthèse. Deux revues systématiques ont également été évaluées avec l'outil AMSTAR et ont été jugées être de qualité moyenne à élevée. Une étude écologique réalisée au Canada a été incluse pour tenir compte du contexte canadien, bien que ce type d'étude utilise des données agrégées pour l'analyse, ce qui veut dire qu'elles présentent un risque élevé de biais et de sophisme écologique et que leurs conclusions ne peuvent pas être extrapolées au niveau individuel.

La synthèse a donc principalement porté sur des études comportant des ensembles de données au niveau individuel, ce qui comprenait un éventail de plans d'étude d'observation, y compris de grandes cohortes prospectives de qualité moyenne à élevée, des cohortes rétrospectives de qualité moyenne à faible, ainsi que des études transversales et des séries de cas rétrospectives de basse qualité.

La littérature a évolué rapidement et les études plus récentes sur les grandes cohortes comportaient suffisamment de pouvoir pour contrôler de nombreuses variables potentiellement confusionnelles. Elles ont donc fourni de meilleures estimations du lien possible que les études qui font plutôt état d'estimations brutes ou ayant été légèrement corrigées. Les grandes études de cohorte concordent modérément et fournissent une certaine assurance que les recherches futures ne modifieront pas les conclusions tirées de ces études. Il subsiste cependant des lacunes dans les connaissances à cet égard, par exemple à savoir la raison pour laquelle certains groupes ethniques peuvent être plus à risque d'être infectés, sachant que certaines variables confusionnelles comme les facteurs socioéconomiques et les comorbidités n'expliquent pas entièrement cette association. Des facteurs génétiques potentiels, liés aux comorbidités, à l'activité de l'ACE2, à la réponse de cytokines pro-inflammatoires ou à d'autres différences dans la fonction du système immunitaire pouvant être associés au profil immunitaire des groupes ethniques à risque élevé ont été suggérés, mais n'ont pu être expliqués (Tal, 2020).

TABLE DES MATIÈRES

LIEN ENTRE L'ETHNICITÉ ET LE RISQUE D'INFECTION, LA GRAVITÉ DE LA MALADIE ET LE TAUX DE MORTALITÉ EN RAISON DE LA COVID-19

Deux revues systématiques et 61 études d'observation sont présentées dans le tableau ci-dessous et mentionnent le risque d'hospitalisations, de maladie grave, d'admission à l'USI, de mise sous ventilation mécanique, d'insuffisance rénale aiguë ou de mortalité en raison de la COVID-19.

Les revues systématiques incluent les études publiées jusqu'au 15 mai et au 15 juin (D. Pan, 2020 ; Raharja, 2020). Seuls les résultats de 15 études chevauchent ceux qui sont indiqués dans le tableau 1 et dans la revue systématique (Raharja, 2020). La revue systématique comprenait par ailleurs des études écologiques (résultats non résumés) et d'autres études ne portant pas sur le lien entre l'origine ethnique et la COVID-19, mais qui ont été incluses dans les méta-analyses.

Même si la majorité des recherches sur l'origine ethnique provient des États-Unis et du Royaume-Uni, deux études ont été effectuées en France et au Canada, ainsi qu'une étude menée au Brésil (tableau 1). Un nombre de plus en plus grand d'études explorait explorait pourquoi il pourrait y avoir un lien entre l'origine ethnique et le risque d'infection, de gravité ou de mortalité par la COVID-19. L'âge, le sexe, les comorbidités et les facteurs socioéconomiques sont les variables potentiellement confusionnelles ou médiatrices incluses dans les modèles multivariés. Quant aux variables réelles utilisées en ce qui concerne les facteurs socioéconomiques, elles variaient d'une étude à l'autre et incluaient notamment le revenu, l'état du quartier et d'autres indices composites. Dans certaines études cependant, les variables utilisées constituaient plutôt des mesures plus complexes associées à différents facteurs sociétaux ayant pour effet de bloquer l'accès aux soins médicaux, des comportements de recours aux soins de santé ou d'autres disparités. La variabilité des facteurs de risque utilisés dans les modèles ainsi que les différences dans le modèle final utilisé par chacune des études ne facilitent pas la comparaison directe des résultats, comme on l'a vu dans les méta-analyses qui démontraient souvent une grande hétérogénéité entre les études. Il convient également de noter que dans les études qui tiennent compte de l'âge, du sexe, des comorbidités et des facteurs socioéconomiques dans leur analyse, certains groupes ethniques présentent toujours un risque plus élevé d'infection par COVID-19.

Le tableau 1 ci-dessous énumère les études sur l'infection, la gravité et la mortalité par pays en raison de la COVID-19. Un résumé de leur contenu est présenté brièvement ci-dessous.

- Le risque d'infection ou la probabilité de résultat positif au test a été évalué aux États-Unis (n = 18 études), au Royaume-Uni (n = 11) et en France (n = 1) et dans une revue systématique.
    - Il a été démontré que les personnes d'origine ethnique noire, asiatique et hispanique étaient plus susceptibles d'obtenir un résultat positif dans une revue systématique (D. Pan, 2020).
    - Seize études ont examiné des données sur les tests réalisés aux États-Unis et analysé la probabilité de résultats positifs. L'éventail d'analyses était plutôt vaste et les résultats ont souvent été corrigés en fonction d'une fourchette de facteurs individuels, sanitaires et

socioéconomiques. Malgré cela, lorsque l'on compare leurs résultats à ceux des Blancs, les Noirs (neuf études), les Hispaniques (onze études), les Asiatiques (deux études) et les Autochtones/Alaskiens (une étude) ont obtenu un nombre significativement plus grand de résultats positifs (un risque de l'ordre de 1,5 à 3,5 fois plus grand) (tableau 1).

- Onze études ont examiné des données sur les tests au Royaume-Uni et ont indiqué une plus forte probabilité de résultats positifs aux tests comparativement aux Blancs pour les membres des groupes MECNA (3 études sur 4), les Noirs (sept études), les Asiatiques du Sud (deux études) et les Asiatiques (une étude).
- Une enquête effectuée auprès des Américains et des Britanniques a révélé que les Noirs et les Hispaniques avaient un plus grand risque corrigé (pour les facteurs comme le sexe, les comorbidités, l'IMC, le tabagisme) d'obtenir un résultat positif à la COVID-19 comparativement aux Américains blancs, alors que ce n'était pas le cas pour les Asiatiques ou les membres d'autres groupes ethniques. Au Royaume-Uni où différentes catégories ethniques ont été utilisées, utilisées, on a signalé a signalé un risque plus élevé pour les Noirs, les Asiatiques du Sud, les Chinois, les Moyen-Orientaux et les autres, mais pas chez les Asiatiques de l'Est ou les Hispaniques (Lo, 2020).
- Une étude menée en France auprès de personnes ayant reçu une greffe de rein a révélé que l'origine ethnique non blanche était associée à des probabilités plus élevées de la maladie de la COVID-19 après correction en fonction de l'âge, du sexe et des comorbidités (Elias, 2020).

- Le risque de maladie grave a été mesuré au fur et à mesure que les hospitalisations, l'admission à l'USI ou la ventilation mécanique étaient signalées, dans les différentes études, des résultats mitigés ont souvent été identifiés. Les résumés énumérés ci-dessous ont été regroupés par dénominateur pour le cadre de l'échantillonnage, soit l'ensemble de la population, le nombre de cas positifs de COVID-19 ou d'hospitalisation en raison de la COVID-19, puisqu'on jugeait qu'il s'agissait d'une source potentielle d'hétérogénéité. L'analyse, dans laquelle s'opposent les résultats univariés et les résultats corrigés, est également une source d'hétérogénéité entre les études puisque les estimations corrigées pour les comorbidités ou les facteurs socioéconomiques ont généralement entraîné l'atténuation vers le zéro en ce qui concerne les liens avec l'origine ethnique.
  - Hospitalisation : La revue systématique a indiqué un lien avec les Noirs (RR : 1,68 [IC à 95 % : de 1,28 à 2,20], I^2 = 98, k = 13) dans l'analyse univariée et les sous-groupes par pays RR R.-U. 5,47 [IC à 95 % : de 2,51 à 12,06] par rapport à RR É.-U. 1,36 [IC à 95 % : de 1,08 à 1,72] et montré un lien plus important entre les études britanniques. Dans les études qui ont été corrigées en fonction de l'âge, du sexe et des comorbidités, aucun lien n'a été signalé. L'analyse univariée n'a montré aucun lien avec les Hispaniques (RR : 1,00 [IC à 95 % : de 0,95 à 1,06], I^2 = 0, k = 8) alors que l'analyse corrigée a permis d'en établir un. Aucun lien avec les Asiatiques n'a été établi globalement ou dans les analyses corrigées. Cependant, lorsque les analyses ont été sous-regroupées par pays, on a observé un lien avec les Asiatiques dans les études britanniques : RR R.-U. : 2,95 [IC à 95 % : de 1,55 à 5,53] contre RR É.-U. : 0,90 [IC à

95 % : de 0,82 à 1,66]. Aucun lien avec l'admission à l'USI et la ventilation mécanique n'a été relevé dans les méta-analyses corrigées, sauf en ce qui concerne les études du Royaume-Uni qui ont indiqué un risque accru chez les Asiatiques et une surreprésentation des groupes MECNA.

- Huit études américaines ont fourni une analyse de l'origine ethnique selon la gravité dans une population. Comparativement aux Blancs, le nombre d'hospitalisations était plus élevé pour les Noirs (n = 4 études sur 4), les Hispaniques (n = 3 sur 4), les Amérindiens/Alaskiens (n = 1 sur 2), les habitants des îles du Pacifique (0 sur 2) et les autres groupes ethniques (n = 1 sur 1). Dans une étude, un niveau d'hospitalisation inférieur aux prévisions a été signalé pour les Asiatiques. Comparativement aux Blancs, des résultats plus graves ont été indiqués pour les Noirs (n = 2 sur 2), les Hispaniques (n = 2 sur 2) et les Asiatiques (n = 2 sur 2). L'admission aux USI était beaucoup plus fréquente chez les Noirs (n = 2 sur 3) et les Hispaniques (n = 1 sur 2), alors que dans une étude, le recours à la ventilation était plus courant chez les Noirs et les Hispaniques.
- Dix études américaines ont porté sur l'hospitalisation et le risque d'être admis à l'USI pour les cas confirmés de COVID-19. Les hospitalisations étaient beaucoup plus fréquentes chez les Noirs (n = 5 études sur 7), les Hispaniques (n = 3 sur 5), les Asiatiques (n = 1 sur 2), les personnes d'origine ethnique mixte, ainsi que globalement (n = 1 chacune). Aucun lien entre l'origine ethnique et le risque d'admission à l'USI n'a été établi pour les personnes atteintes de la COVID-19 ayant été hospitalisées.
- Deux études du Royaume-Uni ont relevé des taux d'hospitalisation plus élevés chez les enfants des groupes MECNA que chez les Blancs alors qu'une deuxième étude a indiqué un risque plus élevé d'hospitalisation chez les Noirs et les groupes ethniques mixtes, mais non chez les Asiatiques.
- Huit études du Royaume-Uni font état d'hospitalisations et d'admissions à l'USI parmi les cas confirmés de COVID-19. Les résultats obtenus au Royaume-Uni n'ont révélé aucun lien parmi les groupes de MECNA (n = 2 études sur 2) et un lien à haut risque pour les Noirs pour les Noirs (n = 2 sur 2), les Asiatiques du Sud (n = 2 sur 2) et les Asiatiques (n = 1 sur 1). L'admission à l'USI était également liée à des groupes de MECNA (n = 4 sur 4), d'Asiatiques du Sud (n = 2 sur 3) et de Noirs (n = 2 sur 2). Une étude a révélé des de plus fortes probabilités de recours à la ventilation mécanique chez les Noirs et les Asiatiques.

- Le syndrome inflammatoire multisystémique de l'enfant (SIME) et un lien potentiel avec l'origine ethnique ont été indiqués dans trois études, soit deux du Royaume-Uni et une de France. Dans l'ensemble de ces études, une fréquence plus élevée a été indiquée pour des ethnies non blanches ayant reçu un diagnostic de SIME et cette différence était significative dans la plus vaste étude.
- Le taux de mortalité était semblable à la gravité lorsque les dénominateurs étaient soit la population en général, soit une population hospitalisée en raison de COVID-19.

- Les revues systématiques ne font état d'aucun lien avec la mortalité chez les Noirs et les Hispaniques dans les analyses corrigées. Elles font cependant état d'un risque plus élevé chez les Asiatiques qui ont été mis sous ventilation mécanique comparativement aux Blancs avec une hétérogénéité significative entre les études et un risque de mortalité plus élevé notable entre les différents groupes ethniques dans les études britanniques (Raharja, 2020).
- Sept études américaines ont établi une analyse entre taux de mortalité parmi les cas de COVID-19 hospitalisés et l'origine ethnique. Une étude a indiqué de plus fortes probabilités chez les Noirs alors qu'une autre a indiqué de plus faibles probabilités chez les Hispaniques et que la plupart des études n'ont indiqué aucun lien avec les Noirs (n = 5), les Hispaniques (n = 4) ou tous les groupes ethniques minoritaires (n = 1).
- Une étude réalisée aux États-Unis a fait état de la mortalité parmi tous les cas positifs de COVID-19 sans cependant établir de lien avec l'origine ethnique noire.
- Sept études britanniques ont effectué une analyse entre taux de mortalité parmi les cas de COVID-19 hospitalisés et l'origine ethnique. Un lien avec un plus grand risque de mortalité a été indiqué pour les Asiatiques du Sud (n = 2 études sur 3), les Noirs (n = 1 sur 4), les Asiatiques (n = 2), mais aucun n'a été mentionné pour les Asiatiques de l'Est (n = 1), les groupes ethniques mixtes (n = 2) et les groupes MECNA (n = 1).
- Six études menées au Royaume-Uni font état de la mortalité liée à la COVID-19 dans l'ensemble de la population. Deux études ont établi de plus forts liens pour les Noirs (n = 3 études sur 4), les Asiatiques du Sud (n = 2 sur 2), les groupes ethniques mixtes (n = 1 sur 2), les MECNA (n = 1 sur 1) et les Asiatiques (n = 1 sur 2) alors que deux autres, portant sur les Asiatiques et les groupes ethniques mixtes, ont chacune donné des résultats contradictoires indiquant tant des liens protecteurs qu'un risque plus élevé comparativement aux Blancs.
- Une seule étude menée au Brésil a fait état d'un lien avec une mortalité plus élevée dans les groupes ethniques mixtes et noirs.

Tableau 1 : Le lien entre l'origine ethnique et le risque d'infection, la gravité de la maladie et le taux de mortalité dans les revues systémiques (n = 2) et les études d'observation (n = 61)

Référence	Renseignement sur l'étude	Principaux résultats
Susceptibilité, gravité clinique et mortalité associées à la COVID-19		
Revue systématique		
(Raharja, 2020) préimpression, nouveauté	Revue systématique et méta-analyse du lien entre l'origine ethnique et les résultats médiocres. (AMSTAR – haute qualité) Données recueillies jusqu'au 15 juin 2020. 72 articles (13 études écologiques) provenant des États-Unis (54), du Royaume-Uni (15), du Brésil (1) et d'Israël (1), ont été inclus, bien que les données des deux derniers ne figurent pas dans les résultats. Les résultats comprenaient la mortalité, l'hospitalisation, l'USI, ainsi que l'insuffisance respiratoire et rénale. Les résultats de l'analyse portent sur les Noirs, les Asiatiques et les Hispaniques, car il y a eu très peu d'études pour d'autres groupes ethniques autochtones ou d'autres études à l'extérieur des États-Unis et du Royaume-Uni. Une méta-analyse des effets aléatoires a été menée sur les résultats quantitatifs figurant dans 45 études. Les études non incluses dans les méta-analyses ont été résumées de façon descriptive. Leurs résultats sont également indiqués lorsqu'un lien a été identifié et/ou diffère de la méta-analyse.	Les données probantes ne confirment pas que l'origine ethnique est un facteur de risque indépendant pour les résultats médiocres chez les patients atteints de COVID-19. Les méta-analyses présentaient généralement une hétérogénéité élevée (I^2 > 60 %) et, lorsqu'elles ont été examinées, les analyses corrigées pour l'âge, le sexe et les comorbidités atténuaient les liens univariés. Les liens significatifs sont présentés ci-dessous et d'autres résultats d'analyse sont disponibles dans le document. Hospitalisation (20 études) : Comparativement aux Blancs, le lien avec les Noirs (RR : 1,68 [IC à 95 % : de 1,28 à 2,20], I^2 = 98, k = 13) dans l'analyse univariée (RR R.-U. 5,47 [IC à 95 % : de 2,51 à 12,06] par rapport à RR É.-U. 1,36 [IC à 95 % : de 1,08 à 1,72] était significativement différent). - Les études qui ont été corrigées en fonction de l'âge, du sexe et des comorbidités ne font état d'aucun lien. - L'analyse univariée n'a montré aucun lien avec les Hispaniques (RR : 1,00 [IC à 95 % : 0,95 à 1,06], I2 = 0, k = 8) alors que l'analyse corrigée a permis d'établir un lien significatif. - Aucun lien avec les Asiatiques n'a été établi globalement ou dans les analyses corrigées. Cependant, lorsque les analyses ont été sous-regroupées par pays, on a observé un lien dans les

		études britanniques : RR R.-U. : 2,95 [IC à 95 % : 1,55 à 5,53] contre RR É.-U. : 0,90 [IC à 95 % : 0,82 à 1,66]. USI (18 études) : comparativement aux Blancs, un lien univarié avec les Noirs (RR : 1,51 [IC à 95 % : de 1,11 à 2,04], I^2 = 94, k = 10) a été observé, mais aucun lien n'a été constaté après correction en fonction de l'âge, du sexe et des comorbidités. - Le lien non corrigé et corrigé avec l'admission à l'USI n'est pas significatif pour les Asiatiques ou les Hispaniques aux États-Unis. Les études menées au Royaume-Uni ont fait état d'un risque accru d'admission à l'USI chez les Asiatiques. - Cinq études britanniques non incluses dans la méta-analyse ont fait état d'une surreprésentation des communautés de MECNA dans les cohortes admises dans l'USI. Deux études américaines n'ont pas trouvé de lien avec les Noirs. Mortalité (51 études) : comparativement aux Blancs, une association protectrice avec la mortalité globale a été indiquée dans l'ensemble des données non corrigées : Hispaniques (RR : 0,69 [IC à 95 % : de 0,57 à 0,84], I^2 = 76, k = 11), mais ce lien a disparu dans les modèles corrigés en fonction de l'âge, du sexe et des comorbidités. - Les Asiatiques qui se sont retrouvés sous ventilation mécanique présentaient un risque de mortalité plus élevé dans quatre études (RR : 1,39 [IC à 95 % : de 1,07 à 1,80], I^2 = 14, k = 4). - Aucun autre lien avec la mortalité n'a été trouvé dans la méta-analyse effectuée en fonction de la mortalité

		globale, des cas hospitalisés, des cas à l'USI, des cas sous ventilation mécanique ou des cas de lésions rénales aiguës et l'origine ethnique noire, asiatique ou hispanique. Ventilation mécanique (18 études) : comparativement aux Blancs, un lien avec les Asiatiques (RR : 1,39[IC à 95 % : de 1,07 à 1,80], I^2 = 14, k = 4) a été indiqué dans l'analyse univariée et corrigée en fonction de l'âge et du sexe. - Aucun lien avec le risque de mise sous ventilation n'a été observé chez les Noirs ou les Hispaniques, même dans une analyse corrigée (âge, sexe et comorbidités). Insuffisance rénale aiguë (IRA) (8 études) : Comparativement aux Blancs, - Aucun lien avec l'IRA n'a été observé chez les Asiatiques. - Un lien a été signalé pour les Noirs (RR : 1,35 [IC à 95 % : de 1,04 à 1,76], I^2 = 92 %, k = 5) dans l'analyse univariée, mais a disparu dans l'analyse corrigée (âge, sexe et comorbidité).
(D. Pan, 2020)	Revue systématique de l'origine ethnique et des résultats cliniques de la COVID-19. (Cote AMSTAR – de qualité moyenne : le protocole enregistré peut ou non avoir été établi *a priori*. Les études incluses pour chacun des résultats ne sont pas indiquées de façon claire et il n'y a aucune discussion sur l'hétérogénéité). Données recueillies jusqu'au 15 mai 2020	Comparativement aux Blancs, plusieurs études ont révélé que les Noirs, les Asiatiques et les Hispaniques sont plus susceptibles d'obtenir ce qui suit : 1. Résultat positif à la COVID-19 Des preuves mixtes ont été indiquées pour les éléments suivants : 1. Hospitalisation 2. Intubation

	162 études (dont 80 en préimpression) Les fichiers supplémentaires 2 à 6 décrivent chacune des études incluses dans cette revue systématique. Les recherches incluses comprenaient de la littérature primaire, des essais cliniques, des préimpressions et de la littérature grise. L'analyse était descriptive et ne rendait pas compte des résultats des études individuelles, du nombre d'études ou des études qui contribuent à chacun des résultats. Peu d'études portant sur l'origine ethnique avaient été publiées en date du 15 mai 2020.	3. USI 4. Mortalité - Origine ethnique et risque d'infection par le SRAS-CoV-2 : une étude publiée (S. de Lusignan, 2020b) indique que les Noirs étaient plus susceptibles d'obtenir un résultat positif et, de façon similaire dans des préimpressions,, une plus grande susceptibilité a été rapportée dans 14 études pour les Noirs, 3 pour les Asiatiques et 3 pour les Hispaniques comparativement aux Blancs. - Les taux d'hospitalisation, d'intubation et d'admission à l'USI selon l'origine ethnique étaient contradictoires entre les études. Une importante cohorte au Royaume-Uni indique une proportion plus élevée de patients non blancs admis à l'USI. - Mortalité : Huit études n'ont révélé aucun lien avec la mortalité, alors que d'autres ont relevé un lien pour les Noirs (n = 6) et les Asiatiques (n = 3) comparativement aux Blancs. La littérature grise aux États-Unis et au Royaume-Uni fait état d'un taux de mortalité plus élevé chez les personnes d'origine non blanche (principalement les Noirs et les Asiatiques).
États-Unis (É.-U.)		
(Petrilli, 2020)	États-Unis, New York, réseau de santé multicentrique, cohorte prospective, données sur les cas jusqu'au 8 avril, puis suivi jusqu'au 5 mai. N = 5 279 admis à l'hôpital pour COVID-19 Tests positifs pour la COVID-19 n = 5 279 Hospitalisations n = 2 741	- Le risque d'hospitalisation parmi les cas positifs de COVID-19 était beaucoup plus élevé chez les Hispaniques RCC de 1,63 (IC à 95 %, 1,35 à 1,97) et les ethnies mixtes ou autres RCC de 1,6 (IC à 95 %, 1,21 à 2,11) que chez les Blancs. Régression logistique multivariable corrigée en fonction de l'âge, du sexe, du tabagisme, de la semaine d'éclosion et de l'IMC.

	Soins palliatifs ou décès n = 665 Ventilation n = 647	
(Goldfarb, 2020)	Un seul centre médical, cohorte prospective de femmes enceintes. Du 6 mars au 4 mai 2020. 65 Hispaniques (représentant 18 % de la population) et 127 femmes non hispaniques ont présenté des symptômes de COVID-19, mais toutes n'ont pas été testées. Aucune analyse statistique n'a été effectuée en raison de la taille de l'échantillon. L'origine ethnique n'a pas été un facteur de cette disparité qui peut s'expliquer par des facteurs socioéconomiques.	- Les femmes hispaniques étaient plus susceptibles d'obtenir un résultat positif (72 %) 39 sur 54 comparativement à 27 % (22 sur 82) pour les femmes non hispaniques (p < 0,001). Cela correspondait au nombre croissant de cas dans la population hispanique par rapport à la population non hispanique et la population en général après la mise en place des mesures de distanciation physique. - Parmi celles qui ont obtenu un résultat positif, une proportion semblable de femmes ont été admises à l'hôpital. 13 femmes hispaniques sur 39 et 8 femmes non hispaniques /22. De ce nombre, 5 femmes hispaniques et 1 femme non hispanique ont été admises à l'USI. Aucun décès.
(Bandi, 2020)	États-Unis, Chicago, cohorte prospective dans un seul hôpital, cas de COVID-19 pédiatrique. Tous les enfants testés pour le SRAS-CoV-2 ont été inscrits à l'étude qui s'est déroulée du 12 mars au 20 avril 2020. N = 474 enfants examinés, 5,2 % (25) étaient positifs à la COVID-19. (n = 5 enfants ont été hospitalisés) Proportion dans l'échantillon : Blanc 25,1 % Noir 43,2 % Hispanique 24,7 % Asiatique 1,5 %	- Comparativement aux Blancs, les Noirs affichaient un taux de résultats positifs beaucoup plus élevé (6,8 % comparativement à 1,7 %, p = 0,046). - Les Noirs avaient une cote de probabilité corrigée supérieure de 3,1 (IC à 95 %, 1,23 à 5,34) d'obtenir un test positif, après correction pour l'âge et le sexe. - Les Hispaniques ont obtenu des résultats semblables, mais ils n'étaient pas significatifs. - Hospitalisations : 80 % (20 sur 25) étaient Noirs, ce qui est plus élevé que prévu, mais l'auteur n'a pas analysé davantage ce résultat.
(Lo, 2020) préimpression, nouveauté	Enquête longitudinale ciblant la population générale aux États-Unis et au Royaume-Uni avec une application qui	- Risque d'obtenir un résultat positif au test de COVID-19 (rapport de cotes et IC 95 %) :

	invite les utilisateurs à entrer des commentaires chaque jour. Données collectées du 24 mars au 25 mai 2020. Données autodéclarées. Répondants : États-Unis = 179 873, Royaume-Uni = 2 234 728 Modèle multivariable par pays : corrigé en fonction du sexe, des antécédents de diabète, de cardiopathie, de maladie pulmonaire, de maladie rénale et de l'état actuel de fumeur (répondre oui ou non à chacune des questions) et de l'indice de masse corporelle (17 à 18,4, 18,5 à 24,9, 25 à 29,9 et 30 kg/m^2). Modèle multivarié combiné É.-U. et R.-U. – également corrigé en fonction du confinement, des travailleurs de la santé en première ligne, de l'exposition communautaire à la COVID-19, de la densité de population, du revenu et de l'éducation.	○ É.-U. : Noirs 2,49 (1,68 à 3,69), Hispaniques 1,66 (1,18 à 2,34), Asiatiques 1,42 (0,86 à 2,35) Autres 1,32 (0,67 à 2,61). ○ R.-U. : Noirs 1,97 (1,47 à 2,64), Hispaniques 1,71 (0,89 à 3,27), Asiatiques du Sud 1,68 (1,43 à 1,97), Chinois 1,79 (1,08 à 2,96), Asiatiques de l'Est 1,02 (0,55 à 1,87), Moyen-Orientaux 2,10 (1,52 à 1,87), Autres 2,10 (1,52 à 2,91). ○ Données combinées des États-Unis et du Royaume-Uni comparativement à celles des Blancs : Noirs 1,17 (1,10 à 1,25), Hispaniques 1,11 (1,00 à 1,23), Asiatiques 1,06 (1,03 à 1,10), Autres 1,21 (1,17 à 1,25). - Facteurs de risque : les Noirs et Hispaniques étaient plus susceptibles d'être obèses et de souffrir de diabète. - Toutes les minorités ethniques ont déclaré un confinement social plus faible, étaient surreprésentées dans les travailleurs de la santé en première ligne et ont déclaré une plus forte probabilité de contact avec un cas atteint de COVID-19.
(Martinez, 2020) nouveauté	Étude longitudinale de la population générale desservie par le Johns Hopkins Health System (5 hôpitaux et 30 cliniques) du 11 mars au 25 mai 2020. Les données représentent 32 727 personnes ayant subi le test RT-PCR pour le SRAS-CoV-2 (au fil du temps, le risque	- Le taux de tests positifs était significativement différent ($p < 0,001$) d'un groupe à l'autre comparativement aux Hispaniques (42,6 % [IC 95 %, 41,1 % à 44,1 %]), aux Blancs (8,8 % [IC 95 %, 8,4 % à 9,2 %]), aux Noirs (17,6 % [IC 95 %, 16,6 % à 18,3 %]) ou à une autre origine ethnique (17,2 % [IC 95 %, 16,2 % à 18,3 %]). Il n'est pas clair si le taux de tests positifs des Hispaniques est attribuable à une prévalence plus

	est passé de seulement élevé à tous les individus symptomatiques). Statistiques : la proportion de personnes ayant eu un résultat positif et ayant été hospitalisées a été analysée par catégorie ethnique à l'aide d'une analyse de variance omnibus avec correction pour les comparaisons multiples.	élevée de la maladie ou à des taux plus faibles d'utilisation des soins de santé. - Les hospitalisations étaient moins nombreuses pour les Hispaniques (29,1 % [IC 95 %, de 27,0 % à 31,2 %]) que pour les Blancs (40,1 % [IC 95 %, de 37,6 % à 42,5 %]) ou les Noirs (41,7 % [IC 95 %, de 39,5 % à 43,8 %]).
(Lee, 2020) préimpression, nouveauté	É.-U., analyse rétrospective de cohorte des dossiers des patients de 12 hôpitaux du Midwest et de 60 cliniques entre le 4 mars et le 19 août 2020. Le résultat principal portait sur la gravité de la COVID-19 établie en fonction de l'hospitalisation dans les 45 jours qui ont suivi le diagnostic. 5 577 patients atteints de COVID-19 ont été inclus et 866 (n = 15,5 %) ont été hospitalisés dans les 45 jours qui ont suivi le diagnostic. Parmi les personnes hospitalisées, 43,9 % (n = 381) étaient Blancs 19,9 % (n = 172) étaient Noirs 18,6 % (n = 161) étaient Asiatiques 11,8 % (n = 102) étaient Hispaniques Le modèle a été corrigé en fonction de l'âge, du sexe, de la comorbidité, de l'état civil et de la ruralité ou de l'urbanité de la personne.	Indépendamment de la privation du quartier, la race ou l'origine ethnique minoritaire des patients était associée à une augmentation de la gravité de la COVID-19. - Hispaniques (RC 3,8, IC 95 %, de 2,72 à 5,30) - Asiatiques (RC 2,39, IC 95 %, de 1,74 à 3,29) - Noirs (RC 1,50, IC 95 %, de 1,15 à 1,94)
(Hatcher, 2020) nouveauté	É.-U., analyse rétrospective de cohorte pour la COVID-19 dans les populations d'Amérindiens et d'Autochtones de l'Alaska de 23 États (n = 345 093). Les résultats sur l'incidence de l'infection par le SRAS-CoV-2 indiqués entre le 22 janvier et le 3 juillet 2020 montrent une incidence	Incidence cumulée de la COVID-19 : - Amérindiens et Autochtones de l'Alaska : 594 (IC 95 %, de 203 à 1 740 pour 100 000 Amérindiens et Autochtones de l'Alaska)

	3,5 fois plus élevée d'Amérindiens et Autochtones de l'Alaska atteints de la COVID-19.	- Blancs 169 (IC 95 %, de 137 à 209) pour 100 000 Blancs - Les Amérindiens et Autochtones de l'Alaska avaient un risque relatif significativement plus élevé d'être atteints de la COVID-19 (RR 3,5, IC 95 %, de 1,2 à 10,1) comparativement aux Blancs.
(McCarty, 2020) nouveauté	E.-U., analyse rétrospective de cohorte de 9 hôpitaux du Massachusetts, avec 379 patients atteints de la COVID-19. Lien entre la Race/l'origine ethnique des patients et résultats de l'hospitalisation (p. ex., mortalité à l'hôpital, admission à l'USI ou mise sous ventilation mécanique).	- Dans le cadre d'une analyse multivariable tenant compte de l'âge, du sexe, de l'obésité, des comorbidités cardiopulmonaires, de l'hypertension et du diabète, aucune différence significative n'a été observée dans la mortalité à l'hôpital, l'admission à l'USI ou la mise sous ventilation mécanique en fonction de la race ou de l'origine ethnique.
(Karaca-Mandic, 2020) nouveauté	É.-U., cohorte rétrospective qui a examiné la prévalence raciale/ethnique des hospitalisations cumulatives liées à la COVID-19 dans 12 États entre le 30 avril et le 24 juin 2020. La proportion d'hospitalisations selon l'origine ethnique a été comparée à la proportion de chaque ethnie dans la population. Origines ethniques incluses dans le rapport : Hispaniques, Blancs, Noirs, Asiatiques, Amérindiens et Autochtones de l'Alaska. Les données sont descriptives et n'ont pas été corrigées.	Hospitalisations : Le nombre de Blancs hospitalisés était significativement inférieur à la proportion de la population qu'ils représentent dans les 12 États inclus. - Le pourcentage d'hospitalisations chez les patients Noirs dépassait le pourcentage que représente cette population dans les 12 États inclus. - Les hospitalisations d'Hispaniques dépassaient la proportion de la population qu'ils représentent dans 10 États et et cette observation était très prononcée en en Virginie, en Utah et au Rhode Island. - Le nombre d'Asiatiques hospitalisés en raison de la COVID-19 était à peu près équivalent ou inférieur à la proportion qu'ils représentent dans la population. - Des Amérindiens et des Autochtones de l'Alaska ont été signalés dans huit États et parmi eux, l'Arizona et l'Utah présentaient d'importantes disparités.

(Gottlieb, 2020) nouveauté	É.-U., étude rétrospective avec cas-témoins effectuée au Rush University Medical Center de Chicago, en Illinois, entre le 4 mars et le 21 juin 2020, qui a examiné les facteurs de risque associés à l'hospitalisation.	- L'origine ethnique hispanique était un facteur de risque pour l'admission à l'hôpital (RC = 1,52, IC à 95 % = 1,18 à 1,92).
(Rozenfeld, 2020) nouveauté	É.-U., étude respective de cohorte effectuée entre le 28 février et le 27 avril 2020 afin de caractériser les facteurs de risque chez 34 503 patients du Providence Health System.	Risque d'infection par le SRAS-CoV-2 comparativement aux Blancs : - Asiatiques (RC 1,43 ; IC 95 %, de 1,18 à 1,72, p = 0,0002) - Noirs (RC 1,51 ; IC 95 %, de 1,25 à 1,83, p < 0,0001) - Hispaniques (RC 2,07 ; IC 95 %, de 1,77 à 2,41, p < 0,0001).
(McPadden, 2020) préimpression, nouveauté	É.-U., étude rétrospective de cohorte effectuée au Yale New Haven Health (YNHH) sur 7 995 patients atteints du SRAS-CoV-2 entre le 1er mars et le 30 avril 2020. L'étude a évalué l'hospitalisation et le taux de mortalité à l'hôpital.	Race/origine ethnique avec risque accru d'hospitalisation : - Asiatiques (RC 1,58, IC 95 % = 1,02 à 2,41) - Noirs (RC 1,43, IC 95 %, de 1,14 à 1,78) - Hispaniques (RC 1,81, IC 95 %, de 1,50 à 2,18) Parmi les gens qui ont pu quitter l'hôpital, la correction en fonction de l'âge et le taux de mortalité à l'hôpital étaient semblables parmi tous les groupes raciaux et ethniques. Taux de mortalité à l'hôpital, corrigé en fonction de l'âge : - Blancs = 4,3 % - Noirs = 3,3 % - Hispaniques = 3,4 % - Asiatiques = 4,6 % - Hawaïens = 4,0 % - Habitants des îles du Pacifique = 3,1 %
(Emeruwa, 2020) nouveauté	É.-U., New York : étude rétrospective de cohorte sur les femmes (n = 100) qui ont accouché dans deux hôpitaux affiliés à l'association New York-Presbyterian à Manhattan du 13 mars au 23 avril 2020. Le taux d'infection par SRAS-	- Le taux d'infection par le SRAS-CoV-2 était beaucoup plus élevé chez les femmes hispaniques que chez les femmes blanches non hispaniques (18,1 % comparativement à 9,4 %, p < 0,01).

	CoV-2 par groupe racial-ethnique de femmes ayant accouché a été analysé.	- Le taux positif d'infection au SRAS-CoV-2 chez les femmes noires non hispaniques (12,7 %) n'était pas significativement différent.
(Mendy, 2020) préimpression nouveauté	Cohorte rétrospective des cas hospitalisés dans le système de santé de l'Université de Cincinnati (4 hôpitaux) du 13 mars au 31 mai 2020. N = 689 cas (test RT-PCR positif) Modélisation de régression logistique corrigée pour les covariables: âge, sexe, origine ethnique, tabagisme, comorbidités.	- Hospitalisations (31,3 % au total) : Analyses corrigées : Noirs RC 2,23 (IC 95 %, de 1,41 à 3,53) et Hispaniques RC 1,91 (IC 95 %, de 1,11 à 3,29) comparativement aux Blancs. - COVID-19 grave : Analyses corrigées : Noirs RC 3,15 (IC 95 %, de 1,71 à 5,79) et Hispaniques RC 2,78 (IC 95 %, de 1,29 à 5,96) comparativement aux Blancs. - USI (13,2 % au total) : Analyses corrigées : Noirs RC 3,32 (IC 95 %, de 1,56 à 7,07) et Hispaniques RC 3,44 (IC 95 %, de 1,42 à 8,34) comparativement aux Blancs. - Décès : analyse corrigée Noirs RC 3,44 (IC 95 %, de 1,32 à 9,00).
(Kalyanaraman Marcello, 2020)* préimpression nouveauté	Cohorte rétrospective, données du système hospitalier public de New York, New York, du 5 mars au 9 avril, suivi jusqu'au 16 avril 2020. 22 254 patients testés dans la circonscription hospitalière, 13 442 résultats positifs au SARS-CoV-2. Les Noirs et les Hispaniques représentaient environ le tiers des cas de COVID-19, ce qui constitue une surreprésentation de ces groupes ethniques par rapport à la population de New York. Analyse descriptive, utilisation du test test du χ2 (khi carré). Aucune analyse multivariable n'a été effectuée.	- Tests positifs 13 442 sur 22 254 (61 %). 26 % de Noirs et 34 % d'Hispaniques. Tant les Noirs que les Hispaniques ont eu une proportion significativement plus élevée de tests positifs que les Blancs ($p < 0,001$). La proportion plus élevée pourrait être attribuable au fait que les Noirs et les Hispaniques étaient plus susceptibles de se présenter à l'urgence plutôt qu'en consultations externes. - Hospitalisations 6 248 sur 13 442 (46 %). 31 % de Noirs et 34 % d'Hispaniques. Une proportion significativement plus élevée de Noirs ont été hospitalisés $p < 0,001$, mais aucun lien établi pour les Hispaniques. - Décès 1 724 sur 6 248 (28 %). 29 % de Noirs et 31 % d'Hispaniques.

(Price-Haywood, 2020)	Cohorte rétrospective, Louisiane aux États-Unis, système de santé Ochsner, du 1er mars au 11 avril. N = 3 481 tests de COVID-19 positifs dans la circonscription hospitalière La population desservie par cet hôpital est composée à 31 % de Noirs et à 65 % de Blancs. Analyse : – Régression logistique multivariable (hospitalisations) corrigée en fonction l'âge, du sexe, de la cote de l'indice de comorbidité, du fait d'habiter dans une habitation habitation de loyer à faible revenu, du régime public d'assurance maladie. – Analyse de survie (mortalité), corrigée en fonction de l'âge, du sexe et de la cote de l'indice de comorbidité.	- Profil racial des tests positifs à la COVID-19 : 70,4 % de Noirs et 29,6 % de Blancs. - Hospitalisation (N = 1 382) 76,9 % de Noirs. La probabilité que les Noirs soient hospitalisés était plus élevée RC 1,96 (IC 95 %, de 1,62 à 2,37). - USI (N = 474) 80,2 % de Noirs. - Ventilation mécanique (N = 364) 81,6 % de Noirs. - Décès (N = 326) 70,6 % de Noirs. Dans l'analyse de survie, la race noire n'a pas été associée de manière indépendante à la mortalité (HR = 1,14, IC 95 %, de 0,88 à 1,49).
(Azar, 2020)*	Cohorte rétrospective multi hôpital. San Francisco aux É.-U., patients, du 1er janvier au 8 avril 2020 Données globales : n = 140 36 testés pour la COVID-19 n = 1 025 cas de COVID-19 n = 256 personnes hospitalisées n = 110 à l'USI	- Hospitalisation des noirs 52,5 % (n = 32) comparativement à 25,7 % (n = 110) pour les Blancs. - Les rapports d'hospitalisation des Noirs étaient 2,7 (RR) fois plus élevés que pour les Blancs selon un modèle multivariable corrigé en fonction de l'âge, du sexe et des variables sociodémographiques. Remarque : Les Noirs étaient plus susceptibles d'être vus à l'urgence alors qu'ils étaient dans un état grave plutôt que dans un cadre non ambulatoire, ce qui peut expliquer ce lien. - Les admissions en USI étaient plus élevées pour les Noirs (24,6 %) que pour les Blancs (10,7 %). - Les Noirs atteints de COVID-19 habitaient dans des régions où les codes postaux correspondaient à un

		revenu inférieur à celui de tous les autres groupes raciaux et ethniques (p < 0,001). - Il n'y a pas eu de différence significative dans la mortalité entre les différents groupes ethniques.
(Rentsch, 2020)* préimpression	États-Unis, 6 millions de vétérans américains, du 8 février au 4 mai. Cohorte rétrospective. N = 5 630 cas de COVID-19 sur 62 098 vétérans testés. Origine ethnique : Blancs 74 %, noirs 19 %, hispaniques 7 %. Les estimations ont été corrigées en fonction des variables démographiques, médicales et des comportements à haut risque, ainsi que des variables socioéconomiques.	- Les taux de tests pour 1 000 personnes étaient plus élevés pour les Noirs 16,4 (IC 95 %, de 16,2 à 16,7) et les Hispaniques 12,2 (IC 95 %, de 11,9 à 12,5) comparativement aux Blancs 9,0 (IC 95 %, de 8,9 à 9,1). - Comparativement rapport aux Blancs, les Noirs étaient plus susceptibles d'obtenir un résultat positif au test de dépistage RCC de 1,96 (IC 95 %, de 1,81 à 2,12), tout comme les Hispaniques 1,73 (IC 95 %, de 1,53 à 1,96). - Parmi les cas de COVID-19, il n'y avait pas de différence significative dans les taux de mortalité à 30 jours selon le groupe ethnique.
(Gu, 2020)* préimpression nouveauté	Cohorte rétrospective, Michigan aux États-Unis, du 10 mars au 22 avril 2020. N = 5 698 patients testés (témoins non appariés sélectionnés par échantillonnage aléatoire n = 7 211 et témoins appariés par fréquence selon la race, l'âge et le sexe n = 13 351) régression logistique, corrigée en fonction de l'âge, du sexe et des caractéristiques socioéconomiques.	- Facteurs de risque pour un test positif : Taux de tests positifs chez les Noirs (42,6 %) significativement plus élevé que chez les Blancs (13,7 %, p < 0,001). - Hospitalisation des noirs 52,2 % comparativement à 39 % pour les Blancs, p < 0,001 et RC 1,66 (IC 95 %, de 1,09 à 2,52). - USI pour les noirs 27 % comparativement à 14,8 % pour les Blancs, p < 0,001 et RC 1,52 (IC 95 %, de 0,92 à 2,52). - Mortalité des noirs 5,3 % comparativement à 3,0 % pour les Blancs, p < 0,12 et RC 1,17 (IC 95 %, de 0,4-3,45)
(Joseph, 2020) nouveauté	É.-U., étude rétrospective de cohorte pour un seul établissement visant à déterminer si la radiographie des poumons prise lors de l'admission des patients non Blancs	- Les patients non Blancs hospitalisés pour une infection par COVID-19 étaient plus susceptibles d'être dans un état plus grave lors de la radiographie pulmonaire prise

	atteints de la COVID-19 indique qu'ils sont dans un état plus grave que les patients Blancs,, du 27 mars au 10 avril 2020, n = 326 au total (210 non Blancs ; 116 Blancs)	au moment de l'admission que les patients Blancs/non-Hispaniques (différence moyenne corrigée de 1,6, IC 95 %, de 0,5 à 2,7, p < 0,01).
(Antwi-Amoabeng, 2020) prépublication	Étude de cohorte rétrospective pour un seul centre Nevada, aux É.-U., n = 172 patients atteints de la COVID-19, du 12 mars au 8 mai Hispaniques comparativement aux non-Hispaniques Résultats globaux : - 121 hospitalisations - 28 à l'USI 18 décès	- Les Hispaniques ont été significativement plus nombreux à être atteints de COVID-19 (50,6 %) que ce à quoi on aurait pu s'attendre puisqu'ils représentent 25,7 % de la population. - La mortalité était significativement plus élevée dans le groupe des non-Hispaniques (15,3 % comparativement à 5,8 %), p = 0,048. *L'analyse qui tient compte du fait que le groupe des Hispaniques est beaucoup plus jeune, qu'il a moins de comorbidités, qu'il est plus susceptible de ne pas avoir d'assurances et qu'il vit dans des collectivités à faible revenu que le groupe non-Hispanique n'a pas été effectuée.
(Kim, 2020)*	Réseau COVID-NET américain (surveillance couvrant 14 États) : 2 491 cas d'hospitalisation entre le 1er mars et le 2 mai. N = 16 318 cas de COVID-19 n = 2 491 cas de COVID-19 ayant des dossiers complets qui ont pu quitter l'hôpital à compter du 3 mai 2020 ont été analysés. Parmi eux, 47 % sont des Blancs, 30 % sont des Noirs et 12 % sont des Hispaniques. n = 798 à l'USI n = 420 décès n = 246 décès sur 462 parmi ceux qui ont été mis sous ventilation mécanique	Parmi les cas de COVID-19 ayant été hospitalisés, aucun lien n'a été établi entre l'origine ethnique et l'admission à l'USI ou le taux de mortalité.

	Régression logistique multivariable contrôlant l'âge, le sexe et les conditions sous-jacentes comme le tabagisme et le traitement avec les inhibiteurs de l'ECA.	
(Bui, 2020) nouveauté	É.-U., enquêtes sur l'éclosion en Utah, du 6 mars au 5 juin 2020. La composition raciale et ethnique des cas associés à une éclosion en milieu de travail a été comparée à la composition raciale et ethnique globale dans chacun des secteurs de l' Utah.	Bien que 24 % de la main-d'œuvre de l'Utah dans les 15 secteurs touchés ait été identifiée comme Hispanique ou de race autre que blanche (non-Blancs), 73 % (soit 970 sur 1 335) des cas de COVID-19 associés à une éclosion en milieu de travail étaient des personnes qui se sont identifiées comme Hispaniques ou non Blancs.
(Chamie, 2020) nouveauté	Une étude transversale a été effectuée dans un secteur comprenant 16 pâtés de maisons dans le district de Mission à San Francisco du 25 au 28 avril. Des tests sérologiques et RT-PCR ont été effectués sur des résidents qui se sont portés volontaires. N = 3 953 personnes testées, 40 % Hispaniques, 41 % Blancs, 9 % Asiatiques ou habitants des îles du Pacifique, 2 % Noirs et 7 % ethnies mixtes ou autres.	- 83 sur 3 953 ont obtenu un résultat positif lors du test RT-PCR et 95 % des personnes ayant obtenu un résultat positif étaient Hispaniques. - Prévalence parmi les résidents et travailleurs hispaniques : 3,9 % (2,0 à 6,4)/10,4 % (7,0 à 14,8) par rapport aux autres ethnies : 0,2 % (0,0 à 0,4)/0,0 % (0,0 à 2,0). - Une infection récente était plus susceptible d'être identifiée chez les Hispaniques 10,1 (2,81 à 64,6) que chez les autres ethnies. - Les Hispaniques qui ont obtenu un résultat positif lors de cette étude étaient plus susceptibles d'être des hommes, d'occuper un poste en première ligne, d'avoir un faible revenu (50 000 $) et de déclarer avoir été en contact avec une personne atteinte de COVID-19.
(Ko, 2020) nouveauté	É.-U., étude transversale qui a examiné les facteurs associés aux hospitalisations en raison de la COVID-19 en évaluant les données provenant de 70 comtés qui participaient au réseau Coronavirus Disease 2019-Associated Hospitalized Surveillance Network (COVID-NET), ainsi qu'un échantillon d'une population d'adultes	Risque d'hospitalisation par origine ethnique comparativement aux Blancs : - Noirs (RRA de 4,7, IC à 95 %, de 3,8 à 5,9). - Autres ethnies (RRA de 3,5 ; IC à 95 %, de 2,8, 4,3)

	non hospitalisés qui vivent dans la zone de couverture du réseau COVID-NET.	
(A. Pan, 2020) préimpression nouveauté	É.-U., analyse transversale effectuée à Houston entre le 3 mars et le 18 juillet 2020, qui a évalué le nombre d'hospitalisations et le taux de mortalité chez les Noirs comparativement aux Blancs et chez les Hispaniques comparativement aux Blancs dans la région métropolitaine du Grand Houston.	Dans un modèle entièrement corrigé, la probabilité d'hospitalisation plus élevée était statistiquement significative. - Noirs : RCC de 1,42 (IC 95 %, de 1,24 à 1,63). - Hispaniques : RCC de 1,61 (IC 95 %, de 1,46 à 1,78). Aucun lien n'a été établi avec le taux de mortalité.
(Vahidy, 2020) nouveauté	É.-U., étude transversale sur les données recueillies simultanément depuis le 5 mars 2020 par le système du Houston Methodist Hospital sur le lien entre l'origine ethnique et de la susceptibilité à l'infection par le SRAS-CoV-2.	Dans le modèle entièrement corrigé, la probabilité d'infection était plus élevée chez les femmes comparativement aux Blancs : - Noirs : RCC, IC de 1,84, de 1,49 à 2,27). - Hispaniques : RCC, IC de 1,70, de 1,35 à 2,14). - Asiatiques : RCC, IC de 1,46, de 1,09 à 1,95).
(Goyal, 2020) nouveauté	É.-U., étude transversale comprenant 1 000 enfants testés entre le 21 mars et le 28 avril 2020 qui a évalué le lien entre l'origine ethnique des patients et les taux d'infection par le SRAS-CoV-2.	Comparativement aux Blancs (7,3 %), les enfants des minorités avaient des taux plus élevés d'infection par le SRAS-CoV-2 (Noir : (30,0 % ; RR corrigé 2,3 [IC 95 %, de 1,2 à 4,4] ; Hispaniques : 46,4 % ; RR corrigé 6,3 [IC 95 %, de 3,3 à 11,9]).
(Alvarez Retamales, 2020) préimpression nouveauté	États-Unis, données d'observation transversales sur l'admission à l'hôpital à l'échelle nationale tirées du COVID-NET du CDC le 11 juin 2020, afin d'examiner l'écart entre le taux d'hospitalisation par race ou origine ethnique chez 21 221 patients atteints de COVID-19 et hospitalisés dans une population de 328 239 523 personnes.	Différences significatives dans la proportion ethnique de la cohorte de patients atteints de COVID-19 par rapport à la population, soit : - Blancs 38 % comparativement à 60,4 %. - Hispaniques : 19 % comparativement à 18,3 %. - Noirs : 36 % comparativement à 13,4 %. - Asiatiques et habitants des îles du Pacifique : 5 % comparativement à 6 %. - Amérindiens et Autochtones de l'Alaska : 1,6 % comparativement à 1,3 %.

		L'écart le plus marqué est entre les Blancs et les Noirs, puisque les Blancs sont sous-représentés de façon disproportionnée alors que les Noirs sont surreprésentés de façon disproportionnée dans la cohorte de patients atteints de COVID-19 par rapport à la population totale.
(Gross, 2020)	États-Unis, 28 États : étude de prévalence allant jusqu'au 21 avril 2020. Les données du CDC ont été extraites par État ; 28 États et NYC ont des données relatives à l'origine ethnique. L'analyse a été corrigée en fonction de l'âge (mortalité normalisée selon l'âge dans les groupes raciaux de chaque État) et une méta-analyse a été effectuée pour évaluer le lien avec les disparités raciales au niveau de l'État.	- Le risque de décès chez les Noirs comparativement à la population blanche était de 3,57 (IC 95 %, de 2,84 à 4,48). La Pennsylvanie était le seul État où le risque de décès lié à la COVID-19 était plus faible pour les Noirs que pour les Blancs. - Le risque de décès des Hispaniques est de 1,88 (IC 95 %, de 1,61 à 2,19) fois plus élevé que celui des Blancs. 12 États ont indiqué un risque significativement plus élevé de décès lié à COVID-19 pour les Hispaniques.
Royaume-Uni (R.-U.)		
(Leeds, 2020) nouveauté	R.-U., étude de cohorte prospective pour les travailleurs de la santé des hôpitaux du NHS Trust. Un programme de tests parmi les membres du personnel effectué en avril a examiné les caractéristiques de 991 travailleurs de la santé touchés.	- L'âge, le sexe, la profession et l'origine ethnique n'ont pas été associés à un risque accru d'avoir le SRAS-CoV-2.
(Harrison, 2020) préimpression nouveauté	Cohorte prospective, Angleterre, Écosse et Pays de Galles. 260 hôpitaux, du 6 février au 8 mai. N = 30 693 cas soupçonnés et confirmés de COVID-19 Analyse : modèles de régression hiérarchique / régression du modèle des risques proportionnels de Cox, corrigés en fonction de l'âge, du sexe, de l'emplacement.	- Comparativement aux Blancs, l'admission à l'USI était plus fréquente chez les Asiatiques du Sud RC 1,28 (IC 95 %, de 1,09 à 1,52), les Noirs RC 1,36 (IC 95 %, de 1,14 à 1,62) et les autres minorités ethniques RC 1,29 (IC 95 %, de 1,13 à 1,47). - Mortalité comparativement aux Blancs : pour les Asiatiques du Sud HR 1,19 (IC 95 %, de 1,05 à 1,36), HR 1,00 pour les Asiatiques de l'Est (IC 95 %, de 0,74 à 1,35), HR 1,05 pour les Noirs (IC 95 %, de 0,91

		à 1,26), HR 0,99 pour les autres minorités ethniques (IC 95 %, de 0,89 à 1,10). - Le diabète a eu un effet médiateur important (17,8 %, de 8,9 à 65,7) sur la mortalité des Asiatiques du Sud.
(Williamson, 2020) nouveauté	R.-U., OPENSafely, l'interface du système de notification des patients du NHS, pour 24 millions d'adultes enregistrés (soit 40 % de la population), cohorte prospective. N = 12 718 279 personnes ayant des données sur l'origine ethnique formant partie de la population générale incluse dans cette cohorte. Les données du 1er février au 6 mai ont été analysées (selon le modèle multivariable des risques proportionnels de Cox) afin d'obtenir le nombre de décès liés à des cas confirmés de COVID-19 (n = 10 926). Données corrigées en fonction de l'âge, du sexe, de l'IMC, du tabagisme, des comorbidités, de l'asthme, du cancer, des indices socioéconomiques et de l'origine ethnique.	- Mortalité due à la COVID-19 : Comparativement aux Blancs, le risque relatif pour les Noirs est de 1,48 (IC 95 %, de 1,29 à 1,69), de 1,45 (IC 95 %, de 1,32-1,58) pour les Asiatiques du Sud et de 1,43 (IC 95 %, de 1,11-1,84) pour les personnes des groupes ethniques mixtes dans la population. - Un risque plus élevé de décès était associé aux hommes, à ceux qui ont un âge plus avancé, à la privation, au diabète incontrôlé, à l'asthme grave et à d'autres problèmes médicaux. - Compte tenu des facteurs socioéconomiques et médicaux, l'origine ethnique est restée un prédicteur important de la mortalité au sein de la population.
(Razieh, 2020) nouveauté	Cohorte prospective, étude sur la biobanque du R.-U. (N = 502 543). Données sur la COVID entre le 16 mars et le 14 juin. N = 5 623 personnes testées, 1 087 résultats positifs Régression logistique sur l'IMC et l'origine ethnique. Analyse corrigée en fonction de l'âge au moment du test, le sexe, la privation sociale (indice de privation de Townsend), le tabagisme, le cancer (nombre) et les maladies autres que le cancer (nombre), la tension artérielle systolique, le cholestérol LHD, le cholestérol total et l'HbA1c.	- Le risque accru d'être atteint de la COVID-19 pour les Noirs comparativement aux Blancs n'était apparent qu'à des valeurs d'IMC plus élevées (figure 1). Par exemple, à une valeur d'IMC de 25 kg/m^2, le risque n'était pas différent (RC = 0,96 ; IC à 95 % : 0.61, 1,52), alors qu'avec un IMC de 30 ou 35 kg/m^2, le risque d'avoir la COVID-19 était respectivement 1,75 (1,24 à 2,48) et 2,56 (1,63 à 4,03) fois supérieur chez les Noirs.

(McQueenie, 2020) nouveauté	Biobanque du R.-U., cohorte prospective de 502 503 participants Données sur la COVID-19 : 16 mars et 18 mai.	- Les non-Blancs ayant de multiples facteurs de morbidité présentaient un risque d'infection par la COVID-19 près de trois fois [RR 2,81 (2,09 à 3,78)] supérieur à celui des Blancs.
(Woolford, 2020) nouveauté	Biobanque du R.-U., analyse de cohorte prospective des adultes atteints de COVID-19 (n = 470) admis au Royal Oldham Hospital visant à explorer les facteurs prédictifs de décès. Données sur la COVID-19 : Du 16 mars au 1er juin Modèle de régression logistique	Lien entre la mortalité et l'origine ethnique comparativement aux Blancs. - Asiatiques [RC = 0,37, IC 95 %, de 0,18 à 0,76), p < 0,01)]. - Autres origines ethniques [RC = 0,29 (IC 95 %, de 0,10 à 0,88, p = 0,03]. - Il n'y a eu aucun lien significatif entre l'origine ethnique des Noirs et les décès liés à la COVID-19 [RR = 1,18 {IC 95 %, de 0,31 à 4,45), p = 0,81].
(Chadeau-Hyam, 2020) nouveauté	Cohorte prospective, étude sur la biobanque du R.-U. Modèle avec cas-témoin négatif modélisant le risque de test positif à la condition d'avoir été testé. Données recueillies jusqu'au 18 mai N = 4 509 tests (1 325 cas positifs de COVID-19) Statistiques : modèles de régression logistique multivariables et pénalisés corrigés en fonction de l'âge, du sexe, de l'éducation, de l'accession à la propriété, du nombre de personnes dans le ménage, du revenu, du fait d'être un travailleur de la santé, du fait d'être au chômage, du tabagisme, de l'obésité, des comorbidités.	Facteurs de risque pour l'obtention d'un résultat positif ou négatif au test : Noirs comparativement aux Blancs (RC 1,05 [1,02 à 1,08]).
(Lassale, 2020) nouveauté	Cohorte prospective, étude sur la biobanque du R.-U. N = 340 966 (640 cas de COVID-19 du 16 mars au 26 avril) Régression logistique pour estimer le risque d'hospitalisation en raison de la COVID-19. Corrigée en fonction de l'âge, du sexe, de la privation du quartier, du surpeuplement dans le ménage, de l'IMC, du tabagisme,	Hospitalisation comparativement aux Blancs : - Noirs RC 2,66 (IC 95 %, de 1,82 à 3,91). - Asiatiques RC 1,43 (IC 95 %, de 0,91 à 2,26). - Autre groupe non-Blancs RC 1,41 (IC 95 %, de 0,87 à 2,31).

	de l'inflammation, de l'hémoglobine glyquée et de la maladie mentale.	Après avoir contrôlé les facteurs mesurés, il est resté des différences ethniques claires liées au risque d'hospitalisation en raison de la COVID-19. Les facteurs d'atténuation les plus importants ont été les facteurs socioéconomiques.
(Raisi-Estabragh, 2020)	Biobanque du R.-U. (cohorte prospective de > 500 000 participants, recrutés entre 2006 et 2010, âge variant entre 40 et 69 ans) Du 16 mars au 18 mai 2020 N = 4 510 personnes testées pour la COVID, 1 326 résultats positifs. L'analyse est limitée au sein de la cohorte testée ; les personnes testées au R.-U. sont vues comme souffrant actuellement d'une maladie grave.	- Régression logistique multivariée pour les résultats positifs au test de la COVID-19, les non-Blancs avaient une probabilité plus élevée RR 1,59 (IC 95 %, de 1,26 à 1,99) comparativement aux Blancs. Données corrigées en fonction du sexe, de l'origine ethnique, de l'IMC, de l'indice de privation de Townsend et du nombre de personnes dans le ménage.
(Niedzwiedz, 2020)	Biobanque du R.-U. (cohorte prospective de 392 116 participants en Angleterre, recrutés entre 2006 et 2010, âge variant entre 40 et 69 ans) du 16 mars au 3 mai. Modèle de régression logistique corrigé pour les éléments suivants : Correction initiale = âge, sexe et centre d'évaluation Correction complète = corrections indiquées ci-dessus + statut de travailleur de la santé, variables socioéconomiques, variables associées au mode de vie, troubles médicaux.	- Comparativement aux Blancs, il était plus probable que les Noirs RRA de 2,05 (IC 95 %, de 1,39 à 3,03, correction complète) et les Asiatiques du Sud RRA de 2,42 (IC 95 %, de 1,75 à 3,36, correction initiale) aient des résultats positifs au test. - Dans des groupes ethniques définis en fonction du risque de test positif (correction initiale) : - RR pour les Pakistanais de 3,24 (IC 95 %, de 1,73 à 6,07) > RR des Asiatiques provenant d'autres pays du Sud de 3,00 (IC 95 %, de 1,64 à 5,49) > RR des Indiens de 1,98 (IC 95 %, de 1,26 à 3,09) pour un test positif comparativement aux Blancs. - Le RR des Antillais noirs est de 3,51 (IC 95 %, de 2,39 à 5,15) et des Noirs africains de 3,11 (IC 95 %, de 1,97 à 4,91) sont similaires.

(Kolin, 2020) préimpression	Biobanque du R.-U. (cohorte prospective de > 500 000 participants, recrutés entre 2006 et 2010, âge variant entre 40 et 69 ans), examen des 669 premiers cas de COVID-19, 16 mars - date d'extraction des données non fournie. Données corrigées pour l'âge, le sexe, l'indice de masse corporelle, l'indice de privation de Townsend et les antécédents de diabète, d'angine ou d'infarctus du myocarde.	Comparativement aux Blancs - Les Noirs RRA de 3,14 (IC 95 %, de 2,28 à 4,31) présentaient un risque plus élevé d'être atteints de la COVID-19. - Les Asiatiques présentaient également un risque plus élevé d'être atteints de la COVID-19 RRA de 2,03 (IC 95 %, de 1,40 à 2,95). *Le dénominateur est la cohorte/population tirée de la Biobanque.
(Patel, 2020)	Biobanque du R.-U. (cohorte prospective de 418 794 participants, recrutés entre 2006 et 2010, âge variant entre 40 et 69 ans) Les dates ne sont pas précisées. Régression corrigée en fonction de l'âge, du sexe et des facteurs socioéconomiques.	Comparativement aux Blancs, les Noirs RRA de 3,1 (IC 95 %, de 2,0 à 4,8) et les Asiatiques 2,0 (IC 95 %, de 1,2 à 3,1) présentaient un risque accru d'hospitalisation en raison d'un test positif de COVID-19 positif. *Le dénominateur est la cohorte/population tirée de la Biobanque.
(Harman, 2020)*	Petite cohorte d'enfants admis avec la COVID-19 provenant d'un seul centre. Sélectionnés de façon prospective au King's College Hospital de Londres au R.-U., entre le 25 février et le 28 avril 2020.	- Hospitalisation : 9 sur 12 (75 %) étaient d'origine noire, asiatique ou d'une autre minorité alors qu'ils ne représentent que 39 % dans la région du centre de Londres.
(Sapey, 2020) nouveauté	R.-U., University Hospitals Birmingham NHS Foundation Trust (UHB) étude rétrospective de cohorte sur les patients atteints du SRAS-CoV-2 (n = 2 217) admis entre le 10 mars et le 17 avril 2020. L'origine ethnique asiatique du Sud est définie comme incluant les Pakistanais, les Bangladais et les Indiens. Analyse de régression du modèle des risques proportionnels de Cox corrigée en fonction de l'âge, du sexe, de la privation et des comorbidités.	- Maladie grave chez les patients asiatiques du Sud 34 sur 137 (24,8 %) comparativement aux Blancs 54 sur 483 (11,2 %) p < 0,0001. - Admissions à l'USI de patients asiatiques du Sud 86 sur 410 (21,0 %) comparativement aux patients Blancs 133 sur 1 540 (8,6 %), p < 0,001. - Mortalité HR de 1,4 (IC 95 %, de 1,2 à 1,8) pour les Asiatiques du Sud comparativement à celle des Blancs.

		- Aucune différence significative n'a été constatée dans la survie des Noirs comparativement aux Blancs.
(Russell, 2020)* nouveauté	R.-U., Guy's Cancer Center de Londres a mené une étude rétrospective de cohorte afin d'évaluer 156 patients atteints de cancer et ayant reçu un diagnostic de COVID-19 entre le 29 février et le 12 mai 2020 et les caractéristiques cliniques associées lorsque le décès était lié à la COVID-19.	- Pour les cancéreux ayant reçu un diagnostic de COVID-19, un lien positif statistiquement significatif a pu être établi avec le décès lié à la COVID-19 pour les Asiatiques comparativement aux Blancs (RC de 3,73 (IC 95 %, de 1,28 à 10,91).
(Martin, 2020) nouveauté	R.-U., étude rétrospective de Leicester sur les patients atteints de COVID-19 dans les hôpitaux universitaires du NHS Trust entre le 1er mars et le 28 avril 2020, ayant évalué les facteurs associés à un résultat positif au test PCR pour le SRAS-CoV-2 avant et après le confinement.	Après correction, comparativement aux Blancs, la probabilité d'obtenir un résultat positif était plus élevée pour d'autres ethnies : - Asiatiques du Sud (RRA de 2,44 IC 95 %, de 2,01 à 2,97). - Noirs (RRA de 2,56 IC 95 %, de 1,71 à 3,84) - Autres ethnies (RRA de 2,53 IC 95 %, de 1,74 à 3,70).
(Perez-Guzman, 2020)* nouveau	R.-U., Londres, étude rétrospective de cohorte du NHS Trust afin d'évaluer les facteurs associés à la mortalité chez 614 patients admis entre le 25 février et le 5 avril dans trois grands hôpitaux londoniens. Ethnies des patients : - MECNA = 40 % (244) - Blancs = 38 % (235) - Origine ethnique inconnue = 22 % (135) Analyse : régression logistique	- En tenant compte de l'âge, du sexe et des comorbidités, les Noirs avaient une probabilité de décès plus élevée que les blancs (RRA de 1,69, IC 95 %, de 1,00 à 2,86). - Ce lien est plus important lorsque l'on tient compte de la gravité de l'infection au moment de l'admission (RRA de 1,85 IC 95 %, de 1,06 à 3,24).
(Ayoubkhani, 2020) préimpression nouveauté	R.-U., étude de cohorte rétrospective pour l'Angleterre et le Pays de Galles afin d'évaluer les décès qui se sont produits entre le 2 mars et le 15 mai 2020, et le lien entre ces décès et les groupes ethniques des minorités.	- Le modèle entièrement corrigé pour les femmes, uniquement pour les femmes noires, a établi un lien avec la mortalité (RRA de 1,29 [IC 95 % de 1,18 à 1,42]). - Chez les hommes, le risque de mortalité lié à la COVID-19 est resté élevé chez les Noirs (1,76 [1,29 [IC 95 %]) de 1,63 à 1,90]), les Bangladais et les Pakistanais (1,35

	Analyse : Modèle des risques proportionnels de Cox.	[1,29 [95 % IC de 1,21 à 1,49]) et les Indiens (1,30 [1,29 [95 % IC de 1,19 à 1,43]).
(Zakeri, 2020) préimpression nouveauté	R.-U., Sud de Londres (King's College Hospital Trust), étude de cohorte avec cas-témoins + rétrospective afin d'examiner le lien entre l'origine ethnique, l'admission à l'hôpital et le taux de mortalité à l'hôpital en raison d'une COVID-19 grave entre le 1er mars et le 2 juin 2020, 872 cas, 3 488 cas-témoins. Parmi tous les cas, - 48,1 % étaient des Noirs, - 33,7 % étaient des Blancs, - 12,6 % étaient d'ethnies mixtes ou autres, - 5,6 % étaient des Asiatiques.	- Comparativement aux Blancs, le risque à l'admission était plus élevé pour les Noirs (RC de 2,28 [IC 95 %, de 1,87 à 2,79]) et les patients d'ethnies mixtes ou autres (RC de 2,66 [IC 95 %, de 2,01 à 3,52]). Les Asiatiques n'ont pas présenté un risque plus élevé à l'admission (RC de 1,04 [IC 95 %, de 0,72 à 1,48]). - Dans les hôpitaux, aucun lien n'a été établi entre le taux de mortalité et les Noirs (HR de 0,84 [IC 95 %, de 0,63 à 1,11]) et les ethnies mixtes ou autres (HR 0.69 [IC 95 %, de 0,43 à 1,10]). Les Asiatiques présentaient un risque plus élevé de mortalité à l'hôpital (HR de 1,54 [IC 95 %, de 0,98 à 2,41]).
(Swann, 2020) préimpression nouveauté	R.-U., cohorte rétrospective multi hôpital (260) en Angleterre, au Pays de Galles et en Écosse, du 17 janvier au 3 juillet 2020, afin d'examiner l'admission à l'USI, le taux de mortalité et le syndrome inflammatoire multisystémique de l'enfant (SIME) et de l'adolescent admis avec une infection par SRAS-CoV-2, n = 651.	- L'admission à l'USI était associée à un âge inférieur à 1 mois, à un âge variant entre 10 et 14 ans et à l'appartenance ethnique noire. Un lien significatif a été établi avec les Noirs RCC de 2,82 (IC 95 %, de 1,41 à 5,57) et avec les autres ethnies RCC de 1,91 (IC 95 %, de 1,07 à 3,34) qui ont été admis à l'USI, mais aucun lien n'a été établi pour les Asiatiques du Sud comparativement aux Blancs. - 11 % des cas ayant été classés comme SIME étaient plus susceptibles d'être d'origine ethnique autre que blanche (64 % (29 sur 45) comparativement à 42 % (148 sur 355) ; p = 0,004).
(Kakkar, 2020)* nouveau	Cohorte rétrospective d'adultes ayant subi un test pour la COVID-19 (n = 3 018) au Sheffield Teaching Hospitals, au R.-U., du 3 janvier au 25 avril 2020.	MECNA comparativement aux Blancs - Test positif : 95 sur 296 comparativement à 631 sur 2 424, p = 0,026.

	MECNA 19 % de la population de Sheffield. Analyse descriptive avec test du χ2 (khi carré).	- Hospitalisation : 86 sur 95 comparativement à 599 sur 631, p0,083 (non significatif). - USI : 20 sur 86 comparativement à 43 sur 599 p < 0,00001. - Un nombre significativement inférieur de tests a été effectué sur le groupe de MECNA comparativement au pourcentage qu'ils représentent dans la population et les personnes MECNA testées étaient significativement plus jeunes que les Blancs.
(Galloway, 2020)* nouveauté	Cohorte rétrospective, Londres au R.-U., 2 hôpitaux, du 1er mars au 17 avril 2020. N = 1 157 admissions à l'hôpital en raison du résultat positif au test RT-PCR pour le SRAS-CoV-2. Analyse : Modèles de régression des risques concurrents, corrigés en fonction de l'âge et du sexe.	- Admission à l'USI comparativement aux Blancs : MECNA HR de 1,53 (IC 95 %, de 1,12 à 2,09). - Mortalité comparativement aux Blancs : MECNA HR de 1,19 (IC 95 %, de 0,89 à 1,58). Un lien a pu être établi avec l'origine ethnique et une maladie plus grave, mais aucun lien n'a pu être établi avec le taux de mortalité parmi les cas hospitalisés.
(Apea, 2020)* préimpression nouveauté	Cohorte rétrospective, 5 hôpitaux, Londres, R.-U., du 1er janvier au 13 mai. N = 1 996 cas de SRAS-CoV-2 Analyse : Une modélisation de régression logistique portant sur l'origine ethnique et le traitement à l'USI sous ventilation mécanique a été effectuée, puis corrigée en fonction de l'âge et du sexe. Modèle des risques proportionnels de Cox corrigé en fonction de l'âge et du sexe	Profil racial des cas 35,2 % de Blancs, 27,0 % d'Asiatiques, 17,0 % de Noirs. - L'admission à l'USI était significative p < 0,001 avec 11 % de Blancs, 20,1 % d'Asiatiques et 18,5 % de Noirs admis à l'USI. - Ventilation mécanique, cotes corrigées en fonction de l'âge et du sexe comparativement aux Blancs dans les cas d'hospitalisation suivants : Asiatiques RC de 1,54 (IC 95 %, de 1,06 à 2,23), Noirs RC de 1,80 (IC 95 %, de 1,20 à 2,71). - Mortalité (dans les 30 jours) : HR de 1,49 pour les Asiatiques (IC 95 %, de 1,19 à 1,86), HR de 1,30 pour les Noirs (IC 95 %, de 1,02 à 1,63) comparativement aux Blancs. Le contrôle des comorbidités a permis d'élargir

		l'intervalle de confiance pour l'origine ethnique, p = 0,09 pour les Noirs. - Mortalité (dans les 90 jours) Asiatiques HR de 1,46 (IC 95 %, de 1,18 à 1,81) comparativement aux Blancs.
(Fletcher, 2020) préimpression	R.-U., étude de cohorte rétrospective pour un seul centre. 2 756 patients admis au Chelsea and Westminster Hospital NHS Foundation Trust, du 1er janvier au 23 avril. Modèle de régression logistique multivariable Remarque : l'origine ethnique était autodéclarée et de nombreuses observations n'étaient pas précisées ce qui a entraîné des estimations insuffisantes.	- Le nombre de personnes qui se présentaient dans des cliniques avec des symptômes de COVID-19 était plus élevé chez les Asiatiques RRA de 1,63 (IC 95 %, de 1,00 à 2,69) et les autres 1,70 (IC 95 %, de 1,21-2,39) comparativement aux Blancs (données corrigées en fonction de l'âge, du sexe et de certains biomarqueurs sanguins). La comparaison corrigée pour les Noirs était similaire, mais non significative. - Aucun lien entre l'admission à l'USI et l'origine ethnique n'a été observé dans cette étude. - Observation d'une tendance d'association de la mortalité chez les Asiatiques, avec un RRA de 2,24, et (IC 95 %, de 1,23-4,50) et un taux similaire pour les Noirs, n'était cependant pas significative.
(S. de Lusignan, 2020a) préimpression	R.-U., revue rétrospective des dossiers médicaux et étude transversale, centre de recherche et de surveillance Oxford RCGP, du 28 janvier au 4 avril 2020. Cas positifs à la COVID-19 n = 587, test négatif n = 3 215. Répartition ethnique : Blancs n = 2 497 (65,7 %) Asiatiques n = 152 (4,0 %) Noirs n = 58 (1,5 %) Ethnicité mixte, autres n = 81 (2,1 %) Informations manquantes n = 1 014 (26,7 %) Régression logistique multivariée.	- Comparativement aux Blancs (15,5 %), les cotes corrigées pour un test positif étaient plus grandes pour les Noirs (62,1 %) RCC de 4,75 (IC 95 %, de 2,65-8,51), corrigées en fonction de l'âge, du sexe, de la privation socioéconomique, de la taille du ménage, de la zone urbaine/rurale, du tabagisme, de l'IMC, de l'hypertension, de la maladie rénale chronique, du diabète, de la maladie cardiaque chronique.

(Wright, 2020) nouveauté	Données transversales sur les patients hospitalisés ayant été testés pour la COVID-19 du 18 mars au 27 avril à Bradford, R.-U. Tests du tests du χ2 (khi carré).	- Taux de mortalité associé aux cas de COVID-19 comparativement aux patients ayant obtenu un résultat négatif. Aucune différence significative dans le taux de mortalité entre les Blancs (25,4 %) et les Asiatiques du Sud (18,1 %) pour les cas hospitalisés de COVID-19 (p = 0,122). Les Asiatiques du Sud étaient cependant beaucoup plus jeunes que les Blancs.
(Hull, 2020) préimpression	R.-U., ensemble de données sur la médecine générale dans l'est de Londres. Étude transversale comptant 1,2 million de personnes dans 157 pratiques avec n = 8 985 cas de COVID-19, du 14 février au 30 avril 2020. Modèle corrigé pour l'âge, le sexe, la privation sociale, les prédicteurs cliniques.	- Les chances d'infection par le SRAS-COV-2, entièrement corrigées pour les autres variables, étaient les suivantes : Asiatiques du Sud RCC de 1,93 IC 95 %, de 1,83 à 2,04) et Noirs RCC de 1,47 (IC 95 %, de 1,38 à 1,57).
(Cook, 2020)	R.-U., personnel du NHS : Les données transversales sur le taux de décès des travailleurs de la santé jusqu'au 22 avril 2020 ont été analysées. 106 cas dont 98 interagissaient directement avec les patients. Les décès des travailleurs de la santé ont représenté de 0,51 à 0,58 % des décès. Aucune analyse statistique.	- La proportion des décès de MECNA (en proportion dans une profession) - Infirmière 71 % (20 %) - Préposés de soutien aux soins de santé 56 % (17 %) - Médecin / dentiste 94 % (44 %) - Autre 29 % (-)
(Riphagen, 2020)	Londres, R.-U., petite série de cas d'enfants atteints du syndrome inflammatoire multisystémique de l'enfant (SIME) maintenant bien reconnu. En dix jours, dans un seul hôpital pédiatrique, huit enfants ont été identifiés à la mi-avril 2020.	- 6 des 8 enfants atteints de cette maladie inflammatoire étaient Noirs. Aucune analyse ou enquête sur ce lien potentiel n'a été effectuée dans le cadre de cette petite étude.
Autres pays		
(Toubiana, 2020)	Paris en France, étude observationnelle prospective du syndrome inflammatoire multisystémique de l'enfant (SIME), du 27 avril au 11 mai (suivi jusqu'au 15 mai). 21 enfants, âge médian de 7,9 ans (entre 3,7 et 16,6 ans)	- 57 % (12 sur 21) étaient Noirs alors que 3 sur 21 étaient Asiatiques. Les données de cette étude étaient insuffisantes pour évaluer le lien, mais les proportions étaient plus élevées que ce à quoi on pourrait

		généralement s'attendre en fonction de la démographie de la population et de ce que l'on sait de la maladie de Kawasaki chez les enfants.
(Elias, 2020) nouveauté	Paris en France, étude de cohorte prospective chez des patients ayant subi une greffe de rein (n = 1 216) avec suivi actif dans deux centres de transplantation de référence entre le 1er mars et le 30 avril 2020.	- L'appartenance ethnique non blanche était liée indépendamment à un risque plus élevé de développer la COVID-19, RCC = 2,17; [95 % CI] de 1,23 à 3,78; p = 0,007).
(Baqui, 2020)*	Brésil, étude trasnversale de la mortalité dans les hôpitaux (à l'échelle du pays). Données collectées du 27 février au 4 mai 2020. N = 6 882 cas dont l'issue est connue. La classification raciale classe la population brésilienne en cinq catégories (pourcentages de la population brésilienne en 2010) : branco (Blancs) (47,5 %), pardo (ethnicité mixte) (43,4 %), preto (Noirs) (7,5 %), amarelo (Asiatiques) (1,1 %) et indígena (Autochtones) (0,4 %). Analyse de régression de Cox corrigée par âge, sexe, groupe ethnique et comorbidités (effets fixes) avec l'état (effet aléatoire).	- La mortalité à l'hôpital était plus élevée chez les personnes d'origine ethnique mixte (1,47) (IC 95 %, de 1,33 à 1,58) et chez les Noirs (1,32) (IC 95 %, de 1,15 à 1,52) comparativement aux Blancs. Après l'âge, l'appartenance ethnique mixte est le facteur de risque le plus influent sur la mortalité.

* = l'étude est également incluse dans (Raharja, 2020). Nouveauté = désigne toute étude ayant été publiée depuis le 1er juin 2020, date à laquelle la première version de cette étude a été achevée. Prépublication = désigne les articles qui n'ont pas été soumis au processus d'évaluation par les pairs. MECNA = minorités ethniques et communautés noire et asiatique, RC = rapport de cotes, HR = risque relatif, RR = rapport de risque, IC à 95 % = intervalle de confiance, I^2 = mesure de l'hétérogénéité dans une méta-analyse, k = nombre d'études.

ORIGINE ETHNIQUE ET EXPOSITION À LA COVID-19 (ÉTUDES SÉROLOGIQUES)

La séroprévalence, d'autres tests sérologiques et des liens avec l'origine ethnique ont été mentionnés dans cinq études. Quatre études de séroprévalence menées aux États-Unis sur la population en générale, les travailleurs de la santé et les femmes enceintes ont montré que la proportion de personnes séropositives était significativement plus élevée dans certaines ethnies : Noirs (n = 3 études sur 4), Hispaniques (n = 3), Asiatiques (n = 1 sur 2) (tableau 2). Une étude menée au Royaume-Uni a examiné la dynamique des anticorps IgG contre le SRAS-CoV-2 pendant

les phases aiguës et convalescentes de l'infection et constaté qu'il y avait une différence dans l'ampleur des résultats avec ELISA, pouvant indiquer que pendant l'infection par COVID-19, les non-Blancs peuvent avoir une charge virale plus élevée (Staines, 2020). Cette constatation nécessitera cependant des recherches plus poussées pour comprendre la signification de l'écart relevé dans cette étude. Les essais enregistrés décrits dans la revue systématique comprenaient des études sur la séroprévalence qui s'ajouteront au corpus d'information (D. Pan, 2020).

Tableau 2 : Études sérologiques sur l'incidence cumulative et la dynamique des anticorps contre le SRAS-COV-2 (n = 5)

Référence	Description de l'étude	Principaux résultats
(Ebinger, 2020)* préimpression nouveauté	É.-U., enquête de séroprévalence dans une vaste cohorte diversifiée d'employés du secteur de la santé, soit 6 062 adultes du comté de Los Angeles. Date : Mai à juin 2020 Analyse : analyses en fonction multivariables corrigées pour des caractéristiques préexistantes, par exemple l'origine ethnique, l'âge, le sexe, l'asthme, l'hypertension	- Comparativement aux Blancs, les Hispaniques (RC 1,80 [IC 95 %, de 1,31, 2,46], P<0,001) et les Noirs (1,72 [1,03, 2,89], P = 0,04) représentaient les principaux facteurs d'association significative à une plus grande probabilité d'être séropositif.
(Flannery, 2020) nouveauté	É.-U., étude de cohorte prospective menée en Pennsylvanie a permis d'effectuer des tests sérologiques sur 1 293 parturientes dans deux centres de Philadelphie entre le 4 avril et le 3 juin 2020, et d'évaluer les différences de race ou d'origine ethnique chez les femmes.	Taux de séroprévalence par race ou ethnie : - Noires (9,7 %; IC 95 %, de 7,3 à 12,5 %) - Hispaniques (10,4 %; IC 95 %, de 5,7 à 17,1 %) - Blanches (2,0 %; IC 95 %, de 0,9 à 3,8 %) - Asiatiques (0,9 %; IC 95 %, de 0,0 à 5,1 %)
(Biggs, 2020) nouveauté	É.-U., étude transversale menée dans deux comtés d'Atlanta entre le 28 avril et le 3 mai 2020 afin d'évaluer la séroprévalence du SRAS-CoV-2 chez 696 personnes.	Taux de séroprévalence total pondéré = 2,5 % (IC 95 %, de 1,4 à 4,5) - Noirs 5,2 % (IC 95 %, de 2,9 à 9,1), p < 0,01 comparativement aux autres ethnies.
(Rosenberg, 2020)	Enquête de séroprévalence dans l'État de New York n = 15 101 adultes, du 19 au 28 avril 2020. Estimation de l'incidence cumulée obtenue en utilisant une pondération post-stratification afin de normaliser la	L'incidence cumulée varie significativement selon l'origine ethnique : - Hispaniques : 29,2 % (IC 95 %, de 27,2 à 31,2 %). - Noirs : 20,2 % (IC 95 %, de 18,1 à 22,3 %).

	population de New York et d'apporter des correctifs à l'aide des caractéristiques du test de détection des anticorps.	- Asiatiques : 12,4 % (IC 95 %, de 9,4 à 15,4 %). - Comparativement aux Blancs 8,1 % (IC 95 %, de 7,4 à 8,7 %), p < 0,0001).
(Staines, 2020) préimpression	Cohorte prospective dans un seul centre, du 29 mars au 22 mai, Londres, R.-U. 177 cas de COVID-19 sur 1 785 sont inclus. Test : IgG du test ELISA pour la COVID-19 développé par Mologic (Bedford au R.-U.) et fabriqué par Omega (Omega Diagnostics de Cambridge au R.-U.) - 2 à 8 % des cas n'ont subi aucune séroconversion.	- L'appartenance à des non-Blancs a été associée à une valeur de densité optique normalisée d'ELISA plus élevée que celles des Blancs, valeur moyenne de 1,06 comparativement à 0,85, p 0,035 (test t non apparié) - L'auteur suggère que ce résultat pourrait être associé à des charges virales plus élevées

* = l'étude est également incluse dans (Raharja, 2020). Nouveauté = désigne toute étude ayant été publiée depuis le 1er juin 2020, date à laquelle la première version de cette étude a été achevée. Prépublication = désigne les articles qui n'ont pas été soumis au processus d'évaluation par les pairs. RC = rapport de cotes, IC 95 % = intervalle de confiance.

ORIGINE ETHNIQUE ET COVID-19 AU CANADA

Malgré une recherche dans la littérature grise, seule une quantité limitée de recherches canadiennes ont été obtenues. Ces recherches incluaient une étude écologique en préimpression, deux rapports d'enquêtes effectuées au Canada, mais non encore publiées, des rapports de surveillance de Services aux Autochtones Canada ainsi que le tableau de bord sur la COVID-19 du Bureau de santé publique de Toronto. Tous ont fourni des résultats pertinents sur l'origine ethnique et la COVID-19 au Canada (tableau 3). La recherche a également permis de déterminer quelles provinces (Ontario / Colombie-Britannique) et/ou unités de santé (Toronto) recueillent ou prévoient de commencer à recueillir des données sur l'origine ethnique des cas de COVID-19. En septembre 2020, seul le Bureau de santé publique de Toronto disposait d'un rapport.

Les données canadiennes disponibles indiquent que les groupes ethniques non Blancs, à l'exception des Asiatiques de l'Est, sont infectés de façon disproportionnée par la COVID-19, ce qui concorde avec d'autres études sur le risque d'infection par la COVID-19 menées dans d'autres pays dans le cadre de la présente synthèse. Ces études soulignent également les inégalités dans les déterminants sociaux de la santé qui peuvent être entraîner un risque accru de COVID-19, ce qui inclut le logement, l'éducation, le revenu, la profession et l'accès aux soins de santé.

- Une enquête transversale conçue pour comparer les répercussions de la COVID-19 sur les Canadiens Noirs à un échantillon « national » représentatif a cependant révélé une plus grande susceptibilité à la COVID-19 chez les Canadiens Noirs tant au niveau individuel que dans leur cercle social. La fréquence de certains facteurs de risque liés à l'utilisation des transports en commun et au fait d'occuper un emploi exigeant des interactions en personne était plus élevée chez les Canadiens Noirs. Ils étaient plus à risque de subir de graves conséquences financières en raison de la pandémie. Ces données concordent donc avec d'autres données tirées d'études similaires publiées aux États-Unis (tableau 1).
- Le tableau de bord créé par le Bureau de santé publique de Toronto montre une proportion plus élevée de cas de COVID-19 dans les groupes ethniques composés de Noirs, d'Hispaniques, d'Asiatiques du Sud-Est, d'Asiatiques du Sud/Indo-Caribéens et de Moyen-Orientaux par rapport à leur représentation dans la communauté.
- L'étude écologique a analysé les données sur le nombre de cas et de décès liés à la COVID-19 par rapport au niveau démographique de la population du Canada en fonction de plusieurs variables, incluant la proportion de Noirs, la proportion de personnes nées à l'étranger, la proportion de personnes âgées de plus de 65 ans, la densité de la population et le revenu médian. Les résultats tirés du modèle binomial négatif multivariable incluent:
    - Le doublement du nombre de cas était associé à une augmentation de 1 % de la proportion de Noirs alors que l'augmentation de 3 % du nombre de cas était associée à une augmentation de 1 % de la population de gens nés à l'étranger.
    - 2,1 fois l'augmentation du taux de mortalité des COVID-19 était, quant à elle, associée à une augmentation de 1 % de la proportion de Noirs dans la population.

Les données sur l'infection par la COVID-19 des populations autochtones du Canada provenaient de la page Web de Services aux Autochtones Canada et des pages Web provinciales de l'Alberta, de la Colombie-Britannique et du Manitoba {{85811;}}. Une analyse effectuée à la fin de juillet a révélé que les populations autochtones du Canada qui se trouvent dans les réserves ont déclaré des taux de COVID-19 correspondant au quart du taux de la population en général ainsi qu'un taux de mortalité d'environ le cinquième de celui de la population en général {{85811;}}. À ce jour, les commentaires et articles publiés dans le Journal de l'Association médicale canadienne (CMAJ)indiquent que les communautés autochtones canadiennes ont réussi dans leurs efforts visant à atténuer les répercussions sur la santé publique {{65290;}}. Les populations autochtones sont également plus susceptibles de vivre dans des collectivités éloignées qui peuvent assurer une certaine protection à une collectivité fermée contre la COVID-19, mais lorsque ces collectivités sont touchées par la COVID-19, elles n'ont alors qu'un accès limité aux soins de santé et sont plus susceptibles d'être dans une mauvaise situation socioéconomique. (Statistique Canada, 2020). Aucune donnée canadienne sur l'origine ethnique et les hospitalisations, la gravité ou la mortalité n'a été relevée. Toutefois, les publications sur le lien entre l'origine ethnique et les problèmes

médicaux ou les facteurs socioéconomiques jugés comme des facteurs de risque pouvant entraîner une forme grave de COVID-19 peuvent être des indicateurs utiles de ce à quoi on pourrait s'attendre d'ici à ce que les données sur la COVID-19 soient disponibles. La recherche a permis de trouver deux publications suggérant que, comparativement aux Blancs, les immigrants noirs, les Autochtones et les immigrants d'Asie du Sud étaient beaucoup plus susceptibles d'avoir un ou plusieurs problèmes de santé associés à un risque plus élevé d'avoir une forme grave de COVID-19 (Lin, 2020).

Tableau 3 : Détails des études et des rapports d'observation effectués au Canada sur le lien entre l'origine ethnique et le risque d'infection par la COVID-19 (n = 5)

Référence	Renseignement sur l'étude	Principaux résultats
Susceptibilité, gravité clinique et mortalité associées à la COVID-19		
Canada		
(Nur, 2020) nouveauté rapport non publié	Un sondage en ligne (transversal) a été effectué du 17 au 30 juin 2020. Il utilisait une stratégie d'échantillonnage pondérée en fonction de l'âge, du sexe, de la région, de l'origine ethnique et du lieu de naissance pour cibler un échantillon représentatif de 1 500 Canadiens et de 400 Canadiens noirs (Noirs). N = 2 322 adultes canadiens	Résultats en ce qui a trait à la COVID-19 : - Les Noirs étaient plus nombreux à déclarer des symptômes de COVID-19 et le traitement associé (10 % comparativement à 7 % à l'échelle nationale). - Les Noirs sont plus nombreux à avoir eu des symptômes de COVID-19 (10 % comparativement à 7 % à l'échelle nationale) ou à connaître quelqu'un ayant eu de tels symptômes (28 % comparativement à 17 % à l'échelle nationale). - Les banlieusards ont obtenu des résultats plus élevés, ce qui veut dire qu'ils étaient plus nombreux à avoir eu des symptômes de COVID-19 (16 % comparativement à 12 % à l'échelle nationale) ou à connaître quelqu'un ayant eu de tels symptômes (34 % comparativement à 18 % à l'échelle nationale).

		- Les Noirs étaient trois fois plus susceptibles de connaître une personne qui est décédée de la COVID-19 (21 % comparativement à 8 % à l'échelle nationale). Facteurs de risque pour la COVID-19 - Les Noirs étaient plus susceptibles de prendre les transports en commun pour se rendre au travail (25 % comparativement à 12 % à l'échelle nationale) (d'autres études ont montré qu'il s'agissait là d'un indicateur de risques plus élevés d'infection à la COVID-19). - Les Noirs sont plus nombreux à déclarer que leur emploi exige des contacts fréquents en direct (61 % comparativement à 50 % à l'échelle nationale). Répercussions de la COVID-19 - Des répercussions financières minimales ont été déclarées par 45 % des répondants Noirs et à l'échelle nationale. - Les hommes Noirs âgés de 45 ans et plus sont plus susceptibles de faire état répercussions financières négatives significatives (38 % comparativement à 22 % à l'échelle nationale) à cet égard. - La confiance financière était plus faible dans les ménages noirs (67 % comparativement à 72 % à l'échelle nationale).
Nous avons demandé une copie du rapport puisqu'il n'était pas disponible en ligne. nouveauté	Enquête sur la COVID-19 menée au sein de la population de la C.-B. (N = 394000). (Informations tirées des articles de presse au 14 août 2020)	- Les données indiquent que les Hispaniques, les Asiatiques de l'Ouest et du Sud et les Noirs ont été touchés de façon disproportionnée par la pandémie et ont éprouvé des difficultés financières en raison de la perte de leur emploi. - L'origine ethnique et l'accès aux soins de santé ont été identifiés comme sources de problèmes, lorsque les

		Japonais, les Coréens, les personnes multiethniques et les Asiatiques du Sud ont mentionné des difficultés à cet égard.
(Bureau de santé publique de Toronto, 2020) nouveauté	Tableau de bord de surveillance pour la COVID-19 à Toronto comprenant les données de proportion établies en fonction de l'identité ethnoraciale et du revenu Données recueillies du 20 mai au 16 août 2020 24 % des données sur l'origine ethnique sont manquantes. Ne comprend pas les cas de COVID-19 dans les établissements de soins de longue durée. Les résultats sont descriptifs et ne comprennent que des observations avec données sur l'origine ethnique.	83 % des cas COVID-19 signalés proviennent d'un groupe ethnique minoritaire alors qu'ils représentent 52 % de la population de Toronto. La liste ci-dessous indique le pourcentage de COVID-19 par rapport au pourcentage de population. - Blancs 17 % comparativement à 48 % - Noirs 22 % comparativement à 9 % - Hispaniques 10 % comparativement à 3 % - Asiatiques du Sud-Est 16 % comparativement à 7 % - Asiatiques du Sud ou Indo-Caribéens 20 % comparativement à 13 % - Moyen-Orientaux 11 % comparativement à 4 % - Asiatiques de l'Est 4 % comparativement à 13 %
(Choi, 2020) préimpression	Étude écologique effectuée à l'échelle du Canada, avec des données recueillies jusqu'au 5 mai 2020. Les données fournies par l'ASPC et Statistique Canada, ainsi que les données provenant de l'approche participative à grande échelle ont été utilisées pour comparer le nombre de cas et de décès liés à la COVID-19 avec les données fournies par les unités de services de santé en fonction de différents prédicteurs pour l'analyse, soit la proportion de Noirs, de personnes nées à l'étranger, le pourcentage de personnes de plus de 65 ans, la densité de la population et le revenu médian. L'analyse des cas et des décès, respectivement, a été effectuée dans un modèle multivariable binomial négatif (en raison des	- Le modèle multivarié utilisé pour évaluer l'infection à la COVID-19 a estimé qu'une augmentation de 1 % de la proportion de résidents Noirs dans une région sanitaire était liée au doublement des taux d'infection par la COVID-19. Il a également estimé qu'une augmentation de 1 % de la proportion de résidents nés à l'étranger était, quant à elle, associée à une hausse de 3 % des taux d'infection par la COVID-19. - Chaque augmentation de 1 % de la proportion de résidents noirs dans une région sanitaire était liée à 2,1 fois le taux de mortalité lié à la COVID-19. Une augmentation de 1 % de la proportion de résidents âgés de 65 ans et plus a été, quant à elle, associée à une hausse de 26 % des décès.

	données de dénombrement trop dispersées) utilisant les prédicteurs indiqués ci-dessus.	
{{85811;}} Rapport de surveillance nouveauté	Données de surveillance : au 20 septembre 2020, 408 cas de COVID-19 avaient été recensés dans les réserves des communautés autochtones.	En date du 31 juillet 2020 : - Le pourcentage d'Autochtones qui vivent dans les réserves et ont été déclarés positifs à la COVID-19 est actuellement au quart du taux observé dans la population canadienne en général. - Le taux de mortalité par COVID-19 pour les Autochtones qui vivent dans les réserves est d'environ un cinquième du taux de mortalité dans la population canadienne en général.

Nouveauté = désigne toute étude ayant été publiée depuis le 1er juin 2020, date à laquelle la première version de cette étude a été achevée.

Prépublication = désigne les articles qui n'ont pas été soumis au processus d'évaluation par les pairs.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. La littérature est extraite de Pubmed, de Scopus, de BioRxiv, de MedRxiv, d'ArXiv, de SSRN, de Research Square et croisée avec la liste de littérature sur la COVID de l'OMS et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley.Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient race, ethnie et origine ethnique. Cette synthèse contient des recherches publiées jusqu'au 7 septembre 2020.
Une recherche élargie dans la littérature canadienne sur l'origine ethnique a également été effectuée en utilisant les termes de recherche indiqués avec COVID-19 ET Canada ou provinces comme termes clés dans Google et sur les sites Web officiels. 464 citations ont été saisies par la recherche; certaines études ont été éliminées, car elles n'étaient pas pertinentes, n'étaient pas des recherches primaires ou des revues systématiques ou n'incluaient pas de plan d'étude. Soixante-treize études ayant analysé un lien avec l'origine ethnique sont incluses dans cette synthèse. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites dans la revue.

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ANNEXE :

Dans les études incluses dans cette synthèse, l'origine ethnique était autodéclarée selon le fait que la personne s'auto-identifie à un ou à plusieurs groupes sociaux parmi une liste d'options prédéfinies. Les listes varient d'un pays à l'autre et d'une étude à l'autre. Le tableau ci-dessous présente les principales catégories de classifications ethniques et ethnoraciales utilisées par les États-Unis et le Royaume-Uni. Certaines études comportaient d'autres options de granularité ou de classification qui sont indiquées ci-dessous.

Définitions

Origine ethnique : Groupe social auquel une personne appartient et auquel elle s'identifie ou est identifiée par d'autres, en raison d'un mélange de facteurs culturels et autres, incluant la langue, le régime alimentaire, la religion, l'ascendance et les caractéristiques physiques traditionnellement associées à la race (voir race). Le concept est de plus en plus utilisé comme synonyme de race, mais la tendance est plus pragmatique que scientifique.

Les classifications **ethnoraciales** désignent la catégorisation administrative des personnes selon des critères ethniques et raciaux à des fins statistiques. Ce terme a été utilisé par le Bureau de santé publique de Toronto.

Catégorie ethnique utilisée dans la synthèse	Acronymes et définitions de la catégorie.
Blanc	Désigne un Blanc non Hispanique. Définition des É.-U. : personne dont l'ascendance vient d'Europe, du Moyen-Orient ou de l'Afrique du Nord. Définition du R.-U. : Désigne un Britannique, un Irlandais ou toute personne dont l'ascendance est blanche.
Noir	Désigne un Noir non hispanique, un Afro-Américain, un Noir britannique, un Noir des Caraïbes, un Africain, un Afro- Caribéen ou un Haïtien. Définition des É.-U. : personne dont l'ascendance vient de l'un des groupes raciaux noirs d'Afrique. Définition du R.-U. : Désigne un Caribéen, un Africain ou toute personne dont l'ascendance est noire.
Hispanique	Latino, Latino-Américain ou Latinx. Remarque : Le Bureau du recensement des États-Unis utilise le terme « hispanique » pour désigner à la fois les personnes hispaniques et latines qui sont nées en Amérique latine ou qui ont des ancêtres provenant d'Amérique latine. Définition des É.-U. : personne dont l'ascendance est Cubaine, Mexicaine, Portoricaine, d'Amérique du Sud ou Centrale, ou de toute autre culture ou antécédence espagnole, peu importe la race.

Autochtone	Désigne les Premières Nations, les Inuits et les Métis (Canada), les Amérindiens et les Autochtones de l'Alaska (États-Unis). Par définition, les peuples autochtones désignent les premières populations d'Amérique du Nord et d'Amérique du Sud.
Habitant des îles du Pacifique	Désigne un natif d'Hawaii. Personne dont l'ascendance vient d'Hawaii, de Guam, de Samoa ou des autres îles du Pacifique.
Asiatique	Désigne toute personne originaire de l'un ou l'autre des premiers peuples de l'Extrême-Orient, de l'Asie du Sud-Est ou du sous-continent indien, y compris, par exemple, le Cambodge, la Chine, l'Inde, le Japon, la Corée, la Malaisie, le Pakistan, les îles des Philippines, la Thaïlande et le Vietnam. Définition du R.-U. : Désigne tout Indien, Pakistanais, Bangladais ou toute personne de toute autre antécédence asiatique.
Chinois	Définition du R.-U. : Désigne tout Chinois ou toute autre personne chinoise.
Mixte	Définition du Royaume-Uni : désigne toute personne blanche et noire des Caraïbes, blanche et noire d'Afrique, blanche et noire de l'Asie, ou toute autre personne ayant une antécédence mixte.
MECNA	Désigne les minorités ethniques et communautés noire et asiatique (ou « Black Asian and minority ethnic group » en anglais), un terme utilisé dans de nombreuses études au Royaume-Uni pour désigner l'origine ethnique non blanche.
Communautés raciales	Désigne les minorités visibles et englobe généralement toutes les personnes qui ne sont pas de race Caucasienne ou de couleur blanche. Au Canada, cela peut inclure ou non les Autochtones, selon le rapport ou l'étude.
Asiatique de l'Est	Constitue une classification racialisée qui désigne les personnes originaires des pays d'Asie de l'Est, soit Chine, Taïwan, Japon, Mongolie, Corée du Nord et Corée du Sud.
Asiatique du Sud	Désigne une personne dont les ancêtres proviennent des pays du sous-continent indien, y compris l'Inde, le Pakistan, le Bangladesh et le Sri Lanka. Les Indo-Caribéens, qui ont été regroupés avec les Asiatiques du Sud, sont des personnes d'origine indienne qui vivent dans les Caraïbes.
Asiatique du Sud-Est	Désigne un groupe de cultures mixtes provenant de 11 pays, soit Brunéi, Birmanie (Myanmar), Cambodge, Timor-Leste, Indonésie, Laos, Malaisie, Philippines, Singapour, Thaïlande et Vietnam.
Moyen-oriental	Désigne les Arabes et Asiatiques occidentaux d'origine moyen-orientale et nord-africaine

Remarques : La capitalisation est conforme au guide de style de l'ASA pour les documents de recherche en sociologie. Définitions de l'origine ethnique ou de la race fournies par le bureau du recensement des États-Unis. Ces définitions représentent un concept social établi d'après la race et l'origine ethnique plutôt que représenter une ségrégation fondée sur la biologie. Catégories de l'origine ethnique établies par le bureau de recensement du Royaume-Uni.

Evidence Snapshot:

Rapid Review on the Impact of School Closures and Re-openings on COVID-19 Transmission

Context

School closures were one of the earliest public health measures implemented to reduce the spread of SARS-CoV-2. The primary aim of this review was to examine the empirical evidence on the effectiveness of school closures and the impact of re-opening schools in reducing community transmission of COVID-19 and decreasing the incidence of COVID-19 in primary and secondary schools.

Key Findings

This rapid review identified 24 studies, including 5 observational studies and 19 ecological studies up to January 25, 2021. Of these, all ecological studies and one prospective cohort study assessed the impact on transmission of COVID-19 in the community, and 4 observational studies assessed the impact on in-school transmission. The key findings were:

- Most observational studies found that school closures and re-openings did not significantly impact within-school and community transmission of COVID-19.
- Findings were mixed across ecological studies that assessed the impact of school closures or re-openings (primary, secondary and/or other schools included) on the spread of COVID-19 in the community early in the pandemic during January 2020 to August 2020.
- Among these, five studies reported that school closures and re-openings did not impact community transmission of COVID-19 and that other public health measures were more effective than school closures.
- Other ecological studies attributed significant reductions in the incidence of COVID-19, the effective reproduction number, and mortality to the closure of schools.

Considerations

The evidence in this review is limited by the inconsistency in the levels of schooling included across the studies, with many of the ecological studies including other types of schools or not describing the type of schools included in their analyses. Most studies were conducted early in the pandemic therefore their findings are likely to be confounded by public health measures that were implemented simultaneously. An important knowledge gap is how the variants of concern and the rollout of COVID-19 vaccinations will impact the effectiveness of school closures or the impact of school re-opening on the spread of COVID-19.

Reference: Emerging Science Group of the Public Health Agency of Canada. Rapid Review on the Impact of School Closures and Re-openings on the COVID-19 Pandemic. May 6, 2021. Full report available from: phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca

Aperçu des éléments de preuve :

Examen rapide de l'impact des fermetures et réouvertures d'écoles sur la transmission de la COVID-19

Contexte

La fermeture des écoles a été l'une des premières mesures de santé publique mises en œuvre pour réduire la propagation du SRAS-CoV-2. L'objectif principal de cette revue était d'examiner les preuves empiriques de l'efficacité des fermetures d'écoles et de l'impact de la réouverture des écoles pour réduire la transmission communautaire de la COVID-19 et d'en diminuer son incidence dans les écoles primaires et secondaires.

Principales constatations

Cet examen rapide a permis d'identifier 24 études, dont 5 études observationnelles et 19 études écologiques jusqu'au 25 janvier 2021. Parmi celles-ci, toutes les études écologiques et une étude de cohorte prospective ont évalué l'impact sur la transmission de la COVID-19 dans la communauté, et 4 études observationnelles ont évalué l'impact sur la transmission en milieu scolaire. Les principales conclusions sont les suivantes :

- La plupart des études observationnelles ont montré que les fermetures et réouvertures d'écoles n'avaient pas d'impact significatif sur la transmission de la COVID-19 au sein d'une école et de la communauté.
- Les résultats sont mitigés dans les études écologiques qui ont évalué l'impact de la fermeture ou de la réouverture des écoles (primaires, secondaires et/ou autres écoles incluses) sur la propagation de la COVID-19 dans la communauté au début de la pandémie, entre janvier 2020 et août 2020.
- Parmi celles-ci, cinq études ont rapporté que la fermeture et la réouverture des écoles n'avaient pas d'impact sur la transmission communautaire de la COVID-19 et que d'autres mesures de santé publique étaient plus efficaces que la fermeture des écoles.
- D'autres études écologiques ont attribué à la fermeture des écoles des réductions significatives de l'incidence de la COVID-19, du nombre effectif de reproductions et de la mortalité.

Facteurs dont il faut tenir compte

Les données de cette revue sont limitées par l'incohérence des niveaux de scolarisation inclus dans les études, de nombreuses études écologiques incluant d'autres types d'écoles ou ne décrivant pas le type d'écoles incluses dans leurs analyses. La plupart des études ayant été menées au début de la pandémie, leurs résultats risquent d'être faussés par les mesures de

santé publique qui ont été mises en œuvre simultanément. Une importante lacune dans les connaissances est la façon dont les variantes de l'inquiétude et le déploiement des vaccinations pour la COVID-19 auront un impact sur l'efficacité de la fermeture des écoles ou l'impact de la réouverture de celles-ci sur la propagation de la COVID-19.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Examen rapide de l'impact des fermetures et réouvertures des écoles sur la pandémie de la COVID-19. Le 6 mai 2021. Rapport complet disponible auprès de : **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Emerging Evidence on COVID-19

Evidence Brief on the Determinants of Individual Adherence to Public Health Interventions for COVID-19

Introduction

What is the evidence on determinants of individual adherence to public health interventions to prevent COVID-19?

An individual's adherence to public health interventions such as social distancing, wearing face masks and washing hands, plays an important role in how effective these interventions will be at controlling the epidemic. This evidence brief identifies and summarizes literature until July 19, 2020 on determinants of individual adherence to public health interventions for COVID-19 to better understand the drivers and barriers of adopting recommended protective behaviors.

Key Points

- 80 studies conducted in many countries evaluated the individual adherence to protective measures against COVID-19 infection in various populations including adults, young adults, university students, children and adolescents, healthcare workers (HCWs), pregnant women, employees, and visitors to hospitals (Tables 1-5).
- Most of these studies were conducted in the initial stages of the epidemic and represent initial adoption of protective behaviours. Many studies (n=28) report better compliance among females compared to males in all age groups. There were few studies on children and adolescents, and many of these noted high compliance in these age groups with a lower compliance among children of high school age.
- Compliance varied across studies, sociodemographic factors and type of protective measure, and was frequently associated with individual knowledge and beliefs.
- Adults > 30 years old were more likely to be compliant with recommended protective behaviors in 13 studies. Other factors positively correlated to adherence in adults include: risk perception (n=7 studies), higher COVID-19 knowledge (n=5), trust in science and government (n=4), increased anxiety levels (n=3), perceived self-efficacy to adopt protective measures (n=3) and Black or Asian ethnicity (n=3).
- Non-adherence in adults was associated with psychological issues such as depression, conspiracy mentality and narcissism (n=5), as well as being a current smoker (n=3).
- In children and adolescents, factors correlated with improved adherence include father's occupation, mother's educational background, location of residence and those with an immigrant background (Chen et al., 2020; Soest, Pedersen, Bakken, & Sletten, 2020).

- Three rapid synthesis reviews were identified that included pre-pandemic literature on adherence to quarantine and individual preventative behaviors (IPC) by HCWS (Table 6).

Overview of the Evidence

Overall, 80 publications pertaining to the adherence to individual protective behaviors recommended by public health to combat the COVID-19 epidemic and the barriers and facilitators associated with these behaviors. Three rapid reviews on adherence and factors that influence adherence to public health interventions to control infectious diseases were also included, however these reviews included only studies published before the pandemic. Of the 83 publications included, 39 preprints were identified, these papers have not completed the peer-review process. The publications reporting on adherence to public health interventions are all observational studies that are at moderate/high risk of bias and thus, are considered medium-low quality. The majority of these studies use a cross-sectional study design and the outcomes are mostly self-reported, which can be biased by recall, response, and social desirability biases. While there are many studies that show similar trends, the conclusions could change with additional research.

A key knowledge gap in this research are studies that evaluate adherence over time. Most of the identified research was conducted in the early stages of the epidemic and only provide a cross-section of whether or not recommended public health behaviors were adopted. In many jurisdictions that situation has changed over time, public messaging and rules have changed with lifting and increasing intensity of different interventions. Studies that longitudinally explore the barriers and facilitators of longer term adherence to protective behaviors are needed to address both those resistant to adopting protective behaviors and the risk of dwindling adherence over time.

CONTENTS

ADHERENCE TO PUBLIC HEALTH INTERVENTIONS IN ADULTS

Fifty-eight studies evaluated adults' adherence to protective behaviors recommended by public health (Table 1). Compliance varied across studies, sociodemographic factors, and type of protective measure and was frequently associated with individual knowledge and beliefs.

- Across 24 studies, females were more likely to adhere to preventive measures than males.
- Adults > 30 years old were more likely to be compliant with recommended protective behaviors in 13 studies.
- Other factors positively correlated to adherence include: risk perception (n=7 studies), higher COVID-19 knowledge (n=5), trust in science and government (n=4), increased anxiety levels (n=3), perceived self-efficacy to adopt protective measures (n=3) and Black or Asian ethnicity (n=3).
- Non-adherence was associated with psychological issues such as depression, conspiracy mentality and narcissism (n=5), as well as being a current smoker (n=3).

Table 1. Fifty-eight studies evaluating adherence to public health measures for COVID-19 and associated factors in adults

Reference	Publication Title	Study Details	Key Outcomes
General Adult Population (18+)			
(Qian et al., 2020) *preprint*	Psychological responses, behavioral changes and public perceptions during the early phase of the COVID-19 outbreak in China: A population based cross-sectional survey	• Cross-sectional study (telephone survey conducted Feb 1-10, 2020) • 1,100 residents of Wuhan (n=510) and Shanghai (n=501) aged 18+ • Public health interventions - avoided eating out and taking public transportation, reduced visits to public places, rescheduling travel plans, increasing surface cleaning, maintaining better indoor ventilation, wearing face mask or goggles, hand-washing	• 401 (78.6%) Wuhan participants and 320 (63.9%) Shanghai participants engaged in all 6 recommended and avoidance behaviors • A high compliance rate of above 90% was observed in all other behaviors in both samples, except for increased surface cleaning • Compliance was associated with increased anxiety levels, perceived risks, and confusion about information reliability
(Wong et al., 2020) *preprint*	The role of institutional trust in preventive and treatment-seeking behaviors during the 2019 novel coronavirus	• Cross-sectional study (online survey conducted Jan 29-30, 2020) • 4,245 residents of Hubei province aged 18+	• The uptake of preventive behaviors was high in the study population • Being under quarantine (aOR=2.35, 95% CI: 1.80-3.08) and having high institutional trust score (aOR=2.23, 95% CI: 1.96-2.53)

	(2019-nCoV) outbreak among residents in Hubei, China	• Public health interventions – avoidance of social interaction, physical contact, and public space, personal protection, seeking treatment	were 2 strong significant determinants of higher preventive behavior scores • The age groups 26-35 years (aOR=1.54, 95% CI: 1.29 -1.83) and 36-45 years (aOR=1.22, 95% CI: 1.01-1.48) had significantly higher preventive behavior scores than those > 45
(Kwok et al., 2020)	Community Responses during Early Phase of COVID-19 Epidemic, Hong Kong	• Cross-sectional study (online survey conducted Jan 2020) • 1,715 residents of Hong Kong aged 18+ • Public health interventions – personal hygiene, disinfecting homes, wearing face masks, travel avoidance, social distancing	• Adoption of enhanced personal hygiene and travel avoidance was high (> 77%) and moderate (40-93%) for different types of social-distancing measures • Higher levels of adoption of social-distancing measures were associated with being female (aOR 1.31, 95% CI: 1.06-1.63, p=0.1), living in the New Territories, perceiving oneself as having a good understanding of COVID-19, and being more anxious
(Lep, Babnik, & Beyazoglu, 2020) *preprint*	The role of information credibility in emotional responses and engagement in self-protective behavior within days of the COVID-19 outbreak: A cross-sectional study	• Cross-sectional study (online survey conducted first week of Mar, 2020) • 1,717 residents of Slovenia aged 18+ • Public health interventions – avoiding crowds, frequent hand washing, avoiding touching one's face	• Perceived credibility of information received by medical professionals and scientists was linked with higher knowledge of self-protective behaviors • Knowledge is linked to higher engagement in self-protective behaviors
(Muto, Yamamoto, Nagasu, Tanaka, & Wada, 2020)	Japanese citizens' behavioral changes and preparedness against COVID-19: How effective is Japan's approach to self-restraint	• Cross-sectional study (online survey conducted Mar 26-28, 2020) • 11,342 residents of Japan aged 20+ • Public health interventions – avoiding poorly ventilated closed space, large gatherings, and	• ~ 76% of participants evaluated themselves as having taken some preventative action • Frequent handwashing was conducted by ~86% and proper coughing etiquette by 77%

preprint		conversations or shouting in close proximity, coughing etiquette	• ~20% of participants are reluctant to implement proper prevention measures. Analysis indicates those that do not follow protective behaviors are more likely to be male, younger (< 30 years old), unmarried, are in lower income household, have a drinking or smoking habit, and have a higher extraversion score.
(Shinan-Altman, 2020) *preprint*	COVID-19 precautionary behavior: The Israeli case in the initial stage of the outbreak	• Cross-sectional study (online survey conducted Mar 12-21, 2020) • 1,407 residents of Israel aged 18+ • Public health interventions – hand washing, avoiding contact with those who have symptoms	• The precautionary behavior score was relatively high among participants • Precautionary behavior was higher for females, older participants, participants with higher levels of knowledge about COVID-19, and participants with greater negative emotional reactions
(Moore, Lee, Hancock, Halley, & Linos, 2020) *preprint*	Experience with Social Distancing Early in the COVID-19 Pandemic in the United States: Implications for Public Health Messaging	• Cross-sectional study (online survey conducted Mar 14-23, 2020) • 7,355 residents of USA aged 18+ • Public health interventions – social distancing	• 39.8% reported not being compliant • The youngest group (18-31) had the lowest compliance rate (52.4%) compared to the other age groups (all > 60%; all p values < .01)
(Machida et al., 2020)	Adoption of personal protective measures by ordinary citizens during the COVID-19 outbreak in Japan	• Cross-sectional study (online survey conducted Feb 25-27, 2020) • 2,400 residents of Japan aged 20+ • Public health interventions – hand hygiene, social distancing, avoiding touching the eyes, nose and mouth, respiratory etiquette, and self-isolation	• 34.7% implemented all 5 protective measures • Prevalence of the 5 protective measures ranged from 59.8-83.8%, with the lowest being avoiding touching the eyes, nose, and mouth • Prevalence is significantly higher in women and older adults compared to men and persons < 65 (women OR: 1.57, older adults OR: 1.83, both p < 0.001)

(Williams, Armitage, Tampe, & Dienes, 2020) *preprint*	Public perceptions and experiences of social distancing and social isolation during the COVID-19 pandemic: A UK-based focus group study	• Focus group conducted online between Mar 28-Apr 4, 2020 • 27 residents of UK aged 18+ • Public health interventions – social distancing and social isolation	• All participants reported high adherence to distancing and isolation guidelines but reported seeing or hearing of non-adherence in others
(Canning, Karra, Dayalu, Guo, & Bloom, 2020) *preprint*	The association between age, COVID-19 symptoms, and social distancing behavior in the United States	• Cross-sectional study (online survey, dates conducted not reported) • 4,676 residents of USA aged 18+ • Public health interventions – social distancing	• ~52% of participants reported going out of their home the previous day (not adhering to social distancing) • Those who experienced shortness of breath have fewer close contacts, with an IRR of 0.49 (95% CI: 0.30–0.78). Having other flulike symptoms reduces the odds of going out by 0.32 (95% CI: 0.18–0.60) and the incidence rate of having close contacts by 42% (IRR = 0.58; 95% CI: 0.38–0.88). • Older people are just as likely to leave their homes as younger people, but people > 50 years had less than half the predicted number of close contacts compared to < 30 year olds
(M. Ã. Czeisler et al., 2020) *preprint*	COVID-19: public compliance with and public support for stay-at-home mitigation strategies	• Cross-sectional study (online survey conducted Apr 2-8, 2020) • 4,676 residents of USA (NY, LA) and Australia aged 18+ • Public health interventions – stay-at-home strategies	• 81.8% reported compliance with recommended quarantine or stay-at-home policies • Compliance was high in both highly-affected (US, NY) and minimally-affected regions (AU, LA)
(Pollak, Dayan, Shoham, &	Predictors of adherence to public health	• Cross-sectional study (online survey conducted Mar 28-Apr 10, 2020) • 654 residents of Israel aged 18+	• 28.7% were defined as non-adherents • Non-adherence was associated with male gender (aOR=1.54, CI 1.03– 2.31), not

Berger, 2020) *preprint*	instructions during the COVID-19 pandemic	• Public health interventions – adherence to medical instructions	having children (aOR = 1.73, 1.13–2.65), smoking (aOR = 2.27, CI 1.42–3.62), high levels of ADHD symptoms (aOR = 1.55, CI 1.07–2.25), high levels of past risk-taking behavior (aOR = 1.41, CI 1.10–1.81), current high psychological distress (aOR = 1.51, CI 1.14–2.01), low perceived risk of COVID-19 (aOR = 1.52, CI 1.22–1.89), low exposure to the instructions (aOR = 1.45, CI 1.14–1.82), and low perceived efficacy of the instructions (aOR = 1.47, CI 1.16–1.85)
(Shahnazi, Ahmadi-Livani, & Pahlavanzadeh, 2020) *preprint*	Assessing preventive health nehaviors from COVID-19 based on the health belief model (HBM) among people in Golestan province: a Cross-sectional study in northern Iran	• Cross-sectional study (online survey conducted Mar 11-16, 2020) • 750 residents of Iran aged 18+ • Public health interventions – avoiding crowded places, social distancing, hand washing, stay-at-home, cough/sneeze etiquette, touching face with hands	• Compliance ranged from 96.8% (avoiding crowded places) to 33.5% (not touching face with hands) • The mean score of preventive behavior was higher in women than men, and greater in urban dwellers than rural dwellers • A one unit increase in the standard deviation of factor scores of self-efficacy and perceived benefits increased the scores of preventive behavior by 0.22 and 0.17 units respectively • A one unit increase in the standard deviation of factor score of perceived barriers and fatalistic beliefs decreased the scores of the preventive behavior by 0.36 and 0.19 units respectively
(Lee & You, 2020)	Psychological and behavioral responses in South Korea during the early stages of	• Cross-sectional study (online survey conducted Feb 25-28, 2020) • 973 residents of South Korea aged 18+	• Participants reported always practicing hand hygiene (67.8%), always wearing a facial mask when outside (63.2%), postponing or canceling social events

	Coronavirus Disease 2019 (COVID-19)	• Public health interventions –hand washing, face masks, social distancing behaviors	(50%), avoiding crowded places (41.5%), and reducing the use of public transportation (38.7%) • Practicing precautionary behaviors is strong associated with perceived risk and response efficacy of the behavior • Specific sociodemographic variables for each behavior are provide in the study (for example, gender, education level, perceived severity, and response efficacy were positive and significant individual predictors of wearing a face mask)
(Jackson, Brown, Shahab, Steptoe, & Fancourt, 2020) *preprint*	COVID-19, smoking, and inequalities: a cross-sectional survey of adults in the UK	• Cross-sectional study (online survey conducted Mar 21-Apr 20) • 53,211 residents of the UK aged 18+ • Public health interventions – following recommendations from authorities to prevent the spread of COVID-19	• Adherence to public health interventions was generally high (96.3%, 95% CI: 96.1-96.4%) • Adherence was lower among current than never smokers (OR 0.70, 95% CI: 0.62-0.78) irrespective of education, but the association was stronger among those with post-16 qualifications
(Clements, 2020)	Knowledge and behaviors toward COVID-19 among U.S. residents during the early days of the pandemic: online questionnaire	• Cross-sectional study (online survey conducted on Mar 17, 2020) • 1,070 residents of the USA aged 18+ • Public health interventions – wearing a mask, avoiding large gatherings	• Participants who reported going to gatherings with more than 50 people, or wearing masks outside the home, were less knowledgeable about COVID-19 and younger compared to participants who did not report these activities • Participants with graduate or professional degrees had 67% greater odds of attending large gatherings and 347-641% greater odds of wearing masks outside the home, compared to those with a high school education

			• Democrats had 30% lower odds of attending large gatherings and 44% lower odds of wearing masks outside the home compared to Republicans • Black participants had 148% increased odds of wearing masks outside the home compared to white participants
(Seale et al., 2020)	COVID-19 is rapidly changing: examining public perceptions and behaviors in response to this evolving pandemic	• Cross-sectional study (online survey conducted Mar 18-24, 2020) • 1,420 residents of Australia aged 18+ • Public health interventions – 6 social distancing strategies, self-isolation, hygiene	• 84.9% of respondents reported undertaking ≥ 1 of 3 hygiene-related behaviors and 93.4% performed ≥1 of 6 avoidance-related behaviors • Adopting avoidance behaviors was associated with trust in government (aOR: 5.5, 95% CI: 3-9.0), higher perceived rating of effectiveness of behaviors (aOR: 4.3, 95% CI: 2.8-6.9), and higher levels of perceived ability to adopt social distancing strategies (aOR: 1.8, 95% CI 1.1-3.0)
(Brouard, Vasilopoulos, & Becher, 2020)	Sociodemographic and psychological correlates of compliance with the COVID-19 public health measures in France	• Cross-sectional study (online survey conducted Mar 16-17, 2020) • 1,010 residents of France aged 18+ • Public health interventions –social distancing strategies, hand hygiene, cough/sneeze etiquette, reducing travel, avoiding crowded places	• Results suggest that age is positively associated with complying with protective measures • Women are more likely to have changed their behavior compared to men • Ideological extremity is associated with a reduced adherence to public health recommendations
(Doğan & Bayraktar, 2020)	COVID-19 with a public health perspective: measures taken in Turkey and public compliance with the measures	• Cross-sectional study (survey conducted on Mar 23-27, 2020) • 178 residents of Turkey aged 18+ • Public health interventions –social distancing strategies, hand hygiene	• 97.2% washed their hands with soap and 91.6% avoided contact with people

(Y. Li, Yao, & Luo, 2020) *preprint*	Perceived stress and its impact on health behavior of Chinese residents during the epidemic of COVID-19: an internet survey	• Cross-sectional study (online survey conducted Feb 14-22, 2020) • 2,449 residents of China aged 18+ • Public health interventions –hand hygiene, wearing a mask	• As perceived stress increased, the frequency of health behaviors such as washing hands and wearing a mask decreased in turn
(Perrotta et al., 2020) preprint	Behaviors and attitudes in response to the COVID-19 pandemic: Insights from a cross-national Facebook survey	• Cross-sectional study (online survey conducted Mar 13-Apr 19, 2020) • 71,612 residents Belgium, France, Germany, Italy, Netherlands, Spain, UK, and the USA aged 18+ • Public health interventions – social distancing, hand hygiene, wearing a face mask, reduced travel	• Overall women have a higher likelihood of adopting preventive behaviors compared to men • Wearing a face mask ranges from 7% in the Netherlands to 60% in Italy • Adopting more frequent hand washing ranges from 87% in Germany to 94% in Spain • Apart from the Netherlands and the UK, women and people > 45 years show the highest adoption rates of face masks
(Cutler, Stantcheva, Alsan, & Yang, 2020) preprint	Disparities in COVID-19 reported incidence, knowledge, and behavior	• Cross-sectional study (online survey conducted Mar 29-Apr 13, 2020) • 5,198 residents of the USA aged 18+ • Public health interventions – stay-at-home and hand hygiene	• Men wash their hands 3.8 times less per 24 hours than women ($p < 0.001$) • African-American and Hispanic respondents wash their hands more frequently than white respondents in a 24 hours period ($p=.020$) • Men are more likely to leave the house frequently than are women (0.74 times, $p < 0.001$) as are African Americans compared to white respondents (0.93 times, $p < 0.001$) • Older Americans (65+) are less likely to leave their homes frequently (-0.36 times, $p =0.018$)

(Barber & Kim, 2020)	COVID-19 worries and behavior changes in older and younger men and women	• Cross-sectional study (online survey conducted Mar 23-31, 2020) • 146 younger adults (18-35) and 156 older adults (65-81) in the USA • Public health interventions – stay-at-home, hand hygiene, wearing a mask, social distancing behaviors, self-isolation	• More than 80% of participants reported washing their hands more frequently, taking more care about cleanliness, no longer shaking hands, and avoiding public places. More than 60% of participants also reported social distancing • Compared with other participants, older men endorsed the fewest number of behavior changes • Older women were the most likely to report social distancing and avoiding public places • For all participants, COVID-19 worry was related to the total number of behavior changes made regardless of age or gender
(Ha, Schensul, Lewis, & Brown, 2020) *preprint*	Early assessment of knowledge, attitudes, anxiety and behavioral adaptations of Connecticut residents to COVID-19	• Cross-sectional study (online survey conducted Mar 23-29, 2020) • 464 residents of the USA aged 21+ • Public health interventions – stay-at-home, hand hygiene, wearing a mask, social distancing behaviors, cough/sneeze etiquette, reduced travel	• Compliance ranged from 21.5% and 9.2% of participants wearing sanitary gloves and wearing a mask when going outside respectively to 96.5% avoiding public transportation, and 100% frequently washing hands, avoiding contact with people, and avoiding events and meetings with a large number of people
(Thang et al., 2020) *preprint*	Preventive behavior of Vietnamese people in response to the COVID-19 pandemic	• Cross-sectional study (online survey conducted Mar 31-Apr 6, 2020) • 2,175 residents of Vietnam aged 18+ • Public health interventions – personal (e.g., face masks, social distancing) and community (e.g., avoiding crowded places) preventive measures	• Using a 9 and 11-item score, the mean level of personal adherence to preventive measures was 7.23 ± 1.63 (range: 1-9) and community preventive measures was 9.57 ± 1.12 (range: 0-11), respectively • The least compliance (45.1%) was found for "measuring body temperature at least twice a week" and the highest for wearing a face mask when going outside (99.5%)

			• Worries about one's health, perceived adaptation of the community to the lockdown, residence in large municipalities, official sources of COVID-19 information, and having a professional role in the health sector (worker or student) were associated with higher adherence scores
(Yousef Yang, peng, Yang, & Rockett, 2020) *preprint*	Changing trends of excess self-protective behavior, and association with belief in prevention myths during the COVID-19 epidemic in China: A panel study	• Prospective longitudinal study (online survey) • 116 residents of China aged 20+ over 5 time points (Feb 5/12/19/26 and Mar 4, 2020) • Public health interventions – excess preventive behaviors (EPB) for example disinfecting clothes, excess hand washing, hoarding masks etc.	• Perceived high risk for contracting COVID-19 was positively associated with each type of selected EPB, and perception of disease severity was positively associated with disinfection of clothes and hoarding of products • Belief in the disease prevention myths (facts about disease prevention that are not true) was positively associated with disinfection of clothes and both hand washing and sanitization • Disinfection of clothes was less prevalent among females than males (OR: 0.34), and among professionals than people in other occupational groups (OR: 0.35) • Hand washing was more prevalent among females than males (OR: 3.48) and less prevalent among the married than the never married (OR: 0.43)
(S. Li, Feng, Liao, & Pan, 2020)	Internet use, risk awareness, and demographic characteristics associated with engagement in Preventive Behaviors and	• Cross-sectional study (online survey conducted Apr 10-14, 2020) • 979 residents of the USA aged 18+ • Public health interventions – wearing a face mask, washing hands, cough/sneeze etiquette, social distancing, staying home, avoiding	• Participants who received more COVID-19–related health information online reported more frequent effort to engage in all types of preventive behaviors • Compared with participants who did not have positive cases in their social circles,

	Testing: cross-sectional survey on COVID-19 in the United States	public transportation, and cleaning frequently touched surfaces	those who had immediate family members or close friends and relatives who tested positive were more likely to get tested • Overall, females, older people, married, and employed individuals more frequently engage in most types of preventive behaviors when compared to their counterparts (males, younger people, single, un-employed) • More educated participants less frequently engaged in multiple preventive behaviors • Ethnic differences were also observed in engagement with preventive behaviors. Compared with whites, African Americans and Asians more frequently wore a facemask in public and stayed at home. Americans reported more frequent effort in cleaning frequently touched surfaces than whites
(Wu, Huang, Xie, & Chen, 2020) *preprint*	People behavior changes in China during COVID-19 pandemic	• Cross-sectional study (online survey conducted Apr 26-30, 2020) • 1,048 residents of China • Public health interventions – social distancing, reduce travel, stay-at-home, wear a mask	• Nearly 80% of participants reduced their out-of-home activities (working, eating, shopping, taking public transportation, and travelling) • 92% wear a mask on the street
(Sutin et al., 2020)	Body mass index, weight discrimination, and psychological, behavioral, and interpersonal responses to the Coronavirus pandemic	• Cross-sectional study (online survey conducted mid-Mar, 2020) • 2,094 residents of the USA with different BMI • Public health interventions – preventive behaviors (e.g., hand hygiene)	• Participants who reported weight discrimination were more likely to engage in preventive behaviors • BMI was unrelated to changes in preventive behaviors

(Iorfa et al., 2020) *preprint*	COVID-19 knowledge, risk perceptions and precautionary behavior among Nigerians: A moderated mediation approach	• Cross-sectional study (online survey conducted Mar 28-Apr 4, 2020) • 1,500 residents of Nigeria aged 18+ • Public health interventions –hand hygiene, avoiding crowded places, testing, wearing a mask, cough/sneeze etiquette, avoiding touching surfaces	• Among females and males, being older, having higher COVID-19 knowledge, and higher risk perception was related to higher precautionary behavior • Females engaged in more precautionary behavior than males • Compliance varied among precautionary measures. 19% of participants reported wearing a mask, 54.4% avoided touching surfaces, 56.8% avoided crowded places, and 66.4% self-isolated
(Liu et al., 2020)	Psychological status and behavior changes of the public during the COVID-19 epidemic in China	• Cross-sectional study (online survey conducted Jan 30-Feb 3, 2020) • 608 residents of China aged 18+ • Public health interventions –hand hygiene, avoiding crowded places, wearing a mask, social distancing	• At least 70.9% of respondents took 3 or more preventive measures to avoid infection • 93.3% respondents avoided going to public places, 83.7% wore a mask and 82.4% engaged in hand hygiene • Anxiety did not appear to be related to public behavior change and preventive measures • Fewer respondents with depression or psychological abnormalities took preventive measures compared with those without depression or psychological abnormalities
(Michela & Carlucci, 2020) *preprint*	Demographic and attitudinal factors of adherence to quarantine guidelines during COVID-19: the Italian model	• Cross-sectional study (online survey conducted Mar 21-26, 2020) • 3,672 quarantined adults in Italy aged 18+ • Public health interventions –hand hygiene, social distancing, cough/sneeze etiquette, cleaning surfaces, wearing a mask, avoiding crowded places	• Respondents exhibited medium to high scores of adherence to quarantine guidelines as measured by a single interval index, with a mean of 32.59 (median= 33; SD= 5·22; range scores 0-44) • Females, being employed, risk perception and risk anxiety were associated with

			significantly higher levels of adherence ($p < 0.001$) compared to their counterparts • Healthcare professional adherence mean ($p < 0.001$) was significantly higher compared the unemployed and employed • For age, the 18-29 age group scored statistically significantly lower ($p < 0.001$) compared to other age groups. Equally, the 50-59 age group was statistically significantly higher ($p < 0.001$) in adherence scores compared to 30-39 group
(Park et al., 2020)	Americans' COVID-19 stress, coping, and adherence to CDC guidelines	• Cross-sectional study (online survey conducted Apr 7-9, 2020) • 1,015 residents of the USA aged 18+ • Public health interventions –adherence to CDC guidelines (social distancing, hand hygiene)	• The most consistent predictors of adherence to CDC guidelines were older age, female gender, and financial security (all with small effect sizes) • Overall, adherence to CDC guidelines was fairly high but varied across interventions: 95.10% avoided eating out and large gatherings, 87.2% engaged in social distancing, and 74.68% engaged in cleaning and disinfecting practices
(Plohl & Musil, 2020)	Modeling compliance with COVID-19 prevention guidelines: the critical role of trust in science	• Cross-sectional study (online survey, date conducted not reported) • 525 global participants aged 18+ • Public health interventions –hand hygiene, compliance to guidelines	• Trust in science and COVID-19 risk perception significantly and directly contribute to explaining compliance with COVID-19 prevention guidelines ($R2 = 0.265$)
(Smith et al., 2020) *preprint*	Factors associated with adherence to self-isolation and lockdown measures in the UK; a cross-sectional survey	• Cross-sectional study (online survey conducted May 6-7, 2020) • 2,240 residents of the UK aged 18+ • Public health interventions – self-isolation	• Factors associated with non-adherence to self-isolation measures included being male, less worried about COVID-19, and perceiving a smaller risk of catching COVID-19

			• 9.7% of participants reported that they or someone in their household had symptoms of COVID-19 in the last 7 days. Of these, 75.1% had left the home in the last 24 hours (non-adherent) • Adherence was also associated with having received help from someone outside the household in the last 7 days
(Haupt et al., 2020) *preprint*	Profiles of social distance compliance: psychological and situational predictors of risky behavior during COVID-19	• Cross-sectional study (online survey conducted Apr 30-May 2, 2020) • 483 residents of the US aged 18+ • Public health interventions –compliance with public health guidelines, risky behavior (e.g., attending gatherings of 5+)	• Risky activity was associated with higher extraversion, need for cognitive closure, behavior activation, and perceived resource scarcity • Risky activity was also associated with less empathy and living space access, as well as younger age • 7 different cluster profile types are constructed to explain associations between variance in risky behavior engagement and responder psychological, sociodemographic and situational factors
(Zajenkowski, Jonason, Leniarska, & Kozakiewicz, 2020)	Who complies with the restrictions to reduce the spread of COVID-19?: personality and perceptions of the COVID-19 situation	• Cross-sectional study (survey conducted Apr 14-30, 2020) • 263 residents of Poland aged 18+ • Public health interventions – compliance with public health guidelines	• Responders scoring low on agreeableness and high on aspects of the Dark Triad traits (i.e., Machiavellianism, psychopathy Factor 1, and narcissistic rivalry) were less likely to comply with public health restrictions • COVID-19 perceptions were found to account for individual differences in public health measure compliance
(Banda et al., 2020)	Knowledge and behaviors related to the	• Cross-sectional study (telephone survey conducted Apr 25-May 23, 2020)	• Use of face masks and hand sanitizers was more frequent among urban residing

preprint	COVID-19 pandemic in Malawi	• 630 residents of Malawi aged 18+ • Public health interventions – use of face masks, hand hygiene, avoiding crowds, stay-at-home	respondents (22.5%) than among rural residents (5.0%) • More than 95% of respondents reported washing their hands more frequently, and ~ 50% reported avoiding crowds. Only 1/5 rural residents and 1/4 urban residents reported staying at home
(Galasso et al., 2020) *preprint*	Gender differences in COVID-19 related attitudes and behavior: evidence from a panel survey in eight OECD countries	• Cross-sectional study (online survey conducted Mar 16-30 and Apr 15-20, 2020) • 21,649 respondents from 8 countries (Australia, Austria, France, Germany, Italy, New Zealand, UK, and US) • Public health interventions – social distancing, hand hygiene, cough/sneeze etiquette, avoiding crowded places, stay-at-home, mask and glove use	• Significant gender differences in compliance with public health rules were observed among survey participants • Public health rule compliance was markedly larger among women than among men
(Bonful et al., 2020) *preprint*	Limiting spread of COVID-19 in Ghana: compliance audit of selected transportation stations in the Greater Accra region of Ghana	• Observational study involving audits of handwashing frequency and physical distancing adherence at public transport stations (conducted Mar 27-29, 2020) • 45 sites in Ghana • Public health interventions - availability of hygiene facilities, source and cleanliness of water, number of handwashing facilities, frequency of handwashing, overcrowding at the handwashing points, social distancing, mask use and information on COVID-19 prevention	• The majority (< 80%) of audit sites did not have adequate hand wash sites, frequency of hand washing was low, and facemask use was only observed among a few passengers • Compliance with COVID-19 prevention measures was inadequate in 13 stations, basic in 16 stations, intermediate in 7 stations, and advanced in 9 stations
(M. É. Czeisler et al., 2020)	Public attitudes, behaviors, and beliefs related to COVID-19,	• Cross-sectional study (online survey conducted May 5-12, 2020)	• Of all 3 cohorts, 77.3% of adults reported self-isolating with 84.6% reporting this behavior in NYC and 83.0% in LA

	stay-at-home orders, nonessential business closures, and public health guidance – United States, New York City, and Los Angeles, May 5-12, 2020	• 3 cohorts (US=1,676, NYC=286, and LA=259) all aged 18+ • Public health intervention – self-isolation, face masks, social distancing	• 74.1% nationwide reported always or often wearing a face mask when in public, with NYC reporting 89.6% and LA 89.8% • Compliance varied significantly across respondent demographics and characteristics
(Al-Hanawi et al., 2020)	Knowledge, attitude and practice toward COVID-19 among the public in the Kingdom of Saudi Arabia: a cross-sectional study	• Cross-sectional study (online survey conducted Mar 20-24, 2020) • 3,388 residents of Saudi Arabia aged 18+ • Public health interventions - avoiding large social events and crowded places, avoiding cultural behaviors, such as shaking hands, practicing social distancing, washing hands after sneezing, coughing, nose-blowing	• The mean score for practices for COVID-19 was 4.34 (SD = 0.87, range: 0–5), indicating overall good practices • Age groups 30–39 ($\beta = 0.039$; $p < 0.001$), 40–49 ($\beta = 0.033$; $p < 0.05$), and 50–59 ($\beta = 0.051$; $p < 0.001$) were associated with better practices than the referent group (18-29) • Compared to women, men have worse practices for COVID-19 ($\beta = -0.064$; $p < 0.001$)
(Marinthe, Brown, Delouvée, & Jolley, 2020)	Looking out for myself: exploring the relationship between conspiracy mentality, perceived personal risk, and COVID-19 prevention measures	• 2 cross-sectional studies (study 1 – conducted online Mar 9, 2020; study 2 – conducted online Mar 17-23, 2020) • 762 residents (study 1 and 229 residents (study 2) of France aged 18+ • Public health interventions – Study 1 was conducted when only gatherings of more than 1,000 people were prohibited. Behaviors studied included normative prevention behaviors (kissing someone, shaking hands) and non normative prevention behaviors (talking to people, taking public transportation, going to a restaurant etc.). Study 2 was conducted during the first week	• In study 1, preventative health behaviors were measured on a 9-point scale ranging from 1= much less than before coronavirus crisis and 9=much more than before coronavirus crisis. The mean adoption of normative prevention behaviors was 6.14 (1.49 SD) and non-normative prevention behaviors was 5.3 (0.66 SD) • Study 1 demonstrated that conspiracy believers are more likely to adopt non-normative prevention behaviors, but not normative ones

		of total confinement and measured compliance with the confinement rule	• In study 2, compliance with the confinement rule was measured on a 7-point scale ranging from 1=not all, to 7=very much. The mean confinement compliance was 6.45 (0.82 SD) • Study 2 demonstrated that people with a heighted conspiracy mentality are less inclined to adopt more extreme and legal normative preventative behaviors
(Daoust, 2020)	Elderly people and responses to COVID-19 in 27 countries	• Cross-sectional study (survey started first week of Apr, 2020) • 72,417 respondents across 27 countries aged 18+ • Public health interventions - wore a face mask outside, washed hands, covered nose and mouth when sneezing or coughing, avoided contact with people who have symptoms, avoid going out in general, avoid taking public transport, social distancing, avoid crowded areas, cleaned frequently touched surfaces avoid touching objects in public	• There is no significant effect of age on one's score of compliance with COVID-19 preventive measures • The baseline level of compliance with preventive measures is quite high (score of 12/16)
(Maher, MacCarron, & Quayle, 2020)	Mapping public health responses with attitude networks: the emergence of opinion-based groups in the UK's early COVID-19 response phase	• Longitudinal study (data collected on Mar 9, 16, and 23, 2020) • 235 participants in the UK aged 18+ • Public health interventions – hand washing, avoiding contact with certain people, reducing hand shaking, avoiding touching face	• Participants reported to be 'science-sceptics' reported significantly lower behavioral compliance at (mean = 5.28, SD = 1.46) compared to those considered 'science-trusters' (mean = 5.70, SD = 1.21)
(de la Vega, Ruíz-Barquín, Boros, &	Could attitudes toward COVID-19 in Spain render men more vulnerable than women?	• 2 cross-sectional studies (online surveys, date conducted not reported) • Study 1 (n = 64) was conducted in a shopping centre in Madrid, Spain and Study 2 (n = 640) online among participants aged 18+	• Compliance was rated on an 11-point scale • Women scored higher than men in compliance with safety measures (8.06 vs. 7.46, $p < 0.001$), proper care to wash

Szabo, 2020)		• Public health interventions – compliance with safety measures and keeping at least 1.5 meters away from others in public places and wearing a mask at all times	hands (8.77 vs. 8.25, p < 0.001), keeping 1.5 meters away from others (7.16 vs. 6.56, p=0.003), and using a mask for protection (1.95 vs. 1.82, p=0.591) • Compliance with safety measures was lower in older age groups: 18-25=6.73 (1.89 SD), 26-50=7.92 (1.64 SD), and 51-72=8.08 (1.56)
(Führer et al., 2020)	COVID-19: knowledge, risk perception and strategies for handling the pandemic	• Cross-sectional study (online survey conducted Mar, 2020) • 1,048 participants from Saxony-Anhalt, Berlin and Schleswig Holstein, Germany aged 18+ • Public health interventions – keeping distance from others, restricting contacts in public spaces, restricted private contacts, avoiding travel, stopped driving tram or avoiding cafes, shopping less often, buying supply of groceries, buying supply of disinfectant, buying respirators	• The most common measures were the observance of minimum distances to others (95.6%) and the reduction of personal contacts (93.4%). Only a minority of those surveyed stated that they had inventories of food (38.3%), disinfectants (15.9%) or breathing masks (15.0%) • Among 79% of respondents who said they had taken action, 41% took action at the end of March when quarantine measures were taken in regions of Italy, while another 13% did not take any precautions until the first infections were found in their state. Only 3 respondents (0.4%) said they had already taken action in response to the spreading coverage in China
(Reuben, Danladi, Saleh, & Ejembi, 2020)	Knowledge, attitudes and practices towards COVID-19: an epidemiological survey in north-central Nigeria	• Cross-sectional study (online survey, date conducted not reported) • 589 residents of north-central Nigeria aged 18+ • Public health interventions - practicing social distancing/self-isolation, improved personal hygiene and using face mask	• 92.7% of respondents practiced social distancing/self-isolation, 96.4% improved personal hygiene, and 82.3% using face masks

(Parsons Leigh et al., 2020)	A national cross-sectional survey of public perceptions, knowledge, and behaviors during the COVID-19 pandemic	• Cross-sectional study (online survey conducted Apr 26-May 1, 2020) • 1,996 respondents from Canada aged 18+ • Public health interventions – self isolating and social/physical distancing	• 842 respondents indicated they were in self-isolation (43.4%, 95% CI: 41.2%-45.6%). • Of those who were not self-isolating (n=1,144), the vast majority (n=1,083, 95.1%, 95% CI: 93.8%-96.4%) reported that they practiced physical distancing always (n=783, 68.8%, (95% CI 66.0%-71.5%) or often (n=300, 26.3%, 95% CI 23.7%-28.9%)
(Alper, Bayrak, & Yilmaz, 2020)	Psychological correlates of COVID-19 conspiracy beliefs and preventive measures: evidence from Turkey	• Cross-sectional study (online survey, dates conducted not reported) • 1,088 residents from Turkey, median age=31 • Public health interventions – leaving the house, avoiding physical contact, avoiding touching your face, washing/disinfecting hands after time outside, avoiding sharing same environment with elders, wearing a mask, covering mouth when coughing or sneezing	• There was no conclusive evidence to suggest any meaningful relationship between conspiracy beliefs and COVID-19-related preventive measures • Female participants were significantly more likely to take preventive measures than male participants ($p < 0.001$)
(de Moura Villela, Edlaine Faria, Mendoza Lopez, Sayuri Sato, & et al., 2020) *preprint*	COVID-19 outbreak in Brazil: adherence to national preventive measures and impact on people's lives	• Cross-sectional study (survey conducted Apr 3-9, 2020) • 23,896 residents of Brazil aged 18+ • Public health interventions – hand hygiene, avoiding touching face, disinfecting cell phone, wearing a mask, cough/sneeze etiquette, physical distancing/isolation, measuring temp twice a week, staying home when experiencing symptoms	• 98.7% of respondents practiced regular handwashing and 92.6% reported adhering to the 1.5-2m physical distancing rule, but only 45.5% wore a face mask when going outside • Older age, being female, living alone, being self-employed, living in the Northeast region, having at least an undergraduate degree, being a health care worker, and having comorbidities were all independently associated with higher adherence to national prevention restrictive measures

(Xie, Campbell, & Zhang, 2020)	Working memory capacity predicts individual differences in social-distancing compliance during the COVID-19 pandemic in the United States	• Cross-sectional study (online survey conducted Mar 13-26, 2020) • 397 participants recruited between March 20-22 and 453 participants recruited between March 24-26 from the US aged 18+ • Public health intervention – held no social gathering with friends, cancelled events or plans to go to an event, stopped going to the church or attending other community activity, and had no handshakes, hugs, or kisses when greeting	• Found that working memory capacity significantly predicted individual differences in social-distancing compliance even after taking into account other mood-related covariates • Participants with higher scores in social-distancing compliance also reported leaving home less and washing their hands more • Social-distancing compliance measure was not significantly correlated with education or income levels of the participants, even though female and older participants tended to show more social-distancing compliance
(Hsu, Lin, Wang, & Jhang, 2020)	How to defend covid-19 in Taiwan? Talk about people's disease awareness, attitudes, behaviors and the impact of physical and mental health	• Cross-sectional study (survey conducted Mar 1-Apr 10, 2020) • 2,132 respondents from Taiwan aged 20+ • Public health interventions - adequate or active compliance with the epidemic prevention measures, correct naming of all prevention processes, compliance with public space regulations, wearing of masks, consultation of experts, scholars, or online media for advice, active maintenance of cleanliness at home, medical waste recycling, sharing of prevention knowledge, reminding persons of inappropriate individual behavior, active community cleaning	• Active compliance with prevention measures and wearing of masks, and sharing of prevention knowledge received the highest compliance scores • The lowest compliance scores were noted for personal and community cleaning
(Almutairi, Mustafa, Alessa, Almutairi, &	Public trust and compliance with the precautionary measures against COVID-19	• Cross-sectional study (online survey, dates conducted not reported) • 1,232 residents of Saudi Arabia aged 18+	• 657 (53.3%) respondents were considered to be practicing poor precautionary measures

Almaleh, 2020)	employed by authorities in Saudi Arabia	• Public health interventions – avoiding public gatherings, obeying night time curfew, avoiding handshakes, hand hygiene, avoiding touching eyes, nose, and mouth with hands, covers nose/mouth when sneezing/coughing, avoiding sharing personal items, using facemask, seeking medical care early, maintaining social distancing	• Precautionary measures with the highest compliance included: "obeys night time curfew" with 98.3%, "avoids public gatherings" with 91.7%, "maintains social distancing during the COVID-19 outbreak" with 89.3% • Precautionary measures with the lowest compliance included: "uses a facemask in public" with 54%, followed by "avoids touching eyes, nose, and mouth with hands" with 37.9%, and "covers nose/mouth when sneezing or coughing with a tissue" with 25.3%
General Population (All Ages)			
(Olapegba & Ayandele, 2020)	Survey data of COVID-19 related knowledge, risk perceptions and precautionary behavior among Nigerians	• Cross-sectional study (online survey conducted Mar 28-Apr 4, 2020) • 1,357 residents of Nigeria aged 15+ • Public health interventions – hand hygiene, wearing a mask, avoiding crowded places	• The majority of participants engaged in protective behaviors such as avoiding crowded places (79%), use hand sanitizer (71.19%), and avoid touching door handles and stair case railings in public spaces (75.76%)
(Shabu, Amen, & Mahmood, 2020) *preprint*	Risk perception and behavioral response to COVID-19 in Iraqi Kurdistan Region	• Cross-sectional study (online survey conducted Mar 20-26, 2020) • 976 teaching faculty and students aged 17+ • Public health interventions – avoiding sneezing/couching, touching face, nose, and eyes, avoiding large gatherings, public places, and traveling to the affected areas, staying at home, using alcohol-based disinfectants, curfew, and wearing mask/gloves	• The percent of the respondents who applied public health measures frequently or always was high for most of the behaviors, except for wearing masks and gloves, and avoiding touching face • There was a significant ($p < 0.001$) weak positive correlation between risk perception with protective behaviors
(Arp et al., 2020) *preprint*	Use of face coverings in public during the COVID-	• Cross-sectional study (direct observations conducted May 16-Jun 1, 2020)	• Females and older adults had higher odds of using face coverings

	19 pandemic: an observational study	• 3,271 residents of WI, USA across all ages (minors, young adults, adults, older adults) • Public health intervention – face mask use in a grocery store	• Shopping at high price index grocery stores was also associated with mask use • Face coverings were used by 41% of the study sample
(Stanislau Affonso de Araújo, Evaldo et al., 2020) *preprint*	Teach, and teach and teach: does the average citizen use masks correctly during daily activities? Results from an observational study with more than 12,000 participants	• Observational study (direct observations conducted Jun 17-19, 2020) • 12,588 people observed in 5 Brazilian cities (no age restriction) • Public health interventions – face mask compliance	• 45.1% of the observed population wore face masks in a correct way with a city by city range of 39.1% to 63.5% • 15.5% (12.7-18.8%) did not use masks at all • 12.9% wore masks but exposed their mouth and nose (9.9-17.6%), 12.0% exposed their nose only (7.9-16.6%), 17.8% touched their mask during use (0.0%-4.0%), and 6.5% wore poorly fitted masks (1.2%-10.7%)

ADHERENCE TO PUBLIC HEALTH INTERVENTIONS IN YOUNG ADULTS AND UNIVERSITY/MEDICAL STUDENTS

Compliance to public health interventions to control COVID-19 was high across six studies specific to young adults (aged 16-29) and university/medical students (Table 2).

- Females were more likely to engage in preventive behaviors compared to men.
- Other factors positively associated with adherence to public health interventions include access to COVID-19 related information, self-control and level of anxiety.
- Self-reported preventative behaviors were negatively correlated with risk perception and being psychologically distressed.
- Among university students, one study found that non-medical students exercised higher compliance with social restrictions while medical students practiced better hand hygiene.

Table 2. Six studies evaluating adherence to public health measures for COVID-19 in young adults and university and medical students

Reference	Publication Title	Study Details	Key Outcomes
Young Adults			
(Imtiaz, Hossain, & Khan, 2020) *preprint*	COVID-19 in Bangladesh: measuring differences in individual precautionary behaviors among young adults	• Cross-sectional study (details of survey not reported) • 350 young adults of Bangladesh aged 16-29 • Public health interventions –precautionary behavior	• The mean precautionary score was highest (26.2) for the people who had completed their postgraduate education compared to those with high school education (24.7) • Psychologically distressed people had lower mean (23.6) precautionary scores than those who were not distressed (mean=25.1), p=0.019 • Females (25.3) had higher precautionary scores than males (23.8), p=0.007 • The self-control score was found to have a significant positive association with the precautionary score
University/Medical Students			
(Taghrir, Borazjani, & Shiraly, 2020)	COVID-19 and Iranian medical students; a survey on their related-knowledge, preventive behaviors and risk perception	• Cross-sectional study (online survey conducted Feb 26-28, 2020) • 240 medical students from Iran, mean age 23.67 • Public health interventions – reducing use of public spaces, cough etiquette, hand washing, disinfecting surfaces, talking with others about preventive behaviors	• 94.2% of participants had high performance in preventive behaviors • Self-reported preventive behaviors and risk perception had a significantly negative correlation. ($r_s = -0.128$; $P < 0.05$) • As preventive behaviors increase, risk perception declines
(Yang, Bin, & He, 2020)	Opinions from the epicenter: an online survey of university students in Wuhan amidst the COVID-19 outbreak	• Cross-sectional study (online survey conducted Jan 28-30, 2020) • 8,252 university students from Wuhan, China • Public health interventions – hand hygiene, wearing a face mask, reducing outdoor activities	• There was positive behavioral compliance among the respondents. Close to 90% of participants would wear a surgical mask when going out, more than two thirds had increased the practice of hand hygiene, and almost all reduced outdoor activities

			• Those with stronger anxiety and fear tended to adopt more stringent practices of mask-wearing and hand hygiene, as a natural behavioral reaction to perceived risks
(Saddik et al., 2020) *preprint*	Increased levels of anxiety among medical and non-medical university students during the COVID-19 pandemic in the United Arab Emirates	• Cross-sectional study (online survey conducted Mar 11-21, 2020) • 1,385 medical (dental and medical) students and non-medical students from the United Arab Emirates • Public health interventions – hygienic behavior, social restrictions	• Compliance was high overall and ranged from 58% wearing gloves and masks, 77% decreasing visits to crowded places, and 85% increasing hand hygiene • Non-medical students exercised higher compliance with social restrictions while medical students practiced better hand hygiene
(Lincango-Naranjo et al., 2020) *preprint*	Paradigms about the COVID-19 pandemic: knowledge, attitudes and practices from medical students	• Cross-sectional study (online survey conducted Apr 6-20, 2020) • 309 medical students from Ecuador • Public health interventions – hand hygiene	• The majority of participants (99%) reported washing hands frequently
(Hamza, Badary, & Elmazar, 2020)	Cross-sectional study on awareness and knowledge of COVID-19 among senior pharmacy students	• Cross-sectional study (online survey conducted Apr 28-30, 2020) • 238 senior pharmacy students in Egypt • Public health interventions - avoidance of public places, masking in public, maintaining social distancing	• Females were more likely to avoid going out in crowded places and maintain social distance than males • Significant associations were noted between public masking and access of COVID-19 related information from television, as well as maintaining a 2 meter social distance and utilizing physicians' advice on COVID-19

ADHERENCE TO PUBLIC HEALTH INTERVENTIONS IN CHILDREN AND ADOLESCENTS

The adherence to protective behaviors in children and adolescents was evaluated in four studies (Table 3). Of these studies, three studies from China (n=2) and Norway (N=1) showed moderate to high compliance rates and one from India showed low compliance rates.

- Female gender was significantly associated with better hand hygiene and overall compliance with the public health interventions.
- Other factors correlated with improved adherence include father's occupation, mother's educational background, location of residence, and those with an immigrant background.
- One study found that the compliance to preventive behaviors of primary school students was generally superior to that of students in high school (Wen et al., 2020).

Table 3. Four studies evaluating adherence to public health measures for COVID-19 and associated factors in children and adolescents

Reference	Publication Title	Study Details	Key Outcomes
Children and Adolescents			
(Chen et al., 2020)	Hand hygiene, mask-wearing behaviors and its associated factors during the COVID-19 epidemic: a cross-sectional study among primary school students in Wuhan, China	• Cross-sectional study (online survey conducted Feb 16-25, 2020) • 8,569 primary school children from Wuhan, China aged 6-13 • Public health interventions – wearing face masks, hand hygiene	• 42.05% and 51.60% of the primary school students showed good hand-washing and mask-wearing behaviors, respectively • Gender (female), grade (3-6), out-going history, father's occupation, and the time filling out the survey were significantly associated with hand hygiene • Grade (5-6), mother's educational background, and residence were associated with mask-wearing
(Saurabh & Ranjan, 2020)	Compliance and psychological impact of quarantine in children and adolescents due to COVID-19 pandemic	• Cross-sectional study (interviews of parents and children, dates conducted not reported) • 121 children and adolescents in India aged 9-18 • Public health interventions – household (e.g., use separate towels) and community (social distancing) preventive measures	• Compliance with quarantine behavior varied from 25.61% (slept in a separate room by themselves) to 83.47% (did not run errands) • Overall compliance to all the behaviors was 7.43%. Compliance with all the household and community protective measures was 10.71% and 17.35%, respectively • The most difficult activity to comply with was not going out of the house to socialize (65.26%)
(Wen et al., 2020)	Knowledge, attitudes, and practices towards	• Cross-sectional study (online survey conducted Mar 2-13, 2020)	• The compliance rates for students were as follows: Reducing unnecessary outings

preprint	COVID-19 among primary and middle school students during the COVID-19 outbreak period in Beijing: an online cross-sectional survey	• 7,377 students in Beijing aged 9-18 • Public health interventions – Reducing unnecessary outings, wearing a mask outside, washing hands frequently, eating a healthy diet, avoiding public transportation, taking hygienic breathing, cleaning and disinfecting regularly, not touching face before disinfecting, taking action when symptoms occur, having rational and effective ventilation, dining separately	(97.1%), wearing a mask outside (92.5%), washing hands frequently (91.3%), eating a healthy diet (86.5%), avoiding public transportation (85.8%), taking hygienic breathing (85.4%), cleaning and disinfecting regularly (78.6%), not touching face before disinfecting (78.3%), taking action when symptoms occur (57.8%), having rational and effective ventilation (39.2%), dining separately (38.6%) • The compliance to effective preventive behaviors of primary school students was generally superior to that of students in high school
(Soest et al., 2020)	Compliance with infection control rules among adolescents in Oslo during the COVID-19 pandemic	• Cross-sectional study (survey conducted Apr 23-May 8, 2020) • 12,686 'youth' in Oslo, Norway • Public health interventions – hand washing, shaking hands, avoiding larger groups, social distancing	• The majority reported following the rules on hand washing (n = 9,915, 84%), not shaking hands/hugging (n = 8,730, 74%) and avoiding larger groups (n = 8,565, 73%). Fewer said they kept a good distance (1-2 meters) from others (n = 5,859, 50%) • The highest support for the rules was seen among girls, young people with an immigrant background, those who live in outer Oslo east

ADHERENCE TO PUBLIC HEALTH INTERVENTIONS IN HEALTHCARE WORKERS (HCWS)

Seven studies evaluated adherence to infection prevention and control protective behaviors against COVID-19 in HCWs (Table 4). Overall adherence varied across studies, healthcare settings, and by the specific behavior.

- The proportion of HCWs that engaged in hand hygiene measures ranged from 79.44% in a group of HCWs from China to 98.2% in a group of frontline doctors from Jordan.

- Two studies demonstrate that being a nurse (vs. doctor, nursing and medical staff, medical and clinical officers) was significantly associated with self-reported compliance to infection control measures. Among these HCW studies, there were conflicting results on gender as a predictor of self-reported compliance.

Table 4. Seven studies evaluating adherence to public health measures for COVID-19 and associated factors in HCWs

Reference	Publication Title	Study Details	Key Outcomes
Healthcare Workers (HCWs)			
(Suleiman et al., 2020)	Preparedness of frontline doctors in Jordan healthcare facilities to COVID-19 outbreak	• Cross-sectional study (online survey conducted Mar 23-27, 2020) • 308 frontline doctors in Jordan, mean age 30.3 ± 5.8 • Public health interventions – adherence to the PPE (Personal Protective Equipment) guidelines	• The adherence scores of these doctors were 8.4 ± 1.5 out of 10 • For example, 88% wash their scrubs, 98.1% wash their hands before seeing a patient, 93.8% avoid high fives and hand shakes, and 91.6% leave their shoes at work our outside the home
(Tamari et al., 2020)	Nationwide survey of COVID-19 prevention measures in Japanese radiotherapy departments via online questionnaire for radiation oncologists	• Cross-sectional study (online survey conducted Apr 16-23, 2020) • 184 radiation oncologists in Japan • Public health interventions – hand hygiene, use of masks/PPE, social distancing	• The majority of the respondents (81.0%) indicated that they had taken some infection control measures • There were differences in compliance between departments • 8.1% of the respondents reported that they used PPE in their radiotherapy practice and 63% engaged in proper social distanced with patients • 96.2% of participants who had direct contact with patients wore masks, and 85.3% who had no direct contact with patients wore masks
(Chatterjee et al., 2020)	Attitude, practice, behavior, and mental health impact of COVID-19 on doctors	• Cross-sectional study (online survey conducted Mar 28-Apr 6, 2020) • 152 doctors in West Bengal, India • Public health interventions – hand hygiene, use of masks/PPE	• The majority of doctors are using a surgical mask (58.6%) but only a few are using N95 masks (19.7%) • 95.4% report they are practicing regular hand hygiene but also report they mostly

			washing their hands on an as-required basis (42.8%) • Only 24.3% have access to PPE and 11.2% are actually using it
(Lai et al., 2020)	Will healthcare workers improve infection prevention and control behaviors as COVID-19 risk emerges and increases, in China?	• Cross-sectional study (survey conducted Jan 15-17, 2020) • 1,581 HCWs in China (n=1581) • Public health interventions – hand hygiene, PPE, terminal cleaning	• Overall, higher education degree, longer work years, female gender (vs. male) had significantly negative effect on the self-reported infection control compliance • Being a nurse (vs. doctors) had significant positive effects on self-reported compliance to infection control measures • Working in high risk departments were associated with increased compliance, while exposure to confirmed or suspected patients reduced infection control compliance
(Zhou, Lai, Zhang, & Tan, 2020)	Compliance measurement and observed influencing factors of hand hygiene based on COVID-19 guidelines in China	• Cross-sectional study (direct observations conducted Mar 5-7, 2020) • HCWs workers from Tongji Hospital and 17 medical groups from other provinces in China • Public health interventions – hand hygiene at 17 moments (e.g., before touching a patient, before aseptic procedure, after using toilet, etc.)	• The overall compliance for 17 moments of hand hygiene was 79.44% • The highest overall compliance was for the moment before wearing gloves (91.67%), and the lowest was the moment after touching patient surroundings (65.56%) • The overall compliance was 85% in the intensive care department, 79.18% in the non-intensive care department; 76.07% in contaminated area, 84.38% in semi contaminated area, and 84.21% in hygienic area
(Martín et al., 2020)	Prevalence of SARS-CoV-2 infection in general practitioners and nurses in primary	• Cross-sectional study (study conducted during first 2 weeks of Apr, 2020)	• The degree of compliance with preventive measures were recorded using a Likert scale of 0-10, with 0 being the lowest

	care and nursing homes in the healthcare area of León and associated factors	• 676 nurses and doctors from primary care centers and nursing homes in the Healthcare Area of León (Spain) • Public health interventions – general compliance with preventative measures	degree of exposure or compliance and 10 the highest • 31% reported high compliance with preventive measures (10 points on the survey)
(Contejean et al., 2020)	Comparing dynamics and determinants of SARS-CoV-2 transmissions among health care workers of adult and pediatric settings in central Paris	• Prospective study conducted Feb 24-Apr 10, 2020 • 336 healthcare workers in Paris, France • Public health interventions – wearing proper PPE, wearing a mask properly, avoiding public transportation, wearing a mask outside home	• The majority of workers recalled a contact without PPE with an index case. PPE was more frequently used in adult settings (56/227) vs. children settings (16/109) • Most employees declared wearing a mask always/most of the time at hospital, but 65/336 (19%) admitted removing masks during breaks in the presence of other colleagues (204/336, 61% during lunch breaks). More than half (201/336, 60%) reported using public transportation, including 112/201 (56%) over one hour per day, but less than 25% (82/334) wore mask outside home

ADHERENCE TO PUBLIC HEALTH INTERVENTIONS IN OTHER POPULATIONS

Five studies on adherence to public health measures aimed to control COVID-19 were identified in four other populations, Table 5. These other populations include pregnant women, employees, visitors to hospitals, and migrants.

Table 5. Five studies on adherence to public health measures for COVID-19 in other populations

Reference	Publication Title	Study Details	Key Outcomes
Pregnant Women			
(Yassa et al., 2020)	Near-term pregnant women's attitude toward, concern about	• Cross-sectional study (details of survey not reported) • 172 pregnant women in Turkey • Public health interventions – self quarantine	• The majority of the women (87.2%) complied with self-quarantine rules

	and knowledge of the COVID-19 pandemic		
Visitors to Hospitals			
(Gunasekaran et al., 2020) *preprint*	Prevalence and acceptance of glove wearing practice among general population when visiting high risk are during local COVID-19 outbreak	• Cross-sectional study (dates not reported) • 40 individuals entering hospitals and 30 entering wet markets in Malaysia • Public health interventions – wearing gloves and face masks	• More individuals visiting wet market (30.0%) were observed with unacceptable glove practice compared to individuals visiting the hospital (8.9%), $\chi 2$ (1) = 5.60, p=0.018 • Men were using more medical grade glove (78.8%) compared to non-medical grade glove (21.2%) while an equal amount of medical (50.0%) and non-medical grade glove (50.0%) was used among female, $\chi 2$ (1) = 6.546, p=0.011 • Glove use was higher among non-Malay (53.3%) compared to Malay (46.7%) in the hospital and glove use was higher among Malay compared to non-Malay (16.7%) visiting wet market, $\chi 2$ (1) = 10.20, p=0.001
(Sahiledengle et al., 2020) *preprint*	Hand washing compliance and COVID-19: a non-participatory observational study among hospital visitors	• Cross-sectional study (direct observations conducted Apr 27-May 3, 2020) • 1,282 individuals entering hospitals in Ethiopia • Public health interventions – hand hygiene	• Only 0.9% (95% CI: 0.4-1.4) of the participants were fully compliant with the recommended hand washing techniques • Most of the participants (47.2%, 95% CI: 44.4-49.9) had minimal compliance and 20.1% (95% CI: 17.8-22.3) were not compliant • There was no difference in the compliances between genders (0.9% vs 0.7%, P = 0.745)
Migrants			
(Mannan & Farhana, 2020)	The COVID-19 pandemic: challenges and reality of	• Cross-sectional study (survey conducted Feb 1-Mar 31, 2020)	• Only 2.74% were officially in quarantine for 14 days. Only 1.98% complied with the 14 days of personal isolation under the Health

preprint	quarantine, isolation and social distancing for the returnee migrants in Bangladesh	• 3,281 returnee migrants from 8 administrative divisions of Bangladesh aged 18+ • Public health interventions – quarantine, isolation, and social distancing for 14 days	Care Rules and only 3.38% were adhered to 14 days of social distancing • In addition to the 14 days of the health warning rule, there is also reluctance to comply with the social distance rule during the epidemic (only 5.05% compliance)
Employees			
(Wang, Yi Wong, & Ho, 2020) *preprint*	Availability of workplace policy for prevention of coronavirus disease 2019 and its relationship with personal protective behaviors: a survey of employees	• Cross-sectional study • 1,048 employees from Hong Kong • Public health interventions – hand hygiene, wearing a face mask, social distancing, household hygiene	• Compliance varied across protective measures (e.g., 77.1% reported always washing hands before meals and 51.2% reported they always avoided leaving their home) • Personal protection behaviors differed between socio-demographic subgroups in terms of age, gender, living arrangement, marital status, educational level and work status • Employees with available workplace guidelines and measures performed personal protection behaviors with higher frequency, and this association was more significant among managers/administrators and manual labourers

SYNTHESIS RESEARCH ON ADHERENCE TO PUBLIC HEALTH INTERVENTIONS

Three reviews on adherence to public health measures aimed to control infectious diseases were identified, Table 6. These reviews did not contain any specific evidence on COVID-19.

Table 6. Three reviews on adherence to public health measures for infectious diseases

Reference	Publication Title	Study Details	Key Outcomes
Reviews			

(Webster et al., 2020)	How to improve adherence with quarantine: rapid review of the evidence	• Rapid evidence review • Search included evidence up until Jan 27, 2020 • AMSTAR: moderate quality • 14 articles included in the review • No articles specific to SARS-CoV-2	• Adherence to quarantine ranged from 0-92.8%. • Main factors associated with adherence were the knowledge people had about the disease and quarantine procedure, social norms, perceived benefits of quarantine and perceived risk of the disease
(Houghton et al., 2020)	Barriers and facilitators to healthcare workers' adherence with infection prevention and control (IPC) guidelines for respiratory infectious diseases: a rapid qualitative evidence synthesis	• Rapid qualitative evidence synthesis • Search included evidence up until Mar 26, 2020 • AMSTAR: good quality • 20 articles included in the review	• Several factors influence HCWs ability and willingness to adhere to IPC guidelines including the guideline content and how it is communicated, support from managers, workplace culture, training, physical space, access to and trust in PPE, and a desire to deliver good patient care
(Brooks, Greenberg, Wessely, & Rubin, 2020) *preprint*	Factors affecting healthcare workers' compliance with social and behavioral infection control measures during emerging infectious disease outbreaks: Rapid evidence review	• Rapid evidence review • Search included evidence up until May 4, 2020 • AMSTAR: moderate quality • 56 articles include in the review	• Staff working in emergency or ICU settings appeared more likely to comply with recommendations than those in other settings • Staff with higher levels of anxiety and higher concern about the risk of infection were more likely to comply • Negative associations were also found to hinder compliance such as observed non-compliance of colleagues, availability of PPE, perceived difficultly and effectiveness, inconvenience, and discomfort

Methods

All of the literature on COVID-19 has been compiled and organized by the Emerging Science Group of the Public Health Agency of Canada since the beginning of the outbreak. This involves a daily scan of the literature for all published and pre-published articles. Searches to retrieve relevant COVID-19 literature are conducted in PubMed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, and Research Square. These are cross-referenced with the literature on the World Health Organization COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier, and Wiley. The daily summary and full scan results are maintained in a RefWorks database and a searchable Excel file. Each article is tagged using various foci to identify the focus of the article (e.g., epidemiology, clinical data, therapeutics etc.). Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. The search terms included in this review were compliance, adherence, and behavior. Each potentially relevant reference was analyzed to confirm its relevance and data was extracted into the review. This review contains research published up until July 19, 2020.

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Nouveaux éléments de preuve sur la COVID-19

Note d'information sur les déterminants de l'adhésion individuelle aux interventions de santé publique pour la COVID-19

Introduction

Quelles sont les données probantes relatives aux déterminants de l'adhésion individuelle aux interventions de santé publique visant à prévenir la COVID-19?

L'adhésion d'une personne à des interventions de santé publique telles que la distanciation sociale, le port de masques faciaux et le lavage des mains, joue un rôle important dans l'efficacité de ces interventions pour contrôler l'épidémie. Cette note d'information recense et résume la littérature publiée avant le 19 juillet 2020 sur les déterminants de l'adhésion individuelle aux interventions de santé publique pour la COVID-19, afin de mieux comprendre les facteurs et les obstacles à l'adoption des comportements de protection recommandés.

Points clés

- Au nombre de 80, les études menées dans de nombreux pays ont évalué l'adhésion individuelle aux mesures de protection contre l'infection par la COVID-19 dans diverses populations, notamment chez les adultes, les jeunes adultes, les étudiants universitaires, les enfants et les adolescents, les travailleurs de la santé, les femmes enceintes ainsi que les employés et les visiteurs des hôpitaux (tableaux 1 à 5).
- La plupart de ces études ont été menées dans les premières phases de l'épidémie et représentent l'adoption initiale de comportements protecteurs. De nombreuses études (n=28) font état d'un meilleur respect des règles par les femmes par rapport aux hommes dans tous les groupes d'âge. Peu d'études ont été menées sur les enfants et les adolescents, mais bon nombre d'entre elles ont constaté un taux de conformité élevé dans ces groupes d'âge, avec un taux de conformité plus faible chez les enfants en âge de fréquenter l'école secondaire.
- La conformité varie selon les études, les facteurs sociodémographiques et le type de mesure de protection, et elle est souvent associée aux connaissances et aux croyances individuelles.
- Treize études ont révélé que les adultes de plus de 30 ans étaient plus susceptibles de respecter les comportements de protection recommandés. D'autres facteurs sont positivement corrélés à l'observance chez les adultes, notamment : la perception du risque (n=7 études), une meilleure connaissance de la COVID-19 (n=5), la confiance dans la science et le gouvernement (n=4), des niveaux d'anxiété accrus (n=3), la perception de l'auto-efficacité à adopter des mesures de protection (n=3) et l'origine ethnique noire ou asiatique (n=3).

- L'inobservance des adultes était associée à des problèmes psychologiques tels que la dépression, la mentalité de conspiration et le narcissisme (n=5), ainsi qu'au fait d'être un fumeur actuel (n=3).
- Chez les enfants et les adolescents, les facteurs corrélés à une meilleure observance comprennent la profession du père, le niveau d'éducation de la mère, le lieu de résidence et les personnes issues de l'immigration (Chen et coll., 2020; Soest, Pedersen, Bakken et Sletten, 2020).
- Trois synthèses rapides ont été recensées. Elles comprennent des documents publiés avant la pandémie qui portent sur le respect des mesures de quarantaine et les comportements préventifs individuels adoptés par les travailleurs de la santé (tableau 6).

Vue d'ensemble des éléments de preuve

Au total, 80 publications relatives à l'adoption de comportements individuels de protection recommandés par la santé publique pour lutter contre l'épidémie de COVID-19 et aux obstacles et éléments facilitants associés à ces comportements. Trois examens rapides sur l'adhésion et les facteurs qui influencent l'adhésion aux interventions de santé publique pour contrôler les maladies infectieuses ont également été inclus, mais ces examens ne comprenaient que des études publiées avant la pandémie. Sur les 83 publications incluses, 39 prétirages ont été recensés; ces articles n'ont pas été soumis au processus d'examen par les pairs. Les publications faisant état de l'adhésion aux interventions de santé publique sont toutes des études d'observation qui présentent un risque modéré/élevé de biais et sont donc considérées comme de qualité moyenne/faible. La majorité de ces études se fondent sur le modèle transversal et les résultats sont pour la plupart autodéclarés; les réponses peuvent donc être faussées par des biais de rappel, de réponse et de désirabilité sociale. Bien que de nombreuses études montrent des tendances similaires, les conclusions pourraient changer dans le cadre de recherches supplémentaires.

Les études qui évaluent l'observance au fil du temps constituent une lacune importante sur le plan des connaissances dans cette recherche. La plupart des recherches recensées ont été menées dans les premiers stades de l'épidémie et ne fournissent qu'un échantillon représentatif de l'adoption ou non des comportements recommandés par la santé publique. Dans de nombreuses juridictions, cette situation a évolué au fil du temps; les messages d'intérêt public et les règles ont changé avec la levée des différentes mesures ou le renforcement de celles-ci. Des études qui explorent longitudinalement les obstacles et les éléments qui facilitent l'adoption à long terme de comportements de protection sont nécessaires pour que l'on puisse se pencher à la fois sur les personnes qui résistent à l'adoption de comportements de protection et sur le risque de diminution de l'adhésion au fil du temps.

CONTENU

L'ADHÉSION AUX INTERVENTIONS DE SANTÉ PUBLIQUE CHEZ LES ADULTES

Cinquante-huit études ont évalué l'adoption par les adultes de comportements de protection recommandés par la santé publique (tableau 1). Le respect des mesures varie selon les études, les facteurs sociodémographiques et le type de mesure de protection, et il est souvent associé aux connaissances et aux croyances individuelles.

- Dans 24 études, les femmes étaient plus susceptibles que les hommes d'adhérer à des mesures préventives.
- Treize études ont révélé que les adultes de plus de 30 ans étaient plus susceptibles de respecter les comportements de protection recommandés.
- D'autres facteurs sont positivement corrélés à l'observance, notamment : la perception du risque (n=7 études), une meilleure connaissance de la COVID-19 (n=5), la confiance dans la science et le gouvernement (n=4), des niveaux d'anxiété accrus (n=3), la perception de l'auto-efficacité à adopter des mesures de protection (n=3) et l'origine ethnique noire ou asiatique (n=3).
- L'inobservance était associée à des problèmes psychologiques tels que la dépression, la mentalité de conspiration et le narcissisme (n=5), ainsi qu'au fait d'être un fumeur actuel (n=3).

Tableau 1. Cinquante-huit études évaluant l'adhésion aux mesures de santé publique pour lutter contre la COVID-19 et les facteurs associés chez les adultes

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Population adulte générale (18+)			
(Qian et coll., 2020) *Préimpression*	Psychological responses, behavioral changes and public perceptions during the early phase of the COVID-19 outbreak in China: A population based cross-sectional survey	• Étude transversale (enquête téléphonique réalisée du 1er au 10 février 2020) • 1 100 résidents de Wuhan (n=510) et de Shanghai (n=501) âgés de 18 ans et plus • Interventions de santé publique – éviter de manger au restaurant et de prendre les transports en commun, réduire les visites dans les lieux publics, reprogrammer les plans de voyage, nettoyer plus souvent les surfaces, maintenir une meilleure ventilation intérieure, porter un masque facial ou des lunettes de protection, se laver les mains	• 401 (78,6 %) participants de Wuhan et 320 (63,9 %) participants de Shanghai ont adopté les 6 comportements recommandés et se sont abstenus d'avoir les comportements à éviter • Un taux de conformité élevé, supérieur à 90 %, a été observé pour tous les autres comportements dans les deux échantillons, à l'exception du nettoyage plus fréquent des surfaces • La conformité était associée à des niveaux d'anxiété accrus, à des risques perçus et à une confusion quant à la fiabilité de l'information
(Wong et coll., 2020) *Préimpression*	The role of institutional trust in preventive and treatment-seeking behaviors during the 2019 novel coronavirus (2019-nCoV) outbreak among residents in Hubei, China	• Étude transversale (enquête en ligne réalisée les 29 et 30 janvier 2020) • 4 245 résidents de la province d'Hubei âgés de 18 ans et plus • Interventions de santé publique – éviter l'interaction sociale, les contacts physiques et l'espace public; prévoir une protection personnelle; rechercher un traitement	• L'adoption de comportements préventifs était élevée dans la population étudiée • Le fait d'être en quarantaine (RCC=2,35; 95 % IC : 1,80 à 3,08) et le fait d'avoir un score élevé de confiance institutionnelle (RCC=2,23; 95 % IC : 1,96 à 2,53) ont été deux déterminants importants de l'augmentation des scores de comportement préventif • Les groupes d'âge de 26 à 35 ans (RCC=1,54; 95 % IC : 1,29 à 1,83) et de 36 à 45 ans (RCC=1,22; 95 % IC : 1,01 à 1,48) ont obtenu des scores de comportement préventif significativement plus élevés que ceux de plus de 45 ans

(Kwok et coll., 2020)	Community Responses during Early Phase of COVID-19 Epidemic, Hong Kong	• Étude transversale (enquête en ligne réalisée en janvier 2020) • 1 715 résidents de Hong Kong âgés de 18 ans et plus • Interventions de santé publique – avoir une bonne hygiène personnelle, désinfecter les habitations, porter un masque facial, éviter les voyages, pratiquer la distanciation sociale	• L'adoption d'une meilleure hygiène personnelle et l'évitement des voyages présentaient un pourcentage élevé (plus de 77 %) et modéré (40 à 93 %) pour différents types de mesures de distanciation sociale • Les niveaux d'adoption de mesures de distanciation sociale étaient plus élevés chez les femmes (RCC 1,31; IC 95 % : 1,06 à 1,63, p=0,1), chez les personnes vivant dans les Nouveaux Territoires, chez les personnes se percevant comme ayant une bonne compréhension de la COVID-19, et chez les personnes étant plus anxieuses
(Lep, Babnik et Beyazoglu, 2020) *Préimpression*	The role of information credibility in emotional responses and engagement in self-protective behavior within days of the COVID-19 outbreak: A cross-sectional study	• Étude transversale (enquête en ligne réalisée la première semaine de mars 2020) • 1 717 résidents de Slovénie âgés de 18 ans et plus • Interventions de santé publique – éviter les foules, se laver fréquemment les mains, éviter de se toucher le visage	• La crédibilité perçue des informations reçues par les professionnels de la santé et les scientifiques était liée à une meilleure connaissance des comportements d'autoprotection • La connaissance est liée à un engagement plus important à l'égard des comportements d'autoprotection
(Muto, Yamamoto, Nagasu, Tanaka et Wada, 2020) *Préimpression*	Japanese citizens' behavioral changes and preparedness against COVID-19: How effective is Japan's approach to self-restraint	• Étude transversale (enquête en ligne réalisée du 26 au 28 mars 2020) • 11 342 résidents du Japon âgés de 20 ans et plus • Interventions de santé publique – éviter les espaces clos mal ventilés, les grands rassemblements et les conversations ou les cris à proximité immédiate, respecter l'étiquette respiratoire	• Environ 76 % des participants ont estimé eux-mêmes avoir pris des mesures préventives • Le lavage fréquent des mains était une mesure adoptée par environ 86 % des participants et l'étiquette respiratoire par 77 % • Environ 20 % des participants sont réticents à mettre en œuvre des mesures de prévention adéquates. L'analyse indique que ceux qui n'adoptent pas de

			comportements protecteurs sont plus souvent des hommes, plus jeunes (moins de 30 ans), célibataires, font partie de ménages à faibles revenus, ont une habitude de boire ou de fumer et ont un score d'extraversion plus élevé.
(Shinan-Altman, 2020) *Préimpression*	COVID-19 precautionary behavior: The Israeli case in the initial stage of the outbreak	• Étude transversale (enquête en ligne réalisée du 12 au 21 mars 2020) • 1 407 résidents d'Israël âgés de 18 ans et plus • Interventions de santé publique – se laver les mains, éviter le contact avec les personnes qui présentent des symptômes	• Le score de comportement de précaution était relativement élevé parmi les participants • Le comportement de précaution était plus élevé chez les femmes, les participants plus âgés, les participants ayant un niveau de connaissance plus élevé sur la COVID-19 et les participants ayant des réactions émotionnelles négatives plus importantes
(Moore, Lee, Hancock, Halley et Linos, 2020) *Préimpression*	Experience with Social Distancing Early in the COVID-19 Pandemic in the United States: Implications for Public Health Messaging	• Étude transversale (enquête en ligne réalisée du 14 au 23 mars 2020) • 7 355 résidents des États-Unis âgés de 18 ans et plus • Interventions de santé publique – distanciation sociale	• 39,8 % ont déclaré ne pas se conformer aux mesures • Le groupe le plus jeune (de 18 à 31 ans) présentait le taux de conformité le plus faible (52,4 %) par rapport aux autres groupes d'âge (tous, moins de 60 %; toutes les valeurs $p < 0,01$)
(Machida et coll., 2020)	Adoption of personal protective measures by ordinary citizens during the COVID-19 outbreak in Japan	• Étude transversale (enquête en ligne menée du 25 au 27 février 2020) • 2 400 résidents du Japon âgés de 20 ans et plus • Interventions de santé publique – avoir une bonne hygiène des mains, respecter la distanciation sociale, éviter le contact avec les yeux, le nez et la bouche, respecter l'étiquette respiratoire et s'isoler volontairement	• 34,7 % ont mis en œuvre l'ensemble des 5 mesures de protection • La prévalence des cinq mesures de protection varie entre 59,8 et 83,8 %, la plus faible étant d'éviter de toucher les yeux, le nez et la bouche • La prévalence est significativement plus élevée chez les femmes et les adultes âgés que chez les hommes et les personnes de moins de 65 ans (femmes

			OU : 1,57 an, personnes plus âgées OU : 1,83, les deux p < 0,001)
(Williams, Armitage, Tampe et Dienes, 2020) *Préimpression*	Public perceptions and experiences of social distancing and social isolation during the COVID-19 pandemic: A UK-based focus group study	• Groupe de discussion mené en ligne entre le 28 mars et le 4 avril 2020 • 27 résidents du Royaume-Uni âgés de 18 ans et plus • Interventions de santé publique – respecter la distanciation sociale et l'isolement social	• Tous les participants ont indiqué qu'ils respectaient beaucoup les directives en matière de distanciation et d'isolement, mais ont déclaré avoir vu ou entendu des cas de non-respect chez d'autres personnes
(Canning, Karra, Dayalu, Guo et Bloom, 2020) *Préimpression*	The association between age, COVID-19 symptoms, and social distancing behavior in the United States	• Étude transversale (enquête en ligne, dates de réalisation non communiquées) • 4 676 résidents des États-Unis âgés de 18 ans et plus • Interventions de santé publique – distanciation sociale	• Environ 52 % des participants ont déclaré être sortis de chez eux la veille (sans respecter la distanciation sociale) • Ceux qui ont souffert d'essoufflement ont moins de contacts étroits, avec un RTI de 0,49 (IC à 95 %) : 0,30 à 0,78). Le fait d'avoir d'autres symptômes de la grippe réduit la probabilité de sortir de 0,32 (IC à 95 %) : 0.18 à 0,60) et le taux d'incidence de contacts étroits de 42 % (RTI = 0,58; IC 95 % : 0,38 à 0,88). • Les personnes âgées sont tout aussi susceptibles de quitter leur domicile que les jeunes, mais les personnes de plus de 50 ans ont eu moins de la moitié du nombre prévu de contacts étroits par rapport aux personnes de moins de 30 ans
(M. Ã. Czeisler et coll., 2020) *Préimpression*	COVID-19 : public compliance with and public support for stay-at-home mitigation strategies	• Étude transversale (enquête en ligne menée du 2 au 8 avril 2020) • 4 676 résidents des États-Unis (N.Y., L.A.) et de l'Australie âgés de 18 ans et plus	• 81,8 % ont déclaré respecter les politiques recommandées en matière de quarantaine ou pour rester à la maison • Le taux de conformité était élevé dans les régions fortement touchées (États-Unis,

		• Interventions de santé publique – adopter des stratégies pour inciter les gens à rester à la maison	New York) et dans les régions faiblement touchées (Australie, Los Angeles)
(Pollak, Dayan, Shoham et Berger, 2020) *Préimpression*	Predictors of adherence to public health instructions during the COVID-19 pandemic	• Étude transversale (enquête en ligne menée du 28 mars au 10 avril 2020) • 654 résidents d'Israël âgés de 18 ans et plus • Interventions de santé publique – respecter les instructions médicales	• 28,7 % ont été définis comme des non-adhérents • L'inobservance était associée au sexe masculin (RCC = 1,54; IC 1,03 à 2,31), au fait de ne pas avoir d'enfants (RCC = 1,73; 1,13 à 2,65), au tabagisme (RCC = 2,27; IC 1,42 à 3,62), à des niveaux élevés de symptômes de TDAH (RCC = 1,55; IC 1,07 à 2,25), à des niveaux élevés de comportements à risque antérieurs (RCC = 1,41; IC 1,10 à 1,81), à une détresse psychologique actuelle élevée (RCC = 1,51; IC 1,14 à 2,01), à un faible risque perçu de COVID-19 (RCC = 1,52; IC 1,22 à 1,89), à une faible exposition aux instructions (RCC = 1,45; IC 1,14 à 1,82) et à une faible efficacité perçue des instructions (RCC = 1,47; IC 1,16 à 1,85)
(Shahnazi, Ahmadi-Livani et Pahlavanzadeh, 2020) *Préimpression*	Assessing preventive health nehaviors from COVID-19 based on the health belief model (HBM) among people in Golestan province: a Cross-sectional study in northern Iran	• Étude transversale (enquête en ligne réalisée du 11 au 16 mars 2020) • 750 résidents de l'Iran âgés de 18 ans et plus • Interventions de santé publique – éviter les lieux bondés, respecter la distanciation sociale, se laver les mains, rester à la maison, respecter l'étiquette respiratoire, éviter de se toucher le visage avec les mains	• Le taux de conformité variait entre 96,8 % (éviter les endroits bondés) et 33,5 % (éviter de se toucher le visage avec les mains) • Le score moyen du comportement préventif était plus élevé chez les femmes que chez les hommes, et plus important chez les citadins que chez les ruraux • Une augmentation d'une unité de l'écart-type des scores factoriels « auto-efficacité » et « bénéfices perçus » a augmenté les scores de comportement

			préventif de 0,22 et 0,17 unité respectivement • Une augmentation d'une unité de l'écart-type des scores factoriels « obstacles perçus » et « croyances fatalistes » a réduit les scores du comportement préventif de 0,36 et 0,19 unité respectivement
(Lee et You, 2020)	Psychological and behavioral responses in South Korea during the early stages of Coronavirus Disease 2019 (COVID-19)	• Étude transversale (enquête en ligne menée du 25 au 28 février 2020) • 973 résidents de la Corée du Sud âgés de 18 ans et plus • Interventions de santé publique – se laver les mains, porter un masque facial, respecter la distanciation sociale	• Les participants ont déclaré qu'ils se lavaient toujours les mains (67,8 %), qu'ils portaient toujours un masque facial lorsqu'ils étaient à l'extérieur (63,2 %), qu'ils reportaient ou annulaient des événements sociaux (50 %), qu'ils évitaient les endroits bondés (41,5 %) et qu'ils réduisaient leur utilisation des transports en commun (38,7 %) • La pratique de comportements de précaution est fortement associée au risque perçu et à l'efficacité de réponse du comportement • Des variables sociodémographiques précises pour chaque comportement sont fournies dans l'étude (p. ex. le sexe, le niveau d'éducation, la gravité perçue et l'efficacité de réponse étaient des prédicteurs individuels positifs et significatifs du port d'un masque facial)
(Jackson, Brown, Shahab, Steptoe et Fancourt, 2020)	COVID-19, smoking, and inequalities: a cross-sectional survey of adults in the UK	• Étude transversale (enquête en ligne menée du 21 mars au 20 avril) • 53 211 résidents du Royaume-Uni âgés de 18 ans et plus	• L'adhésion aux interventions de santé publique était généralement élevée (96,3 %, IC à 95 %) : 96,1 à 96,4 %) • Le taux d'adhésion était plus faible chez les fumeurs actuels que chez les jeunes n'ayant jamais fumé (RC 0,70, IC à 95 %) :

Préimpression		• Interventions de santé publique – respecter les recommandations des autorités pour prévenir la propagation de la COVID-19	0,62 à 0,78) indépendamment du niveau de scolarité, mais l'association était plus forte parmi les personnes ayant obtenu des diplômes après 16 ans
(Clements, 2020)	Knowledge and behaviors toward COVID-19 among U.S. residents during the early days of the pandemic: online questionnaire	• Étude transversale (enquête en ligne réalisée le 17 mars 2020) • 1 070 résidents des États-Unis âgés de 18 ans et plus • Interventions de santé publique – porter un masque, éviter les grands rassemblements	• Les participants qui ont déclaré être allés à des rassemblements de plus de 50 personnes ou avoir porté des masques à l'extérieur de la maison étaient moins bien informés sur la COVID-19 et plus jeunes que les participants qui n'ont pas déclaré ces activités • Les participants ayant un diplôme universitaire ou professionnel étaient 67 % plus susceptibles d'assister à de grands rassemblements et de 347 à 641 % plus susceptibles de porter un masque en dehors de la maison, par rapport à ceux ayant fait des études secondaires • Les démocrates étaient 30 % moins susceptibles d'assister à de grands rassemblements et 44 % moins susceptibles de porter un masque à l'extérieur du foyer par rapport aux républicains • Les participants noirs étaient 148 % plus susceptibles de porter un masque à l'extérieur du domicile que les participants blancs
(Seale et coll., 2020)	COVID-19 is rapidly changing: examining public perceptions and behaviors in response to this evolving pandemic	• Étude transversale (enquête en ligne réalisée du 18 au 24 mars 2020) • 1 420 résidents australiens de 18 ans et plus	• 84,9 % des personnes interrogées ont déclaré avoir adopté au moins 1 des 3 comportements liés à l'hygiène et 93,4 % ont adopté au moins 1 des 6 comportements liés à l'évitement

		• Interventions de santé publique – 6 stratégies de distanciation sociale, isolement volontaire, hygiène	• L'adoption de comportements d'évitement était associée à la confiance dans le gouvernement (RCC : 5,5; 95 % IC : 3 à 9,0), une meilleure perception de l'efficacité des comportements (RCC : 4,3; 95 % IC : 2,8 à 6,9), et des niveaux plus élevés de capacité perçue à adopter des stratégies de distanciation sociale (RCC : 1,8; 95 % IC 1,1 à 3,0)
(Brouard, Vasilopoulos et Becher, 2020)	Sociodemographic and psychological correlates of compliance with the COVID-19 public health measures in France	• Étude transversale (enquête en ligne réalisée les 16 et 17 mars 2020) • 1 010 résidents de France âgés de 18 ans et plus • Interventions de santé publique – stratégies de distanciation sociale, hygiène des mains, étiquette respiratoire, réduction des déplacements, évitement des lieux bondés	• Les résultats suggèrent que l'âge est positivement associé au respect des mesures de protection • Les femmes sont plus susceptibles d'avoir changé de comportement que les hommes • L'extrémité idéologique est associée à une moindre adhésion aux recommandations de santé publique
(Doğan et Bayraktar, 2020)	COVID-19 with a public health perspective: measures taken in Turkey and public compliance with the measures	• Étude transversale (enquête menée du 23 au 27 mars 2020) • 178 résidents de la Turquie âgés de 18 ans et plus • Interventions de santé publique – stratégies de distanciation sociale, hygiène des mains	• 97,2 % se sont lavé les mains avec du savon et 91,6 % ont évité le contact avec les gens
(Y. Li, Yao et Luo, 2020) *Préimpression*	Perceived stress and its impact on health behavior of Chinese residents during the epidemic of COVID-19: an internet survey	• Étude transversale (enquête en ligne menée du 14 au 22 février 2020) • 2 449 résidents de Chine âgés de 18 ans et plus • Interventions de santé publique – hygiène des mains, port d'un masque	• À mesure que le stress perçu augmentait, la fréquence des comportements de santé comme le lavage des mains et le port d'un masque diminuait

(Perrotta et coll., 2020) Préimpression	Behaviors and attitudes in response to the COVID-19 pandemic: Insights from a cross-national Facebook survey	• Étude transversale (enquête en ligne menée du 13 mars au 19 avril 2020) • 71 612 résidents de 18 ans et plus en Belgique, en France, en Allemagne, en Italie, aux Pays-Bas, en Espagne, au Royaume-Uni et aux États-Unis • Interventions de santé publique – distanciation sociale, hygiène des mains, port d'un masque facial, réduction des déplacements	• Dans l'ensemble, les femmes sont plus susceptibles que les hommes d'adopter des comportements préventifs • Le port d'un masque facial varie de 7 % aux Pays-Bas à 60 % en Italie • L'adoption d'un lavage des mains plus fréquent va de 87 % en Allemagne à 94 % en Espagne • En dehors des Pays-Bas et du Royaume-Uni, les femmes et les personnes de plus de 45 ans affichent les taux d'adoption du masque facial les plus élevés
(Cutler, Stantcheva, Alsan et Yang, 2020) Préimpression	Disparities in COVID-19 reported incidence, knowledge, and behavior	• Étude transversale (enquête en ligne menée du 29 mars au 13 avril 2020) • 5 198 résidents des États-Unis âgés de 18 ans et plus • Interventions de santé publique – adopter une bonne hygiène des mains et rester à la maison	• Les hommes se lavent les mains 3,8 fois moins souvent dans une période de 24 heures que les femmes ($p < 0,001$) • Les répondants afro-américains et hispaniques se lavent les mains plus fréquemment que les répondants blancs au cours d'une période de 24 heures ($p=0,020$) • Les hommes sont plus susceptibles de quitter la maison fréquemment que les femmes (0,74 fois, $p < 0,001$), tout comme les Afro-Américains par rapport aux répondants blancs (0,93 fois, $p < 0,001$) • Les Américains plus âgés (65 ans et plus) sont moins susceptibles de quitter fréquemment leur domicile (-0,36 fois, $p =0,018$)
(Barber et Kim, 2020)	COVID-19 worries and behavior changes in older and younger men and women	• Étude transversale (enquête en ligne réalisée du 23 au 31 mars 2020)	• Plus de 80 % des participants ont déclaré se laver les mains plus fréquemment, faire plus attention à la propreté, ne plus serrer la main et éviter les lieux publics. Plus de

		• 146 jeunes adultes (de 18 à 35 ans) et 156 adultes plus âgés (de 65 à 81 ans) aux États-Unis • Interventions en matière de santé publique – rester à la maison, adopter une bonne hygiène des mains, porter le masque, adopter des comportements de distanciation sociale, s'isoler volontairement	60 % des participants ont également déclaré respecter la distanciation sociale • Par rapport aux autres participants, les hommes plus âgés sont ceux qui ont adopté le moins de changements de comportement • Les femmes âgées sont les plus nombreuses à déclarer respecter la distanciation sociale et éviter les lieux publics • Pour tous les participants, l'inquiétude relative à la COVID-19 était liée au nombre total de changements de comportement effectués, indépendamment de l'âge ou du sexe
(Ha, Schensul, Lewis et Brown, 2020) *Préimpression*	Early assessment of knowledge, attitudes, anxiety and behavioral adaptations of Connecticut residents to COVID-19	• Étude transversale (enquête en ligne réalisée du 23 au 29 mars 2020) • 464 résidents des États-Unis âgés de 21 ans et plus • Interventions en matière de santé publique – rester à la maison, adopter une bonne hygiène des mains, porter le masque, adopter des comportements de distanciation sociale, respecter l'étiquette respiratoire, réduire les déplacements	• Le taux de conformité variait de 21,5 % des participants portant des gants de protection et de de 9,2 % portant un masque lorsqu'ils sortaient à l'extérieur à 96,5 % évitant les transports publics et 100 % se lavant fréquemment les mains, évitant le contact avec les gens et évitant les événements et réunions avec un grand nombre de personnes
(Thang et coll., 2020) *Préimpression*	Preventive behavior of Vietnamese people in response to the COVID-19 pandemic	• Étude transversale (enquête en ligne menée du 31 mars au 6 avril 2020) • 2 175 résidents du Vietnam âgés de 18 ans et plus • Interventions de santé publique – mesures préventives personnelles (p. ex. masques faciaux, éloignement social) et communautaires (p. ex. éviter les lieux bondés)	• En utilisant un score de 9 et 11 points, le niveau moyen d'adhésion personnelle aux mesures préventives était de 7,23 ± 1,63 (étendue : 1 à 9) et les mesures préventives communautaires étaient de 9,57 ± 1,12 (étendue : 0 à 11), respectivement

			• Le taux de conformité le plus faible (45,1 %) a été constaté pour « la mesure de la température corporelle au moins deux fois par semaine » et le plus élevé pour le port d'un masque facial lors de sorties à l'extérieur (99,5 %) • Les inquiétudes concernant la santé, la perception de l'adaptation de la communauté au confinement, le fait de vivre dans de grandes municipalités, les sources officielles d'information sur la COVID-19 et le fait d'avoir un rôle professionnel dans le secteur de la santé (travailleur ou étudiant) ont été associés à des scores d'adhésion plus élevés
(Yousef Yang, peng, Yang et Rockett, 2020) *Préimpression*	Changing trends of excess self-protective behavior, and association with belief in prevention myths during the COVID-19 epidemic in China: Une étude de panel	• Étude longitudinale prospective (enquête en ligne) • 116 résidents de la Chine âgés de 20 ans et plus à 5 moments dans le temps (5/12/19/26 février et 4 mars 2020) • Interventions de santé publique – comportements préventifs excessifs, par exemple désinfection des vêtements, lavage excessif des mains, accumulation de masques, etc.	• La perception d'un risque élevé de contracter la COVID-19 était positivement associée à chaque type de comportement préventif excessif sélectionné, et la perception de la gravité de la maladie était positivement associée à la désinfection des vêtements et à l'accumulation de produits • La croyance dans les mythes sur la prévention des maladies (faits sur la prévention des maladies qui ne sont pas vrais) a été positivement associée à la désinfection des vêtements ainsi qu'au lavage et à la désinfection des mains • La désinfection des vêtements était moins répandue chez les femmes que chez les hommes (CR : 0,34), et parmi les professionnels que chez les personnes

			appartenant à d'autres groupes professionnels (CR : 0,35) • Le lavage des mains était plus fréquent chez les femmes que chez les hommes (CR : 3,48) et moins fréquents chez les personnes mariées que chez les personnes jamais mariées (CR : 0,43)
(S. Li, Feng, Liao et Pan, 2020)	Internet use, risk awareness, and demographic characteristics associated with engagement in Preventive Behaviors and Testing: cross-sectional survey on COVID-19 in the United States	• Étude transversale (enquête en ligne réalisée du 10 au 14 avril 2020) • 979 résidents des États-Unis âgés de 18 ans et plus • Interventions de santé publique – porter un masque facial, se laver les mains, respecter l'étiquette respiratoire, respecter la distanciation sociale, rester à la maison, éviter les transports en commun et nettoyer les surfaces fréquemment touchées	• Les participants qui ont reçu plus d'information en ligne sur la santé liée à la COVID-19 ont déclaré faire plus souvent des efforts pour adopter tous les types de comportements préventifs • Par rapport aux participants qui n'ont pas eu de cas positifs dans leur entourage, ceux dont des membres de la famille immédiate ou des amis et parents proches ont reçu un diagnostic positif sont plus susceptibles de se faire dépister • Dans l'ensemble, les femmes, les personnes âgées, les personnes mariées et les personnes ayant un emploi adoptent plus fréquemment la plupart des types de comportements préventifs que leurs homologues (hommes, jeunes, célibataires, sans emploi) • Des participants plus instruits étaient moins souvent engagés dans de multiples comportements préventifs • Des différences ethniques ont également été observées en ce qui concerne l'adoption de comportements préventifs. Par rapport aux Blancs, les Afro-Américains et les Asiatiques portent plus

			fréquemment un masque en public et restent à la maison. Les Américains ont signalé des efforts plus fréquents que les Blancs pour nettoyer les surfaces fréquemment touchées
(Wu, Huang, Xie et Chen, 2020) *Préimpression*	People behavior changes in China during COVID-19 pandemic	• Étude transversale (enquête en ligne réalisée du 26 au 30 avril 2020) • 1 048 résidents de la Chine • Interventions de santé publique – respecter la distanciation sociale, réduire les déplacements, rester à la maison, porter un masque	• Près de 80 % des participants ont réduit leurs activités hors du domicile (travailler, manger, faire des courses, prendre les transports en commun et voyager) • 92 % portent un masque dans la rue
(Sutin et coll., 2020)	Body mass index, weight discrimination, and psychological, behavioral, and interpersonal responses to the Coronavirus pandemic	• Étude transversale (enquête en ligne réalisée à la mi-mars 2020) • 2 094 résidents des États-Unis ayant un IMC différent • Interventions de santé publique – comportements préventifs (p. ex. l'hygiène des mains)	• Les participants qui ont signalé une discrimination liée au poids étaient plus susceptibles d'adopter des comportements préventifs • L'IMC n'était pas lié aux changements de comportements préventifs
(Iorfa et coll., 2020) *Préimpression*	COVID-19 knowledge, risk perceptions and precautionary behavior among Nigerians: A moderated mediation approach	• Étude transversale (enquête en ligne menée du 28 mars au 4 avril 2020) • 1 500 résidents du Nigeria âgés de 18 ans et plus • Interventions de santé publique – adopter une bonne hygiène des mains, éviter les endroits bondés, se faire tester, porter le masque, respecter l'étiquette respiratoire, éviter de toucher les surfaces	• Chez les femmes et les hommes, le fait d'être plus âgés, d'avoir une meilleure connaissance de la COVID-19 et une perception plus élevée du risque était lié à un comportement plus prudent • Les femmes adoptent un comportement plus prudent que les hommes • Le respect des mesures de précaution varie. 19 % des participants ont déclaré porter un masque, 54,4 % ont évité de toucher les surfaces, 56,8 % ont évité les endroits bondés et 66,4 % se sont isolés volontairement

(Liu et coll., 2020)	Psychological status and behavior changes of the public during the COVID-19 epidemic in China	• Étude transversale (enquête en ligne réalisée du 30 janvier au 3 février 2020) • 608 résidents de Chine âgés de 18 ans et plus • Interventions de santé publique – adopter une bonne hygiène des mains, éviter les lieux bondés, porter le masque, respecter la distanciation sociale	• Au moins 70,9 % des personnes interrogées ont pris 3 mesures préventives ou plus pour éviter l'infection • 93,3 % des personnes interrogées évitent d'aller dans les lieux publics, 83,7 % portent un masque et 82,4 % se lavent les mains • L'anxiété ne semble pas être liée au changement de comportement du public et aux mesures préventives • Moins de répondants souffrant de dépression ou d'anomalies psychologiques ont pris des mesures préventives par rapport à ceux qui n'en souffraient pas
(Michela et Carlucci, 2020) *Préimpression*	Demographic and attitudinal factors of adherence to quarantine guidelines during COVID-19: the Italian model	• Étude transversale (enquête en ligne menée du 21 au 26 mars 2020) • 3 672 adultes de 18 ans et plus mis en quarantaine en Italie • Interventions de santé publique – avoir une bonne hygiène des mains, respecter la distanciation sociale, respecter l'étiquette respiratoire, nettoyer les surfaces, porter le masque, éviter les lieux bondés	• Les répondants ont obtenu des scores de moyens à élevés en matière de respect des directives de quarantaine, mesurés par un indice d'intervalle unique, avec une moyenne de 32,59 (médiane = 33; ET = 5 22; étendue : 0 à 44) • Chez les femmes, le fait d'être employées, la perception du risque et l'anxiété liée au risque étaient associés à des niveaux d'observance beaucoup plus élevés ($p < 0,001$) comparativement à leurs homologues • La moyenne de l'observance chez les professionnels de la santé ($p < 0,001$) était significativement plus élevée que celle des chômeurs et des salariés • En ce qui concerne l'âge, la tranche des 18 à 29 ans a obtenu un score

			statistiquement inférieur ($p < 0,001$) par rapport aux autres tranches d'âge. De même, le groupe des 50 à 59 ans a obtenu des scores d'observance statistiquement plus élevés ($p < 0,001$) que le groupe des 30 à 39 ans
(Park et coll., 2020)	Americans' COVID-19 stress, coping, and adherence to CDC guidelines	• Étude transversale (enquête en ligne menée du 7 au 9 avril 2020) • 1 015 résidents des États-Unis âgés de 18 ans et plus • Interventions de santé publique – respect des directives du CDC (distanciation sociale, hygiène des mains)	• Les prédicteurs les plus cohérents du respect des directives du CDC étaient l'âge, le sexe féminin et la sécurité financière (tous avec un effet de faible ampleur) • Dans l'ensemble, le respect des directives du CDC était assez élevé, mais variait selon les interventions : 95,10 % évitent de manger au restaurant et se rendre dans les grands rassemblements, 87,2 % s'engagent dans des pratiques de distanciation sociale et 74,68 % adoptent des pratiques de nettoyage et de désinfection
(Plohl et Musil, 2020)	Modeling compliance with COVID-19 prevention guidelines: the critical role of trust in science	• Étude transversale (enquête en ligne, date de réalisation non communiquée) • 525 participants mondiaux âgés de 18 ans et plus • Interventions de santé publique – hygiène des mains, respect des directives	• La confiance dans la science et la perception du risque lié à la COVID-19 contribuent de manière significative et directe à expliquer le respect des directives de prévention de la COVID-19 ($R2 = 0,265$)
(Smith et coll., 2020) *Préimpression*	Factors associated with adherence to self-isolation and lockdown measures in the UK; a cross-sectional survey	• Étude transversale (enquête en ligne réalisée les 6 et 7 mai 2020) • 2 240 résidents du Royaume-Uni âgés de 18 ans et plus • Interventions de santé publique – isolement volontaire	• Les facteurs associés au non-respect des mesures d'isolement volontaire sont notamment le fait d'être un homme, d'être moins préoccupé par la COVID-19 et de percevoir un risque moindre de contracter la COVID-19

			• 9,7 % des participants ont déclaré qu'eux-mêmes ou un membre de leur foyer avaient eu des symptômes de COVID-19 au cours des 7 derniers jours. Parmi ceux-ci, 75,1 % avaient quitté le domicile au cours des dernières 24 heures (inobservance) • L'observance était également associée au fait d'avoir reçu de l'aide d'une personne extérieure au ménage au cours des 7 derniers jours
(Haupt et coll., 2020) *Préimpression*	Profiles of social distance compliance: psychological and situational predictors of risky behavior during COVID-19	• Étude transversale (enquête en ligne réalisée du 30 avril au 2 mai 2020) • 483 résidents des États-Unis âgés de 18 ans et plus • Interventions de santé publique – respecter les directives de santé publique, éviter les comportements à risque (p. ex. participation à des rassemblements de plus de 5 personnes)	• L'activité à risque était associée à une extraversion plus élevée, à un besoin de fermeture cognitive, à l'activation du comportement et à la perception d'une pénurie de ressources • L'activité à risque était également associée à une moindre empathie et à un accès plus restreint à l'espace de vie, ainsi qu'à un âge plus précoce • Sept différents types de profils de grappes sont créés pour expliquer les associations entre la variance dans l'adoption de comportements à risque et les facteurs psychologiques, sociodémographiques et situationnels des répondants
(Zajenkowski, Jonason, Leniarska et Kozakiewicz, 2020)	Who complies with the restrictions to reduce the spread of COVID-19?: personality and perceptions of the COVID-19 situation	• Étude transversale (enquête menée du 14 au 30 avril 2020) • 263 résidents de Pologne âgés de 18 ans et plus • Interventions de santé publique – respect des lignes directrices en matière de santé publique	• Les répondants ayant obtenu un score faible pour le caractère agréable et élevé pour certains aspects des traits de la triade noire (c.-à-d. le machiavélisme, la psychopathie Facteur 1 et la rivalité narcissique) étaient moins susceptibles de

			respecter les restrictions de santé publique • Les perceptions de la COVID-19 expliquent les différences individuelles dans le respect des mesures de santé publique
(Banda et coll., 2020) *Préimpression*	Knowledge and behaviors related to the COVID-19 pandemic in Malawi	• Étude transversale (enquête téléphonique réalisée du 25 avril au 23 mai 2020) • 630 résidents du Malawi âgés de 18 ans et plus • Interventions de santé publique – utiliser un masque facial, avoir une bonne hygiène des mains, éviter les foules, rester à la maison	• L'utilisation de masques faciaux et de désinfectants pour les mains était plus fréquente parmi les répondants résidant en milieu urbain (22,5 %) que parmi ceux résidant en milieu rural (5,0 %) • Plus de 95 % des personnes interrogées ont déclaré se laver les mains plus fréquemment et environ 50 % ont déclaré éviter les foules. Seuls 1/5 des résidents ruraux et 1/4 des résidents urbains ont déclaré rester à la maison
(Galasso et coll., 2020) *Préimpression*	Gender differences in COVID-19 related attitudes and behavior: evidence from a panel survey in eight OECD countries	• Étude transversale (enquête en ligne réalisée du 16 au 30 mars et du 15 au 20 avril 2020) • 21 649 répondants de 8 pays (Australie, Autriche, France, Allemagne, Italie, Nouvelle-Zélande, Royaume-Uni et États-Unis) • Interventions de santé publique – respecter la distanciation sociale, avoir une bonne hygiène des mains, respecter l'étiquette respiratoire, éviter les endroits bondés, rester à la maison, utiliser des masques et des gants	• Des différences significatives entre les sexes en matière de respect des règles de santé publique ont été observées parmi les participants à l'enquête • Le respect des règles de santé publique était nettement plus important chez les femmes que chez les hommes
(Bonful et coll., 2020) *Préimpression*	Limiting spread of COVID-19 in Ghana: compliance audit of selected transportation	• Étude d'observation comprenant des vérifications de la fréquence du lavage des mains et du respect de la distanciation physique dans les stations de transport en commun (menée du 27 au 29 mars 2020)	• La majorité (moins de 80 %) des sites de vérification ne disposaient pas d'emplacements adéquats pour le lavage des mains, la fréquence de lavage des

	stations in the Greater Accra region of Ghana	• 45 sites au Ghana • Interventions de santé publique – disponibilité des installations d'hygiène, source et propreté de l'eau, nombre d'installations de lavage des mains, fréquence du lavage des mains, surpopulation dans les points de lavage des mains, distanciation sociale, utilisation de masques et information sur la prévention de la COVID-19	mains était faible et le port du masque n'a été observé que chez quelques passagers • Le respect des mesures de prévention de la COVID-19 était insuffisant dans 13 stations, de base dans 16 stations, intermédiaire dans 7 stations, et avancée dans 9 stations
(M. É. Czeisler et coll., 2020)	Public attitudes, behaviors, and beliefs related to COVID-19, stay-at-home orders, nonessential business closures, and public health guidance – United States, New York City, and Los Angeles, May 5-12, 2020	• Étude transversale (enquête en ligne réalisée du 5 au 12 mai 2020) • 3 cohortes (É.-U.=1 676, N.Y.=286, et L.A.=259) toutes âgées de 18 ans et plus • Intervention de santé publique – isolement volontaire, masques faciaux, distanciation sociale	• Sur les 3 cohortes, 77,3 % des adultes ont déclaré s'isoler, 84,6 % à New York et 83,0 % à Los Angeles • 74,1 % des personnes interrogées dans l'ensemble du pays ont déclaré porter toujours ou souvent un masque facial lorsqu'elles sont en public, 89,6 % à New York et 89,8 % à Los Angeles • Le respect des mesures varie considérablement en fonction de la démographie et des caractéristiques des répondants
(Al-Hanawi et coll., 2020)	Knowledge, attitude and practice toward COVID-19 among the public in the Kingdom of Saudi Arabia: a cross-sectional study	• Étude transversale (enquête en ligne réalisée du 20 au 24 mars 2020) • 3 388 résidents de l'Arabie saoudite âgés de 18 ans et plus • Interventions de santé publique – éviter les grands événements sociaux et les lieux bondés, éviter les comportements culturels tels que la poignée de main, respecter la distanciation sociale, se laver les mains après un éternuement, une toux et après s'être mouché	• Le score moyen pour les pratiques de lutte contre la COVID-19 était de 4,34 (ET = 0,87, étendue : 0 à 5), indiquant l'adoption de bonnes pratiques en général • Les groupes d'âge de 30 à 39 ans (β = 0,039; pβ = 0,033; pβ = 0,051; p • Par rapport aux femmes, les hommes ont de moins bonnes pratiques pour éviter la propagation de la COVID-19 (β = −0,064; p

(Marinthe, Brown, Delouvée et Jolley, 2020)	Looking out for myself: exploring the relationship between conspiracy mentality, perceived personal risk, and COVID-19 prevention measures	• Deux études transversales (étude 1 – réalisée en ligne le 9 mars 2020; étude 2 – réalisée en ligne du 17 au 23 mars 2020) • 762 résidents (étude 1) et 229 résidents (étude 2) de France âgés de 18 ans et plus • Interventions de santé publique – L'étude 1 a été menée alors que seuls les rassemblements de plus de 1 000 personnes étaient interdits. Les comportements étudiés comprenaient des comportements de prévention normatifs (embrasser quelqu'un, lui serrer la main) et des comportements de prévention non normatifs (parler aux gens, prendre les transports en commun, aller au restaurant, etc.) L'étude 2 a été menée pendant la première semaine de confinement total et a mesuré le respect de la règle de confinement	• Dans l'étude 1, les comportements de santé préventifs ont été mesurés sur une échelle de 9 points allant de 1 = beaucoup moins qu'avant la crise du coronavirus à 9 = beaucoup plus qu'avant la crise du coronavirus. L'adoption moyenne de comportements de prévention normatifs était de 6,14 (1,49 ET) et de comportements de prévention non normatifs de 5,3 (0,66 ET) • L'étude 1 a démontré que les personnes qui croient à une conspiration sont plus susceptibles d'adopter des comportements de prévention non normatifs, mais pas des comportements de préventions normatifs • Dans l'étude 2, le respect de la règle de confinement a été mesuré sur une échelle de 7 points allant de 1=pas du tout à 7= beaucoup. Le taux moyen de respect des mesures de confinement était de 6,45 (0,82 ET) • L'étude 2 a démontré que les personnes ayant une forte mentalité de conspiration sont moins enclines à adopter des comportements préventifs normatifs plus extrêmes et légaux
(Daoust, 2020)	Elderly people and responses to COVID-19 in 27 countries	• Étude transversale (l'enquête a débuté la première semaine d'avril 2020) • 72 417 répondants dans 27 pays, âgés de 18 ans et plus • Interventions de santé publique – porter un masque facial à l'extérieur, se laver les mains,	• L'âge n'a pas d'effet significatif de l'âge sur le score de conformité aux mesures préventives de lutte contre la COVID-19 • Le niveau de base du respect des mesures préventives est assez élevé (score de 12/16)

		se couvrir le nez et la bouche lorsqu'on éternue ou qu'on tousse, éviter le contact avec les personnes qui présentent des symptômes, éviter de sortir en général, éviter de prendre les transports en commun, respecter la distanciation sociale, éviter les endroits bondés, nettoyer les surfaces fréquemment touchées, éviter de toucher des objets en public	
(Maher, MacCarron et Quayle, 2020)	Mapping public health responses with attitude networks: the emergence of opinion-based groups in the UK's early COVID-19 response phase	• Étude longitudinale (données recueillies les 9, 16 et 23 mars 2020) • 235 participants au Royaume-Uni âgés de 18 ans et plus • Interventions de santé publique – se laver les mains, éviter le contact avec certaines personnes, réduire les poignées de mains, éviter de toucher le visage	• Les participants qui ont déclaré être « sceptiquesà l'égard de la science » ont fait état d'une conformité comportementale significativement plus faible (moyenne = 5,28; ET = 1,46) que les personnes considérées comme « ayant confiance dans la science » (moyenne = 5,70; ET = 1,21)
(de la Vega, Ruíz-Barquín, Boros et Szabo, 2020)	Could attitudes toward COVID-19 in Spain render men more vulnerable than women?	• 2 études transversales (enquêtes en ligne, date de réalisation non communiquée) • L'étude 1 (n = 64) a été menée dans un centre commercial à Madrid, en Espagne, et l'étude 2 (n = 640) a été menée en ligne parmi des participants âgés de 18 ans et plus • Interventions de santé publique – respecter les mesures de sécurité et maintenir une distance d'au moins 1,5 mètre par rapport aux autres dans les lieux publics et porter un masque à tout moment	• Le respect des mesures a été évalué sur une échelle de 11 points • Les femmes ont obtenu un score plus élevé que les hommes en ce qui concerne les mesures de sécurité (8,06 contre 7,46; p < 0,001), le lavage des mains (8,77 contre 8,25; p < 0,001), le maintien d'une distance de 1,5 mètre par rapport aux autres (7,16 contre 6,56; p=0,003) et l'utilisation d'un masque de protection (1,95 contre 1,82; p=0,591) • Le respect des mesures de sécurité était plus faible dans les tranches d'âge plus élevées : 18 à 25=6,73 (1,89 ET), 26 à 50=7,92 (1,64 ET) et 51 à 72=8,08 (1,56)

(Führer et coll., 2020)	COVID-19 : knowledge, risk perception and strategies for handling the pandemic	• Étude transversale (enquête en ligne réalisée en mars 2020) • 1 048 participants de Saxe-Anhalt, Berlin et Schleswig-Holstein, en Allemagne, âgés de 18 ans et plus • Interventions de santé publique – se tenir à distance des autres, limiter les contacts dans les espaces publics, limiter les contacts privés, éviter les déplacements, cesser de prendre le tramway ou éviter les cafés, faire les courses moins souvent, faire des provisions, acheter du désinfectant, acheter des respirateurs	• Les mesures les plus courantes sont le respect des distances minimales par rapport aux autres (95,6 %) et la réduction des contacts personnels (93,4 %). Seule une minorité des personnes interrogées ont déclaré avoir des stocks de nourriture (38,3 %), de désinfectants (15,9 %) ou de masques respiratoires (15,0 %) • Sur 79 % de personnes interrogées qui ont déclaré avoir pris des mesures, 41 % ont agi à la fin mars lorsque des mesures de quarantaine ont été prises dans certaines régions d'Italie, tandis que 13 % n'ont pris aucune précaution avant que les premières infections ne soient découvertes dans leur État. Seuls 3 répondants (0,4 %) ont déclaré avoir déjà pris des mesures en réponse à la propagation étendue en Chine
(Reuben, Danladi, Saleh et Ejembi, 2020)	Knowledge, attitudes and practices towards COVID-19: an epidemiological survey in north-central Nigeria	• Étude transversale (enquête en ligne, date de réalisation non communiquée) • 589 résidents du centre-nord du Nigeria âgés de 18 ans et plus • Interventions de santé publique – pratique de la distanciation sociale/isolement volontaire, amélioration de l'hygiène personnelle et utilisation d'un masque facial	• 92,7 % des répondants ont pratiqué la distanciation sociale/isolement volontaire, 96,4 % ont amélioré leur hygiène personnelle et 82,3 % ont utilisé des masques faciaux
(Parsons Leigh et coll., 2020)	A national cross-sectional survey of public perceptions, knowledge, and behaviors during the COVID-19 pandemic	• Étude transversale (enquête en ligne réalisée du 26 avril au 1er mai 2020) • 1 996 répondants du Canada âgés de 18 ans et plus • Interventions de santé publique – isolement volontaire et distanciation sociale/physique	• 842 répondants ont indiqué qu'ils se sont isolés volontairement (43,4 %, IC 95 %) : 41,2 % à 45,6 %). • Parmi ceux qui ne se sont pas isolés volontairement (n=1 144), la grande majorité (n=1 083, 95,1 %, IC 95 %) : 93,8

			à 96,4 %) ont déclaré qu'ils pratiquaient la distanciation physique toujours (n=783; 68,8 % (IC 95 % 66,0 à 71,5 %) ou souvent (n=300, 26,3 %, IC 95 % 23,7 à 28,9 %)
(Alper, Bayrak et Yilmaz, 2020)	Psychological correlates of COVID-19 conspiracy beliefs and preventive measures: evidence from Turkey	• Étude transversale (enquête en ligne, dates de réalisation non communiquées) • 1 088 résidents de Turquie, âge médian = 31 ans • Interventions de santé publique – quitter la maison, éviter les contacts physiques, éviter de se toucher le visage, se laver/désinfecter les mains après une sortie à l'extérieur, éviter de partager le même environnement avec des personnes âgées, porter un masque, se couvrir la bouche lorsqu'on tousse ou éternue	• Il n'y a pas eu de preuve concluante suggérant une relation significative entre les croyances de conspiration et les mesures préventives liées à la COVID-19 • Les participantes étaient significativement plus susceptibles de prendre des mesures préventives que les participants (p < 0,001)
(de Moura Villela, Edlaine Faria, Mendoza L opez, Sayuri Sato et coll., 2020) *Préimpressi on*	COVID-19 outbreak in Brazil: adherence to national preventive measures and impact on people's lives	• Étude transversale (enquête menée du 3 au 9 avril 2020) • 23 896 résidents du Brésil âgés de 18 ans et plus • Interventions de santé publique – avoir une bonne hygiène des mains, éviter de se toucher le visage, désinfecter le téléphone portable, porter un masque, respecter l'étiquette respiratoire, respecter la distanciation physique/isolement, prendre sa température deux fois par semaine, rester à la maison en cas de symptômes	• 98,7 % des personnes interrogées se lavent régulièrement les mains et 92,6 % déclarent respecter la règle de distanciation physique de 1,5 à 2 m, mais seulement 45,5 % portent un masque facial lorsqu'ils sortent • Le fait d'être âgé, d'être une femme, de vivre seul, d'être travailleur indépendant, de vivre dans la région du Nord-Est, d'avoir au moins un diplôme de premier cycle, d'être un travailleur de la santé et le fait d'avoir des comorbidités étaient tous indépendamment associés à une plus grande adhésion aux mesures nationales de prévention et de restriction
(Xie, Campbell et	Working memory capacity predicts	• Étude transversale (enquête en ligne menée du 13 au 26 mars 2020)	• On a constaté que la capacité de mémoire de travail permettait de prédire de

Zhang, 2020)	individual differences in social-distancing compliance during the COVID-19 pandemic in the United States	• 397 participants recrutés entre le 20 et le 22 mars et 453 participants recrutés entre le 24 et le 26 mars aux États-Unis, âgés de 18 ans et plus • Intervention de santé publique – pas de rassemblement avec des amis, annulation d'événements ou de projets de participation à un événement, pas de visite à l'église ni de participation à d'autres activités communautaires, et pas de poignée de main, d'accolade ou de baiser lors de la salutation	manière significative les différences individuelles en matière de respect de la distanciation sociale, même en tenant compte d'autres covariables liées à l'humeur • Les participants ayant obtenu des scores plus élevés en matière de respect de la distanciation sociale ont également déclaré quitter moins souvent la maison et se laver davantage les mains • La mesure du respect de la distanciation sociale n'a pas été significativement corrélée avec le niveau de scolarité ou de revenu des participants, même si les femmes et les participants plus âgés avaient tendance à montrer un plus grand respect de la distanciation sociale
(Hsu, Lin, Wang et Jhang, 2020)	How to defend covid-19 in Taiwan? Talk about people's disease awareness, attitudes, behaviors and the impact of physical and mental health	• Étude transversale (enquête menée du 1er mars au 10 avril 2020) • 2 132 répondants de Taïwan âgés de 20 ans et plus • Interventions de santé publique – respect adéquat ou actif des mesures de prévention des épidémies, dénomination correcte de tous les processus de prévention, respect de la réglementation relative aux espaces publics, port de masques, consultation d'experts, d'universitaires ou de médias en ligne pour obtenir des conseils, maintien actif de la propreté à domicile, recyclage des déchets médicaux, partage des connaissances en matière de prévention, rappel des	• Le respect actif des mesures de prévention et le port de masques, ainsi que le partage des connaissances en matière de prévention ont obtenu les meilleurs scores de conformité • Les scores de conformité les plus faibles ont été relevés pour le nettoyage sur les plans personnel et communautaire

		comportements individuels inappropriés, nettoyage actif au sein de la communauté	
(Almutairi, Mustafa, Alessa, Almutairi et Almaleh, 2020)	Public trust and compliance with the precautionary measures against COVID-19 employed by authorities in Saudi Arabia	• Étude transversale (enquête en ligne, dates de réalisation non communiquées) • 1 232 résidents de l'Arabie saoudite âgés de 18 ans et plus • Interventions de santé publique – éviter les rassemblements publics, respecter le couvre-feu nocturne, éviter les poignées de main, avoir une bonne hygiène des mains, éviter de se toucher les yeux, le nez et la bouche avec les mains, se couvrir le nez et la bouche lorsqu'on éternue ou qu'on tousse, éviter de partager des objets personnels, porter un masque facial, se faire soigner tôt, maintenir une distance sociale	• 657 (53,3 %) des répondants ont été considérés comme appliquant de mauvaises mesures de précaution • Les mesures de précaution les plus respectées comprenaient : « respecte le couvre-feu nocturne » avec 98,3 %, « évite les rassemblements publics » avec 91,7 %, « maintient une distance sociale pendant l'épidémie de COVID-19 » avec 89,3 % • Les mesures de précaution les moins respectées comprenaient : « utilise un masque facial en public » avec 54 %, suivie de « évite de toucher les yeux, le nez et la bouche avec les mains » avec 37,9 %, et de « couvre le nez et la bouche lorsqu'il éternue ou tousse avec un mouchoir » avec 25,3 %
Population générale (tous âges)			
(Olapegba et Ayandele, 2020)	Survey data of COVID-19 related knowledge, risk perceptions and precautionary behavior among Nigerians	• Étude transversale (enquête en ligne menée du 28 mars au 4 avril 2020) • 1 357 résidents du Nigeria âgés de 15 ans et plus • Interventions de santé publique - avoir une bonne hygiène des mains, porter un masque, éviter les lieux bondés	• La majorité des participants ont adopté des comportements de protection, comme éviter les endroits bondés (79 %), utiliser du désinfectant pour les mains (71,19 %) et éviter de toucher les poignées de porte et les rampes d'escalier dans les espaces publics (75,76 %)
(Shabu, Amen et Mahmood, 2020)	Risk perception and behavioral response to COVID-19 in Iraqi Kurdistan Region	• Étude transversale (enquête en ligne menée du 20 au 26 mars 2020) • 976 enseignants et étudiants âgés de 17 ans et plus	• Le pourcentage de personnes interrogées qui appliquent fréquemment ou toujours des mesures de santé publique est élevé pour la plupart des comportements, à l'exception du port du masque et de

Préimpression		• Interventions de santé publique : éviter d'éternuer ou de tousser, éviter de se toucher le visage, le nez et les yeux, éviter les grands rassemblements et les lieux publics, éviter de se rendre dans les zones touchées, rester chez soi, utiliser des désinfectants à base d'alcool, respecter le couvre-feu et porter un masque ou des gants	gants et du fait d'éviter de se toucher le visage • Il y avait une corrélation positive faible et significative ($p < 0,001$) entre la perception du risque et les comportements de protection
(Arp et coll., 2020) *Préimpression*	Use of face coverings in public during the COVID-19 pandemic: an observational study	• Étude transversale (observations directes effectuées du 16 mai au 1er juin 2020) • 3 271 résidents du Wisconsin aux États-Unis, de tous âges (mineurs, jeunes adultes, adultes, personnes âgées) • Intervention de santé publique – utilisation d'un masque facial dans une épicerie	• Les femmes et les personnes âgées sont plus susceptibles d'utiliser des couvre-visage • Les achats dans les épiceries où les prix sont élevés ont également été associés à l'utilisation de masques • 41 % des personnes faisant partie de l'échantillon d'étude ont utilisé des couvre-visage
(Stanislau Affonso de Araújo, Evaldo et coll., 2020) *Préimpression*	Teach, and teach and teach: does the average citizen use masks correctly during daily activities? Results from an observational study with more than 12,000 participants	• Étude d'observation (observations directes effectuées du 17 au 19 juin 2020) • 12 588 personnes observées dans 5 villes brésiliennes (pas de restriction d'âge) • Interventions de santé publique – respect du port de masques faciaux	• 45,1 % de la population observée portait un masque facial de manière correcte, l'étendue ville par ville étant de 39,1 % à 63,5 % • 15,5 % (12,7 à 18,8 %) n'ont pas du tout utilisé de masques • 12,9 % portaient un masque, mais exposaient leur bouche et leur nez (9,9 à 17,6 %), 12,0 % exposaient leur nez uniquement (7,9 à 16,6 %), 17,8 % touchaient leur masque pendant l'utilisation (0,0 à 4,0 %) et 6,5 % portaient un masque mal ajusté (1,2 à 10,7 %)

ADHÉSION AUX INTERVENTIONS DE SANTÉ PUBLIQUE CHEZ LES JEUNES ADULTES ET LES

ÉTUDIANTS UNIVERSITAIRES/MÉDECINE

La conformité aux interventions de santé publique pour contrôler la propagation de la COVID-19 était élevée dans six études visant précisément les jeunes adultes (16 à 29 ans) et les étudiants universitaires/médecine (tableau 2).

- Les femmes sont plus susceptibles d'adopter des comportements préventifs que les hommes.
- D'autres facteurs sont positivement associés à l'adhésion aux interventions de santé publique, notamment l'accès à l'information sur la COVID-19, la maîtrise de soi et le niveau d'anxiété.
- Les comportements préventifs signalés ont été négativement corrélés à la perception du risque et à la détresse psychologique.
- Parmi les étudiants universitaires, une étude a révélé que les étudiants qui n'étaient pas en médecine respectaient davantage les restrictions sociales, tandis que les étudiants en médecine pratiquaient une meilleure hygiène des mains.

Tableau 2. Six études évaluant l'adhésion aux mesures de santé publique pour lutter contre la COVID-19 chez les jeunes adultes et les étudiants universitaires/médecine

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Jeunes adultes			
(Imtiaz, Hossain et Khan, 2020) *Préimpression*	COVID-19 in Bangladesh: measuring differences in individual precautionary behaviors among young adults	• Étude transversale (détails de l'enquête non communiqués) • 350 jeunes adultes du Bangladesh âgés de 16 à 29 ans • Interventions de santé publique – comportement de précaution	• Le score moyen de précaution était le plus élevé (26,2) pour les personnes ayant terminé leurs études supérieures par rapport à celles ayant fait des études secondaires (24,7) • Les personnes en détresse psychologique avaient des scores de précaution moyens (23,6) plus faibles que ceux des personnes qui n'étaient pas en détresse (moyenne=25,1), p=0,019 • Les femmes (25,3) ont obtenu un score de précaution plus élevé que les hommes (23,8), p=0,007

			• Il a été constaté que le score de maîtrise de soi était significativement associé au score de précaution
Étudiants universitaires/médecine			
(Taghrir, Borazjani et Shiraly, 2020)	COVID-19 and Iranian medical students; a survey on their related-knowledge, preventive behaviors and risk perception	• Étude transversale (enquête en ligne menée du 26 au 28 février 2020) • 240 étudiants en médecine d'Iran, âge moyen 23,67 ans • Interventions de santé publique – réduire l'utilisation des espaces publics, respecter l'étiquette respiratoire, se laver les mains, désinfecter les surfaces, discuter avec d'autres des comportements préventifs	• 94,2 % des participants ont obtenu de bons résultats en matière de comportements préventifs • Les comportements préventifs et la perception du risque signalés par les personnes interrogées ont une corrélation négative significative. (rs = -0,128; P < 0,05) • La perception du risque diminue à mesure que les comportements préventifs augmentent
(Yang, Bin et He, 2020)	Opinions from the epicenter: an online survey of university students in Wuhan amidst the COVID-19 outbreak	• Étude transversale (enquête en ligne réalisée les 28 et 30 janvier 2020) • 8 252 étudiants universitaires de Wuhan, Chine • Interventions de santé publique – hygiène des mains, port d'un masque facial, réduction des activités de plein air	• Il y avait une conformité comportementale positive chez les répondants. Près de 90 % des participants portaient un masque chirurgical lors de leurs sorties, plus des deux tiers avaient renforcé la pratique de l'hygiène des mains et presque tous avaient réduit les activités de plein air • Les personnes plus anxieuses et effrayées avaient tendance à adopter des pratiques plus strictes en matière de port de masque et d'hygiène des mains, en réaction naturelle aux risques perçus
(Saddik et coll., 2020) *Préimpression*	Increased levels of anxiety among medical and non-medical university students during the COVID-19	• Étude transversale (enquête en ligne réalisée du 11 au 21 mars 2020) • 1 385 étudiants en médecine (dentaire et médecine) et étudiants d'autres programmes des Émirats arabes unis	• Le taux de conformité était globalement élevé et variait entre 58 % pour le port de gants et de masques, 77 % pour la diminution des visites dans les lieux très fréquentés et 85 % pour l'amélioration de l'hygiène des mains

	pandemic in the United Arab Emirates	• Interventions de santé publique – comportement hygiénique, restrictions sociales	• Les étudiants d'autres programmes que la médecine respectaient mieux les restrictions sociales, tandis que les étudiants en médecine avaient une meilleure hygiène des mains
(Lincango-Naranjo et coll., 2020) *Préimpression*	Paradigms about the COVID-19 pandemic: knowledge, attitudes and practices from medical students	• Étude transversale (enquête en ligne réalisée du 6 au 20 avril 2020) • 309 étudiants en médecine d'Équateur • Interventions de santé publique – hygiène des mains	• La majorité des participants (99 %) ont déclaré se laver fréquemment les mains
(Hamza, Badary et Elmazar, 2020)	Cross-sectional study on awareness and knowledge of COVID-19 among senior pharmacy students	• Étude transversale (enquête en ligne réalisée du 28 au 30 avril 2020) • 238 étudiants en pharmacie en Égypte • Interventions de santé publique – éviter les lieux publics, porter le masque en public, maintenir la distance sociale	• Les femmes sont plus susceptibles que les hommes d'éviter de sortir dans des endroits bondés et de maintenir une distance sociale • Des associations significatives ont été notées entre le port du masque en public et l'accès à l'information sur la COVID-19 à partir de la télévision, ainsi que le maintien d'une distance sociale de 2 mètres et l'utilisation des conseils des médecins sur la COVID-19

ADHÉSION AUX INTERVENTIONS DE SANTÉ PUBLIQUE CHEZ LES ENFANTS ET LES ADOLESCENTS

Le respect des comportements de protection chez les enfants et les adolescents a été évalué dans quatre études (tableau 3). Parmi ces études, trois études réalisées en Chine (n=2) et en Norvège (N=1) ont montré des taux de conformité modérés à élevés et une étude réalisée en Inde a montré des taux de conformité faibles.

- Le sexe féminin a été associé de manière significative à une meilleure hygiène des mains et au respect général des interventions de santé publique.

- Parmi les autres facteurs en corrélation avec une meilleure observance, citons la profession du père, le niveau d'éducation de la mère, le lieu de résidence et les personnes issues de l'immigration.
- Une étude a montré que le respect des comportements préventifs des élèves de l'école primaire était généralement supérieur à celui des élèves du secondaire (Wen et coll., 2020).

Tableau 3. Quatre études évaluant l'adhésion aux mesures de santé publique pour lutter contre la COVID-19 et les facteurs associés chez les enfants et les adolescents

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Enfants et adolescents			
(Chen et coll., 2020)	Hand hygiene, mask-wearing behaviors and its associated factors during the COVID-19 epidemic: a cross-sectional study among primary school students in Wuhan, China	• Étude transversale (enquête en ligne menée du 16 au 25 février 2020) • 8 569 élèves de l'école primaire de Wuhan, en Chine, âgés de 6 à 13 ans • Interventions de santé publique – port de masques faciaux, hygiène des mains	• 42,05 % et 51,60 % des élèves de l'école primaire ont montré de bons comportements en matière de lavage des mains et de port de masque, respectivement • Le sexe (féminin), l'année d'études (3e à 6e), les antécédents de sortie, la profession du père et le temps passé à remplir l'enquête ont été associés de manière significative à l'hygiène des mains • L'année d'études (5e à 6e), le niveau d'éducation de la mère et le lieu de résidence étaient associés au port du masque
(Saurabh et Ranjan, 2020)	Compliance and psychological impact of quarantine in children and adolescents due to COVID-19 pandemic	• Étude transversale (entretiens avec les parents et les enfants, dates de réalisation non communiquées) • 121 enfants et adolescents de 9 à 18 ans en Inde • Interventions de santé publique – mesures préventives au niveau des ménages (par exemple, utilisation de serviettes distinctes) et de la communauté (distanciation sociale)	• Le respect du comportement de quarantaine varie de 25,61 % (ont dormi seuls dans une chambre séparée) à 83,47 % (n'ont pas fait de courses) • Le respect global de tous les comportements était de 7,43 %. Le respect de toutes les mesures de protection des ménages et de la communauté était de 10,71 % et 17,35 %, respectivement

			• L'activité la plus difficile à respecter était de ne pas sortir de la maison pour socialiser (65,26 %)
(Wen et coll., 2020) *Préimpression*	Knowledge, attitudes, and practices towards COVID-19 among primary and middle school students during the COVID-19 outbreak period in Beijing: an online cross-sectional survey	• Étude transversale (enquête en ligne menée du 2 au 13 mars 2020) • 7 377 étudiants de 9 à 18 ans à Pékin • Interventions de santé publique – Réduire les sorties inutiles, porter un masque à l'extérieur, se laver fréquemment les mains, avoir une alimentation saine, éviter les transports en commun, respirer de manière hygiénique, nettoyer et désinfecter régulièrement, ne pas se toucher le visage avant de désinfecter, agir lorsque des symptômes apparaissent, avoir une ventilation rationnelle et efficace, manger séparément	• Les taux de conformité pour les étudiants étaient les suivants : Réduire les sorties inutiles (97,1 %), porter un masque à l'extérieur (92,5 %), se laver fréquemment les mains (91,3 %), avoir une alimentation saine (86,5 %), éviter les transports en commun (85,8 %), respirer de manière hygiénique (85,4 %), nettoyer et désinfecter régulièrement (78,6 %), ne pas se toucher le visage avant de désinfecter (78,3 %), agir lorsque les symptômes se manifestent (57,8 %), avoir une ventilation rationnelle et efficace (39,2 %), manger séparément (38,6 %) • Le respect de comportements préventifs efficaces par les élèves de l'école primaire était généralement supérieur à celui des élèves du secondaire
(Soest et coll., 2020)	Compliance with infection control rules among adolescents in Oslo during the COVID-19 pandemic	• Étude transversale (enquête menée du 23 avril au 8 mai 2020) • 12 686 « jeunes » à Oslo, Norvège • Interventions de santé publique – se laver les mains, se serrer la main, éviter les grands groupes, respecter la distanciation sociale	• La majorité d'entre eux ont déclaré suivre les règles concernant le lavage des mains (n = 9 915, 84 %), ne pas se serrer la main/se serrer dans les bras (n = 8 730, 74 %) et éviter les grands groupes (n = 8 565, 73 %). Moins nombreux sont ceux qui ont déclaré avoir gardé une bonne distance (1 à 2 mètres) par rapport aux autres (n = 5 859, 50 %) • Le soutien le plus important à l'égard des règles a été constaté chez les filles, les jeunes issus de l'immigration et ceux qui vivent dans la périphérie est d'Oslo

ADHÉSION AUX INTERVENTIONS DE SANTÉ PUBLIQUE CHEZ LES TRAVAILLEURS DE LA SANTÉ

Sept études ont évalué l'adhésion aux comportements de prévention et de contrôle des infections contre la COVID-19 chez les travailleurs de la santé (tableau 4). L'adhésion globale varie selon les études, les établissements de santé et les comportements spécifiques.

- La proportion de travailleurs de la santé qui ont pris des mesures d'hygiène des mains allait de 79,44 % dans un groupe de travailleurs de la santé de Chine à 98,2 % dans un groupe de médecins de première ligne de Jordanie.
- Deux études démontrent que le fait d'être infirmière (par opposition à médecin, personnel infirmier et médical, agents médicaux et cliniques) était significativement associé à la conformité autodéclarée aux mesures de contrôle des infections. Parmi ces études sur les travailleurs de la santé, les résultats sont contradictoires en ce qui concerne le sexe en tant que prédicteur de la conformité déclarée.

Tableau 4. Sept études évaluant l'adhésion aux mesures de santé publique pour lutter contre la COVID-19 et les facteurs associés chez les travailleurs de la santé

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Travailleurs de la santé			
(Suleiman et coll., 2020)	Preparedness of frontline doctors in Jordan healthcare facilities to COVID-19 outbreak	• Étude transversale (enquête en ligne réalisée du 23 au 27 mars 2020) • 308 médecins de première ligne en Jordanie, âge moyen 30,3 ± 5,8 • Interventions de santé publique – respect des directives relatives aux EPI (équipements de protection individuelle)	• Les scores d'adhésion de ces médecins étaient de 8,4 ± 1,5 sur 10 • Par exemple, 88 % des personnes interrogées lavent leur blouse, 98,1 % se lavent les mains avant de voir un patient, 93,8 % évitent les « tape m'en cinq » et les poignées de main, et 91,6 % laissent leurs chaussures au travail ou en dehors de la maison
(Tamari et coll., 2020)	Nationwide survey of COVID-19 prevention measures in Japanese radiotherapy departments via online	• Étude transversale (enquête en ligne réalisée du 16 au 23 avril 2020) • 184 radio-oncologues au Japon • Interventions de santé publique – hygiène des mains, utilisation de masques/EPI, distanciation sociale	• La majorité des personnes interrogées (81,0 %) ont indiqué avoir pris certaines mesures de lutte contre l'infection • Il y a eu des différences de conformité entre les services

	questionnaire for radiation oncologists		• 8,1 % des personnes interrogées ont déclaré utiliser des EPI dans leur pratique de la radiothérapie et 63 % ont pris une distance sociale appropriée avec les patients • 96,2 % des participants qui ont eu un contact direct avec les patients portaient un masque, et 85,3 % qui n'ont pas eu de contact direct avec les patients portaient un masque
(Chatterjee et coll., 2020)	Attitude, practice, behavior, and mental health impact of COVID-19 on doctors	• Étude transversale (enquête en ligne menée du 28 mars au 6 avril 2020) • 152 médecins au Bengale occidental, en Inde • Interventions de santé publique – hygiène des mains, utilisation de masques/EPI	• La majorité des médecins utilisent un masque chirurgical (58,6 %), mais seuls quelques-uns utilisent des masques N95 (19,7 %) • 95,4 % déclarent qu'ils pratiquent une hygiène des mains régulière, mais déclarent également qu'ils se lavent principalement les mains en fonction des besoins (42,8 %) • Seuls 24,3 % ont accès à l'EPI et 11,2 % l'utilisent réellement
(Lai et coll., 2020)	Will healthcare workers improve infection prevention and control behaviors as COVID-19 risk emerges and increases, in China?	• Étude transversale (enquête menée du 15 au 17 janvier 2020) • 1 581 travailleurs de la santé en Chine (n=1581) • Interventions de santé publique – hygiène des mains, EPI, nettoyage des terminaux	• Dans l'ensemble, un diplôme d'études supérieures, des années de travail plus longues, le sexe féminin (par rapport au sexe masculin) ont eu un effet négatif significatif sur le respect des mesures de lutte contre les infections autodéclarées • Le fait d'être infirmière (par opposition aux médecins) a eu des effets positifs significatifs sur l'autodéclaration de la conformité aux mesures de lutte contre les infections • Le fait de travailler dans des services à haut risque était associé à une meilleure

			conformité, tandis que l'exposition à des patients confirmés ou suspectés réduisait la conformité au contrôle des infections
(Zhou, Lai, Zhang et Tan, 2020)	Compliance measurement and observed influencing factors of hand hygiene based on COVID-19 guidelines in China	• Étude transversale (observations directes effectuées du 5 au 7 mars 2020) • Travailleurs de l'hôpital de Tongji et de 17 groupes médicaux d'autres provinces de Chine • Interventions de santé publique – hygiène des mains à 17 moments (par exemple, avant de toucher un patient, avant une procédure aseptique, après être allé aux toilettes, etc.)	• La conformité globale pour 17 moments liés à l'hygiène des mains était de 79,44 % • La conformité globale la plus élevée était associée au moment précédant le port de gants (91,67 %), et la plus faible au moment après avoir touché l'environnement du patient (65,56 %) • La conformité globale était de 85 % dans le service des soins intensifs, 79,18 % dans le service des soins non intensifs, 76,07 % dans la zone contaminée, 84,38 % dans la zone semi-contaminée et 84,21 % dans la zone hygiénique
(Martín et coll., 2020)	Prevalence of SARS-CoV-2 infection in general practitioners and nurses in primary care and nursing homes in the healthcare area of León and associated factors	• Étude transversale (étude menée pendant les deux premières semaines d'avril 2020) • 676 infirmières et médecins de centres de soins primaires et de maisons de retraite dans la zone de soins de santé de León (Espagne) • Interventions de santé publique – respect général des mesures préventives	• Le degré de conformité aux mesures préventives a été enregistré sur une échelle de Likert de 0 à 10, 0 étant le degré d'exposition ou de conformité le plus faible et 10 le plus élevé • 31 % ont déclaré un taux élevé de respect des mesures préventives (10 points dans l'enquête)
(Contejean et coll., 2020)	Comparing dynamics and determinants of SARS-CoV-2 transmissions among health care workers of adult and pediatric settings in central Paris	• Étude prospective réalisée du 24 février au 10 avril 2020 • 336 travailleurs de la santé à Paris, France • Interventions de santé publique – porter un EPI approprié, porter un masque correctement, éviter les transports en commun, porter un masque à l'extérieur du domicile	• La majorité des travailleurs ont rappelé un contact sans EPI avec un cas index. Les EPI ont été plus souvent utilisés dans des environnements d'adultes (56/227) que dans des environnements d'enfants (16/109) • La plupart des salariés ont déclaré porter un masque toujours/la plupart du temps à

			l'hôpital, mais 65/336 (19 %) ont admis enlever leur masque pendant les pauses en présence d'autres collègues (204/336, 61 % pendant les pauses déjeuner). Plus de la moitié (201/336, 60 %) ont déclaré utiliser les transports en commun, dont le 112/201 (56 %) plus d'une heure par jour, mais moins de 25 % (82/334) portaient un masque en dehors de chez eux

L'ADHÉSION AUX INTERVENTIONS DE SANTÉ PUBLIQUE DANS D'AUTRES POPULATIONS

Cinq études sur l'adhésion aux mesures de santé publique visant à contrôler la COVID-19 ont été recensées dans quatre autres populations, tableau 5. Ces autres populations comprennent les femmes enceintes, les employés, les visiteurs des hôpitaux et les migrants.

Tableau 5 Cinq études sur l'adhésion aux mesures de santé publique pour lutter contre la COVID-19 dans d'autres populations

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Femmes enceintes			
(Yassa et coll., 2020)	Near-term pregnant women's attitude toward, concern about and knowledge of the COVID-19 pandemic	• Étude transversale (détails de l'enquête non communiqués) • 172 femmes enceintes en Turquie • Interventions de santé publique – autosurveillance	• La majorité des femmes (87,2 %) ont respecté les règles d'autodiscipline
Visiteurs dans les hôpitaux			
(Gunasekaran et coll., 2020) *Préimpression*	Prevalence and acceptance of glove wearing practice among general population when visiting high risk are during local COVID-19 outbreak	• Étude transversale (dates non communiquées) • 40 personnes fréquentant les hôpitaux et 30 fréquentant les marchés traditionnels de produits frais en Malaisie • Interventions de santé publique – port de gants et de masques	• On a observé un plus grand nombre de personnes fréquentant le marché traditionnel de produits frais (30,0 %) qui n'avaient pas de bonnes pratiques pour le port de gants par rapport aux personnes visitant l'hôpital (8,9 %), $\chi 2$ (1) = 5,60, p=0,018

			• Les hommes utilisent davantage de gants de qualité médicale (78,8 %) que de gants de qualité non médicale (21,2 %), tandis que les femmes utilisent autant de gants de qualité médicale (50,0 %) que de gants de qualité non médicale (50,0 %), $\chi 2$ (1) = 6 546, p=0,011 • L'utilisation de gants était plus élevée chez les non-Malais (53,3 %) que chez les Malais (46,7 %) à l'hôpital et l'utilisation de gants était plus élevée chez les Malais que chez les non-Malais (16,7 %) dans le marché traditionnel de produits frais, $\chi 2$ (1) = 10,20, p=0,001
(Sahiledengle et coll., 2020) *Préimpression*	Hand washing compliance and COVID-19: a non-participatory observational study among hospital visitors	• Étude transversale (observations directes effectuées du 27 avril au 3 mai 2020) • 1 282 personnes entrant dans les hôpitaux en Éthiopie • Interventions de santé publique – hygiène des mains	• Seulement 0,9 % (95 % IC : 0,4 à 1,4) des participants ont pleinement respecté les techniques de lavage des mains recommandées • La plupart des participants (47,2 %, 95 % IC : 44,4 à 49,9) présentaient une conformité minimale et 20,1 % (95 % IC : 17,8 à 22,3) n'étaient pas conformes • Il n'y a pas de différence dans les conformités entre les sexes (0,9 % contre 0,7 %, P = 0,745)
Migrants			
(Mannan et Farhana, 2020) *Préimpression*	The COVID-19 pandemic: challenges and reality of quarantine, isolation and social distancing	• Étude transversale (enquête menée du 1er février au 31 mars 2020) • 3 281 migrants de retour de 8 divisions administratives du Bangladesh âgés de 18 ans et plus	• Seulement 2,74 % ont été officiellement en quarantaine pendant 14 jours. Seulement 1,98 % ont respecté les 14 jours d'isolement personnel prévus par les règles de soins de santé et seulement 3,38 % ont

	for the returnee migrants in Bangladesh	• Interventions de santé publique – quarantaine, isolement et distanciation sociale pendant 14 jours	respecté les 14 jours de distanciation sociale • En plus des 14 jours prévus dans la règle d'avertissement sanitaire, il y a aussi une réticence à respecter la règle de la distanciation sociale pendant l'épidémie (seulement 5,05 % s'y sont conformés)
Employés			
(Wang, Yi Wong et Ho, 2020) *Préimpression*	Availability of workplace policy for prevention of coronavirus disease 2019 and its relationship with personal protective behaviors: a survey of employees	• Étude transversale • 1 048 employés de Hong Kong • Interventions de santé publique – hygiène des mains, port d'un masque facial, distanciation sociale, hygiène domestique	• La conformité varie selon les mesures de protection (par exemple, 77,1 % ont déclaré se laver toujours les mains avant les repas et 51,2 % ont déclaré qu'ils évitaient toujours de quitter leur domicile) • Les comportements en matière de protection personnelle diffèrent selon les sous-groupes sociodémographiques en termes d'âge, de sexe, de conditions de vie, de situation matrimoniale, de niveau d'éducation et de statut professionnel • Les employés disposant de directives et de mesures sur le lieu de travail ont eu plus souvent des comportements de protection personnelle, et cette association était plus importante chez les directeurs/administrateurs et les travailleurs manuels

RECHERCHE DE SYNTHÈSE SUR L'ADHÉSION AUX INTERVENTIONS DE SANTÉ PUBLIQUE

Trois examens sur le respect des mesures de santé publique visant à contrôler les maladies infectieuses ont été recensés, au tableau 6. Ces examens ne contenaient pas de preuves précises sur la COVID-19.

Tableau 6 Trois études sur le respect des mesures de santé publique pour les maladies infectieuses

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Revues			
(Webster et coll., 2020)	How to improve adherence with quarantine: rapid review of the evidence	• Examen rapide des données probantes • Les recherches ont porté sur des données probantes recueillies jusqu'au 27 janvier 2020 • AMSTAR : qualité modérée • 14 articles sont inclus dans l'examen • Aucun article propre au SRAS-CoV-2	• Le respect de la quarantaine varie de 0 à 92,8 %. • Les principaux facteurs associés à l'adhésion étaient les connaissances des personnes sur la maladie et la procédure de quarantaine, les normes sociales, les avantages perçus de la quarantaine et le risque perçu lié à la maladie
(Houghton et coll., 2020)	Barriers and facilitators to healthcare workers' adherence with infection prevention and control (IPC) guidelines for respiratory infectious diseases: a rapid qualitative evidence synthesis	• Synthèse rapide de données probantes qualitatives • Les recherches ont porté sur des données probantes recueillies jusqu'au 26 mars 2020 • AMSTAR : bonne qualité • 20 articles sont inclus dans l'examen	• Plusieurs facteurs influencent la capacité et la volonté des travailleurs de la santé de respecter les directives de CPI, notamment le contenu des directives et la manière dont elles sont communiquées, le soutien des responsables, la culture du lieu de travail, la formation, l'espace physique, l'accès et la confiance dans les EPI et le désir de fournir de bons soins aux patients
(Brooks, Greenberg, Wessely et Rubin, 2020) *Préimpression*	Factors affecting healthcare workers' compliance with social and behavioral infection control measures during emerging infectious disease outbreaks: Examen rapide des données probantes	• Examen rapide des données probantes • Les recherches ont porté sur des données probantes recueillies jusqu'au 4 mai 2020 • AMSTAR : qualité modérée • 56 articles sont inclus dans l'examen	• Le personnel travaillant dans les situations d'urgence ou dans les unités de soins intensifs semble plus enclin à respecter les recommandations que celui travaillant dans d'autres contextes • Le personnel plus anxieux et plus préoccupé par le risque d'infection était plus enclin à se conformer • Il a également été constaté que des associations négatives entravaient le respect des règles, comme le non-respect observé de la part des collègues, la disponibilité des EPI, la perception de la difficulté et de l'efficacité, les désagréments et l'inconfort

Méthodes

Toute la littérature sur la COVID-19 a été compilée et classée par le Groupe des sciences émergentes de l'Agence de la santé publique du Canada depuis le début de l'épidémie. Cela suppose une recension quotidienne de la littérature pour tous les articles publiés et prépubliés. Les recherches pour trouver de la littérature pertinente sur la COVID-19 sont menées dans PubMed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square. Elles sont mises en correspondance avec les publications figurant sur la liste de littérature de l'Organisation mondiale de la santé au sujet de la COVID et les centres d'information COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de la recension sont conservés dans une base de données Refworks et un fichier Excel qui peut être consulté. Chaque article est étiqueté en fonction de divers critères permettant de déterminer le thème central de l'article (p. ex. épidémiologie, données cliniques, thérapeutique, etc.) Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour y relever des citations pertinentes sur la COVID-19 et le SARS-CoV-2. Les termes de recherche inclus dans cet examen étaient la conformité, l'adhésion et le comportement. Chaque référence potentiellement pertinente a été analysée pour confirmer sa pertinence, et des données ont été extraites et incluses dans la recension de la littérature. Cette revue contient des recherches publiées jusqu'au 19 juillet 2020.

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Emerging Evidence on COVID-19

Evidence Brief on Age-Dependent Transmission

Introduction

What is the evidence for age-dependent transmission of SARS-CoV-2?

It is important to establish whether there are differences in the potential to transmit SARS-CoV-2 among children of different age groups (preschool 0-4 years old, primary school 5-11 years old, intermediate 12-13 years old and high school 14-19 years old) compared to adults. This evidence brief is an update to the June 22, 2020 version and includes COVID-19 literature up to July 20, 2020 that measures age-dependent transmission or estimates transmission scenarios among children of different age groups such as in school.

Key Points

- Empirical evidence suggests that a low proportion of SARS-CoV-2 cases occur in children <19 years old. Of the cases in children, a large proportion may be asymptomatic, but they are still capable of transmitting the virus (Table 1).
- Few contact tracing or outbreak studies have reported children <19 years old as the index case (Table 1). However, there are instances where an infected child has passed SARS-CoV-2 to an adult or another child. Most studies conclude that children have not been the main drivers of transmission of SARS-CoV-2 to date.
- One study estimated the relative infectivity of children to adults to be 85% (65-110%). However, few children were the index case in the household outbreaks investigated, which resulted in the study being underpowered (Dattner et al., 2020). In a systematic review, pooled odds ratio of being an infected contact in children compared with adults for all contact tracing studies was reported as 0.44 (0.29, 0.69) (Viner et al., 2020).
- Viral load in symptomatic children was shown to be the same as adults in three studies of symptomatic COVID-19 cases (Table 2).
- Six publications use mathematical models to investigate the impact of relaxing intervention measures by targeting different age groups on the epidemic (Table 1).
    - Re-opening schools: the most recent model examines the risk of opening schools in a low transmission vs. high community transmission scenario, indicating opening schools in low transmission scenarios along side other public health interventions did not result in a large spike in cases. Two other mathematical models demonstrate that allowing younger children (pre-school and primary school aged) to return to school would have the smaller impact on the basic reproduction number (R0) , whereas the return of secondary school grades will have

the greatest impact (Di Domenico, Pullano, Sabbatini, Boëlle, & Colizza, 2020; Keeling et al., 2020).

- Of the three models that analyzed lifting interventions by age groups, results suggest that relaxing measures by age group could reduce the impact of COVID-19. Specifically, releasing younger individuals (0-19) from strict lockdown can lead to lower overall fatality rates compared to the simultaneous release of all individuals after a lockdown (Castilho, Gondim, & Marchesin, 2020; Zhao & Feng, 2020).

Overview of the Evidence

The evidence for age-dependent transmission of SARS-CoV-2 has been directly and indirectly explored in a number of predictive models. These models are based on scenarios and are parameterized using observational data from the outbreak; caution should be exercised in using these findings, as the extent to which the results can be generalized to the local context is variable.

Empirical evidence from surveillance, estimates of transmission and descriptions of transmission clusters or outbreaks are obtained from data collected during retrospective outbreak investigations, which have a moderate to high risk of bias. Many studies identified in this brief are in preprint format and have not completed a peer-review process. There is some evidence that may allow estimation of transmission rates among child age groups compared to adults, this evidence is accumulating rapidly and there is a high probability that estimates or conclusions will change as additional evidence becomes available.

CONTENTS

EVIDENCE OF AGE-DEPENDANT TRANSMISSION AND TRANSMISSION POTENTIAL

The age distribution of COVID-19 cases has shown strong age dependence with fewer cases documented in children, and few transmission events attributed to transmission from an infected child. In this updated review, several studies were added from cluster investigations and school community investigations conducted in countries in Asia, Europe, Australasia, North America and South America that add a significant update to this review.

It is hypothesized that the apparent age-dependence we see in epidemiological data may have several contributing factors including that children may be less susceptible to infection and/or are less prone to showing clinical symptoms when infected. Several studies in Table 1 provide evidence that a significantly lower proportion of children are infected with SARS-CoV-2 compared to adult populations, that children are less susceptible to SARS-CoV-2 infection than adults and that they may be less likely to have symptoms. This susceptibility appears to increase between 10 and 20 years old. Models like the one by Davies et al. show the impact of different rates of transmission by age and the impact of assumptions around how readily asymptomatic or paucisymptomatic transmission occurs (Davies et al., 2020).

Contact tracing studies in Table 1, such as the results from South Korea, agree that children are infrequently identified as the index case or a contact in cluster investigations. However, a unique finding of this study was that the few 10-19 year old index cases had a high rate of transmission (18.6%) compared to their household contacts (Park et al., 2020). Speculation around this increase in transmission includes that children in this age group are taller, and can contaminate more shared air with adults and that they may be less likely to adhere to optimal personal hygiene behaviors. Across other studies a child <18 years old is rarely implicated as the index case in a family or non-household cluster (Table 1).

Similarly, there were seven investigations within school communities. Even though cases were identified in the school, most were not attributed to transmission at school and instead were attributed to transmission from a family member at home. Two of the school investigations from Chile and France reported very high seroprevalence after school closures (Fontanet, Tondeur et al., 2020; Torres et al., 2020). The study in France was in one of the epicenters of an outbreak, and was thought to have been going on for approximately 3 weeks before the school closed. The results were high seroprevalence across all age groups in this investigation (Fontanet, Tondeur et al., 2020). The study from a school community in Santiago Chile indicated that the there was high prevalence among the preschool teachers and parents due to meetings that had taken place in the first few weeks of schools opening (Torres et al., 2020).

Table 1: Twenty-three studies that inform age-dependent factors of COVID-19 transmission including predictive models (n=2), contact tracing studies (n=10), school/daycare studies of transmission (n=7), synthesis research on age related transmission (n=4)

Reference	Title	Study Description	Key Outcomes
Predictive Models of age-dependent transmission			
(Davies et al., 2020)	Age-dependent effects in the transmission and control of COVID-19 epidemics	Dynamic transmission models were fit to a range of available data on the age distribution of reported cases, and 2studies that looked for infections among close contacts, to estimate the age-specific susceptibility to SARS-CoV-2 infection and the age-specific fraction of infections that develop full clinical symptoms of COVID-19. Data from China, Italy, Japan, Singapore, Canada and South Korea was used. The model examined epidemiological evidence to better understand whether children have lower susceptibility to infection, lower propensity to show clinical symptoms or both. The model accounting for both fit the data best.	• Susceptibility to SARS-CoV-2 infection in <20 yo is approximately half that of adults aged over 20 years. Relative susceptibility to infection was 0.40 (0.25-0.57) in 0-9 yo vs. 0.88 (0.70-0.99) in 60-69 yo. • Clinical symptoms manifest in 21% (95% credible interval: 12–31%) of infections in 10-19 yo, rising to 69% (57–82%) of infections in >70 yo. • Results were consistent across countries and intervention contexts. • These results show that interventions targeting schoolchildren may be less effective than for other respiratory infections. • Age-structure of a population is important for estimating the burden of SARS-CoV-2. • A comparison of COVID-19 vs. influenza in 3 cities with different age structures indicates that school closures delay the COVID-19 peak 1-6 days and decreased it by 10-19% vs. 10-89 days and 17-35% for influenza.
(Lau, Grenfell, Nelson, & Lopman, 2020)	Characterizing super-spreading events and age-specific infectivity of COVID-19 transmission in Georgia, USA	Individual-level spatiotemporal mechanistic framework to statistically integrate case data with geo-location data and aggregate mobility data, enabling a more granular understanding of the transmission dynamics of COVID-19. Data: March 1- May 3, the analysis included the 5 most infected counties with n=9559 COVID-19 cases with demographic information.	• They did not look at children as a separate age group because there were not enough observations. Younger children seem to be less susceptible to SARS-CoV-2. • We estimate that the infected children and adults <60 yo may be 2.38 [1.30, 3.51] times more transmissible than infected elderly (>=60 yo), and the former may be the main driver of super-spreading.

Surveillance / Contact Tracing Data			
(Park et al., 2020) *new*	Contact tracing during Coronavirus Disease outbreak, South Korea, 2020	Summary of S. Korea's retrospective cluster investigations from Jan 20- Mar 27 59073 contacts of 5706 COVID-19 cases were traced. RT-PCR was used to determine COVID-19 status. They did not test asymptomatic contacts and had different thresholds for testing household vs. non-household contacts. Age category: # index/# contacts traced 0–9: 29 (0.5%)/ 237 (0.4%) 10–19: 124 (2.2%)/ 457 (0.8%) 20–29: 1695 (29.7%)/ 15810 (26.8%) 30–39: 668 (11.7%)/ 8,636 (14.6%) 40–49: 807 (14.1%)/ 9709 (16.4%) 50–59: 1107 (19.4%)/ 11353 (19.2%) 60–69: 736 (12.9%)/ 8490 (14.4%) 70–79: 338 (5.9%)/ 2,389 (4.0%) >80: 202 (3.5%) / 1992 (3.4%) • Index and contracts in the 20-29 year group and the 50-59 year group represented the larges age categories identified as the index case and traced for COVID-19 infection. In this study, the index case was the first case to be identified in time since they could not confirm who transmitted to whom.	• Overall: o 11.8% (95% CI 11.2%–12.4%) of household contacts were infected o 1.9% (95% CI 1.8%–2.0%) of non-household contacts were infected. • Index case age category: positive/N (%, 95% CI) in household contacts. 0–9: 3/57 (5.3%,1.3–13.7) 10–19: 43/231 (18.6%,14.0–24.0) 20–29: 138/12393 (1.1%, 0.9–1.3) 30–39: 70/7,407 (0.9%, 0.7–1.2) 40–49: 206/1749 (11.8%, 10.3–13.4) 50–59: 300/2045 (14.7%, 13.2–16.3) 60–69: 177/1039 (17.0%, 14.8–19.4) 70–79: 86/477 (18.0%, 14.8–21.7) ≥80: 50/348 (14.4%, 11.0–18.4) o Note transmission from a 10-19 year old index case to household contacts was significantly higher that other younger age groups. • Index case age category: positive/N (%, 95% CI) in non-household contacts. 0–9: 2/180 (1.1%, 0.2–3.6) 10–19: 2/226 (0.9%, 0.1–2.9) 20–29: 138/12393 (1.1%, 0.9–1.3) 30–39: 70/7,407 (0.9%, 0.7–1.2) 40–49: 161/7960 (2.0%, 1.7–2.3) 50-59: 166/9308 (1.8%, 1.5–2.1) 60–69: 215/7451 (2.9%, 2.5–3.3) 70–79: 92/1912 (4.8%, 3.9–5.8) • ≥80: 75/1,644 (4.6%, 3.6–5.7)
(Van Der Hoek et al., 2020)	[De rol van kinderen in de transmissie van	Data from the Dutch surveillance system Osiris was analysed up to May 11, 2020.	• 0.9%, 369/42788 confirmed COVID-19 cases in the Netherlands have been 0-18 yo.

new	SARS-CoV-2] in Dutch	This is preliminary data and the study is on going. Family cluster investigations were prospective enrolment at first confirmed case between March 23 and April 16. N=54 families Note: schools were closed during this study period.	○ 0-3 yo, 74 cases ○ 4-11 yo, 38 cases ○ 12-18 yo, 257 cases • There was no difference between Ct values of children or adults. • Results of a transmission pair analysis indicated 21 cases of parent to child transmission and 2 cases of child-to-child transmission within a household. • None of the 43 contacts of 10 COVID-19 cases under 18 yo developed infections compared to adults where secondary transmission was 8.3%. • In the family investigations, children were less likely to report symptoms in the last 14 days (67%) vs. adults (91%) or have specific respiratory symptoms (25% vs. 78%) • Seroconversion at 2-3 weeks post initial investigation: ○ 1-5 yo, 21% (3/14) ○ 6-11 yo, 13% (4/31) ○ 12-17 yo, 32% (12/38) ○ 18-45 yo, 31% (11/35) ○ >45 yo, 43% (13/30) • The study concluded that children can become infected, but they do not appear to contribute as much to transmission as adults.
(Sun et al., 2020) *new*	Children infected with SARS-CoV-2 from family clusters	Analysis of 74 children admitted to a Wuhan hospital Jan 28- Mar3. Cases were confirmed by RT-PCR.	• In all pediatric cases at least one adult family member was infected before the children in the household.
(Somekh et al., 2020) *new*	The role of children in the dynamics of intra family Coronavirus 2019 spread in densely populated area	Bnei Brak, Israel, which is one of the most crowded cities in the world and the city with the highest rates of children per family in Israel.	• 13 family clusters were investigated. ○ 12/13 index cases were adults exposed at the synagogue, holiday feast, work or unknown in 50%. ○ 1/13 was 14.5 yo that was exposed at Yeshiva.

		Children 0–19 years of age comprise 50% of the 200,000 population. The average number of children in a family is 4.57.
		In each family cluster all members were tested by RT-PCR
			• RT-PCR positive cases within these clusters included [relative risk of being positive compared to >18yo]
			  ○ >18 yo: 58.3%, 21/36
			  ○ 5-17 yo: 32.5%, 13/40 [0.61, 95%CI 0.39–0.96, p=0.037]
			  ○ 0-4 yo: 11.8%, 2/18 [0.47, 95%CI 0.30–0.71, p<0.002]
			• The study concludes they could not show a dominant role for children in transmission of SARS-CoV-2 even in a densely populated city with a high proportion of children.

(Dattner et al., 2020) *new*	The role of children in the spread of COVID-19: Using household data from Bnei Brak, Israel, to estimate the relative susceptibility and infectivity of children	Data from Bnei Brak up to May 2 was used for analysis. Epidemiological cluster investigations of 637 households were included. Estimates were generated from a stochastic dynamic model.	• Most index cases were adults. • Adults had a higher risk of being infected than children (44% vs. 25%). • Children under 1 yo had a higher risk of being infected compared to those aged 1-4 yo. • Their model estimates that children may have a lower infectivity compared to adults. Relative infectivity 85% (65-110%). Few child index cases meant this estimate is underpowered.
(Lavezzo et al., 2020) p*reprint*	Suppression of COVID-19 outbreak in the municipality of Vo, Italy	Two population surveys were conducted to collect nasopharyngeal swabs from 2,812 and 2,343 in the municipality of Vo, Italy.	• No infections were detected in either survey in 234 tested children ranging from 0-10 yo, despite 13 of them living in the same household as infected people. Based on household secondary infection rate positive children were expected.
(Zhang et al., 2020)	Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China	Contact surveys were conducted in two cities: Wuhan and Shanghai. The surveys were conducted from Feb 1 to Feb 10. The dataset included 1245 contacts in Wuhan and 1296 in Shanghai.	• Susceptibility to SARS-CoV-2 infection increased with age. Young individuals (aged 0-14 yo) had a lower risk of infection than individuals aged 15-64 yo {OR = 0.34 [95% confidence interval (CI): 0.24 to 0.49], p < 0.0001}.

(Mizumoto, Omori, & Nishiura, 2020) *preprint*	Age specificity of cases and attack rate of novel coronavirus disease (COVID-19)	Summarized Japan's cases up to March 7. 313 domestically acquired cases from 2496 close contacts that were investigated.	• The attack rate was low among children (male 7.2%, female 3.0%) compared to adults which peaked in the 50-59 age group (22.23%, 21.9%). As these were all exposed or symptomatic-suspected COVID-19 samples, it appears that the risk of disease given exposure is low among children.
(Bi et al., 2020)	Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study	Summary of case data from Jan 14 to Feb 12, 2020, the Shenzhen Center for Disease Control and Prevention. There were 391 SARS-CoV-2 cases and 1286 close contacts identified through symptomatic surveillance and contact tracing.	• Transmission from a child to adult was not documented. • The authors conclude that children had a similar risk of infection as adults. However, there are few observations and large uncertainty in the data for the child age categories. • Contact-based (exposed) testing results by age: 0-9= 14.9%, 10-19= 5.7%, 20-59= 10.3-17.2%. • Symptom-based testing results by age: 0-9 & 10-19= 2.1%, 20-59=7.9-24.3%.
(Danis et al., 2020)	Cluster of Coronavirus Disease 2019 (COVID-19) in the French Alps, February 2020	Ski Chalet outbreak in the French Alps February 2020. The index case spread SARS-CoV-2 to 11 people at the chalet during a 4 day stay.	• A pediatric case in this outbreak visited 3 different schools while symptomatic and no secondary cases were caused by this case.
School and Daycare Investigations			
(Yung et al., 2020) *new*	Novel coronavirus 2019 transmission risk in educational settings	Case reports of cases that attended daycare and secondary school from contact tracing studies in February and March in Singapore. Schools were not closed in Singapore, but they cancelled extracurricular activities, staggered breaks, and cohorted children. A strict cleaning protocol was also implemented. Daycares with a positive case closed for 14 days.	• 3 incidents are reported: ○ A 12 year old and a 5 year old were identified through contact tracing of an adult case they had contact with. None of the 8 symptomatic contacts at the secondary school or 34 in the preschool tested SARS-CoV-2 positive by RT-PCR. ○ The 3rd cluster was an adult staff member at a preschool. Up to 16 staff members were infected. 77 children (8 symptomatic) all tested negative.

			The 23% of children not swabbed did not develop symptoms.
(National Centre for Immunisation Research and Surveillance, 2020) *new*	COVID-19 in schools – the experience in NSW	In New south Wales between March and Mid-April 9 students and 9 staff from 15 different schools were diagnosed with SARS-CoV-2 infection. 735 students and 128 staff were close contacts.	• 2 children were potential secondary cases. • Most of the cases and observations were from high schools (12 cases/ 695 contacts). 235 contacts received RT-PCR tests and 75 received serology tests 30 days post exposure. One serology test was positive. • 1/263 close contact (53 tested) was identified from all the close contacts of 6 cases across 5 primary schools.
(Heavey, Casey, Kelly, Kelly, & McDarby, 2020) *new*	No evidence of secondary transmission of COVID-19 from children attending school in Ireland, 2020	The retrospective epidemiological investigations here targeted any case that had attended schools as a student or employee prior to school closures (Mar 12) in Ireland. Only symptomatic contacts were tested.	• 3 adults and 3 children had 1155 contacts between school, sports, music (woodwind instruments) and choir practice. • Only 1 transmission event was detected, this occurred outside of school between 2 infected adults and a susceptible adult.
(Armann et al., 2020) *new*	Anti-SARS-CoV-2 IgG antibodies in adolescent students and their teachers in Saxony, Germany (SchoolCoviDD19): very low seroprevalence and transmission rates	Seroprevalence survey conducted in eastern Saxony Germany among 13 secondary schools (grade 8-11) May 25- June 30, 2020. Anti-SARS-CoV-2 IgG were assessed using 3 assays starting with Diasorin Liaison, Abbott Diagnostics and Euroimmun to confirm results. 1538 students and 507 teachers participated in this study. The community PCR confirmed prevalence was 0.15% (based on surveillance data).	• Overall seroprevalence was 0.6% o Students 0.7%, 12/1538 (5 had confirmed COVID-19 and 22 had family members with confirmed COVID-19) o Teachers 0.2%, 1/507 (2 had family members with confirmed COVDI-19) • No clusters of cases were identified even from schools with COVID-19 cases prior to lockdown (March 13). • This paper concludes that students and teachers do not seem to play a crucial role in driving SARS-CoV-2.
(Fontanet et al., 2020) *new*	SARS-CoV-2 infection in primary schools in northern France	Retrospective cohort in France. Serological tests and questionnaire data were collected April 28-30 to measure exposure among	• Infection attack rate (IAR), no difference between groups (P = 0.29) o Students (primary school 6-11 yo) 45/510 (8.8%) o Teachers 3/42 (7.1%)

		primary school families and staff from February/March 2020. Before school closures Feb 14 there were 3 infected students.	○ Non-teaching staff 1/28 (3.6%) ○ Parents 76/641 (11.9%) ○ Relatives 14/119 (11.8%) • Familial clustering of cases was documented by the high proportion of antibodies among parents (61.0% versus 6.9%; P <0.0001) and relatives s (44.4% versus 9.1%; P = 0.002) of infected pupils. • Asymptomatic cases were reported in 41.4% of children and 9.9% of adults. Only 2 adults were hospitalized in this study group.
(Torres et al., 2020) *new*	SARS-CoV-2 antibody prevalence in blood in a large school community subject to a COVID-19 outbreak: a cross-sectional study	Santiago Chile outbreak March 12 (10 days after schools opened). 52 cases from a large school community (K-12, N=2950) were identified. The school was closed and the community was quarantined. Seroprevalence survey was conducted May 4-19 of all students and staff. Test used: The Novel Coronavirus (2019-nCoV) IgG/IgM Test Kit (Colloidal gold) from Genrui Biotech Inc, China, High school students had a significantly lower seropositivity (p=0.01) than other students. Among seropositive cases 40% (95%CI: 30-50%) of students and 18% (95%CI: 8-34%) of staff reported no symptoms.	• N=1009 students, 235 staff were included in the study ○ Preschool 12.3% (95%CI 7.8-18.6), N=147 ○ Elementary 10.8% (7.81-14.7), 286 ○ Middle School 11.9% (8.81-15.9), 295 ○ High School 5.7% (3.6-8.9), 281 ○ Teachers 20.6% (14.7-27.6), 165 ○ Support Staff 7.1% (2.4-15.9), 70 • Students had a higher seropositivity than staff p=0.003. • The primary school had higher seropositive staff and analysis of contact rates indicated children with more contacts were more likely to be seropositive. • Sources with the greatest likelihood of possible contagion in students were: a home caregiver (OR: 27.9), a household relative (OR: 5.4), a classmate (OR: 3.2), and teacher (OR: 2.2) This study attributes the age distribution to preschool parent-teacher meetings.
(Fontanet, Tondeur et al., 2020) *preprint, new*	Cluster of COVID-19 in northern France: a retrospective	After 2 cases from a high school were identified in Oise France, part of the epicenter, a retrospective seroepidemiology study was conducted March 30- April 4th to	• 452/661 participants reported symptoms. • 10 participants were hospitalized (9 were SARS-CoV-2 seropositive) and there were no deaths. Serology Results: • 171/661 had antibodies

	closed cohort study	investigate the pupils, teaches and non-teaching staff serology levels.
		Response rate was 37%, this low level of participation may reflect a bias in the sample.
		They also sampled a nearby blood bank for comparison.
			• IAR of 25.9% (95%CI; 22.6-29.4)
			  ○ Pupils = 38.3%
			  ○ Teachers = 43.4%
			  ○ Non-teaching staff = 59.3%
			  ○ Parents = 11.4%
			  ○ Siblings = 10.2%
			• IFR 0% (one-sided 97.5% CI:0 - 2.1).
			• Hospitalization rate 5.3% (95%CI: 2.4 –9.8).
			• The blood donor samples had seropositive rates of (3.0%, 95%CI = 1.1- 6.4).
			• Based on the epidemiological information there appears to have been an outbreak at this high school from the last week of January to mid-February when schools closed.

Synthesis Research			

(Li et al., 2020)	The role of children in transmission of SARS-CoV-2: a rapid review	Rapid Review (search date Apr30):
		Evidence for four categories:
		1) studies reporting documented cases of SARS-CoV-2 transmission by infected children;
		2) studies presenting indirect evidence on the potential of SARS-CoV-2 transmission by (both symptomatic and asymptomatic) children;
		3) studies reporting cluster outbreaks of COVID-19 in schools; and,
		4) studies estimating the proportions of children infected by SARS-CoV-2.
			• 16 studies included
			• Conclusions:
			  ○ Case series and outbreak reports detailing transmission in children are few. Those studies which are available demonstrate that transmission by children is possible but do not quantify the likelihood of transmission in children compared to adults.
			  ○ There is little evidence on transmission dynamics in school settings. Given the current paucity of data, further investigation and close monitoring will be essential where schools have re-opened and in settings where schools have remained open.
			  ○ Children are infected, but perhaps less frequently than adults.

(Ludvigsson, 2020a)	Children are unlikely to be the main drivers of the COVID-19 pandemic: a systematic review	Systematic review up to May 12, (no protocol, data extraction or quality assessment = low quality). The authors screened 600 papers to identify key papers for the review.	• Children make up a small percentage of cases across studies. • Children tend to have milder disease. • Children are rarely the index case in household transmission events. • Even asymptomatic children have viral loads, but opening daycares and schools is unlikely to have an impact on the bigger picture of mortality.
(Viner et al., 2020) *preprint*	Susceptibility to and transmission of COVID-19 amongst children and adolescents compared with adults: a systematic review and meta-analysis	Rapid systematic review up to May 16. Includes 18 studies on contact tracing and population screening. The analysis dichotomized age at <20 yo.	• Pooled odds ratio of being an infected contact in children compared with adults for all contact tracing studies was 0.44 (0.29, 0.69). • There was heterogeneity across countries in terms of the proportion of children infected. • There is weak evidence that children and young people play a lesser role in transmission of SARS-CoV-2 at a population level.
(Zhu et al., 2020)	Children are unlikely to have been the primary source of household SARS-CoV-2 infections	A review of the literature up to March 31. They looked for evidence of the role of children in transmission of SARS-CoV-2.	• 3/31 clusters investigated had a pediatric index case. This suggests that children are not the primary source of household transmission.

IAR= Infection Attack Rate, IFR= Infection fatality rate, CI= confidence interval.

One of the hypotheses suggested to explain why children seem to transmit SARS-CoV-2 less frequently than adults is that their viral load may be lower. Three studies were included in this review, two used RT-PCR cycle counts to estimate viral load and the third cultured virus from RT-PCR positive samples. All three studies (Table 2) sampled only symptomatic cases, and all agreed that the viral load was not different from adults.

Two case studies (Table 2) of several SARS-CoV-2 infected children failed to detect transmission to their caregivers, with the possible exception of an infant who may or may not have been the index case in her family.

Studies measuring the proportion of SARS-CoV-2 infection in children have consistently reported lower infection prevalence compared to adults regardless of whether the sampling frame is targeted at potentially exposed, high risk populations or targeted at the general population (Desmet et al., 2020; Gudbjartsson et al., 2020; Johansen et al., 2020; Ludvigsson, 2020b)

Table 2: Nine studies that describe viral load (n=3) and proportion of SARS-CoV-2 by age group or SARS-CoV-2 case studies (n=2) of transmission and synthesis of research (n=1) on children

Reference	Title	Study Description	Key Outcomes
Viral Load in Samples from Symptomatic Cases of Different Age Groups			
(Baggio et al., 2020) *preprint, new*	SARS-CoV-2 viral load in the upper respiratory tract of children and adults with early acute COVID-19	Switzerland, single center cross-sectional study of viral load among children and adults tested within 5 days of symptom onset by RT-PCR. Data collected March 10-May 26. N=405	• Viral load in log10 RNA copies/mL, o Child (0-11 yo): 6.13 ± 2.02 (range 3.06-9.21) o Adolescent (12-19 yo): 5.85 ± 2.32 (range 2.36-9.42) o Young adult (20-45 yo): 5.91 ± 1.88 (range 2.37-9.39) o Adult (>45 yo): 6.33 ± 2.05 (range 2.49-9.39) • No correlation between viral load and age was found in this study.
(L'Huillier, Torriani, Pigny, Kaiser, & Eckerle, 2020) *new*	Culture-competent SARS-CoV-2 in nasopharynx of symptomatic neonates, children, and adolescents	Switzerland, case series of 23 children. They cultured SARS-CoV-2 from the upper respiratory tract samples between Jan 25- Mar 31. 23/638 patients <16 years were SARS-CoV-2 positive. Samples were collected a median of 2 days post symptom onset.	• 12/23 children had virus that could be cultured. o Median viral RNA load (VRL) at diagnosis was 3.0×10^6 copies/mL o Mean VRL 4.4×10^8 [IQR 6.9×10^3–4.4×10^8] copies/mL o Peak VRL 5.3×10^9 copies/mL • The data show that viral load at diagnosis is comparable to that of adults, and that symptomatic children of all ages shed infectious virus in early acute illness.

(Jones et al., 2020)	An analysis of SARS-CoV-2 viral load by patient age	Jan 1 to Apr 26 virology laboratories at Charité, Berlin screened 59,831 patients for COVID-19 infection, 3,712 (6.2%) with a positive real-time RT-PCR result.
		School groups: kindergarten (ages 0-6), grade school (ages 7-11), high school (ages 12-19), university (ages 20-25), adult (26-45 years), and mature (age over 45).
			• Although there were fewer children tested than adults, the proportion positive:
			  ○ By 10 year blocks,
			  ▪ 1-10 yo=2.25%
			  ▪ 11-20 yo=3.9%
			  ▪ adult age groups 4.96-6.25%
			  ▪ elderly 7.8-10.69%
			  ○ By school group,
			  ▪ kindergarten =2.10%
			  ▪ grade school =2.57%
			  ▪ high school 4.13%
			  ▪ university 5.82%
			  ▪ adults 5.27%
			  ▪ mature adults 7.56%
			• Viral load was reported to be not significantly different across age groups by the author.
			• The viral load was back translated to: 43k 1-10 yo, 63k 11-20 yo, 183k 21-30 yo, 164k 31-40 yo. P=0.008 by kurkal-wallis test.

Case studies			
(Wongsawat et al., 2020)	Risk of novel coronavirus 2019 transmission from children to caregivers: a case series	This study reports on 3 cases in children in Thailand. The children were exposed by an infected family member.	• Caregivers of the mildly sick children did not develop an infection to SARS-CoV-2.
(Cai et al., 2020)	A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features	Case series of pediatric cases. N=10 describes the clinical course of each case. One case may have transmitted to her parents, although it is plausible that she had a shorter incubation period.	• A 3 month old infant that became ill with COVID-19 prior to her parents. They were from Wuhan and exposure of the infant is unknown.

Only Report on Proportion of Children Infected with SARS-CoV-2			
(Gudbjartsson et al., 2020)	Spread of SARS-CoV-2 in the Icelandic population	This study describes the results of two sampling techniques in Iceland. 1) symptom/contact history and 2) population screening.	• Targeted testing of children: (<10 years) 38/564 positive (6.7%) vs. older ages 1183/8635 (13.7%). There was a gradual increase in the proportion that tested positive between 10 and 20 years. • The population screening group detected 0/848 children positive vs. 100/12232 (0.8% 95%CI 0.7-1.0) in older ages groups, this is despite the school remaining open in Iceland. • Children in Iceland had lower positive tests compared to other age groups despite not closing their schools.
(Johansen et al., 2020)	Infection prevention guidelines and considerations for paediatric risk groups when reopening primary schools during COVID-19 pandemic, Norway, April 2020	Summary of a risk assessment and IPC guidelines developed by the Norwegian Institute for Public Health. Data up to May 11	• 8135 COVID-19 cases in Norway o 0-5 yo 0.9%, n=72 o 6-13 yo 2.0%, n=162 o 14-19 yo 4.2%, n=341 o >19 yo 93%, n=7560 • The rest of the document includes guidelines for school re-opening.
(Desmet et al., 2020)	No SARS-CoV-2 carriage observed in children attending daycare centers during the first weeks of the epidemic in Belgium	An on-going study in Belgium of nasopharyngeal carriage in daycare children was on-going at the start of the epidemic. From March 2-12 samples collected across 8 daycare centers were tested for SARS-CoV-2.	• 0/84 positive samples from children age 6 months to 30 months. • There was no evidence of SARS-CoV-2 transmission at these daycare facilities.
Synthesis Research			

(Ludvigsson, 2020b)	Systematic review of COVID-19 in children show milder cases and a better prognosis than adults	A systematic review of COVID-19 in children including evidence (45 papers) up to March 18.	• The proportion of cases that were <19 yo was small across countries. In China 2% (n=44672 cases) were 0-19 yo. Italian reported 1.2% (n=22 512 cases) were children. This is consistent with SARS where 6.9% of cases were children and none died (Caselli & AricÃ², 2020).

THE IMPACT OF RELAXING INTERVENTION MEASURES BY TARGETING DIFFERENT AGE GROUPS

Six publications use mathematical models to investigate the impact of relaxing intervention measures by targeting different age groups on the epidemic (Table 1). In the context of re-opening schools, two mathematical models demonstrate that allowing younger children (pre-school and primary school aged) to return to school would have the smaller impact on R, whereas the return of secondary school grades will have the greatest impact (Di Domenico et al., 2020; Keeling et al., 2020). A more recent model examines several European countries and estimates that countries with low transmission and high intensity interventions for controlling the epidemic can fully reopen schools, however if community transmission is high, then care should be taken to re-open schools slowly (Stage, Shingleton, Ghosh, & et al., 2020).

Of the three models that analyzed lifting interventions by age groups, results suggest that relaxing measures by age group could reduce the impact of COVID-19. Specifically, releasing younger individuals (0-19) from strict lockdown would result in lower overall fatality rates compared to the simultaneous release of all individuals after a lockdown (Castilho et al., 2020; Zhao & Feng, 2020).

Table 3: Six publications that investigate the impact of relaxing intervention measures by targeting different age groups on the epidemic.

Reference	Publication Title	Study Description	Key Outcomes
Returning to School			
(Stage et al., 2020)	Shut and re-open: the role of schools in the spread of COVID-19 in Europe	Investigates the effect of school closure and subsequent reopening on the transmission of COVID-19, by considering Denmark, Norway, Sweden, and German states as case studies.	• The effect of school closure on growth rate of the epidemic has a noticeable reduction in the growth rate approximately 9 days after implementation. • Large-scale reopening of schools while controlling or suppressing the epidemic appears feasible in

			countries such as Denmark or Norway, where community transmission is generally low. • School reopening can contribute to significant increases in the growth rate in countries like Germany, where community transmission is relatively high.
(Keeling et al., 2020) *preprint*	The impact of school reopening on the spread of COVID-19 in England	Using an SEIR model, eight strategies for reopening primary and secondary schools in England starting on June 1 were analyzed.	• The study predicts that reopening schools with half class sizes, or that is focused on younger children is unlikely to push R above 1, although there is noticeable variation between the regions of the country. • Since older children have a greater number of social contacts and therefore a greater potential for transmission, reopening secondary schools results in larger increases in case burden compared to only reopening primary schools. • The more year groups allowed to return to school at one time, the greater the effect on R, with the return of secondary school grades having the greatest impact.
(Di Domenico et al., 2020) *preprint*	Expected impact of reopening schools after lockdown on COVID-19 epidemic in Île-de-France	This stochastic discrete age-structured epidemic model was used to assess the impact of reopening schools in the Île-de-France region of France after the withdrawal of lockdown scheduled for May 11. Authors explore several scenarios of partial, progressive, or full school reopening combined with moderate social distancing interventions and large-scale tracing, testing, and isolation.	• Results indicate that reopening all schools on this date would lead to a 2nd wave similar to the 1st and overwhelm the ICU system. • If just pre-schools and primary schools opened and middle/high schools reopen 1 month later following a progressive protocol, the ICU capacity would not be overwhelmed and would reach at most 72% capacity (95% CI: 55-83%). • There is no difference in the epidemic risk if pre-school and primary schools are reopened promptly or progressively, allowing full attendance for the younger children.

			• Full attendance for middle and high school students is not recommended.
Lifting Interventions by Age Group			
(Castilho et al., 2020) *preprint*	Assessing the efficiency of different control strategies for the Coronavirus (COVID-19) epidemic	This SEIR model was used to explore four different strategies to lift interventions in Brazil. These strategies based on age groups were analyzed using 3 age classes: children (0 to 19), adults (20 to 59), and elderly (60 to 100). The strategies include: 1) splitting the effort equally among the 3 groups, 2) stronger isolation (x2) of the elderly compared to infants/adults, 3) stronger isolation (x2) of infants/adults compared to the elderly, 4) stronger isolation (x2) of adults compared to infants/elderly.	• Results indicate that stronger isolation of the elderly compared to children and adults is the best strategy. • All other options result in 7.5% more deaths. • Authors also found that social distancing among adults has the greatest impact on R0.
(Scala, Flori, & Spelta, 2020) *preprint*	Between geography and demography: key interdependencies and exit mechanisms for COVID-19	This SIOR model analyzed the impact of mobility restrictions and age-based lockdowns in Italy during the outbreak.	• The most intensively interacting age-class are the young (0-19) and the old (70+). Mitigation strategies geared towards these two classes can produce a significant impact on diffusion rates in the post-lock down phase.
(Zhao & Feng, 2020) *preprint*	Staggered release policies for COVID-19 control: costs and benefits of sequentially relaxing restrictions by age	This SEIR model investigated the impact of sequential timing of relaxing restrictions across age groups in reducing health risks from COVID-19.	• Results show that releasing the least vulnerable group of a population before other groups will reduce the overall number of deaths. • A properly constructed sequential release of age-defined subgroups (young, middle-aged, old) from strict lockdown can lead to lower overall fatality rates compared to the simultaneous release of all individuals after a lockdown.

			• However, the timing of each step of the staggered release is very important. For example, releasing the middle-aged group too soon after releasing the young group would cause a drastic increase infections and deaths.

OTHER EVIDENCE SYNTHESIS PRODUCTS CONDUCTED TO LOOK AT TRANSMISSION AMONG DIFFERENT AGE GROUPS.

The synthesis products below were identified during our search. These products are part of the grey literature and inform the topic of transmission of SARS-CoV-2 in select age groups.

Table 3: Synthesis products that are up to date or evergreen and present information on transmission in different age groups.

Reference	Publication Title	Study Description	Key Outcomes
Rapid Review			
NCCMT Rapid Review	Rapid review: what is the specific role of daycares and schools in COVID-19 transmission?	Updated July 9, 2020 1. What is known about the likelihood of transmission of COVID-19 amongst children and adults in daycare and schools and among children to their household members? 2. What is known about likelihood of transmission of COVID-19 by infants, toddlers, and school-aged children to others in other settings?	• 23 publications are summarized that show some potential transmission of SARS-CoV-2 among children of different ages. No transmission among young daycare age children was identified. • A potential outbreak in a high school is described, however the results are based on serology 6 weeks after schools closed in an epicenter.
COVID-Explained	COVID-19 and children: our crowd-sourced data	Updated July 8, 2020. Researchers and students at Brown, MIT, Harvard, Mass General and elsewhere crowd sourcing data on COVID-19 in daycares and camps in the USA.	• They report 970 daycare settings with 27234 students and a total of 42 cases (0.15%). Among staff infections were 106/9587 (1.01%). • There is also information from camps.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an Excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: age-dependent, children and transmission. This review contains research published up to July 20, 2020. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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Nouveaux éléments de preuve sur la COVID-19

Note d'information sur la transmission en fonction de l'âge

Introduction

Quelles sont les preuves de la transmission du SRAS-CoV-2 en fonction de l'âge?

Il est important de déterminer s'il existe des différences dans le potentiel de transmission du SRAS-CoV-2 entre les enfants de différents groupes d'âge (préscolaire 0 à 4 ans, école primaire 5 à 11 ans, intermédiaire 12 à 13 ans et secondaire 14 à 19 ans) par rapport aux adultes. Cette note d'information est une mise à jour de la version du 22 juin 2020 et inclut la littérature sur la COVID-19 jusqu'au 20 juillet 2020 qui mesure la transmission en fonction de l'âge ou estime les scénarios de transmission parmi les enfants de différents groupes d'âge, comme à l'école.

Points clés

- Les données empiriques suggèrent qu'une faible proportion des cas de SRAS-CoV-2 survient chez les enfants de moins de 19 ans. Parmi les cas chez les enfants, une grande partie d'entre eux peuvent être asymptomatiques, mais ils sont toujours capables de transmettre le virus (tableau 1).
- Peu d'études sur les contacts ou les épidémies ont rapporté des enfants de moins de 19 ans comme cas index (tableau 1). Toutefois, il existe des cas où un enfant infecté a transmis le SRAS-CoV-2 à un adulte ou à un autre enfant. La plupart des études concluent que les enfants n'ont pas été les principaux vecteurs de transmission du SRAS-CoV-2 à ce jour.
- Une étude a estimé que l'infectiosité relative des enfants par rapport aux adultes était de 85 % (65 à 110 %). Cependant, peu d'enfants ont été le cas index dans les foyers étudiés, ce qui a entraîné une sous-estimation de l'étude (Dattner et coll., 2020). Dans une revue systématique, le rapport de cotes mis en commun pour être un contact infecté chez les enfants par rapport aux adultes pour toutes les études de recherche des contacts a été rapporté comme étant de 0,44 (0,29; 0,69) (Viner et coll., 2020).
- La charge virale chez les enfants symptomatiques s'est révélée être la même que celle des adultes dans trois études de cas symptomatiques de COVID-19 (tableau 2).
- Six publications utilisent des modèles mathématiques pour étudier l'impact de l'assouplissement des mesures d'intervention en ciblant différentes tranches d'âge sur l'épidémie (tableau 1).
    - Réouverture des écoles : le modèle le plus récent examine le risque d'ouverture des écoles dans un scénario de faible transmission par rapport à un scénario de forte transmission communautaire, indiquant que l'ouverture des écoles dans des scénarios de faible transmission parallèlement à d'autres interventions de santé publique n'a pas entraîné une forte hausse des

cas. Deux autres modèles mathématiques démontrent que le retour à l'école des enfants plus jeunes (en âge préscolaire et primaire) aurait un impact plus faible sur le taux de reproduction de base (R0), tandis que le retour aux études secondaires aurait l'impact le plus important (Di Domenico, Pullano, Sabbatini, Boëlle et Colizza, 2020; Keeling et coll., 2020).

- Sur les trois modèles qui ont analysé la levée de mesures par groupes d'âge, les résultats suggèrent que l'assouplissement des mesures par groupe d'âge pourrait réduire l'impact de la COVID-19. Plus précisément, la libération de jeunes individus (0 à 19 ans) après un confinement strict peut entraîner un taux de mortalité global plus faible que la libération simultanée de tous les individus après un confinement (Castilho, Gondim et Marchesin, 2020; Zhao et Feng, 2020).

Vue d'ensemble des éléments de preuve

Les preuves de la transmission du SRAS-CoV-2 en fonction de l'âge ont été directement et indirectement explorées dans un certain nombre de modèles prédictifs. Ces modèles sont fondés sur des scénarios et sont paramétrés à partir des données d'observation de l'épidémie; il convient d'utiliser ces résultats avec prudence, car la mesure dans laquelle ils peuvent être généralisés au contexte local est variable.

Les preuves empiriques issues de la surveillance, des estimations de la transmission et des descriptions des groupes de transmission ou des foyers sont obtenues à partir des données recueillies lors d'enquêtes rétrospectives sur les foyers, qui présentent un risque de biais modéré à élevé. De nombreuses études recensées dans ce dossier sont en version préliminaire et n'ont pas fait l'objet d'un processus d'évaluation par les pairs. Certains éléments peuvent permettre d'estimer les taux de transmission parmi les groupes d'âge des enfants par rapport aux adultes, ces éléments s'accumulent rapidement et il est fort probable que les estimations ou les conclusions changent à mesure que d'autres éléments deviennent disponibles.

CONTENU

PREUVES DE LA TRANSMISSION EN FONCTION DE L'ÂGE ET DU POTENTIEL DE TRANSMISSION

La répartition par âge des cas de COVID-19 a montré une forte dépendance à l'âge, avec moins de cas documentés chez les enfants, et peu d'événements de transmission attribués à la transmission à partir d'un enfant infecté. Dans cette mise à jour, plusieurs études ont été ajoutées à partir d'enquêtes sur les grappes et les communautés scolaires menées dans des pays d'Asie, d'Europe, d'Australasie, d'Amérique du Nord et d'Amérique du Sud, qui apportent une mise à jour importante à cette revue.

On suppose que l'apparente dépendance de l'âge que nous constatons dans les données épidémiologiques peut avoir plusieurs facteurs contributifs, notamment le fait que les enfants peuvent être moins sensibles à l'infection et/ou sont moins enclins à présenter des symptômes cliniques lorsqu'ils sont infectés. Plusieurs études du tableau 1 montrent qu'une proportion nettement plus faible d'enfants sont infectés par le SRAS-CoV-2 par rapport aux populations adultes, que les enfants sont moins susceptibles d'être infectés par le SRAS-CoV-2 que les adultes et qu'ils sont peut-être moins susceptibles d'avoir des symptômes. Cette susceptibilité semble augmenter entre 10 et 20 ans. Des modèles comme celui de Davies et coll. montrent l'impact des différents taux de transmission selon l'âge et l'impact des hypothèses concernant la facilité avec laquelle la transmission asymptomatique ou paucisymptomatique se produit (Davies et coll., 2020).

Les études de recherche de contacts du tableau 1, telles que les résultats de la Corée du Sud, s'accordent à dire que les enfants sont rarement identifiés comme cas index ou comme contact dans les enquêtes par grappes. Cependant, une conclusion unique de cette étude était que les quelques cas index âgés de 10 à 19 ans avaient un taux de transmission élevé (18,6 %) par rapport à leurs contacts familiaux (Park et coll., 2020). Les spéculations autour de cette augmentation de la transmission incluent le fait que les enfants de ce groupe d'âge sont plus grands, qu'ils peuvent contaminer davantage l'air partagé avec les adultes et qu'ils sont moins susceptibles d'adhérer à des comportements d'hygiène personnelle optimaux. Dans d'autres études, un enfant de moins de 18 ans est rarement impliqué comme cas index dans un groupe familial ou non familial (tableau 1).

De même, il y a eu sept enquêtes au sein des communautés scolaires. Même si des cas ont été recensés à l'école, la plupart n'ont pas été attribués à une transmission à l'école, mais à une transmission par un membre de la famille à la maison. Deux des enquêtes scolaires menées au Chili et en France ont fait état d'une séroprévalence très élevée après la fermeture des écoles (Fontanet, Tondeur et coll., 2020; Torres et coll., 2020). L'étude en France a été menée dans l'un des épicentres d'une épidémie, et aurait duré environ 3 semaines avant la fermeture de l'école. Les résultats ont montré une séroprévalence élevée dans tous les groupes d'âge de cette enquête (Fontanet, Tondeur et coll., 2020). L'étude d'une communauté scolaire de Santiago au Chili a indiqué qu'il y avait une forte prévalence parmi les enseignants et les parents des écoles maternelles en raison des réunions qui avaient eu lieu au cours des premières semaines d'ouverture des écoles (Torres et coll., 2020).

Tableau 1 : Vingt-trois études qui informent sur les facteurs de transmission de la COVID-19 en fonction de l'âge, y compris des modèles prédictifs (n=2), des études de recherche de contacts (n=10), des études de transmission en milieu scolaire/garderie (n=7), des recherches de synthèse sur la transmission liée à l'âge (n=4)

Référence	Titre	Description de l'étude	Principaux résultats
Modèles prédictifs de transmission en fonction de l'âge			
(Davies et coll., 2020)	Age-dependent effects in the transmission and control of COVID-19 epidemics	Des modèles dynamiques de transmission ont été adaptés à une série de données disponibles sur la répartition par âge des cas déclarés et à deux études qui ont recherché les infections parmi les contacts proches, afin d'estimer la sensibilité par âge à l'infection par le SRAS-CoV-2 et la fraction par âge des infections pour lesquelles des symptômes cliniques complets de COVID-19 sont développés. Des données de la Chine, de l'Italie, du Japon, de Singapour, du Canada et de la Corée du Sud ont été utilisées. Le modèle a examiné les données épidémiologiques pour mieux comprendre si les enfants sont moins sensibles à l'infection, moins enclins à présenter des symptômes cliniques ou les deux. Le modèle qui tient compte des deux correspond le mieux aux données.	• La sensibilité à l'infection par le SRAS-CoV-2 chez les moins de 20 ans est environ la moitié de celle des adultes âgés de plus de 20 ans. La sensibilité à l'infection était de 0,40 (0,25 à 0,57) chez les 0 à 9 ans contre 0,88 (0,70 à 0,99) chez les 60 à 69 ans. • Les symptômes cliniques se manifestent dans 21 % des cas (intervalle crédible de 95 % : 12 à 31 %) des infections chez les 10 à 19 ans, passant à 69 % (57 à 82 %) des infections chez les personnes âgées de plus de 70 ans. • Les résultats sont cohérents d'un pays à l'autre et d'un contexte d'intervention à l'autre. • Ces résultats montrent que les interventions ciblant les écoliers peuvent être moins efficaces que pour d'autres infections respiratoires. • La structure par âge d'une population est importante pour estimer la charge du SRAS-CoV-2. • Une comparaison entre les cas de COVID-19 et de grippe dans trois villes ayant des structures d'âge différentes indique que les fermetures d'écoles retardent le pic de COVID-19 de 1 à 6 jours et le réduisent de 10 à 19 %, contre 10 à 89 jours et 17 à 35 % pour la grippe.
(Lau, Grenfell, Nelson et Lopman, 2020)	Characterizing super-spreading events and age-specific infectivity of COVID-19	Cadre mécaniste spatio-temporel au niveau individuel pour intégrer statistiquement les données de cas avec les données de géolocalisation et les données de mobilité agrégées, permettant une compréhension	• Ils n'ont pas considéré les enfants comme un groupe d'âge distinct, faute d'observations suffisantes. Les jeunes enfants semblent être moins sensibles au SRAS-CoV-2. • Nous estimons que les enfants et les adultes infectés de moins de 60 ans peuvent être des vecteurs de

	transmission in Georgia, USA	plus granulaire de la dynamique de transmission de la COVID-19. Données : Du 1er mars au 3 mai, l'analyse a inclus les 5 comtés les plus infectés (n=9 559 cas de COVID-19) avec des informations démographiques.	transmission 2,38 [1,30; 3,51] fois plus élevés que les personnes âgées infectées (>=60 ans), et que les premiers peuvent être le principal facteur de la super-diffusion.
Surveillance/Données de recherche des contacts			
(Park et coll., 2020) *nouveau*	Contact tracing during Coronavirus Disease outbreak, South Korea, 2020	Résumé des enquêtes en grappes rétrospectives menées en Corée du Sud du 20 janvier au 27 mars; 59 073 contacts de 5 706 cas de COVID-19 ont été retracés. La RT-PCR a été utilisée pour déterminer le statut de COVID-19. Ils n'ont pas testé les contacts asymptomatiques et avaient des seuils différents pour tester les contacts domestiques et non domestiques. Catégorie d'âge : # index/# contacts tracés 0 à 9 : 29 (0,5 %)/237 (0,4 %) 10 à 19 : 124 (2,2 %)/457 (0,8 %) 20 à 29 : 1695 (29,7 %)/15 810 (26,8 %) 30 à 39 : 668 (11,7 %)/8 636 (14,6 %) 40 à 49 : 807 (14,1 %)/9709 (16,4 %) 50 à 59 : 1107 (19,4%)/11 353 (19,2%) 60 à 69 : 736 (12,9 %)/8490 (14,4 %) 70 à 79 : 338 (5,9 %)/2 389 (4,0 %) >80 : 202 (3,5 %)/1992 (3,4 %) • L'index et les personnes ayant contracté le virus dans les groupes des 20 à 29 ans et des 50 à 59 ans représentaient les plus grandes catégories d'âge identifiées comme cas index et ayant été tracées pour l'infection à la COVID-19.	• Dans l'ensemble : o 11,8 % (95 % IC, 11,2 % à 12,4 %) des contacts familiaux étaient infectés o 1,9 % (95 % IC, 1,8 % à 2,0 %) des contacts non domestiques ont été infectés. • Catégorie d'âge du cas index : positive/N (%, IC 95 %) dans les contacts du ménage. 0 à 9 : 3/57 (5,3 %,1,3 à 13,7) 10 à 19 : 43/231 (18,6 %,14,0 à 24,0) 20 à 29 : 138/12 393 (1,1 %, 0,9 à 1,3) 30 à 39 : 70/7 407 (0,9 %, 0,7 à 1,2) 40 à 49 : 206/1 749 (11,8 %, 10,3 à 13,4) 50 à 59 : 300/2 045 (14,7 %, 13,2 à 16,3) 60 à 69 : 177/1 039 (17,0 %, 14,8 à 19,4) 70 à 79 : 86/477 (18,0 %, 14,8 à 21,7) ≥80 : 50/348 (14,4 %, 11,0 à 18,4) o Il convient de noter que la transmission d'un cas index de 10 à 19 ans aux contacts du ménage était significativement plus élevée que pour les autres groupes d'âge plus jeunes. • Catégorie d'âge des cas index : positive/N (%, IC 95 %) dans les contacts hors du ménage. 0 à 9 : 2/180 (1,1 %, 0,2 à 3,6) 10 à 19 : 2/226 (0,9 %, 0,1 à 2,9) 20 à 29 : 138/12 393 (1,1 %, 0,9 à 1,3) 30 à 39 : 70/7 407 (0,9 %, 0,7 à 1,2)

		Dans cette étude, le cas index a été le premier cas à être identifié à temps, car ils ne pouvaient pas confirmer qui avait transmis à qui.	40 à 49 : 161/7 960 (2,0 %, 1,7 à 2,3) 50-59 : 166/9 308 (1,8 %, 1,5 à 2,1) 60 à 69 : 215/7 451 (2,9 %, 2,5 à 3,3) 70 à 79 : 92/1 912 (4,8 %, 3,9 à 5,8) • ≥80 : 75/1 644 (4,6 %, 3,6 à 5,7)
(Van Der Hoek et coll., 2020) *nouveau*	[De rol van kinderen in de transmissie van SARS-CoV-2] en hollandais	Les données du système de surveillance néerlandais Osiris ont été analysées jusqu'au 11 mai 2020. Il s'agit de données préliminaires et l'étude est en cours. Les enquêtes sur les grappes familiales étaient des inscriptions prospectives lors du premier cas confirmé entre le 23 mars et le 16 avril. N=54 familles Note : les écoles ont été fermées pendant cette période d'étude.	• 0,9 %, 369/42 788 cas confirmés de COVID-19 aux Pays-Bas touchaient des personnes âgées de 0 à 18 ans. o 0 à 3 ans, 74 cas o 4 à 11 ans, 38 cas o 12 à 18 ans, 257 cas • Il n'y avait aucune différence entre les valeurs de Ct des enfants et des adultes. • Les résultats d'une analyse des paires de transmission ont indiqué 21 cas de transmission de parent à enfant et 2 cas de transmission d'enfant à enfant au sein d'un ménage. • Aucun des 43 contacts de 10 cas de COVID-19 de moins de 18 ans n'a développé d'infection par rapport aux adultes où la transmission secondaire était de 8,3 %. • Dans les enquêtes familiales, les enfants ont moins tendance à signaler des symptômes au cours des 14 derniers jours (67 %) que les adultes (91 %) ou à présenter des symptômes respiratoires spécifiques (25 % contre 78 %) • Séroconversion à 2 ou 3 semaines après l'enquête initiale : o 1 à 5 ans, 21 % (3/14) o 6 à 11 ans, 13% (4/31) o 12 à 17 ans, 32% (12/38) o 18 à 45 ans, 31% (11/35) o >45 ans, 43 % (13/30)

			• L'étude a conclu que les enfants peuvent être infectés, mais qu'ils ne semblent pas contribuer autant à la transmission que les adultes.
(Sun et coll., 2020) *nouveau*	Children infected with SARS-CoV-2 from family clusters	Analyse de 74 enfants admis dans un hôpital de Wuhan du 28 janvier au 3 mars. Les cas ont été confirmés par RT-PCR.	• Dans tous les cas pédiatriques, au moins un membre adulte de la famille a été infecté avant les enfants du ménage.
(Somekh et coll., 2020) *nouveau*	The role of children in the dynamics of intra family Coronavirus 2019 spread in densely populated area	Bnei Brak, Israël est l'une des villes les plus peuplées du monde et la ville qui a le taux le plus élevé d'enfants par famille en Israël. Les enfants de 0 à 19 ans représentent 50 % des 200 000 habitants. Le nombre moyen d'enfants dans une famille est de 4,57. Dans chaque grappe familiale, tous les membres ont été testés par RT-PCR	• 13 grappes familiales ont été étudiées. o 12/13 cas index étaient des adultes ayant été exposés à la synagogue, lors d'un repas en période de fête, au travail ou à un endroit inconnu dans 50 % des cas. o 1/13 des cas avaient 14,5 ans et ont été exposés à la yeshiva. • Les cas de RT-PCR positifs dans ces grappes comprenaient [risque relatif d'être positif par rapport aux personnes >18 ans] o >18 ans : 58,3 %, 21/36 o 5 à 17 ans : 32,5 %, 13/40 [0,61, 95 %CI 0,39 à 0,96, p=0,037] o 0 à 4 ans : 11,8 %, 2/18 [0,47, 95%CI 0,30 à 0,71, p<0,002] • L'étude conclut qu'ils n'ont pas pu montrer un rôle dominant des enfants dans la transmission du SRAS-CoV-2, même dans une ville très peuplée où la proportion d'enfants est élevée.
(Dattner et coll., 2020) *nouveau*	The role of children in the spread of COVID-19: Using household data from Bnei Brak, Israel, to estimate the relative	Les données de Bnei Brak recueillies jusqu'au 2 mai ont été utilisées pour l'analyse. Des enquêtes épidémiologiques par grappes de 637 ménages ont été incluses. Les estimations ont été générées à partir d'un modèle dynamique stochastique.	• La plupart des cas index étaient des adultes. • Les adultes ont un risque plus élevé d'être infectés que les enfants (44 % contre 25 %). • Les enfants de moins de 1 an ont un risque plus élevé d'être infectés que ceux âgés de 1 à 4 ans. • Leur modèle estime que les enfants peuvent avoir une infectiosité plus faible que les adultes. Infectiosité

	susceptibility and infectivity of children		relative 85 % (65 à 110 %). Le peu de cas index d'enfants signifie que cette estimation est sous-évaluée.
(Lavezzo et coll., 2020) *préimpression*	Suppression of COVID-19 outbreak in the municipality of Vo, Italy	Deux enquêtes de population ont été menées pour recueillir des prélèvements nasopharyngés auprès de 2 812 et 2 343 personnes dans la municipalité de Vo, en Italie.	• Aucune infection n'a été détectée dans les deux enquêtes chez 234 enfants testés âgés de 0 à 10 ans, bien que 13 d'entre eux vivent dans le même foyer que des personnes infectées. D'après le taux d'infection secondaire des ménages, on s'attendait à ce que les enfants soient positifs.
(Zhang et coll., 2020)	Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China	Des enquêtes de contact ont été menées dans deux villes : Wuhan et Shanghai. Les enquêtes ont été menées du 1er au 10 février. L'ensemble de données comprenait 1 245 contacts à Wuhan et 1 296 à Shanghai.	• La vulnérabilité à l'infection par le SRAS-CoV-2 augmente avec l'âge. Les jeunes individus (0 à 14 ans) ont un risque d'infection plus faible que les individus âgés de 15 à 64 ans {CR = 0,34 [intervalle de confiance (IC) de 95 %] : 0,24 à 0,49], p < 0,000 1}.
(Mizumoto, Omori et Nishiura, 2020) *Préimpression*	Age specificity of cases and attack rate of novel coronavirus disease (COVID-19)	Résumé des cas au Japon jusqu'au 7 mars. 313 cas d'infections contractées au pays auprès de 2 496 contacts étroits qui ont fait l'objet d'une enquête.	• Le taux d'attaque était faible chez les enfants (7,2 % chez les hommes, 3,0 % chez les femmes) par rapport aux adultes qui ont atteint un pic dans la tranche d'âge des 50 à 59 ans (22,23 %, 21,9 %). Comme il s'agissait de tous les échantillons COVID-19 exposés ou suspectés d'être symptomatiques, il semble que le risque de maladie, compte tenu de l'exposition, soit faible chez les enfants.
(Bi et coll., 2020)	Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study	Résumé des données sur les cas du 14 janvier au 12 février 2020, au Centre de contrôle et de prévention des maladies de Shenzhen. Il y a eu 391 cas de SRAS-CoV-2 et 1 286 contacts étroits identifiés grâce à la surveillance symptomatique et à la recherche des contacts.	• La transmission d'un enfant à un adulte n'a pas été documentée. • Les auteurs concluent que les enfants présentent un risque d'infection similaire à celui des adultes. Cependant, il y a peu d'observations et une grande incertitude dans les données pour les catégories d'âge des enfants.

			• Résultats des tests par contact (exposition) selon l'âge : 0 à 9= 14,9 %, 10 à 19= 5,7 %, 20 à 59= 10,3 à 17,2 %. • Résultats des tests basés sur les symptômes par âge : 0 à 9 et 10 à 19= 2,1 %, 20 à 59=7,9 à 24,3 %.
(Danis et coll., 2020)	Cluster of Coronavirus Disease 2019 (COVID-19) in the French Alps, February 2020	Février 2020 : flambée épidémique au chalet de ski dans les Alpes françaises. Le cas index a propagé le SRAS-CoV-2 à 11 personnes au chalet pendant un séjour de 4 jours.	• Un cas pédiatrique dans cette épidémie a visité 3 écoles différentes alors que ce cas était symptomatique et qu'aucun cas secondaire n'a été causé par ce cas.
Enquêtes sur les écoles et les garderies			
(Yung et coll., 2020) *nouveau*	Novel coronavirus 2019 transmission risk in educational settings	Rapports de cas de personnes ayant fréquenté une garderie et une école secondaire dans le cadre d'études de recherche de contacts en février et mars à Singapour. Les écoles n'ont pas été fermées à Singapour, mais elles ont annulé les activités parascolaires, échelonné les pauses et regroupé les enfants. Un protocole de nettoyage strict a également été mis en place. Les garderies ayant un cas positif ont fermé pendant 14 jours.	• 3 incidents sont signalés : o Un enfant de 12 ans et un enfant de 5 ans ont été identifiés grâce à la recherche d'un cas d'adulte avec lequel ils ont été en contact. Aucun des 8 contacts symptomatiques de l'école secondaire ou des 34 de l'école maternelle n'a été testé positif au SRAS-CoV-2 par RT-PCR. o La troisième grappe était un membre adulte du personnel d'une école maternelle. Jusqu'à 16 membres du personnel ont été infectés. 77 enfants (8 symptomatiques) ont tous reçu un résultat négatif au test. Les 23 % d'enfants qui n'ont pas fait l'objet d'un prélèvement n'ont pas développé de symptômes.
(National Centre for Immunisation Research and Surveillance, 2020)	COVID-19 in schools – the experience in NSW	En Nouvelle-Galles-du-Sud, entre mars et la mi-avril, 9 élèves et 9 membres du personnel de 15 écoles différentes ont été diagnostiqués comme étant atteints d'une infection par le SRAS-CoV-2.	• 2 enfants étaient des cas secondaires potentiels. • La plupart des cas et des observations provenaient d'écoles secondaires (12 cas/695 contacts). 235 contacts ont reçu des tests RT-PCR et 75 ont reçu des tests sérologiques 30 jours après l'exposition. Un test sérologique s'est avéré positif.

nouveau		735 étudiants et 128 membres du personnel étaient des contacts étroits.	• 1/263 contacts étroits (53 testés) ont été identifiés parmi tous les contacts étroits de 6 cas dans 5 écoles primaires.
(Heavey, Casey, Kelly, Kelly et McDarby, 2020) *nouveau*	No evidence of secondary transmission of COVID-19 from children attending school in Ireland, 2020	Les enquêtes épidémiologiques rétrospectives ont ciblé ici tout cas ayant fréquenté des écoles en tant qu'étudiant ou employé avant la fermeture des écoles (12 mars) en Irlande. Seuls les contacts symptomatiques ont été testés.	• 3 adultes et 3 enfants ont eu 1 155 contacts entre l'école, le sport, la musique (instruments à vent en bois) et la pratique de la chorale. • Un seul cas de transmission a été détecté; il s'est produit en dehors de l'école entre deux adultes infectés et un adulte sensible.
(Armann et coll., 2020) nouveau	Anti-SARS-CoV-2 IgG antibodies in adolescent students and their teachers in Saxony, Germany (SchoolCoviDD19): very low seroprevalence and transmission rates	Enquête de séroprévalence menée en Saxe orientale, en Allemagne, auprès de 13 écoles secondaires (de la 8e à la 11e année) du 25 mai au 30 juin 2020. Les IgG anti-SARS-CoV-2 ont été évalués à l'aide de 3 tests, en commençant par Diasorin Liaison, Abbott Diagnostics et Euroimmun pour confirmer les résultats. 1 538 étudiants et 507 enseignants ont participé à cette étude. La PCR communautaire a confirmé une prévalence de 0,15 % (sur la base des données de surveillance).	• La séroprévalence globale était de 0,6 % o Étudiants 0,7 %, 12/1 538 (5 avaient une COVID-19 confirmée et 22 avaient des membres de leur famille avec une COVID-19 confirmée) o Enseignants 0,2 %, 1/507 (2 avaient des membres de leur famille avec une COVDI-19 confirmée) • Aucune grappe de cas n'a été identifiée, même dans les écoles ayant des cas de COVID-19 avant le confinement (13 mars). • Ce document conclut que les étudiants et les enseignants ne semblent pas jouer un rôle crucial dans la lutte contre le SRAS-CoV-2.
(Fontanet et coll., 2020) nouveau	SARS-CoV-2 infection in primary schools in northern France	Retrospective cohort in France. Des tests sérologiques et des données de questionnaires ont été recueillis du 28 au 30 avril pour mesurer l'exposition des familles et du personnel des écoles primaires à partir de février/mars 2020. Avant la fermeture des écoles le 14 février, il y avait 3 élèves infectés.	• Taux d'attaque de l'infection (TAI), aucune différence entre les groupes (P = 0,29) o Élèves (école primaire 6-11 ans) 45/510 (8,8 %) o Enseignants 3/42 (7,1 %) o Personnel non enseignant 1/28 (3,6 %) o Parents 76/641 (11,9 %) o Famille 14/119 (11,8 %) • Le regroupement des cas en grappes familiales a été documenté par la forte proportion d'anticorps chez

			les parents (61,0 % contre 6,9 %; P < 0,000 1) et les proches (44,4 % contre 9,1 %; P = 0,002) des élèves infectés. • Des cas asymptomatiques ont été signalés chez 41,4 % des enfants et 9,9 % des adultes. Seuls deux adultes ont été hospitalisés dans ce groupe d'étude.
(Torres et coll., 2020) nouveau	SARS-CoV-2 antibody prevalence in blood in a large school community subject to a COVID-19 outbreak: a cross-sectional study	Foyer d'éclosion à Santiago au Chili, le 12 mars (10 jours après l'ouverture des écoles). 52 cas provenant d'une grande communauté scolaire (K-12, N=2 950) ont été identifiés. L'école a été fermée et la communauté a été mise en quarantaine. Une enquête de séroprévalence a été menée du 4 au 19 mai auprès de l'ensemble des étudiants et du personnel. Test utilisé : La trousse de test IgG/IgM (or colloïdal) du nouveau coronavirus (2019-nCoV) de Genrui Biotech Inc, Chine Les élèves du secondaire ont eu une séropositivité significativement plus faible (p=0,01) que les autres élèves. Parmi les cas séropositifs, 40 % (95 % IC : 30 à 50 %) des étudiants et 18 % (95%CI : 8 à 34 %) du personnel n'ont pas signalé de symptômes.	• N=1 009 étudiants, 235 membres du personnel ont été inclus dans l'étude o Préscolaire 12,3 % (95 % IC 7,8 à 18,6), N=147 o Primaire 10,8 % (7,81 à 14,7), 286 o Intermédiaire 11,9 % (8,81 à 15,9), 295 o Secondaire 5,7 % (3,6 à 8,9), 281 o Enseignants 20,6 % (14,7 à 27,6), 165 o Personnel de soutien 7,1 % (2,4 à 15,9), 70 • Les étudiants avaient une séropositivité plus élevée que le personnel p=0,003. • La séropositivité était plus élevée chez le personnel de l'école primaire et l'analyse des taux de contact indiquait que les enfants ayant plus de contacts étaient plus susceptibles d'être séropositifs. • Les sources présentant la plus grande probabilité de contagion possible chez les étudiants étaient : une aide à domicile (CR : 27,9), un parent du ménage (CR : 5,4), un camarade de classe (CR : 3,2), et un professeur (CR : 2,2) Cette étude attribue la répartition selon l'âge aux réunions parents-professeurs dans les écoles maternelles.
(Fontanet, Tondeur et coll., 2020) préimpression, nouveau	Cluster of COVID-19 in northern France: a retrospective	Après l'identification de deux cas dans un lycée de l'Oise, en France, qui fait partie de l'épicentre, une étude rétrospective de séroépidémiologie a été menée du 30 mars au 4 avril pour étudier les niveaux	• 452/661 participants ont déclaré des symptômes. • 10 participants ont été hospitalisés (9 étaient séropositifs pour le SRAS-CoV-2) et il n'y a eu aucun décès. Résultats de la sérologie : • 171/661 avait des anticorps

	étude de cohorte fermée	sériques des élèves, des enseignants et du personnel non enseignant. Le taux de réponse était de 37 %; ce faible niveau de participation peut refléter un biais dans l'échantillon. Ils ont également prélevé des échantillons dans une banque de sang voisine pour les comparer.	• TAI de 25,9 % (95%CI; 22,6 à 29,4) o Élèves = 38,3 % o Enseignants = 43,4 % o Personnel non enseignant = 59,3 % o Parents = 11,4 % o Frères et sœurs = 10,2 % • TLI 0 % (CI unilatéral 97,5 % : 0 à 2,1). • Taux d'hospitalisation 5,3 % (95 % IC : 2,4 à 9,8). • Les échantillons des donneurs de sang ont eu des taux de séropositivité de (3,0 %, 95 % IC = 1,1 à 6,4). • D'après les informations épidémiologiques, il semble qu'il y ait eu une épidémie dans ce lycée entre la dernière semaine de janvier et la mi-février, lorsque les écoles ont fermé.
Recherche de synthèse			
(Li et coll., 2020)	The role of children in transmission of SARS-CoV-2: a rapid review	Examen rapide (date de recherche : 30 avril) : Preuves pour quatre catégories : 1) études faisant état de cas documentés de transmission du SRAS-CoV-2 par des enfants infectés; 2) études présentant des preuves indirectes du potentiel de transmission du SRAS-CoV-2 par des enfants (tant symptomatiques qu'asymptomatiques); 3) études signalant des flambées de COVID-19 en grappes dans les écoles; et 4) études estimant les proportions d'enfants infectés par le SRAS-CoV-2.	• 16 études ont été réalisées • Conclusions : o Les séries de cas et les rapports d'épidémies détaillant la transmission chez les enfants sont peu nombreux. Les études disponibles démontrent que la transmission par les enfants est possible, mais ne quantifient pas la probabilité de transmission chez les enfants par rapport aux adultes. o Il existe peu de données sur la dynamique de la transmission en milieu scolaire. Étant donné le manque actuel de données, il sera essentiel de mener des enquêtes plus approfondies et d'assurer un suivi étroit dans les cas où les écoles ont rouvert et dans les milieux où les écoles sont restées ouvertes. o Les enfants sont infectés, mais peut-être moins fréquemment que les adultes.

(Ludvigsson, 2020a)	Children are unlikely to be the main drivers of the COVID-19 pandemic: a systematic review	Examen systématique jusqu'au 12 mai, (pas de protocole, extraction de données ou évaluation de la qualité = faible qualité). Les auteurs ont passé en revue 600 articles afin d'isoler les articles clés pour l'examen.	• Les enfants représentent un faible pourcentage des cas dans l'ensemble des études. • Les enfants ont tendance à avoir des effets moins graves de la maladie. • Les enfants sont rarement le cas index dans les événements de transmission des ménages. • Même les enfants asymptomatiques ont une charge virale, mais l'ouverture de garderies et d'écoles n'aura probablement pas d'impact sur le tableau général de la mortalité.
(Viner et coll., 2020) *Préimpression*	Susceptibility to and transmission of COVID-19 amongst children and adolescents compared with adults: a systematic review and meta-analysis	Examen systématique rapide jusqu'au 16 mai. Comprend 18 études sur la recherche des contacts et le dépistage de la population. L'analyse a dichotomisé l'âge à <20 ans.	• Le rapport de cotes cumulé d'être un contact infecté chez les enfants par rapport aux adultes pour toutes les études de recherche des contacts était de 0,44 (0,29; 0,69). • Il y avait une hétérogénéité entre les pays en termes de proportion d'enfants infectés. • Il n'existe que peu de preuves que les enfants et les jeunes jouent un rôle moindre dans la transmission du SRAS-CoV-2 au niveau de la population.
(Zhu et coll., 2020)	Children are unlikely to have been the primary source of household SARS-CoV-2 infections	Une revue de la littérature jusqu'au 31 mars. Ils ont cherché des preuves du rôle des enfants dans la transmission du SRAS-CoV-2.	• 3/31 des grappes étudiées comptaient un cas index pédiatrique. Cela suggère que les enfants ne sont pas la principale source de transmission au sein des ménages.

TAI = taux d'attaque de l'infection, TLI = taux de létalité de l'infection, IC = intervalle de confiance.

L'une des hypothèses avancées pour expliquer pourquoi les enfants semblent transmettre le SRAS-CoV-2 moins fréquemment que les adultes est que leur charge virale pourrait être plus faible. Trois études ont été incluses dans cette revue, deux ont utilisé des cycles de RT-PCR pour estimer la charge virale et la troisième a cultivé le virus à partir d'échantillons positifs RT-PCR. Les trois études (tableau 2) n'ont porté que sur des cas symptomatiques, et toutes ont convenu que la charge virale n'était pas différente de celle des adultes.

Deux études de cas (tableau 2) de plusieurs enfants infectés par le SRAS-CoV-2 n'ont pas permis de détecter la transmission à leurs soignants, à l'exception peut-être d'un nourrisson qui peut ou non avoir été le cas index dans sa famille.

Les études mesurant la proportion d'infection par le SRAS-CoV-2 chez les enfants ont systématiquement fait état d'une prévalence d'infection inférieure à celle des adultes, que la base d'échantillonnage soit destinée aux populations potentiellement exposées et à haut risque ou à la population générale (Desmet et coll., 2020; Gudbjartsson et coll., 2020; Johansen et coll., 2020; Ludvigsson, 2020b)

Tableau 2 : Neuf études qui décrivent la charge virale (n=3) et la proportion de cas de SRAS-CoV-2 par groupe d'âge ou des études de cas de transmission du SRAS-CoV-2 (n=2) et synthèse des recherches (n=1) sur les enfants

Référence	Titre	Description de l'étude	Principaux résultats
Charge virale dans les échantillons provenant de cas symptomatiques de différentes tranches d'âge			
(Baggio et coll., 2020) *préimpression, nouveau*	SARS-CoV-2 viral load in the upper respiratory tract of children and adults with early acute COVID-19	Suisse, étude transversale à centre unique de la charge virale chez les enfants et les adultes testés dans les 5 jours suivant l'apparition des symptômes par RT-PCR. Données recueillies du 10 mars au 26 mai. N=405	• Charge virale en log10 copies d'ARN/mL, o Enfant (0 à 11 ans) : 6,13 ± 2,02 (étendue 3,06 à 9,21) o Adolescent (12 à 19 ans) : 5,85 ± 2,32 (étendue 2,36 à 9,42) o Jeune adulte (20 à 45 ans) : 5,91 ± 1,88 (étendue 2,37 à 9,39) o Adulte (>45 ans) : 6,33 ± 2,05 (étendue 2,49 à 9,39) • Aucune corrélation entre la charge virale et l'âge n'a été trouvée dans cette étude.
(L'Huillier, Torriani, Pigny, Kaiser et Eckerle, 2020) *nouveau*	Culture-competent SARS-CoV-2 in nasopharynx of symptomatic neonates, children, and adolescents	Suisse, série de cas de 23 enfants. Ils ont cultivé le SRAS-CoV-2 à partir d'échantillons des voies respiratoires supérieures entre le 25 janvier et le 31 mars. 23/638 patients <16 ans avaient obtenu un résultat positif pour le SRAS-CoV-2. Les échantillons ont été prélevés en moyenne deux jours après l'apparition des symptômes.	• 12/23 enfants avaient un virus qui pouvait être cultivé. o La charge médiane d'ARN viral (VRL) au moment du diagnostic était de $3,0 \times 10^6$ copies/mL o VRL moyen $4,4 \times 10^8$ [EI $6,9 \times 10^3$, $4,4 \times 10^8$] copies/mL o VRL de pointe $5,3 \times 10^9$ copies/mL • Les données montrent que la charge virale au moment du diagnostic est comparable à celle des adultes, et que les enfants symptomatiques

			de tous âges éliminent le virus infectieux au début de la phase aiguë de la maladie.
(Jones et coll., 2020)	An analysis of SARS-CoV-2 viral load by patient age	Du 1er janvier au 26 avril, les laboratoires de virologie Charité, à Berlin, ont examiné 59 831 patients pour une infection à la COVID-19, dont 3 712 (6,2 %) ont obtenu un résultat positif en RT-PCR en temps réel. Groupes scolaires : maternelle (0 à 6 ans), école primaire (7 à 11 ans), école secondaire (12 à 19 ans), université (20 à 25 ans), adultes (26 à 45 ans) et adultes (plus de 45 ans).	• Bien qu'il y ait moins d'enfants testés que d'adultes, la proportion est positive : o Par blocs de 10 ans, ▪ 1 à 10 ans=2,25 % ▪ 11 à 20 ans=3,9 % ▪ groupes d'âge adulte 4,96 à 6,25 % ▪ personnes âgées 7,8 à 10,69 % o Par groupe scolaire, ▪ Maternelle =2,10 % ▪ École primaire =2,57 % ▪ École secondaire = 4,13 % ▪ Université = 5,82 % ▪ Adultes = 5,27 % ▪ Adultes matures = 7,56 % • Selon l'auteur, la charge virale n'est pas significativement différente d'un groupe d'âge à l'autre. • La charge virale a été à nouveau traduite : 43k 1 à 10 ans, 63 k 11 à 20 ans, 183 k 21 à 30 ans, 164 k 31 à 40 ans. P=0,008 par le test de kurkal-wallis.
Études de cas			
(Wongsawat et coll., 2020)	Risk of novel coronavirus 2019 transmission from children to caregivers: a case series	Cette étude fait état de 3 cas d'enfants en Thaïlande. Les enfants ont été exposés par un membre de la famille infecté.	• Les personnes qui s'occupaient des enfants légèrement malades n'ont pas développé d'infection au SRAS-CoV-2.
(Cai et coll., 2020)	A case series of children with 2019	Série de cas pédiatriques. N=10 décrit l'évolution clinique de chaque cas. Un cas peut avoir été	• Un bébé de 3 mois qui est tombé malade de la COVID-19 avant ses parents. Ils étaient de

	novel coronavirus infection: clinical and epidemiological features	transmis à ses parents, bien qu'il soit plausible qu'elle ait eu une période d'incubation plus courte.	Wuhan et l'exposition du nourrisson est inconnue.
Seul rapport sur la proportion d'enfants infectés par le SRAS-CoV-2			
(Gudbjartsson et coll., 2020)	Spread of SARS-CoV-2 in the Icelandic population	Cette étude décrit les résultats de deux techniques d'échantillonnage en Islande. 1) les symptômes/antécédents de contact et 2) le dépistage de la population.	• Tests ciblés sur les enfants : (<10 ans) 38/564 positifs (6,7 %) contre 1183/8635 plus âgés (13,7 %). La proportion de personnes ayant obtenu un résultat positif au test a augmenté progressivement entre 10 et 20 ans. • Le groupe de dépistage de la population a détecté 0/848 enfants positifs contre 100/12 232 (0,8 % IC 95 % 0,7 à 1,0) dans les groupes d'âge plus âgés, et ce malgré le fait que l'école reste ouverte en Islande. • En Islande, les enfants ont eu moins de tests positifs que les autres groupes d'âge, bien que les écoles n'aient pas été fermées.
(Johansen et coll., 2020)	Infection prevention guidelines and considerations for paediatric risk groups when reopening primary schools during COVID-19 pandemic, Norway, April 2020	Résumé d'une évaluation des risques et des lignes directrices de CPI élaborées par l'Institut norvégien de la santé publique. Données jusqu'au 11 mai	• 8 135 cas de COVID-19 en Norvège o 0 à 5 ans 0,9 %, n=72 o 6 à 13 ans 2,0 %, n=162 o 14 à 19 ans 4,2 %, n=341 o >19 ans 93 %, n=7 560 • Le reste du document comprend des lignes directrices pour la réouverture des écoles.
(Desmet et coll., 2020)	No SARS-CoV-2 carriage observed in	Une étude en cours en Belgique sur le portage nasopharyngé chez les enfants en garderie était en cours au début de l'épidémie. Du 2 au	• 0/84 échantillons positifs d'enfants âgés de 6 mois à 30 mois. • Il n'y avait aucune preuve de transmission du SRAS-CoV-2 dans ces garderies.

	children attending daycare centers during the first weeks of the epidemic in Belgium	12 mars, des échantillons recueillis dans 8 garderies ont été testés pour le SRAS-CoV-2.	
Recherche de synthèse			
(Ludvigsson, 2020b)	Systematic review of COVID-19 in children show milder cases and a better prognosis than adults	Une revue systématique de la COVID-19 chez les enfants, y compris des données probantes (45 articles) jusqu'au 18 mars.	• La proportion de cas de moins de 19 ans était faible dans tous les pays. En Chine, 2 % (n=44 672 cas) étaient âgés de 0 à 19 ans. Les Italiens ont déclaré que 1,2 % (n=22 512 cas) étaient des enfants. Cela correspond au SRAS où 6,9 % des cas étaient des enfants et aucun n'est mort (Caselli & AricÃ², 2020).

L'IMPACT DE L'ASSOUPLISSEMENT DES MESURES D'INTERVENTION EN CIBLANT DIFFÉRENTES TRANCHES D'ÂGE

Six publications utilisent des modèles mathématiques pour étudier l'impact de l'assouplissement des mesures d'intervention en ciblant différentes tranches d'âge sur l'épidémie (tableau 1). Dans le contexte de la réouverture des écoles, deux modèles mathématiques démontrent que le retour à l'école des enfants plus jeunes (en âge préscolaire et primaire) aurait un impact plus faible, tandis que le retour aux études secondaires aurait l'impact le plus important (Di Domenico, et coll., 2020; Keeling et coll., 2020). Un modèle plus récent examine plusieurs pays européens et estime que les pays où la transmission est faible et où les interventions visant à contrôler l'épidémie sont très intensives peuvent rouvrir complètement les écoles, mais si la transmission communautaire est élevée, il faut alors s'assurer de rouvrir les écoles lentement (Stage, Shingleton, Ghosh et coll., 2020).

Sur les trois modèles qui ont analysé la levée de mesures par groupes d'âge, les résultats suggèrent que l'assouplissement des mesures par groupe d'âge pourrait réduire l'impact de la COVID-19. Plus précisément, la libération de jeunes individus (0 à 19 ans) après un confinement strict entraînerait un taux de mortalité global plus faible que la libération simultanée de tous les individus après un confinement (Castilho et coll., 2020; Zhao et Feng, 2020).

Tableau 3 : Six publications qui étudient l'impact de l'assouplissement des mesures d'intervention en ciblant différentes tranches d'âge sur l'épidémie.

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Retour à l'école			
(Stage et coll., 2020)	Shut and re-open: the role of schools in the spread of COVID-19 in Europe	Étudie l'effet de la fermeture et de la réouverture ultérieure des écoles sur la transmission de la COVID-19, en considérant le Danemark, la Norvège, la Suède et les États allemands comme des études de cas.	• L'effet de la fermeture des écoles sur le taux de croissance de l'épidémie se traduit par une réduction sensible du taux de croissance environ 9 jours après la mise en œuvre. • La réouverture à grande échelle des écoles tout en contrôlant ou en supprimant l'épidémie semble possible dans des pays comme le Danemark ou la Norvège, où la transmission communautaire est généralement faible. • La réouverture des écoles peut contribuer à une augmentation significative du taux de croissance dans des pays comme l'Allemagne, où la transmission communautaire est relativement élevée.
(Keeling et coll., 2020) *Préimpression*	The impact of school reopening on the spread of COVID-19 in England	À l'aide d'un modèle SEIR, huit stratégies de réouverture des écoles primaires et secondaires en Angleterre à partir du 1er juin ont été analysées.	• L'étude prévoit que la réouverture des écoles dont les classes sont à moitié pleines ou qui s'adressent à des enfants plus jeunes ne fera probablement pas passer la cote R au-dessus de 1, bien qu'il y ait des variations notables entre les régions du pays. • Comme les enfants plus âgés ont un plus grand nombre de contacts sociaux et donc un plus grand potentiel de transmission, la réouverture des écoles secondaires entraîne une augmentation plus importante de la charge de travail par rapport à la seule réouverture des écoles primaires. • Plus le nombre de groupes d'âge autorisés à retourner à l'école en même temps est élevé, plus

			l'effet sur la cote R est important, le retour des niveaux de l'école secondaire ayant le plus grand impact.
(Di Domenico et coll., 2020) *Préimpression*	Expected impact of reopening schools after lockdown on COVID-19 epidemic in Île-de-France	Ce modèle stochastique discret d'épidémie structurée par âge a été utilisé pour évaluer l'impact de la réouverture des écoles dans la région Île-de-France, en France, après la levée du confinement prévue pour le 11 mai. Les auteurs explorent plusieurs scénarios de réouverture partielle, progressive ou totale de l'école, combinés à des interventions modérées de distanciation sociale et à un dépistage, un suivi et un isolement à grande échelle.	• Les résultats indiquent que la réouverture de toutes les écoles à cette date entraînerait une 2e vague similaire à la 1re et submergerait le système des USI. • Si seules les écoles maternelles et primaires ouvraient et que les collèges et lycées rouvraient un mois plus tard en suivant un protocole progressif, la capacité de l'ICU ne serait pas dépassée et atteindrait au maximum 72 % de sa capacité (95 % IC : 55 à 83 %). • Il n'y a pas de différence dans le risque d'épidémie si les écoles maternelles et primaires sont rouvertes rapidement ou progressivement, permettant la pleine fréquentation des plus jeunes enfants. • Il n'est pas recommandé aux élèves des collèges et des lycées d'assister à tous les cours.
Levée des interventions par groupe d'âge			
(Castilho et coll., 2020) *Préimpression*	Assessing the efficiency of different control strategies for the Coronavirus (COVID-19) epidemic	Ce modèle SEIR a été utilisé pour explorer quatre stratégies différentes pour lever les interventions au Brésil. Ces stratégies basées sur les groupes d'âge ont été analysées en utilisant 3 classes d'âge : les enfants (0 à 19 ans), les adultes (20 à 59 ans) et les personnes âgées (60 à 100 ans). Les stratégies comprennent : 1) la répartition de l'effort à parts égales entre les 3 groupes, 2) un isolement plus rigoureux (x2) des personnes âgées par rapport aux enfants/adultes,	• Les résultats indiquent que la meilleure stratégie consiste à isoler davantage les personnes âgées par rapport aux enfants et aux adultes. • Toutes les autres options entraînent 7,5 % de décès en plus. • Les auteurs ont également constaté que la distance sociale entre les adultes a le plus grand impact sur le R0.

		3) un isolement plus rigoureux (x2) des nourrissons/adultes par rapport aux personnes âgées, 4) un isolement plus rigoureux (x2) des adultes par rapport aux nourrissons et aux personnes âgées.	
(Scala, Flori et Spelta, 2020) *Préimpression*	Between geography and demography: key interdependencies and exit mechanisms for COVID-19	Ce modèle SIOR a analysé l'impact des restrictions de mobilité et du confinement selon l'âge en Italie pendant l'épidémie.	• Les classes d'âge qui interagissent le plus intensément sont les jeunes (0 à 19 ans) et les personnes âgées (70+). Les stratégies d'atténuation axées sur ces deux classes peuvent avoir un impact significatif sur les taux de diffusion dans la phase de post-confinement.
(Zhao et Feng, 2020) *Préimpression*	Staggered release policies for COVID-19 control: costs and benefits of sequentially relaxing restrictions by age	Ce modèle SEIR a étudié l'impact du calendrier séquentiel de l'assouplissement des restrictions dans les différents groupes d'âge sur la réduction des risques sanitaires liés à la COVID-19.	• Les résultats montrent que le fait de déconfiner le groupe le moins vulnérable d'une population avant les autres groupes réduira le nombre total de décès. • Une libération séquentielle correctement construite de sous-groupes définis par âge (jeunes, personnes d'âge moyen, personnes âgées) d'un confinement strict peut conduire à un taux de mortalité global plus faible que la libération simultanée de tous les individus après un confinement. • Toutefois, le calendrier de chaque étape du déconfinement échelonné est très important. Par exemple, si l'on déconfine le groupe d'âge moyen trop tôt après avoir déconfiné le groupe jeune, cela entraînerait une augmentation drastique du nombre d'infections et de décès.

AUTRES PRODUITS DE SYNTHÈSE EVIDENCE RÉALISÉS POUR EXAMINER LA TRANSMISSION ENTRE DIFFÉRENTS GROUPES D'ÂGE.

Les produits de synthèse ci-dessous ont été recensés au cours de notre recherche. Ces produits font partie de la littérature grise et nous informent sur le thème de la transmission du SRAS-CoV-2 dans certaines tranches d'âge.

Tableau 3 : Des produits de synthèse actualisés ou évolutifs qui présentent des informations sur la transmission dans différentes tranches d'âge.

Référence	Titre de la publication	Description de l'étude	Principaux résultats
Examen rapide			
Examen rapide du CCNMO	Examen rapide : quel est le rôle spécifique des garderies et des écoles dans la transmission de la COVID-19?	Mis à jour le 9 juillet 2020 1. Que sait-on sur la probabilité de transmission de la COVID-19 chez les enfants et les adultes dans les garderies et les écoles et des enfants aux membres de leur ménage? 2. Que sait-on sur la probabilité de transmission de la COVID-19 par les nourrissons, les tout-petits et les enfants d'âge scolaire à d'autres personnes dans d'autres contextes?	• 23 publications sont résumées; elles montrent une certaine transmission potentielle du SRAS-CoV-2 chez les enfants de différents âges. Aucune transmission parmi les jeunes enfants en âge d'aller à la garderie n'a été observée. • Une épidémie potentielle dans une école secondaire est décrite, mais les résultats sont basés sur la sérologie obtenue 6 semaines après la fermeture des écoles dans un épicentre.
Explication de la COVID	La COVID-19 et les enfants : nos données participatives	Mis à jour le 8 juillet 2020. Les chercheurs et les étudiants de Brown, du MIT, de Harvard, de Mass General et d'ailleurs se pressent pour obtenir des données sur la COVID-19 dans les garderies et les camps aux États-Unis.	• Ils font état de 970 garderies accueillant 27 234 élèves et d'un total de 42 cas (0,15 %). Quant aux infections chez le personnel, on observe 106 cas sur 9587 (1,01 %). • Il y a aussi des informations provenant des camps.

Méthodologies

Une recension quotidienne de la littérature (publiée et prépubliée) est effectuée par le Groupe des sciences émergentes de l'ASPC. Cette recension a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver de la littérature pertinente sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont mises en correspondance avec les publications figurant sur la liste de littérature de l'OMS au sujet de la COVID, et les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de la recension sont conservés dans une base de données Refworks et une liste Excel qui peut être consultée. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour y relever des citations pertinentes sur la COVID-19 et le SARS-CoV-2. Les termes de recherche utilisés sont notamment : selon l'âge, enfants et transmission. Cette revue contient des recherches publiées avant le 20 juillet 2020. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, lesquelles ont été extraites et incluses dans la recension de la littérature.

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Emerging Evidence on COVID-19

Evidence Brief of Pregnancy and Severity of COVID-19

Introduction

Are pregnant women at higher risk of severe COVID-19 disease than non-pregnant women of reproductive age?

Pregnant women are potentially a vulnerable population, and may be expected to experience different symptoms and disease outcomes compared to the general population due to physiological changes during pregnancy. The objective of this evidence brief was to summarize studies conducted on COVID-19 related outcomes among pregnant women to assess whether there is evidence indicating their COVID-19 disease outcomes are more severe than the general population. This brief focused on COVID-19 disease outcomes and did not summarize birth outcomes or neonate outcomes, and includes studies published up to July 13, 2020.

Key Points

- Studies looking at severity of COVID-19 disease among pregnant women compared to non-infected pregnant women or non-pregnant COVID-19 cases present variable results that are not comparable from one study to the next due to their study design.
- Prospective studies of pregnant women in the population find a low proportion of women were infected with COVID-19 during the initial stage of the epidemic (note this was not compared to infection in the general population). Many COVID-19 positive pregnant women were asymptomatic at the time of enrollment, which ranged from first trimester visits to delivery. Many of these studies report close to zero hospitalizations or severe outcomes (Table 1).
- Prospective and retrospective case series report on a spectrum of COVID-19 disease severity outcomes in pregnant women, with significant heterogeneity across estimates between studies and within the systematic review meta-analyses (Table 2 & 3). Most of these studies did not indicate that the proportions reported were higher or different from the general population. A summary of the range in proportions reported across studies for each outcome is listed below:
    - Severe COVID-19 disease: 5.3% - 26.1%
    - Critical COVID-19 disease: 1.4% - 5%
    - Mortality: 0 – 2.0% / ICU mortality: 15.4%
    - Hospitalized for COVID-19: 0% - 28%
    - Oxygen therapy among hospitalized COVID-19 cases: 7% - 32%
    - ICU overall COVID-19 cases: 2% -10%
    - Mechanical Ventilation overall COVID-19 cases: 2 - 3.4% / ICU: 11 - 61.5%

    - ECMO overall COVID-19 cases: 0.03% - 2.3%
    - Induction of delivery due to COVID-19 disease: 9% - 19.0%
- One study based on USA surveillance data reported that the adjusted risk ratio for hospitalizations among pregnant women during the beginning of the epidemic was 5.4 times that of non-pregnant women of reproductive age (Ellington et al., 2020). This study also reported higher adjusted relative risk of ICU admission 1.5 times and mechanical ventilation 1.7 times, but no difference in the adjusted relative risk of mortality. This data could not distinguish hospitalizations for COVID-19 from other reasons for hospital admission (e.g., pregnancy-related treatment, or labor and delivery, which are common during pregnancy), thus it is unknown what proportion of the risk of hospitalization between pregnant and non-pregnant women can be attributed to pregnancy versus a possible increased risk due to COVID-19 during pregnancy.
- Another large hospital dataset from New York, USA compared the hospitalization rates of weeks one and four of the epidemic between pregnant women [RR 14.81 (95%CI 2.07-107.38) N=3064] and total hospitalizations [RR 46.99 (95% CI, 36.72-60.15) N=21980] (Tekbali et al., 2020). The study concludes that the increase in risk of the general population being hospitalized was more than for pregnant women in the first month of the epidemic. However, without a measure of excess hospitalizations due to COVID-19, these results are difficult to interpret.
- A study from China, documented that pregnant women were more likely to be admitted to the hospital sooner and with more mild symptoms compared to non-pregnant COVID-19 cases, which may bias outcomes such as hospitalization when comparing pregnant women to non-pregnant populations (Wang, Wang, & Xiong, 2020).
- There was no association with COVID-19 status and spontaneous abortion in the first trimester (S. Cosma et al., 2020b).
- There was some indication that women in the third trimester are more likely to have clinical symptoms and be diagnosed with pneumonia related to SARS-CoV-2 infection compared to those in the first trimester (Crovetto et al., 2020).
- Risk factors for severe COVID-19 disease among pregnant women included age>35, comorbidities and/or obesity (Table 2 & 3) (Cohen, Vignaux, & Jacquemard, 2020; Khalil et al.; Vivanti et al., 2020).

Overview of the Evidence

A range of retrospective and prospective case series and cohorts, case-control studies, cross-sectional data from surveillance and systematic reviews of relevant outcomes were identified, and provide evidence for this review. Retrospective observational studies, case reports and case series are considered to have a high risk of bias. The case-control study in this review did not have a large enough sample size to detect a difference between groups. The prospective studies and cohort designs have moderate to low risk of bias. Included

systematic reviews were evaluated using the AMSTAR quality assessment tool, and only reviews of moderate and high quality were summarized as those of low quality were missing key methodological steps. Those systematic reviews that were also evaluated by McMaster Plus are noted along with their quality score.

A large amount of heterogeneity across studies was identified for most outcomes that relate to severity of COVID-19 in pregnant women. This is likely due to variation in where and how the observations were collected, as well as the wide variability in sample size.

CONTENTS

OBSERVATIONAL STUDIES

Observational study data that has exposed and unexposed, diseased and healthy individuals in the sampling frame are needed to address the question of whether pregnant women are at higher risk of severe COVID-19 disease. Recent research from the USA and surveillance data from the CDC (July 16, 2020) suggest that pregnant women are at higher risk of hospitalization (3381/10156), ICU admission (160/3302) and mechanical ventilation (63/2856), but their risk for death is the same. These conclusions are supported by an MMWR paper based on the same surveillance data, in which the authors analyzed COVID-19 outcomes for all women of reproductive age (Ellington et al., 2020). Their analysis reports significantly higher adjusted risk ratios for hospitalization, ICU admittance and mechanical ventilation among women who are pregnant, controlling for age, ethnicity and presence of comorbidities. However, due to the nature of this dataset it is unknown if hospitalization, ICU or mechanical ventilation were due to COVID-19 disease, or due to conditions related to pregnancy.

Another large hospitalizations dataset from New York in the beginning of the epidemic compared the hospitalization rates of pregnant women vs. total hospitalizations (Tekbali et al., 2020). They report that the increased risk of hospitalization for pregnant women over the first four weeks of the epidemic in New York was lower [RR 14.81 (95%CI 2.07-107.38) N=3064] than for the rest of the population [RR 46.99 (95% CI, 36.72-60.15) N=21980] (Tekbali et al., 2020). This analysis did not control for any potential confounders and the results imply that the increased risk of hospitalization was lower during the first four weeks of the epidemic for pregnant women compared to the general population. However, the reasons for this difference were not explored. Another study from China documented that pregnant women were more likely to be admitted to the hospital sooner and with more mild symptoms compared to non-pregnant COVID-19 cases

(Wang et al., 2020). During pregnancy women may be admitted to the hospital for several reasons that would be unrelated to COVID-19 (e.g., to deliver, for pregnancy related complications and illness) which makes it difficult to interpret the high relative risk for hospitalization presented by (Ellington et al., 2020) or the lower increase in risk of hospitalization for pregnant women in the first four weeks of the epidemic in New York (Tekbali et al., 2020).

Several studies prospectively enrolled pregnant women attending the first trimester visit, a third trimester visit, or at delivery during the pandemic. Enrolled women were screened for SARS-CoV-2 infection and the impact of COVID-19 infection was evaluated compared to non-infected pregnant women (S. Cosma et al., 2020a; S. Cosma et al., 2020b; Fassett et al., 2020; Mohr-Sasson et al., 2020; Ruggiero, Somigliana, Tassis, & et al., 2020). There was no evidence that COVID-19 infection is associated with spontaneous abortions [RR 1.28 (95%CI 0.53-3.08)] in first trimester pregnancies (S. Cosma et al., 2020b). Two studies reported infected first trimester pregnancies were largely asymptomatic and none were hospitalized (S. Cosma et al., 2020a; Crovetto et al., 2020). Serological evidence of exposure to SARS-CoV-2 in first trimester and third trimester women report risk of exposure is the same, and that women in the third trimester were more likely to be hospitalized (0% vs. 9%) and treated for pneumonia (0% vs. 4.2%) (Crovetto et al., 2020). Post-partum complications resulting in re-admittance to the hospital was reported to be significantly higher in COVID-19 positive cases 12.9% (N=70) compared to non-COVID-19 controls 4.5% (N=605), p<0.001 (Prabhu et al., 2020). Other studies conclude that most infected pregnant women are not at higher risk of hospitalization compared to non-infected pregnant women (Fassett et al., 2020; Mohr-Sasson et al., 2020). In one study, there was no evidence of an association with COVID-19 status among pregnant women and other risk factors (e.g., age and comorbidities) (Ruggiero et al., 2020).

There were few deaths recorded among the observational studies (Table 1-3) of pregnant women. One study of USA surveillance data concluded that mortality was the same among pregnant and non-pregnant women with COVID-19 of reproductive age (Ellington et al., 2020).

Table 1: Observational studies (cohorts, case control studies), N=10 published June 8- July 10*, that compared pregnant COVID-19 cases to severity outcomes in the general population or severe outcomes in non-infected pregnant groups.

Reference	Country	Dates	Trimester	Study Design	Key outcomes
Primary Research					
(Ellington et al., 2020)	USA	Jan 22- Jun 7	Not specified	Cross-section of surveillance data Data represents 50 states Women age 15-44 with confirmed COVID-19	Hospitalization: pregnant 31.5%, control 5.8% aRR 5.4 (95%CI 5.1-5.6) (Data were not available to distinguish hospitalization for COVID-19–related circumstances (e.g., worsening respiratory status) from hospital

				N=91412 (8207 pregnant)	admission for pregnancy-related treatment or procedures (e.g., delivery).) ICU aRR 1.5 (95%CI 1.2-1,8) Mechanical Ventilation aRR 1.7 (95%CI 1.2-2.4) Mortality : pregnant 0.2% and control 0.2% aRR 0.9 (95%CI 0.5-1.5) *Adjusted for comorbidities, age, ethnicity
(S. Cosma et al., 2020a)	Italy	Apr 16 – Jun 4	1st trimester	Prospective cohort – consecutive pregnant women (n=138) attending their 12 week appointment at a single hospital	Prevalence 10.1% 14/138 (8 seropositive, 6 RT-PCR) None of the patients were hospitalized or treated for pneumonia associated with COVID-19
(Prabhu et al., 2020)	USA	Mar 22-Apr 27	> 20 weeks	Prospective cohort- women (n=675) admitted for delivery at 3 New York hospitals	COVID-19 cases 10.4% (70/675), 55 asymptomatic Readmission for postpartum complication COVID-19 12.9% vs. control 4.5%, p<0.001 ICU 1 No woman had mechanical ventilation No maternal deaths
(Fassett et al., 2020)	USA	Apr 6- May 11	3rd trimester	Prospective Cohort – women (N=3963) admitted to delivery at the KPSC hospitals in southern California	Prevalence COVID-19: 0.43%; 95% CI 0.23-0.63%, (17/3923) All COVID-19 cases were asymptomatic on admission
(Tekbali et al., 2020)	USA	Mar 2- Mar 29	NR	Analysis of the COVID-19 cases collected from a 14 hospital database.(N=21980 admissions of which 3064 were pregnant)	Over the four week period the relative risk of hospital admission for COVID-19 increased: Pregnant: RR 14.81 (95%CI 2.07-107.38) All hospital admissions : RR 46.99 (95% CI, 36.72-60.15) Study does not try to adjust for age or other confounders/risk factors. It is also discussed that reproductive age women are younger and less likely to be symptomatic or get tested, and most of the

					admissions for pregnant women were for labor and delivery
(Mohr-Sasson et al., 2020)	Israel	NR	3rd trimester	Case-control study comparing 11 pregnant COVID-19 cases with 25 age-matched non-pregnant controls. This study was underpowered	Hospitalization 7/11 pregnant vs. 20/25 controls p=0.29, lower admission rate, but not significant Noted clinical measures of severity that were different in the COVID-19 group: • Lymphocyte count to WBC was significantly reduced in the pregnant group compared to the controls [13.6% (4.5–19.3) vs. 26.5% (15.7–29.9); p=0.003, • pCO2 was significantly lower [39 (31–43 vs.46 (45–57); p=0.004] • base excess was significantly elevated [(−2.9)[(−7.9) − (−1.7)] vs. 0.4(0.05–2); p=0.004]
(Crovetto et al., 2020) *Preprint*	Spain	Apr 14- May 5	1st Trimester (N=372) and 3rd trimester (N=502)	Cohort of pregnant women (N=874) at their first trimester appointment or delivery. Serology, and a questionnaire collected data on previous COVID-19 status	Seropositivity to SARS-CoV-2 were the same in 1st trimester (14.3%) and 3rd trimester patients (14.1%), the authors concluded there is no difference in susceptibility between 1st and 3rd trimester. Hospital admission for COVID-19 was 0% and 9.9% for 1st and 3rd trimester. Severity of COVID-19, 1st vs. 3rd trimester Asymptomatic 70.4% vs. 52.1% Mild: 29.6% vs. 43.7% Pneumonia 0% vs. 4.2% There were higher proportions of symptomatic infections in the 3rd trimester, which is in line with other studies where a high proportion are in the 3rd trimester.

(S. Cosma et al., 2020b)	Italy	Feb 22- May 21	1st trimester	Case control study comparing spontaneous abortion and COVID-19 status	Cumulative incidence of COVID-19 between the cases (11/100, 11%) and the controls (12/125, 9.6%) (p=0.73) was the same. Logistic regression analysis confirmed that COVID-19 was not an independent predictor of abortion (1.28, 95%CI 0.53-3.08).
(RUGGIERO et al., 2020)	Italy	Apr 7 – May 6	3rd trimester	Cohort of all women delivering (N=315) at an obstetrics hospital in Milan	COVID-19 8.9%, 95%CI: 6.2–12.5%, 28/315 There was no difference between the COVID-19 group and the control group in terms of risk factors or disease outcomes.
(Wang et al., 2020)	China	Dec 8 – Apr 1	NR	Retrospective study of 30 pregnant COVID-19 cases and 42 non-pregnant COVID-19 cases in Wuhan	Pregnant women were admitted to the hospital earlier (0.25 vs. 11.00 days; P<0.001), and with milder symptoms. The proportion of asymptomatic pregnant women were 26.7% vs. 0% among non-pregnant COVID-19 cases.

* The most recent systematic review on this topic searched the literature up to June 8, 2020 and is described in Table 2.
aRR= adjusted risk ratio, RR= risk ratio

SYSTEMATIC REVIEWS

There were 38 studies that identified as a systematic review, meta-analysis, scoping review, rapid review or umbrella review and had outcomes on severity of COVID-19 in pregnant women. Only nine of these were considered of moderate or high quality with most reviews failing to describe *a priori* development of a protocol and to a lesser extent other key components of conducting synthesis research.

Studies included in the systematic reviews vary depending on search date, inclusion and exclusion criteria. Most included studies are case reports and case series with some of the newer ones also identifying case control studies. Meta-analysis or raw data on the proportions of hospitalization, severe/critical COVID-19, ICU admission, oxygen therapy, mechanical ventilation and death are reported in the systematic reviews and most have a significant amount of heterogeneity across studies (Table 2). A comparable proportion in a non-pregnant population was not reported in most reviews as the data is based largely on case series. Sources of heterogeneity likely include the selection procedure for inclusion in a study, e.g., prospective enrollment, retrospective medical records, or just a summary of a couple of cases without details of selection. There is also likely

variation depending on the spectrum of COVID-19 severity, outpatient clinic vs. hospital case selection, admittance to labor and delivery or hospitalized for COVID-19.

Table 2: Summary of the findings of systematic reviews evaluated to be of moderate or high quality (9/38) using the AMSTAR quality assessment tool with outcomes relevant to severity of COVID-19 in pregnant women.

Reference	Study Design	Quality (AMSTAR)	# Studies/ Observations/ Details	Key Outcomes
Systematic Review				
(Khalil et al., 2020)	Systematic Review and meta-analysis. Search data June 8, 2020.	High	17 studies with > 15 observations (86 included in qualitative summary) global/ 25676 pregnancies/ most women were in the 3rd trimester or post partum	Asymptomatic: 253/1205, 14.5% (5.6–32.5%), I^2=97.0% Prevalence of Risk Factors across samples: • Obesity 509/1725, 38.2% (23.6–55.4%), I^2=97% • Any co-morbidity 252/776, 32.5% (29.3–35.8%), I^2=0% ICU: 159/1591, 7% (95%CI 4-11), I^2=82% Oxygen Support: 295/1623, 18.2% (9.8–31.1%), I^2=95.5% Mechanical Ventilation 92/1680, 3.4% (1.5–7.7%), I^2=90.2% ECMO 13/1896, 0.7% (0.4–1.2%), I^2=0.0% Mortality 43/2650, 0.9% (0.3–2.9%), I^2=84.4% Deliver due to COVID-19 related reason: 95/497, 19.0% (8.9–36.0%), I^2=89.4% - ICU in pregnant women with COVID-19 was ~7% across studies for pregnant women, which is higher than 4.2% (CDC COVID-19 Response Team, 2020) reported by USA surveillance data for the reproductive age group. - ICU admittance was associated with older age (>35) and comorbidities (p<0.05). Trimester of pregnancy, ethnicity and obesity did not explain the heterogeneity in ICU or maternal death.
(Trippella et al., 2020)	Systematic Review. Search	Moderate	37 (China and Other countries)/275	Oxygen therapy: 36/275 (13%) ICU: 10/275 (4%) Mechanical ventilation: 5/275 (2%)

	date April 18, 2020. Includes epidemiological studies, case reports	(9/10 McMaster Plus)	pregnancies, 239 deliveries	ECMO: 1/275 (0.03%) Mortality: 1/275 (0.03%) The majority of pregnant women had mild or moderate disease with a low incidence of severe complications and low mortality rates.
(Huntley et al., 2020)	Systematic Review. Reports of >10 observations. Search date April 29, 2020. Includes mainly case reports and case series.	High (9/10 McMaster Plus)	13 (China, US, Italy, Data Jan-Apr 4)/538 pregnancies % 438 deliveries	Mild COVID-19: 86.1% (81.5–89.7) Severe COVID-19: 15.3% (11.1–20.8) ICU admission: 3.0% (95% CI 1.6–5.9, 8/263) Critical disease: 1.4% (95% CI 0.5–4.1, 3/209) Deaths: 0% (95% CI 0.0–1.1, 0/348) Approximately 1 in 3 pregnant women with SARS-CoV-2 had a comorbidity across studies.
(Juan et al., 2020)	Systematic Review. Search date April 20, 2020. Includes 9 case series and 15 case reports.	Moderate (8/10 McMaster Plus)	24 (China, Australia, Canada, France, Korea, Iran, Italy, Sweden, Turkey, USA)/324 pregnancies/ maternal age 20-44 and gestational age 5-41 weeks	Severe pneumonia 0-14% across studies, most admitted to ICU One case series from Iran of severe COVID-19 pregnant women had 7 death/9 ICU admitted cases on mechanical ventilation. This review also summarizes comorbidities and reports the frequency to be similar to the general population.
(Gao, Ye, & Zhang, 2020) *Preprint*	Systematic Review. Search Date April 16,	Moderate	14 (China, USA)/ 236 pregnancies	Pregnant Women Severe case or death MA: 12%, 95%CI: 0.03~0.20, I^2 =0%, P=0.006 Co-morbidities MA: 33%, 95%CI: 0.21~0.44, I^2=70%, P=0.000

	2020. Only studies with >5 observations. Includes case reports, case series and observational studies			
(Smith et al., 2020)	Systematic Review. Search date March 28, 2020 Includes: case series and 1 controlled before and after study design.	Moderate (8/10 McMaster Plus)	9 (China)/ 92 pregnancies	Hospitalized:34.7%, 32/92 Oxygen therapy: 28.1%, 9/32 hospitalized ICU: 3.1%, 1/32 hospitalized Mortality: 0/32 Many pregnant women captured across these studies were asymptomatic and afebrile at presentation. Lymphopenia: 66.7% (similar to SARS 67% and MERS 50%) and was NOT associated with worse prognosis in pregnant women. ICU and mortality for pregnant women with SARS-CoV-2 appears lower than for SARS (15-18%/30%) and MERS (25-27%/ 60%)
(Yang, Wang, Zhu, & Liu, 2020)	Systematic Review. Search date March 26, 2020 Includes case reports, case series and 1 case control.	Moderate	18/114 pregnancies	Severe/Critical: 5.3%, 6/114 ECMO 0.9%: 1/114 The only case-control study suggested no differences in preeclampsia, gestational diabetes mellitus, and premature rupture of membrane between COVID-19 and non-COVID-19 groups. In general, the clinical characteristics of pregnant women are similar to those of non-pregnant adults
(Gajbhiye, Modi, & Mahale, 2020) *Preprint*	Systematic Review. Search Date May 3, 2020.	Moderate	50 (china, USA, Iran, Australia, Canada, Korea, Honduras, Jordan, Spain, Peru, Sweden,	ICU with mechanical ventilation: 11% Oxygen therapy: 24% ECMO: 2.3%, 10/441 Deaths: 2.0%, 9/441

	Includes case series, case reports.		Turkey, Italy, Portugal, Switzerland, India)/ 441 pregnancies, 387 deliveries/ 95% of the women were in the 3rd trimester	
(Sun et al., 2020) *Preprint*	Systematic Review. Search Date March 11, 2020.	High	17/ 21 SARS, 11 MERS, 41 COVID-19 pregnancies	Hospital stay >15 days: COVID-19 (50% [95%CI -0·19-1·19], p>0·05) MERS: (80% [95%CI 0·45-1·15], p<0·05) Fatality Rate COVID-19: 0% MERS: 40% ([95%CI -0·03-0·83], p>0·05) SARS: 25% ([95%CI 0·01-0·49], p<0·05)

CASE SERIES

Case series and case reports are the most common study design used to describe COVID-19 impacts on pregnancy. As this review question was about whether there is more severe COVID-19 disease among pregnant women we targeted new case series with more than 30 observations. There were 16 case reports published between June 8-July 10 that were excluded by this cut point.

Table 3: Case series (>30 women) published June 8- July 10 summarizing the probability of severe outcomes in pregnant COVID-19 cases.

Reference	Country	Dates	Trimester	Study Design	Key outcomes
Primary Research					

(Cohen et al., 2020)}	France	Not specified	1-3 (27 weeks median, range 4-34)	Survey of pregnant women with COVID-19 in France (self-identified) N=194. Only data on RT-PCR confirmed cases was analysed, N= 88. Recruitment bias	Hospitalization 18/88 (20%) Severe disease with oxygen therapy 6/88 (7%) Uterine contractions 15/88 (2 severe) Delivery: 14/88 (1 severe) Severe disease was seen in older women p=0.009., higher BMI p=0.002, and those with diabetes (50% vs. 5%) p=0.006
(Vivanti et al., 2020)	France	Mar 12- Apr 13	14 weeks and 2 days postpartum	Retrospective multicenter review of medical records (N=100)	Hospitalized 52/100 ICU 10/100 Oxygen therapy 32/100 Risk factors for hospitalization: - BMI high vs. lower p=0.003 - Not significant were maternal age, gestational age, parity, and comorbidities.
(Sentilhes et al., 2020)	France	Mar 1- Apr 3	NR	Retrospective case series of all pregnant women with COVID-10 (N=54) in Strasbourg	Oxygen therapy 24.1%, 13/54 Mechanical ventilation in 3/13 ECMO 1/13 Medically indicated premature birth (>37 weeks) due to severe COVID-19: 5/54
(Lokken, Walker, & Adams Waldorf, 2020)	USA	Jan21- Apr 17	2nd trimester (N=20), 3rd trimester (N=23)	Retrospective Case series of pregnant women with hospital entries for COVID-19 (N=46) in Washington State hospitals	Severe 15%, 6/46 (all overweight or with comorbidities) Hospitalization: 16%, 7/46 ICU 1/46
(Khoury et al., 2020)	USA	Mar 13 – Apr 12	Term	Prospective cohort of COVID-19 cases (N=241) that gave birth across 5 New York medical centers	Asymptomatic 42.1%, 102/241 Mild 26.5%,, 64/241 Severe 26.1%, 63/241 Critical 5%, 12/241 ICU 7.1%, 17/241 Mechanical ventilation 3.7%, 9/241 Deaths 0%

					Risk Factors: BMI was associated with severity p=0.001
(Blitz et al., 2020)	USA	Mar 1- May 6	NR	Case Series of COVID-19 confirmed cases in pregnant women (N=462) in 10 hospitals in New York state	Severe or critical 15.2% 70/462 ICU 18.6%, 13/70 Deaths 15.4%, 2/13 (and overall) Invasive mechanical ventilation 61.5%, 8/13 5 emergency deliveries were performed in the ICU cases prior to invasive mechanical ventilation due to COVID-19 symptoms.
(San-Juan et al., 2020)	Spain	Mar 5- Apr 6	2nd trimester (N=9), 3rd trimester (N=22)	Retrospective cohort, patients enrolled at diagnosis (N=52)	COVID-19 pneumonia was diagnosed in 61.5%, 32/54 Oxygen therapy 56%,18/32 ARDS 25%, 8/32 ICU 6.4%, 2/32 Mortality 0/32

* The most recent systematic review on this topic searched the literature up to June 8, 2020 and is described in Table 2.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: pregnancy or pregnant or maternal
This review contains research published up to July 14, 2020
Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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Preuve émergente sur la COVID-19

Synthèse en bref des données probantes sur la grossesse et la gravité de la COVID-19

Introduction

Les femmes enceintes ont-elles un risque plus élevé d'être atteintes d'une forme grave de COVID-19 que les femmes non enceintes en âge de procréer?

Les femmes enceintes représentent une population potentiellement vulnérable et l'on peut s'attendre à ce qu'elles présentent des symptômes et une évolution de la maladie différents de ceux de la population en général en raison des changements physiologiques qu'elles vivent pendant la grossesse. L'objectif de cette synthèse en bref vise à faire synthétiser les études sur l'évolution de la COVID-19 chez les femmes enceintes afin d'évaluer s'il existe des données probantes indiquant que l'évolution de cette maladie est plus grave chez ces femmes que dans la population en général. Ce document porte sur l'évolution de la COVID-19, mais n'inclut aucune donnée de synthèse en ce qui concerne l'issue de la grossesse ou l'évolution de la maladie chez les nouveau-nés, et comprend des études publiées jusqu'au 13 juillet 2020.

Points clés

- Les études portant sur la gravité de la COVID-19 chez les femmes enceintes comparativement aux femmes enceintes non infectées ou aux femmes non enceintes atteintes de la COVID-19 présentent des résultats variables non comparables d'une étude à l'autre en raison du plan de chacune des études.
- Des études prospectives sur les femmes enceintes révèlent qu'une faible proportion de ces femmes ont été infectées par la COVID-19 pendant la première phase de l'épidémie (à noter que cela n'a pas été comparé au taux d'infection dans la population en général). Les femmes qui se sont inscrites aux études en étaient à différentes étapes de leur grossesse allant des premières visites pendant le premier trimestre à l'accouchement et bon nombre d'entre elles étaient positives à la COVID-19 et asymptomatiques. Bon nombre de ces études font état de presque zéro hospitalisation ou évolution grave (tableau 1).
- Les séries de cas prospectifs et rétrospectifs indiquent un spectre de gravité de l'infection associée à la COVID-19 chez les femmes enceintes, avec une hétérogénéité importante entre les estimations découlant des études et les méta-analyses de la revue systématique (tableaux 2 et 3). La plupart de ces études n'indiquaient pas que les proportions déclarées étaient plus élevées que dans la population en général ou différentes de celles-ci. Voici un résumé de l'éventail de proportions déclarées dans les études pour chaque résultat découlant de l'évolution de la maladie :

  - Maladie grave associée à la COVID-19 : entre 5,3 % et 26,1 %
  - Maladie très grave associée à la COVID-19 : entre 1,4 % et 5 %
  - Mortalité : entre 0 % et 2,0 %/mortalité pendant le séjour dans les USI : 15,4 %
  - Hospitalisation en raison de la COVID-19 : entre 0 % et 28 %
  - Oxygénothérapie utilisée parmi les cas d'infection à la COVID-19 ayant exigé une hospitalisation : entre 7 % et 32 %
  - Taux global de COVID-19 dans les USI : entre 2 % et 10 %
  - Taux global de COVID-19 ayant exigé l'utilisation d'un ventilateur mécanique : entre 2 % et 3,4 %/dans les USI : entre 11 % et 61,5 %
  - Taux global de COVID-19 ayant exigé une ECMO : entre 0,03 % et 2,3 %
  - Accouchement provoqué en raison de la COVID-19 : entre 9 % et 19,0 %
- Une étude fondée sur des données de surveillance aux États-Unis a révélé que le risque relatif ajusté pour les hospitalisations chez les femmes enceintes au début de l'épidémie était 5,4 fois supérieur à celui des femmes non enceintes en âge de procréer (Ellington et coll., 2020). Cette étude a également indiqué un risque relatif ajusté 1,5 fois supérieur pour l'admission aux soins intensifs et 1,7 fois supérieur pour le ventilateur mécanique, mais aucune différence dans le risque relatif ajusté de mortalité. Ces données n'ont pas permis de faire une distinction entre les hospitalisations en raison de la COVID-19 et des autres motifs d'admission à l'hôpital (p. ex., traitements liés à la grossesse, au travail et à l'accouchement, qui sont courants pendant la grossesse). On ne sait donc pas quelle proportion du risque d'hospitalisation chez les femmes enceintes et celles qui ne le sont pas peut être attribuée à la grossesse plutôt qu'à un risque accru possible en raison de la COVID-19 pendant la grossesse.
- Un autre grand ensemble de données provenant des hôpitaux de New York, aux États-Unis, a comparé les taux d'hospitalisation pendant les semaines un et quatre de l'épidémie chez les femmes enceintes [RRA de 14,81 (2,07 à 107,38, IC à 95 %) N=3 064] aux hospitalisations totales [RRA de 46,99 (36,72 à 60,15, IC à 95 %)) N=21 980] (Tekbali et coll., 2020). L'étude a conclu que l'augmentation du risque d'hospitalisation dans la population en général était supérieure à celle des femmes enceintes pendant le premier mois de l'épidémie. Toutefois, sans éléments permettant de mesurer les hospitalisations supplémentaires associées à la COVID-19, ces résultats sont difficiles à interpréter.
- Une étude menée en Chine a révélé que les femmes enceintes étaient plus susceptibles d'être admises plus tôt à l'hôpital et de présenter des symptômes plus bénins que les femmes non enceintes atteintes de COVID-19, ce qui peut fausser les résultats comme en ce qui concerne les hospitalisations, lorsqu'on compare les femmes enceintes aux populations non enceintes (Wang, Wang et Xiong, 2020).
- Il n'y avait aucun lien entre le fait d'être atteinte de COVID-19 et l'avortement spontané au cours du premier trimestre (S. Cosma et coll., 2020b).
- Selon certaines indications, les femmes qui en sont à leur troisième trimestre sont plus susceptibles d'avoir des symptômes cliniques et de recevoir un diagnostic de pneumonie liée à une infection par le SRAS-CoV-2 que celles qui en sont à leur premier trimestre (Crovetto et coll., 2020).

- Les facteurs de risque de maladie grave liée à la COVID-19 chez les femmes enceintes comprenaient l'âge (> 35 ans), les comorbidités ou l'obésité (tableaux 2 et 3) (Cohen, Vignaux et Jacquemard, 2020; Khalil et coll.; Vivanti et coll., 2020).

Vue d'ensemble des éléments de preuve

Un éventail de séries de cas et de cohortes rétrospectives et prospectives, d'études cas-témoins, de données transversales provenant de la surveillance et de l'examen systématique de l'évolution pertinente de la maladie a été établi et fournit des données probantes pour cet examen. Les études d'observation rétrospectives, les rapports de cas et les séries de cas sont jugés présenter un risque élevé de biais. La taille de l'étude cas/témoins de cette étude n'était pas assez grande pour permettre de déceler une différence entre les groupes. Les études prospectives et les cohortes présentent un risque modéré à faible de biais. Les examens systématiques inclus ont été évalués à l'aide de l'outil d'évaluation de la qualité AMSTAR, et seuls les examens de qualité moyenne et élevée ont été résumés puisque ceux de faible qualité ne comportaient pas d'étapes méthodologiques clés. Les examens systématiques ayant également été évalués par McMaster Plus sont mentionnés, avec leur cote de qualité.

Les études ont révélé une grande hétérogénéité en ce qui concerne l'évolution et la gravité de la COVID-19 chez les femmes enceintes. Cette homogénéité est probablement attribuable aux variations liées à l'endroit et à la façon dont les observations ont été notées, ainsi qu'à la grande variabilité dans la taille des échantillons.

CONTENU

ÉTUDES D'OBSERVATION

Des données d'études d'observation sur des femmes exposées et non exposées, malades et en santé dans la base d'échantillonnage sont nécessaires pour déterminer si les femmes enceintes sont plus à risque de contracter une forme grave de la COVID-19. Les données des recherches récentes menées aux États-Unis et les données de surveillance du CDC (16 juillet 2020) suggèrent que les femmes enceintes sont plus à risque d'être hospitalisées (3 381/10 156), d'être admisses aux soins intensifs (160/3 302) et de devoir être mises sous ventilateur mécanique (63/2 856), mais que leur risque de décès est le même. Ces conclusions sont

appuyées par un document du MMWR fondé sur les mêmes données de surveillance, dans lequel les auteurs ont analysé l'évolution de la COVID-19 chez l'ensemble des femmes en âge de procréer (Ellington et coll., 2020). Leur analyse révèle un taux de risque ajusté beaucoup plus élevé en ce qui concerne l'hospitalisation, l'admission aux soins intensifs et le recours au ventilateur mécanique chez les femmes enceintes, compte tenu de l'âge, de l'origine ethnique et de la présence de comorbidités. Toutefois, en raison de la nature de cet ensemble de données, on ne sait pas si l'hospitalisation, le séjour aux soins intensifs ou le recours au ventilateur mécanique étaient attribuables à la COVID-19 ou à des problèmes liés à la grossesse.

Un autre important ensemble de données sur les hospitalisations émanant de New York au début de l'épidémie comparait les taux d'hospitalisation des femmes enceintes par rapport au nombre total d'hospitalisations (Tekbali et coll., 2020). Il indiquait que le risque accru d'hospitalisation des femmes enceintes pendant les quatre premières semaines de l'épidémie à New York était plus faible [RRA de 14,81 (2,07 à 107,38, IC à 95 %)) N=3 064] que pour le reste de la population [RR 46,99 (36,72 à 60,15, IC à 95 %)) N=21 980] (Tekbali et coll., 2020). Cette analyse n'a cependant pas pu contrôler certaines variables confusionnelles et ses résultats sous-entendent que le risque accru d'hospitalisation était plus faible chez les femmes enceintes pendant les quatre premières semaines de l'épidémie que dans la population en général. Toutefois, les raisons de cette différence n'ont pas été examinées. Une autre étude menée en Chine a révélé que les femmes enceintes étaient plus susceptibles d'être admises à l'hôpital plus tôt avec des symptômes plus bénins comparé aux femmes non enceintes atteintes de COVID-19.

(Wang et coll., 2020). Pendant la grossesse, les femmes ont pu être admises à l'hôpital pour différentes raisons sans lien avec la COVID-19 (par exemple, pour accoucher, en raison de complications et de maladies liées à la grossesse), ce qui rend difficile l'interprétation du risque relatif élevé d'hospitalisation présenté par (Ellington et coll., 2020) ou la plus faible augmentation du risque d'hospitalisation des femmes enceintes pendant les quatre premières semaines de l'épidémie à New York (Tekbali et coll., 2020).

Pendant la pandémie, plusieurs études ont inscrit de manière prospective des femmes enceintes qui allaient à l'hôpital dans le cadre d'un rendez-vous pendant le premier trimestre ou le troisième trimestre ou au moment de leur accouchement. Ces femmes ont été soumises à un dépistage de l'infection par le SRAS-CoV-2 et les répercussions de l'infection par COVID-19 a ont été évalué par rapport aux femmes enceintes non infectées (S. Cosma et coll., 2020a; S. Cosma et coll., 2020b; Fassett et coll., 2020; Mohr-Sasson et coll., 2020; Ruggiero, Somigliana, Tassis et coll., 2020). Il n'a pas été démontré que l'infection par COVID-19 était associée à des avortements spontanés [RRA de 1,28 (0,53 à 3,08, IC à 95 %))] pendant le premier trimestre de la grossesse (S. Cosma et coll., 2020b). Deux études ont indiqué que les femmes infectées, qui en étaient au premier trimestre, étaient en grande partie asymptomatiques et qu'aucune n'avait été hospitalisée (S. Cosma et coll., 2020a; Crovetto et coll., 2020). Les signes sérologiques de l'exposition au SRAS-CoV-2 pendant le premier et le troisième trimestre indiquent que le risque d'exposition était le même et que les femmes qui en étaient au troisième trimestre étaient plus susceptibles d'être hospitalisées (0 % c. 9 %) et traitées pour une pneumonie (0 % c. 4,2 %) (Crovetto et coll., 2020). Les complications post-partum ayant entraîné une réadmission à l'hôpital ont été signalées comme étant significativement plus élevées chez les femmes ayant

été déclarées positives à la COVID-19 par rapport aux femmes témoins non atteintes de COVID-19 dans une proportion de 12,9 % (N=70) et de 4,5 % (N=605), p< 0,001 respectivement (Prabhu et coll., 2020). D'autres études ont conclu que bon nombre des femmes enceintes infectées ne présentaient pas de risque d'hospitalisation plus élevé que les femmes enceintes non infectées (Fassett et coll., 2020; Mohr-Sasson et coll., 2020). Dans une étude, aucune preuve n'a pu établir de lien entre la situation liée à la COVID-19 chez les femmes enceintes et d'autres facteurs de risque (par exemple, l'âge et les comorbidités) (Ruggiero et coll., 2020).

Peu de décès ont été enregistrés dans les études d'observation (tableau 1-3) chez les femmes enceintes. Une étude avec données de surveillance aux États-Unis a conclu que le taux de mortalité était le même chez les femmes enceintes et non enceintes en âge de procréer atteintes de COVID-19 (Ellington et coll., 2020).

Tableau 1 : Études d'observation (cohortes, études de comparaison avec témoins), N=10 publiées entre le 8 juin et le 10 juillet* ayant comparé les cas de femmes enceintes atteintes de COVID-19 à la gravité de la maladie dans la population en général ou à des infections graves parmi les groupes de femmes enceintes non infectées.

Référence	Pays	Dates	Trimestre	Plan de l'étude	Principaux résultats
Recherche originale					
(Ellington et coll., 2020)	États-Unis	22 janvier au 7 juin	Non précisé	Échantillon représentatif des données de surveillance Données représentant 50 États Femmes de 15 à 44 ans dont la COVID-19 a été confirmée N=91 412 (8 207 étaient enceintes)	Hospitalisation : femmes enceintes 31,5 %, groupe de contrôle 5,8 % RRA de 5,4 (5,1 à 5,6, IC à 95 %) (Aucune donnée permettant de faire une distinction entre les hospitalisations en raison de circonstances liées à la COVID-19 (par exemple, aggravation de l'état respiratoire) et les admissions à l'hôpital pour un traitement ou des procédures liés à la grossesse (par exemple, l'accouchement).) RRA de 1,5 dans les USI (1,2 à 1,8, IC à 95 %) RRA de 1,7 avec le ventilateur mécanique (1,2 à 2,4, IC à 95 %) Mortalité : femmes enceintes 0,2 % et groupe de contrôle 0,2 % avec RRA de 0,9 (0,5 à 1,5, IC à 95 %) *Ajusté pour les comorbidités, l'âge, l'ethnicité
(S. Cosma et coll., 2020a)	Italie	16 avril au 4 juin	1er trimestre	Cohorte prospective - femmes enceintes (n=138)	Prévalence de 10,1 % 14/138 (8 séropositives, 6 RT-PCR)

				qui se présentent à leur visite à 12 semaines de grossesse dans un seul hôpital	Aucune des patientes n'a été hospitalisée ou traitée pour une pneumonie associée à la COVID-19
(Prabhu et coll., 2020)	États-Unis	22 mars au 27 avril	> 20 semaines	Cohorte prospective - femmes (n=675) admises pour accoucher dans 3 hôpitaux de New York	10,4 % (70/675) de cas de COVID-19, 55 asymptomatiques Réadmission pour complications post-partum 12,9 % de COVID-19 contre 4,5 %, p<0,001 pour le groupe de contrôle USI 1 Aucune femme n'a eu besoin du ventilateur mécanique Aucun décès maternel
(Fassett et coll., 2020)	États-Unis	6 avril au 11 mai	3e trimestre	Cohorte prospective - femmes (N=3 963) admises pour accoucher dans les hôpitaux du KPSC en Californie du Sud	Prévalence de COVID-19 : 0,43 %; IC à 95 % 0,23 à 0,63 %, (17/3 923) Tous les cas de COVID-19 étaient asymptomatiques lors de leur admission
(Tekbali et coll., 2020)	États-Unis	2 mars au 29 mars	N.d.	Analyse des cas de COVID-19 tirée d'une base de données de 14 hôpitaux (N=21 980 admissions, dont 3 064 femmes enceintes)	Pendant cette période de quatre semaines, le risque relatif d'admission à l'hôpital pour la COVID-19 a augmenté : Enceinte : RRA de 14,81 (2,07 à 107,38, IC à 95 %) Toutes les admissions à l'hôpital : RRA de 46,99 (36,72 à 60,15, IC à 95 %) L'étude n'a pas essayé d'ajouter les données en fonction de l'âge ou d'autres facteurs de confusion ou de risque. Il est également mentionné que les femmes en âge de procréer étaient plus jeunes et moins susceptibles de présenter des symptômes ou de se faire dépister, et que la plupart des femmes enceintes se présentaient à l'hôpital parce qu'elles étaient en plein travail et pour accoucher.

(Mohr-Sasson et coll., 2020)	Israël	N.d.	3e trimestre	Étude cas-témoins comparant 11 cas de COVID-19 chez des femmes enceintes avec groupe témoin de 25 femmes non enceintes appariées par âge. Cette étude ne comportait pas suffisamment de candidates.	Hospitalisation 7/11 femmes enceintes contre 20/25 dans le groupe témoins p=0,29, soit un taux d'admission plus faible, mais non significatif Mesures cliniques de gravité distinctes en ce qui concerne le groupe de femmes atteintes de COVID-19 : • la numération lymphocytaire par rapport au nombre de globules blancs était sensiblement inférieure dans le groupe de femmes enceintes par rapport au groupe témoin [13,6 % (4,5 à 19,3) contre 26,5 % (15,7 à 29,9); p=0,003, • la pCO2 était nettement inférieure [39 (31 à 43 contre 46 (45 à 57); p=0,004] • l'excès de base était nettement élevé [(-2,9) [(-7,9) à (-1,7)] par rapport à 0,4 (0,05 à 2); p=0,004]
(Crovetto et coll., 2020) *Prépublication*	Espagne	14 avril au 5 mai	1er trimestre (N=372) et 3e trimestre (N=502)	Cohorte de femmes enceintes (N=874) lors de leur rendez-vous au premier trimestre ou de leur accouchement. Sérologie, et un questionnaire a permis de recueillir des données sur leur situation précédente liée à la COVID-19	La séropositivité au SRAS-CoV-2 étant la même au 1er trimestre (14,3 %) et au 3e trimestre (14,1 %), les auteurs ont conclu qu'il n'y a pas de différence de susceptibilité entre le 1er et le 3e trimestre. L'admission à l'hôpital pour des raisons liées à la COVID-19 était de 0 % et de 9,9 % pour les 1er et 3e trimestres respectivement. Gravité de la COVID-19 entre le 1er et le 3e trimestre Asymptomatique : 70,4 % contre 52,1 % Bénigne : 29,6 % contre 43,7 % Pneumonie : 0 % contre 4,2 % Les proportions d'infections symptomatiques étaient plus élevées pendant le troisième trimestre, ce qui est conforme à d'autres études dans

					lesquelles une proportion plus élevée avait été remarquée pendant le troisième trimestre.
(S. Cosma et coll., 2020b)	Italie	22 février au 21 mai	1er trimestre	Étude cas/témoins visant à comparer les avortements spontanés et la situation liée à la COVID-19	L'incidence cumulée de COVID-19 entre les cas (11/100, 11 %) et les témoins (12/125, 9,6 %) (p=0,73) était la même. L'analyse de régression logistique a confirmé que la COVID-19 n'était pas un prédicteur indépendant de l'avortement (1,28, IC à 95 % 0,53 à 3,08).
(RUGGIERO et coll., 2020)	Italie	7 avril au 6 mai	3e trimestre	Cohorte comprenant toutes les femmes qui accouchent (N=315) dans un hôpital obstétrique de Milan	COVID-19 : 8,9 %, 6,2 à 12,5 %, IC à 95 %, 28/315 Il n'y avait aucune différence entre le groupe de femmes atteintes de la COVID-19 et le groupe témoin en ce qui concerne les facteurs de risque ou d'évolution de la maladie.
(Wang et coll., 2020)	Chine	8 décembre au 1er avril	N.d.	Étude rétrospective de 30 cas de COVID-19 chez des femmes enceintes et de 42 cas de COVID-19 chez des femmes non enceintes à Wuhan	Les femmes enceintes ont été admises à l'hôpital plus tôt (0,25 contre 11,00 jours; P<0,001), avec des symptômes plus légers. La proportion de femmes enceintes asymptomatiques était de 26,7 % contre 0 % pour les cas de COVID-19 chez les femmes non enceintes.

* L'étude systématique la plus récente à ce sujet a examiné la littérature publiée jusqu'au 8 juin 2020 et est décrite dans le tableau 2.

RRA= ratio de risque ajusté, RR= ratio de risque

REVUES SYSTÉMATIQUES

38 études ont été identifiées comme étant des revues systématiques, une méta-analyse, une revue exploratoire, une revue rapide ou une revue d'ensemble et incluaient de l'information sur la gravité de la COVID-19 chez les femmes enceintes. Seules neuf de ces études ont été jugées de qualité moyenne ou élevée, la plupart ne décrivant pas le développement *a priori* d'un protocole et, dans une moindre mesure, d'autres éléments clés de la recherche de synthèse.

Les études incluses dans les revues systématiques varient en fonction de la date de recherche, ainsi que des critères d'inclusion et d'exclusion. La plupart des études incluses sont des exposés de cas de cas et des séries de cas, alors que certaines des plus récentes ont également mentionné des études de comparaison avec les témoins. Les méta-analyses ou les données brutes sur les proportions d'hospitalisation, d'état grave ou sévère associé à la COVID-19, d'admission en USI, de recours à l'oxygénothérapie, d'utilisation du ventilateur mécanique et de décès sont indiqués dans les revues systématiques et bon nombre démontrent une grande hétérogénéité entre les études (tableau 2). Une proportion comparable dans une population de femmes non enceintes n'a pas été signalée dans la plupart des études, puisque les données sont fondées en grande partie sur des séries de cas. Les sources d'hétérogénéité comprennent probablement la procédure de sélection pour l'inclusion dans une étude, par exemple, l'inscription prospective, les dossiers médicaux rétrospectifs ou un simple résumé de quelques cas, sans détails sur la sélection. Il est également probable qu'il y ait des variations dans le spectre de gravité de la COVID-19, de la sélection des cas en clinique externe ou à l'hôpital, de l'admission en raison du travail et de l'accouchement ou de l'hospitalisation liée à la COVID-19.

Tableau 2 : Résumé des conclusions des revues systématiques évaluées comme étant de qualité moyenne ou élevée (9/38) à l'aide de l'outil d'évaluation de la qualité AMSTAR avec des résultats pertinents en ce qui concerne la gravité de la COVID-19 chez les femmes enceintes.

Référence	Plan de l'étude	Qualité (AMSTAR)	Nombre d'études/Observations/Détails	Principaux résultats
Revue systématique				
(Khalil et coll., 2020)	Revue systématique et méta-analyse. Recherche de données effectuée le 8 juin 2020.	Élevée	17 études avec > 15 observations (86 ont été incluses dans le résumé qualitatif) global/25 676 grossesses/la plupart des femmes étaient au 3e trimestre ou en post-partum	Asymptomatiques : 253/1 205, 14,5 % (5,6 à 32,5 %), I^2=97,0 % Prévalence des facteurs de risque dans les échantillons : • Obésité : 509/1 725, 38,2 % (23,6 à 55,4 %), I^2=97 % • Toute comorbidité : 252/776, 32,5 % (29,3 à 35,8 %), I^2=0 % USI : 159/1 591, 7 % (4 à 11, IC à 95 %), I^2=82 % Oxygénothérapie : 295/1 623, 18,2 % (9,8 à 31,1 %), I^2=95,5 % Ventilateur mécanique : 92/1 680, 3,4 % (1,5 à 7,7 %), I^2=90,2 %

				ECMO : 13/1 896, 0,7 % (0,4 à 1,2 %), I^2=0,0 % Mortalité : 43/2 650, 0,9 % (0,3 à 2,9 %), I^2=84,4 % Accouchement pour toute raison liée à la COVID-19 : 95/497, 19,0 % (8,9 à 36,0 %), I^2=89,4 % - Les femmes enceintes atteintes de COVID-19 qui ont dû être hospitalisées dans l'USI étaient d'environ 7 % dans l'ensemble des études sur les femmes enceintes, ce qui est supérieur aux taux de 4,2 % (CDC COVID-19 Response Team, 2020) indiqué par les données de surveillance des États-Unis pour le groupe en âge de procréer. - L'admission en USI était associée à un âge plus avancé (>35 ans) et à des comorbidités (p<0,05). Le trimestre, l'ethnicité et l'obésité n'expliquent pas l'hétérogénéité en ce qui concerne l'USI ni le décès de la mère.
(Trippella et coll., 2020)	Revue systématique. Date de la recherche : 18 avril 2020. Comprend des études épidémiologiques, des exposés de cas	Modérée (9/10 McMaster Plus)	37 (Chine et autres pays)/275 grossesses, 239 accouchements	Oxygénothérapie : 36/275 (13 %) USI : 10/275 (4 %) Ventilateur mécanique : 5/275 (2 %) ECMO: 1/275 (0,03 %) Mortalité : 1/275 (0,03 %) La majorité des femmes enceintes étaient atteintes d'une forme bénigne ou modérée de la maladie avec faible incidence de complications graves et faible taux de mortalité.
(Huntley et coll., 2020)	Revue systématique.	Élevée	13 (Chine, États-Unis, Italie, données pour janvier à	Bénin : 86,1 % (81,5 à 89,7) Grave : 15,3 % (11,1 à 20,8)

	Rapports sur >10 observations. Date de la recherche : 29 avril 2020. Comprend principalement des exposés de cas et des séries de cas.	(9/10 McMaster Plus)	avril 4)/538 grossesses 438 accouchements	Admission à l'USI : 3,0 % (1,6 à 5,9, IC à 95 %, 8/263) Maladie grave : 1,4 % (0,5 à 4,1, IC à 95 %, 3/209) Décès : 0 % (0,0 à 1,1, IC à 95 %, 0/348) Entre les études, environ une femme enceinte sur trois atteinte du SRAS-CoV-2 présentait une comorbidité.
(Juan et coll., 2020)	Revue systématique. Date de la recherche : 20 avril 2020. Comprend 9 séries de cas et 15 exposés de cas.	Modérée (8/10 McMaster Plus)	24 (Chine, Australie, Canada, France, Corée, Iran, Italie, Suède, Turquie, États-Unis)/324 grossesses/âge de la mère de 20 à 44 ans et âge gestationnel de 5 à 41 semaines	Pneumonie sévère de 0 à 14 % selon les études, la plupart des femmes ayant été admises à l'USI Une série de cas en Iran de femmes enceintes atteintes d'une grave infection à la COVID-19 a entraîné 7 décès/9 cas admis à l'USI sous ventilateur mécanique. Cette revue résume également les comorbidités et indique que leur fréquence est similaire à celle de la population en général.
(Gao, Ye et Zhang, 2020) *Prépublication*	Revue systématique. Date de la recherche : 16 avril 2020. Uniquement les études comportant plus de 5 observations. Comprend des exposés de cas, des séries de cas et des études d'observation.	Modérée	14 (Chine, États-Unis)/236 grossesses	Femmes enceintes Cas grave ou décès MA : 12 %, 0,03~0,20, IC à 95 % I^2 =0 %, P=0,006 Comorbidités MA : 33%, 0,21~0,44, IC à 95 % I^2=70 %, P=0,000

(Smith et coll., 2020)	Revue systématique. Date de la recherche : 28 mars 2020 Comprend : des séries de cas et un plan d'étude avant/après.	Modérée (8/10 McMaster Plus)	9 (Chine)/92 grossesses	Hospitalisation : 34,7 %, 32/92 Oxygénothérapie : 28,1 %, 9/32 hospitalisées USI : 3,1 %, 1/32 hospitalisées Mortalité : 0/32 De nombreuses femmes enceintes prises en compte dans ces études étaient asymptomatiques et afébriles lors de la présentation. Lymphopénie : 66,7 % (comme le SRAS 67 % et le MERS 50 %) et n'était PAS associé à un pronostic plus défavorable chez les femmes enceintes. Le séjour à l'USI et la mortalité des femmes enceintes atteintes du SRAS-CoV-2 semblent plus faibles que pour le SRAS (15 à 18 %/30 %) et le MERS (25 à 27 %/60 %)
(Yang, Wang, Zhu et Liu, 2020)	Revue systématique. Date de la recherche : 26 mars 2020 Comprend des exposés de cas, des séries de cas et une comparaison avec les témoins.	Modérée	18/114 grossesses	Grave/critique : 5,3 %, 6/114 ECMO 0,9 % : 1/114 La seule étude cas/témoins n'a révélé aucune différence en ce qui concerne la prééclampsie, le diabète sucré de la grossesse et la rupture prématurée des membranes entre les groupes de femmes atteintes ou non de COVID-19. En général, les caractéristiques cliniques des femmes enceintes sont similaires à celles des femmes adultes non enceintes.
(Gajbhiye, Modi et Mahale, 2020) *Prépublication*	Revue systématique. Date de la recherche : 3 mai 2020.	Modérée	50 (Chine, États-Unis, Iran, Australie, Canada, Corée, Honduras, Jordanie, Espagne, Pérou, Suède, Turquie, Italie, Portugal, Suisse, Inde)/441 grossesses,	USI avec ventilateur mécanique : 11 % Oxygénothérapie : 24 % ECMO : 2,3 %, 10/441 Décès : 2,0 %, 9/441

	Comprend des séries de cas, des exposés de cas.		387 accouchements/95 % des femmes étaient au 3e trimestre	
(Sun et coll., 2020) *Prépublication*	Revue systématique. Date de la recherche : 11 mars 2020.	Élevée	Grossesses : 17/21 SRAS, 11 MERS, 41 COVID-19	Séjour à l'hôpital > 15 jours : COVID-19 (50 % [0,19 à 1,19, IC à 95 %], p > 0,05) MERS : (80 % [0,45 à 1,15, IC à 95 %], p < 0,05) Taux de mortalité : COVID-19 : 0 % MERS : 40 % ([0,03 à 0,83, IC à 95 %], p > 0,05) SRAS : 25 % ([0,01 à 0,49, IC à 95 %], p < 0,05)

SÉRIE DE CAS

Les séries de cas et les exposés de cas constituent le modèle d'étude le plus couramment utilisé pour décrire les effets de la COVID-19 sur la grossesse. Comme cette revue visait à savoir si la COVID-19 était plus grave chez les femmes enceintes, nous avons ciblé de nouvelles séries de cas comportant plus de 30 observations. Seize exposés de cas publiés entre le 8 juin et le 10 juillet ont été exclus en fonction de ce point de découpage.

Tableau 3 : Série de cas (>30 femmes) publiée entre le 8 juin et le 10 juillet résumant la probabilité de résultats graves dans les cas de COVID-19 chez les femmes enceintes.

Référence	Pays	Dates	Trimestre	Plan de l'étude	Principaux résultats
Recherche originale					
(Cohen et coll., 2020)}	France	Non précisé	1 à 3 (27 semaines médianes, fourchette de 4 à 34)	Enquête sur les femmes enceintes atteintes de COVID-19 en France (auto-identification) N=194. Seules les données sur les cas	Hospitalisation : 18/88 (20 %) Maladie grave avec oxygénothérapie : 6/88 (7 %) Contractions utérines : 15/88 (2 graves) Accouchement : 14/88 (1 grave) Une maladie grave a été observée chez les femmes âgées (p=0,009), chez celles qui avaient un IMC plus

				confirmés par test RT-PCR ont été analysées, N= 88. Biais de recrutement	élevé (p=0,002) et chez celles qui étaient diabétiques (50 % contre 5 %) (p=0,006)
(Vivanti et coll., 2020)	France	12 mars au 13 avril	14 semaines et 2 jours après l'accouchement	Examen rétrospectif multicentrique des dossiers médicaux (N=100)	Hospitalisation : 52/100 USI : 10/100 Oxygénothérapie : 32/100 Facteur de risque pour l'hospitalisation : - IMC élevé ou bas : p=0,003 - L'âge de la mère, l'âge gestationnel, la parité et les comorbidités n'étaient pas significatifs.
(Sentilhes et coll., 2020)	France	1er mars au 3 avril	N.d.	Série de cas rétrospective de toutes les femmes enceintes atteintes de COVID-19 (N=54) à Strasbourg	Oxygénothérapie : 24,1 %, 13/54 Ventilateur mécanique : 3/13 ECMO : 1/13 Naissance prématurée médicalement indiquée (>37 semaines) en raison d'une COVID-19 grave : 5/54
(Lokken, Walker et Adams Waldorf, 2020)	États-Unis	21 janvier au 17 avril	2e trimestre (N=20), 3e trimestre (N=23)	Série de cas rétrospectifs de femmes enceintes ayant été hospitalisées en raison de la COVID-19 (N=46) dans les hôpitaux de l'État de Washington	Grave : 15 %, 6/46 (toutes en surpoids ou avec des comorbidités) Hospitalisation : 16 %, 7/46 USI : 1/46
(Khoury et coll., 2020)	États-Unis	13 mars au 12 avril	Durée	Cohorte prospective de cas de COVID-19 (N=241) ayant donné naissance dans cinq centres médicaux de New York	Asymptomatiques : 42,1 %, 102/241 Bénigne : 26,5 %, 64/241 Grave : 26,1 %, 63/241 Critique : 5 %, 12/241 USI : 7,1 %, 17/241 Ventilateur mécanique : 3,7 %, 9/241 Décès : 0 Facteurs de risque : L'IMC était associé à la gravité, p=0,001

(Blitz et coll., 2020)	États-Unis	1er mars au 6 mai	N.d.	Série de cas de COVID-19 confirmés chez des femmes enceintes (N=462) dans dix hôpitaux de l'État de New York	Grave ou critique : 15,2 % 70/462 USI : 18,6 %, 13/70 Décès : 15,4 %, 2/13 (et globalement) Ventilateur mécanique invasif : 61,5 %, 8/13 5 accouchements d'urgence ont été effectués dans les cas se trouvant à l'USI avant que le ventilateur mécanique invasif ne soit utilisé en raison des symptômes de COVID-19.
(San-Juan et coll., 2020)	Espagne	5 mars au 6 avril	2e trimestre (N=9), 3e trimestre (N=22)	Cohorte rétrospective, patientes inscrites au moment du diagnostic (N=52)	Pneumonie associée à la COVID-19 diagnostiquée chez 61,5 %, 32/54 Oxygénothérapie : 56 %, 18/32 SDRA : 25 %, 8/32 USI : 6,4 %, 2/32 Mortalité : 0/32

* L'étude systématique la plus récente à ce sujet a examiné la littérature publiée jusqu'au 8 juin 2020 et est décrite dans le tableau 2.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont menées par Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont recoupées avec la littérature de la liste de littérature COVID de l'OMS, et les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-COV-2. Termes de recherche utilisés comprennent : pregnancy ou pregnant ou maternal
Cet examen contient les recherches publiées jusqu'au 14 juillet 2020
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites dans l'examen.

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Emerging Evidence on COVID-19

Evidence Brief on SARS-CoV-2 Variants of Concern and Transmission in Children

Introduction

What is the global evidence on whether SARS-CoV-2 variants of concern (VOCs) have changed transmission in children and transmission patterns in schools?

Several SARS-CoV-2 variants of concern (VOCs) have been identified since December 2020. As of March 26, 2021, these included B.1.1.7, B.1.351, P.1 (1) and B.1.429 (2) which have acquired enhanced infectivity and transmissibility. The new variants have quickly spread to many countries globally and are being intensely studied to understand their clinical and epidemiological impacts. This evidence brief identifies and summarizes the existing evidence up to March 26, 2021 on transmission of the VOCs in children and the impact on in-school transmission.

Key Points

- Web-scraped media data of school related COVID-19 outbreaks across Canada indicate that an increasing number of VOC related school outbreaks have been reported from January to March 2021.
- Overall, nine studies were identified COVID-19 VOC transmission in children. Of these, five focused only on transmission of VOCs in children, three assessed transmission patterns in schools and one study evaluated both (Tables 1 and 2). Currently, all studies focused on B.1.1.7 transmission patterns in children in the UK during November 2020 to January 2021 as the proportion of cases associated with B.1.1.7 increased steadily from the end of November onward (3).
- Five studies found that B.1.1.7 does not disproportionately affect children (<11 years old) and youth (11-19 years old). The increased transmissibility of the variant is observed in both adults and children, which suggested that the variant is not particularly adapted to any age group. A modelling study as well as epidemiological evidence of B.1.1.7 transmission in the UK identified that VOC transmission was not driven by children.
    - A single study reported that there were increased cases of B.1.1.7 in children and youth <20 years compared to older adults (> 70 years). However, schools remained open

during the community lockdown, which would result in school-age children having higher contact rates and risk of being exposed compared to adults over 70 years (4).

- Among children and young people hospitalized, there was no evidence of more severe disease (e.g., requiring ventilation support) with B.1.1.7 infection. This suggested that clinical course does not differ appreciably.
- Evidence identified that transmission in school-aged children was strongly correlated with the level of community transmission.
    - None of the studies estimated the likelihood of school outbreaks associated with VOCs compared to the original SARS-CoV-2 variant.
    - There was no evidence identified that schools were playing a large role in driving B.1.1.7 transmission in the community (5).
    - There was a reduction of cases in children and youth following school closures which may be due to both a reduction in cases and a reduction in testing of this age group. Reopening schools are expected to increase the proportion of VOC cases in children relative to the level of VOC community transmission (6, 7).
    - There was insufficient evidence to quantify the effect of VOC transmission in schools compared to transmission in the wider community.
- A single report in the UK estimated that children under ten are about half as likely as adults to transmit the B.1.1.7 variant. Thus, while secondary attack rates from B.1.1.7 cases in children increased 30-50%, the secondary attack rates for VOC child cases were still half that seen in VOC adult cases (3). This finding is similar to the original SARS-CoV-2 variant attack rates.
- Predictive models indicate that the stringency of public health measures other than school closures, particularly with a more transmissible VOC, is the most important determinant of the epidemic trajectory and that schools being open or closed has minimal impact on the epidemic course overall.

Overview of Evidence

Eight studies pertaining to transmission of VOC B.1.1.7 in children and patterns of transmission in schools were included in this review. The studies reporting transmission in children were mainly observational with the majority being retrospective cohort studies exploring the B.1.1.7 variant transmission in the UK during fall 2020 to early winter 2021. There was also one surveillance data

analysis, one prevalence study and two predictive models. The predictive models were focused on variant transmission and school closures.

A formal risk of bias assessment was not conducted. These observational studies are moderate to high risk of bias due to the retrospective nature of the study design and whether the sample is representative of the population and sufficiently large to obtain generalizable results. The retrospective studies obtained surveillance data in children from large national databases while others focused on small numbers of cases in a specific setting. In addition, due to the nature of the study designs these studies may be at higher risk for missing information bias, selection biases and confounding.

Quantitative predictive models were included. These do not identify actual outcomes of strategies that have been tested, but rather present a range of plausible outcomes within the theoretical scenarios being studied. Their results are useful to compare different options as part of a decision-making process, however the results need to be interpreted with caution as the models will vary on their assumptions, input values based on the epidemic period and region specific parameters used.

A key knowledge gap in this research is the lack of high-quality studies of transmission of VOCs in children and transmission patterns in schools. Although current evidence from a small number of studies on B.1.1.7 reports similar findings, there is the possibility that conclusions could change with further research. There is limited evidence evaluating the severity and clinical course of treatment and further studies that follow these outcomes closely in children are needed. Furthermore, studies of the effects from other VOCs are needed to provide understanding about the role these variants have in transmission of SARS-CoV-2 in children and school settings. Additional evidence is also needed on the clinical epidemiology of VOCs in children. Further research is also needed to investigate whether VOC transmission in schools have a different epidemiology than the original SARS-CoV-2 variant and may need re-evaluation of public health measures in this setting.

CONTENTS

COVID-19 CANADIAN SCHOOL OUTBREAKS

A summary of data on the number of school related outbreaks in Canada that included two or more people are summarized in Figure 1. The proportion of outbreaks associated with VOCs increased between January and March 2021. While this data is imperfect, it provides a snapshot of the proportion of school-based outbreaks attributed to VOCs up to the end of March 2021.

The data in Figure 1 is based on webscraping media reports conducted by the Outbreak Response Unit in CIRID and has the following caveats:

- Due to the volume of school outbreaks and the limited information provided about them by some jurisdictions, the database includes only school outbreaks that are referenced in the media, and not those reported by public health in these provinces, for both original strain and VOC-associated outbreaks.
- Unnamed schools are not captured in the webscraping database.
- Therefore, the total number of outbreaks in schools in the webscraping database is likely an underestimate for both original strain and VOC-associated outbreaks.
- The reported date represents the date the outbreak was declared if available, otherwise it represents the earliest date the outbreak was reported in the media.

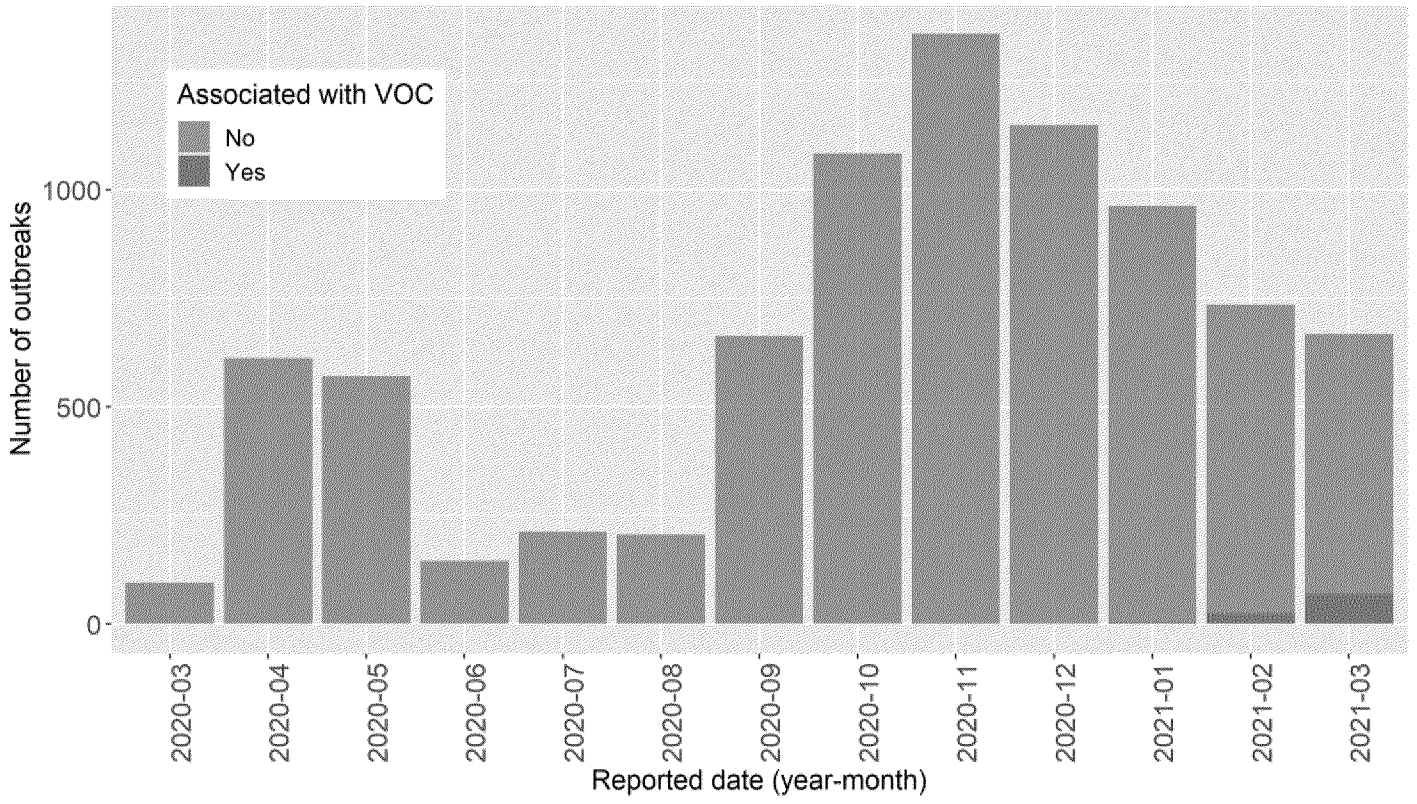

Figure 1: Outbreaks in Canadian schools reported by the media between March 2020 and March 2021

COVID-19 VOC TRANSMISSION IN CHILDREN

The current research has only evaluated the impact of B.1.1.7 on transmission and severity of disease in children in six studies (Table 1). All the studies detail outcomes of B.1.1.7 transmission in children from the UK during November 2020 to January 2021.

- Five studies found that B.1.1.7 does not disproportionately transmit more in children compared to adults (3, 8-11). The increased transmissibility of the variant is observed in both adults and children.
    - Transmission of B.1.1.7 in children correlated strongly with community transmission (5, 9, 10).
    - S-gene target failure (SGTF), which serves as a proxy for B.1.1.7 cases, was studied in adults and children and no difference in SGTF mean excess growth rates between children up to high school (5% (95% CI 1-8%)) and adults (6% (95% CI 4-9%)) were reported (10). This suggested that there are increased VOC infections compared to the original SARS-CoV-2 variant. However, the growth is similar in both children and adults. Furthermore, this study found no evidence that VOC transmission was driven by children (10).
    - A single report in the UK found that children under ten are about half as likely to transmit the B.1.1.7 variant compared to adults >20 years. Although, secondary attack rates from B.1.1.7 cases in children increased 30-50%, the secondary attack rates in VOC child cases were still half that seen in VOC adult case, similar to the original SARS-CoV-2 variant attack rates (3).
    - A modelling study found that data did not support a hypothesis that children were more susceptible to infection from VOCs than the original SARS-CoV-2 variant (11).
- A single study reported that there were increased cases of B.1.1.7 in children <20 years compared to older adults (>70 years old). The authors identified that given the community was in lockdown, but the schools were open, the children had a higher contact rate and risk of being exposed than the older adults (4).
- Two studies evaluated severity of disease in children:
    - One study found no evidence of more severe disease having occurred in children and young people during November 2020 to January 2021 in the UK when the proportion of cases associated with B.1.1.7 was rapidly increasing compared to cases seen in March to May 2020 (8).

- Another study evaluated viral load between children with the variant and those with the original SARS-CoV-2 variant and found no difference, which suggested that infection with the B.1.1.7 VOC does not result in a different clinical course compared to the original strain (10).

Table 1: Evidence of transmission of variants in children (n=6)

STUDY	METHOD	KEY OUTCOMES
Surveillance Data Analysis (n=2)		
Mensah 2021 (9) Surveillance data analysis UK Jul – Dec 2020	Analysis of SARS-CoV-2 infection rates based on Public Health England daily reports during the school year from July to December 2020, including the effect of a national month-long lockdown whilst keeping schools open in November 2020. Three educational settings: preschools (nursery, preschool<5 yr olds), primary schools (reception, age 5-11) and secondary schools (age 11-18) compared to adults (age 16-64) or young adults (age 18-29). Infection rate ratios were used to compare groups. Denominators for each group were taken from the census data.	• Infection rates in adults and children increased rapidly after the week of Nov 23, 2020. • Infection rates in children increased with the cases in the community August through November when the community locked down. In November 2020 schools remained open during lockdown, infection rates in children decreased more slowly than adult cases and the decrease showed a 1 week lag in children. After lockdown, cases in adults started to increase quickly which also coincided with the emergence of B.1.1.7. Cases in secondary school-aged children also increased at a similar rate to adults, whereas those in younger children increased more slowly. • Age specific infection rates were highest in young adults > secondary school children > primary school children > preschool-aged children. The relative rates compared to preschool-aged children were 1.91 (95% CI, 1.74–2.09) primary, 5.17 (95% CI 4.73–5.65) secondary and 10.73 (95% CI, 9.84–11.71) young adults during the week of 19 October 2020. These relative differences continued through the end of 2020 when B.1.1.7 rapidly spread through the UK despite schools being closed at the end of November. • A strong and statistically significant (P<0.001) correlation was observed between weekly SARS-CoV-2 infection rates in adults and the three educational cohorts, with the strongest correlation observed for secondary school-aged children which was seen through to the end of 2020.

Public Health England 2021 (3) Surveillance data analysis UK Sep 2020- Jan 2021	Surveillance data was analyzed from a total of 6,008 VOC cases and 68246 cases sequenced from 20 September 2020 until 4 January 2021. Contact tracing data 30 November 2020 to 20 December 2020 included 386 805 cases of which 90401/212943 were S-gene target failure (SGTF, a proxy for B.1.1.7) from those with TaqPath data and 3801/ 9321 were B.1.1.7 when sequenced.	• Epidemiologically the age-sex profile was similar between sequenced cases B.1.1.7 (Sept 2020-Jan 2021) and cases identified by SGTF (Dec 2020- Jan 2021) compared to non-B.1.1.7/ non-SGTF cases. • 0-9 year-olds represented 6.1% of B.1.1.7 isolates compared to non-B.1.1.7 at 4.0% among sequenced cases. • Contact tracing data report estimated attack rates are 10-70% higher across age groups. E.g., 0-9 year-olds had a 9.0% secondary attack rate for B.1.1.7 vs. 6.1% for non-B.1.1.7 cases. SGTF attack rates were similarly 30-50% higher, in 0-9 year-olds it was 8.9% for SGTF and 6.2% for non-SGTF. Similar to the originalSARS-CoV-2 variant, children under the age of ten are about half as likely as adults >20 years to transmit the variant to others.
Cohort Studies (n=3)		
Brookman 2021 (8) Retrospective cohort UK Feb 2021	Characteristics of children and young people (age <19 years) admitted with acute respiratory COVID-19 between March 1 and May 31, 2020 (n=20) were compared to those admitted Nov 1, 2020, and Jan 19, 2021 (n=60) to King's College Hospital for SARS-CoV-2 infection.	• No difference in demographics e.g., age, sex, ethnicity or deprivation score were identified between waves 1 and 2. • Severe disease necessitating oxygen therapy or ventilatory support was infrequent in both waves and was lower as a proportion of total admission in the second wave than in the first. • These November 2020 to January 2021 data show that many children and young people have been admitted to hospital due to the higher prevalence of SARS-CoV-2 in the hospital's community. The findings in this paper were in line with national data. • There was no evidence of more severe disease having occurred in children and young people since B.1.1.7 increased in circulation, suggesting that infection with the B.1.1.7 variant does not result in a different clinical course to the original strain.
Volz 2021 (4) *Preprint* Retrospective cohort UK	This study included an analysis of S-gene target failures (SGTF) a proxy for	• Analysis of trends during lockdown (November 2020) show that non-SGTF cases decreased, but SGTF cases increased across jurisdictions in the UK.

Jan 2021	B.1.1.7 and non-SGTF cases across England areas between November 8 to December 12, 2020. Age-distributions were assessed.	• After standardizing the cases to the population composition, there are significantly more SGTF cases among individuals aged 0-19 as compared to non-SGTF cases. • The authors suggest differences between the age-distributions of VOC and non-VOC community cases may result from the overall increase in transmissibility of the VOC (especially during a time where lockdown was in force, but schools were open).
Walker 2021 (10) *Preprint* Retrospective cohort UK Sep 2020- Jan 2021	This was a large community surveillance study in the UK. Data were analyzed from nose and throat swabs (n=1,553,687) collected and tested by RT-PCR. S-gene target failures (SGTF) was used as a proxy for B.1.1.7. Cycle threshold (Ct) values (a proxy for viral load), percentage of positives, population positivity and growth rates in SGTF vs non-SGTF positives was assessed by age.	• In the sample 0.98% were positive: 8545 non-SGTF and 3531 SGTF. From early November 2020 to December 31, 2020, the SGTF positives increased e.g., London samples 15% to 38% to 81%. • In November the non-SGTF cases remained stable and the SGTF cases increased adding to the SARS-CoV-2 cases rather than replacing the non-SGTF cases. The growth rate was similar in adults and children. • No association with Ct values (a proxy for viral load) and SGTF cases was identified. • In some regions SGTF cases in younger individuals emerged first, but this was not consistent across regions. No evidence of difference in SGTF growth rates between children up to high school (5% (1-8%)) and adults (6% (4-9%)). This supports B.1.1.7 not being particularly adapted to transmit more in children.
Predictive model (n=1)		
Davies 2021 (11) Predictive model UK Mar 2021	An age-and regionally-structured mathematical model of SARS-CoV-2 transmission was conducted using Google mobility data and social contact surveys. They used this model to test four different hypotheses to assess which had the best fit.	• The age-and regionally-structured mathematical model found the hypothesis that lower Ct values (an indicator for higher viral load) which supports that VOCs are more transmissible than pre-existing variants fits the model better than the hypothesis that children were more susceptible to infection with the VOC than pre-existing variants.

COVID-19 VOC TRANSMISSION PATTERNS IN SCHOOLS

Four studies were identified on COVID-19 transmission patterns in schools, three of which were predictive models (Table 2). Specifically, these studies explored the impact of school closures on transmission. The modelling studies assessed the reproduction number R(t), which indicates the ability of a disease to spread, for different scenarios of closures. R values greater than 1 indicate that cases will increase. These models showed that school closures did have some impact on reducing VOC community incidence, however transmission among school-aged children correlated most strongly with the level of community transmission. These models identified that transmission in schools contributes to but was not driving the spread of VOCs.

- One modelling study found that the reductions in cases and R(t) were largest with continual full national lockdown until April 19, 2021 compared to any of the scenarios with some schools reopened. Reopening primary schools and exam critical years only, or having primary schools open continuously with secondary schools on a two-weeks on-off rotation, will lead to a lower increase in cases and R than if all schools stayed open (6).
- Another modelling study found similar results that strict restrictions in community mobility along with closure of schools will reduce R(t) below 1 (11).
- A UK cohort study found that there was a large rise in school absences in secondary school settings in some regions in London due to the increased cases of the B.1.1.7 variant. This was not observed in primary school settings. There was also a positive correlation between cases in schools and cases in the community. Furthermore, there was no evidence identified that schools were playing a large role in driving the transmission in the community (5).
- A Canadian modelling study estimated that B.1.1.7 would result in a higher likelihood of an outbreak that is 3.6 times and 4.2 times that of an outbreak from original SARS-CoV-2 variant, even with strict control measures in place for adults and children respectively. This increase is predicted irrespective of whether schools are closed or open in scenarios where the community is open due to poor public health interventions and high community transmission risk. The modelling identified that schools do not have a large impact on the trajectory of the epidemic (7).

Table 2: Evidence of VOC transmission in schools (n=4)

STUDY	METHOD	KEY OUTCOMES
Predictive modelling studies (n=3)		
Davies 2021 (11) Predictive model UK Mar 2021	A transmission model fitted to seven NHS regions in England was used to project epidemic changes under different control measures from mid-December 2020 to the end of June 2021. The study is modelled on the assumption of increased transmissibility of the variants. Four scenarios were compared: (i) a moderate-stringency scenario; (ii) a high-stringency scenario with schools open; (iii) the same high-stringency scenario, but with schools closed until 15 February 2021; and (iv) a very high-stringency scenario with schools closed.	• The transmission model found that regardless of control measures, all regions were projected to experience a new wave of COVID-19 cases and deaths in early 2021, peaking in February if no substantial control measures were introduced or mid-January if strong control measures were in place. • The model also predicted that more stringent measures (iii and iv) would lead to larger rebound cases when simulated restrictions were lifted in March 2021. • The authors suggest that closing schools along with restrictions in the community can succeed in reducing R below 1.
Panovska-Griffiths 2021 (6) *Preprint* Predictive model UK Feb 2021	The Covasim model, calibrated until January 25, 2021, was used to simulate the impact of a full national lockdown (FNL) with schools closed until April 19, 2021 versus four different partial national lockdown (PNL) scenarios with different elements of schooling open: 1) PNL staggered start 2) PNL full-return 3) PNL with primary and critical exam years (Y11 and Y13) only returning to school and 4) PNL with primary full-time and secondary schools rotating two-weeks in class and two weeks online learning. The study is modelled on the assumption that the new variant is more transmissible, and that the	• The modelling suggests that the reduction in cases and in R is largest with continual FNL until April 19, 2021 compared to any of the scenarios with some schools reopened. Reopening primary schools and exam critical years only, or having primary schools open continuously with secondary schools on a two-weeks on-off rotation, will lead to a lower increase in cases and R than if all schools open. • National lockdown will reduce the number of cases by early March to a similar level as in October with R also falling and remaining below 1. • Across each scenario, the number of new infections is expected to decrease over January and early February lockdowns.

	relative proportion of the new strain increased from September 1, 2020 to January 31, 2021 following a logistic growth function, such that 30% of infections in December and 90% of infections by the end of January 2021 were caused by the new variant.	• Impacts upon deaths are lagged, with plateauing of cumulative deaths seen from February in each scenario. This is due to the vaccine effect having been modelled with a delay of 21 days. Overall, when schools open, we predict a rise in the number of infections and increase in R, and a possible shift in R above 1 once society opens also.
Yuan 2021 (7) *Preprint* Predictive model Toronto Jul– Nov 2020	Using a deterministic age-household-location structured extended SEIR model fitted to demographic data from Toronto, the model is calibrated to epidemiological data between July 31 and November 23, 2020. The model was developed to mimic transmission in households, the community and schools. The new VOC is based on B.1.1.7, assumed to have a 50% increased transmission probability and assumes children will be 70% as susceptible as adults. They also assume it will be the dominant strain after 1 month. The study modelled the impact of the new variant of concern assuming higher susceptibility of children and youth to the new variant.	• Compared to the baseline with the variant strain and the community restricted/ schools closed, which resulted in near epidemic control, the variant strain was estimated to increase the number of cases 3.6x for adults and 4.2x in children and youth. • The scenarios run considering the new variant indicate that schools closing do not have a large impact on the trajectory of the epidemic January to May 2021 as with stage 2 opening (partial opening) of the community the prediction was 7x or 7.5x more cases with schools closed vs. open. • Exponential increases in cases were predicted regardless of whether schools were open or closed in scenarios where the community is fully opened (stage 3) due to weak public health interventions and high community transmission risk.
Cohort studies (n=1)		
Southhall 2021 (5) *Preprint* Retrospective cohort UK	Analysis of absenteeism of pupils and teachers was conducted to assess the impact of the new variant, B.1.1.7. Specific regions were evaluated to assess the differential impact of the new variant. London and Kent were chosen due to the high number of new variant compatible cases reported, while Devon and the West Midlands were chosen due to having	• A large rise in the number of absences per school in secondary school settings was observed in the South East and Greater London in December but not in other regions or primary school settings. • Authors suspect absences were related to increased transmissibility of the new B.1.1.7 variant which contributed to the rise of cases in secondary schools in these regions.

Sep-Dec 2020	had fewer reported cases compatible with the new variant. Additionally, on the 3rd December 2020, Devon was in tier 2 and the West Midlands was in tier 3.	• A positive correlation was found between cases in the community and cases in schools in most regions. • No significant evidence to suggest that schools are playing a significant role in driving transmission in the community. • Careful monitoring may be required as schools re-open to determine the effect associated with opening schools upon community incidence. • In London, Kent and the West Midlands, a weak correlation between cases in secondary school pupils and community cases that increases with lag time, indicating that an increase in community cases is most positively correlated with an increase in school cases in pupils at a later date. • The same result was observed for primary school pupils in Kent and the West Midlands. However, a negligible correlation between community cases and cases in primary school children in London across all time lags was observed.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included:
SCHOOL TRANSMISSION TERMS: (B.1.1.7 or 501Y.V1 or B.1351 or 501Y.V2 or P1 or P2 or B1.1.1.28 or B.1.1.33 or 501Y.V3 or B.1.426 or variant) AND school AND transmission
CHILDREN TERMS: B.1.1.7 or 501Y.V1 or 202012/01 or B.1351 or 501Y.V2 or P1 or P2 or B1.1.1.28 or B.1.1.33 or 501Y.v3 B.1.426 or variant) AND (children or adolescent)
This review contains research published up to March 26, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Grey Literature

A grey literature search was conducted to compliment the database search. The grey literature focused on key websites that reports on B.1.1.7 variants, including Public Health England and SPOR Evidence Alliance. The original grey literature search was conducted on March 24-March 26, 2021.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

Prepared by: Kusala Pussegoda, Lisa Waddell Emerging Science Group, PHAC.

Knowledge mobilized by the Office of the Chief Science Officer: phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref des données probantes sur les variants préoccupants du SRAS-CoV-2 et leur transmission chez les enfants

Introduction

Quelles sont les données probantes à l'échelle internationale sur la question de savoir si les variants préoccupants du SRAS-CoV-2 (COV) ont modifié la transmission chez les enfants et les modes de transmission dans les écoles?

Plusieurs variants préoccupants du SRAS-CoV-2 ont été identifiées depuis décembre 2020. Ainsi, en date du 26 mars 2021, ceux-ci comprenaient les variants B.1.1.7, B.1.351, P.1 (1) et B.1.429 (2) qui ont une plus grande infectiosité et sont plus transmissibles. Les nouveaux variants se sont rapidement répandus dans de nombreux pays et font l'objet d'études intensives pour comprendre leurs impacts cliniques et épidémiologiques. Cette synthèse en bref sur les données probantes indique et résume les données probantes disponibles jusqu'au 26 mars 2021 sur la transmission des variants préoccupants chez les enfants et l'impact sur la transmission dans les écoles.

Points clés

- Les données des médias recueillies sur le Web à propos des éclosions de COVID-19 dans les écoles partout au Canada indiquent qu'un nombre croissant d'éclosions de variants préoccupants ont été signalées dans les écoles de janvier à mars 2021.
- Au total, neuf études ont porté sur la transmission des variants préoccupants associés à la COVID-19 chez les enfants. De ce nombre, cinq portaient uniquement sur la transmission des variants préoccupants chez les enfants, trois ont évalué les modes de transmission dans les écoles et une étude a évalué les deux (tableaux 1 et 2). À l'heure actuelle, toutes les études ont porté sur les modèles de transmission du variant B.1.1.7 chez les enfants au Royaume-Uni entre novembre 2020 et janvier 2021, car la proportion de cas associés au B.1.1.7 a augmenté régulièrement à compter de la fin de novembre (3).
- Cinq études ont révélé que le variant B.1.1.7 ne touche pas de façon disproportionnée les enfants (< 11 ans) et les jeunes (âgés de 11 à 19 ans). L'augmentation de la transmissibilité de ce variant a été observée chez les adultes et les enfants, ce qui donne à penser que le variant n'est pas particulièrement adapté à quelque groupe d'âge que ce soit. Une étude de

modélisation ainsi que des données épidémiologiques sur la transmission du B.1.1.7 au Royaume-Uni ont révélé que les enfants n'étaient pas un vecteur dans la transmission des variants préoccupants.

  - Une seule étude a révélé une augmentation des cas associés au variant B.1.1.7 chez les enfants et les jeunes de moins de 20 ans comparativement aux adultes plus âgés (âgés de plus de 70 ans). Les écoles sont toutefois restées ouvertes pendant le confinement de la collectivité, ce qui fait que les enfants d'âge scolaire présentaient des taux de contact plus élevés et un risque d'exposition plus élevé que les adultes de plus de 70 ans (4).

- Chez les enfants et les jeunes hospitalisés, il n'y avait aucun signe de maladie plus grave (p. ex., nécessitant une ventilation assistée) en raison d'une infection par le B.1.1.7. Cela suggère que l'évolution clinique du virus n'est pas très différente.
- Les données probantes ont cependant démontré que la transmission chez les enfants d'âge scolaire était fortement corrélée avec le niveau de transmission dans la collectivité.
  - Aucune des études n'a estimé la probabilité d'éclosions dans les écoles associées aux variants préoccupants comparativement à la souche originale du SRAS-CoV-2.
  - Rien n'indique non plus que les écoles jouent un rôle important dans la transmission du B.1.1.7 dans la collectivité (5).
  - Il y a même une réduction du nombre de cas chez les enfants et les jeunes à la suite des fermetures d'école, ce qui peut être attribuable tant à une réduction du nombre de cas qu'à une réduction du nombre de tests pour ce groupe d'âge. La réouverture des écoles devrait accroître la proportion de cas associés aux variants préoccupants chez les enfants par rapport au niveau de transmission de variants préoccupants dans la communauté (6, 7).
  - Il n'y avait cependant pas suffisamment d'éléments de preuve pour quantifier l'effet de la transmission des variants préoccupants dans les écoles comparativement à la transmission dans l'ensemble de la collectivité.
- Selon un seul rapport publié au Royaume-Uni, les enfants de moins de dix ans sont deux fois moins susceptibles que les adultes de transmettre le variant B.1.1.7. Ainsi, alors que les taux d'attaque secondaires du B.1.1.7 chez les enfants ont augmenté de 30 à 50 %, les taux d'attaque secondaires chez les enfants étaient toujours deux fois moins élevés que ceux observés chez les adultes ayant eu une infection associée aux variants préoccupants (3). Ce résultat est semblable aux taux d'attaque du variant du SRAS-CoV-2.

- Les modèles prédictifs indiquent que la rigueur des mesures de santé publique autres que la fermeture des écoles, en particulier avec des variants préoccupants plus transmissibles, est le déterminant le plus important de la trajectoire de l'épidémie et que l'ouverture ou la fermeture des écoles a un impact minime sur le cours global de l'épidémie.

Vue d'ensemble des éléments de preuve

Huit études portant sur la transmission du variant B.1.1.7 chez les enfants et les modes de transmission dans les écoles ont été incluses dans la présente revue. Les études faisant état de la transmission chez les enfants étaient principalement observationnelles, la majorité étant des études de cohorte rétrospectives explorant la transmission du variant B.1.1.7 au Royaume-Uni de l'automne 2020 jusqu'au début de l'hiver 2021. On a également trouvé une analyse des données de surveillance, une étude de prévalence et deux modèles prédictifs. Les modèles prédictifs étaient axés sur la transmission des variants et les fermetures d'écoles.

Aucune évaluation officielle du risque de biais n'a été effectuée. Ces études d'observation présentent un risque de biais modéré à élevé en raison de la nature rétrospective du plan d'étude et de la question de savoir si l'échantillon est représentatif de la population et suffisamment grand pour obtenir des résultats généralisables. Les études rétrospectives ont permis d'obtenir des données de surveillance sur les enfants à partir de grandes bases de données nationales, tandis que d'autres portaient sur un petit nombre de cas dans un contexte particulier. De plus, en raison de la nature des plans d'étude, ces études peuvent présenter un risque plus élevé de biais en raison des informations manquantes, ainsi que des biais de sélection et de confusion.

Des modèles prédictifs quantitatifs ont été inclus. Même si ces modèles n'ont pas permis de déterminer les résultats réels des stratégies mises à l'essai, ils offrent un éventail de résultats plausibles en ce qui concerne les scénarios théoriques à l'étude. Bien que leurs résultats soient utiles pour comparer différentes options dans le cadre d'un processus décisionnel, il faut cependant faire preuve de prudence au moment de les interpréter, puisque ces modèles ont utilisé différentes hypothèses de base ainsi que des valeurs variables, notamment la période et les paramètres propres à la région.

L'absence d'études de grande qualité sur la transmission des variants préoccupants chez les enfants et sur les modes de transmission dans les écoles représente une lacune clé de cette recherche. Bien que les données actuelles associées à un petit nombre d'études sur le variant B.1.1.7 comportent des constatations semblables, il est possible que les conclusions changent avec d'autres recherches. Il existe peu de données probantes permettant d'évaluer la gravité et le déroulement clinique du

traitement, et d'autres études qui suivent de près ces résultats chez les enfants sont donc nécessaires. En outre, des études sur les effets des autres variants préoccupants seront nécessaires pour mieux comprendre le rôle que jouent ces variants dans la transmission du SRAS-CoV-2 chez les enfants et en milieu scolaire. Il faudra aussi des données supplémentaires sur l'épidémiologie clinique des variants préoccupants chez les enfants. D'autres recherches seront également nécessaires pour déterminer si la transmission des variants préoccupants dans les écoles a une épidémiologie différente de la souche originale du SRAS-CoV-2 et pourrait nécessiter une réévaluation des mesures de santé publique dans ce contexte.

TABLE DES MATIÈRES

ÉCLOSIONS DE COVID-19 EN MILIEU SCOLAIRE AU CANADA

Un résumé des données sur le nombre d'éclosions en milieu scolaire au Canada qui ont touché deux personnes ou plus est présenté à la figure 1. La proportion des éclosions associées aux variants préoccupants a augmenté entre janvier et mars 2021. Bien que ces données soient imparfaites, elles donnent un aperçu de la proportion d'éclosions en milieu scolaire attribuées aux variants préoccupants jusqu'à la fin de mars 2021.

Les données de la figure 1 sont fondées sur des reportages diffusés sur le Web et réalisés par l'Unité d'intervention en cas d'éclosion du Centre de l'immunisation et des maladies respiratoires infectieuses (CIMRI) et comportent les mises en garde suivantes :

- En raison du volume d'éclosions en milieu scolaire et de l'information limitée fournie à leur sujet par certaines administrations, la base de données ne comprend que les éclosions dans les écoles mentionnées dans les médias, et non celles déclarées par la santé publique dans ces provinces, tant en ce qui concerne la souche originale que les variants préoccupants.

- Lorsqu'aucun nom n'était indiqué pour l'école, les données associées n'ont pas été saisies dans la base de données Web.
- Par conséquent, le nombre total d'éclosions en milieu scolaire indiqué dans la base de données de recherche en ligne est probablement une sous-estimation, tant pour les éclosions associées à la souche originale que pour celles liées aux variants préoccupants.
- La date déclarée représente la date à laquelle l'éclosion a été déclarée si elle est disponible, sinon elle représente la date la plus hâtive à laquelle l'éclosion a été mentionnée dans les médias.

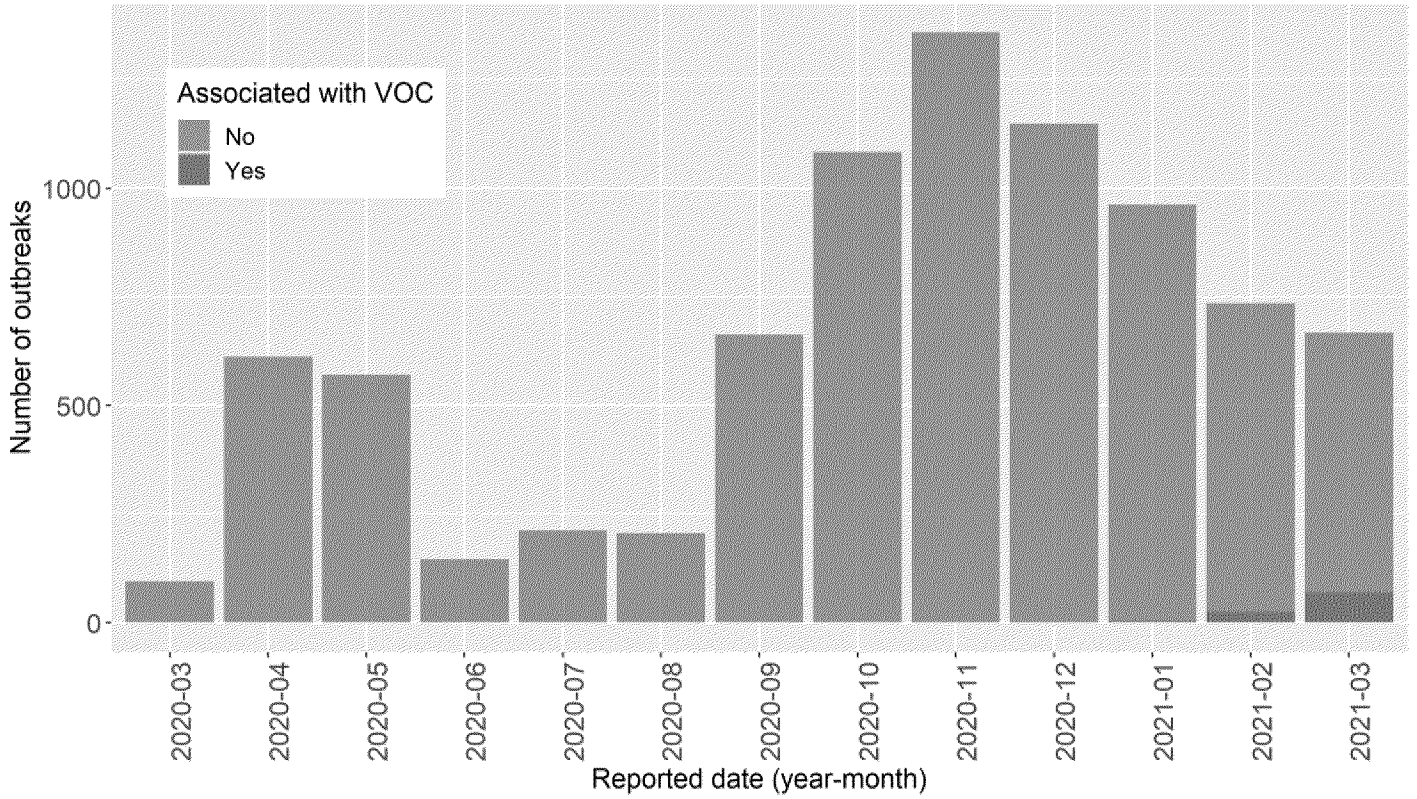

Figure 1 : Éclosions dans les écoles canadiennes mentionnées par les médias entre mars 2020 et mars 2021

TRANSMISSION DES VARIANTS PRÉOCCUPANTS ASSOCIÉS À LA COVID-19 CHEZ LES ENFANTS

Seules six études ont évalué l'impact du variant B.1.1.7 sur la transmission et la gravité de la maladie chez les enfants (tableau 1). Toutes les études présentent en détail les résultats de la transmission du variant B.1.1.7 chez les enfants du Royaume-Uni entre novembre 2020 et janvier 2021.

- Cinq études ont révélé que le variant B.1.1.7 ne se transmettait pas de façon disproportionnée chez les enfants que chez les adultes (3, 8 à 11). La transmissibilité accrue du variant a été observée chez les adultes et les enfants.
    - La transmission du variant B.1.1.7 chez les enfants était fortement corrélée avec la transmission dans la collectivité (5, 9, 10).
    - La défaillance cible du gène S (SGTF), qui sert de substitut pour les cas associés au variant B.1.1.7, a été étudiée chez les adultes et les enfants et aucune différence n'a été signalée dans les taux de croissance moyens de la SGTF chez les adultes (6 % (IC à 95 %, 4 à 9 %)) et chez les enfants (jusqu'au niveau de l'école secondaire) (5 % (IC à 95 %, 1 à 8 %) (10). Cela donne à penser qu'il y a une augmentation du nombre d'infections associées aux variants préoccupants par rapport aux infections associées à la souche originale du SRAS-CoV-2. La croissance est cependant semblable chez les enfants et les adultes. En outre, cette étude n'a trouvé aucune preuve que les enfants pouvaient être un vecteur dans la transmission des variants préoccupants (10).
    - Un seul rapport publié au Royaume-Uni a révélé que les enfants de moins de dix ans étaient environ deux fois moins susceptibles de transmettre le variant B.1.1.7 que les adultes de plus de 20 ans. Bien que les taux d'attaque secondaires du B.1.1.7 chez les enfants aient augmenté de 30 à 50 %, ces taux étaient toujours deux fois moins élevés que ceux observés chez les adultes ayant eu une infection associée aux variants préoccupants, comme l'indiquent les données obtenues pour les taux d'attaque de la souche originale du SRAS-CoV-2 (3).
    - Une étude de modélisation a révélé que les données n'appuyaient pas l'hypothèse selon laquelle les enfants étaient plus susceptibles d'être infectés par les variants préoccupants que par la souche originale du SRAS-CoV-2 (11).
- Une seule étude a révélé une augmentation des cas associés au variant B.1.1.7 chez les enfants et les jeunes de moins de 20 ans comparativement aux adultes plus âgés (âgés de plus de 70 ans). Les auteurs ont déterminé qu'étant donné que la collectivité était en confinement, mais que les écoles étaient ouvertes, les enfants présentaient un taux de contact et un risque d'exposition plus élevés que les adultes plus âgés (4).
- Deux études ont évalué la gravité de la maladie chez les enfants :
    - Une étude n'a révélé aucune preuve d'une maladie plus grave chez les enfants et les jeunes entre novembre 2020 et janvier 2021 au Royaume-Uni, alors que la proportion

de cas associés au variant B.1.1.7 augmentait rapidement par rapport au nombre de cas observés entre mars et mai 2020 (8).

- Une autre étude a évalué la charge virale chez les enfants atteints d'une infection causée par le variant et ceux atteints par la souche originale du SRAS-CoV-2 et n'a révélé aucune différence, ce qui signifie que l'infection par le variant B.1.1.7 n'entraîne pas une évolution clinique différente de celle de la souche originale (10).

Tableau 1 : Preuve de transmission des variants chez les enfants (n = 6)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Analyse des données de surveillance (n = 2)		
Mensah 2021 (9) Analyse des données de surveillance Royaume-Uni Juillet à décembre 2020	Analyse des taux d'infection par le SRAS-CoV-2 établie à l'aide des rapports quotidiens de la santé publique de l'Angleterre publiés pendant l'année scolaire, de juillet à décembre 2020, ce qui inclut l'effet qu'a eu un confinement national d'une durée d'un mois pendant lequel les écoles sont restées ouvertes (en novembre 2020). Les données concernant trois établissements d'enseignement ont été examinées : des établissements préscolaires (maternelle et prématernelle pour les enfants de moins de 5 ans), des écoles primaires (enfants âgés de 5 à 11 ans) et des	• Les taux d'infection chez les adultes et les enfants ont augmenté rapidement après la semaine du 23 novembre 2020. • Les taux d'infection chez les enfants ont augmenté au même rythme que dans la collectivité entre août et novembre, pendant le confinement. En novembre 2020, alors que les écoles restaient ouvertes pendant le confinement, les taux d'infection chez les enfants ont diminué plus lentement que les cas chez les adultes, et cette diminution était en retard d'une semaine chez les enfants. Après le confinement, les cas chez les adultes ont commencé à augmenter rapidement, ce qui a également coïncidé avec l'émergence du variant B.1.1.7. Le nombre de cas chez les enfants en âge d'aller à l'école secondaire a également augmenté à un taux semblable à celui des adultes, tandis que le nombre de cas chez les enfants plus jeunes a augmenté plus lentement. • Les taux d'infection selon l'âge étaient les plus élevés chez les jeunes adultes, puis chez les enfants qui allaient à l'école secondaire, ainsi que des enfants qui allaient à l'école primaire et des enfants d'âge préscolaire. Les taux relatifs par rapport aux enfants d'âge préscolaire étaient de 1,91 (IC à 95 %, 1,74 à 2,09) pour le primaire, de 5,17 (IC à 95 %, 4,73 à 5,65) pour le secondaire et de 10,73 (IC à 95 %, 9,84–11,71) pour les

	écoles secondaires (âgés de 11 à 18 ans) comparativement aux adultes (âgés de 16 à 64 ans) ou aux jeunes adultes (âgés de 18 à 29 ans). Les ratios des taux d'infection ont été utilisés pour comparer les données des différents groupes. Les dénominateurs pour chacun des groupes proviennent des données du recensement.	jeunes adultes pendant la semaine du 19 octobre 2020. Cet écart relatif s'est poursuivi jusqu'à la fin de 2020, lorsque le variant B.1.1.7 s'est rapidement répandu au Royaume-Uni, malgré la fermeture des écoles à la fin du mois de novembre. • Une corrélation forte et statistiquement significative ($P < 0,001$) a été observée entre les taux hebdomadaires d'infection par le SRAS-CoV-2 chez les adultes et les trois cohortes en milieu scolaire, la plus forte ayant été observée chez les enfants qui allaient à l'école secondaire et qui a perduré jusqu'à la fin de 2020.
Public Health England 2021 (3) Analyse des données de surveillance Royaume-Uni Septembre 2020 à janvier 2021	Des données de surveillance provenant d'un total de 6 008 cas de variants préoccupants et de 68 246 cas séquencés entre le 20 septembre 2020 et le 4 janvier 2021 ont été analysées. Les données sur la recherche des contacts établies entre le 30 novembre 2020 et le 20 décembre 2020 portaient sur 386 805 cas, dont 90 401 sur 212 943 provenait de TaqPath et étaient associées à la négativation de la détection du gène S (SGTF, un substitut pour le variant B.1.1.7) alors	• Sur le plan épidémiologique, le profil âge-sexe était semblable entre les cas séquencés pour le variant B.1.1.7 (entre septembre 2020 et janvier 2021) et les cas à SGTF (décembre 2020 et janvier 2021) comparativement aux cas non liés au variant B.1.1.7 ou sans SGTF. • Les enfants de 0 à 9 ans représentaient 6,1 % des isolats du variant B.1.1.7, comparativement à 4,0 % parmi les cas qui ont été séquencés • Les données sur la recherche des contacts indiquent que les taux d'attaque sont de 10 à 70 % plus élevés dans tous les groupes d'âge. P. ex., les enfants de 0 à 9 ans avaient un taux d'attaque secondaire de 9,0 % pour le variant B.1.1.7 comparativement à 6,1 % pour les autres cas. Les taux d'attaques pour les cas à SGTF étaient également de 30 à 50 % plus élevés, soit de 8,9 % pour les 0 à 9 ans et de 6,2 % pour les cas sans SGTF. Comme pour la souche originale du SRAS-CoV-2, cela indique que les enfants de moins de dix ans sont environ deux fois moins susceptibles que les adultes de plus de 20 ans de transmettre le variant aux autres.

	que les données de 3 801 sur 9 321 cas, une fois séquencées, ont plutôt été associées au variant B.1.1.7.	
Études de cohorte (n = 3)		
Brookman 2021 (8) Cohorte rétrospective. Royaume-Uni Février 2021	Les caractéristiques des enfants et des jeunes (âgés de moins de 19 ans) admis avec la forme respiratoire aiguë de la COVID-19 entre le 1er mars et le 31 mai 2020 (n = 20) ont été comparées à celles des personnes admises entre le 1er novembre 2020 et le 19 janvier 2021 (n = 60) à l'Hôpital King's College pour une infection au SRAS-CoV-2.	• Aucune différence démographique (p. ex., âge, sexe, origine ethnique ou cote de privation) n'a été relevée entre les première et deuxième vagues. • Les maladies graves nécessitant une oxygénothérapie ou un soutien respiratoire étaient peu fréquentes dans les deux vagues et représentaient une proportion plus faible du nombre total de personnes admisses lors de la deuxième vague que pendant la première. • Les données de novembre 2020 à janvier 2021 montrent que de nombreux enfants et jeunes ont été hospitalisés en raison de la prévalence plus élevée du SRAS-CoV-2 à l'hôpital. Les constatations présentées dans cette étude étaient conformes aux données nationales. • Rien n'indiquait de maladies plus graves chez les enfants et les jeunes depuis que le variant B.1.1.7 circule plus, ce qui donne à penser que l'infection par ce variant n'entraîne pas une évolution clinique différente de celle de la souche originale.
Volz 2021 (4) *Préimpression* Cohorte rétrospective. Royaume-Uni Janvier 2021	Cette étude comprenait une analyse des cas associés à la négativation de la détection du gène S (SGTF), un substitut pour le variant B.1.1.7 et non SGTF dans les différentes régions d'Angleterre entre le 8 novembre et le 12 décembre 2020. Les répartitions selon l'âge ont été évaluées.	• L'analyse des tendances pendant le confinement (novembre 2020) montre que les cas sans SGTF ont diminué, mais que les cas à SGTF ont augmenté dans l'ensemble des juridictions du Royaume-Uni. • Après avoir normalisé les cas en fonction de la composition de la population, on peut voir beaucoup plus de cas à SGTF chez les personnes de 0 à 19 ans que chez les personnes sans SGTF. • Les auteurs suggèrent que les différences entre les répartitions selon l'âge des cas dans la communauté associés ou non aux variants préoccupants peuvent découler de l'augmentation globale de la

		transmissibilité des variants préoccupants (surtout pendant une période où un confinement était en vigueur, mais où les écoles étaient ouvertes).
Walker 2021 (10) *Préimpression* Cohorte rétrospective. Royaume-Uni Septembre 2020 à janvier 2021	Il s'agissait d'une vaste étude de surveillance communautaire effectuée au Royaume-Uni. Les données ont été analysées à partir d'écouvillons provenant de la gorge et du nez (n = 1 553 687) recueillis et testés par RT-PCR. La négativation de la détection du gène S (SGTF) a été utilisée comme substitut pour le variant B.1.1.7. Les valeurs du seuil de cycle (Ct) (indicateur de la charge virale), le pourcentage de cas positifs, la positivité de la population et les taux de croissance chez les cas à SGTF par rapport aux cas positifs sans SGTF ont été évalués selon l'âge.	• Dans l'échantillon, 0,98 % ont obtenu un résultat positif, soit 8 545 sans SGTF et 3 531 à SGTF. Entre le début de novembre 2020 et le 31 décembre 2020, les résultats positifs pour les cas à SGTF ont augmenté (par exemple, dans le cas de Londres, les pourcentages d'échantillons sont passés de 15 % à 38 % à 81 %). • En novembre, les cas sans SGTF sont demeurés stables et les cas à SGTF ont augmenté, ce qui a fait augmenter le nombre de cas de SRAS-CoV-2 plutôt que de remplacer les cas sans SGTF. Le taux de croissance était semblable chez les adultes et les enfants. • Aucun lien n'a été déterminé entre les valeurs Ct (indicateur de la charge virale) et les cas à SGTF. • Dans certaines régions, les cas à SGTF chez les jeunes sont apparus en premier, mais ce n'était pas uniforme d'une région à l'autre. Il n'y a eu aucune preuve de différence dans les taux de croissance de la SGTF entre les enfants jusqu'à l'école secondaire (5 % (1 à 8 %)) et les adultes (6 % (4 à 9 %)). Cela vient appuyer le fait que le variant B.1.1.7 n'est pas particulièrement adapté pour être plus transmissible chez les enfants.
Modèle prédictif (n = 1)		
Davies 2021 (11) Modèle prédictif Royaume-Uni Mars 2021	Un modèle mathématique de la transmission du SRAS-CoV-2 structuré selon l'âge et les régions a été réalisé à l'aide des données de mobilité Google et des sondages sur les contacts sociaux. Ce modèle a été utilisé	• Le modèle mathématique structuré en fonction de l'âge et de la région a permis de dégager l'hypothèse selon laquelle des valeurs Ct plus faibles (un indicateur d'une charge virale plus élevée) qui appuient le fait que les variants préoccupants sont plus transmissibles que les souches préexistantes, correspond mieux au modèle que l'hypothèse selon laquelle les enfants étaient plus susceptibles d'être infectés par les variants préoccupants que les souches préexistantes.

	pour mettre à l'essai quatre hypothèses différentes afin d'évaluer laquelle était la plus appropriée.	

MODES DE TRANSMISSION DU VARIANT PRÉOCCUPANT DE LA COVID-19 EN MILIEU SCOLAIRE

Quatre études ont été recensées sur les modèles de transmission de la COVID-19 en milieu scolaire, dont trois étaient des modèles prédictifs (tableau 2). Plus précisément, ces études ont exploré l'impact des fermetures d'écoles sur la transmission. Les études de modélisation ont évalué le nombre de reproductions R(t), qui indique la capacité d'une maladie à se propager, associé à différents scénarios de fermeture. Les valeurs R supérieures à 1 indiquent que le nombre de cas augmentera. Ces modèles ont montré que les fermetures d'écoles ont eu une certaine incidence sur la réduction de l'incidence des variants préoccupants dans la collectivité, mais que la transmission chez les enfants d'âge scolaire était plus fortement corrélée au niveau de la transmission dans la collectivité. Ces modèles ont permis de déterminer que la transmission en milieu scolaire contribue à la propagation des variants préoccupants, mais qu'elle n'en est pas le vecteur principal.

- Une étude de modélisation a révélé que les réductions du nombre de cas et de R(t) ont été les plus importantes lors d'un confinement national complet continu jusqu'au 19 avril 2021, comparativement à n'importe lequel des scénarios associés à la réouverture de certaines écoles. La réouverture des écoles primaires et des niveaux comportant des examens obligatoires, ou l'ouverture continue des écoles primaires et l'ouverture des écoles secondaires en alternance avec deux semaines en classe et deux semaines d'apprentissage en ligne, entraînera une augmentation plus faible du nombre de cas et du R(t) que si toutes les écoles restaient ouvertes (6).
- Une autre étude de modélisation a permis d'obtenir des résultats semblables indiquant que des restrictions strictes à la mobilité communautaire et la fermeture des écoles réduiront le R(t) à moins de 1 (11).
- Une étude de cohorte effectuée au Royaume-Uni a révélé qu'il y avait une forte augmentation des absences dans les établissements d'enseignement secondaire dans certaines régions de Londres en raison de l'augmentation des cas associés au variant B.1.1.7. Cela n'a pas été observé dans les écoles primaires. On a également vu une corrélation positive entre les cas dans les écoles et les cas dans la collectivité. En outre, rien n'indique non

plus que les écoles jouent un rôle important dans la transmission de l'infection dans la collectivité (5).

- Une étude de modélisation canadienne a estimé que le variant B.1.1.7 entraînerait une probabilité d'éclosion plus élevée de 3,6 fois et de 4,2 fois qu'avec la souche originale du SRAS-CoV-2, même si des mesures de contrôle strictes étaient mises en place pour les adultes et les enfants respectivement. Cette augmentation devrait se produire, peu importe si les écoles sont fermées ou ouvertes dans des scénarios où la collectivité reste ouverte en raison de mauvaises interventions en matière de santé publique et d'un risque élevé de transmission dans la collectivité. La modélisation a permis de déterminer que les écoles n'ont pas d'impact important sur la trajectoire de l'épidémie (7).

Tableau 2 : Preuve de la transmission des variants préoccupants en milieu scolaire (n = 4)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Études de modélisation prédictive (n = 3)		
Davies 2021 (11) Modèle prédictif Royaume-Uni Mars 2021	Un modèle de transmission adapté à sept régions NHS en Angleterre a été utilisé pour effectuer des projections quant aux effets que différentes mesures de contrôle auraient sur l'épidémie entre la mi-décembre 2020 et la fin de juin 2021. L'étude est modélisée sur l'hypothèse d'une transmissibilité accrue des variants. Quatre scénarios ont été comparés : (i) un scénario moyennement restrictif; (ii) un scénario très strict dans lequel les écoles sont ouvertes; (iii) le même scénario très strict, mais en gardant les écoles fermées jusqu'au 15 février 2021; et (iv) un scénario très strict dans lequel les écoles sont fermées.	• Le modèle de transmission a révélé que, peu importe les mesures de contrôle mises en œuvre, toutes les régions devraient connaître une nouvelle vague de cas de COVID-19 et de décès au début de 2021, vague qui atteindra un sommet en février si aucune mesure de contrôle importante n'est mise en œuvre ou à la mi-janvier si des mesures de contrôle rigoureuses sont en place. • Le modèle prévoyait également que des mesures plus strictes (iii et iv) créeraient à un plus grand nombre de cas de rebonds lorsque les restrictions simulées seraient levées en mars 2021. • Les auteurs suggèrent que la fermeture des écoles et les restrictions dans la communauté pourraient réussir à réduire le R(t) en dessous de 1.
Panovska-Griffiths 2021 (6) *Préimpression* Modèle prédictif Royaume-Uni Février 2021	Le modèle Covasim, calibré jusqu'au 25 janvier 2021, a été utilisé pour simuler l'impact d'un confinement national complet (CNC) avec fermeture des écoles jusqu'au 19 avril 2021 par rapport à quatre scénarios différents de confinement national partiel (CNP) avec différents établissements scolaires ouverts : 1) CNP avec un début décalé; 2) CNP avec retour de tous les élèves; 3) CNP avec ouverture des écoles primaires et seuls les élèves dont les niveaux comportent des examens obligatoires	• La modélisation suggère que la réduction du nombre de cas et du R(t) est plus importante avec un CNC continu jusqu'au 19 avril 2021 comparativement à n'importe lequel des scénarios avec réouverture de certaines écoles. La réouverture des écoles primaires et des niveaux comportant des examens obligatoires, ou l'ouverture continue des écoles primaires et l'ouverture des écoles secondaires en alternance avec deux semaines en classe et deux semaines d'apprentissage en ligne, entraînera une augmentation plus faible du nombre de cas

	(11e et 13e années) seront de retour à l'école; et 4) CNP avec ouverture des écoles primaires à plein temps et des écoles secondaires en alternance avec deux semaines en classe et deux semaines d'apprentissage en ligne. L'étude est fondée sur l'hypothèse selon laquelle le nouveau variant est plus transmissible et la proportion relative de la nouvelle souche a augmenté entre le 1er septembre 2020 et le 31 janvier 2021 en raison d'une fonction de croissance logistique, 30 % des infections détectées en décembre et 90 % des infections détectées à la fin de janvier 2021 auraient été causés par le nouveau variant.	et du R(t) que si toutes les écoles restaient ouvertes. • Le confinement national complet ramènera le nombre de cas d'ici le début de mars à un niveau semblable à celui d'octobre puisque le R(t) sera également en baisse et restera inférieur à 1. • Dans chaque scénario, le nombre de nouvelles infections devrait diminuer en janvier et au début de février. • Les répercussions sur les décès seront cependant décalées, avec un plafonnement des décès cumulatifs à compter de février dans chacun des scénarios. Cela est dû au fait que l'effet du vaccin a été modélisé avec un délai de 21 jours. Dans l'ensemble, si les écoles ouvrent, nous prédisons une augmentation du nombre d'infections et une augmentation du R(t), et un changement possible du R(t) supérieur à 1 une fois que le confinement prendra fin.
Yuan 2021 (7) *Préimpression* Modèle prédictif Toronto Juillet à novembre 2020	À l'aide d'un modèle déterministe de type SEIR élargi fondé sur l'âge, la ville où vit le ménage et adapté aux données démographiques de Toronto, le modèle a été étalonné en fonction des données épidémiologiques obtenues entre le 31 juillet et le 23 novembre 2020. Le modèle a été élaboré pour imiter la transmission dans les ménages, la collectivité et les écoles. Le nouveau variant préoccupant est basé sur le B.1.1.7 et on suppose que la probabilité de transmission augmentera de 50 % et que les enfants seront 70 % plus sensibles que les adultes. Le modèle suppose	• Si on compare la souche de référence et le variant et qu'on tient compte des restrictions imposées à la collectivité et des fermetures d'écoles, qui ont permis un contrôle quasi complet de l'épidémie, on estime que le variant entraînerait une augmentation de 3,6 fois le nombre de cas chez les adultes et de 4,2 fois le nombre de cas chez les enfants et les jeunes. • Les scénarios qui tiennent compte du nouveau variant indiquent que la fermeture des écoles n'a que peu d'impact sur la trajectoire de l'épidémie de janvier à mai 2021, puisqu'avec une réouverture de la communauté (étape 2) (ouverture partielle), on prévoyait un nombre de cas 7 fois ou

	également que ce variant sera la souche dominante après un mois. L'étude a modélisé l'impact du nouveau variant préoccupant en supposant une plus grande susceptibilité des enfants et des jeunes à ce nouveau variant.	7,5 fois plus élevé si les écoles étaient fermées plutôt qu'ouvertes. • Des augmentations exponentielles du nombre de cas ont été prédites, peu importe si les écoles étaient ouvertes ou fermées dans les scénarios dans lesquels la collectivité est entièrement ouverte (étape 3) en raison de la faiblesse des interventions en santé publique et du risque élevé de transmission dans la collectivité.
Études de cohorte (n = 1)		
Southhall 2021 (5) *Préimpression* Cohorte rétrospective. Royaume-Uni Septembre à décembre 2020	Une analyse de l'absentéisme des élèves et des enseignants a été effectuée pour évaluer l'impact du nouveau variant B.1.1.7. Des évaluations ont été effectuées dans des régions précises afin d'évaluer l'incidence différentielle du nouveau variant Londres et Kent ont été choisis en raison du nombre élevé de nouveaux cas associés au variant, tandis que Devon et les West Midlands ont été choisis parce qu'il y avait moins de cas déclarés associés à ce variant. En outre, le 3 décembre 2020, Devon était au niveau 2 alors que les West Midlands étaient au niveau 3.	• Une forte augmentation du nombre d'absences dans les établissements d'enseignement secondaire a été observée dans le Sud-Est et le Grand Londres en décembre, mais pas dans d'autres régions ou établissements d'enseignement primaire. • Les auteurs soupçonnent que les absences étaient liées à la transmissibilité accrue du nouveau variant B.1.1.7, qui a contribué à l'augmentation des cas dans les écoles secondaires de ces régions. • On a constaté une corrélation positive entre les cas dans la collectivité et les cas dans les écoles dans la plupart des régions. • Il n'y a cependant pas de preuve importante indiquant que les écoles jouent un rôle important dans la transmission dans la collectivité. • Il pourra être nécessaire de surveiller attentivement la réouverture des écoles pour déterminer l'effet associé à leur ouverture sur l'incidence dans la collectivité. • À Londres, dans le Kent et dans les West Midlands, une faible corrélation entre les cas parmi les élèves du secondaire et les cas dans la collectivité a augmenté avec le

		temps, ce qui indique qu'une augmentation des cas dans la collectivité est corrélée de façon plus positive avec une augmentation des cas dans les écoles à une date ultérieure. • Le même résultat a été observé chez les élèves des écoles primaires de Kent et des West Midlands. Cependant, la corrélation était négligeable entre les cas dans les communautés et les cas chez les enfants d'âge primaire à Londres, quel que soit le type de décalage choisi pour la réouverture.

Méthodologies :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé était effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-COV-2. Les termes de recherche utilisés comprenaient :
TERMES ASSOCIÉS À LA TRANSMISSION DANS LES ÉCOLES : (B.1.1.7 ou 501Y.V1 ou B.1351 ou 501Y.V2 ou P1 ou P2 ou B1.1.1.28 ou B.1.1.33 ou 501Y.V3 ou B.1.426 ou variant) ET school ET transmission
TERMES ENFANTS : B.1.1.7 ou 501Y.V1 ou 202012/01 ou B.1351 ou 501Y.V2 ou P1 ou P2 ou B1.1.1.28 ou B.1.1.33 ou 501Y.v3 B.1.426 ou variant) ET (children ou adolescent)
La présente revue contient des recherches publiées jusqu'au 26 mars 2021.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

Littérature grise

Une recherche dans la littérature grise a été effectuée afin de compléter la recherche dans la base de données. La littérature grise portait sur les principaux sites Web qui font état des variants B.1.1.7, incluant Public Health England et SPOR Evidence Alliance. La recherche dans la littérature grise a été effectuée du 24 au 26 mars 2020.

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

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Emerging Evidence on COVID-19

Rapid Review on the Impact of School Closures and Re-openings on COVID-19 Transmission

Introduction

What is the impact of school closures/re-openings on community transmission of COVID-19 and on the incidence of COVID-19 in primary and secondary schools?

Jurisdictions continue to implement a variety of non-pharmaceutical interventions (NPIs) to limit the spread of SARS-CoV-2 and the impact of COVID-19. Globally, closing schools was one of the earliest public health measures implemented, however this has not only disrupted the education and daily routines of students, but also the lives of teachers and parents.

While school closures have been implemented to combat the spread of SARS-CoV-2, they were also associated with negative effects on student's mental health, academic progress, and increased stress in parents and teachers (1). With a lack of school-based peer interactions and daily routines, students experience increased distress, loneliness, anxiety and depressive symptoms (1,2). School routines are crucial for maintaining the well-being of students with mental health or special education needs (3). In addition, school closures have been associated with reduced academic achievement due to delayed educational progress (1,4,5). It is uncertain whether virtual learning is equally effective and many students from low-income households lack access to, and accommodations with, online materials (5).

Given the negative impacts of school closures, it is important to consider whether they are significantly effective in reducing the impact of COVID-19. Initially, it was assumed that school closures would be effective in mitigating the spread of SARS-CoV-2 based on the evidence from the influenza epidemic (6,7). In contrast, modelling studies conducted in Ontario and Canada during the first and second waves found that school closures had limited impact on reducing the transmission of COVID-19 compared with other NPIs (8–10). Other modelling studies reported modest effects of school closures in delaying peak case numbers early in the pandemic (11,12) while some studies showed a smaller magnitude of effect when compared with other public health measures (13,14). Early modelling studies relied on the underlying assumption that there is a low transmission risk in children. Although modelling studies are excellent for making informed predictions, their accuracy is dependent on the assumptions and the quality of data used. Overall, there was a need to assess the potential benefits of school closures in reducing the spread of COVID-19.

This review summarizes empirical studies on the effectiveness of school closures and the impact of re-opening schools in reducing community transmission of COVID-19 and decreasing the incidence of COVID-19 in primary and secondary schools. The principal focus was the impact of primary and secondary school

closures, although if studies also included data from other types of schools this was included as well. Predictive modelling studies were excluded. This review summarizes literature until January 25th, 2021.

Key Points

- Twenty-four studies were identified on the topic of school closures or re-openings to limit the spread of COVID-19. There were 5 observational studies providing individual level data (two cohort studies, one cross-sectional study, and two cluster and outbreak investigations), and 19 ecological studies providing population level data.
- Most observational studies assessing the impact of school closures/re-openings on the spread of COVID-19 in schools reported no significant effects. Four studies found no difference in incidence of cases both before and after closing schools for the holidays, following children who stayed at home vs went to school with strict surveillance, or following school re-opening (15–18).
- Overall, the evidence from the ecological studies assessing community transmission was mixed. Five studies reported that school closures and re-openings were not significantly associated with reduction in the transmission and incidence of COVID-19, and were much less effective in reducing transmission when compared with other NPIs (19–23). Four studies reported a reduction in the incidence of COVID-19 in the community ranging from 8% to 62% following school closures (24–27) and other studies reported a significant reduction in the effective reproduction number (Rt) (28–30). Three studies attributed significant reductions in mortality to school closures (27,31,32) and one study reported increased mortality with delayed school closures (33).
- Many of the studies included post-secondary schools and half of the ecological studies did not describe what schools were included in their analyses.
- All of the ecological studies included in this review analyzed data on school closures/re-openings early in the pandemic, between January-August 2020, when multiple NPIs were implemented simultaneously so it was not possible to isolate the impact of school closures/re-openings on the number of cases of COVID-19 in the community.
- Only one of the ecological studies described if there was adherence to infection prevention and control (IPAC) measures in the schools assessed (23).
- Ecological studies are considered a low level of evidence due to the research design, the multiple confounding factors and the high degree of variability in the results, therefore there is a high degree of uncertainty with the evidence from the ecologic studies.

Overview of the Evidence

Twenty-four articles published prior to January 25, 2021 were identified on the impact of school closures/re-openings on the spread of COVID-19. This includes a cross-sectional study (n=1), cohort studies (n=2), cluster and outbreak investigations (n=2), and ecological studies (n=19). Eleven of these are studies are preprints or studies that have not been peer-reviewed.

The five observational studies use individual-level data to assess the effectiveness of school closures or the impact of school re-openings on COVID-19 transmission in schools and the community. Observational studies have moderate to high risk of bias if the study sample is not representative of the population. Cohort studies are one of the strongest observational study designs, especially if prospective, and can be used to determine a temporal relationship between school closures/re-openings and COVID-19 outcomes. These studies are at risk of selection bias if losses to follow-up occur or if confounding factors vary between groups. Cross-sectional studies provide a good picture of the impact of school closures at a particular point in time but with the use of self-reported data, there is a risk for recall bias so these studies cannot establish causation. Cluster and outbreak investigations are also at high risk of bias. Although these studies are useful, they are very situation specific and may not provide data that is generalizable to other populations.

The 19 ecological studies use population-level data mostly from publicly available data on COVID-19 outcomes. Ecological studies can be useful as an initial approach for determining public health trends and if there are strong associations observed, this can provide the opportunity for more carefully designed studies. However, these studies are at high risk of bias. It is important to note that ecological studies are prone to the ecological fallacy because what occurs at population-level may not occur at an individual level. There are many confounding factors involved in ecological studies so these studies are lower quality. Additionally, these studies were conducted very early in the pandemic simultaneously with other public health measures, therefore the findings are likely to change as new data becomes available.

An important limitation to be considered with this review is the inconsistency of the levels of schooling that were included in the measures of efficacy across studies. Most studies did not provide information on what schools were included when determining the impact of school closures on the spread of COVID-19. Some studies measured primary and secondary school closures alone, or in combination with other types of schools, therefore the magnitude of effect varies across studies. Additionally, the relative impact of school closures and re-openings will vary according to the time of implementation, level of community transmission, and the structure of populations from different countries. Overall, the confidence in this evidence is low given that the studies vary by several factors and were conducted at different times in a number of countries.

An important knowledge gap to consider is how the new variants of concern and the rollout of COVID-19 vaccinations will impact the transmission of COVID-19 within schools and the community. The evidence in this review pre-dates the introduction of the variants of concern, therefore it is unknown how this will impact the effectiveness of school closures or the impact of school opening on the spread of COVID-19.

CONTENTS

OBSERVATIONAL STUDIES

There were 5 observational studies that assessed the impact of school closures/re-openings on transmission of COVID-19 in schools using individual-level data (Table 1). IPAC measures implemented by the schools were similar across most of the observational studies: masks, physical distancing, frequent cleaning, reduced class sizes and hand hygiene. One cohort study did not report whether or not IPAC measures were implemented in the school (14). The implementation of IPAC measures in schools can act as a mediating variable with the results from these studies because of its ability to reduce transmission and risk of infection.

- Four studies found little or no impact of school closures or re-opening on transmission of COVID-19 in schools and the community:
    - A prospective cohort study that analyzed the association between school re-opening dates and COVID-19 cases across twenty-one regions in Italy found SARS-CoV-2 incidence among students was lower than the general population in 19/21 regions (16).
    - A retrospective cohort study found no evidence of transmission in schools prior to school closures despite several introductions and analysis of COVID-19. Infection attack rates (IAR) among family and relatives compared to teachers and staff of infected and not infected pupils provides evidence that most infections were likely acquired within the household (15).
    - A cross-sectional study comparing children in a school group with strict surveillance and a stay-at-home group found no significant differences in number of cases of SARS-CoV-2 in the children in each group (18).
    - A cluster investigation study reported a very low secondary attack rate overall after school re-opening, but that it was higher in secondary schools (6.6%) than in elementary schools (0.38%) (17).
    - A large outbreak was reported from a high school in Jerusalem, but this was confounded by the fact that the mask mandate was lifted as there was a heatwave shortly after re-opening (34).

Table 1: Observational studies assessing the impact of school closures or re-openings on the transmission of COVID-19 in schools and the community (n=5)

STUDY	METHOD	KEY OUTCOMES
Cohort studies (n=2)		
Gandini (2020) *preprint* (16) Prospective cohort study and cross-sectional study Italy	This study analyzed the association between school re-opening dates and COVID-19 cases across twenty-one Italian regions by using a database on positive cases in elementary, middle and high school. IPAC measures included: temperature control, hand hygiene, mask mandate for students/staff, physical distancing, ban on sports and music, and reduced duration of school.	• There was no evidence that the second SARS-CoV-2 wave was driven by schools re-opening across the regions. • SARS-CoV-2 incidence among students was lower than the general population of all but two Italian regions. • The increase in reproduction number R_t was not associated with the different school opening dates.

Sep-Nov 2020	Several COVID-19 outcomes were measured during school re-openings: growth of incidence, reproduction number (R_t), and secondary infections.	• School closures implemented in two regions did not affect the decline of R_t.
Fontanet (2020) *preprint* (15) Retrospective cohort study France Feb-Apr 2020	This retrospective cohort study included primary school pupils, teachers, non-teaching staff, parents, and relatives exposed to SARS-CoV-2 in February and March from 6 schools. IPAC measures were not described. A questionnaire covering sociodemographic information and history of recent symptoms was completed by participants. Blood samples were also tested for the presence of anti-SARS-CoV-2 antibodies using a flow-cytometry-based assay. Three introductions of SARS-CoV-2 occurred prior to school closures. Spread within schools vs families was investigated in this sero-epidmiological study. The infection attack rate (IAR) was compared between school contacts and family contacts to understand the potential impact of the school closure.	• The IAR was 45/510 (8.8%), 3/42 (7.1%), 1/28 (3.6%), 76/641 (11.9%) and 14/119 (11.8%) among primary school pupils, teachers, non-teaching staff, parents, and relatives, respectively (P = 0.29). • No secondary infections from COVID-19 introductions in schools was detected. • Among pupils who were infected, their parents were significantly more likely to be infected (61.0% versus 6.9%; P <0.0001), The same was identified among relatives of infected pupils compared to non-infected pupils (44.4% versus 9.1%; P = 0.002) • Transmission did not appear to be impacted by the closure of schools.
Cross-sectional studies (n=1)		
Kriger (2020) (18) Cross-sectional study Israel Mar-May 2020	During a national lockdown, an alternative school was used for healthcare workers' children to attend with strict symptom surveillance. Families with children who remained at home were compared to children at this alternative school. IPAC measures in the school included: daily disinfecting, face mask use by staff, and frequent hand washing. This cross-sectional study included 70 children who attended the alternative primary school and 36 who stayed home, along with their 78 parents. Data was collected through a short questionnaire; nasopharyngeal and oropharyngeal swabs were obtained and tested for SARS-CoV-2 by RT-PCR, and	• Symptoms were reported in approximately 16% of children in both groups: those who attended the school (11/70) and those who did not (6/36). • Positive serology tests showing previous exposure was detected in less than 2% of each group and they were not significantly different from each other. • There was no evidence of increased infection in those at school compared with those at home.

	blood was collected for SARS-CoV-2 IgA and IgG titres.	
Cluster and outbreak investigations (n=2)		
Larosa (2020) (17) Cluster investigation Italy Sep-Oct 2020	This cluster investigation analyzed the transmission of COVID-19 in 41 classes of 36 schools upon their re-opening in northern Italy. The secondary attack rate was measured in students and teachers in elementary and secondary schools (middle and high schools). IPAC measures included: mask mandate for high school students only, physical distancing, and ban of extracurricular activities.	• The secondary attack rate for COVID-19 was reported to be higher in secondary schools (6.6%) than in elementary schools (0.38%).
Stein-Zamir (2020) (34) Outbreak investigation Israel May-Jun 2020	This outbreak investigation study assessed the epidemiological characteristics of a high school outbreak in Jerusalem that displayed mass COVID-19 transmission upon school reopening on May 17th. The high school included grades 7 to 12. An extreme heatwave occurred upon the re-opening of the school. IPAC measures: face mask use was lifted for 3 days during the heatwave, physical distancing was below the standard in overcrowded classes, and extracurricular activities were not banned.	• It was reported that the proportion of the 10–19 years-olds was 19.8% (938/4,747) of the cases before May 24th, and then increased to 40.9% (316/772) after May 24th. • Testing of the whole school revealed that 153 students (attack rate: 13.2%) and 25 staff members (attack rate: 16.6%) were COVID-19 positive. • COVID-19 rates were higher in grades 7-9 than in grades 10-12.

CI = confidence interval, NPI = non-pharmaceutical intervention, Rt = effective reproduction number, SE = standard error, p = p-value, IPAC = infection prevention and control

ECOLOGICAL STUDIES

Nineteen ecological studies were identified that assessed the impact of school closures or re-openings on the spread of COVID-19 (Table 2). All ecological studies in Table 2 use population-level data to estimate the effectiveness of school closures or re-openings on preventing the spread COVID-19 in the community.

Overall, the evidence from the ecological studies assessing community transmission was mixed (n=19):

- Five studies reported that school closures and re-openings were not significantly associated with reduction in the transmission and incidence of COVID-19:
    - In a Japan study, the closure of primary and secondary schools was not found to be effective in decreasing the incidence of COVID-19 (21).

  - An ecological study in Germany found no significant effect on infections that could be attributed to school and day-care closures (22).
  - Child-to-child transmission in primary, secondary schools and childcare facilities in Germany was low and school reopening was not associated with a change in transmission (23).
  - A global study found that school closures were less effective than other NPIs (19).
  - A USA study found that closing schools was found to have the smallest reduction in Rt compared to 6 other NPIs that were assessed (20).
- Four studies reported a reduction in the incidence of COVID-19 ranging from 8% to 62% following school closures (24–27). Three studies reported a significant reduction in Rt:
  - A global study estimated an overall reduction in infection of 12% with closures of primary, secondary and tertiary educational institutions (28).
  - A USA study found that the closure of educational facilities was associated with a significant reduction in Rt compared to states without this policy (29).
  - A Hong Kong study reported a 44% reduction in transmission during the first 2 weeks of school closures including kindergartens up to tertiary and post-tertiary institutions, and tutorial centres (30).
- Three studies reported significant reductions in mortality with school closures (27,31,32) and one study reported increased mortality with delayed school closures (33).

Table 2: Ecological studies assessing the effectiveness of school closures or re-openings on reducing spread of COVID-19 in the community (n=19)

STUDY	METHOD	KEY OUTCOMES
Global (n=10)		
An (2021) *preprint* (19) Ecological study Global Jan-Jul 2020	This study aimed to identify associations between six NPIs and the number of COVID-19 infections. Using worldwide data on NPIs and COVID-19 infections between Jan-Jul 2020, analysis was conducted on the short-term and long-term effects of NPIs on new infection rates 5, 9, 12, and 21 days after their adoption. IPAC measures and level of schooling included in the study were not described. NPIs examined included mask mandates, international travel restrictions, domestic lockdowns, mass gathering bans, restaurant closures, and school closures.	• School closures took more time than other NPIs to show efficacy. After a time lag, the impact of school closures on new case rates was -0.492 (SE=0.16) at 12 days ($p<0.01$), -0.722 (SE=0.148) at 21 days ($p<0.001$), and -0.824 (SE=0.0967) at 30 days ($p<0.001$). • School closures were not found to have significant effects on population-adjusted infections in the long-term (90^{th} to 120^{th} day).

Banholzer (2020) *preprint* (25) Ecological study 20 countries Apr 2020	In this study, the impact of NPIs on the relative reduction of new COVID-19 cases using a Bayesian hierarchical model with a time-delayed effect for each NPI. IPAC measures were not described. NPIs examined included: (1) primary school closures, (2) border closures, (3) public event bans, (4) gathering bans, (5) venue closures, (6) lockdowns prohibiting public movements without valid reason, and (7) work bans on non-essential business activities.	• The mean reduction of new COVID-19 cases with primary school closures was 8% (95% CI: 0 to 23%). • Compared to other NPIs examined, school closures appeared to be one of the least effective NPIs.
Banholzer (2021) *preprint* (24) Ecological study 20 countries Feb-May 2020	Using a semi-mechanistic Bayesian hierarchical model, this study aimed to measure the effectiveness of seven NPIs in reducing the number of new infections. IPAC measures were not described. NPIs examined included: (1) primary school closures, (2) border closures, (3) public event bans, (4) gathering bans, (5) venue closures, (6) lockdowns prohibiting public movements without valid reason, and (7) work bans on non-essential business activities.	• The relative reduction of new COVID-19 cases with primary school closures was 17% (95% CI: 2% to 36%). • This reduction was lower than two other NPIs: event bans and venue closures.
Brauner (2021) (26) Ecological study 41 countries Jan-May 2020	This study estimated the effectiveness of NPIs in 41 countries using a Bayesian hierarchical model by linking intervention implementation dates to national case and death counts. Intervention effect sizes were categorized by the median reductions in the reproduction number R_t of <17.5% (small), between 17.5 and 35% (moderate), and >35% (large). NPIs examined included: limiting gatherings to <1000 or <100, or <10, closing some businesses, closing most businesses, closing schools and universities, and stay at home orders. IPAC measures were not described.	• The percentage reduction in Rt associated with closing both schools and universities in conjunction was 38% (95% CI: 16 to 54%) which was categorized as a large effect size. • The individual effects of school closures was not measured.

Klimek-Tulwin (2020) (35) Ecological study Global Mar 2020	This study aimed to assess the effect of school closures on COVID-19 cases globally by measuring correlation between the incidence rate on the day of school closure and the incidence rate in the following days. IPAC measures and level of schooling included in the study were not described.	• The results indicate that there was a strong correlation between the day of educational facilities closure and the incidence rate in the following days (16^{th} (p = 0.004), 30^{th} (p = 0.002), and 60^{th} (p = 0.031) days since the 100^{th} confirmed case in each country). • Early closure of schools is statistically significantly correlated with lower incidence rates further on during the different phases of the epidemic.
Papadopoulos (2020) *preprint* (36) Ecological study Global Jan-Apr 2020	The impact of lockdown measures was assessed globally using publicly available data. The timing and association of early NPIs with log10 national deaths (LogD) and log10 national cases (LogC) was compared between nations. IPAC measures and level of schooling included in the study were not described.	• Early generalised school closure (p=0.050, regression coefficient β=-0.012, 95% CI: 0 to -0.024) was associated with reduced LogC (log10 national cases).
Pasdar (2020) *preprint* (32) Ecological study 22 countries May 2020	The aim of this study was to determine the associations between NPIs and COVID-19 outcomes. Associations with NPIs were assessed with their respective stringency index (rs) on several outcomes that form the epidemic curve: mean mortality rate, time to peak, peak deaths per 100,000 population, cumulative deaths after peak per 100,000 population and ratio of the mean slope of the descending curve to the mean slope of the ascending curve. IPAC measures and level of schooling included in the study were not described.	• School closures were effective against all outcomes, except time to reaching the peak of the epidemic curve. • The strongest association was seen in cumulative deaths after peak, per 100,000 (rs = -0.744, p = 0.009). • In non-European countries, school closures were most effective against mean mortality rate (rs = -0.757, p = 0.049).
Esra (2020) *preprint* (28) Ecological study Global Jan-May 2020	This study used globally reported data on SARS-CoV-2 cases to fit a Bayesian model framework to estimate the association with NPIs and transmission. NPIs examined include stay home mandates, gathering limits, school closures (primary, secondary and tertiary educational	• There was an estimated mean reduction in Rt of 12% (95% CI: 5-19%) with school closures (primary, secondary and tertiary educational institutions).

	institutions), and mask policies. IPAC measures were not described.	
Jüni (2020) (37) Ecological study Global Mar 2020	This prospective study of geopolitical areas aimed to determine whether climate or public health interventions are associated with reducing transmission of COVID-19. A weighted random effects regression was used to determine the association between epidemic growth (ratios of rate ratios [RRR]) and climate measures and public health interventions such as school closures, restrictions of mass gatherings, and measures of social distancing during an exposure period 14 days previously. IPAC measures and level of schooling included in the study were not described.	• Strong negative associations with epidemic growth were found for school closures (RRR - 0.63, 95% CI: 0.52 to 0.78). • This association was more pronounced in areas that implemented 2 or 3 NPIs compared to 1 NPI.
Stokes (2020) *preprint* (31) Ecological study Global Jun 2020	This study examined the variation of NPIs in 130 countries in two periods: 1) prior to first COVID-19 death and 2) 14-days-post first COVID-19 death. This study examined associations with daily COVID-19 deaths per million and each 24 day period (time between virus transmission and mortality). IPAC measures and level of schooling included in the study were not described.	• Stricter/earlier school closures were associated with the largest reductions in COVID-19 deaths (-1.23 per million (95% CI: -2.20 to -0.27)) compared to other NPIs.
North America (n=5)		
Auger (2020) (27) Ecological study USA Mar-May 2020	This study aimed to determine if school closures were associated with a decrease in the cumulative incidence of COVID-19 and mortality. The impact of primary and secondary school closures was assessed using publicly available data from all 50 states. IPAC measures were not described.	• Results showed that school closures were associated with a significant decline in incidence of COVID-19 (−62% [95% CI: −71% to −49%]) and in mortality (−58% [95% CI: −68% to −46%]). • These associations were stronger in states with a low cumulative incidence of COVID-19 at the time of the school closure.
Dreher (2020) *preprint* (29) Ecological study	This study aimed to measure the impact of NPIs on the effective reproduction number (R_t) of COVID-19 in US states. The average R_t was measured during the weeks after each state reached 500 cases. R_t	• Educational facilities closure was associated with a significant reduction in R_t compared to states without this policy the week following 500 cases (ß = -0.17, 95% CI: -0.30 to -0.05, p = 0.009).

USA Apr 2020	was measured at the week immediately following 500th Case (days +1 to +7) and at a one-week delay from 500th case (days +8 to +14). NPIs examined included: stay at home order, educational facilities closure, and non-essential business closure. IPAC measures and level of schooling included in the study were not described.	• From days 8 to 14 after the 500th case date, educational facilities closure was associated with a significant reduction in R_t compared to controls (ß = -0.12, 95% CI: -0.21 to -0.04, p = 0.006).
Krishnamachari (2020) *preprint* (38) Ecological study USA May 2020	This study aimed to examine the effects of NPIs on the cumulative incidence rates of COVID-19 in the USA on a state-level in the 25 most populated cities, while adjusting for socio-demographic risk factors. A negative binomial regression was used to calculate adjusted rate ratios by comparing two levels of a binary variable: "above median value," and "median value and below" for days to implementing an NPI. NPIs assessed in this study included: days to closing of non-essential business; days to stay home orders; days to restrictions on gathering, days to restaurant closings and days to school closing. IPAC measures and level of schooling included in the study were not described.	• Days to school closing was associated with cumulative incidence on days 35 and 42, with an adjusted rate ratio of 1.59 (95% CI: 1.03 to 2.44, p=0.04) at 35 days, and adjusted rate ratio of 1.64 (95% CI: 1.07 to 2.52, p=0.04) at 42 days. • Delays in closing schools was positively associated with cumulative incidence at the state level.
Liu (2020) *preprint* (20) Ecological study USA Feb-Apr 2020	This study estimated the impact of nine different NPIs on reduction of the effective reproduction number (Rt) by using the daily number of reported new cases and inferred infections in 50 states. IPAC measures and level of schooling included in the study were not described.	• Closing schools was found to moderately reduce Rt by about 10% (95% CI: 7%-14%). • This reduction was smaller than 6 other NPIs assessed (stay-at-home order, face masks, gathering ban, non-essential business closure, declaration of state of emergency and interstate travel restriction).

Yehya (2020) (33) Ecological study USA Jan-Apr 2020	In this study, a state-level analysis was conducted to determine association between later implemented NPIs with higher mortality rates. Using a multivariable negative binomial regression, the association was tested between timing of emergency declarations and school closures with 28-day mortality. Day 1 for each state was set to when they recorded ≥ 10 deaths. IPAC measures and level of schooling included in the study were not described.	• Later school closure was associated with more deaths (adjusted mortality rate ratio aMRR 1.05; 95% CI: 1.01 to 1.09; p = 0.008).
Asia (n=2)		
Cowling (2020) (30) Ecological study Hong Kong Jan-Feb 2020	This study examined the effect of public health interventions on the incidence of COVID-19 and on the daily effective reproduction number (R_t). Laboratory-confirmed COVID-19 cases and on the daily effective reproduction number (R_t) were estimated to estimate changes in transmissibility over time. School closures included kindergartens up to tertiary and post-tertiary institutions, and tutorial centres. IPAC measures were not described.	• The estimated R_t was 1.28 (95% CI: 1.26–1.30) during the 2-week period before the start of the school closures and 0.72 (95% CI: 0.70–0.74) during the first 2 weeks of school closures, corresponding to a 44% (95% CI: 34–53%) reduction in transmissibility • R_t calculated from hospitalisation data was 1.10 (1.06–1.12) before the start of the school closures and reduced to 0.73 (0.68–0.77) after school closures, corresponding to a 33% (95% CI: 24–43%) reduction in transmissibility.
Kentaro (2020) (21) Ecological study Japan Mar 2020	This study aimed to assess the effectiveness of primary and secondary school closure on COVID-19 incidence nine days after implementation. IPAC measures were not described. Using a Bayesian method, time-series analyses were conducted and local linear trend models were developed for the number of newly reported cases of COVID-19.	• The school closure intervention was not effective in decreasing the incidence of COVID-19. • The newly reported COVID-19 cases continued to rise (α - 0.08, 95% CI: −0.36 to 0.65).
Europe (n=2)		

Wieland (2020) (22) Ecological study Germany Mar-Apr 2020	The aim of this study was to assess the effectiveness of different NPIs against the spread of COVID-19 over time. School closures included day-care closures as well. IPAC measures were not described. Using publicly available data on daily reported German cases, exponential growth models for infections and reproduction numbers were estimated and investigated with respect to change points in the time series.	• There was no significant effect found on COVID-19 infections that could be attributed to school and day-care closures.
Ehrhardt (2020) (23) Ecological study Germany Feb-Aug 2020	This study aimed to assess the transmission of SARS-CoV-2 among children in primary schools, secondary schools and childcare facilities in Baden-Württemberg, Germany after school reopening in May. IPAC measures included: reduced class size, disinfecting, hand hygiene, and banning of sports and music in primary and secondary schools. An epidemic curve was used to show the daily new cases after the schools reopened.	• Child-to-child transmission in schools was low. • The study estimated that one secondary case originates per 25 infectious school days (days that cases spent at school during infectious period). • School re-openings were not associated with a change in transmission of SARS-CoV-2.

CI = confidence interval, NPI = non-pharmaceutical intervention, Rt = effective reproduction number, SE = standard error, p = p-value, IPAC = infection prevention and control

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms included: school AND closure OR re-opening. References were also used to search for additional relevant studies. The literature search was confined to English and French language. This review contains research published up to January 25th, 2021. Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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Nouvelles données sur la COVID-19

Examen rapide de l'impact des fermetures et réouvertures d'écoles sur la transmission de la COVID-19

Introduction

Quel est l'impact des fermetures/réouvertures des écoles sur la transmission communautaire de la COVID-19 et sur l'incidence de celle-ci dans les écoles primaires et secondaires ?

Les juridictions continuent de mettre en œuvre une variété d'interventions non pharmaceutiques (INP) pour limiter la propagation du SRAS-CoV-2 et l'impact de la COVID-19. À l'échelle mondiale, la fermeture des écoles a été l'une des premières mesures de santé publique mises en œuvre, mais cette mesure a non seulement perturbé l'éducation et la routine quotidienne des élèves, mais aussi la vie des enseignants et des parents.

Si les fermetures des écoles ont été mises en œuvre contrer la propagation du SRAS-CoV-2, elles ont également été associées à des effets négatifs sur la santé mentale des élèves, les progrès scolaires et l'augmentation du stress chez les parents et les enseignants (1). En l'absence d'interactions avec leurs pairs à l'école et de routine quotidienne, les élèves ressentent davantage de détresse, de solitude, d'anxiété et de symptômes dépressifs (1,2). Les routines scolaires sont essentielles au maintien du bien-être des élèves ayant des besoins en matière de santé mentale ou d'éducation spécialisée (3). En outre, les fermetures des écoles ont été associées à une baisse des résultats scolaires en raison d'un retard dans la progression de l'enseignement (1, 4, 5). Il n'est pas certain que l'apprentissage virtuel soit aussi efficace et de nombreux étudiants issus de foyers à faibles revenus n'ont pas accès aux matériels en ligne et ne peuvent pas s'y adapter (5).

Compte tenu des impacts négatifs de la fermeture des écoles, il est important de se demander si elles sont significativement efficaces pour réduire l'impact de la COVID-19. Au départ, on a supposé que les fermetures d'écoles seraient efficaces pour atténuer la propagation du SRAS-CoV-2, en se basant sur les données de l'épidémie de la grippe (6,7). En revanche, des études de modélisation menées en Ontario et au Canada au cours de la première et de la deuxième vague ont montré que la fermeture des écoles avait un impact limité sur la réduction de la transmission de la COVID-19 par rapport aux autres INP (8–10). D'autres études de modélisation ont fait état d'effets modestes de la fermeture des écoles pour retarder le pic de cas au début de la pandémie (11,12) tandis que certaines études ont montré un effet de moindre ampleur par rapport à d'autres mesures de santé publique (13,14). Les premières études de modélisation reposaient sur l'hypothèse sous-jacente selon laquelle le risque de transmission est faible chez les enfants. Bien que les études de modélisation soient excellentes pour faire des prévisions éclairées, leur précision dépend des hypothèses et de la qualité des données utilisées. Dans l'ensemble, il était nécessaire d'évaluer les avantages potentiels de la fermeture des écoles pour réduire la propagation de la COVID-19.

Cette revue résume les études empiriques sur l'efficacité de la fermeture des écoles et l'impact de la réouverture des écoles sur la réduction de la transmission communautaire de la COVID-19 et la diminution de l'incidence de celle-ci dans les écoles primaires et secondaires. L'accent a été mis principalement sur l'impact de la fermeture des écoles primaires et secondaires, mais si les études comprenaient également des données sur d'autres types d'écoles, celles-ci étaient également incluses. Les études de modélisation prédictive ont été exclues. Cette revue résume la littérature jusqu'au 25 janvier 2021.

Points clés

- Vingt-quatre études ont été identifiées sur le thème de la fermeture ou de la réouverture des écoles pour limiter la propagation de la COVID-19. Il y avait 5 études observationnelles fournissant des données au niveau individuel (deux études de cohorte, une étude transversale et deux enquêtes sur des grappes et des épidémies), et 19 études écologiques fournissant des données au niveau de la population.
- La plupart des études observationnelles évaluant l'impact des fermetures/réouvertures des écoles sur la propagation de la COVID-19 dans les écoles n'ont signalé aucun effet significatif. Quatre études n'ont trouvé aucune différence dans l'incidence des cas avant et après la fermeture des écoles pour les vacances, en suivant les enfants qui sont restés à la maison par rapport à ceux qui sont allés à l'école avec une surveillance stricte, ou après la réouverture des écoles (15–18).
- Dans l'ensemble, les résultats des études écologiques évaluant la transmission communautaire sont mitigés. Cinq études ont rapporté que les fermetures et réouvertures des écoles n'étaient pas significativement associées à une réduction de la transmission et de l'incidence de la COVID-19, et qu'elles étaient beaucoup moins efficaces pour réduire la transmission par rapport à d'autres INP (19–23). Quatre études ont rapporté une réduction de l'incidence de la COVID-19 dans la communauté allant de 8 % à 62 % suite à la fermeture des écoles (24–27) et d'autres études ont rapporté une réduction significative du nombre effectif de reproductions (Rt) (28–30). Trois études ont attribué des réductions significatives de la mortalité à la fermeture des écoles (27, 31, 32) et une étude a signalé une augmentation de la mortalité en cas de fermeture tardive des écoles (33).
- Un grand nombre d'études incluaient des écoles postsecondaires et la moitié des études écologiques ne décrivaient pas quelles écoles étaient incluses dans leurs analyses.
- Toutes les études écologiques incluses dans cette revue ont analysé des données sur les fermetures/réouvertures des écoles au début de la pandémie, entre janvier et août 2020, lorsque plusieurs IPN ont été mises en œuvre simultanément ; il n'a donc pas été possible d'isoler l'impact des fermetures/réouvertures d'écoles sur le nombre de cas de COVID-19 dans la communauté.
- Une seule des études écologiques a décrit si les mesures de prévention et de contrôle des infections (PCI) étaient respectées dans les écoles évaluées (23).
- Les études écologiques sont considérées comme un faible niveau de preuve en raison de la conception de la recherche, des multiples facteurs de confusion et du haut degré de variabilité des résultats, il y a donc un haut degré d'incertitude avec les preuves provenant des études écologiques.

Aperçu des données probantes

Vingt-quatre articles publiés avant le 25 janvier 2021 ont été identifiés sur l'impact des fermetures/réouvertures des écoles sur la propagation de la COVID-19. Il s'agit d'une étude transversale (n=1), d'études de cohorte (n=2), d'enquêtes sur les grappes et les épidémies (n=2) et d'études écologiques (n=19). Onze de ces études sont des prépublications ou des études qui n'ont pas été examinées par des pairs.

Les cinq études observationnelles utilisent des données au niveau individuel pour évaluer l'efficacité de la fermeture des écoles ou l'impact de la réouverture de celles-ci sur la transmission de la COVID-19 dans les écoles et la communauté. Les études observationnelles présentent un risque de biais modéré à élevé si l'échantillon de l'étude n'est pas représentatif de la population. Les études de cohorte sont l'un des modèles d'étude observationnelle les plus solides, surtout si elles sont prospectives, et peuvent être utilisées pour déterminer une relation temporelle entre les fermetures/réouvertures d'écoles et les résultats de la COVID-19. Ces études sont exposées à un risque de biais de sélection en cas de perte de suivi ou si les facteurs de confusion varient d'un groupe à l'autre. Les études transversales donnent une bonne image de l'impact de la fermeture des écoles à un moment donné, mais avec l'utilisation de données autodéclarées, il existe un risque de la partialité de rappel, de sorte que ces études ne peuvent pas établir de lien de causalité. Les enquêtes sur les grappes et les épidémies présentent également un risque élevé de partialité. Bien que ces études soient utiles, elles sont très spécifiques à une situation et peuvent ne pas fournir de données généralisables à d'autres populations.

Les 19 études écologiques utilisent des données au niveau de la population, provenant pour la plupart de données accessibles au public sur les résultats de la COVID-19. Les études écologiques peuvent être utiles en tant qu'approche initiale pour déterminer les tendances en matière de santé publique et si de fortes associations sont observées, elles peuvent offrir l'occasion de mener des études conçues plus soigneusement. Toutefois, ces études présentent un risque élevé de partialité. Il est important de noter que les études écologiques sont sujettes au sophisme écologique, car ce qui se produit au niveau de la population ne se produit pas forcément au niveau individuel. Les études écologiques comportent de nombreux facteurs de confusion et sont donc de moindre qualité. En outre, ces études ont été menées très tôt dans la pandémie, en même temps que d'autres mesures de santé publique, de sorte que les conclusions sont susceptibles de changer à mesure que de nouvelles données sont disponibles.

Une limite importante à prendre en compte dans cette analyse est l'incohérence des niveaux de scolarité inclus dans les mesures d'efficacité entre les études. La plupart des études n'ont pas fourni d'informations sur les écoles prises en compte pour déterminer l'impact de la fermeture des écoles sur la propagation de la COVID-19. Certaines études ont mesuré les fermetures d'écoles primaires et secondaires seules, ou en combinaison avec d'autres types d'écoles, par conséquent l'ampleur de l'effet varie selon les études. En outre, l'impact relatif des fermetures et réouvertures des écoles variera en fonction du moment de leur mise en œuvre, du niveau de transmission communautaire et de la structure des populations des différents pays. Dans

l'ensemble, la confiance dans ces preuves est faible étant donné que les études varient en fonction de plusieurs facteurs et ont été menées à des moments différents dans un certain nombre de pays.

Une importante lacune dans les connaissances à prendre en compte est la manière dont les nouvelles variantes préoccupantes et le déploiement de la vaccination contre la COVID-19 auront un impact sur la transmission de la COVID-19 dans les écoles et la communauté. Les données de cette étude datent d'avant l'introduction des variantes préoccupantes, on ne sait donc pas comment cela influencera l'efficacité des fermetures des écoles ou l'impact de l'ouverture des écoles sur la propagation de la COVID-19.

CONTENU

ÉTUDES OBSERVATIONNELLES

Cinq études observationnelles ont évalué l'impact des fermetures/réouvertures des écoles sur la transmission de la COVID-19 dans les écoles en utilisant des données au niveau individuel (tableau 1). Les mesures PCI mises en œuvre par les écoles étaient similaires dans la plupart des études observationnelles : masques, distance physique, nettoyage fréquent, classes de taille réduite et hygiène des mains. Une étude de cohorte n'a pas indiqué si des mesures PCI avaient été mises en œuvre ou non en milieu scolaire (14). La mise en œuvre de mesures PCI dans les écoles peut agir comme une variable médiatrice avec les résultats de ces études en raison de sa capacité à réduire la transmission et le risque d'infection.

- Quatre études n'ont trouvé que peu ou pas d'impact de la fermeture ou de la réouverture des écoles sur la transmission de la COVID-19 dans les écoles et la communauté :
    - Une étude de cohorte prospective qui a analysé l'association entre les dates de réouverture des écoles et les cas de COVID-19 dans vingt et une régions d'Italie a révélé que l'incidence du SRAS-CoV-2 chez les étudiants était inférieure à celle de la population générale dans 19 des 21 régions (16).
    - Une étude de cohorte rétrospective n'a trouvé aucune de preuve de transmission dans les écoles avant la fermeture des écoles, malgré plusieurs introductions et analyses de COVID-19. Les taux d'attaque de l'infection (TAI) chez les membres de la famille et les proches par rapport aux enseignants et au personnel des élèves infectés et non infectés montrent que la plupart des infections ont probablement été contractées au sein du foyer (15).
    - Une étude transversale comparant les enfants d'un groupe scolaire soumis à une surveillance stricte et d'un groupe restant à la maison n'a révélé aucune différence significative dans le nombre de cas de SRAS-CoV-2 chez les enfants de chaque groupe (18).

- Une étude d'enquête par grappes a rapporté un très faible taux d'attaque global après la réouverture des écoles, mais qu'il était plus élevé dans les écoles secondaires (6,6 %) que dans les écoles primaires (0,38 %) (17).
- Une épidémie importante a été signalée dans un lycée de Jérusalem, mais elle a été compliquée par le fait que le port du masque a été levé en raison d'une vague de chaleur peu après la réouverture (34).

Tableau 1 : Études observationnelles évaluant l'impact de la fermeture ou de la réouverture des écoles sur la transmission de la COVID-19 dans les écoles et la communauté (n=5)

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Études de cohorte (n=2)		
Gandini (2020) *préimpression* (16) Étude de cohorte prospective et étude transversale Italie Sep-Nov 2020	Cette étude a analysé l'association entre les dates de réouverture des écoles et les cas de COVID-19 dans vingt et une régions italiennes en utilisant une base de données sur les cas positifs dans les écoles primaires, les collèges et les lycées. Les mesures PCI comprenaient : contrôle de la température, hygiène des mains, obligation de porter un masque pour les élèves et le personnel, éloignement physique, interdiction de faire du sport et de la musique et réduction de la durée de l'école. Plusieurs résultats sur la COVID-19 ont été mesurés pendant la réouverture des écoles : croissance de l'incidence, nombre de reproduction (R_t) et infections secondaires.	• Rien n'indique que la deuxième vague de SRAS-CoV-2 ait été provoquée par la réouverture des écoles dans les régions. • L'incidence du SRAS-CoV-2 chez les étudiants était inférieure à celle de la population générale dans toutes les régions italiennes sauf deux. • L'augmentation du nombre de reproductions R_t n'était pas associée aux différentes dates d'ouverture des écoles. • Les fermetures des écoles mises en œuvre dans deux régions n'ont pas affecté le déclin de la R_t.
Fontanet (2020) *préimpression* (15) Étude de cohorte rétrospective France Fév-Avril 2020	Cette étude de cohorte rétrospective a inclus des élèves des écoles primaires, des enseignants, du personnel non enseignant, des parents et des proches exposés au SRAS-CoV-2 en février et mars dans 6 écoles. Les mesures PCI n'ont pas été décrites. Un questionnaire couvrant les informations sociodémographiques et l'historique des symptômes récents a été rempli par les participants. Les échantillons de sang ont également été testés pour la présence d'anticorps anti-SARS-CoV-2 en utilisant un	• Le TAI était de 45/510 (8,8 %), 3/42 (7,1 %), 1/28 (3,6 %), 76/641 (11,9 %) et 14/119 (11,8 %) chez les élèves de l'école primaire, les enseignants, le personnel non enseignant, les parents et les proches, respectivement (P = 0,29). • Aucune infection secondaire due à l'introduction de la COVID-19 dans les écoles n'a été détectée. • Parmi les élèves infectés, leurs parents étaient significativement plus susceptibles d'être infectés (61,0 % contre 6,9 % ; P <0,0001), La même chose a été identifiée parmi les parents

	biotest basé sur la cytométrie en flux. Trois introductions du SRAS-CoV-2 ont eu lieu avant la fermeture des écoles. La propagation au sein des écoles et des familles a été étudiée dans cette étude séroépidémiologique. Le taux d'attaque de l'infection (TAI) a été comparé entre les contacts scolaires et les contacts familiaux afin de comprendre l'impact potentiel de la fermeture de l'école.	des élèves infectés par rapport aux élèves non infectés (44,4 % contre 9,1 % ; P = 0,002) • La transmission ne semble pas avoir été affectée par la fermeture des écoles.
Études transversales (n=1)		
Kriger (2020) (18) Étude transversale Israël Mars-Mai 2020	Lors d'un confinement national, une autre école a été utilisée pour les enfants des travailleurs de la santé, avec une surveillance stricte des symptômes. Les familles dont les enfants sont restés à la maison ont été comparées aux enfants de cette école alternative. Les mesures PCI dans l'école comprenaient : une désinfection quotidienne, le port d'un masque facial par le personnel et le lavage fréquent des mains. Cette étude transversale a inclus 70 enfants qui ont fréquenté l'autre école primaire et 36 qui sont restés à la maison, ainsi que leurs 78 parents. Les données ont été recueillies au moyen d'un court questionnaire ; des écouvillons nasopharyngés et oropharyngés ont été obtenus et testés pour le SARS-CoV-2 par RT-PCR, et du sang a été prélevé pour les titres IgA et IgG du SARS-CoV-2.	• Des symptômes ont été signalés chez environ 16 % des enfants des deux groupes : ceux qui fréquentaient l'école (11/70) et ceux qui ne la fréquentaient pas (6/36). • Des tests sérologiques positifs montrant une exposition antérieure ont été détectés dans moins de 2 % de chaque groupe et ils n'étaient pas significativement différents les uns des autres. • Il n'y avait aucune preuve d'une augmentation de l'infection chez les enfants scolarisés par rapport aux enfants à domicile.
Enquêtes sur les grappes et les épidémies (n=2)		
Larosa (2020) (17) Enquête sur les grappes Italie Sep-Oct 2020	Cette enquête sur les grappes a analysé la transmission de la COVID-19 dans 41 classes de 36 écoles lors de leur réouverture dans le nord de l'Italie. Le taux d'attaque secondaire a été mesuré chez les élèves et les enseignants des écoles primaires et secondaires (collèges et lycées). Les mesures du PCI comprenaient : le port d'un masque réservé aux élèves du secondaire, l'éloignement physique et l'interdiction des activités extrascolaires.	• Le taux d'attaque de la COVID-19 serait plus élevé dans les écoles secondaires (6,6 %) que dans les écoles primaires (0,38 %).

Stein-Zamir (2020) (34) Enquête sur les épidémies Israël Mai-Juin 2020	Cette étude d'enquête sur les épidémies a évalué les caractéristiques épidémiologiques d'une épidémie survenue dans un lycée de Jérusalem qui a présenté une transmission massive de la COVID-19 à la réouverture de l'école le 17 mai. Le lycée comprenait les classes de la 7 à la 12 années. Une vague de chaleur extrême s'est produite lors de la réouverture de l'école. Mesures PCI : le port du masque facial a été levé pendant 3 jours durant la canicule, l'éloignement physique était inférieur à la norme dans les classes surchargées et les activités périscolaires n'ont pas été interdites.	• Il a été rapporté que la proportion des 10-19 ans était de 19,8 % (938/4 747) des cas avant le 24 mai, puis a augmenté à 40,9 % (316/772) après cette même date. • Les tests effectués sur l'ensemble de l'école ont révélé que 153 élèves (taux d'attaque : 13.2 %) et 25 membres du personnel (taux d'attaque : 16.6 %) étaient des cas positifs de la COVID-19. • Les taux de COVID-19 étaient plus élevés dans les classes de 7e à la 9e année que dans les classes de la 10e à la 12e année.

IC = intervalle de confiance, INP = intervention non pharmaceutique, Rt = nombre effectif de reproductions, ES = erreur standard, p = valeur p, PCI = prévention et contrôle des infections

ÉTUDES ÉCOLOGIQUES

Dix-neuf études écologiques ont été identifiées pour évaluer l'impact de la fermeture ou de la réouverture des écoles sur la propagation de la COVID-19 (tableau 2). Toutes les études écologiques du tableau 2 utilisent des données au niveau de la population pour estimer l'efficacité de la fermeture ou de la réouverture des écoles sur la prévention de la propagation de la COVID-19 dans la communauté.

Dans l'ensemble, les résultats des études écologiques évaluant la transmission communautaire sont mitigés (n=19) :

- Cinq études ont rapporté que les fermetures et réouvertures des écoles n'étaient pas significativement associées à une réduction de la transmission et de l'incidence de la COVID-19 :
    - Dans une étude japonaise, la fermeture des écoles primaires et secondaires ne s'est pas avérée efficace pour réduire l'incidence de la COVID-19 (21).
    - Une étude écologique menée en Allemagne n'a révélé aucun effet significatif sur les infections qui pourrait être attribué à la fermeture des écoles et garderies (22).
    - La transmission d'enfant à enfant dans les écoles primaires, secondaires et les structures d'accueil en Allemagne était faible et la réouverture des écoles n'était pas associée à une modification de la transmission (23).
    - Une étude mondiale a révélé que les fermetures d'écoles étaient moins efficaces que les autres INP(19).

  - Une étude américaine a montré que la fermeture des écoles avait la plus faible réduction sur l'incidence de la pauvreté par rapport à 6 autres INP qui ont été évaluées (20).
- Quatre études ont rapporté une réduction de l'incidence de la COVID-19 allant de 8 % à 62 % suite à la fermeture des écoles (24-27). Trois études ont rapporté une réduction significative de la Rt :
  - Une étude mondiale a estimé une réduction globale de l'infection de 12 % avec la fermeture des établissements d'enseignement primaire, secondaire et tertiaire (28).
  - Une étude américaine a montré que la fermeture d'établissements d'enseignement était associée à une réduction significative de la Rt par rapport aux États n'ayant pas adopté cette politique (29).
  - Une étude réalisée à Hong Kong a fait état d'une réduction de 44 % de la transmission pendant les deux premières semaines de fermeture des écoles, y compris les écoles maternelles, les établissements d'enseignement supérieur et postsecondaire et les centres de tutorat (30).
- Trois études ont fait état de réductions significatives de la mortalité en cas de fermeture des écoles (27, 31, 32) et une étude a signalé une augmentation de la mortalité en cas de fermeture tardive des écoles (33).

Tableau 2 : Études écologiques évaluant l'efficacité de la fermeture ou de la réouverture des écoles sur la réduction de la propagation de la COVID-19 dans la communauté (n=19)

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Global (n=10)		
An (2021) *préimpression* (19) Étude écologique Global Jan-Jul 2020	Cette étude visait à identifier les associations entre six INP et le nombre d'infections par la COVID-19. À l'aide de données mondiales sur les INP et les infections de COVID-19 entre janvier et juillet 2020, une analyse a été menée sur les effets à court et à long terme des INP sur les taux de nouvelles infections 5, 9, 12 et 21 jours après leur adoption. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits. Les INP examinées comprenaient les mandats de port de masque, les restrictions aux voyages internationaux, les confinements nationaux, les interdictions de rassemblement de masse, les fermetures de restaurants et les fermetures d'écoles.	• Les fermetures des écoles ont mis plus de temps que les autres INP à montrer leur efficacité. Après un décalage temporel, l'impact de la fermeture des écoles sur les taux de nouveaux cas était de -0,492 (ES=0,16) à 12 jours (p<0,01), -0,722 (ES=0,148) à 21 jours (p<0,001) et -0,824 (ES=0,0967) à 30 jours (p<0,001). • Les fermetures des écoles n'ont pas eu d'effets significatifs sur les infections ajustées à la population à long terme (90^{e} à 120^{e} jour).

Banholzer (2020) *préimpression* (25) Étude écologique 20 pays Avril 2020	Dans cette étude, l'impact des INP sur la réduction relative des nouveaux cas de COVID-19 en utilisant un modèle hiérarchique bayésien avec un effet différé dans le temps pour chaque INP. Les mesures PCI n'ont pas été décrites. Les INP examinés sont les suivants : (1) fermetures des écoles primaires, (2) fermetures de frontières, (3) interdictions d'événements publics, (4) interdictions de rassemblements, (5) fermetures de lieux, (6) confinements interdisant les mouvements publics sans raison valable, et (7) interdictions de travail pour les activités commerciales non essentielles.	• La réduction moyenne des nouveaux cas de COVID-19 avec la fermeture des écoles primaires était de 8 % (IC 95 % : 0 à 23 %). • Par rapport aux autres INP examinées, la fermeture des écoles semble être l'une des INP les moins efficaces.
Banholzer (2021) *préimpression* (24) Étude écologique 20 pays Fév-Mai 2020	En utilisant un modèle hiérarchique bayésien semi-mécanique, cette étude visait à mesurer l'efficacité de sept INP dans la réduction du nombre de nouvelles infections. Les mesures PCI n'ont pas été décrites. Les INP examinés sont les suivants : (1) fermetures des écoles primaires, (2) fermetures de frontières, (3) interdictions d'événements publics, (4) interdictions de rassemblements, (5) fermetures de lieux, (6) confinements interdisant les mouvements publics sans raison valable, et (7) interdictions de travail pour les activités commerciales non essentielles.	• La réduction relative des nouveaux cas de COVID-19 avec la fermeture des écoles primaires était de 17 % (IC 95 % : 2 % à 36 %). • Cette réduction était inférieure à celle de deux autres INP : les interdictions d'événements et les fermetures de lieux.
Brauner (2021) (26) Étude écologique 41 pays Janvier-Mai 2020	Cette étude a estimé l'efficacité des INP dans 41 pays à l'aide d'un modèle hiérarchique bayésien en reliant les dates de mise en œuvre de l'intervention aux comptages nationaux des cas et des décès. Les tailles d'effet des interventions ont été catégorisées par les réductions médianes du nombre de reproductions R_t de <17.5 % (petit), entre 17,5 et 35 % (modéré), et >35 % (important).</17,5 %> Les INP examinées comprenaient : la limitation des rassemblements à <1000 ou <100, ou <10, la fermeture de certaines entreprises, la	• Le pourcentage de réduction de la R_t associé à la fermeture conjointe des écoles et des universités était de 38 % (IC 95 % : 16 à 54 %), ce qui a été classé comme une taille d'effet importante. • Les effets individuels des fermetures d'écoles n'ont pas été mesurés.

	fermeture de la plupart des entreprises, la fermeture des écoles et des universités, et l'ordre de rester à la maison. Les mesures PCI n'ont pas été décrites.	
Klimek-Tulwin (2020) (35) Étude écologique Global Mars 2020	Cette étude visait à évaluer l'effet de la fermeture des écoles sur les cas de COVID-19 au niveau mondial en mesurant la corrélation entre le taux d'incidence le jour de la fermeture de l'école et le taux d'incidence les jours suivants. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	• Les résultats indiquent qu'il existe une forte corrélation entre le jour de la fermeture des établissements d'enseignement et le taux d'incidence dans les jours suivants (26^{e} [p = 0,004], 30^{e} [p = 0,002] et 60^{e} [p = 0,031] jours depuis le 100^{e} cas confirmé dans chaque pays). • La fermeture précoce des écoles est corrélée de manière statistiquement significative avec des taux d'incidence plus faibles au cours des différentes phases de l'épidémie.
Papadopoulos (2020) *préimpression* (36) Étude écologique Global Janvier-Avril 2020	L'impact des mesures de confinement a été évalué au niveau mondial à l'aide de données accessibles au public. Le moment et l'association des INP précoces avec les décès nationaux log10 (LogD) et les cas nationaux log10 (LogC) ont été comparés entre les nations. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	• Fermeture généralisée précoce des écoles (p=0,050, coefficient de régression β=-0,012, IC 95 % : 0 à -0,024) était associée à une réduction du LogC (log10 des cas nationaux).
Pasdar (2020) *préimpression* (32) Étude écologique 22 pays Mai 2020	L'objectif de cette étude était de déterminer les associations entre les INP et les résultats de la COVID-19. Les associations avec les INP ont été évaluées à l'aide de leur indice de rigueur (irr) respectif sur plusieurs résultats qui forment la courbe épidémique : taux de mortalité moyen, temps jusqu'au pic, décès au pic pour 100 000 habitants, décès cumulés après le pic pour 100 000 habitants et rapport entre la pente	• Les fermetures d'écoles ont été efficaces pour tous les résultats, à l'exception du temps nécessaire pour atteindre le pic de la courbe épidémique. • L'association la plus forte a été observée dans les décès cumulés après le pic, pour 100 000 (irr = -0,744, p = 0,009). • Dans les pays non européens, la fermeture des écoles a été la plus

	moyenne de la courbe descendante et la pente moyenne de la courbe ascendante. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	efficace contre le taux de mortalité moyen (irr = -0,757, p = 0,049).
Esra (2020) *préimpression* (28) Étude écologique Global Janvier-Mai 2020	Cette étude a utilisé les données rapportées au niveau mondial sur les cas de SRAS-CoV-2 pour adapter un cadre de modèle bayésien afin d'estimer l'association avec les INP et la transmission. Les INP examinées comprennent les mandats de rester à la maison, les limites de rassemblement, les fermetures d'écoles (établissements d'enseignement primaire, secondaire et tertiaire) et les politiques de port des masques. Les mesures PCI n'ont pas été décrites.	• Il y a eu une réduction moyenne estimée de la Rt de 12 % (IC 95 % : 5-19 %) avec des fermetures d'écoles (établissements d'enseignement primaire, secondaire et tertiaire).
Jüni (2020) (37) Étude écologique Global Mars 2020	Cette étude prospective de zones géopolitiques visait à déterminer si les interventions climatiques ou de santé publique sont associées à la réduction de la transmission du COVID-19. Une régression pondérée des effets aléatoires a été utilisée pour déterminer l'association entre la croissance de l'épidémie (ratios de taux [RT]) et les mesures climatiques et les interventions de santé publique telles que les fermetures des écoles, les restrictions des rassemblements de masse et les mesures de distanciation sociale au cours d'une période d'exposition 14 jours auparavant. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	• Des associations négatives fortes avec la croissance épidémique ont été trouvées pour les fermetures des écoles (RT - 0,63, IC 95 % : 0.52 à 0,78). • Cette association était plus prononcée dans les zones qui ont mis en œuvre 2 ou 3 INP par rapport à 1 INP.

Stokes (2020) *préimpression* (31) Étude écologique Global Juin 2020	Cette étude a examiné la variation des INP dans 130 pays sur deux périodes : 1) avant le premier décès par COVID-19 et 2) 14 jours après le premier décès par COVID-19. Cette étude a examiné les associations avec les décès quotidiens par million de COVID-19 et chaque période de 24 jours (temps entre la transmission du virus et la mortalité). Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	• Les fermetures d'écoles plus strictes/précoces ont été associées aux réductions les plus importantes du nombre de décès par COVID-19 (-1,23 par million [IC 95 % : -2,20 à -0,27]) par rapport aux autres INP.
Amérique du Nord (n=5)		
Auger (2020) (27) Étude écologique É-U Mars-Mai 2020	Cette étude visait à déterminer si la fermeture des écoles était associée à une diminution de l'incidence cumulée du COVID-19 et de la mortalité. L'impact des fermetures d'écoles primaires et secondaires a été évalué à l'aide de données publiques disponibles dans les 50 États. Les mesures PCI n'ont pas été décrites.	• Les résultats ont montré que la fermeture des écoles était associée à une baisse significative de l'incidence de la COVID-19 (-62 % [IC 95 % : -71 % à -49 %]) et de la mortalité (-58 % [IC 95 % : -68 % à -46 %]). • Ces associations étaient plus fortes dans les états ayant une faible incidence cumulée de COVID-19 au moment de la fermeture de l'école.
Dreher (2020) *préimpression* (29) Étude écologique É-U Avril 2020	Cette étude visait à mesurer l'impact des INP sur le nombre effectif de reproductions (R_t) de COVID-19 dans les états américains. Le R_t moyen a été mesuré pendant les semaines suivant l'atteinte de 500 cas par chaque état. R_t a été mesuré à la semaine suivant immédiatement le 500^e cas (jours +1 à +7) et à une semaine de retard par rapport au 500^e cas (jours +8 à +14). Les INP examinées sont les suivantes : ordre de rester à la maison, fermeture d'établissements d'enseignement et fermeture d'entreprises non essentielles. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	• La fermeture des établissements d'enseignement était associée à une réduction significative de la R_t par rapport aux États sans cette politique la semaine suivant 500 cas (ß = -0,17, IC 95 % : -0,30 à -0,05, p = 0,009). • Du 8^e au 14^e jour après la 500^e date de cas, la fermeture des établissements d'enseignement était associée à une réduction significative de R_t par rapport aux témoins (ß = -0,12, IC 95 % : -0,21 à -0,04, p = 0,006).

Krishnamachari (2020) *préimpression* (38) Étude écologique É-U Mai 2020	Cette étude visait à examiner les effets des INP sur les taux d'incidence cumulée du COVID-19 aux États-Unis au niveau des 25 villes les plus peuplées, tout en ajustant les facteurs de risque sociodémographiques. Une régression binomiale négative a été utilisée pour calculer les ratios de taux ajustés en comparant deux niveaux d'une variable binaire : « valeur supérieure à la médiane », et « valeur médiane et inférieure » pour les jours de mise en œuvre d'un INP. Les INP évalués dans cette étude comprennent : les jours de fermeture des commerces non essentiels, les jours d'ordre de rester à la maison, les jours de restriction des rassemblements, les jours de fermeture des restaurants et les jours de fermeture des écoles. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	• Le nombre de jours avant la fermeture de l'école était associé à l'incidence cumulée aux jours 35 et 42, avec un rapport de taux ajusté de 1,59 (IC 95 % : 1.03 à 2,44, p=0,04) à 35 jours, et ratio de taux ajusté de 1,64 (IC 95 % : 1.07 à 2,52, p=0,04) à 42 jours. • Le retard dans la fermeture des écoles était positivement associé à l'incidence cumulée au niveau de l'État.
Liu (2020) *préimpression* (20) Étude écologique É-U Févr-Avril 2020	Cette étude a estimé l'impact de neuf INP différents sur la réduction du nombre effectif de reproductions (Rt) en utilisant le nombre quotidien de nouveaux cas signalés et d'infections déduites dans 50 États. Les mesures PCI et le niveau de scolarité inclus dans l'étude n'ont pas été décrits.	• On a constaté que la fermeture des écoles réduisait modérément d'environ 10 % (IC 95 % : 7 %-14 %). • Cette réduction était inférieure à celle de six autres INP évalués (ordre de rester à la maison, masques faciaux, interdiction de rassemblement, fermeture d'entreprise non essentielle, déclaration de l'état d'urgence et restriction des déplacements entre États).
Yehya (2020) (33) Étude écologique É-U Janvier-Avril 2020	Dans cette étude, une analyse au niveau de l'État a été réalisée pour déterminer l'association entre les INP mis en œuvre plus tard et les taux de mortalité plus élevés. À l'aide d'une régression binomiale négative multivariable, l'association entre le moment de la déclaration de l'état d'urgence et de la fermeture des écoles et la mortalité à 28 jours a été testée. Le jour 1 pour chaque État a été fixé au moment où ils ont enregistré ≥ 10 décès. Les mesures PCI et le niveau de	• La fermeture plus tardive des écoles a été associée à un plus grand nombre de décès (ratio de taux de mortalité ajusté aMRR 1,05 ; IC 95 % : 1.01 à 1,09 ; p = 0,008).

	scolarité inclus dans l'étude n'ont pas été décrits.	
Asie (n=2)		
Cowling (2020) (30) Étude écologique Hong Kong Janv.-Févr. 2020	Cette étude a examiné l'effet des interventions de santé publique sur l'incidence de la COVID-19 et sur le nombre de reproductions effectif quotidien (R_t). Les cas de COVID-19 confirmés en laboratoire et le nombre de reproductions effectif quotidien (R_t) ont été estimés pour estimer les changements de transmissibilité dans le temps. Les fermetures d'écoles ont concerné les garderies jusqu'aux établissements d'enseignement supérieur et postuniversitaire, ainsi que les centres de tutorat. Les mesures PCI n'ont pas été décrites.	• Le R_t estimé était de 1,28 (IC 95 % : 1.26-1,30) au cours de la période de deux semaines précédant le début de la fermeture des écoles et 0,72 (IC 95 % : 0,70-0,74) pendant les 2 premières semaines de fermeture des écoles, ce qui correspond à une baisse de 44 % (IC 95 % : 34-53 %) de réduction de la transmissibilité • Le R_t calculé à partir des données d'hospitalisation était de 1,10 (1,06-1,12) avant le début des fermetures d'écoles et a diminué à 0,73 (0,68-0,77) après les fermetures des écoles, ce qui correspond à une réduction de 33 % (IC 95 % : 24-43 %) de réduction de la transmissibilité.
Kentaro (2020) (21) Étude écologique Japon Mars 2020	Cette étude visait à évaluer l'efficacité de la fermeture des écoles primaires et secondaires sur l'incidence du COVID-19 neuf jours après sa mise en œuvre. Les mesures PCI n'ont pas été décrites. En utilisant une méthode bayésienne, des analyses de séries chronologiques ont été effectuées et des modèles de tendances linéaires locales ont été développés pour le nombre de nouveaux cas de COVID-19 ont été développés pour le nombre de nouveaux cas de COVID-19.	• L'intervention de fermeture de l'école n'a pas été efficace pour diminuer l'incidence de la COVID-19. • Les cas de COVID-19 nouvellement signalés ont continué à augmenter (α - 0,08, IC 95 % : -0.36 à 0,65).
Europe (n=2)		

Wieland (2020) (22) Étude écologique Allemagne Mars-Avril 2020	L'objectif de cette étude était d'évaluer l'efficacité de différentes INP contre la propagation de la COVID-19 sur un certain temps. Les fermetures des écoles incluent également les fermetures de garderies. Les mesures PCI n'ont pas été décrites. À l'aide de données accessibles au public sur les cas quotidiens signalés en Allemagne, des modèles de croissance exponentielle pour les infections et les nombres de reproductions ont été estimés et étudiés par rapport aux points de changement dans la série chronologique.	• On n'a pas trouvé d'effet significatif sur les infections à COVID-19 qui pourrait être attribué à la fermeture des écoles et des garderies.
Ehrhardt (2020) (23) Étude écologique Allemagne Févr. — août 2020	Cette étude visait à évaluer la transmission du SRAS-CoV-2 chez les enfants des écoles primaires, des écoles secondaires et des structures d'accueil du Baden-Württemberg, en Allemagne, après la réouverture des écoles en mai. Les mesures du PCI comprenaient : la réduction de la taille des classes, la désinfection, l'hygiène des mains et l'interdiction du sport et de la musique dans les écoles primaires et secondaires. Une courbe épidémique a été utilisée pour montrer les nouveaux cas quotidiens après la réouverture des écoles.	• La transmission d'enfant à enfant dans les écoles était faible. • L'étude a estimé qu'un cas secondaire est généré pour 25 jours d'école infectieuse (jours que les cas ont passé à l'école pendant la période infectieuse). • La réouverture des écoles n'a pas été associée à une modification de la transmission du SRAS-CoV-2.

IC = intervalle de confiance, INP = intervention non pharmaceutique, Rt = nombre effectif de reproductions, ES = erreur standard, p = valeur p, PCI = prévention et contrôle des infections

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé la littérature sur la COVID-19 depuis le début de l'épidémie et est mis à jour quotidiennement. Les recherches pour retrouver la littérature pertinente sur la COVID-19 sont effectuées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et croisées avec les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats de l'analyse complète sont conservés dans une base de données Refworks et dans une liste Excel qui peut être consultée. Une recherche ciblée par mots-clés a été menée dans ces bases de données afin d'identifier les citations pertinentes sur la COVID-19 et SARS-COV-2. Les termes de recherche comprenaient : école ET fermeture OU réouverture. Les références ont également été utilisées pour rechercher d'autres études pertinentes. La recherche documentaire s'est limitée aux langues anglaise et française. Cette revue contient les recherches publiées jusqu'au 25 janvier 2021. Chaque référence potentiellement pertinente a été

examinée pour confirmer qu'elle contenait des données pertinentes et les données pertinentes ont été extraites dans l'examen.

Révision par les pairs

Le présent document a fait l'objet d'une révision par les pairs, par un expert en la matière, ainsi que d'un examen rédactionnel et d'un examen des aspects scientifiques et politiques par le Bureau du directeur scientifique.

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Emerging Evidence on COVID-19

Evidence Brief on the Risk of COVID-19 Transmission in Flight, Update 2

Introduction

What is the evidence on transmission of COVID-19 during air travel and on assessing the risk and mitigation strategies around air travel?

Many changes have been implemented by airlines during the pandemic to reduce the risk of SARS-CoV-2 transmission during air travel. This evidence brief summarizes the literature on in-flight transmission of SARS-CoV-2, the characteristics of these events and the strategies used or studied to mitigate transmission in an airplane or during boarding and disembarkation. The first update of this review contained literature published up to October 28, 2020. This is the second update and includes studies up until April 26, 2021.

What's New

- Twenty-nine additional studies were added in this update (published between Oct 28, 2020 and Apr 26, 2021; nine new flight investigations (Table 1), nine reviews and risk assessments on in-flight transmission (Table 2) and eleven new simulation studies on reduction of respiratory virus spread and the relative impact of mitigation strategies during air travel (Table 3). These new studies bring the total number of studies included in this review to 64.

- Several studies estimated attack rates that varied depending on the proximity to the infected case when seated on the airplane. Estimates varied, but the attack rates were consistently low, particularly with mandatory face masks.

- Four risk assessments were added to this update and provide estimated overall probabilities of acquiring COVID-19 during a flight at different points in the pandemic. These estimates varied widely depending on the data used, assumptions of the model and whether or not the model accounted for under-reporting of in-flight transmission.

Key Points

- Twenty-six flight investigations (contact tracing or cohorts) were identified, of these nine reported no secondary cases (five on repatriation and four on commercial flights) and seventeen reported likely transmission from in-flight exposure. Whole genome sequencing results were available for five investigations and aided in linking cases to an on-flight single exposure. Implications of emerging Variants of Concern were not addressed in any of the captured studies.

- The overall attack rate of SARS-CoV-2 among passengers on short to medium-haul flights (1.5-2.5 hours long) was low.
- No transmissions from passengers to crew or between crew members were documented on repatriation flights.
- Most in-flight transmission events occurred on flights without mandatory face masks. Transmission was primarily passenger to passenger, although four studies reported transmission event(s) from passenger to crew. On flights with mandatory mask use, some transmission events occurred that were thought to be due to either incorrect mask use (e.g., not covering the nose) or to the removal of a mask to eat or drink.
- Symptom and temperature checks were conducted on some flights. Lack of adherence by passengers to self-report symptoms led to transmission on at least one flight.
- Proximity to an index case (two-row radius) was a risk factor in investigations where seating charts were available.
- The most common enhanced public health measures were in-flight physical distancing, enhanced cleaning, mandatory face masks, hand hygiene, physical distancing during boarding and disembarking, designated crew only areas, and quarantine areas for unwell passengers. One survey of passengers and crew indicated that both the passengers and crew felt safer after implementation of enhanced safety measures to curb transmission and felt that most measures were feasible to implement, apart from physical distancing of 1.5-2m while in-flight.

- Mitigating the risk of SARS-CoV-2 transmission during air travel was discussed directly in 14 reviews and risk assessments (Table 2) and indirectly in 24 reviews, predictive models, simulation experiments, environmental monitoring studies and *in silico* studies (Table 3).
  - The key findings of the SARS-CoV-2 literature on transmission during flights is that multiple interventions are needed to maximally reduce the risk of transmission (Table 2); this is summarized well in the Appendix figure from the Aviation Public Health Initiative report lead by Harvard (1).
    - A meta-analysis found that from January–June 2020, the risk of being infected with SARS-CoV-2 in an airplane cabin was estimated to be 1 case for every 1.7 million travelers.
    - The longer the duration of the flight, the higher the infection risk. Removing masks for meal service led to increased risk.
    - Public health measures to maintain physical distancing during boarding, disembarkation and in-flight, enhanced cleaning, hand hygiene and universal mask use for duration of flight implemented in a layered approach significantly reduce the risk of transmission.

- Airplane ventilation systems are designed to quickly refresh cabin air and this level of ventilation substantially reduces the time particles remain in the cabin compared to other indoor environments and thus reduces the opportunity for transmission, particularly when coupled with other public health measures (Table 2 & 3).
- Adherence to public health measures by passengers and crew are a critical factor to the impact of these measures to reduce the risk of transmission, such as symptom screening guidelines and on-board procedures.

- The indirect literature investigates the aerodynamics of droplets and aerosols to characterize high risk situations, or simulates boarding and in-flight movements to suggest strategies for minimizing interaction of people and maximizing the distance between people in flight (Table 3).
  - In-flight particle concentrations in the air in airplanes are lower than that of retail/grocery stores, restaurants, office spaces, homes, and other forms of transport.
  - Passengers who sneeze or cough while standing or moving about the cabin spread their respiratory droplets considerably further than those seated.
  - Wearing a face mask significantly decreased the spread of droplets (>90%).
  - Boarding an airplane by groups of related individuals, those seated in back of plane and window seats first as well as other more complicated algorithms were shown to reduce the interaction with other people. Decreasing the amount of carry-on luggage was also found to reduce interactions on-board. Although some strategies such as increasing the number of boarding groups or social distancing may sacrifice efficiency (i.e., longer total boarding/disembarkation time), they can significantly reduce the risk of infection.
  - Grouping families and strategically spacing passengers on flights that are not at capacity improves physical distance between passengers. Algorithms developed by researchers were presented to maximize this concept and demonstrated the potential performance of these algorithms compared to middle seat empty or aisle seat empty strategies. Across all of these strategies, their effectiveness decreased on fuller airplanes.

Overview of the Evidence

The in-flight transmission events recorded across studies were investigated through contact tracing investigations and cohorts. The cluster/outbreak investigations are at risk of bias due to their retrospective and descriptive nature. Cohorts were available for repatriation flights and are at lower risk of bias because the passengers and crew were followed-up in a uniform manner for a specific time period.

Other types of evidence include review literature ranging from good quality systematic reviews to commentaries. There was good agreement in the information and recommendations across the different review literature.

Quantitative risk assessments, predictive models, simulation experiments and other *in silico* studies were highly variable in their objectives and approaches. No attempt to assess the validity of these studies was conducted. These studies aim to mimic a real world scenario usually to explore options for different interventions. Their results should be interpreted with caution as they may not reflect what would happen in a field setting.

There were only a small number of flights for which epidemiological investigations of possible transmission events had been undertaken. These events are likely under-reported and/or under-investigated due to the logistics and available resources for contact tracing. It is also difficult to classify instances of in-flight transmission as acquisition of SARS-CoV-2 may occur prior to departure, at various points during travel, or during quarantine/upon arrival. Whole genome sequencing may help in linking cases to an on-flight single exposure. Future investigations, risk assessments, and predictive models should also address the implications that emerging SARS-CoV-2 variants and their attributes (e.g., increased transmissibility) may have on in-flight transmission risk, as well as vaccination status of both travellers and airline staff in mitigating risk.

CONTENTS

TRANSMISSION EVENTS ON AIRPLANES

The full extent of COVID-19 exposure associated with airplanes is not known. The table below lists 26 studies (9 are new since the last review update) where the possibility of in-flight SARS-CoV-2 transmission was investigated. Seventeen report transmission occurred and 9 report no transmission occurred during the flights. Several studies of repatriation flights where many precautions were taken report no transmission to the crew (2-7).

Symptom and temperature screening at the airport were mentioned in a few investigations. The failure of individuals to self-report and adhere to the screening guidelines demonstrate that screening was not an effective control measure on its own; it needs to be used in conjunction with other precautions. This was

demonstrated well in the business class outbreak reported by Khanh et al. (2020) where one index case caused 15 secondary cases on a flight where masks were not mandatory (8).

Many of the larger transmission events occurred before the mandatory use of face masks on flights (8-11) or other risk reduction strategies had been implemented. There are also a few instances where transmission events occurred even though face masks were mandatory (12-15). Investigations that examined adherence and proper use of face masks during these transmission events, reported both incorrect use of the mask (e.g., not covering the nose) and eating and drinking on the plane for a period of time when the mask was removed. One epidemiological investigation suggested in-flight SARS-CoV-2 transmission from a passenger to a flight attendant and then secondary transmission a few days later to another flight attendant who shared the crew resting area and ground transportation with the infected flight attendant (use of face masks on the flights was not mentioned) (16).

An investigation of 18 England-bound flights report the overall SARS-CoV-2 transmission on short to medium-haul flights (1.5-2.5 hours) to be low, with an attack rate of only 0.2% (95%CI 0.1-0.5) among flight-only contacts (17). The attack rate was higher for contacts who sat within a two-seat radius of the infectious cases (3.8% 95%CI 1.3-10.6%); however, the highest risk was among co-travellers with multiple non-flight exposures to the infected case (AR 13% 95%CI 7.6-21.4). Other outbreaks with seating charts, where available, were able to show the proximity of secondary cases to the index cases, which showed those seated within two rows of the index case were at higher risk of acquiring COVID-19 (8, 17, 18). However there were several cases across the outbreaks that were seated much further away and the mode or circumstance of transmission was not obvious (could have been from movement in cabin, shared restrooms, or fomite transmission) and cannot be confirmed (8, 9, 19, 20).

Across outbreak reports it was frequently mentioned that the window seat should be a safer seat as there are fewer contacts with other people compared to the aisle seats, however one investigation found that being in a window seat was a higher risk than the aisle seat (9). This was an unexpected finding that the authors could not explain. Table 3 describes studies that look at the potential differences in risk of sitting in different areas and seats on an airplane.

Whole genome sequencing (WGS) was undertaken in five investigations. In all cases it helped to identify cases linked to the same source and, particularly in the Australian and New Zealand investigations, WGS added a layer of information that the epidemiological investigation would have missed (9, 12, 21).

Several limitations are observed across these investigations mainly related to limitations in the data obtained. For example, pre/post flight contacts between index case and secondary contacts could not be excluded (8, 9, 15, 16, 18, 20, 22), and for some investigations, seating location was not known (8, 13).

Table 1: A list of transmission events that have occurred during flights (n=26)

STUDY	METHOD	KEY OUTCOMES
Flights with secondary cases identified		

Blomquist (2021) (17) *new* Cohort UK Dec 2020	Identified infections among passengers 18 England-bound flights with infectious cases using national case management datasets. Passengers were considered to be infectious during the flight if lab results were positive 7 days before or 2 days after the flight. Note: whole genome sequencing could not be applied as this data was not available for index and secondary cases from the same flight.	- The investigation determined 5 cases to be linked to potential aircraft transmission, 55 infectious passengers and 2313 co-passengers, with 2221 flight-only contacts. The overall SARS-CoV-2 transmission on short to medium-haul flights was estimated to be low. - The following attack rates were estimated: - 0.2% (95%CI 0.1-0.5) among all flight-only contacts. - 3.8% (95%CI 1.3-10.6) among contact-traced flight-only contacts who sat within a two-seat radius. - 13.0% (95%CI 7.6%-21.4%) among co-travellers with multiple non-flight exposures to infectious cases.
Swadi (2021) (21) *new* Outbreak Investigation New Zealand Sep 2020	A comprehensive investigation into the potential source of COVID-19 infections among 7 travelers that were on a flight from Dubai, UAB on Sept 29th 2020, with a stop in Kuala Lumpur, Malaysia, and landed in Auckland, New Zealand (18 hour duration). These 7 passengers had been seated within 4 rows of each other. The lineage of the genomes obtained from the 7 passengers was determined. Mask use was not mandatory. Post aircraft transportation to quarantine facilities was physically distanced where possible, and mask use was mandated.	- During the required 14-day managed isolation and quarantine period, 7 passengers who had traveled on the flight received positive SARS-CoV-2 test results. - The 7 passengers had begun their journeys from 5 different countries before a layover in Dubai; pre-departure SARS-CoV-2 test results prior to boarding were negative for 5. None of the passengers reported close contact at the Dubai airport. - Among the 7 passengers, 2 were probably index case-patients infected before the flight, 4 were probably infected during the flight, and the remaining passenger was probably infected while in isolation. - 5/7 cases wore masks and gloves while on the flight, including the two index cases, while the other two cases did not. - Genomic analysis found that the sequences obtained from all 7 cases were assigned to lineage B.1 and were genetically identical.
Eichler (2021) (12)	Investigated the origin of multiple COVID-19 cases	- Genomic sequence and epidemiological analysis identified a multi-branched chain of transmission

new Outbreak investigation New Zealand Aug 2020	identified after 14 days in post travel quarantine.	that included international and domestic air travel and probable aerosol transmission in the quarantine hotel (not summarized below). - The index case was identified to be a repatriated citizen returning to New Zealand from India. - Three secondary cases from the index case's 18 hour (35% occupancy) international flight on a Boeing 747 were identified by whole genome analysis. All three cases sat within 2 rows from each other, and were required to wear facemasks. - In-flight infection transmission also occurred from one of the secondary cases, who was unknowingly exposed during quarantine and released from quarantine before they were positive, to three passengers during an 85 minute domestic flight (50% capacity) on a Boeing 737. The three cases sat near one another (in front of each other) while the infectious case sat at a distance. - Note: All flight passengers wore masks during the flights.
Mun (2021) (16) *new* Case series South Korea Feb-Mar 2020	This case series describes two flight attendants diagnosed with COVID-19 who shared the crew's resting area and ground transportation, and discusses the risks experienced by flight attendants.	- The first case became ill on Feb 21, 2020 and was diagnosed on Feb 25, 2020. Thorough epidemiologic investigations suggested in-flight disease transmission as the source of infection as the flight attendant had worked during a flight on February 15th, 2020 which had on-board 39 Korean Catholic pilgrims coming from Tel Aviv, Israel. Soon after their return to South Korea, 30 pilgrims were diagnosed with COVID-19. There were no other identified sources for this case. After the flight, she continued to work between February 19 and February 22, 2020. - After the first flight attendant was diagnosed with COVID-19, a 2-week self-quarantine period was imposed on all crew members (n=30). Only one crew member was diagnosed with COVID-19 during this quarantine on Mar 6, 2020. While the two flight attendants worked on different decks of the plane, they had shared the crew's resting area and ground transportation after the first flight attendant had developed symptoms.

Wang (2021) (20) *new* Cluster Investigation China Feb 2020	Contact tracing activities of a family cluster of COVID-19. The reported cluster involved 3 confirmed cases, 2 asymptomatic infections, and a total of 34 close contacts within the family, of which 8 were visiting relatives from other provinces, and 1 was on the same flight as a confirmed case.	- The source of infection in this cluster was a family member's girlfriend who travelled via plane from Guizhou province. This case had close contact with a confirmed case on the plane while waiting in line for the bathroom as well as getting on and off the plane.
Murphy (2020) (19) Outbreak Investigation Ireland Jun-Aug 2020	An outbreak investigation into COVID-19 cases linked to an international flight into Ireland in the summer, 2020. Masks were worn by 9 cases, not worn by 1 child case and was unknown for 3.	- 13 cases were linked to a single international flight (duration 7.5h). The cases had come from three different continents. - Only 49 passengers and 12 crew were on the flight. No data on the crew or 11 passengers. - Whole genome sequencing showed 5 strains from passengers matched suggesting a single point source of infection. The index case(s) was not identified through the epidemiological investigation, but plausible theories suggest a proportion of cases acquired COVID-19 in-flight. - 4 of the flight cases were not seated near a positive case, had no contact in transit, wore face masks in-flight and would not have been considered a close contact. - A social network is shown to demonstrate how the flight cases spread SARS-CoV-2 to 46 secondary contacts in the community.
Speake (2020) (9) Cluster Investigation Australia Mar 2020	The flight, an Airbus A330-200, on Mar 19, 2020 from New South Wales to Perth (duration 5h) had 28 business class and 213 economy passengers. An epidemiologic and whole-genome sequencing investigation were undertaken.	- 29 passengers on the flight had SARS-CoV-2, and an additional 35 had compatible symptoms by tested negative. 18 from cruise ships and 10 domestic/international travellers. - Based on WGS 18 cases were considered primary: 13 Ruby Princess, 4 Ovation of the Seas and 1 traveller from the US. - 11 secondary cases, 3 did not have WGS and were classified as possible, 8 are considered to have occurred in-flight. The 8 did not know each other, 4 from USA and 4 Australians

	Mask use was rare on this flight and inconsistent.	- Among the 11 secondary cases, 8 were within 2 rows of an infected case and 3 were more distant. All secondary cases were from the mid section despite 5 infectious cases in the aft cabin. - 64% in were in a window seat, risk ratio 5.2 (95%CI 1.6-15.4). - WGS allowed proper attribution of cases to in-flight transmission.
Khanh (2020) (8) Cluster Investigation Vietnam Mar 2020	Flight from London, UK to Hanoi, Vietnam on March 2, 2020 (duration 10h). All successfully traced passengers and crew were interviewed, tested and quarantined. At arrival, there were temperature checks and symptom screening and some countries (not UK) had to undergo SARS-CoV-2 testing. Facemasks were not mandatory on airplanes.	- There were 16 crew and 201 passengers. The index case started to experience symptoms the day before the flight, she was seated in business class. - 14 passengers and 1 crew were identified as positive during the contact tracing investigation. - 12 were in business class and 92% were seated within 2 meters of the index case and 1 was more than 2 meters, risk ratio 7.3 (95%CI 1.2-46.2). - Three other contacts (2 passengers and 1 flight attendant) did not have a close encounter with the index case as they were in economy class.
Choi (2020) (10) Cluster Investigation Hong Kong Mar 2020	A study examining confirmed COVID-19 cases in Hong Kong and travel history identified 4 people that shared a flight from Boston, USA to Hong Kong, China March 9, 2020. The airplane was a Boeing 700-300ER (duration >15h), with 294 passengers. Not all passengers were tested. No mandatory quarantine or airport screening was in place. Use of facemasks was not mentioned.	- The cluster included 2 passengers (a married couple) in business class and 2 crew. - The couple both had symptom onset on March 10, so they were already infected during travel. - The flight attendants developed symptoms March 16 and 18. One of 2 flight attendants spent 5 days in Boston, the other could not be confirmed. - Their viral sequences all matched 100% and were not sequences that had been seen in Hong Kong. However, close matches were identified from Toronto, New York and Boston. - Based on this analysis the authors conclude it is likely that the couple transmitted SARS-CoV-2 to the flight attendants during the flight.
Hoehl (2020) (18)	102 passengers of a flight from Tel Aviv, Israel to Frankfurt, Germany March 9,	- The tourist group was tested for SARS-CoV-2 on arrival, 7 of 24 were positive. On the flight the 7 positive from the tourist group were symptomatic

Outbreak Investigation Germany Mar 2020	2020. 24 members were from a tourist group that unknowingly at the time had had contact with an infected hotel manager 7 days prior. No preventative measures were taken on the flight. Crew were not followed-up. Antibody tests were offered, however many passengers did not get tested, so additional transmission events may not have been detected.	(n=4), presymptomatic (n=2) and asymptomatic (n=1). - 1 of 71 other passengers with follow-up data reported having a positive RT-PCR test 4 days after the flight. 7 of 71 reported symptoms of COVID-19 within 14 days of the flight; one was confirmed with IgG serology and PRNT test. - Both confirmed cases are considered likely on-board transmission events, they were sitting within 2 rows of an index case.
Bae (2020) (13) Cohort South Korea Mar 2020	299 passengers were on an evacuation flight from Milan, Italy to South Korea (duration 11 h) March 31, 2020. Medical checks were conducted before the flight, everyone wore N95 respirators except when eating and social distancing was observed on embarkation and disembarkation. All evacuees were under medical observation during a 14 day quarantine with RT-PCR testing on day 1 and day 14.	- Based on RT-PCR testing and no development of symptoms, 6 evacuees had asymptomatic COVID-19. - One evacuee, who self quarantined for 3 weeks before the flight and then 2 weeks after the flight, had an RT-PCR positive test on day 14 of quarantine in South Korea. The authors suggest her exposure must have been on the flight where she was 3 rows from an asymptomatic case and they shared the same washroom.
Zhang (2020) (14) *preprint* Cohort China Mar 2020	During the month of March all passengers and crew suspected of being infected with SARS-CoV-2 on 830 international flights bound for Beijing were enrolled (n=4492/ 130000 total passengers). Suspects were quarantined, tested and epidemiological	- Of the 4492 suspect cases, 161 became confirmed upon testing (mean age 28·6 years). 94/830 flights (>10%) had a case on it. - On one flight Madrid to Beijing (duration 10h 18m), a cluster of eleven COVID-19 cases with a history of close contact were identified. No secondary cases from the passengers within two rows were identified. - Two cases may have been exposed on their flight as they did not have a plausible non-flight

	investigations were conducted. Universal facemask use was implemented. It was noted that many passengers were also wearing other protective clothing, gloves and goggles.	exposure to COVID-19. Assuming these 2 cases were infected on the aircraft, the attack rate (AR) was 0.14% (0.0-0.34%) across 94 flights with 14505 passengers - Universal facemask use and airplane ventilation systems were considered protective against transmission.
Pavli (2020) (23) Cluster Investigations Greece Feb-Mar 2020	Contact tracing activities of international passengers arriving or departing from Greece Feb 26- Mar 9, 2020. No public health measures were noted.	- 18 flights with 21 index cases and 891 passengers and 90 crew were traced. - Of the 21 index cases, 6 were symptomatic, 12 were pre-symptomatic and 2 developed symptoms 5-7 days after the flight. - 5 secondary cases were identified that many have been in-flight transmission from one flight (Israel to Greece, duration 2h) with two COVID-19 cases. The secondary cases were seated within 2 seats of an index case.
Eldin (2020) (22) Case report France Feb 2020	A case investigation of a French national who developed COVID-19 shortly after returning to France. He had left France February 13 for Bangui, Central African Republic and returned to Marseille, France with his partner on February 24th via Yaoundé, Cameroon.	- This investigation suggests that transmission occurred on the flight from Bangui to Yaoundé where French nationals were on the same plane as the first case of COVID-19 diagnosed in Cameroon after the February 24th flight. - The case developed symptoms shortly after returning to Marseille France. The flight is the most plausible point of exposure.
Yang (2020) (11) Cluster Investigation China Jan-Feb 2020	A flight from Singapore to Hangzhou (duration 5h) carrying 325 people on January 23, 2020. Seat assignments were not obtained, so physical proximity of the index and other cases is not known. Masks were worn by flight attendants, but not by most passengers.	- The index case developed a fever on the flight and did not wear a mask, he was identified during disembarkation and tested positive. All passengers were quarantined for 14 days. 11 other passengers developed symptoms and tested positive for an AR=3.4%

Chen (2020) (15) Cluster Investigation China Jan-Feb 2020	A flight from Singapore to Hangzhou (duration 5h) carrying 335 people on January 24, 2020. The flight was strictly managed because 100 people on the flight were from Wuhan. All passengers were quarantined for 14 days. Facemasks were worn on the flight except when eating and drinking.	- 16/335 COVID-19 cases were diagnosed among passengers, attack rate 4.8%. None of the crew were infected. - Only one passenger did not have a plausible epidemiological history of exposure prior to the flight. On the flight, he was seated near 4 infected passengers from Wuhan for approximately 1 hour and did not wear his facemask properly (not tight and nose not covered).
Kong (2020) (24) Retrospective cohort China Jan 2020	This paper details the travel and potential transmission of SARS-CoV-2 from an index case in tour group A to 3 other tour groups that were in Europe Jan 16-28. Shared flights and lodging were considered in the epidemiological investigation. Face mask use or other precautions were not mentioned.	- Transmission within the tour group (group A) resulted in 13 confirmed or suspected infections and could have occurred on flights, bus or during tours. The first case was hospitalized Jan 22, and others in the group fell ill starting Jan 26. - It seems unlikely that transmission from Group A to Group B tour group occurred on a January 16 flight as the 3 cases in Group B were not identified until January 29. - It is plausible that transmission from Group A to two others and a tour guide from group C and- an independent traveller,-occurred on a Jan 28 flight. - It is also plausible that transmission from Group A to 3 people in Group D occurred at lodging shared by both groups Jan 22.
Flights with no secondary cases identified		
Karim (2020) (5) *new* Descriptive Study Malaysia Feb-Apr 2020	This article summarizes the repatriation of Malaysian citizens using chartered commercial aircraft. The mission objectives were to repatriate as many citizens based on aircraft capacity and prevent onboard transmission of the disease to flight personnel. All flight team personnel underwent	- There were 82 positive cases detected among the repatriated citizens. Secondary transmission among repatriated citizens during the flight was not investigated. - There was a single positive case of a healthcare worker involved in the mission, based on the sample taken on arrival of the flight. This worker was asymptomatic and did not test positive again upon repeat testing (potential false positive or sampling error). No investigation into how the worker may have acquired infection was

	briefing on in-flight safety procedures and use of personal protective equipment (PPE). All repatriates were required to wear face masks and sanitise their hands upon boarding the flight.	described. There were no infections involving flight team members who worked with the case.
Ruonan (2021) (25) *new* Surveillance analysis China Jan-Apr 2020	Analyzed Guangzhou imported case data from The National Information Management System for Infectious Diseases Reports of the China Disease Control and Prevention Information System.	- Out of 34 flights, 10 (29.4%) had more than 3 cases on-board. There is no clear evidence of the spread of COVID-19 on any of the flights.
Kim (2020) (6) *new* Cohort South Korea Mar 2020	Describes a repatriation flight of 80 Koreans from Iran to Korea, with a direct transfer of passengers between airplanes in Dubai. Strict infection prevention precautions were implemented (i.e., vinyl curtains to separate clean and contaminated zones, PPE, face masks, and social distancing). Passengers with symptoms in the last two weeks were designated as 'patients under investigation' (PUI). Everyone aboard the flight was screened for SARS-CoV-2 upon arrival into Korea and completed a mandatory 14-day medical quarantine.	- One passenger was identified as a PUI during the first leg of the flight but tested negative upon arrival and one additional passenger was categorized as a PUI during the second leg of the flight upon developing a fever tested positive upon arrival. No additional passengers, aircrew, medical staff, or others involved in the evacuation, developed signs of infection during the 14-day observation period.
Suzuki (2021) (7) *new* Cohort Japan	Measured serum antibody titers for SARS-CoV-2 in 10 healthcare workers who were engaged in the operation of charter flights for the evacuation of	- Median compliance with PPE was 90% (range 70-100%, n=8). - The number of positive cases on each of the five flights was 3, 2, 2, 1, and 0, respectively.

Feb-Mar 2020	Japanese residents from Hubei Province. All participants wore PPE. Blood samples were collected at enrollment (after February 14th) and at every 2 weeks after enrollment until 4 weeks after the final participation in the evacuation operation.	- All samples from all healthcare workers were seronegative, indicating that PPE was effective in protecting staff during repatriation flights.
Draper (2020) (26) Contact tracing investigation Australia Mar-Apr 2020	Two flights with an infected crew member were identified in Northern Territory, Australia. All 555 passengers were considered close contacts necessitating contact tracing and quarantining activities. There were 28 cases and 527 close contacts over the two months. 94% follow-up rate was achieved. No public health measures or mask wearing noted.	- Due to a delay in getting manifests, it was almost a week before the flight passengers were notified (n=195 people to quarantine). - 326 air passengers from other flights were also monitored with 131 quarantined for being in the same row or within 2 rows of an infected case. - No secondary cases (0%, 95%CI 0-1.1%) from flights were identified.
Cornelius (2020) (2) Descriptive Study USA Jan-Mar 2020	This article summarizes the repatriation of USA citizens by US Department of health and human services air medical evacuation crews.	- The study included 39 flights with > 2000 individuals. - The article describes in depth the precautions taken to transport many potentially infected individuals. Best practices for IPC during air transport are described in the paper. No cases were identified of emergency workers acquiring COVID-19 during evacuation flights.
Nir-Paz (2020) (3) Cohort Israel Feb 2020	This article describes the repatriation of 11 citizens from the Diamond Princess cruise ship. Before boarding a 13.5 hour flight Feb 20, 2020 all 11 citizens had a negative SARS-CoV-2 RT-PCR test result.	- Two of the repatriated citizens (a couple), were SARS-CoV-2 positive upon arrival. Thus, it is assumed that they were infectious on the airplane. - No secondary cases were identified among the other repatriated citizens or 4 crew members. - Everyone on the flight were observed to wear their facemask except for eating and drinking.

	Precautions were taken, everyone wore surgical or FFP2 masks and crew had minimal interaction with passengers.	
Schwartz (2020) (27) Case reports Canada Jan 2020	Reports on the index case who arrived in Toronto on Jan 22, after taking a 15hr flight from China with 350 people onboard. No public health measures or mask wearing noted.	- No secondary COVID-19 cases were identified despite public health follow-up.
Qian (2020) (28) Contact-tracing investigation China Jan 2020	12 cases had taken a flight Ningbo to Zhejiang, China following a super spreading event at a temple in Ningbo. No public health measures or mask wearing noted.	- Eleven of these cases were linked to the temple; the exposure of one case was unknown, but not considered to have occurred on the flight. No secondary cases are known to have occurred from the flight. - The results of contact-tracing investigations identified 88 cases of COVID-19 admitted to five hospitals in Zhejiang province, China.

AR = attack rate

TRANSMISSION POTENTIAL OF SARS-COV-2 ON AIRPLANES

Fourteen citations are included in Table 2. These are a mixed group of review literature, commentaries, reports, a passenger survey and quantitative risk assessments that examine the risk of SARS-CoV-2 transmission while flying.

The report released by the Aviation Public Health Initiative (APHI) October 27, 2020 is the most comprehensive assessment of the risk of SARS-CoV-2 transmission from gate-to-gate (1). This report evaluates the available evidence and considers expert opinion and simulation results in its evaluation of reducing risk transmission of SARS-CoV-2 on flights. They outline why a layered risk mitigation strategy is necessary and the importance of compliance from passengers and the airlines. Similar conclusions and recommendations are described in the other reviews and commentaries in Table 2.

A single passenger and crew survey examined the impact and perception of enhanced safety measures to reduce the risk of SARS-CoV-2 transmission gate-to-gate (4). There was positive feedback about implemented changes such as crew only restrooms, frequent cleaning of restrooms, designated quarantine areas on the plane, masking everyone, use of face shields, frequent hand hygiene (alcohol gel provided to all passengers), and symptom and temperature checks. Passengers reported physical distancing of 1.5-2m could be maintained at check-in, pre-boarding and boarding, but not in-flight. Crew found that handing passengers

surgical masks, face shields and alcohol gel prior to the flight was impractical as passengers often had their hands full already with multiple pieces of carry-on luggage.

A meta-analysis found that from January–June 2020, the risk of being infected with SARS-CoV-2 in an airplane cabin was estimated to be 1 case for every 1.7 million travelers (95%CI 712000 to 8 million) (29). This analysis also showed the risk was substantially decreased with implemented mitigation measures where the risk in March 2020 was 1:425,062 and from April-September 2020, the risk was 1:7.1 million. Other quantitative risk assessments outlined in Table 2 also provide risk estimates of SARS-CoV-2 on airplanes and in many cases they estimate the risk of transmission is higher than the meta-analysis. While we know in-flight transmission has been under-reported and the risk of in-flight transmission varies depending on many factors and the parameters in the models, the variability across estimates from different studies cannot be reconciled due to the variation in approaches across analyses.

The combination of masks, social distancing among passengers, improved ventilation and vacant middle seats at 66% capacity, can reduce the number of infections by more than 50%, and N95 or surgical masks (ASTM 3) reduced infection risk to 0 (30). Infection probabilities for a 2 hour flight without face masks was comparable to a 12 hour flight where all passengers wore high efficiency facemasks (31). This study also found that removing mask for meal service increased risk. Further, removing roughly one-third of the passengers by keeping the middle seats empty and increasing social distancing while boarding can significantly reduce the infection risk (by 35-50%) compared to the full airplane (32, 33). One risk assessment estimated that a flight in the USA on June 30, 2020 had a risk of contracting SARS-CoV-2 of 1/4300 on a full flight and 1/7700 if the middle seat empty policy was in place (these numbers depend on the disease activity in the population) (34). The longer the duration of the flight, the higher the SARS-CoV-2 infection risk (31, 35).

Table 2: Reviews, reports, passengers survey and risk assessments related to SARS-CoV-2 transmission on airplanes (N=14)

STUDY	METHOD	KEY OUTCOMES
Pang (2021) (29) *Preprint* *new* Systematic review USA[1] Apr 2021[1]	Systematic review of COVID-19 cases related to air travel up to Sept 2020. The review was limited to flights with passenger index cases and did not include transmissions amongst air crew, ground crews, or airport staff. A quantitative approach was used to estimate the risk of air travel transmission. Correction factors were used in risk estimates for	- As of August 2020, there were at least 2866 index cases that were documented air passengers. - Fewer than 50 documented potential secondary cases associated with air travel during the pandemic were reported. - Mask use on reviewed flights ranged from use unknown to mandatory N95 use. - From January–June 2020, the risk of being infected with SARS-CoV-2 in an airplane cabin is estimated to be 5.927×10^{-7} or 1:1.7 million. Uncertainty in the correction factors and a 95% credible interval indicate risk ranges from 1 case for every 712,000 travelers to 1 case for every 8 million travelers.

	asymptomatic transmission and underreporting. Transmission risk was calculated for three time periods of interest: (1) January–June 2020 the period covered by the literature, (2) the month of March 2020 when the global spread of COVID-19 was occurring, and (3) April–September 2020 to account for the sharp drop in worldwide air travel and increased use of COVID-19 testing.	- For the month of March 2020, the risk is estimated to be 2.353×10^{-6} or 1:425,062. - From April-September 2020, the risk is estimated to be 1.413×10^{-7} or 1:7.1 million.
Sun (2021) (36) *new* Literature Review China[1] Apr 2021[1]	Narrative review of publications related to the COVID-19 pandemic and air transportation published in 2020.	- A summary of literature on airport screening operations and boarding strategies. - Summarizes the existing (2020) literature regarding in-flight operations in the presence of COVID-19 and in-flight transmission events. - Conclude that widely available, robust data for whether there are transmission occurs despite proper mask use on airplanes would yield more valuable insights.
Bielecki (2021) (37) *new* Literature Review Switzerland[1] Feb 2021[1]	Narrative review of topics related to air-travel in the pandemic period. Topics included traveller numbers, peri-flight prevention, and testing recommendations and in-flight SARS-CoV-2 transmission, photo-epidemiology of mask use, the pausing of air travel to mass gathering events, and quarantine measures and their effectiveness.	- Air travel numbers have significantly declined (51.6% decrease compared to 2019). - Flying will be safer by optimizing screening procedures, minimizing the risk of allowing pre- or asymptomatic cases to board (i.e., testing), and implementation of/adherence to simple hygiene measures and physical distancing that prevent the spread of diseases. Passenger screening is inadequate to detect all infectious cases. - High airflow and use of HEPA filters onboard planes make it unlikely to catch the virus from someone who is not seated close by. - Infection risk during flights is low: 1 infection per 54 h of flight and zero infections during a 12-h flight.

Khatib (2020) (38) *new* Literature Review Canada[1] Dec 2020[1]	Narrative review of literature on SARS-CoV-2 transmission risks and infection prevention strategies used by commercial air travel. Authors provide recommendations and propose strategies to mitigate the spread of COVID-19.	- Air quality aboard modern aircraft is very safe (HEPA filters are 99.97% effective in removing particles between 0.1 and 0.3 µm in diameter and 100% of larger particles). - Further study is needed to examine the interaction between airflow and resulting particle dispersion, but authors recommend turning on the personal airflow (gasper) above each passenger to improve travel comfort, air quality and reduce person-to-person transmission of exhaled contaminants. - Risk is highest during boarding and disembarkation. - A window seat is thought to be the safest option- though recent real-world outbreak studies are questioning this. - Recommendations included: masks should be used, frequent hand sanitization promoted and physical distancing ensured when feasible from boarding to disembarkation. High-frequency touchpoints should be disinfected between flights and in-flight. Pre-screening and pre-testing measures should be used in addition to the preventive measures enforced onboard. The implementation of a standardized digital health pass for COVID-19 and more robust contact tracing may be key factors to allow for a gradual safe return to air travel.
Marcus (2020) (1) Aviation Public Health Initiative Report from the Harvard TH Chan School of Public Health USA[1] Sep 2020[1]	This excellent quality APHI Report includes data up to September 28, 2020 This research-led guidance report reflects a mixture of literature review, *in silico* models and expert engagement to assess the following question: *In the midst of this complex, novel coronavirus crisis, how can aviation leaders advance an independent evidence-based*	- Layered non-pharmaceutical interventions (NPIs) significantly reduce the risk of disease transmission and includes: optimal ventilation, disinfection of surfaces, wearing face masks, procedures to encourage social distancing particularly during embarkation and disembarkation, but also during flight (e.g. no queuing for the restrooms or walking about the plane and minimizing interaction with crew.) - Airplane ventilation is highly sophisticated and delivers high amounts of clean air to the cabin which rapidly disperses exhaled air. - Crew and Passenger Behavior: Public safety on board and airplane depends a lot on individual behaviours: first health attestations and screening

	program to reduce the risks of SARS-CoV-2 disease transmission and with that, enhance the safety and confidence of its workforce and passengers?	pre-boarding, mandatory facemasks, social distancing and orderly conduct to avoid congestion combined with hand washing and cleaning. This is encouraged via the penalty of being on a "no-fly" list for non-compliance. - Overall, there is limited data on in-flight transmission, however it appears that a very low number of infections could be attributed to in-flight transmission and there is evidence that NPIs, particularly mask use, resulted in no transmission despite infectious passengers onboard. They describe 13 manuscripts (also included in Table 1) of studying in-flight transmission. Of note, no crew from repatriation flights acquired SARS-Cov-2, a demonstration that adherence to NPIs is effective. - Layered risk mitigation strategies can significantly reduce the risk of transmission, but require compliance from passengers and the airlines.
Freedman (2020) (39) Literature Review NA[1] Sep 2020[1]	Narrative review of all publications of possible in-flight SARS-CoV-2 up to Sep 21, 2020. This review summarized transmission events by attributes such as mask wearing on the flight in an attempt to describe and quantify the risk under different scenarios and considerations such as differing incidence rates of SARS-Co-V-2 at origin and destination, intensity of viral load in index cases, flight duration, masking practices onboard, pre-flight screening and passenger spacing. There were not enough data points to quantify the risk.	- Describe 4 well documented flights, three included in Table 1 (8-10) and the forth is an online inventory of flights to Hong Kong that reported transmission to 2 passengers, 1 seated with 5 index cases, masks were used on-board (duration 8 h). - 3 single transmission events have been reported, 2 were published (15, 18). - 6 high risk flights with no transmission are listed, 1 is published (27). The inventory of flights from Hong Kong lists many flights with positive passengers and no secondary transmission attributable to the flight. - 5 evacuation flights of which 3 are published (3, 13) are listed with one possible transmission event. The review states >1.7 million passengers were repatriated by their government or a cruse ship company during the pandemic, few have been documented in the literature. - Flights lists with known COVID-19 cases were identified from Canada and Australia. These lists are for other passengers to self identify and isolate. US CDC is also collecting data, but has not published any findings.

		- What risk factors have been identified? Clear clustering of cases where seat plans were available, but some transmission occurred to people > 2 rows from the index case. The flights with large transmission clusters occurred before face masks were mandated on flights and several high-risk flights with no transmission had mandatory masks.
Shaimoldina (2020) (40) *new* Commentary NA[1] Dec 2020[1]	A public dataset of international flight infection information was used to analyze the trend in flight traffic and infections during the pandemic. Based on existing literature, the authors then describe challenges of prevention of SARS-CoV-2 infected individuals from boarding flights and solutions for flight resumption.	- Flight infections have decreased and air travel has been significantly reduced. - Preventing SARS-CoV-2 infected individuals from boarding flights is challenging due to testing accuracy, asymptomatic cases and many other factors including the inability to maintain physical distance and density of passengers on a plane. - Solutions may include hotel quarantine for arriving passengers, mandatory PPE, airport diagnosis, and rapid imaging/biomarker diagnosis by advanced high-technology.
Harries (2020) (41) Commentary NA[1] Aug 2020[1]	How safe is it to fly? This commentary looks at the publications available up to August 2020. Historical outbreaks have been reported for tuberculosis, influenza like illness, SARS-CoV-1.	- Ventilation in an aircraft is very good. However it can be disrupted by passengers moving around, coughing etc. - Aisle seats tend to have more contact with others compared to a window seat. - They suggest following available guidance: wear a well-fitting mask and a face shield or glasses, use alcohol wipes to wipe surfaces, do not congregate or que for the washroom, change seats if near a symptomatic person, avoid drinking and eating if possible. - Use same precautions in the airport and exercise physical distancing when possible.
Pongpirul (2020) (4) Passenger and crew survey Thailand	This study targeted passengers and crew of two repatriation flights operated by Thai Airways (TG476 from Sydney 9.25h and TG492 from Auckland to Bangkok	- Response rate for the online questionnaire was low: 22.5% - Several risk reduction measures were implemented and well received. These included crew only restrooms, frequent cleaning of restrooms, designated quarantine areas on the plane, masking everyone, use of face shields, frequent hand

Apr 2020	11.5h), total 335 passengers and 35 crew. An online questionnaire was administered to get individual feedback about social distancing, mask wearing, and other procedures put in place to reduce the risk of SARS-CoV-2 transmission. In depth interviews were conducted with crew.	hygiene (alcohol gel provided to all passengers), symptom and temp checks. - Physical distancing of 1.5-2m could be maintained at checking, pre-boarding and boarding, but not in-flight. - Crew found that handing passengers surgical masks, face shields and alcohol gel prior to the flight was impractical as passengers often had their hands full already with multiple pieces of carry-on luggage.
Horstman (2021) (30) *new* Risk assessment US[1] Mar 2021[1]	Applied computer fluid dynamic results of virus transport and concentration, past data on Influenza transmission in airplanes, and the Wells Riley quanta estimation, to estimate infections risk of an arbitrary airborne viral infection on Boeing 737-600 airplanes. The parameters and data in the analysis were then compared to field data on SARS-CoV-2 on an airplane. Note: Field data based on the transmission event described by Hoehl (2020) in Table 1. Investigators assumed the virus emission rate was 1.6 ± 1.2 x 10^5 genome copies/m^3h that corresponded to 1267 viruses/minute released, and an Influenza human 50% infectious dose (HID_{50}) of 2554 copies/quanta.	- In a 3-hour flight, infection risk of an airborne infection was approximately 50% for passengers sitting in the vicinity (i.e., a single row) of infected cases (positioned at the 12^{th} row aisle seats), estimated as 2-3 infections per 131 passengers. - When the analysis was compared to field data where 4 symptomatic infected cases led to 2 secondary infections, SARS-CoV-2 was found to be less infectious and lie mid-range of the applied Influenza infectious dose data. - Masks, social distancing among passengers by 2.9 feet, vacant middle seat at 66% capacity, reduced the risk of transmission by more than 48%. The use of N95 masks and surgical masks (ASTM 3) reduced the number of secondary infections to 0.

Wang (2021) (31) *new* Quantitative Risk Assessment UK[1] Feb 2021[1]	Estimate inflight SARS-CoV-2 infection probability for a range of scenarios using experimental aerosol dispersion data and a modified Wells-Riley equation. Scenarios were varied based on quanta generation rates and face mask efficiencies, and specified for a B777-200 aircraft.	- Infection probabilities for a 2 hour flight without face masks were comparable to a 12 hour flight where all passengers wore high efficiency facemasks. Overall, infection probabilities were higher in the economy class cabins (MID-AFT) compared to the business class (FWD) sections. - Individual infection probabilities during a 2 hour unmasked flight ranged from 4.5%-60.2%. The average infection probabilities based on the number of infected passengers on the flight ranged from 0.1%-2.5% in the same scenario. For a 12 hour unmasked flight individual infection probabilities ranged from 24.1%-99.6%, average infection probability 0.8%-10.8%. - The use of high/low efficiency masks by passengers during a 12 hour flight except during 1 hour meal service increased average infection probabilities by ~59% to ~8%, compared to when masks were worn for the entire flight.
McCarthy (2021) (32) *new* Quantitative risk assessment NA* Jan 2021*	This mechanistic transmission model assumes that the probability of SARS-CoV-2 infection is additive over sub-activities. Sub-activities that together make up the air travel activity include boarding the plane, moving to and entering one's seat, sitting on the plane for the duration of the flight, and finally leaving ones seat and disembarking the plane. The model also assumes a three-hour long flight and that there is no direct physical contact between participants and that all surfaces are disinfected. It also assumes that all passengers are compliant	The relative benefits of different mitigation strategies on the airplane can be explored: - Time spent seated was the most important factor in total risk score. - Mask-wearing, making masks mandatory, given what we currently know, could be a (cost-) effective strategy for risk reduction. - Keeping the middle seat vacant unless there is a party of three travelling together at least halves the risk, under a very wide range of decay assumptions. - Managing boarding is less costly than leaving seats empty, but the analysis found that the total impact will be lower.

	with the boarding and masking policies. This is a risk-cost-benefit decision analysis framework that can be applied to many settings, including airplanes. The analysis can produce relative risks.	
Hu (2020) (35) *new* Quantitative Risk Assessment China Dec 2019- Mar 2020	This risk assessment applies epidemiological data from airplane passengers (n= 9,265 passengers and 175 index cases, on 291 airplanes) and close contacts to estimated attack rates (AR) and reproduction number (R_0) prior to the lockdown in Wuhan. Relative risk among seats by proximity to the index case was also estimated. AR upper bound was estimated, based on the assumption 34 and 69 close contacts were infected on the flight departing Wuhan.	- The overall risk of SARS-CoV-2 transmission on planes with high efficiency air filtration devices was reported to be relatively low. The estimated AR upper bound was 0.60% (95% CI: 0.43%-0.84%), and R0 ranged from 0.12 to 0.19. - Transmission risk was variable by seat distance from infected case(s) and duration of the trip. - The seats immediately adjacent to the index cases were the highest risk, AR of 9.2% (95% CI: 5.7% - 14.4%), relative risk (RR) of these seats compared to others seats on the airplane was 27.8 (95% CI: 14.4 - 53.7). The middle seats had the highest AR (0.7%, 95%CI 0.4% - 1.2%), followed by the window seats (0.6%, 95%CI 0.3% - 1.0%) and the aisle seats (0.6%, 95%CI 0.3% - 1.0%). - Lower bounds of AR estimates linked to air travel increased from 0.0% (95%CI 0.0% - 0.6%) to 0.4% (95%CI 0.02% - 2.2%), and upper bounds from 0.7% (95%CI 0.5%-1.0%) to 1.2% (95% CI 0.4% 3.3%) when trip duration increased from 1.5 hours to 3.3 hours. However these results were not significant due to limited data on secondary cases based on flight times.
Arnold (2020) (34) *Preprint* Quantitative Risk Assessment USA Jun 2020	This risk assessment calculates the risk of SARS-CoV-2 infection resulting from exposure on an airplane. It did not account for loading/unloading, going to the bathroom, length of the flight, and made some assumptions about the	- Based on the assumptions, the risk of contracting COVID-19 from a nearby passenger on a flight in the USA on June 30, 2020 was about 1 in 4,300 on a full flight. - Under the "middle seat empty" policy, that risk falls to in 7,700. - These numbers are based on the estimate that 1 in 120 Americans have Covid-19 on a given day,

	"protection" afforded by the seat backs as a barrier between rows. It is based on economy class in airplanes with 6 seats in a row.	40,000 confirmed cases per day x 10 x 7 days is about 1/120 of the US population of 330,000,000. - They suggest wearing a mask could reduce the risk by 82% (not part of the risk assessment and no reference.)

INDIRECT ANALYSES OF RESPIRATORY INFECTION TRANSMISSION RISK ON AIRPLANES AND POSSIBLE MITIGATION STRATEGIES

Several simulation and *in silico* models have been developed to explore ways to minimize the risk of transmitting an infectious disease on an airplane or during embarkation and disembarkation. There were nine studies on boarding/disembarking an airplane, six on optimal seating patterns to minimize in-flight transmission and seven on the aerodynamics of respiratory droplets in an airplane when coughing and sneezing that have been published during the pandemic (Table 3). A single review of these aerodynamic studies up to June 2020 and a systematic review on evidence for influenza transmission are also listed in Table 3. These studies look at strategies for boarding to minimize passenger interactions and seating plans to maximize distance and interaction with other people. The studies that look at ventilation on the airplane and how coughing or sneezing impacts airflow describe the distance and range of droplets and aerosols from various seats (e.g., window, middle, aisle) and when standing or walking about the cabin (Table 3).

Several predictive, simulation and *in silico* models have been developed to explore ways to assess and minimize the risk of transmitting an infectious disease during boarding and disembarkation. A variety of boarding/disembarkation methods were investigated across nine studies. Overall, increasing the number of boarding groups, decreasing carry-on luggage, and avoiding interaction with other passengers (i.e., boarding back of plane and window seats first) was found to decrease risk of infection significantly, albeit with a sacrifice in overall efficiency (i.e., lengthier boarding/disembarkation time) in some scenarios (42-49).

Environmental monitoring studies, *in silico* models, and simulation experiments provide risk estimates and mitigation strategies for transmission while in-flight. In-flight particle concentrations in the air in airplanes are lower than that of retail/grocery stores, restaurants, office spaces, homes, and other forms of transport (50, 51). Further, simulation experiments of in-flight aerosol transmission and surface contamination find that air in the cabin is rapidly renewed (52). When surgical masks were used in simulations, there was a >90% reduction in droplets released during the cough simulation compared to no mask (51).

The seats immediately adjacent to the index cases have the highest infection risk, followed by the row directly behind and in front (35, 51-53). The travel distance of cough particles is heavily influenced by the direction and type of cough (54, 55). There is conflicting evidence on what seats (aisle, middle, or window) have a higher infection risk. Standing or walking about the cabin can lead to much further spread of respiratory

droplets and aerosols (56). Differences in risk between different airplanes as well as business and economy seats are also discussed (57, 58).

An ECDC systematic review on evidence for influenza transmission (59) reports on transmission during flights reported in the literature was largely consistent with findings from the COVID-19 literature; low number of secondary cases and seating of a secondary case was usually within two rows of an infected person. Interestingly the length of the flight was not associated with risk of transmission in the studies captured in this review.

Table 3: Studies and reviews that examined the aerodynamics of respiratory droplets on airplanes and mitigation strategies for respiratory infections on planes (n=24)

STUDY	METHOD	KEY OUTCOMES
Simulation and *in silico* models		
Boarding/Disembarkation		
Cotfas (2021) (48) *new* Predictive model Romania[1] Mar 2021[1]	Use an agent-based model and stochastic simulation approach to investigate the impacts of the Reverse Pyramid method on average boarding time and health risk to aisle and window seat passengers. Assessments were based on social distancing by maintaining distances of 1-2 meters between passengers when walking down the aisle, keeping the middle seat empty, and different carry on luggage policies.	- When minimizing the health risk to passengers was the primary objective the optimal solution was to assign an equal number of window seat passengers to 1 and 2 boarding groups, and an equal number of aisle seat passengers to boarding groups 2 and 3. This option was robust to changes in luggage volume and aisle social distance. The option reduced health risk among aisle seat passengers by 22.76%-35.31%, when compared to other simulations which minimized boarding time. - Scenarios that reduce boarding time, and health risks to a lesser degree, are also discussed.
Milne (2021) (43) *new* Predictive Model NA[1] Feb 2021[1]	In these stochastic simulation experiments and agent-based models, the authors assess six boarding methods and compare their performance with that of the two best boarding methods used to date with social distancing according to four performance metrics. Three of the metrics are	- Increased luggage = increased boarding time. - In a scenario where there is 1 m aisle distancing, the back-to-front by row – WilMA method has shorter boarding times, fewer seat interferences, and less aisle seat risk than the baseline back-to-front method for each luggage scenario. The baseline back-to-front by row method has less window seat risk

	related to the risk of the virus spreading to passengers during boarding. The fourth metric is the time to complete boarding. The two "best" baseline boarding methods are back-to-front by row and modified reverse pyramid half zone (see figures for description). The back-to-front by row – WilMA method boards the passengers one row at a time starting from the rear of the airplane. The five other boarding methods are created by adjusting the back-to-front by row – WilMA method so that some of the window seat passengers board earlier. In particular, k rows of window seat passengers will board the airplane before any aisle seat passengers. In the five new methods, the value of k ranges between 2 and 6.	for the higher volumes of luggage scenarios. - In a scenario where there is 2 m aisle distancing, the back-to-front by row – WilMA – offset 3 method is superior to the baseline modified reverse pyramid half zone method because its boarding time is about the same and it has less significantly less aisle seat risk and window seat risk. The back-to-front by row – WilMA method has the lowest window seat risk.
Xie (2021) (44) *new* Predictive Model NA[1] Jan 2021[1]	Quantitatively compare the disembarkation process of a Boeing 737-300 before and after adopting disembarkation management strategies. Two strategies are investigated: Strategy I: Where there is one infected passenger, ground crews first disinfect cabin aisles before the disembarkation process begins, then passengers in front of the infected patient disembark from the front door while passengers in the rear of the case disembark from the rear door. The patient and his or her "close contacts" disembark	- The number of high-risk passengers decreased by 72% after adopting Strategy I. - After adopting Strategy II, the number of high-risk passengers again decreased by 27%. - Although both strategies sacrifice efficiency (i.e., longer total disembarkation time), they also significantly reduce the risk of infection.

	only after all passengers have left the cabin. Strategy II: Where there are multiple infected passengers, passengers are evacuated from the front door or rear door from traversed columns that do not contain patients or close contacts. After the passengers have left the cabin, the cases and "close-contacts" leave from the front or back door without picking up their luggage. After the cases have left, the ground crews perform a second disinfection of the cabin. After disinfection, the remaining passengers leave through the front or rear door.	
Milne (2020) (42) *new* Predictive Model NA[1] Nov 2020[1]	In these stochastic simulation experiments and agent-based models, the authors adapt the Reverse Pyramid method for social distancing when an airplane is boarded using a jet bridge that connects the terminal the airplane's front door. They assess the impact of number of boarding groups (2 vs. 6) to show the resulting impact on four performance evaluation metrics. The first performance metric is the average boarding time. The second performance metric is the number of type-3 seat interferences during the boarding (i.e., switching seats, moving out into aisle to allow window passenger access to seat). The third and the fourth performance metrics	- As the number of boarding groups increases from two to four, average boarding times decrease. - When the number of boarding groups increases from 3 to 6, the aisle seat risk decreases significantly from 44% to 21%. - As the volume of luggage carried aboard the airplane decreases, the risk duration decreases significantly. - Doubling the aisle social distance from 1 m to 2 m increases the average boarding time and decreases both aisle and window seat risks.

	pertain to seated passengers' health while later boarding passengers pass them	
Schwarzbach (2020) (60) *new* Simulation experiment NA[1] Oct 2020[1]	Evaluate the applicability of technology-based social distancing methods while boarding in an aircraft cabin environment using a radio propagation simulation based on a three-dimensional aircraft model. They perform a ray tracing propagation simulation in a section of a modeled Airbus A321 aircraft cabin.	- The authors demonstrate that commonly utilized Receiver Signal Strength Indicator (RSSI) measurements can lead to false-positive and false-negative encounter classification, depending on the path-loss model tuning, lowering the reliability and user acceptance of technology-aided social distancing options. - From an application point of view, a possible implementation of the proposed technological approaches could look at the following: Real-time proximity warning, Post-processing contact tracing, Boarding/deboarding scheduling.
Delcea (2021) (49) *new* Predictive Model Romania [1] May 2020[1]	Estimate the number of passengers for each boarding group assuming reverse pyramid boarding with the middle seats unoccupied. Apply agent-based modeling and a stochastic simulation to evaluate impacts on boarding time and health risk to passengers in each scenario.	- If the objective is to minimize health risk among passengers, then reverse pyramid boarding first group should be those with window seats in the rear half of the airplane, the third group should be passengers with aisle seats in the front half of the airplane, with the second boarding group being the remaining passengers. This arrangement was found to be the most ideal as it reduced health risk to aisle seat passengers by 25% and by 22% for window seat passengers, while increasing boarding time by 2%.
Milne (2020) (45) Predictive Model NA[1]	In these stochastic simulation experiments, the authors assess nine adaptations of boarding methods according to four	- Average boarding time is the comparable measurement between several scenarios.

Aug 2020[1]	performance metrics. Three of the metrics are related to the risk of the virus spreading to passengers during boarding. The fourth metric is the time to complete boarding of the two-door airplane when apron buses transport passengers to the airplane.	- Increased social distance (1m to 2m) = increased boarding time. - Increased proportion of people with luggage = increased boarding time. - Seating the window seat passengers before aisle seat passengers decreases the risk of seat interference (where the aisle seat has to get up to let the window seat in). - Aisle seat risk is higher when social distance is lower (1m), luggage is carried, when boarding is random. - The author indicates that window seat risk is less than aisle seat risk during boarding, but does not estimate what the difference may be.
Schultz (2020) (46) Predictive model UK[1] Jul, 2020[1]	A cellular automata model that models the movement of passengers during the boarding process. They do not consider facemasks. They model distance to index case and contact time to estimate transmission risk.	- The model shows that compared to random boarding of people, boarding groups (e.g., families) together individually will result in the shortest boarding time 41% of the random scenario and least transmission risk 0.09 compared to 0.57-0.62 for any of the random scenarios when the plane is half-full. These boarding times were relatively stable at 75% and 100% capacity; however, transmission risk increased to 0.31 and 0.66 for the boarding in groups, individually scenario.
Cotfas (2020) (47) Predictive Model NA[1] May 2020[1]	An agent-based model is used to simulate the passenger boarding process, mainly interactions with agents and other people. (used NetLogo platform) They model the length of time to board the plane under a number of scenarios and considering hand luggage storage times.	- Back to Front boarding of the plane took the longest time, but had the lowest health risk in the simulation. - The risk is similarly low if a 2-meter social distance is maintained when boarding. - Boarding is more efficient and less risky when passengers do not have luggage to store.

	The outcome is about length of time already seated passengers come into contact with other people either as they pass by down the aisle or due to having to get up to let a person into the window or middle seat.	
In-flight transmission and seating		
Dietrich (2021) (33) *new* Environmental monitoring and predictive model study USA[1] Apr 2021[1]	Used bacteriophage MS2 virus dispersion data as a surrogate for SARS-CoV-2 and modeled the relationship between SARS-CoV-2 exposure and aircraft seating proximity. Both full occupancy and vacant middle seat occupancy scenarios were considered.	- Compared with exposures in full occupancy scenarios, relative exposure risk to an individual passenger in vacant middle seat scenarios was reduced by 23% to 57%. - The 23% exposure reduction was observed for a single passenger who was in the same row and two seats away from the SARS-CoV-2 source, empty middle seat between. - A 57% in a scenario involving a three-row section that contained a mix of SARS-CoV-2 sources and other passengers - Overall exposure risk reduction in a full 120-passenger cabin with vacant middle seats ranged from 35.0% to 39.4%.
Desai (2021) (57) *new* *In silico* study USA[1] Feb 2021[1]	Modeled the airflow, transport of oral and nasal expired particles (e.g. CO_2 and coronavirus) at different seat positions inside Airbus Airbus 380 and Boeing B747 aircraft. Simulations considered First, Business and Economy class sections in each aircraft. Seat positions were ranked based on CO_2 mass fraction, temperature, and velocity corresponding to passenger nose positions at each seat location.	- Seat ranking across aircrafts were highly variable. - In the first class section: The Airbus best ranked seat was warmer than the Boeing best ranked seat, but has worse circulation. - In business class: Airbus best ranked seat was colder, but offered better circulation than the Boeing best ranked seat. The Airbus seat was located in the side bank of the seats on the aisle side and the Boeing seat was is located next to the window.

		- In economy class: The best ranked seat for the Airbus was located next to the window while the best ranked seat for the Boeing was the middle seat in the side bank of the seats. The Airbus seat had a higher temperature, lower CO2 concentration, and lower air velocity, the trade-off for a warmer seat was worse circulation. - Overall, airbus economy best ranked seat was both warm and with good circulation; the Boeing seat performed worse in all these areas.
Ghorbani (2020) (61) preprint *In silico* study NA[1] Oct 2020[1]	The model, Monte Carlo Simulations, optimizes the number of passengers and their arrangements under a social distancing measure for the airline industry for single aisle and double aisle scenarios.	- The figures in the paper depict optimal arrangement of passengers in an airplane. Key to safely increasing the number of passengers is to group families closely together.
Salari (2020) (62) *In silico* study NA[1] Jun 2020[1]	A mixed integer programming (MIP) model to properly assign passengers to seats on an airplane while effectively preserving two types of social distancing: keeping the passengers seated far enough away from each other and providing a safe distance between seat assignments and the aisle. They use an airbus A320 with 20 row, single aisle and three seats on each side. The MIP model ran a number of scenarios: - Middle seat empty - Social distance of 3.3 ft when seated - Aisle seat empty	- If social distance is completely adhered to, no aisle seat use and no one within 3.3ft, the max load is 20 passengers in a 120-seat plane. - If passengers can sit in the aisle seat, this increases to 30 passengers socially distanced 3.3ft+. Sitting in the aisle should include strategies to limit movement / possible exposure of people moving around the plane. - Middle seat blocking policy lead to less multiple people within 3.3.ft compared to the leave the aisle seat open policy. - The more people on the plane, the more people were seated close to each other and thus considered to be in increasingly higher risk situations with 1, 2 or 3+ people within 3.3.ft. See figures for illustration.

	- Hybrid	
Wagner (2009) (58) Quantitative Risk assessment USA[1] Dec 2009[1]	This quantitative risk assessment estimates the possibility of within-flight transmission of H1N1. The simulation uses a Boeing 747.	- Even during long flights, a low to moderate within-flight transmission risk if the source case travels First Class. - Index sits in first class: • 0-1 infections could occur during a 5-hour flight, • 1-3 during an 11-hour flight • 2-5 during a 17-hour flight. - However, within-flight transmission could be significant, particularly during long flights, if the source case travels in Economy Class. - Index sits in economy class: • 2-5 infections could occur during a 5-hour flight, • 5-10 during an 11-hour flight • 7-17 during a 17-hour flight
Hertzberg (2018) (63) Environmental monitoring study and an *in silico* study USA[1] Mar 2018[1]	During flu season on 10 transcontinental US flights, they chronicled behaviors and movements of individuals in the economy cabin on single-aisle aircraft and did some environmental sampling. They simulated transmission during flight based on these data. This data-driven, dynamic network transmission model of droplet-mediated respiratory disease is unique.	- None of the 229 environmental samples were positive. - The results indicate there is low probability of direct transmission to passengers not seated in close proximity to an infectious passenger.
Aerosol Simulations on an Airplane		
Talaat (2021) (52) *new*	Studies in-flight aerosol transmission and surface contamination using a	- Particles take 2–3 min to deposit or leave the system as air in the cabin is rapidly renewed.

Simulation experiment USA[1] Feb 2021[1]	computational model of a cabin zone of a Boeing 737. The investigation aims to understand the effect of reducing passenger capacity (from 60 to 40) and to compare to alternative intervention measures such as using sneeze shields (sneeze guards) between passengers on a full capacity flight. The investigation considers a wide range of particle sizes (1–50 µm). This study does not take into account more than one infection on board, human behaviour e.g. talking, eating, drinking, adherence to mask wearing, or moving down the aisles.	- Aerosol in the 1 µm–20 µm size range is concentrated within one row of the index patient, and virtually, no particles make it past two rows from the index patient. Larger particles such as 50 µm particles are only present in the row of the index patient. - A relatively small fraction (21–26%) of exhaled particles are directly removed by the ventilation system. The majority of the particles deposit on surfaces in the cabin, with more 1 µm particles depositing on the walls than on the ground (10–14% vs 3%–6%). - The most contaminated surfaces in the full capacity model (60 passengers) with no sneeze guards are the passengers (including the index patient) at 31% deposition fraction followed by the seats at 27%. In the reduced capacity model with no sneeze guards and the full capacity model with sneeze guards, total deposition on passengers is reduced to 21% and 15%, respectively. - The total inhalable fraction is the lowest in the full capacity model with sneeze guards (0.5%) followed by the reduced passenger capacity model without sneeze guards (0.7%) and then the full capacity model without sneeze guards (1.7%). However, reduction in passenger capacity and use of sneeze guards eliminates the direct transmission of 50 µm particles. Although these particles deliver a much smaller inhalable fraction compared to 1 µm particles, they contain substantially more virions than 1 µm particles due to their volume.
Kinahan (2021) (53) *new*	Aerosol dispersion and deposition in two wide-body aircraft (Boeing 767-300 and Boeing 777-200 at	- The maximum exposure, 0.0947-0.4614%, occurs in a seat next to a source, with the next highest risk of

Simulation experiment USA[1] Jan 2021[1]	30,000 ft) was measured using fluorescent and DNA-tagged microspheres. Experimental data included over 300 releases from a simulated SARS-CoV-2-infected passenger in seats while in-flight. The tests were designed to measure the aerosol concentration within passenger breathing zones in neighboring seats and rows from the simulated infected passenger. The breathing releases included a mix of tests with the mannequin not wearing a mask and tests with a mask. This study does not take into account more than one infection on board, or human behaviour (e.g., talking, eating, drinking, or adherence to mask wearing).	inhalation typically occurring in the seats in front and behind the simulated infected passenger. This maximum exposure risk equates to a minimum reduction of 99.54% of 1 µm aerosols from the index source to the breathing zone of a typical passenger seated directly next to the source. - Less than 0.03% of tracer particles settle out on solid surfaces during testing, with the highest concentration on the surfaces closest to each release location. Notably horizontal surfaces, such as arm rests were typically higher than vertical surfaces such as seatbacks and inflight entertainment (IFE) systems. - The average reduction with a mask in total particles counted was 15.6%.
Rivero-Rios (2021) (50) *new* Biological monitoring study USA July 2020	Particulate matter (PM) concentrations were measured in a variety of indoor spaces including 19 flights, retail/grocery stores, restaurants, office spaces, homes, and other transport (private cars, buses, trains). Flights were chosen to cover a range of flight durations/destinations and aircraft models and including the following stages of air travel: Terminal (departure), Boarding, Taxiing (out), Climbing, Cruising, Descending, Taxiing (in), Disembarkation, and Terminal (arrival).	- In-flight particle concentration in the air in aircraft was lower than that of retail/grocery stores, restaurants, office spaces, homes, and other transport tested. - Particles with diameters smaller than 1 µm dominate the total particle number concentrations (because they are the most difficult to remove by filtration). - PM concentrations exhibited a V-shape pattern, with high levels at boarding and a continued decrease and stable minimum concentration during cruising. Slight increases in particle mass concentration during food service were observed. When the plane began descending, particle concentrations started increasing and an abrupt increase was typically observed once

		the cabin door was opened and the disembarkation process began. - Air exchange rates in the cabin are rapid during flight, reducing the number of particles in the cabin significantly. Ambient air at altitude contains fewer particles than air at the surface, contributing to low cruising particle number and mass concentrations and also explains the decrease and increase observed during climbing and descending.
Kotb (2020) (56) *In silico* study Egypt[1] Sep 2020[1]	In this computational fluid dynamic (CFD) modeling simulation to examine what happens to respiratory droplets when expelled by a sneeze or cough by a person moving around an airplane cabin.	- The airflow of coughing and sneezing droplets produced from the moving passengers could reach seated passengers several rows from the source compared to when standing still. Cough distance 1.1m, sneeze went further when standing still. - Comparing the droplets spread range resulting from the moving passenger and stand-still one, the quicker the passenger moves, the further the droplets spread. - Figures illustrate coughing/sneezing during standing and in motion in an economy class airplane cabin.
Silcott (2020) (51) *Unpublished* Simulation experiments USA Aug 2020	The simulations used 767-300 and 777-200 aircrafts/models to study aerosol penetrations by an infected COVID-19 passenger into the area around them. 300 replications were conducted including terminal loading and unloading. Inflight simulations conducted in the hanger and at 35 000ft. This study does not take into account human behaviour e.g. talking, eating, drinking, adherence	- High air exchange rates 1.8 x 108 on aircraft. Cumulative particle exposure was 10x less on the airplane compared to a residential house. - Particles were in the cabin less than 6 minutes (vs. 1.5h in a house). Air particulate removal was 15x faster than in a house and 5x faster than in a modern hospital isolation room. - Surgical masks were used in simulations, there was a >90% reduction in droplets released during the cough simulation compared to no mask.

	to mask wearing or other modes of transmission e.g. fomite.	- Sharing a row with a COVID-19 case is the highest risk, the row behind and in front are the next highest risk. There was little practical difference in risk between seats. See figures in paper. - The individual air nozzle did not make a difference to the risk. - During embarking and disembarking, keeping the air circulating, loading in small groups may reduce risk. There was low risk of jet wave exposure from an infected person already sitting on the plane.
Yan (2020) (54) Simulation experiment Australia[1] Aug 2020[1]	This study developed a computational model to mimic a Boeing 737 economy section with three rows and 9 manikins. This cough flow rate	- The cough flow was found to have a long and effective impact on contaminants transport, up to 4 s (or 8x longer than the cough). - A wide range of sizes of droplets was dispersed in the direction of the cough due to the strong jet-effects of coughing compared to what occurs with ventilated flow. (see figures in paper)
Yang (2018) (55) *In silico* study Australia[1] Dec 2017[1]	Using computational fluid dynamics, this study investigated the effect of cough-jet on local airflow and containment transport in a typical airplane cabin. The particle dispersion from a cough in a three-seat airplane row was simulated.	- The travel distance of cough particles was heavily influenced by the direction and type of cough. The aisle seat person coughing resulted in longer particle travel distance than the middle and window seat. The middle seat was considered the most at risk of exposure seat.
Reviews		
Jayaweera (2020) (64) Review Sri Lanka[1] Jun 2020[1]	Literature Review on aerodynamics of SARS-CoV-2 in droplets and aerosols – in an Airplane Cabin (see appendix). The section of the review that focuses on airplane cabins.	- They describe the flow of air in the cabin and reports a complete air exchange within 2-3 minutes, which should be good for quickly dissipating virus-laden droplets. They also indicate the air is passed through a HEPA filter, which can remove particles >0.3 µm. Cough-jet trajectories with no mask,

		surgical mask and N95 mask are described in the paper.
Leitmeyer (2016) (59) Systematic Review ECDC[1] Aug 2016[1]	A systematic review was conducted on air travel association with the spread of influenza through infected passengers and potential for in-flight transmission. 14 publication, 11 from H1N1 pandemic were included. The systematic review is high quality and includes studies up to October 2015	- Across studies, 2165/4252 traceable passengers were followed-up and of these 163 secondary cases were identified (7.5% secondary attack rate). 42% were seated within two rows of the index case. - The length of the flight was not associated with risk of transmission in this review.

[1] Country of study based on author affiliations and date of study based on publication date.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Sciences Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: flight or airplane or aircraft or plane. The search netted 649 citations (507 from initial search up to October 28, 2020 and 147 from updated search conducted April 26, 2021), which were screened for relevance to the review. Additional references to relevant synthesis research not related to SARS-CoV-2 or the current pandemic were identified through citations in articles on the current pandemic and an additional google search was executed May 4, 2021 to identify any new non-indexed reports using (COVID-19 or SARS-CoV-2) AND (flight OR plane). Potentially relevant citations were examined to confirm it had relevant data and relevant data is extracted into the review.
This review contains research published up to April 26, 2021.

Peer-review
This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX

NPI table from Marcus (2020) (1) highlights the interventions that can be used together to help minimize the risk of SARS-CoV-2 transmission when flying.

Table 1.1 Non-pharmaceutical Interventions that can be used to Control Transmission of the Novel Coronavirus SARS-CoV-2, where Layering NPIs can create Additive and/or Synergistic Benefits in Reducing the Risk of Exposure to COVID-19 for Passengers and Crewmembers during Air Travel

Phase of Gate-to-Gate Passenger Journey	Non-Pharmaceutical Interventions that can be Layered to Mitigate Risk of SARS-CoV-2 Transmission during Air Travel													
	Section 6.0 Testing & Screening			Section 7.0 Face Coverings			Section 8.0 Process Management		Section 9.0 Cleaning & Disinfection				Section 10.0 Physical Engineering	
NPI Layering Intervention	*Health Symptom Self-screening*	*Temperature Screening*	*Viral Testing*	*Mask*	*Respirator*	*Face Shield*	*Limiting Cabin Service*	*Boarding and Deplaning*	*Cleaning*	*Electrostatic Spray*	*UV Disinfection*	*Anti-microbial Coatings*	*Ventilation*	*Enhanced Ventilation for Boarding/Deplaning*
Preparation of Airplane	–	–	–	++	–	–	–	–	++	++	*	*	–	–
Pre-Boarding	++	++	*	++	–	–	++	++	++	–	–	–	++	*
On Board at Cruise	–	▲	–	++	▲	▲	++	–	++	–	–	*	++	–
Deplaning	–	*	–	++	–	–	–	++	++	–	–	–	++	*

NPIs Non-pharmaceutical Interventions

– Not applicable
++ Recommended
* Desirable/optional
▲ May be appropriate under certain circumstances

Route of Transmission:

- Direct contact with infectious droplets
- Inhalation of infectious aerosols
- Indirect contact with infectious agents contaminating inanimate surfaces (fomites)

Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur le risque de transmission du COVID-19 en vol, mise à jour 2

Introduction

Quelles sont les preuves de la transmission du COVID-19 lors des voyages aériens, et de l'évaluation du risque et des stratégies d'atténuation autour des voyages aériens?

De nombreux changements ont été mis en œuvre par les compagnies aériennes pendant la pandémie, afin de réduire le risque de transmission du SRAS-CoV-2 lors des voyages aériens. Le présent document résume la documentation sur la transmission du SRAS-CoV-2 en vol, les caractéristiques de ces événements et les stratégies utilisées ou étudiées pour atténuer la transmission dans un avion ou pendant l'embarquement et le débarquement. La première mise à jour de cette revue contenait la littérature publiée jusqu'au 28 octobre 2020. Il s'agit de la deuxième mise à jour et elle inclut les études jusqu'au 26 avril 2021.

Quoi de neuf?

- Vingt-neuf études supplémentaires ont été ajoutées dans cette mise à jour (publiées entre le 28 octobre 2020 et le 26 avril 2021; neuf nouvelles études en vol [tableau 1], neuf examens et évaluations des risques sur la transmission en vol [tableau 2] et onze nouvelles études de simulation sur la réduction de la propagation des virus respiratoires, et l'impact relatif des stratégies d'atténuation pendant les voyages aériens [tableau 3]. Ces nouvelles études portent à 64 le nombre total d'études incluses dans cette revue.

- Plusieurs études ont estimé des taux d'attaque qui varient en fonction de la proximité du cas infecté lorsqu'on est assis dans l'avion. Les estimations varient, mais les taux d'attaque étaient toujours faibles, notamment lorsque le port du masque était obligatoire.

- Quatre évaluations des risques ont été ajoutées à cette mise à jour. Elles fournissent des estimations des probabilités globales de contracter le COVID-19 pendant un vol à différents moments de la pandémie. Ces estimations varient largement en fonction des données utilisées, des hypothèses du modèle et de la prise en compte ou non par le modèle de la sous-déclaration des transmissions en vol.

Points clés

- Vingt-six études sur les vols (recherche des contacts ou cohortes) ont été identifiées, dont neuf n'ont pas rapporté de cas secondaires (cinq sur des rapatriements et quatre sur des vols commerciaux) et dix-sept ont rapporté une transmission probable par exposition en vol. Les résultats du séquençage

du génome entier étaient disponibles pour cinq études et ont permis de relier les cas à une exposition unique en vol. Les implications des nouveaux variants préoccupants n'ont été abordées dans aucune des études capturées.

- Le taux d'attaque global du SRAS-CoV-2 parmi les passagers de vols courts et moyen-courriers (d'une durée de 1,5 à 2,5 heures) était faible.
- Aucune transmission de passagers à l'équipage ou entre membres d'équipage n'a été documentée sur les vols de rapatriement.
- La plupart des cas de transmission en vol se sont produits sur des vols où le port du masque n'était pas obligatoire. La transmission se faisait principalement de passager à passager, bien que quatre études aient rapporté un ou plusieurs événements de transmission de passager à équipage. Sur les vols où le port du masque était obligatoire, certains événements de transmission sont survenus et on pense qu'ils sont dus à une mauvaise utilisation du masque (p. ex., le fait de ne pas couvrir le nez) ou au retrait du masque pour manger ou boire.
- Des contrôles de symptômes et de température ont été effectués sur certains vols. Le manque d'adhésion des passagers à l'autodéclaration des symptômes a entraîné une transmission sur au moins un vol.
- La proximité d'un cas de référence (rayon de deux rangées) était un facteur de risque dans les études où des plans de cabine étaient disponibles.
- Les mesures de santé publique renforcées les plus courantes étaient la distanciation physique en vol, le nettoyage renforcé, les masques obligatoires, l'hygiène des mains, la distanciation physique lors de l'embarquement et du débarquement, les zones réservées à l'équipage et les zones de quarantaine pour les passagers malades. Un sondage mené auprès des passagers et des membres d'équipage a révélé que ces derniers se sentaient plus en sécurité après la mise en œuvre de mesures de sécurité renforcées pour enrayer la transmission et qu'ils estimaient que la plupart des mesures étaient réalisables, à l'exception de la distance physique de 1,5 à 2 m en vol.

- L'atténuation du risque de transmission du SRAS-CoV-2 pendant les voyages aériens a été abordée directement dans 14 examens et évaluations des risques (tableau 2) et indirectement dans 24 examens, modèles prédictifs, expériences de simulation, études de surveillance environnementale et études *in silico* (tableau 3).
  - Les principales conclusions de la littérature sur la transmission du SRAS-CoV-2 pendant les vols sont que de multiples interventions sont nécessaires pour réduire au maximum le risque de transmission (tableau 2); ceci est bien résumé dans la figure de l'annexe du rapport de l'Aviation Public Health Initiative dirigée par l'Université Harvard (1).
    - Une méta-analyse a révélé qu'entre janvier et juin 2020, le risque d'être infecté par le SRAS-CoV-2 dans une cabine d'avion était estimé à 1 cas pour 1,7 million de voyageurs.

- Plus la durée du vol est longue, plus le risque d'infection est élevé. Le retrait des masques pour le service des repas a entraîné une augmentation du risque.
- Les mesures de santé publique visant à maintenir une distance physique pendant l'embarquement, le débarquement et le vol, le renforcement du nettoyage, l'hygiène des mains et le port universel du masque pendant la durée du vol, mises en œuvre dans le cadre d'une approche à plusieurs niveaux, réduisent considérablement le risque de transmission.
- Les systèmes de ventilation des avions sont conçus pour rafraîchir rapidement l'air de la cabine et ce niveau de ventilation réduit considérablement le temps pendant lequel les particules restent dans la cabine par rapport à d'autres environnements intérieurs et réduit ainsi les possibilités de transmission, en particulier lorsqu'il est associé à d'autres mesures de santé publique (tableaux 2 et 3).
- L'adhésion des passagers et de l'équipage aux mesures de santé publique est un facteur essentiel de l'impact de ces mesures visant à réduire le risque de transmission, tout comme les directives de dépistage des symptômes et les procédures à bord.

- La littérature indirecte étudie l'aérodynamique des gouttelettes et des aérosols pour caractériser les situations à haut risque, ou simule les mouvements d'embarquement et en vol pour suggérer des stratégies visant à minimiser l'interaction des personnes et à maximiser la distance entre les personnes en vol (tableau 3).
  - Les concentrations en nombre et en masse de particules en vol dans les avions sont inférieures à celles des magasins de détail/épiceries, des restaurants, des bureaux, des habitations et d'autres moyens de transport.
  - Les passagers qui éternuent ou toussent en étant debout ou en se déplaçant dans la cabine propagent leurs gouttelettes respiratoires beaucoup plus loin que ceux qui sont assis.
  - Le port d'un masque facial a considérablement réduit la propagation des gouttelettes (>90 %).
  - Il a été démontré que l'embarquement dans un avion par groupes d'individus apparentés, les personnes assises en premier à l'arrière de l'avion et aux hublots, ainsi que d'autres algorithmes plus complexes, réduisent l'interaction avec les autres personnes. On également constaté que la diminution du nombre de bagages à main réduisait les interactions à bord. Bien que certaines stratégies telles que l'augmentation du nombre de groupes d'embarquement ou la distanciation sociale puissent sacrifier l'efficacité (c'est-à-dire une durée totale d'embarquement/débarquement plus longue), elles peuvent réduire considérablement le risque d'infection.

- Le regroupement des familles et l'espacement stratégique entre les passagers sur les vols qui ne sont pas au maximum de leur capacité améliorent la distance physique entre les passagers. Les algorithmes développés par les chercheurs ont été présentés pour maximiser ce concept et ont démontré les performances potentielles de ces algorithmes par rapport aux stratégies de siège central vide ou de siège côté couloir vide. Toutes ces stratégies ont vu leur efficacité diminuer sur des avions plus pleins.

Vue d'ensemble des éléments de preuve

Les événements de transmission en vol enregistrés dans les différentes études ont été étudiés par le biais d'études de recherche de contacts et de cohortes. Les études sur les groupes et les épidémies présentent un risque de distorsion en raison de leur nature rétrospective et descriptive. Des cohortes étaient disponibles pour les vols de rapatriement et le risque de distorsion est jugé moindre, car les passagers et l'équipage ont été suivis de manière uniforme pendant une période spécifique.

Parmi les autres types de preuves, citons la littérature d'analyse, allant des examens systématiques de bonne qualité aux commentaires. Il y avait une bonne concordance dans les renseignements et les recommandations entre les divers documents passés en revue.

Les évaluations quantitatives des risques, les modèles prédictifs, les expériences de simulation et autres études *in silico* étaient très variables dans leurs objectifs et leurs approches. Aucune tentative d'évaluation de la validité de ces études n'a été effectuée. Ces études visent à imiter un scénario du monde réel, généralement pour explorer divers choix d'interventions. Leurs résultats doivent être interprétés avec prudence, car ils peuvent ne pas refléter ce qui se passerait sur le terrain.

Il n'y avait qu'un petit nombre de vols pour lesquels des études épidémiologiques sur d'éventuels événements de transmission avaient été entreprises. Ces événements sont probablement sous-déclarés ou sous-enquêtés en raison de la logistique et des ressources disponibles pour la recherche des contacts. Il est également difficile de classer les cas de transmission en vol, car l'infection au SRAS-CoV-2 peut se produire avant le départ, à divers moments du voyage, ou pendant la quarantaine/à l'arrivée. Le séquençage du génome entier peut aider à établir un lien entre les cas et une exposition unique en vol. Les étudess, évaluations des risques et modèles prédictifs à venir devraient également porter sur les implications des variants émergents du SRAS-CoV-2 et leurs attributs (p. ex., transmissibilité accrue) sur le risque de transmission en vol, ainsi que sur le statut vaccinal des voyageurs et du personnel des compagnies aériennes pour atténuer le risque.

CONTENU

ÉVÉNEMENTS DE TRANSMISSION DANS LES AVIONS

L'étendue complète de l'exposition au COVID-19 associée aux avions n'est pas connue. Le tableau ci-dessous énumère 26 études (9 sont nouvelles depuis la dernière mise à jour de l'examen) dans lesquelles la possibilité de transmission du SRAS-CoV-2 en vol a été étudiée. Dix-sept rapportent qu'une transmission a eu lieu et 9 rapportent qu'aucune transmission n'a eu lieu pendant les vols. Plusieurs études portant sur des vols de rapatriement où de nombreuses précautions ont été prises ne rapportent aucune transmission à l'équipage (2-7).

Le dépistage des symptômes et de la température à l'aéroport a été mentionné dans quelques études. L'incapacité des personnes à se déclarer et à respecter les directives de dépistage démontre que le dépistage n'est pas une mesure de contrôle efficace en soi; il doit être utilisé en conjonction avec d'autres précautions. Cela a été bien démontré dans l'épidémie de la classe affaires rapportée par Khanh et coll. (2020) où un cas de référence a provoqué 15 cas secondaires sur un vol où les masques n'étaient pas obligatoires (8).

Bon nombre des événements de transmission les plus importants se sont produits avant le port obligatoire de masques sur les vols (8-11) ou la mise en œuvre d'autres stratégies de réduction des risques. Il existe également quelques cas où des événements de transmission se sont produits alors que les masques faciaux étaient obligatoires (12-15). Les études qui ont examiné l'adhésion et l'utilisation correcte des masques faciaux lors de ces événements de transmission ont rapporté à la fois une utilisation incorrecte du masque (p. ex., il ne couvrait pas le nez), et le fait de manger et de boire dans l'avion pendant le retrait du masque. Une étude épidémiologique a suggéré une transmission en vol du SRAS-CoV-2 d'un passager à un agent de bord, puis une transmission secondaire quelques jours plus tard à un autre agent de bord qui a partagé la zone de repos de l'équipage et les transports terrestres avec l'agent de bord infecté (l'utilisation de masques faciaux sur les vols n'a pas été mentionnée) (16).

Une étude portant sur 18 vols à destination de l'Angleterre rapporte que la transmission globale du SRAS-CoV-2 sur les vols courts et moyen-courriers (1,5-2,5 heures) est faible, avec un taux d'attaque de seulement 0,2 % (IC 95 %, 0,1-0,5) parmi les contacts en vol seulement (17). Le taux d'attaque était plus élevé chez les contacts qui étaient assis dans un rayon de deux sièges des cas infectieux (3,8 %; IC95 % : 1,3-10,6 %); cependant, le risque le plus élevé se trouvait chez les covoyageurs ayant eu de multiples expositions hors vol au cas infecté (AR 13 %; IC95 % : 7,6-21,4). D'autres épidémies pour lesquelles on disposait d'un plan des sièges, lorsqu'il était disponible, ont pu montrer la proximité des cas secondaires par rapport aux cas de référence, ce qui a montré que les personnes assises dans les deux rangs du cas de référence avaient un risque plus élevé de contracter le COVID-19 (8, 17, 18). Cependant, dans l'ensemble des épidémies, plusieurs cas ont été observés dans des endroits beaucoup plus éloignés et le mode ou les circonstances de

transmission n'étaient pas évidents (ils auraient pu provenir d'un déplacement dans la cabine, de toilettes partagées ou d'une transmission par vecteur) et ne peuvent être confirmés (8, 9, 19, 20).

Dans les rapports d'épidémies, il est souvent mentionné que le siège côté hublot devrait être plus sûr, car il y a moins de contacts avec d'autres personnes que sur les sièges côté couloir. Cependant, une étude a montré que le fait d'être sur un siège côté hublot présentait un risque plus élevé que le siège côté couloir (9). Il s'agit d'un résultat inattendu que les auteurs n'ont pas pu expliquer. Le tableau 3 décrit les études qui examinent les différences potentielles de risque liées au fait d'être assis dans différentes zones et sur différents sièges d'un avion.

Le séquençage du génome entier (SGE) a été entrepris dans cinq études. Dans tous les cas, il a permis d'identifier les cas liés à la même source et, dans les études australienne et néo-zélandaise, il a permis d'obtenir des renseignements que l'étude épidémiologique n'aurait pu fournir (9, 12, 21).

Plusieurs limites sont observées dans ces études; elles sont principalement liées aux limitations des données obtenues. Par exemple, les contacts avant/après le vol entre le cas de référence et les contacts secondaires n'ont pas pu être exclus (8, 9, 15, 16, 18, 20, 22), et pour certaines études, le lieu de séjour n'était pas connu (8, 13).

Tableau 1 : Liste des événements de transmission qui se sont produits pendant les vols (n = 26)

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Vols avec cas secondaires identifiés		
Blomquist (2021) (17) *nouveau* Cohorte ROYAUME-UNI Déc. 2020	Infections identifiées parmi 18 passagers sur des vols limités à l'Angleterre, avec des cas infectieux, en utilisant des ensembles de données de gestion de cas nationaux. Les passagers ont été considérés comme infectieux pendant le vol si les résultats de laboratoire étaient positifs sept jours avant ou deux jours après le vol. Note : le séquençage du génome entier n'a pas pu être appliqué, car ces données n'étaient pas disponibles pour les cas de	- L'étude a permis de déterminer que cinq cas étaient liés à une transmission potentielle par avion, 55 passagers infectieux et 2 313 copassagers, avec 2 221 ayant eu des contacts uniquement en vol. La transmission globale du SRAS-CoV-2 à court et à moyen terme a été estimée faible. - Les taux d'attaque suivants ont été estimés : - 0,2 % (IC 95 %, 0,1- -0,5) parmi tous les contacts en vol seulement. - 3,8 % (IC 95 %, 1,3- -10,6) parmi les personnes ayant eu des contacts seulement en vol, qui se sont assises dans un dans un rayon de deux sièges. - 13,0 % (IC 95 %, 7,6 %- -21,4 %) parmi les covoyageurs ayant eu de multiples expositions non aériennes à des cas infectieux.

	référence et secondaires du même vol.	
Swadi (2021) (21) *nouveau* Étude sur les épidémies Nouvelle-Zélande Sept. 2020	Une étude approfondie sur la source potentielle des infections au COVID-19 chez sept voyageurs qui étaient sur un vol de Dubaï, UAB, le 29 septembre 2020, avec une escale à Kuala Lumpur, Malaisie, et un atterrissage à Auckland, Nouvelle-Zélande (durée : 18 heures). Ces sept passagers avaient été assis à quatre rangées les uns des autres. Il a été possible de déterminer la lignée des génomes obtenus à partir des sept passagers. L'utilisation du masque n'était pas obligatoire. Le transport après le vol vers les installations de quarantaine a été éloigné physiquement dans la mesure du possible, et le port du masque a été rendu obligatoire.	- Au cours de la période requise de 14 jours d'isolement et de quarantaine gérée, sept passagers qui avaient voyagé sur le vol ont reçu des résultats positifs aux tests de dépistage du SRAS-CoV-2. - Les sept passagers avaient commencé leur voyage depuis cinq pays différents avant une escale à Dubaï. Les résultats des tests de dépistage du SRAS-CoV-2 effectués avant l'embarquement étaient négatifs pour cinq d'entre eux. Aucun des passagers n'a signalé de contact rapproché à l'aéroport de Dubaï. - Parmi les sept passagers, deux étaient probablement des cas de référence infectés avant le vol, quatre ont été probablement infectés pendant le vol, et le dernier passager a été probablement infecté pendant son isolement. - Cinq des sept cas ont porté des masques et des gants pendant le vol, y compris les deux cas de référence, tandis que les deux autres cas ne l'ont pas fait. - L'analyse génomique a montré que les séquences obtenues à partir des sept cas étaient attribuées à la lignée B.1 et génétiquement identiques.
Eichler (2021) (12) *nouveau* Étude sur les épidémies Nouvelle-Zélande Août 2020	Étude sur l'origine des multiples cas de COVID-19 identifiés après 14 jours de quarantaine post-voyage.	- La séquence génomique et l'analyse épidémiologique ont permis d'identifier une chaîne de transmission à ramifications multiples comprenant des voyages aériens internationaux et nationaux et une probable transmission par aérosol dans l'hôtel de quarantaine (non résumée ci-dessous). - Le cas de référence a été identifié comme étant un citoyen rapatrié d'Inde qui revenait en Nouvelle-Zélande. - Trois cas secondaires provenant du cas de référence du vol international de 18 heures (35 % d'occupation) sur un Boeing 747 ont été identifiés par analyse du génome entier. Les trois

		cas étaient assis à deux rangées l'un de l'autre et devaient porter des masques faciaux. - La transmission de l'infection en vol s'est également produite à partir d'un des cas secondaires qui a été exposé sans le savoir pendant la quarantaine et libéré de la quarantaine avant d'être positif; trois passagers ont été infectés pendant un vol intérieur de 85 minutes (capacité de 50 %) sur un Boeing 737. Les trois cas étaient assis les uns à côté des autres (en face les uns des autres), tandis que le cas infectieux est assis à l'écart. - Note : Tous les passagers portaient des masques pendant les vols.
Mun (2021) (16) *nouveau* Série de cas Corée du Sud Février-Mars 2020	Cette série de cas décrit deux agents de bord ayant reçu un diagnostic de COVID-19, qui ont partagé l'aire de repos de l'équipage et les transports terrestres. Elle traite des risques encourus par les agents de bord.	- Le premier agent est tombé malade le 21 février 2020 et a été diagnostiqué le 25 février 2020. Des étudess épidémiologiques approfondies ont suggéré que la transmission de la maladie en vol était la source de l'infection, car l'agent de bord avait travaillé pendant un vol le 15 février 2020, qui avait à son bord 39 pèlerins catholiques coréens venant de Tel-Aviv, Israël. Peu après leur retour en Corée du Sud, 30 pèlerins ont reçu un diagnostic de COVID-19. Il n'y avait pas d'autres sources identifiées dans ce cas. Après le vol, l'agent a continué à travailler entre le 19 et le 22 février 2020. - Après que le premier agent de bord eut reçu un diagnostic de COVID-19, une période d'autoquarantaine de deux semaines a été imposée à tous les membres de l'équipage (n=30). Un seul membre d'équipage a reçu un diagnostic de COVID-19 pendant cette quarantaine, le 6 mars 2020. Bien que les deux agents de bord travaillaient sur des ponts différents de l'avion, ils avaient partagé la salle de repos de l'équipage et les transports terrestres après que le premier agent de bord eut développé des symptômes.
Wang (2021) (20) *nouveau*	Activités de recherche au sein d'un groupe familial en contact avec le COVID-19. Le groupe signalé comprenait	- La source d'infection dans ce groupe était la petite amie d'un membre de la famille qui avait voyagé par avion depuis la province de Guizhou. Ce cas a été en contact étroit avec un cas

Étude sur les groupes Chine Février 2020	trois cas confirmés, deux infections asymptomatiques et un total de 34 contacts étroits au sein de la famille, dont huit rendaient visite à des parents d'autres provinces, et 1 était sur le même vol qu'un cas confirmé.	confirmé dans l'avion, alors qu'elle faisait la queue pour les toilettes, et qu'elle montait et descendait de l'avion.
Murphy (2020) (19) Enquête sur l'éclosion Irlande De juin à août 2020	Une enquête sur l'éclosion de cas de COVID-19 lors d'un vol international à destination de l'Irlande pendant l'été 2020. Dans cette étude, 9 personnes portaient un masque, 1 enfant n'en portait pas et aucun détail n'est indiqué pour les 3 autres personnes.	Ce vol international (d'une durée de 7,5 h) a donné lieu à 13 cas. Les cas provenaient de trois continents différents. L'avion ne comptait que 49 passagers et 12 membres d'équipage. Aucune autre donnée n'est disponible pour les membres d'équipage ou les 11 autres passagers. Le séquençage du génome entier (SGE) a montré que les 5 souches provenant des passagers étaient appariés, ce qui suggère une source unique d'infection. L'enquête épidémiologique n'a pas permis de déterminer le ou les cas index, mais des théories plausibles suggèrent qu'une proportion des cas aurait attrapé la COVID-19 pendant le vol. Parmi les personnes qui auraient attrapé le virus en vol, 4 n'étaient pas assises près d'un cas positif, n'avaient aucun contact pendant le voyage, portaient des masques pendant le vol et n'auraient pas eu ce qui est jugé comme des contacts étroits avec d'autres. - L'exemple d'un réseau social est utilisé pour montrer comment un cas en vol peut entraîner la propagation du SRAS-CoV-2 à 46 contacts secondaires dans la collectivité.
Speake (2020) (9) Enquête sur les grappes Australie Mars 2020	Le 19 mars 2020, un Airbus A330-200 reliant la Nouvelle-Galles du Sud à Perth (vol d'une durée de 5 h) transportait 28 passagers en classe affaires et 213 en classe économique.	29 passagers de ce vol ont été atteints de SRAS-CoV-2 alors que 35 autres ont présenté des symptômes compatibles, mais avec des résultats négatifs. 18 personnes provenaient de navires de croisière alors que 10 autres étaient des voyageurs nationaux et internationaux. Le SGE a permis d'établir que 18 cas étaient des cas considérés comme primaires : 13 provenant du

	Une étude épidémiologique et de séquençage du génome complet a été effectuée. Lors de ce vol, peu de personnes portaient le masque et lorsqu'il était porté, il l'était de façon inconsistante.	Ruby Princess, 4 provenant du Ovation of the Seas et 1 voyageur venu des États-Unis. Parmi les 11 cas secondaires, 3 n'avaient pas de SGE et ont été classés comme possibles, alors que 8 contagions ont été considérées comme ayant eu lieu en vol. Les 8 cas ne se connaissaient pas, et 4 venaient des États-Unis alors que les 4 autres venaient d'Australie. Des 11 cas secondaires, 8 se trouvaient à moins de 2 rangées d'un cas infecté alors que 3 étaient plus loin. Tous les cas secondaires provenaient de la section centrale de l'avion, malgré 5 cas d'infection qui se trouvaient dans la partie arrière de la cabine. 64 % des répondants occupaient un siège près du hublot avec un rapport de risque de 5,2 (IC à 95 %, de 1,6 à 15,4). - Le SGE a permis d'attribuer correctement les cas à la transmission en vol.
Khanh (2020) (8) Enquête sur les grappes Vietnam Mars 2020	Vol de Londres (Royaume-Uni) à Hanoï (Vietnam) le 2 mars 2020 (durée : 10 h). Tous les passagers et membres d'équipage qui ont été retracés avec succès ont été interrogés, testés et mis en quarantaine. Lors de l'arrivée, des contrôles de température et un dépistage des symptômes ont été effectués et les passagers de certains pays (pas le Royaume-Uni) ont dû subir des tests de dépistage pour le SRAS-CoV-2. Le port du masque n'étaient pas obligatoire à bord des avions.	Cet avion comptait 16 membres d'équipage et 201 passagers. Le cas index, assis en classe affaires, a commencé à avoir des symptômes la veille du vol. Pendant l'enquête de recherche de contacts, 14 passagers et 1 membre d'équipage ont été jugés positifs. 12 personnes étaient en classe affaires et 92 % d'entre elles étaient assis à moins de 2 mètres du cas index et 1 autre se trouvait à plus de 2 mètres, rapport de risque de 7,3 (IC à 95 %, de 1,2 à 46,2). Trois autres contacts (2 passagers et 1 agent de bord) n'ont pas eu de contact étroit avec le cas index, car ils étaient en classe économique.
Choi (2020) (10) Enquête sur les grappes Hong Kong	Une étude portant sur les cas confirmés de COVID-19 à Hong Kong et sur l'historique de voyage des personnes a permis d'identifier quatre	La grappe comprenait 2 passagers (un couple marié) en classe affaires et 2 membres d'équipage.

Mars 2020	personnes qui ont pris un vol en partance de Boston, aux États-Unis, à destination de Hong Kong, en Chine, le 9 mars 2020. L'avion était un Boeing 700-300ER (vol d'une durée de plus de 15 h), avec 294 passagers. Les passagers n'ont pas tous été soumis à des tests. Il n'y avait ni quarantaine obligatoire ni contrôle à l'aéroport. L'utilisation des masques n'a pas été mentionnée.	Le couple a eu des symptômes le 10 mars, ce qui veut dire qu'il était déjà infecté au moment du voyage. Les agents de bord ont développé des symptômes le16 et 18 mars. L'un des 2 agents de bord a passé 5 jours à Boston, mais les déplacements de l'autre n'ont pu être confirmés. Leurs séquences virales étaient 100% identiques et n'étaient pas les séquences vues à Hong Kong. Cependant, des correspondances étroites ont été effectuées avec des cas à Toronto, à New York et à Boston. - D'après cette analyse, les auteurs concluent qu'il est probable que le couple a transmis le SRAS-CoV-2 aux agents de bord pendant le vol.
Hoehl (2020) (18) Enquête sur l'éclosion Allemagne Mars 2020	102 passagers d'un vol en partance de Tel-Aviv (Israël) à destination de Francfort (Allemagne), le 9 mars 2020. 24 personnes faisaient partie d'un groupe de touristes qui, sans le savoir, avaient été en contact avec un gérant d'hôtel infecté 7 jours auparavant. Aucune mesure préventive n'a été prise pendant le vol. L'équipage n'a pas fait l'objet d'un suivi. Des tests d'anticorps ont été offerts, mais de nombreux passagers n'ont pas été testés, ce qui veut dire d'autres événements de transmission n'ont peut-être pas été détectés.	A leur arrivée, le groupe de touristes a été testé pour le SRAS-CoV-2 et 7 personnes sur 24 ont obtenu un résultat positif. Sur ce vol, les 7 membres du groupe ayant obtenu des résultats positifs étaient symptomatiques (n = 4), présymptomatiques (n = 2) et asymptomatiques (n = 1). 1 seul des 71 autres passagers pour lequel des données de suivi ont été obtenues a déclaré avoir subi un test RT-PCR positif 4 jours après le vol. 7 des 71 personnes ont indiqué avoir eu des symptômes de la COVID-19 dans les 14 jours suivant le vol. L'une d'elles a obtenu un résultat positif à la suite d'un test sérologique de l'IgG et d'un test PRNT. - Les deux cas confirmés sont considérés comme des événements probables de transmission à bord; ils se trouvaient à moins de deux rangées d'un cas index.
Bae (2020) (13) Étude de cohorte Corée du Sud Mars 2020	299 passagers ont pris un vol d'évacuation en provenance de Milan, en Italie, à destination de la Corée du Sud (vol d'une durée de 11 h) le 31 mars 2020. Des	Selon les résultats du test RT-PCR et l'absence de symptômes, 6 personnes évacuées étaient asymptomatiques. - L'une des personnes évacuées, qui s'est mise en quarantaine pendant trois semaines avant le vol,

	examens médicaux ont été effectués avant le vol, tout le monde portait des masques N95, sauf quand une distanciation sociale était respectée au moment de l'embarquement et du débarquement et pendant les repas. Toutes les personnes évacuées ont été en observation médicale pendant une quarantaine qui a duré 14 jours et ont subi des tests RT-PCR les jours 1 et 14.	puis deux semaines après le vol, a subi un test RT-PCR positif le 14e jour de sa quarantaine en Corée du Sud. Les auteurs suggèrent que l'exposition s'est probablement produite pendant le vol puisqu'elle se trouvait à 3 rangées d'un cas asymptomatique et qu'ils ont partagé la même toilette.
Zhang (2020) (14) *préimpression* Étude de cohorte Chine Mars 2020	Au cours du mois de mars, tous les passagers et membres d'équipage soupçonnés d'avoir été infectés par le SRAS-CoV-2 sur 830 vols internationaux à destination de Pékin ont été inscrits (n = 4 492/130 000 passagers au total). Les suspects ont été mis en quarantaine, testés et des enquêtes épidémiologiques ont été effectuées Le port universel du masque avait été mis en place. On a également remarqué que de nombreux passagers portaient d'autres vêtements de protection, des gants et des lunettes de protection.	Des 4 492 cas suspects, 161 ont été confirmés après des tests (âge moyen de 28,6 ans). On trouvait un cas dans 94 vols sur 830 (> 10 %). Lors d'un vol entre Madrid et Pékin (durée du vol de 10 h 18), une grappe de 11 cas de COVID-19 ayant des antécédents de contact étroit a été identifiée. Aucun cas secondaire de passagers assis dans les deux rangées autour n'a été identifié. Il se pourrait que deux cas aient été exposés pendant le vol, car ils n'avaient pas d'expositions plausibles à la COVID-19, autre que le vol. En supposant que ces 2 cas ont été infectés pendant le vol, le taux d'attaque était de 0,14 % (entre 0,0 et 0,34 %) sur 94 vols avec 14 505 passagers. Le port universel du masque et les systèmes de ventilation des avions étaient considérés comme une protection contre la transmission.
Pavli (2020) (23) Enquête sur les grappes Grèce	Activités de recherche des contacts pour des passagers internationaux en provenance de la Grèce ou à destination de ce pays entre	On a retracé 18 vols comprenant 21 cas index, 891 passagers et 90 membres d'équipage. Des 21 cas index, 6 étaient symptomatiques, 12 étaient pré-symptomatiques et 2 ont présenté des symptômes 5 à 7 jours après le vol.

Entre février et mars 2020	le 26 février et le 9 mars 2020. Aucune mesure de santé publique n'a été notée.	En outre, 5 cas secondaires ont également été identifiés. Il est fort possible que cette transmission ait eu lieu pendant un même vol (d'Israël en Grèce, durée de 2 h) où se trouvaient 2 cas de COVID-19. Les cas secondaires se trouvaient à moins de deux sièges d'un cas index.
Eldin (2020) (22) Fiche d'observation France Février 2020	Enquête sur un ressortissant français qui a développé la COVID-19 peu après son retour en France. Il avait quitté la France le 13 février pour Bangui, en République centrafricaine, et il était retourné à Marseille, en France, avec son partenaire le 24 février en passant par Yaoundé, au Cameroun.	Cette enquête suggère que la transmission s'est produite lors du vol entre Bangui et Yaoundé, où des ressortissants français se trouvaient dans le même avion que le premier cas de COVID-19 diagnostiqué au Cameroun après le vol du 24 février. Le ressortissant français a développé des symptômes peu après son retour à Marseille, en France. Le vol est le point d'exposition le plus plausible.
Yang (2020) (11) Enquête sur les grappes Chine Entre janvier et février 2020	Un vol de Singapour à Hangzhou (vol d'une durée de 5 h) transportant 325 personnes le 23 janvier 2020. Le plan de cabine n'a pas été obtenu, ce qui veut dire que la proximité physique entre le cas index et d'autres cas n'est pas connue. Les agents de bord portaient des masques, mais pas la plupart des passagers.	- Le cas index a développé une fièvre pendant le vol et ne portait pas de masque. Il a été identifié au moment du débarquement et a subi des tests qui se sont révélés positifs. Tous les passagers ont été mis en quarantaine pendant 14 jours. 11 autres passagers ont développé des symptômes et ont reçu un résultat positif, ce qui donne un taux d'attaque de 3,4 %.
Chen (2020) (15) Enquête sur les grappes Chine Entre janvier et février 2020	Un vol de Singapour à Hangzhou (vol d'une durée de 5 h) transportant 335 personnes le 24 janvier 2020. Le vol a été géré de façon stricte parce que 100 personnes qui s'y trouvaient venaient de Wuhan.	L'on a diagnostiqué 16 cas de COVID-19 sur 335 passagers, soit un taux d'attaque de 4,8 %. Aucun des membres de l'équipage n'a été infecté. - Seul un passager n'avait pas d'antécédents épidémiologiques plausibles d'exposition avant le vol. Pendant le vol, il a été assis pendant 1 heure près de 4 passagers infectés en provenance de Wuhan et il n'a pas porté son masque de façon appropriée (non serré et nez non couvert).

	Tous les passagers ont été mis en quarantaine pendant 14 jours. Les gens ont porté un masque pendant tout le vol, sauf au moment de manger et de boire.	
Kong (2020) (24) Cohorte rétrospective. Chine Janvier 2020	Ce document décrit en détail le voyage et la transmission potentielle du SRAS-CoV-2 d'un cas index du groupe A à trois autres groupes de voyageurs qui ont été en Europe du 16 au 28 janvier. Les vols et l'hébergement partagés ont été pris en compte dans l'enquête épidémiologique. L'utilisation d'un masque ou d'autres précautions n'ont pas été mentionnées.	La transmission dans le groupe de touristes (groupe A) a entraîné 13 infections confirmées ou présumées qui auraient pu se produire à bord d'un avion, d'un autobus ou pendant des visites guidées. Le premier cas a été hospitalisé le 22 janvier, et d'autres membres du groupe sont tombés malades à compter du 26 janvier. Il semble peu probable que la transmission du groupe A au groupe B se soit produite lors du vol du 16 janvier, puisque les 3 cas du groupe B n'ont été identifiés que le 29 janvier. Il est plausible que la transmission du groupe A à deux autres, à un guide touristique du groupe C et à un voyageur indépendant se soit produite sur un vol le 28 janvier. - Il est également plausible que la transmission du groupe A à trois personnes du groupe D se soit produite dans le lieu l'hébergement partagés par les deux groupes le 22 janvier.
Vols sans cas secondaires identifiés		
Karim (2020) (5) *nouveau* Étude descriptive Malaisie Février-Avril 2020	Cet article résume le rapatriement des citoyens malaisiens à l'aide d'un avion commercial affrété. La mission avait pour but de rapatrier autant de citoyens que possible en fonction de la capacité de l'avion et d'empêcher la transmission de la maladie au personnel de bord. Tout le personnel de bord a suivi une séance d'information sur les procédures de sécurité en vol et sur l'utilisation des	- On a détecté 82 cas positifs parmi les citoyens rapatriés. La transmission secondaire parmi les citoyens rapatriés pendant le vol n'a pas été étudiée. - Un seul cas positif a été relevé chez un travailleur de la santé impliqué dans la mission, sur la base de l'échantillon prélevé à l'arrivée du vol. Ce travailleur était asymptomatique; lorsqu'il a refait le test, le résultat était négatif (possiblement faux positif ou erreur d'échantillonnage). Aucune étude sur la façon dont le travailleur a pu contracter l'infection n'a été décrite. Il n'y a pas eu d'infection chez les membres d'équipage qui ont travaillé sur le cas.

	équipements de protection individuelle (EPI). Tous les rapatriés devaient porter des masques et se désinfecter les mains à l'embarquement.	
Ruonan (2021) (25) *nouveau* Analyse de la surveillance Chine Janvier-Avril 2020	Nous avons analysé les données sur les cas importés de Guangzhou à partir du Système national de gestion de l'information pour les rapports sur les maladies infectieuses du Système d'information sur le contrôle et la prévention des maladies en Chine.	- Sur 34 vols, 10 (29,4 %) avaient plus de trois cas à bord. Il n'y a aucune preuve évidente de la propagation du COVID-19 sur chacun des vols.
Kim (2020) (6) *nouveau* Cohorte Corée du Sud Mars 2020	Décrit un vol de rapatriement de 80 Coréens de l'Iran vers la Corée, avec un transfert direct des passagers entre avions à Dubaï. Des précautions strictes de prévention des infections ont été mises en place (c'est-à-dire des rideaux en vinyle pour séparer les zones propres et contaminées, des EPI, des masques faciaux et une distanciation sociale). Les passagers présentant des symptômes au cours des deux dernières semaines ont été désignés comme « patients faisant l'objet d'examens » (PUI). Toutes les personnes à bord du vol ont subi un dépistage du SRAS-CoV-2 à leur arrivée en Corée et ont été soumises à une quarantaine médicale obligatoire de 14 jours.	- Un passager a été identifié comme étant un PUI pendant la première partie du vol, mais le test s'est avéré négatif à l'arrivée et un autre passager a été catégorisé comme étant un PUI pendant la deuxième partie du vol après avoir développé une fièvre et le test s'est avéré positif à l'arrivée. Aucun autre passager, équipage, personnel médical ou autre personne ayant participé à l'évacuation n'a développé de signes d'infection pendant la période d'observation de 14 jours.
Suzuki (2021) (7) *nouveau*	Mesure des titres d'anticorps sériques pour le SRAS-CoV-2 chez 10 travailleurs de la santé qui ont participé à	- Le taux médian de conformité à l'EPI était de 90 % (intervalle 70-100 %, n=8).

Cohorte Japon Février-Mars 2020	l'exploitation des vols affrétés pour l'évacuation des résidents japonais de la province du Hubei. Tous les participants portaient un EPI. Des échantillons de sang ont été prélevés lors de l'inscription (après le 14 février) et toutes les deux semaines après l'inscription jusqu'à quatre semaines après la participation finale à l'opération d'évacuation.	- Le nombre de cas positifs sur chacun des cinq vols était respectivement de 3, 2, 2, 1 et 0. - Tous les échantillons de l'ensemble du personnel de santé étaient séronégatifs, ce qui indique que l'EPI a permis de protéger efficacement le personnel lors des vols de rapatriement.
Draper (2020) (26) Enquête sur la recherche des contacts Australie Entre mars et avril 2020	Deux vols avec un membre d'équipage infecté ont été signalés dans le Territoire du Nord, en Australie. Les 555 passagers ont tous été considérés comme des contacts étroits qui exigeaient des activités de recherche de contacts et de mise en quarantaine. Il y a eu 28 cas et 527 contacts étroits au cours de ces deux mois. Un taux de suivi de 94 % a été atteint. Aucune mesure de santé publique ni aucune mention du port de masque n'a été notée.	En raison d'un retard dans l'obtention des manifestes, il a fallu presque une semaine avant que les passagers du vol ne soient avisés (n = 195 personnes qui ont dû se mettre en quarantaine). On a également surveillé 326 passagers aériens qui ont pris d'autres vols, dont 131 ont été mis en quarantaine parce qu'ils se trouvaient dans la même rangée ou à moins de 2 rangées d'un cas infecté. - Aucun cas secondaire (0 %, IC à 95 % : entre 0 et 1,1 %) associé à ces vols n'a été identifié.
Cornelius (2020) (2) Étude descriptive États-Unis Entre janvier et mars 2020	Cet article résume le rapatriement de citoyens américains par les équipes d'évacuation médicale aérienne du ministère de la Santé et des Services sociaux des États-Unis.	L'étude a porté sur 39 vols comptant plus de 2 000 personnes. - L'article décrit en détail les précautions prises pour transporter de nombreuses personnes potentiellement infectées. Les pratiques exemplaires en matière de protocoles de contrôle et de prévention des infections pendant le transport aérien sont décrites dans le document. Aucun cas de COVID-19 acquis pendant ces vols d'évacuation n'a été identifié chez les travailleurs des interventions d'urgence.

Nir-Paz (2020) (3) Étude de cohorte Israël Février 2020	Cet article décrit le rapatriement de 11 citoyens qui se trouvaient sur le navire de croisière Diamond Princess. Avant d'embarquer dans un vol de 13,5 heures le 20 février 2020, les 11 citoyens ont d'abord obtenu un résultat négatif au test RT-PCR pour le SRAS-CoV-2. Des précautions ont été prises, tout le monde portait des masques chirurgicaux ou des masques FFP2 et l'équipage n'a eu qu'un minimum d'interactions avec les passagers.	Deux des citoyens rapatriés (un couple) étaient séropositifs au SRAS-CoV-2 à leur arrivée. On suppose donc qu'ils étaient infectieux lorsqu'ils ont pris l'avion. Aucun cas secondaire n'a été identifié parmi les autres citoyens rapatriés ou parmi les 4 membres d'équipage. - Tous les passagers du vol ont porté leur masque, sauf pour manger et boire.
Schwartz (2020) (27) Études de cas Canada Janvier 2020	Rapports sur le cas index qui est arrivé à Toronto le 22 janvier, après un vol de 15 heures en provenance de la Chine avec 350 personnes à bord. Aucune mesure de santé publique ni aucune mention du port de masque n'a été notée.	- Aucun cas secondaire de COVID-19 n'a été relevé malgré le suivi de la santé publique.
Qian (2020) (28) Enquête sur la recherche des contacts Chine Janvier 2020	12 cas ont pris un vol de Ningbo à Zhejiang, en Chine, après un événement de super-propagation du virus dans un temple de Ningbo. Aucune mesure de santé publique ni aucune mention du port de masque n'a été notée.	Onze de ces cas étaient liés au temple; l'exposition pour un cas était inconnue, mais on ne pensait pas qu'elle avait eu lieu pendant le vol. Aucun cas secondaire n'est connu pour s'être produit à la suite du vol. Les résultats des enquêtes de recherche des contacts ont permis d'identifier 88 cas de COVID-19 admis dans cinq hôpitaux de la province du Zhejiang, en Chine.

TA = taux d'attaque

POTENTIEL DE TRANSMISSION DU SRAS-COV-2 EN AVION

Quatorze citations sont incluses dans le tableau 2. Il s'agit d'un groupe mixte de documents de synthèse, de commentaires, de rapports, d'un sondage auprès des passagers et d'évaluations quantitatives des risques qui examinent le risque de transmission du SRAS-CoV-2 en vol.

Le rapport publié par l'Aviation Public Health Initiative (APHI) le 27 octobre 2020 constitue l'évaluation la plus complète du risque de transmission du SRAS-CoV-2 de porte à porte (1). Le présent rapport évalue les preuves disponibles et tient compte de l'avis d'experts et des résultats de simulations dans son évaluation de la réduction du risque de transmission du SRAS-CoV-2 sur les vols. Ils expliquent pourquoi une stratégie d'atténuation des risques à plusieurs niveaux est nécessaire et l'importance de la conformité des passagers et des compagnies aériennes. Des conclusions et recommandations similaires sont décrites dans les autres examens et commentaires du tableau 2.

Un seul sondage auprès des passagers et des équipages a permis d'examiner l'impact et la perception des mesures de sécurité renforcées visant à réduire le risque de transmission du SRAS-CoV-2 de porte à porte (4). Les changements mis en œuvre, tels que les toilettes réservées à l'équipage, le nettoyage fréquent des toilettes, les zones de quarantaine désignées dans l'avion, le port du masque pour tous, l'utilisation d'écrans faciaux, l'hygiène fréquente des mains (gel alcoolisé fourni à tous les passagers) et les contrôles des symptômes et de la température, ont suscité des réactions positives. Les passagers ont indiqué qu'une distance physique de 1,5 à 2 m pouvait être maintenue lors de l'enregistrement, du pré-embarquement et de l'embarquement, mais pas en vol. L'équipage a constaté que remettre aux passagers des masques chirurgicaux, des écrans faciaux et du gel alcoolisé avant le vol n'était pas pratique, car les passagers avaient souvent déjà les mains pleines avec plusieurs bagages à main.

Une méta-analyse a révélé que, de janvier à juin 2020, le risque d'être infecté par le SRAS-CoV-2 dans une cabine d'avion était estimé à 1 cas pour 1,7 million de voyageurs (IC 95 %, 712 000 à 8 millions) (29). Cette analyse a également montré que le risque a été considérablement réduit grâce aux mesures d'atténuation mises en œuvre. En mars 2020, le risque était de 1:425 062 et d'avril à septembre 2020, il était de 1:7,1 millions. D'autres évaluations quantitatives du risque présentées dans le tableau 2 fournissent également des estimations du risque de transmission du SRAS-CoV-2 en avion et, dans de nombreux cas, elles estiment que le risque de transmission est plus élevé que la méta-analyse. Bien que nous sachions que la transmission en vol a été sous-déclarée et que le risque de transmission en vol varie en fonction de nombreux facteurs et des paramètres des modèles, la variabilité des estimations provenant de différentes études ne peut être réconciliée en raison de la variation des approches entre les analyses.

L'effet combiné du port de masques, d'une distanciation sociale entre les passagers, d'une ventilation améliorée et de sièges intermédiaires vacants à 66 % de leur capacité, peut réduire le nombre d'infections de plus de 50 %, et les masques N95 ou chirurgicaux (ASTM 3) réduisent le risque d'infection à 0 (30). Les probabilités d'infection pour un vol de 2 heures sans masque facial étaient comparables à celles d'un vol de 12 heures où tous les passagers portaient des masques à haute efficacité (31). Cette étude a également révélé que le retrait du masque pour le service des repas augmentait le risque. De plus, le fait de retirer environ un tiers des passagers en gardant les sièges du milieu vides et d'augmenter la distance sociale pendant l'embarquement peut réduire considérablement le risque d'infection (de 35 à 50 %) par rapport à un avion

complet (32, 33). Une évaluation des risques a estimé qu'un vol aux États-Unis le 30 juin 2020 présentait un risque de contracter le SRAS-CoV-2 de 1/4300 sur un vol complet et de 1/7700 si la politique du siège central vide était en place (ces chiffres dépendent de l'activité de la maladie dans la population) (34). Plus la durée du vol est longue, plus le risque d'infection par le SRAS-CoV-2 est élevé (31, 35).

Tableau 2 : Examens, rapports, sondage auprès des passagers et évaluations des risques liés à la transmission du SRAS-CoV-2 dans les avions (N=14)

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Pang (2021) (29) *Préimprimé* *nouveau* Examen systématique USA1 Avril 20211	Examen systématique des cas de COVID-19 liés à des voyages aériens jusqu'en septembre 2020. L'examen s'est limité aux vols avec des cas de référence de passagers et n'a pas inclus les transmissions entre l'équipage aérien, le personnel au sol ou le personnel de l'aéroport. Une approche quantitative a été utilisée pour estimer le risque de transmission par les voyages aériens. Des facteurs de correction ont été utilisés dans les estimations de risque pour la transmission asymptomatique et la sous-déclaration. Le risque de transmission a été calculé pour trois périodes d'intérêt : (1) de janvier à juin 2020, période couverte par la littérature; (2) le mois de mars 2020 lorsque la propagation mondiale du COVID-19 se produisait; et (3) d'avril à septembre 2020 pour tenir compte de la forte baisse des voyages aériens dans le monde et de l'utilisation accrue des tests de dépistage du COVID-19.	- En août 2020, il y avait au moins 2 866 cas de référence documentés qui étaient des passagers aériens. - Moins de 50 cas secondaires potentiels documentés associés aux voyages aériens pendant la pandémie ont été signalés. - L'utilisation des masques sur les vols examinés allait de l'utilisation inconnue à l'utilisation obligatoire du N95. - De janvier à juin 2020, le risque d'être infecté par le SRAS-CoV-2 dans une cabine d'avion est estimé à 5,927 x 10-7 ou 1:1,7 million. L'incertitude des facteurs de correction et un intervalle crédible à 95 % indiquent que le risque varie de 1 cas pour 712 000 voyageurs à 1 cas pour 8 millions de voyageurs. - Pour le mois de mars 2020, le risque est estimé à 2,353 x 10-6 ou 1:425 062. - D'avril à septembre 2020, le risque est estimé à 1,413 x10-7 ou 1:7,1 millions.

Soleil (2021) (36) *nouveau* Revue de la littérature Chine[1] Avril 2021[1]	Revue narrative des publications relatives à la pandémie de COVID-19 et au transport aérien publiées en 2020.	- Un résumé de la documentation sur les opérations de contrôle des aéroports et les stratégies d'embarquement. - Résume la littérature existante (2020) concernant les opérations en vol en présence du COVID-19 et les événements de transmission en vol. - La conclusion est que des données robustes et largement disponibles sur les cas de transmission, malgré l'utilisation correcte du masque dans les avions, permettraient d'obtenir des renseignements plus utiles.
Bielecki (2021) (37) *nouveau* Revue de la littérature Suisse[1] Février 2021[1]	Examen narratif des sujets liés au transport aérien en période de pandémie. Parmi les sujets abordés, citons le nombre de voyageurs, la prévention et les recommandations de dépistage en vol, la transmission du SRAS-CoV-2 en vol, la photo-épidémiologie du port du masque, l'interruption des voyages aériens vers les rassemblements de masse, ainsi que les mesures de quarantaine et leur efficacité.	- Le nombre de voyages aériens a considérablement diminué (baisse de 51,6 % par rapport à 2019). - Les vols seront plus sûrs si l'on optimise les procédures de dépistage, si l'on minimise le risque de laisser monter à bord des cas pré ou asymptomatiques (c'est-à-dire si l'on procède à des tests), et si l'on met en œuvre/respecte des mesures d'hygiène simples et de distanciation physique qui empêchent la propagation des maladies. Le contrôle des passagers est insuffisant pour détecter tous les cas infectieux. - Grâce à la circulation d'air élevée et à l'utilisation de filtres HEPA à bord des avions, il est peu probable d'attraper le virus d'une personne qui n'est pas assise à proximité. - Le risque d'infection pendant les vols est faible : Une seule infection par 54 heures de vol et aucune infection pendant un vol de 12 heures.
Khatib (2020) (38) *nouveau* Revue de la littérature Canada[1] Déc. 2020[1]	Examen narratif de la littérature sur les risques de transmission du SRAS-CoV-2 et les stratégies de prévention de l'infection dans le cadre du transport aérien commercial. Les auteurs fournissent des recommandations et proposent des stratégies	- La qualité de l'air à bord des avions modernes est très sûre (les filtres HEPA sont efficaces à 99,97 % pour éliminer les particules comprises entre 0,1 et 0,3 µm de diamètre et 100 % des particules plus grosses). - Des études supplémentaires sont nécessaires pour examiner l'interaction entre le débit d'air et la dispersion des particules qui en résulte, mais les auteurs recommandent d'allumer le débit d'air personnel (*ventilation*) au-dessus de chaque passager pour améliorer le confort durant le voyage, la qualité de l'air, et pour réduire la

	pour atténuer la propagation du COVID-19.	transmission de personne à personne des contaminants exhalés. - Le risque est le plus élevé lors de l'embarquement et du débarquement. - On pense qu'un siège côté hublot est l'option la plus sûre, bien que des études récentes sur des épidémies réelles remettent en question cette hypothèse. - Parmi les recommandations, citons l'utilisation de masques, la promotion d'une désinfection fréquente des mains et l'instauration d'une distance physique, lorsque cela est possible, entre l'embarquement et le débarquement. Les points de contact les plus fréquents doivent être désinfectés entre les vols et pendant le vol. Des mesures de présélection et de prétestage doivent être utilisées en plus des mesures préventives appliquées à bord. La mise en place d'un laissez-passer numérique standardisé pour le COVID-19 et une recherche plus solide des contacts pourraient être des facteurs clés pour permettre un retour progressif et sûr aux voyages aériens.
Marcus (2020) (1) Aviation Public Health Initiative Report from the Harvard TH Chan School of Public Health É.-U.[1] Septembre 2020[1]	Ce rapport de l'APHI comprend les données disponibles jusqu'au 28 septembre 2020 Le présent rapport d'orientation axé sur la recherche évalue la question indiquée ci-dessous à l'aide d'un mélange de revues de la littérature, de modèles *in silico* et d'opinons d'experts : *Au milieu de cette crise complexe et nouvelle de coronavirus, comment les chefs de file du secteur de l'aviation peuvent-ils faire progresser un programme indépendant fondé sur des*	Les interventions non pharmaceutiques à plusieurs niveaux réduisent considérablement le risque de transmission de la maladie. Elles incluent notamment une ventilation optimale, la désinfection des surfaces, le port de masques, des procédures visant à encourager la distanciation sociale, tout particulièrement au moment de l'embarquement et du débarquement, mais aussi pendant le vol (p. ex., pas de file d'attente pour les toilettes ou éviter de se déplacer dans l'avion et réduire au minimum les interactions avec l'équipage). La ventilation des avions est très sophistiquée et fournit une grande quantité d'air pur à la cabine, qui disperse rapidement l'air expiré. Comportement des membres de l'équipage et des passagers : La sécurité du public à bord des avions dépend beaucoup des comportements individuels, y compris les certificats de santé et les vérifications

	données probantes afin de réduire les risques de transmission du SRAS-CoV-2 et, par le fait même, améliorer la sécurité et la confiance des employés et des passagers?	avant l'embarquement, le port obligatoire du masque, le respect de la distanciation sociale et l'adoption de comportements ordonnés pour éviter la congestion, sans oublier le lavage des mains et le nettoyage. Ces bons comportements sont fortement encouragés elle sera inscrite sur une liste d'interdiction de vol pour cause de non-respect. Dans l'ensemble, il n'existe que peu de données sur la transmission pendant le vol, mais il semble qu'un très faible nombre d'infections pourrait être attribué à ce type de transmission. Il existe également des preuves que les interventions non pharmaceutiques, tout particulièrement le port du masque, n'ont pas entraîné de transmission malgré le fait que certains passagers infectieux se trouvaient dans les avions. Ils décrivent 13 manuscrits (également inclus dans le tableau 1) portant sur l'étude de la transmission en vol. Il faut également noter qu'aucun des équipages des vols de rapatriement n'a contracté le SRAS-CoV-2, ce qui démontre que l'utilisation et le respect des interventions non pharmaceutiques sont efficaces. - Des stratégies d'atténuation des risques à plusieurs niveaux peuvent réduire grandement le risque de transmission, mais exigent la conformité tant des passagers que des compagnies aériennes.
Freedman (2020) (39) Analyse bibliographique N.d.[1] Septembre 2020[1]	Examen narratif de toutes les publications sur la transmission du SRAS-CoV-2 en vol, disponibles jusqu'au 21 septembre 2020. Cet examen résume les événements de transmission à l'aide d'attributs comme le port du masque pendant le vol pour tenter de décrire et de quantifier le risque selon différents scénarios et considérations, comme les	Décrit 4 vols bien documentés, dont trois sont indiqués dans le tableau 1 (5 à 7), alors que le quatrième est un inventaire en ligne des vols à destination de Hong Kong qui ont signalé une transmission à 2 passagers, 1 assis avec 5 cas index, alors que les personnes portaient des masques dans l'avion (vol d'une durée de 8 h). 3 événements de transmission uniques ont été signalés et 2 ont été publiés (9, 11). 6 vols à haut risque sans transmission sont répertoriés, 1 a été publié (17). L'inventaire des vols en provenance de Hong Kong comprend de nombreux vols avec des

	taux d'incidence différents du SRAS-CoV-2 au point d'origine et à destination, l'intensité de la charge virale dans les cas index, la durée du vol, les pratiques associées au port de masque dans l'avion, les vérifications effectuées avant le vol et la distanciation entre les passagers. Il n'y avait pas suffisamment de points de données pour quantifier le risque.	passagers ayant eu un résultat positif et aucune transmission secondaire attribuable au vol. 5 vols d'évacuation dont 3 ont été publiés (3, 13) sont répertoriés avec un événement de transmission possible. Selon cet examen, plus de 1,7 million de passagers ont été rapatriés par leur gouvernement ou une compagnie de navires de croisière pendant la pandémie, mais peu de ces rapatriements ont été documentés. Des listes de vols contenant des cas connus de COVID-19 ont été signalées au Canada et en Australie. Ces listes permettent aux autres passagers de s'auto-identifier et de s'isoler. Le CDC des États-Unis recueille également des données, mais n'a publié aucune conclusion. Quels facteurs de risque ont été signalés? Grappe évidente avec cas lorsque des plans de cabine étaient disponibles, mais une certaine transmission a tout de même touché les personnes se trouvant à plus de 2 rangées du cas index. Les vols avec d'importantes grappes de transmission ont été effectués avant que les masques ne soient obligatoires pendant les vols et plusieurs vols à haut risque sans transmission ont exigé que les passagers portent des masques.
Shaimoldina (2020) (40) *nouveau* Commentaire NA[1] Déc. 20201	Un ensemble de données publiques sur les infections liées aux vols internationaux a été utilisé pour analyser la tendance du trafic aérien et des infections pendant la pandémie. En se basant sur la littérature existante, les auteurs décrivent ensuite les défis à relever pour empêcher les personnes infectées par le SRAS-CoV-2 de monter à bord des avions et les	- Les infections en vol ont diminué et les voyages en avion ont été considérablement réduits. - Il est difficile d'empêcher les personnes infectées par le SRAS-CoV-2 de monter à bord des avions en raison de la précision des tests, des cas asymptomatiques et de nombreux autres facteurs, notamment l'impossibilité de maintenir une distance physique et la densité des passagers dans un avion. - Les solutions peuvent inclure la mise en quarantaine des passagers dans les hôtels, l'obligation de porter un EPI, le diagnostic dans les aéroports et le diagnostic rapide par imagerie/biomarqueurs grâce à une technologie de pointe.

	solutions pour la reprise des vols.	
Harries (2020) (41) Commentaires N.d.[1] Août 2020[1]	Est-il sécuritaire de prendre l'avion? Ce commentaire examine les publications disponibles jusqu'en août 2020. Des éclosions historiques ont été signalées pour la tuberculose, les maladies semblables à la grippe et le SRAS-CoV-1.	La ventilation dans un avion est très bonne. Elle peut toutefois être perturbée par les déplacements des passagers, la toux, etc. Les sièges près de l'allée ont tendance à entraîner plus de contacts avec les autres personnes que les sièges près des hublots. Ils recommandent de suivre les documents d'orientation disponibles : porter un masque bien ajusté et un écran facial ou des lunettes, d'utiliser des lingettes imbibées d'alcool pour essuyer les surfaces, de ne pas se rassembler ou de faire la file pour aller à la toilette, de changer de siège si l'on se trouve près d'une personne symptomatique, ainsi que d'éviter de boire et de manger si possible. Prenez les mêmes précautions à l'aéroport et assurez-vous de respecter, dans la mesure du possible, la distanciation physique.
Pongpirul (2020) (4) Sondage réalisé auprès des passagers et des membres d'équipage Thaïlande Avril 2020	Cette étude a porté sur les passagers et les membres d'équipage de deux vols de rapatriement effectués par Thai Airways (TG476 en provenance de Sydney, soit un vol d'une durée de 9,25 h et TG492 entre Auckland et Bangkok, soit un vol de 11,5 h), pour un total de 335 passagers et de 35 membres d'équipage. Un questionnaire en ligne a été utilisé pour obtenir des commentaires individuels sur la distanciation sociale, le port du masque et d'autres procédures mises en place	Le taux de réponse au questionnaire en ligne était faible puisqu'il n'était que de 22,5 %. Plusieurs mesures de réduction des risques ont été mises en œuvre et bien accueillies. Cela incluait notamment les toilettes réservées à l'équipage, le nettoyage fréquent des toilettes, les zones de quarantaine désignées dans l'avion, le port du masque pour tout le monde, l'utilisation d'écrans faciaux, l'hygiène des mains fréquente (gel d'alcool fourni à tous les passagers), la vérification des symptômes et la prise de température. Parmi les conclusions obtenues, notons le fait que les passagers ont déclaré qu'il était possible de maintenir une distance physique de 1,5 à 2 m lors de la vérification, du pré-embarquement et de l'embarquement, mais pas en vol. En raison des bagages à main, les membres de l'équipage ont déclaré qu'il n'était pas pratique de

	pour réduire le risque de transmission du SRAS-CoV-2. Des entrevues approfondies ont été menées auprès des membres de l'équipage.	remettre des masques chirurgicaux, des écrans faciaux et du gel alcoolisé aux passagers avant le vol.
Horstman (2021) (30) *nouveau* Évaluation des risques US[1] Mar. 2021[1]	Application des résultats de la dynamique des fluides informatiques du transport et de la concentration des virus, des données antérieures sur la transmission de la grippe dans les avions et de l'estimation des quanta de Wells Riley, pour estimer le risque d'infection d'une infection virale aérienne arbitraire dans les avions de type Boeing 737-600. Les paramètres et les données de l'analyse ont ensuite été comparés aux données de terrain sur le SRAS-CoV-2 dans un avion. Note : Données de terrain basées sur l'événement de transmission décrit par Hoehl (2020) dans le tableau 1. Les enquêteurs ont supposé que le taux d'émission du virus était de 1,6 ± 1,2 x10^5 copies du génome/m^3h, ce qui correspondait à 1 267 virus libérés par minute, et à une dose infectieuse humaine de 50 % (HID_{50}) de 2 554 copies/quanta.	- Au cours d'un vol de trois heures, le risque d'infection par voie aérienne était d'environ 50 % pour les passagers assis à proximité (c'est-à-dire dans une seule rangée) des cas infectés (positionnés aux sièges de la 12e rangée de l'allée); on estime alors à deux ou trois le nombre d'infections pour 131 passagers. - Lorsque l'analyse a été comparée aux données de terrain où quatre cas d'infection symptomatique ont entraîné deux infections secondaires, le SRAS-CoV-2 s'est avéré moins infectieux et se situe au milieu de la fourchette des données appliquées aux doses infectieuses de grippe. - Les masques, la distance sociale entre les passagers de 2,9 pieds, le siège central vacant à 66 % de sa capacité ont réduit le risque de transmission de plus de 48 %. L'utilisation de masques N95 et de masques chirurgicaux (ASTM 3) a permis de réduire à zéro le nombre d'infections secondaires.

Wang (2021) (31) *nouveau* Évaluation quantitative des risques UK[1] Fév. 2021[1]	Estimer la probabilité d'infection par le SRAS-CoV-2 en vol pour une série de scénarios en utilisant les données expérimentales de dispersion des aérosols et une équation de Wells-Riley modifiée. Les scénarios ont été variés en fonction des taux de génération de quanta et de l'efficacité des masques faciaux, et spécifiés pour un avion B777-200.	- Les probabilités d'infection pour un vol de deux heures sans masque facial étaient comparables à celles d'un vol de 12 heures où tous les passagers portaient des masques à haute efficacité. Dans l'ensemble, les probabilités d'infection étaient plus élevées dans les cabines de la classe économique (MID-AFT) que dans celles de la classe affaires (FWD). - Les probabilités d'infection individuelle au cours d'un vol non masqué de deux heures variaient de 4,5 % à 60,2 %. Les probabilités moyennes d'infection basées sur le nombre de passagers infectés sur le vol variaient de 0,1 % à 2,5 % dans le même scénario. Pour un vol de 12 heures sans port du masque, les probabilités d'infection individuelles variaient de 24,1 % à 99,6 %, la probabilité d'infection moyenne étant de 0,8 % à 10,8 %. - L'utilisation de masques à haute/faible efficacité par les passagers pendant un vol de 12 heures, à l'exception de l'heure de repas, a fait passer les probabilités moyennes d'infection de ~59 % à ~8 %, par rapport au cas où les masques étaient portés pendant tout le vol.
McCarthy (2021) (32) *nouveau* Évaluation quantitative des risques NA* Jan 2021*	Ce modèle de transmission mécaniste suppose que la probabilité d'infection par le SRAS-CoV-2 est cumulative et liée aux sous-activités. Les sous-activités qui, ensemble, constituent l'activité de voyage aérien comprennent l'embarquement dans l'avion, le déplacement vers et dans le siège, le fait de s'asseoir dans l'avion pendant la durée du vol, et enfin le fait de quitter son siège et de débarquer de l'avion. Le modèle suppose également que le vol dure	Les avantages relatifs de différentes stratégies d'atténuation sur l'avion peuvent être explorés : - Le temps passé en position assise était le facteur le plus important du score de risque total. - Le port du masque, rendu obligatoire, compte tenu de ce que nous savons actuellement, pourrait être une stratégie (rentable) de réduction des risques. - Le fait de laisser le siège du milieu vacant, à moins qu'un groupe de trois personnes ne voyage ensemble, réduit au moins de moitié le risque, dans un très large éventail d'hypothèses de dégradation. - Gérer l'embarquement est moins coûteux que de laisser des sièges vides, mais l'analyse a montré que l'impact total est moindre.

	trois heures, qu'il n'y a pas de contact physique direct entre les participants et que toutes les surfaces sont désinfectées. Il suppose également que tous les passagers respectent les politiques d'embarquement et de port du masque. Il s'agit d'un cadre d'analyse décisionnelle risque-coût-bénéfice qui peut être appliqué à de nombreux contextes, y compris celui des avions. L'analyse peut produire des risques relatifs.	
Hu (2020) (35) *nouveau* Évaluation quantitative des risques Chine Déc 2019- Mar 2020	Cette évaluation du risque applique les données épidémiologiques des passagers d'avions (n= 9 265 passagers et 175 cas de référence, sur 291 avions) et des contacts proches pour estimer les taux d'attaque (TA) et le nombre de reproductions (R_0) avant le verrouillage de Wuhan. Le risque relatif entre les sièges selon la proximité du cas de référence a également été estimé. La limite supérieure du TA a été estimée sur la base de l'hypothèse que 34 et 69 contacts proches ont été infectés sur le vol au départ de Wuhan.	- Le risque global de transmission du SRAS-CoV-2 dans les avions équipés de dispositifs de filtration de l'air à haute efficacité serait relativement faible. La limite supérieure estimée du TA était de 0,60 % (IC 95 % : 0,43 %-0,84 %), et R_0 variait de 0,12 à 0,19. - Le risque de transmission était variable selon la distance du siège par rapport au(x) cas infecté(s) et à la durée du voyage. - Les sièges immédiatement adjacents aux cas de référence étaient les plus à risque, avec un TA de 9,2 % (IC 95 % : 5,7 % — 14,4 %), le risque relatif (RR) de ces sièges par rapport aux autres sièges de l'avion était de 27,8 (IC 95 % : 14,4 - 53,7). Les sièges du milieu présentaient le TA le plus élevé (0,7 %, IC 95 % : 0,4 % — 1,2 %), suivis des sièges côté hublot (0,6 %, IC 95 % : 0,3 % - 1,0 %) et des sièges côté couloir (0,6 %, IC 95 % : 0,3 % — 1,0 %). - Les limites inférieures des estimations de TA liées aux voyages en avion sont passées de 0,0 % (IC 95 % : 0,0 % — 0,6 %) à 0,4 % (IC 95 % : 0,02 % - 2,2 %), et les limites supérieures de 0,7 % (IC 95 % : 0,5 % — 1,0 %) à 1,2 % (IC 95 % : 0,4 % - 3,3 %) lorsque la durée du voyage est passée de 1,5 heure

		à 3,3 heures. Cependant, ces résultats n'étaient pas significatifs en raison des données limitées sur les cas secondaires par rapport au temps de vol.
Arnold (2020) (34) *Prépublication* Évaluation quantitative des risques États-Unis Juin 2020	Cette évaluation des risques permet de calculer le risque d'infection par le SRAS-CoV-2 à la suite d'une exposition dans un avion. Cette évaluation ne tenait pas compte de l'embarquement et du débarquement, de l'accès à la toilette et de la durée du vol et a fait certaines suppositions en ce qui concerne la « protection » offerte par les dossiers de siège comme barrière entre les rangées. Elle utilise les données provenant des passagers qui se trouvaient en classe économique dans des avions comportant 6 sièges par rangée.	Selon ces hypothèses, le risque d'attraper la COVID-19 d'un passager à proximité sur un vol aux États-Unis le 30 juin 2020 était d'environ 1 sur 4 300 si l'avion était rempli. Lorsque la politique du « siège central vide », ce risque descend à 7 700. Ces chiffres sont fondés sur l'estimation selon laquelle 1 Américain sur 120 a la COVID-19 à n'importe quel jour, ce qui donne 40 000 cas confirmés par jour x 10 x 7 jours, donc environ 1/120 de la population américaine de 330 000 000. Cette évaluation suggère que le port du masque pourrait réduire le risque de 82 % (n'est pas inclus dans le taux d'attaque et ne contient aucune référence).

ANALYSES INDIRECTES DU RISQUE DE TRANSMISSION DES INFECTIONS RESPIRATOIRES À BORD DES AVIONS ET STRATÉGIES D'ATTÉNUATION POSSIBLES

Plusieurs modèles de simulation et *in silico* ont été développés pour explorer les moyens de minimiser le risque de transmission d'une maladie infectieuse dans un avion ou lors de l'embarquement et du débarquement. Neuf études sur l'embarquement et le débarquement d'un avion, six sur la configuration optimale des sièges pour minimiser la transmission en vol et sept sur l'aérodynamique des gouttelettes respiratoires dans un avion lors de la toux et des éternuements ont été publiées pendant la pandémie (tableau 3). Un examen unique de ces études aérodynamiques jusqu'en juin 2020 et un examen systématique des preuves de la transmission de la grippe sont également répertoriés dans le tableau 3. Ces études portent sur les stratégies d'embarquement permettant de minimiser les interactions entre les passagers et sur les plans des sièges pour maximiser la distance et l'interaction avec les autres personnes. Les études portant sur la ventilation à bord d'un avion et sur l'impact de la toux ou des éternuements sur la circulation de l'air

décrivent la distance et la portée des gouttelettes et des aérosols à partir de différents sièges (par exemple, hublot, milieu, couloir) et lorsque l'on est debout ou que l'on marche dans la cabine (tableau 3).

Plusieurs modèles prédictifs, de simulation et *in silico* ont été développés pour explorer les moyens d'évaluer et de minimiser le risque de transmission d'une maladie infectieuse lors de l'embarquement et du débarquement. Diverses méthodes d'embarquement et de débarquement ont été examinées dans neuf études. Dans l'ensemble, on a constaté qu'en augmentant le nombre de groupes d'embarquement, en réduisant le nombre de bagages à main et en évitant l'interaction avec les autres passagers (c'est-à-dire en embarquant à l'arrière de l'avion et en commençant par les sièges côté hublot), le risque d'infection diminuait de manière significative, bien qu'il faille sacrifier l'efficacité globale (c'est-à-dire le temps d'embarquement et de débarquement) dans certains scénarios (42-49).

Les études de surveillance de l'environnement, les modèles *in silico* et les expériences de simulation fournissent des estimations du risque et des stratégies d'atténuation pour la transmission en vol. Le nombre de particules en vol et les concentrations massiques dans les avions sont inférieurs à ceux des magasins de détail/épiceries, des restaurants, des bureaux, des maisons et d'autres formes de transport (50, 51). En outre, des expériences de simulation de la transmission d'aérosols en vol et de la contamination de surface montrent que l'air de la cabine est rapidement renouvelé (52). Lorsque des masques chirurgicaux ont été utilisés dans des simulations, on a constaté une réduction de plus de 90 % des gouttelettes libérées pendant la simulation de la toux par rapport à l'absence de masque (51).

Les sièges immédiatement adjacents aux cas de référence présentent le risque d'infection le plus élevé, suivis par la rangée directement derrière et devant (35, 51-53). La distance de déplacement des particules de toux est fortement influencée par la direction et le type de toux (54, 55). Il existe des données contradictoires sur les sièges (couloir, milieu ou hublot) qui présentent un risque d'infection plus élevé. Le fait de rester debout ou de marcher dans la cabine peut entraîner une propagation beaucoup plus importante des gouttelettes respiratoires et des aérosols (56). Les différences de risque entre les différents avions, ainsi que les sièges en classe affaires et économiques, sont également discutées (57, 58).

Une revue systématique de l'ECDC sur les preuves de la transmission de la grippe (59) rapporte que la transmission pendant les vols que rapporte la littérature était largement cohérente avec les résultats de la littérature sur le COVID-19; le nombre de cas secondaires est faible et le siège d'un cas secondaire se trouve généralement à moins de deux rangées d'une personne infectée. Il est intéressant de noter que la durée du vol n'était pas associée au risque de transmission dans les études prises en compte dans cette revue.

Tableau 3 : Études et analyses portant sur l'aérodynamique des gouttelettes respiratoires dans les avions et sur les stratégies d'atténuation des infections respiratoires dans les avions (n=24)

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Simulation et modèles *in silico*		

Embarquement/Débarquement		
Cotfas (2021) (48) *nouveau* Modèle prédictif Roumanie[1] Mar. 2021[1]	Utiliser un modèle à base d'agents et une approche de simulation stochastique pour étudier les impacts de la méthode de la pyramide inversée sur le temps moyen d'embarquement et le risque sanitaire pour les passagers assis dans les allées et les hublots. Les évaluations étaient basées sur la distanciation sociale en maintenant une distance de 1 à 2 mètres entre les passagers lorsqu'ils marchent dans l'allée, en gardant le siège du milieu vide et en appliquant différentes politiques en matière de bagages à main.	- Lorsque la minimisation du risque sanitaire pour les passagers était l'objectif principal, la solution optimale consistait à affecter un nombre égal de passagers en siège côté hublot aux groupes d'embarquement 1 et 2, et un nombre égal de passagers en siège côté couloir aux groupes d'embarquement 2 et 3. Cette option était imposante quant aux changements du volume de bagages et de la distance sociale de l'allée. Elle a permis de réduire de 22,76 % à 35,31 % le risque pour la santé des passagers du siège côté couloir, par rapport à d'autres simulations qui minimisaient le temps d'embarquement. - Les scénarios permettant de réduire le temps d'embarquement et, dans une moindre mesure, les risques sanitaires sont également examinés.
Milne (2021) (43) *nouveau* Modèle prédictif NA[1] Fév. 2021[1]	Dans ces expériences de simulation stochastique et ces modèles basés sur des agents, les auteurs évaluent six méthodes d'embarquement et comparent leurs performances à celles des deux meilleures méthodes d'embarquement utilisées à ce jour avec la distanciation sociale selon quatre paramètres de performance. Trois de ces paramètres sont liés au risque de propagation du virus aux passagers durant l'embarquement. La quatrième mesure est le temps nécessaire pour achever l'embarquement. Les deux « meilleures » méthodes d'embarquement de base sont	- Plus il y a de bagages = plus le temps d'embarquement est long - Dans un scénario où la distance entre les allées est de 1 m, la méthode d'arrière à l'avant par rangée — WilMA présente des temps d'embarquement plus courts, moins d'interférences entre les sièges et moins de risques pour les sièges côté allée que la méthode de base à l'envers pour chaque scénario de bagages. La méthode de base d'arrière à l'avant par rangée présente moins de risques pour les sièges côté hublot dans les scénarios où le volume de bagages est plus élevé. - Dans un scénario où la distance entre les allées est de 2 m, la méthode d'arrière à l'avant par rangée — WilMA — décalée de trois est supérieure à la méthode de base de la demi-zone en pyramide inversée modifiée parce que

	l'embarquement à l'envers par rangée et la demi-zone pyramidale inversée modifiée (voir les figures pour la description). La méthode d'arrière à l'avant par rangée — WilMA fait monter les passagers une rangée à la fois en commençant par l'arrière de l'avion. Les cinq autres méthodes d'embarquement sont créées en ajustant la méthode d'embarquement d'arrière à l'avant par rangée — WilMA de façon à ce que certains des passagers assis aux hublots embarquent plus tôt. En particulier, les passagers en siège côté hublot des rangées K embarqueront dans l'avion avant les passagers en siège côté couloir. Dans les cinq nouvelles méthodes, la valeur du K se situe entre 2 et 6.	le temps d'embarquement est à peu près le même et qu'elle comporte moins de risques liés aux sièges côté allée et aux sièges côté hublot. La méthode d'arrière à l'avant par rangée — WilMA présente le plus faible risque pour les sièges côté hublot.
Xie (2021) (44) *nouveau* Modèle prédictif NA[1] Jan. 2021[1]	Comparer quantitativement le processus de débarquement d'un Boeing 737-300 avant et après l'adoption de stratégies de gestion du débarquement. Deux stratégies sont étudiées : Stratégie I : Lorsqu'il y a un seul passager infecté, les équipes au sol commencent par désinfecter les allées de la cabine avant de commencer le processus de débarquement, puis les passagers situés devant le patient infecté débarquent par la porte avant, tandis que les passagers situés à l'arrière du cas débarquent par la porte arrière. Le patient et ses	- Le nombre de passagers à haut risque a diminué de 72 % après l'adoption de la stratégie I. - Après l'adoption de la stratégie II, le nombre de passagers à haut risque a de nouveau diminué de 27 %. - Bien que ces deux stratégies sacrifient l'efficacité (c'est-à-dire une durée totale de débarquement plus longue), elles réduisent également de manière significative le risque d'infection.

	« contacts proches » ne débarquent que lorsque tous les passagers ont quitté la cabine. Stratégie II : Lorsqu'il y a plusieurs passagers infectés, les passagers sont évacués par la porte avant ou la porte arrière à partir des colonnes traversées qui ne contiennent pas de patients ou de contacts proches. Après que les passagers ont quitté la cabine, les valises et les « contacts proches » sortent par la porte avant ou arrière sans récupérer leurs bagages. Après le départ des bagages, les équipes au sol procèdent à une seconde désinfection de la cabine. Après la désinfection, les autres passagers sortent par la porte avant ou arrière.	
Milne (2020) (42) *nouveau* Modèle prédictif NA[1] Nov. 2020[1]	Dans ces expériences de simulation stochastique et ces modèles à base d'agents, les auteurs adaptent la méthode de la pyramide inversée pour la distanciation sociale lors de l'embarquement dans un avion à l'aide d'une passerelle d'avion à réaction qui relie le terminal à la porte avant de l'avion. Ils évaluent l'impact du nombre de groupes d'embarquement (2 contre 6) pour montrer l'impact résultant sur quatre mesures d'évaluation des performances. La première mesure de performance est le temps moyen d'embarquement. La deuxième mesure de performance est le nombre de mouvements de	- Lorsque le nombre de groupes d'embarquement passe de deux à quatre, le temps moyen d'embarquement diminue. - Lorsque le nombre de groupes d'embarquement passe de 3 à 6, le risque lié au siège côté couloir diminue sensiblement, passant de 44 % à 21 %. - Plus le volume des bagages transportés à bord de l'avion diminue, plus la durée du risque diminue de manière significative. - Le fait de doubler la distance sociale de l'allée, de 1 m à 2 m, augmente la durée moyenne de l'embarquement et diminue les risques liés aux sièges de l'allée et des hublots.

	siège de type 3 pendant l'embarquement (c'est-à-dire changement de siège, déplacement dans l'allée pour permettre au passager du hublot d'accéder à son siège). Les troisième et quatrième paramètres de performance concernent la santé des passagers assis pendant que les passagers embarquant plus tard les dépassent.	
Schwarzbach (2020) (60) *nouveau* Expérience de simulation NA[1] Oct. 2020[1]	Évaluer l'applicabilité des méthodes de distanciation sociale basées sur la technologie lors de l'embarquement dans la cabine d'un avion en utilisant une simulation de propagation radio basée sur un modèle d'avion tridimensionnel. Ils effectuent une simulation de propagation par traçage de rayons dans une section de la cabine modélisée d'un avion Airbus A321.	- Les auteurs démontrent que les mesures de l'indicateur de force du signal de réception (RSSI) couramment utilisées peuvent conduire à une classification de faux positifs et de faux négatifs en fonction du réglage du modèle de prévision d'affaiblissement, ce qui réduit la fiabilité et l'acceptation par les utilisateurs des options de distanciation sociale assistées par la technologie. - Du point de vue de l'application, une mise en œuvre possible des approches technologiques proposées pourrait ressembler à ce qui suit : Avertissement de proximité en temps réel, recherche des contacts après traitement, programmation de l'embarquement et du débarquement.
Delcea (2021) (49) *nouveau* Modèle prédictif Roumanie [1] Mai 2020[1]	Estime le nombre de passagers pour chaque groupe d'embarquement en supposant un embarquement en pyramide inversée avec les sièges du milieu inoccupés. Applique une modélisation basée sur les agents et une simulation stochastique	- Si l'objectif est de minimiser le risque sanitaire parmi les passagers, le premier groupe d'embarquement en pyramide inversée devrait être constitué de ceux qui ont des sièges côté hublot dans la moitié arrière de l'avion, le troisième groupe devrait être constitué de passagers ayant des sièges

	pour évaluer les impacts sur le temps d'embarquement et le risque sanitaire pour les passagers dans chaque scénario.	côté couloir dans la moitié avant de l'avion, le deuxième groupe d'embarquement étant constitué des autres passagers. Cette disposition s'est avérée être la meilleure, car elle réduit de 25 % le risque sanitaire pour les passagers assis du côté de l'allée et de 22 % pour les passagers assis à côté d'un hublot, tout en augmentant de 2 % le temps d'embarquement.
Milne (2020) (45) Modèle prédictif N.d.[1] Août 2020[1]	Dans ces expériences de simulation stochastique, les auteurs ont évalué neuf adaptations des méthodes d'embarquement en fonction de quatre mesures de rendement. Trois des mesures sont liées au risque que le virus se propage aux passagers au moment de l'embarquement. La quatrième mesure est le temps qu'il faut pour monter à bord d'un avion à deux portes lorsque les autobus d'aéroport transportent des passagers sur l'aire de circulation avant qu'ils n'embarquent dans l'avion.	Le temps d'embarquement moyen est la mesure comparable entre les différents scénarios. Augmentation de la distance sociale (de 1 m à 2 m) = augmentation du temps d'embarquement Augmentation de la proportion de personnes qui ont des bagages = augmentation du temps d'embarquement Le fait d'asseoir les passagers près des hublots avant ceux qui occuperont les sièges près de l'allée réduit le risque d'interférence avec le siège (lorsque la personne assise dans le siège près de l'allée doit se lever pour permettre à la personne qui s'assoit près du hublot de passer). Le risque lié au siège près de l'allée est plus élevé lorsque la distanciation physique est plus faible (1 m), que les personnes ont des bagages et que l'embarquement est aléatoire. L'auteur indique que le risque associé au siège près du hublot est inférieur au risque lié au siège près de l'allée pendant

		l'embarquement, mais sans cependant estimer la différence.
Schultz (2020) (46) Modèle prédictif R.-U.[1] Juillet 2020[1]	Modèle d'automate cellulaire qui modélise les déplacements des passagers pendant le processus d'embarquement. Ne tient pas compte des masques. Modélise la distance jusqu'au cas index ainsi que le temps de contact pour estimer le risque de transmission.	- Le modèle montre que, comparativement à l'embarquement aléatoire, le fait de faire embarquer ensemble les membres des groupes (p. ex., les familles) réduira le temps d'embarquement puisque celui-ci sera 41 % plus court que le scénario aléatoire. Ce type d'embarquement « groupé » entraîne également le risque de transmission le plus faible, soit de 0,09 comparativement à une valeur variant entre 0,57 et 0,62 pour n'importe lequel des scénarios aléatoires lorsque l'avion est à moitié plein. Ces temps d'embarquement étaient relativement stables à 75 % et à 100 % de la capacité de l'avion, toutefois, le risque de transmission a augmenté à une valeur variant entre 0,31 et 0,66 pour l'embarquement en groupe, par rapport à un scénario individuel.
Cotfas (2020) (47) Modèle prédictif N.d.[1] Mai 2020[1]	Un modèle basé sur des agents est utilisé pour simuler le processus d'embarquement des passagers, principalement en ce qui concerne les interactions avec les agents et d'autres personnes (la plateforme NetLogo a été utilisée pour ce faire). Ils ont modélisé le temps nécessaire pour embarquer dans l'avion en fonction d'un certain nombre de scénarios et ont tenu compte du temps pour ranger les bagages à main. Le résultat porte donc sur le temps pendant lequel les passagers déjà assis sont en contact avec d'autres	L'embarquement de l'arrière à l'avant de l'avion a pris le plus de temps, mais selon la simulation, c'était ce cas que le risque pour la santé était le plus faible. Le risque est tout aussi faible si une distanciation physique de 2 mètres est maintenue pendant l'embarquement. - L'embarquement est plus efficace et moins risqué lorsque les passagers n'ont aucun bagage à ranger.

	personnes, soit lorsque ces dernières circulent dans l'allée, soit parce qu'ils doivent se lever pour laisser entrer une personne qui doit aller s'asseoir au centre ou près du hublot.	
Transmission et répartition des sièges en vol		
Dietrich (2021) (33) *nouveau* Surveillance de l'environnement et étude des modèles prédictifs USA[1] Avril 2021[1]	Utilisation des données de dispersion du virus du bactériophage MS2 comme substitut du SRAS-CoV-2 et modélisation de la relation entre l'exposition au SRAS-CoV-2 et la proximité des sièges d'avion. Les deux scénarios d'occupation complète et d'occupation vacante du siège central ont été envisagés.	- Par rapport aux expositions dans les scénarios d'occupation complète, le risque d'exposition relatif pour un passager individuel dans les scénarios de siège central vacant a été réduit de 23 % à 57 %. - La réduction de 23 % de l'exposition a été observée pour un seul passager qui se trouvait dans la même rangée et à deux sièges de la source du SRAS-CoV-2, avec un siège central vide entre les deux. - On obtient 57 % dans un scénario impliquant une section à trois rangées contenant un mélange de sources de SRAS-CoV-2 et d'autres passagers. - La réduction globale du risque d'exposition dans une cabine complète de 120 passagers avec des sièges centraux vacants allait de 35,0 % à 39,4 %.
Desai (2021) (57) *nouveau* Étude*in silico* USA[1] Fév. 2021[1]	Modélisation de l'écoulement de l'air, du transport des particules expirées par voie orale et nasale (par exemple, CO_2 et coronavirus) à différentes positions du siège à l'intérieur des avions Airbus 380 et Boeing B747. Les simulations ont pris en compte les sections de première classe, de classe affaires et de classe économique dans chaque avion. Les positions des	- Le classement des sièges d'un avion à l'autre était très variable. - Dans la section de première classe : Le siège le mieux classé d'Airbus était plus chaud que le siège le mieux classé de Boeing, mais la circulation y était moins bonne. - En classe affaires : Le siège le mieux classé d'Airbus était plus froid, mais offrait une meilleure circulation que le siège le mieux classé de Boeing. Le siège de l'Airbus était situé dans la

	sièges ont été classées en fonction de la fraction de masse de CO_2, de la température et de la vitesse correspondant aux positions du nez des passagers pour chaque siège.	rangée latérale des sièges, côté couloir, et le siège du Boeing était situé près d'un hublot. - En classe économique : Le siège le mieux classé pour l'Airbus était situé côté hublot, tandis que le siège le mieux classé pour le Boeing était le siège du milieu dans la rangée latérale de sièges. Le siège de l'Airbus avait une température plus élevée, une concentration de CO_2 plus faible et une vitesse de l'air plus faible, la contrepartie pour un siège plus chaud étant une moins bonne circulation. - Dans l'ensemble, le siège d'Airbus le mieux classé en économie était à la fois chaud et doté d'une bonne circulation; le siège de Boeing était moins performant dans tous ces domaines.
Ghorbani (2020) (61) préimpression Étude *in silico* N.d.[1] Octobre 2020[1]	Le modèle appelé simulations de Monte-Carlo optimise, pour le secteur du transport aérien, le nombre de passagers et leur aménagement, dans le respect des mesures de distanciation sociale, pour des scénarios d'avions comportant une seule ou deux allées.	- Les figures présentées dans le document montrent l'aménagement optimal des sièges des passagers dans un avion. La clé pour augmenter le nombre de passagers en toute sécurité consiste à s'assurer de regrouper les familles.
Salari (2020) (62) Étude *in silico* N.d.[1] Juin 2020[1]	Un modèle de programmation linéaire mixte est utilisé pour répartir correctement les passagers dans les sièges tout en s'assurant de respecter deux types de distanciation physique, c'est-à-dire garder les passagers assis assez loin les uns des autres et assurer une distance sécuritaire entre l'allée et les sièges qui ont été attribués. Un Airbus A320 avec 20 rangées de sièges, une allée et trois sièges de	Si la distanciation physique est respectée entièrement, si aucun siège près de l'allée n'est utilisé et si personne ne se trouve à moins de 1 m d'une autre personne, la charge maximale sera de 20 passagers dans un avion de 120 places. Si les passagers peuvent s'asseoir dans le siège près de l'allée, le total passe à 30 passagers ayant une distanciation sociale de 1 m et plus. Le fait de s'asseoir près de l'allée doit inclure des stratégies visant à limiter les déplacements et

	chaque côté a été utilisé pour ce faire. Ce modèle a permis de réaliser un certain nombre de scénarios : - Siège central vide - Distanciation physique de 1 m une fois la personne assise - Siège près de l'allée vide - Hybride	l'exposition possible des personnes qui se déplacent dans l'avion. La politique qui vise à bloquer les sièges du centre permet de réduire le nombre de personnes dans un rayon de 1 m par rapport à la politique de n'asseoir personne dans les sièges près des allées. Plus il y a de passagers dans l'avion, plus les personnes se retrouvent assises à proximité les unes des autres, ce qui veut dire que le risque va en augmentant lorsque 1, 2 ou 3 personnes ou plus se retrouvaient dans un rayon de 1 m. Voir les illustrations dans les figures.
Wagner (2009) (58) Évaluation quantitative des risques É.-U.[1] Décembre 2009[1]	Cette évaluation quantitative des risques permet d'estimer la possibilité de transmission de la grippe H1N1 pendant un vol. La simulation utilise un Boeing 747.	Même lors de longs vols, le risque de transmission en vol est faible à modéré si le cas index voyage en première classe. Si le cas index se trouve en première classe, • De 0 à 1 infection pourrait survenir pendant un vol de 5 heures, • De 1 à 3 infections pourraient survenir pendant un vol de 11 heures, • De 2 à 5 infections pourraient survenir pendant un vol de 17 heures. Cependant, la transmission en vol pourrait être importante, particulièrement pendant les longs vols, si le cas index se déplace en classe économique. Si le cas index se trouve en classe économique, • De 2 à 5 infections pourraient survenir pendant un vol de 5 heures,

		• De 5 à 10 infections pourraient survenir pendant un vol de 11 heures, • De 7 à 17 infections pourraient survenir pendant un vol de 17 heures.
Hertzberg (2018) (63) Étude de surveillance de l'environnement et étude *in silico* É.-U.[1] Mars 2018[1]	Pendant la saison de la grippe sur 10 vols transcontinentaux aux É.-U., les auteurs ont établi la chronique des comportements et des déplacements des personnes dans la cabine économique d'un avion avec une seule allée et ont procédé à un échantillonnage environnemental. Ils ont simulé la transmission en vol à partir de ces données. Ce modèle axé sur les données et dynamique, de transmission en réseau de maladies respiratoires par gouttelettes, est unique en son genre.	Aucun des 229 échantillons prélevés dans l'environnement ne s'est révélé positif. - Les résultats indiquent qu'il y a une faible probabilité de transmission directe aux passagers qui ne sont pas assis à proximité d'un passager infectieux.
Simulations d'aérosols dans un avion		
Talaat (2021) (52) *nouveau* Expérience de simulation USA[1] Fév. 2021[1]	Étude de la transmission des aérosols en vol et de la contamination des surfaces à l'aide d'un modèle de calcul de la zone de la cabine d'un Boeing 737. L'étude vise à comprendre l'effet de la réduction de la capacité du nombre de passagers (de 60 à 40) et à la comparer à d'autres mesures d'intervention telles que l'utilisation d'écrans anti-éternuements (pare-haleine) entre les passagers d'un vol au maximum de sa capacité. L'étude prend en compte une large	- Les particules mettent 2 à 3 minutes pour se déposer ou quitter le système, car l'air de la cabine est rapidement renouvelé. - L'aérosol situé dans le spectre de dimension de 1 µm–20 µm est concentré à une rangée du patient de référence, et pratiquement aucune particule ne dépasse deux rangées du patient de référence. Les particules plus grandes, telles que celles de 50 µm, ne sont présentes que dans la rangée du patient de référence. - Une fraction relativement faible (21-26 %) des particules exhalées est

	gamme de tailles de particules (1-50 µm). Cette étude ne tient pas compte de la présence de plus d'une infection à bord, du comportement humain (parler, manger, boire, respecter le port du masque ou se déplacer dans les allées).	directement éliminée par le système de ventilation. La majorité des particules se déposent sur les surfaces dans la cabine et plus de particules de 1 µm se déposant sur les parois que sur le sol (10-14 % contre 3-6 %). - Les surfaces les plus contaminées dans le modèle au maximum de sa capacité (60 passagers) sans pare-haleine sont les passagers (y compris le patient de référence) avec une fraction de dépôt de 31 %, suivis des sièges avec 27 %. Dans le modèle à capacité réduite sans pare-haleine et dans le modèle au maximum de sa capacité avec pare-haleine, le dépôt total sur les passagers est réduit à 21 % et 15 %, respectivement. - La fraction respirable totale est la plus faible dans le modèle au maximum de sa capacité avec pare-haleine (0,5 %), suivi du modèle à capacité réduite pour passagers sans pare-haleine (0,7 %), puis du modèle au maximum de sa capacité sans pare-haleine (1,7 %). Cependant, la réduction du nombre de passagers et l'utilisation de pare-haleine éliminent la transmission directe de particules de 50 µm. Bien que ces particules laissent échapper une fraction respirable beaucoup plus faible que les particules de 1 µm, elles contiennent nettement plus de virions que les particules de 1 µm en raison de leur volume.
Kinahan (2021) (53) *nouveau* Expérience de simulation USA[1] Jan. 2021[1]	La dispersion et le dépôt d'aérosols dans deux avions gros porteurs (Boeing 767-300 et Boeing 777-200 à 30 000 pieds) ont été mesurés à l'aide de microsphères fluorescentes et marquées à l'ADN. Les données expérimentales	- Durant la simulation, l'exposition maximale, de 0,094 7 à 0,461 4 %, se produit dans un siège situé à côté d'une source, le risque d'inhalation le plus élevé suivant se produisant généralement dans les sièges situés devant et derrière le passager infecté. Ce risque d'exposition maximal équivaut à une réduction minimale de

	portaient sur une simulation de plus de 300 rejets d'un passager infecté par le SRAS-CoV-2 dans les sièges pendant le vol. Les tests ont été conçus pour mesurer la concentration d'aérosols dans les zones de respiration des passagers des sièges et des rangées voisines du passager infecté durant la simulation. Les rejets respiratoires comprenaient un mélange de tests avec le mannequin ne portant pas de masque et de tests avec un masque. Cette étude ne tient pas compte de la présence de plus d'une infection à bord ni du comportement humain (par exemple, parler, manger, boire ou respecter le port du masque).	99,54 % des aérosols à particules de 1 µm de la source de référence par rapport à la zone de respiration d'un passager type assis directement à côté de la source. - Moins de 0,03 % des particules décelables se déposent sur les surfaces solides pendant les essais, la concentration la plus élevée se trouvant sur les surfaces les plus proches de chaque point de rejet. On note que les surfaces horizontales comme les accoudoirs étaient généralement plus élevées que les surfaces verticales telles que les dossiers de sièges et les systèmes de divertissement à bord (IFE). - Avec le port du masque, la réduction moyenne du nombre total de particules comptées était de 15,6 %.
Rivero-Rios (2021) (50) *nouveau* Étude de suivi biologique États-Unis Juillet 2020	Les concentrations de particules (PM) ont été mesurées dans divers espaces intérieurs, notamment 19 vols, des magasins de détail/épiceries, des restaurants, des bureaux, des habitations et d'autres moyens de transport (voitures privées, bus, trains). Les vols ont été choisis de manière à couvrir un éventail de durées/destinations de vol et de modèles d'avions, et les étapes suivantes du voyage aérien : Terminal (départ), embarquement, taxi (sortie), montée, en vol, descente, taxi (entrée), débarquement et terminal (arrivée).	- Le nombre de particules durant le vol et les concentrations massiques dans les avions étaient inférieures à celles des magasins de détail/épiceries, des restaurants, des bureaux, des habitations et des autres moyens de transport testés. - Les particules dont le diamètre est inférieur à 1 µm dominent les concentrations totales en nombre de particules (car elles sont les plus difficiles à éliminer par filtration). - Les concentrations de particules présentaient une forme en V, avec des niveaux élevés à l'embarquement, une diminution continue et une concentration minimale stable pendant le vol. De légères augmentations de la concentration de masse des particules pendant le service des aliments ont été

		observées. Lorsque l'avion a commencé à descendre, les concentrations de particules ont commencé à augmenter et une augmentation brutale a été observée une fois que la porte de la cabine a été ouverte et que le processus de débarquement a commencé. - Le taux de renouvellement de l'air dans la cabine est rapide pendant le vol, ce qui réduit considérablement le nombre de particules dans la cabine. L'air ambiant en altitude contient moins de particules que l'air à la surface, ce qui contribue aux faibles concentrations en nombre et en masse de particules en altitude, et explique également la diminution et l'augmentation observées pendant la montée et la descente.
Kotb (2020) (56) Étude *in silico* Égypte[1] Septembre 2020[1]	Cette simulation avec modélisation informatique de la dynamique des fluides numériques est utilisée pour examiner ce qui arrive aux gouttelettes respiratoires lorsqu'elles sont expulsées par l'éternuement ou la toux d'une personne qui se déplace dans une cabine d'avion.	L'écoulement de l'air des gouttelettes produites par les toux et éternuements des passagers qui se déplacent pouvait atteindre les passagers se trouvant à plusieurs rangées de la source, comparativement à ceux qui restaient immobiles. Si la personne tousse et qu'elle se trouve à 1,1 m, l'éternuement aura une plus grande portée si la personne reste immobile. En comparant la plage de propagation des gouttelettes résultant d'un passager en mouvement et d'un passager immobile, plus le passager se déplace rapidement, plus les gouttelettes se propagent. - Les chiffres illustrent le fait de tousser ou d'éternuer debout et en mouvement dans une cabine d'avion de classe économique.

Silcott (2020) (51) *Non publiée* Expériences de simulation États-Unis Août 2020	Les simulations ont utilisé les modèles d'avion 767-300 et 777-200 pour étudier les pénétrations d'aérosol associées à un passager infecté par la COVID-19 dans la zone autour d'eux. Ces simulations ont été effectuées à 300 reprises, y compris avec l'embarquement et le débarquement. Les simulations en vol ont été effectuées dans le hangar et à une altitude de 35 000 pi. Cette étude ne tient pas compte du comportement humain, p. ex., parler, manger, boire, adhérence à porter le masque ou d'autres modes de transmission, p. ex., transmission par fomites.	Taux d'échange d'air élevé de 1,8 x 10^8 dans l'avion. L'exposition cumulative aux particules était de 10x moins élevée dans l'avion que dans une maison. Les particules se trouvaient dans la cabine moins de 6 minutes (contre 1,5 h dans une maison). L'élimination des particules dans l'air était 15x plus rapide que dans une maison et 5x plus rapide que dans une chambre d'isolement moderne d'un hôpital. Des masques chirurgicaux ont été utilisés dans les simulations. On a pu voir une réduction de plus de 90 % des gouttelettes libérées pendant la simulation de la toux comparativement au taux obtenu sans masque. Le fait de partager une rangée avec une personne atteinte de COVID-19 comporte le risque le plus élevé, alors que la rangée derrière et celle qui est devant offrent le deuxième niveau de risque le plus élevé. En fait, il y avait peu de différences pratiques du risque entre les sièges. Voir les données dans le document. La buse d'air individuelle ne fait aucune différence en ce qui concerne le risque. Pendant l'embarquement et le débarquement, si l'on s'assure de garder une circulation d'air, l'embarquement en petits groupes peut réduire le risque. Il y avait un faible risque d'exposition aux ondes du jet d'une personne infectée qui était déjà assise dans l'avion.
Yan (2020) (54) Expérience de simulation Australie[1]	Cette étude a mis au point un modèle informatique pour imiter une section économique de	On a constaté que le flux causé par la toux avait une portée longue et efficace en ce qui concerne le déplacement des

Août 2020[1]	Boeing 737 avec trois rangées et neuf mannequins.	contaminants, soit jusqu'à 4 s (ou 8x plus long qu'une simple toux). Un large éventail de gouttelettes de toutes tailles ont été dispersées dans la direction de la toux en raison du fort jet d'air associé à la toux, comparativement à ce qui se produit lorsque le flux d'air circule sous l'effet de la ventilation de l'avion (voir les figures sur papier).
Yang (2018) (55) Étude *in silico* Australie[1] Décembre 2017[1]	À l'aide de la mécanique des fluides numérique, cette étude a étudié l'effet du jet d'air associé à la toux sur le flux d'air local et le transport des particules dans un espace confiné comme une cabine d'avion type. La dispersion des particules émises par la toux a été simulée dans une rangée d'avions avec trois sièges.	- La distance de déplacement des particules associées à la toux était fortement influencée par la direction et le type de toux. La toux de la personne assise près de l'allée a créé une distance de déplacement des particules plus longue que celle qui se produisait lorsque la personne était assise sur le siège central ou près du hublot. Le siège du milieu a été considéré comme le siège le plus à risque d'exposition.
Bilans		
Jayaweera (2020) (64) Revue Sri Lanka [1] Juin 2020[1]	Revue de la littérature sur l'aérodynamique du virus SRAS-CoV-2 dans les gouttelettes et les aérosols dans une cabine d'avion (voir l'annexe). Nous nous sommes intéressés à la partie de la revue qui porte sur les cabines d'avion.	- Elle décrit la circulation de l'air dans la cabine et indique qu'un échange d'air complet est effectué en 2 à 3 minutes, ce qui devrait être bon pour dissiper rapidement les gouttelettes chargées de virus. Elle indique également que l'air passe à travers un filtre HEPA, qui peut éliminer les particules dont la taille est inférieure à 0,3 µm. Les trajectoires des jets de toux lorsque la personne ne porte pas de masque, lorsqu' elle porte un masque chirurgical et lorsqu'elle porte un masque N95 sont décrites dans le document.
Leitmeyer (2016) (59) Revue systématique ECDC[1] Août 2016[1]	Une revue systématique a été effectuée à propos du lien entre le transport aérien et la propagation de la grippe chez les passagers infectés et la possibilité de transmission en	Dans l'ensemble des études, 2 165/4 252 passagers pouvant être retracés ont été suivis et de ces passagers, 163 cas secondaires ont pu être identifiés (taux d'attaque secondaire de 7,5 %). 42 %

	vol. 14 publications, 11 sur la pandémie de grippe H1N1 ont été incluses. La revue systématique est de haute qualité et comprend des études jusqu'en octobre 2015.	des personnes étaient assises à moins de deux rangées du cas index. - La durée du vol n'a pas été associée à un risque de transmission dans cette étude.

[1] Pays de l'étude basé sur les affiliations des auteurs et date de l'étude basée sur la date de publication.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le Groupe des sciences émergentes de l'ASPC. La numérisation a compilé la littérature sur le COVID-19 depuis le début de l'épidémie et une mise à jour est effectuée quotidiennement. Les recherches pour retrouver de la documentation pertinente sur le COVID-19 sont effectuées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square, et font l'objet d'une vérification de concordance avec les centres d'information sur le COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats de l'analyse complète sont conservés dans une base de données Refworks et dans une liste Excel pouvant être consultée. Une recherche ciblée par mots-clés est effectuée dans ces bases de données, afin d'identifier les citations pertinentes sur le COVID-19 et SRAS-COV-2. Les termes de recherche utilisés comprenaient : vol ou avion, ou aéronef ou avion. La recherche a permis d'obtenir 649 citations (507 à partir de la recherche initiale jusqu'au 28 octobre 2020 et 147 à partir de la recherche actualisée menée le 26 avril 2021), qui ont été examinées pour leur pertinence à étudier. Des références supplémentaires à des recherches de synthèse pertinentes non liées au SRAS-CoV-2 ou à la pandémie actuelle ont été identifiées par le biais de citations dans des articles sur la pandémie actuelle et une recherche supplémentaire sur Google a été effectuée le 4 mai 2021 pour identifier tout nouveau rapport non indexé en utilisant (COVID-19 ou SRAS-CoV-2) ET (vol OU avion). Les citations potentiellement pertinentes ont été examinées pour confirmer qu'elles contenaient des données pertinentes, et les données pertinentes ont été extraites pour étude.
Ce bilan contient les recherches publiées jusqu'au 26 avril 2021.

Révision par les pairs

Le présent document a fait l'objet d'un examen par les pairs, par un expert en la matière, ainsi que d'un examen rédactionnel et d'un examen des aspects scientifiques de la politique par le Bureau de la Conseillère scientifique en chef.

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ANNEXE

Tableau de Marcus (2020) (1) qui met en évidence les interventions qui peuvent être utilisées ensemble pour permettre de minimiser le risque de transmission du SRAS-CoV-2 en vol.

Table 1.1 Non-pharmaceutical Interventions that can be used to Control Transmission of the Novel Coronavirus SARS-CoV-2, where Layering NPIs can create Additive and/or Synergistic Benefits in Reducing the Risk of Exposure to COVID-19 for Passengers and Crewmembers during Air Travel

Phase of Gate-to-Gate Passenger Journey	Non-Pharmaceutical Interventions that can be Layered to Mitigate Risk of SARS-CoV-2 Transmission during Air Travel													
	Section 6.0 Testing & Screening			Section 7.0 Face Coverings			Section 8.0 Process Management		Section 9.0 Cleaning & Disinfection				Section 10.0 Physical Engineering	
NPI Layering Intervention	*Health Symptom Self-screening*	*Temperature Screening*	*Viral Testing*	*Mask*	*Respirator*	*Face Shield*	*Limiting Cabin Service*	*Boarding and Deplaning*	*Cleaning*	*Electrostatic Spray*	*UV Disinfection*	*Anti-microbial Coatings*	*Ventilation*	*Enhanced Ventilation for Boarding/Deplaning*
Preparation of Airplane	–	–	–	++	–	–	–	–	++	++	*	*	–	–
Pre-Boarding	++	++	*	++	–	–	++	++	++	–	–	–	++	*
On Board at Cruise	–	▲	–	++	▲	▲	++	–	++	–	–	*	++	–
Deplaning	–	*	–	++	–	–	–	++	++	–	–	–	++	*

NPIs Non-pharmaceutical Interventions

– Not applicable
++ Recommended
* Desirable/optional
▲ May be appropriate under certain circumstances

Route of Transmission:

- Direct contact with infectious droplets
- Inhalation of infectious aerosols
- Indirect contact with infectious agents contaminating inanimate surfaces (fomites)

Emerging Evidence on COVID-19

Evidence Brief of Size of Gatherings and Characteristics of High Risk Transmission Events

Introduction

What evidence is available on the thresholds or allowable sizes of gatherings or events?

Are there characteristics of gathering events that would make them high risk of transmission of SARS-CoV-2?

This review will address the state of the evidence up to August 18, 2020 with respect to the size of community-based gatherings as well as the characteristics of gatherings that are associated with transmission of SARS-CoV-2. It does not include transmission at home, in congregate living settings (e.g., long-term care facilities, prisons, dormitories) or healthcare organizations, however, it does distinguish social gatherings where people generally do or do not know each other.

Key Points

- Fifty-five studies were identified, including modelling studies, risk assessments, ecological and epidemiologic studies and outbreak reports.
- The studies showed a clear relationship between increased gathering size and risk, but there was not a consistent assessment of different gathering size thresholds (Table 1).
    - An ecological study estimated a 36% reduction in Ro if the cut-off for gathering size was 10 people, compared to 21% if it was 100 people, and a 2% reduction in Ro if the cut-off for gathering size was 1000 people (Brauner et al., 2020). Another study estimated overall 10% reduction in infections associated with gathering size restrictions (Esra et al., 2020).
    - Two models explored thresholds for epidemic collapse, one identified a gathering cut off of 23 people (St-Onge , 2020) and another identified limiting contacts to seven people per 5-day period (Zhao, 2020).
- Several predictive models that employ a network structure were developed to explore the impact of different sizes, types of gatherings and whether they included people that knew each other or did not know each other (Table 1).
    - Small closed community networks (e.g., where groups of people only interact with a chosen group of other people and there is limited interaction outside of that network) were identified as having a low risk of virus introduction. The risk increased with increasing bridges to other networks (e.g., commuting to work in another place, attending a sporting event) (Scott et al., 2020; Sneppen et al., 2020).

  - Random mixing events such as public transit, restaurants/bars and sporting events were high-risk events because people from many small networks mixed and, if transmission occurred could then take the virus back to their network (Scott et al., 2020).
- There were a number of studies that evaluated the risk associated with certain activities:
  - One assessment estimated the relative risk of going to a nightclub was 200-fold higher than eating at a restaurant (Dalton et al., 2020). This was consistent with another study that found >50% attack rate in direct contacts at night clubs (Prakash et al., 2020), a qualitative risk assessment that identified nightclubs, karaoke, restaurant, gymnasiums, ski resorts and cruise ships as high risk gathering settings (Dalton et al., 2020) and a study in Hong Kong found that 30.4% of cases were linked to exposure to bars and bands (Adam et al., 2020).
  - Large gatherings are associated with the largest outbreaks. A carnival in Germany, for example, was associated with 1,700 cases (Walker et al., 2020). Sporting events were associated with approximately 50-100 cases (Leclerc et al., 2020). Small gatherings, such as interactions among household members, had the majority of documented transmission events but usually result in a small number of secondary cases (<5).
  - Other common gathering settings where transmission events were documented included family gatherings (birthday parties, meals etc.), religious gatherings, weddings, social settings, gyms, shopping facilities, shared accommodations and a variety of workplaces from office environments to factory type settings (such as food processing plants).
- Non-pharmaceutical interventions, such as individual hand hygiene practices and community mask wearing and limiting the number of individual contacts, can reduce the risk of a transmission event occurring during gatherings, particularly gatherings of random individuals (Scott et al., 2020).
- Super spreading events (SSEs) have been associated with large gatherings and the following characteristics (Table 3):
  - The index case is often asymptomatic or mildly symptomatic.
  - Several studies have estimated that 10-20% of COVID-19 cases cause ~80% of new infections (Adam et al., 2020; Pozderac et al., 2020, James et al., 2020, Laxminara et al., 2020).
  - The risk of transmission in closed environments is higher than in open-air environments (OR 18.7 (6.0-57.9) (Nishiura et al., 2020).
  - Most transmission events were attributed to the number of close and sustained contact; loud talking, shouting and singing have all been associated with high attack rates.
- These findings need to be considered in light of other individual factors that can affect transmission, such as viral load (Pfefferle et al., 2020) and that some people may have a higher Ro than others e.g., women had a higher Ro than men in Korean clusters (Kim & Jiang, 2020).

Overview of the Evidence

The risk of transmission during gatherings and the relationship of the size of that gathering to the risk of transmission has been directly and indirectly explored in a number of predictive models. Many of the models more directly exploring this question are preprints and still need to undergo the peer-review process. These models are based on scenarios and are parameterized using observational data from the outbreak. The extent to which the findings can be generalized to the local context is variable and should be used with caution.

Published ecological studies estimate the impact of gatherings on the epidemic based on studying the changes in the trajectory of the epidemic after policies to limit gathering sizes were implemented and/or lifted in a region or country. By nature, these studies are at high risk of bias and ecological fallacy.

Estimates of transmission rates and descriptions of SSEs or outbreaks are obtained from data collected during retrospective outbreak investigations, which have a high risk of bias. Thus, these studies are considered to be of low quality and there is a high probability that the conclusion will change as additional evidence becomes available.

CONTENTS

THRESHOLDS FOR GATHERING EVENTS

Eleven agent-based and other network models explore the impact of different restrictions on gatherings and how segmented groups that have minimal random contacts can be protective (Block et al., 2020; Deforche et al., 2020; Kain et al., 2020; Leng et al., 2020; Phillips et al., 2020; Scott et al., 2020; Sneppen et al., 2020; St-Onge et al., 2020; Szapudi, 2020; Weiner et al., 2020; Zhao, 2020). Some of the models explore and explain the concept of small-segmented community networks providing increased protection to an introduction of the virus and the activities that degrade the protection of a segmented network. Activities classified as random gathering events where unknown people mix, such as transportation, commuting to a workplace outside of the segmented network, social places such as bars and restaurants, or sporting events, were considered to degrade the protection afforded by having a segmented community. Other models look at super spreading activities and how the number of contacts in a gathering may lead to a higher number of transmission events. Few studies provided threshold values for gatherings or even explored the implications of different cut offs.

One ecological study reported the impact of gathering size restrictions generally to be a 10% reduction in infections (Esra et al., 2020). Another study estimated a 2% reduction of Ro if the cut-off for different gatherings was 1000 people, compared to 21% if it was 100 people and 36% if it was 10 people (Brauner et

al., 2020). Two other models explored thresholds for epidemic collapse, one suggested a gathering cut off of 23 people under one scenario (St-Onge et al., 2020) and another suggested limiting contacts to seven people per 5-day period (P. J. Zhao, 2020).

Two risk assessments evaluate the risk associated with certain activities and try to put individual risk into perspective. The first estimates the risk of transmission was approximately 1 infection per 3,836, (Range: 626 to 31,800) unprotected community-level contacts in the USA on May 31, 2020 (Bhatia & Klausner, 2020). A qualitative risk assessment from Australia describes several high-risk gathering settings and estimates a 200 fold difference in the relative risk of going to a restaurant for dinner versus a nightclub (Dalton et al., 2020). Other settings unpacked in this risk assessment include karaoke clubs, gymnasiums, ski resorts and cruise ships (Dalton et al., 2020).

Given the evidence is primarily predictive models, risk assessments and ecological studies, the extent that the estimates can be generalized beyond the populations and scenarios studied is unknown. It should also be noted that most epidemiological studies on the impact of non-pharmaceutical interventions (NPI's) are not included in this review, as they do not isolate the effect of gathering size restrictions from other NPIs that were implemented almost simultaneously.

Table 1: Thirteen predictive models and risk assessments that explore the impact of gatherings and risk of transmission.

Reference	Study Description	Relevant Outcomes
Predictive Models		
(Phillips et al., 2020) *preprint*	Agent-based model to explore outbreak potential in daycares/schools in Ontario. They explored different ratios of child-educator ratios. The simulations considered 2:8, 3:7, 2:15, 1:15 and 1:30 ratios of teacher to child.	Conclusion: A ratio of 3:7 was most protective and the 2:15 model performed far worse. - Doubling class size from 8 to 15 to 30 doubled the outbreak size. - Drivers of increased risk/impact of larger classes= • higher probability that someone is positive • more students affected when class is quarantined • outbreak size is larger due to a higher number of exposed individuals
(Weiner et al., 2020) *preprint*	Age-of-infection model developed to explore the impact of NPIs on the potential second wave in Illinois. Model starts August 1, 2020. For comparison, Arizona and Florida are also modelled. Data is borrowed from other states already experiencing their second wave e.g., Texas.	- In the two scenarios run, the strict scenario limits on gatherings, closing bars and indoor dining to bring super spreading under control (assuming 80% of cases come from 10-20% of infected people) prevents a second wave.

(Szapudi, 2020) *preprint*	SIR model with modification using a power-law model that allows for inclusion of social connection networks.	- This model shows that by stopping super-spreading events through NPIs, the pandemic is significantly slowed.
(Kain et al., 2020)	SEIR model parameterized for COVID-19 epidemic dynamics by estimating a time-varying transmission rate that incorporates the impact of NPIs that change over time, in five epidemiologically distinct settings:Los Angeles and Santa Clara Counties, California; Seattle (King County), Washington; Atlanta (Dekalb and Fulton Counties), Georgia; and Miami (Miami-Dade County), Florida.	- Effective reproduction number (Re) dropped below 1 rapidly following social distancing orders in mid-March, 2020 - Re started increasing in late May 2020 in LA, Miami, and Atlanta and in June 2020 in Santa Clara and Seattle. - The authors show decreasing the risk of super-spread events (crowded enclosed spaces) is effective.
(Deforche et al., 2020)	SEIR model: Incidence data and deaths in 35 countries (includes Canada) data until mid-May 2020. The authors explore which mobility changes during lockdown were significantly associated with the changes in disease transmission.	- Reductions in individuals using transit and going to work were highly correlated with a reduction in the incidence of COVID-19 in the multi-variable model. - Retail and recreation changes were most significant/ highly associated with Rt changes: Mean reduction of Rt of 0.50 (95% CI 0.18 – 0.81), or an average reduction of 22% (95% CI 8 – 35) in transmission. - Thus, across countries the parameter retail/recreation indicates that venues such as bars, restaurants, malls, mass gatherings provide optimal circumstance for the spread of SARS-CoV-2, as opposed to individual factors.
(Block et al., 2020)	Stochastic Model: Adopting a social network approach, the authors evaluate the effectiveness of three distancing strategies designed to keep the curve flat and aid compliance in a post-lockdown world. They demonstrate that a strategic social network-based reduction of contact strongly enhances the effectiveness of social distancing measures while keeping risks lower.	Three approaches to defining a closed contact network were evaluated to be protective, all of which can be protective if closely adhered to. - Individuals choose their contact partners based on similarity of a predetermined individual characteristic. This facilitates forming small groups e.g., neighbourhood/ small organization. - Individuals consider who their contact partners interact with and do not see people outside of a defined contact network. - Build bubbles through repeat contacts. Individuals decide who they want to interact with. This can be used with work

		units as well. It is difficult for the virus to penetrate these micro-communities.
(Leng et al., 2020) *preprint*	Individual-based model: Using the UK as a case study, a mathematical model was used to assess the effectiveness of various social bubble strategies as part of a gradual lockdown exit strategy.	- Using a base case where non-essential shops and schools are closed, the household attack rate is 20% and Ro=0.8, a number of social bubble strategies are simulated. Results demonstrate that in this base case scenario, social bubbles reduced cases and fatalities by 17% compared to an un-clustered increase of contacts. - Clustering contacts outside the household into exclusive social bubbles is an effective strategy of increasing contacts while limiting some of the associated increase in epidemic risk (e.g., 2 families interact).
(Scott et al., 2020)	Australian agent-based open source model "Covasim". This model allows for contact networks and random/clustered interactions, specifically: households; schools; workplaces; social networks; cafés and restaurants; pubs and bars; public transport; places of worship; professional sport; community sport; beaches; entertainment (cinemas, performing arts venues etc.); national parks; public parks; large events (concerts, festivals, sports games etc.); child care; and aged care.	- The model indicated that the largest risk was re-opening bars and restaurants, followed by workplaces and large events. - Social gatherings <10 were the least risky type of gathering. - The model also implies that it could take more than two months to identify an increase in cases. - The largest risk in a resurgence was allowing individuals to have large contact networks, particularly where there is mixing of individuals who do not know each other. - Random mixing of a large number of people at sporting events for example, is risky because it exposes the individual's smaller, clustered network (home/work/close contacts) to potential introduction of the virus.
(Sneppen & et al., 2020) *preprint*	This agent-based model explored the impact of super-spreading events. In the base model super-spreading events had little effect on the epidemic, however under various intervention strategies, limiting diffuse social contacts – random gathering events - in settings such as bars, transportation, restaurants, parties, concerts and lecture halls is far more effective than limiting the same	- Limiting random gathering events had a large impact on the risk of super spreading events in this model under scenarios where various intervention strategies are implemented.

	amount of contact events in the home and work setting.	
(Zhao, 2020) *preprint*	Social network model: The epidemic is dependant on network connectivity and time to spread. Thus, transmission of the virus is affected by public health interventions such as isolation, quarantine and physical distancing. This social network model explores the level of NPIs needed to contain the COVID-19 pandemic. Contact definition: a spouse, two children, a friend, a neighbor, a colleague, and a cashier during grocery shopping.	- Without social distancing, if a single individual is infected with COVID-19, the average probability that any given person will be infected is 1 in 1.03 million. - After shutting down all non-essential businesses in Italy on March 21, the average number of unique contacts per individual over each viral generation period is expected to be 6.6, leading to a predicted reproductive number of 0.97 - The epidemic in the U.S. can be controlled by limiting the average number of contacts per person to 7 unique individuals over each 5-day period.
(St-Onge et al., 2020) *preprint*	Canadian authors from Laval University provide SIS/SIR models using a network science framework to look at the impact of having structures aka gatherings (groups/ classrooms/ sports teams etc.)	- Demonstrate that localized epidemics can collapse if the group or gathering size remains below a threshold. - The threshold for the mesoscopic localization regime, with a transmission rate $\beta = 0.07$ was 23 people and below.
Risk Assessments		
(Dalton et al., 2020)	This is a qualitative risk assessment on re-opening where they examine the characteristics of retail and recreational situations for high risk of super spreading events. Assumption is that up to 80% of cases may be caused by 10-20% of infected people and some setting characteristics are higher risk than others. Case studies used nightclub and karaoke rooms, gymnasiums, ski resorts, cruise ships, churches and religious gatherings.	- High risk venues should only start to open after low risk venues have been open a sufficient time to know there is no spike in cases. - The relative risk of going to a nightclub is 200 fold higher than eating at a restaurant. - Case study setting characteristics: Nightclubs: 100s of people, close proximity, poor ventilation, social behaviours. Karaoke rooms: 10 people, enclosed room. Gymnasiums: high touch surfaces and increased risk of droplet/aerosol transmission >1.5 meters. Dance/aerobic classes are higher risk where higher respiration rate and movement may be associated with further transmission.

		Ski resorts: unclear Cruise ships: 19 cruise ships had cases prior to March 2020. The design and close contacts allow high attack rates. Screening of crew and passengers is unlikely to prevent COVID-19 cases even in low transmission areas. Churches: Activities include singing and sharing a meal. Several outbreaks have been related to these activities.
(Bhatia et al., 2020)	Risk Assessment: What is the average probability of acquiring COVID-19 infection, being hospitalized, or dying from an unprotected community-level contact in US? Estimates of individual level probability for COVID-19 infection may inform more accurate risk perceptions and facilitate re-engagement with social activity. Among the 100 most populous US Counties, for the week ending May 30, 2020, the median daily case incidence is 5.92 per 100,000, (Range, 0.65 - 35).	- The median probability of COVID-19 infection transmission is 1 infection per 3836, (Range: 626 to 31,800) unprotected (e.g., without social distancing, wearing of masks, hand hygiene, etc.) community-level contact. - For a 50 to 64 year old individual, the estimated median probability of hospitalization is 1 hospitalization per 852,000, (Range: 139,000 to 7,080,000) community level person-contacts and the median probability of a fatality is 1 fatality per 19.1 million, (Range,:3.13 million to 159,000,000 million) community-level person-contacts
Ecological Studies – impact of policies to restrict gatherings on the epidemic		
(Esra et al., 2020) *preprint*	Ecological study: Bayesian model framework to estimate transmission associated with NPIs in 26 countries and 34 US states.	- The estimated overall reduction in infection associated with different NPIs was: • 23% (95% CI: 18-27%) associated with household confinement • 10% (95% CI: 1-18%) with limits on gatherings • 12% (95% CI: 5-19%) with school closures • 17% (95% CI: 6-28%) with mask policies. - 12% (95% CI: 9-15%) overall
(Brauner et al., 2020) *preprint*	Ecological study: Bayesian hierarchical model, by linking non-pharmaceutical interventions (NPI) implementation dates to national case and death counts. Chronological data on NPIs in 41 countries between January and May 2020 was analysed.	Estimate the mean reduction in Ro across the countries for eight NPIs: - Mandating mask-wearing in (some) public spaces (2%; 95% CI: -14%–16%) – this NPI had been implemented after most other NPIs were fully implemented. - Limiting gatherings to:

	Each NPI's effect as a multiplicative (percentage) reduction in the reproduction number R. Many of these were implemented at the same time, however the authors claim their model was able to estimate individual intervention effect due to the large dataset. They present a lengthy sensitivity analysis. Results are averaged across countries, some countries may have had more success than others, this is not reflected in this analysis. (Canada and the USA are not studied)	• 1,000 people or less (2%; 20%–22%), • 100 people or less (21%; 1%–39%), • 10 people or less (36%; 16%–53%), - Closing some high-risk businesses (31%; - 13%–46%), - Closing most nonessential businesses (40%; 22%–55%), - Closing schools and universities (39%; 21%–55%), the model cannot distinguish between these and there may be additive effects such as parents staying home that increases the impact of these NPIs - Issuing stay-at-home orders (18%; 4%–31%).

SIR= susceptible – infected –recovered model, SEIR= susceptible-exposed-infected-recovered, NPI= non-pharmaceutical interventions. Ro= basic reproduction number, Rt= effective reproduction number.

CHARACTERISTICS OF COMMUNITY GATHERING TRANSMISSION EVENTS

Super spreading events (SSEs) or outbreaks include multiple people acquiring infection. Gatherings provide an opportunity for SSEs to occur. By limiting certain high-risk activities and implementing public health measures, including limiting the size of gatherings, the risk of SARS-CoV-2 transmission and the likelihood of super spreading events should be reduced.

Table 2 highlights the importance of controlling super spreaders or SSEs. Retrospective analyses estimate that a large proportion of cases (80%) are due to a small proportion of those infected (10-20%) (Adam et al., 2020; Pozderac et al., 2020; James et al., 2020b; Laxminarayan et al., 2020). One ecological study of North American professional sports reported an association with professional games played early in the epidemic and the number of cases and COVID-19 mortality in that city, which was attributed to large gatherings associated with the game (Wing, Simon, & Carlin, 2020).

Three studies quantify the impact of gathering size restrictions and individual contacts (Jarvis et al., 2020; Scire et al., 2020; Zhang et al., 2020). These studies provide an estimate of the change in behaviour and may help to parameterize or estimate incremental changes in contact patterns that are tolerable at different points in the epidemic.

Table 2: Estimates on the importance of controlling super spreading cases and events.

Reference	Study Description	Relevant Outcomes
Estimates of Impact		

(Wing et al., 2020) *preprint*	Ecological study to compare COVID-19 caseload and mortality between cities that hosted many vs. few NHL, NBA and NCAA games in the first quarter of 2020.	- Found an association with the number of games: • Each NHL or NBA game lead to an additional 783 cases and 52 deaths March - mid-May, 2020. - NCAA games were associated with 31 cases and 2.4 deaths.
(Pozderac & Skinner, 2020) *preprint*	Model to estimate the variation in infectiousness by examining the variation in early-time growth rates of new cases among different subpopulations in the USA.	- Estimates the dispersion of the epidemic and reports that 88% of the case likely were from 10% of the cases.
(A. James et al., 2020b) *preprint*	Analysis of New Zealand's epidemic. COVID-19 cases =1499 Children under 10 were under-represented. Children infected fewer people/ lower secondary attack rate. Asymptomatic cases transmitted to fewer people than clinical cases. Serial interval ~5 days	- Super spreading is a significant contributor to the epidemic dynamics, with 20% of cases among adults responsible for 65-85% of transmission.
(Laxminarayan et al., 2020) *preprint*	This study analyses the epidemiological data from two states in India. Case identification and contact tracing investigations.	- The analysis indicates that 5.4% of cases accounted for 80% of infected contacts.
(Adam et al., 2020) *preprint*	This study analyses the super spreading events in Hong Kong across 135 clusters	- The analysis inferred 20% of infections were responsible for 80% of the transmission events in Hong Kong. - One notable cluster of 106 cases traced to bars and bands accounted for 30.4% of the local transmission early in the epidemic.
Impact of Gathering Restrictions		
(Saidan et al., 2020)	This study calculates context specific Ro based on cluster investigations. This transmission model (SIR) was developed to only model clusters compared and not the entire population.	- Estimated Ro by gathering type • Weddings/ party Ro=5 • Religious gatherings Ro=2.5 • Processing plants (meat) Ro=2.0
(Scire et al., 2020)	Switzerland February 27 - April 22, 2020: Strict gathering rules of <5 people in public places was implemented and self-quarantine for 10 days for anyone with symptoms. Using surveillance data for the number of cases, Ro was calculated for different periods of the epidemic. Sensitivity analysis indicates this result is not an artifact of testing intensity.	- Prior to the gathering restrictions Ro was between 1.5-2. After gathering restrictions were put in place Ro dropped to between 0.6-0.8 in the first third of April 2020.

(Jarvis et al., 2020)	UK survey on contact patterns before and after lockdown. Survey was done the day after lockdown, so it can't really measure longer term adherence.	- 74% reduction in the number of daily contacts (10.8 contacts per day to 2.8). - This would be expected to reduce Ro from 2.6 to 0.62 (95%CI 0.37-0.53) for all types of contacts.
(J. Zhang et al., 2020)	Contact patterns in Wuhan and Shanghai were assessed before and after lockdown using a survey run February 1-10, 2020. 'Contact' was a conversation of three or more words in the presence of another person and/or direct contact.	- Age weighted mean contacts per day was 14.0-18.8 at baseline and reduced to 1.9-2.1 during the outbreak period ($p<0.001$). Overall, contacts during the outbreak mostly occurred at home with household members (94.1% in Wuhan and 78.5% in Shanghai). - The interventions (lockdown) were predicted to block transmission for a Ro before the interventions of 6-7.8.

Table 3 lists repositories of SSEs and outbreaks of COVID-19, studies that investigate the characteristics of these clusters, review literature that summarizes COVID-19 SSEs associated with gatherings and primary epidemiological investigations that implicate gatherings. This list is not exhaustive but describes a wide range of situations under which transmission events have been documented. There are limitations to the research and resources presented in this section including biases that may make some SSEs more likely to be identified and documented. For example, social events are more likely to be recalled than everyday activities and events are more easily traced. Further, some settings may be better represented because they have the infrastructure in place to monitor and identify outbreaks (e.g., prisons or long-term care facilities may have routine monitoring and testing).

Databases of SSEs compiled by researchers and journalists were identified; the most comprehensive one currently has more than 1,400 SSEs documented from the primary and grey literature (Table 3). All include descriptions of the size, setting and other attributes, such as the activity associated with the SSE.

Cluster investigations that estimate the risk of transmission from an infected person or the impact of type of gathering on the size and extent of the transmission event are important to help inform high or low risk situations (Table 3) (Kim et al., 2020; Liu et al., 2020; Pfefferle et al., 2020). These investigations report that a small number of cases may be responsible for the majority of transmission events and that risk of transmission is highly variable. The latter studies are based on retrospective contact tracing investigations, which are at a high risk of bias and may not represent the spectrum of transmission events at gatherings that have occurred. Underreporting of transmission events from gatherings, particularly random mixing events such as public transportation, is highly likely as these events would be difficult to investigate.

General observations across super spreading events (SSEs) that have occurred outside of the household include (Table 3):

- Often the index case was asymptomatic or mildly symptomatic at the time of the transmission event.

- Most SSEs occurred in indoor environments.
- Most are associated with crowded spaces and a prolonged period of time spent in that space or close and intense contact with the infected person (Leclerc, Fuller, Knight, Funk, & Knight, 2020; Swinkels, 2020).
    - Activities such as close range interactions at elderly care homes and events with significant singing, loud conversation or shouting have been associated with SSEs.
- High-risk settings are places where a large number of people congregate. These include large group accommodations, confined working environments, and mass gatherings. (Note household accounts for 50-60%, (Swinkels, 2020)).
    - Approximately 15% of SSEs are associated with entertainment/leisure; dining, sports and fitness, parties, bars and nightclubs.
    - Approximately 5% of SSEs are associated with indoor shopping malls and supermarkets (three SSEs have been associated with outdoor markets).
    - Approximately 3% of SSEs are associated with religious gatherings.
    - Approximately 2% of SSEs are associated with schools.
    - Work environment SSEs (~7%) mostly include office environments followed by food processing plants. Few clusters were associated with working outdoors.
        - Food processing plant outbreaks globally have largely occurred in refrigerated processing environments over other types of facilities. This may be due to the working environment being favourable to SARS-CoV-2 persistence (low temperature and humidity, solid metallic surfaces), work places being crowded and transportation/accommodation being shared, and the workforce being unlikely to not work despite being symptomatic (Chong, Ng, Hori, & et al., 2020; Durand-Moreau et al., 2020).
    - Approximately 7% of SSEs have occurred in shared accommodation such as worker dormitories, prisons, and long-term care facilities.
    - Transportation (~1%) has also been associated with a few clusters including buses, flights and trains.

Table 3: Studies and repositories that summarize the characteristics of gathering events associated with transmission.

Reference	Study Description	Relevant Outcomes
Repositories of COVID-19 Transmission events		
(Swinkels, 2020)	Super Spreading Events Around the World [Google Sheet]. Update version August 15, 2020	- Project includes over 1,400 SSE events. The spreadsheet is available for download and analysis. *The summary*

	- Transmission events with >5 secondary cases are included in this list. - Sources are both primary literature and grey literature. - Details include location, setting, description, indoor, # cases, index date, reference, other settings. - They tag SSEs associated with loud vocalization and those that occur in a refrigeration setting.	*proportions in the text came from this work.* • Currently 21 SSEs are listed from Canada.
(Institute for Investigative Journalism, Concordia, 2020)	Project pandemic A Canadian list of clusters reported across Canada, compiled as a joint initiative of Canadian journalists. *This site is not freely accessible, but is a data repository that is not available elsewhere.*	As of August 18: - 58 food processing plant clusters, the largest was >650 infected - 53 detention facilities have reported clusters.
(Leclerc et al., 2020)	This rapid review and database of SSE events compiled literature up to June 7 2020 and after that, the effort has not been comprehensive. Details include setting, indoor, country, details, reference, date, number of clusters, total cases and attack rates.	SSE Setting / COUNT N=265 / % Building site 4 1.5% Conference 5 1.9% Elderly care 21 7.9% Food processing plant 21 7.9% Funeral 2 0.8% Hospital 9 3.4% Hotel 3 1.1% Household 38 14.3% Shared accommodation 30 11.3% Meal 17 6.4% Party 14 5.3% Prison 6 2.3% Public 6 2.3% Religious 22 8.3% School 11 4.2% Ship 5 1.9% Shipyard 1 0.4% Shopping 8 3.0% Sport 22 8.3% Transport 1 0.4%
Characteristics of Transmission Events and their Association with Gathering		
(Kuebart & Stabler, 2020)	This paper studies SSEs in Germany and considers the socio-spatial spread of SARS-CoV-2 and the drivers associated with spread.	- This article highlights the importance of place, crowd, and activity as facilitators of transmission:

		• A regional outbreak in Western Germany centred on the Heinsberg district (February 2020). • Tourists returning to their home regions while carrying an infection. • Infection networks based on specific focus places or events.
(Kim & Jiang, 2020) *preprint*	This study investigated the properties of the network of cases occurring in Korea. (n=3,127 cases) - Longitudinal transmission network - 147 clusters were identified - 12 had 20 or more cases	- Women had a higher Ro than men. - Older adults (not in long-term care) had higher Ro than young/middle age adults. - Religious gatherings, gyms, long-term care facilities and customer call center caused the longest transmission events.
(On Kwok et al., 2020)	The analysed epidemiological data up to March 3, 2020 from Hong Kong, Japan and Singapore to evaluate the presence and likelihood of clusters or transmission events. The mean cluster sizes were 2.54 (HK), 1.92 (JP) and 3.32 (SG); while the maximum were 16 (HK), 28 (JP) and 31 (SG).	- The probability of observing secondary case clusters of size ≥4 ranged from 10.6% – 21.5% of clusters.
(Adam et al., 2020) *preprint*	This study analyses the super spreading events in Hong Kong across 135 clusters.	- The analysis inferred 20% of infections were responsible for 80% of the transmission events in Hong Kong. - One notable cluster of 106 cases traced to bars and bands accounted for 30.4% of the local transmission early in the epidemic.
(Hamner et al., 2020)	High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice - Skagit County, Washington, March 2020.	- Among 61 people that attended choir practice on March 10, 2020, the secondary attack rate was 53% among confirmed individuals and 87% among all potential cases. - Singing has been attributed as the cause of the high attack rate.
(Nishiura et al., 2020) *preprint*	This article looks at epidemiological data on 11 clusters of 110 cases total that occurred in Japan as of 26 February: 4 in Tokyo and 1 each in Aichi, Fukuoka, Hokkaido, Ishikawa, Kanagawa and Wakayama prefectures.	- All clusters were associated with indoor environments: gym, restaurant, hospital, and a festival where eating occurred in tents. - This study estimated the odds of transmitting in a closed environment vs. open-air environment was OR 18.7 (95%CI 6.0-57.9). There was no control for confounders or potential interaction with other predictors in this analysis.

(S. Zhao et al., 2020) *preprint*	The analysis of the outbreak on the Diamond Cruise ship, February 2020.	- The dispersion term (k) was estimated to be 44 (95%CI 6-88), which is significantly larger than 1 and implies a lower chance of super-spreading events. In comparison to SARS and other coronaviruses, COVID-19 has less super spreading potential and high potential to persist in a population.
Synthesis of Clusters		
(Leclerc et al., 2020)	Systematic review, search date March 31, 2020, that summarizes 201 transmission clusters.	- Characteristics of clusters: • Indoor or indoor/outdoor settings (21/22). • Large clusters, such as those linked to churches and ships fewer than 100 cases (181/201). • > than 100 cases have been recorded in hospitals, elderly care, worker dormitories, food processing plants (9 clusters), prisons, schools (8 clusters), shopping and ship settings. • Clusters of 50-100 cases: sports, bar, wedding, work, conference. • Household was the most common cluster venue and these were usually <10 people.
(Bouffanais & Lim, 2020)	Comment on super spreading hotspots for COVID-19.	- 95% of Singapore's cases have occurred in dormitories that house migrant workers (42,000 cases or 12.5% of the people living in the dormitories).
(Prakash, 2020) *preprint*	This synthesis is not conducted using standard systematic review methodology although a thorough search was conducted. They identified 20 situations that resulted in 418 infections across 32 instances from 44 individuals (8 had mild symptoms, 36 were asymptomatic).	- Situation (transmission rate): • Meals/ family events 15.7% to 66.7%. • Meetings (1 hour private meeting, 72.7% (43.6-98.0). • Open workspace with people movement (78.7% (CI. 70.3-85.3%)). • Singing (e.g., 2 hour practice 86.7% (CI.76.2- 93.2%), (Hamner et al., 2020)). • Prayer service (resulted in 1-7 secondary infections per infected individual). • Travelling in a car (closed environment) and talking had a high risk (100% (CI.20-100%)).

		• Public transportation, wearing a mask with no talking (~0%). • Hotels 53.3% (30.1-75.2%)/cruise ships 28.1% (27.3-29.0%) where space is shared for days . • Direct interaction with an infected sales agent 25.0% (10.2-49.5%). • Nightclub, attack rate among direct contacts >50%, among patrons of the nightclub 6.27% (5.15-7.61%) (Adam et al., 2020). • Restaurant overall attack rate (9.9% (CI: 5.3-17.7%) vs. those in the flow of the air conditioner 45.0% (25.8-65.8%). - Across all these super spreading events, number of infections caused depends on the number of close contacts and in most cases the index case was not detectable at the time of transmission.
(Y. Liu, Eggo, & Kucharski,)	This short communication summarizes 9 outbreaks resulting in 48 secondary infections among 137 people in late January.	- This makes for a secondary attack rate of 35% (95%: 27-44). • 3 outbreaks are meals in the home ARs (100%, 31%, 44%). • 1 restaurant meal (21%). • 4 unknown meals (100%, 87.5%, 11.7%, 21%). • 1 Chalet in France (45%).
Primary Research of Clusters		
(Walker et al., 2020)	Germany's first super spreading event.	- The Heinsberg outbreak associated with attending a carnival session on February 15, 2020. - Resulted in Germany's first large outbreak. More than 1,700 cases have been traced back to this event.
(Pfefferle et al., 2020)	This study uses viral genomics and variant calling to follow-up viral transmission during the initial outbreak in Hamburg Germany. They provide evidence of high viral dose transmission and low viral dose transmission.	- Patient 0 had contact with 132 people at his work place within the two days before developing symptoms. These transmission events are considered to be low dose transmission events. - One high risk contact co-worker and his spouse became positive for SARS-CoV-2. 1/33 high risk interactions and 0/98 low risk interactions were positive.

		- The spouse was asymptomatic, but virus was cultured from her oropharyngeal swab and both she and the index case viral load decreased quickly in the first 5 days of illness. - A familial cluster also demonstrates evidence of minority sequence variants, which is indicative of a high viral load exposure by droplets.
(Ghinai et al., 2020)	Chicago outbreaks associated with a family gathering and funeral.	- Index case had recently travelled and was mildly symptomatic at the time of transmission. Transmission events include sharing a meal and attending the funeral where there was a fair amount of contact (handshaking and hugging) - The birthday party was in a home with 9 family members (hugging, sharing food). - Church service transmission due to close conversation and sitting within one row for 90 minutes.
(A. James et al., 2020a)	Arkansas church outbreak in March 2020.	- Two pre-symptomatic people attended church gatherings and resulting attack rate was 35/92 and at least 26 additional cases in the community.
(Shen, Xu et al., 2020)	Jiaxing city outbreaks where gathering events included weddings, birthday parties and work.	- The secondary attack rate (SAR) was 0.6% (3/473). Cases that tested positive had contact with the index case; ate at the same table during the wedding, had close conversations, spent extended periods in the same room. The SAR among close contacts was 29% (2/7).
(Breton et al., 2020)	The first cluster of cases in France associated with a church week of prayer February 17-21, 2020, n=2000 Ro= 1.4 Serial interval = 4 days.	- The epidemic threshold was estimated as 4 cases per day. - The curve of incidence shows that the epidemic begun before a sanitary alert was given and that some of the attendees to the Christian week of prayer displayed symptoms before the event.
(Chaw et al., 2020; Wong, Jamaludin, Alikhan, & Chaw, 2020)	Cluster of cases in Malaysia related to Tablighi Jamaat's religious gathering. 19/75 attendees were infected at the event, they caused 52 secondary cases. - Negative binomial model was used to explore risk factors.	- The strongest attack rate (AR) was the gathering: (14.8% 95% CI: 7.1, 27.7]). - Household ARs of symptomatic cases were higher (14.4% 95% CI: 8.8, 19.9]) than asymptomatic or pre-symptomatic cases (5.4% 95% CI: 1.2, 9.6]).

		- Low ARs (< 1%) were observed for workplace and social settings.
(Chen et al., 2020)	A retrospective study of 141 COVID-19 cases in Chongquing January-February 2020. 90 were part of clusters and 51 were considered sporadic.	- 82% of clustered cases were associated with exposure at a family gathering.
(Adam et al., 2020) *preprint*	A notable cluster early in the epidemic in Hong Kong.	- 106 cases traced to bars and bands accounted for 30.4% of the local transmission in Hong Kong early in the epidemic. - This is thought to have been caused by a series of super spreading events among staff, bands, and patrons.
(Ye et al., 2020)	(in Chinese) An outbreak in Ningbo associated with a Buddhist rally in which the index case used shared transportation by bus.	- The overall attack rate was 37/1,283, 2.88% and infection rate 48/1,008, 4.76%. However, the bus attack rate 33.82% (23/68), and infection rate 38.24% (26/68) accounted for most of the transmission. - The presumed index case had started showing symptoms 1 day before participating in the event.
(Y. F. Liu et al., 2020 (in Chinese); Wu et al., 2020; Y. Zhang et al., 2020)	Cluster investigation in Tianjin up to February 22, 2020. N=115 cases in 33 clusters.	- 28 familial clusters. - 1 work place cluster (index case infected >6 people). - 3 transport clusters (2 airplanes, 1 train). - 1 department store cluster (1 infected sales associate infected 20 patrons and 3 co-workers).
(Correa-Martínez et al., 2020)	An outbreak associated with a ski resort town, Ishgl, Austria. Recognised by a local hospital, University Hospital Münster (UKM) in Germany. N-19 cases.	- 36/90 COVID cases had recently visited Ischgl (39.6%), a ski resort town. An apres-ski bar where a bar-keeper tested positive was also frequented by many of the positive cases. This bar is considered the potential source of the SSE.
(Park et al., 2020)	This report describes an outbreak of COVID-19 at a call center in Korea. Of 1,143 individuals tested for COVID, 97 (8.5%) were positive. The majority of these employees (94/97) were working on an 11th floor call center with 216 employees.	- The attack rate was 43.5% (95% CI: 36.9-50.4%). The household secondary attack rate among symptomatic cases was 16.2% (95% CI: 11.6-22%).
(Shen et al., 2020) *preprint*	The first outbreak investigation involved transportation to a worship event on buses. A second outbreak involving a 30-person workshop with shared transportation.	- Outbreak 1: Bus #2 had an attack rate of 34.3%, and no one on bus #1 was infected.

	Tracing from index case to secondary cases and relative time spent in proximity of index case are part of the investigation.	- In the second outbreak, the overall attack rate was 48.3%. - Fans and air conditioning units on recirculation mode are hypothesized to have helped circulate the virus within the room/bus. They suggest that airborne transmission must be partially responsible for the high attack rates.
(Qian et al., 2020) *preprint*	This study analyzed all outbreaks involving 3 or more cases reported to the municipal health commissions in China January 4-February 11, 2020. 318 indoor outbreaks are described across 120 cities. 80% of the outbreaks involved <5 people.	- 318 indoor outbreaks involving family (129), relatives (133), socially connected people (29) and socially disconnected people (24) are described across 120 cities. 80% of the outbreaks involved <5 people. 83 outbreaks had multiple venues so total >100% (n=318) - 79.9% occurred within a home, - 34.0% transportation, - 4.4% at restaurant, - 2.2% shopping venue and - 9.7% at other venues.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: social AND (network, gathering, cluster, outbreak), superspread* OR (super spread*). Approximately 278 citations were screened for relevance and additional outbreaks were drawn from the list of outbreak papers in previous reviews of super spreading events and workplace/indoor transmission events. This review contains research published up to August 18, 2020

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Nouveaux éléments de preuve sur la COVID-19

Note d'information sur la taille des rassemblements et les caractéristiques des événements à risque élevé de transmission

Introduction

Quelles sont les preuves disponibles quant au nombre maximal de participants à des rassemblements ou à des événements ou quant à la taille permise pour de telles activités?

Y a-t-il caractéristiques propres aux rassemblements qui feraient en sorte que ceux-ci présentent un risque élevé de transmission du SRAS-CoV-2?

Cette revue portera sur l'état des données probantes en date du 18 août 2020 en ce qui concerne la taille des rassemblements communautaires ainsi que les caractéristiques des rassemblements qui sont associés à la transmission du SRAS-CoV-2. Elle n'inclut pas la transmission à domicile, dans les lieux de vie collectifs (par exemple, les établissements de soins de longue durée, les prisons, les dortoirs) ou les centres de soins de santé, mais les rassemblements sociaux où les gens se connaissent ou non y sont distingués.

Points clés

- Cinquante-cinq études ont été recensées, dont des études de modélisation, des évaluations des risques, des études écologiques et épidémiologiques et des rapports sur les éclosions.
- Les études ont montré une relation claire entre l'augmentation de la taille du rassemblement et le risque, mais il n'y a pas eu d'évaluation cohérente des différents seuils déterminant la taille maximale d'un rassemblement (tableau 1).
    - Une étude écologique a estimé une réduction de 36 % du R0 si la taille limite des rassemblements était de 10 personnes, contre 21 % si elle était de 100 personnes, et une réduction de 2 % du R0 si la taille limite des rassemblements était de 1000 personnes (Brauner et coll., 2020). Une autre étude a estimé à 10 % la réduction globale du nombre d'infections associées aux restrictions de la taille des rassemblements (Esra et coll., 2020).
    - Deux modèles ont exploré des seuils permettant de faire chuter l'épidémie, l'un a relevé une limite de 23 personnes dans un rassemblement (St-Onge, 2020) et l'autre a relevé une limitation des contacts à sept personnes par période de 5 jours (Zhao, 2020).
- Plusieurs modèles prédictifs utilisant une structure de réseau ont été élaborés pour explorer l'impact de différentes tailles et types de rassemblements et pour savoir s'ils incluent des personnes qui se connaissent ou non (tableau 1).
    - Les petits réseaux communautaires fermés (par exemple, lorsque des groupes de personnes n'interagissent qu'avec un groupe choisi d'autres personnes et qu'il y a une interaction limitée

en dehors de ce réseau) ont été identifiés comme présentant un faible risque d'introduction de virus. Le risque augmente avec la multiplication des passerelles vers d'autres réseaux (par exemple, se rendre au travail dans un autre lieu, assister à un événement sportif) (Scott et coll., 2020; Sneppen et coll., 2020).

- Les événements qui supposent le mélange aléatoire des personnes, comme les transports publics, les restaurants/bars et les événements sportifs étaient des événements à risque élevé parce que les personnes de nombreux petits réseaux se mélangeaient et, s'il y avait transmission, les personnes atteintes pouvaient ramener le virus dans leur réseau (Scott et coll., 2020).

- Un certain nombre d'études ont évalué le risque associé à certaines activités :
  - Une évaluation a estimé que le risque relatif associé à la fréquentation d'une boîte de nuit était 200 fois plus élevé que de manger au restaurant (Dalton et coll., 2020). Cette constatation concorde avec une autre étude qui a révélé un taux d'attaque >50 % lors de contacts directs dans des boîtes de nuit (Prakash et coll., 2020); avec une évaluation qualitative des risques qui a identifié les boîtes de nuit, le karaoké, les restaurants, les gymnases, les stations de ski et les bateaux de croisière comme des lieux de rassemblement à risque élevé (Dalton et coll., 2020); et avec une étude réalisée à Hong Kong ayant révélé que 30,4 % des cas étaient liés à une exposition dans des bars et à des spectacles de groupes de musique (Adam et coll., 2020).
  - Les grands rassemblements sont associés aux plus importantes éclosions. À titre d'exemple, un carnaval en Allemagne a été associé à 1 700 cas (Walker et coll., 2020). Les événements sportifs ont été associés à environ 50 à 100 cas (Leclerc et coll., 2020). Les petits rassemblements, tels que les interactions entre les membres d'un ménage, font partie de la majorité des cas de transmission documentés, mais n'ont généralement donné lieu qu'à un petit nombre de cas secondaires (<5).
  - Parmi les autres lieux de rassemblement courants où les événements de transmission ont été documentés figurent les réunions familiales (fêtes d'anniversaire, repas, etc.), les rassemblements religieux, les mariages, les milieux sociaux, les gymnases, les centres commerciaux, les logements partagés et divers lieux de travail, allant des bureaux aux usines (comme les usines de transformation des aliments).
- Les interventions non pharmaceutiques, telles que les pratiques individuelles d'hygiène des mains et le port du masque dans la communauté et la limitation du nombre de contacts individuels, peuvent réduire le risque qu'un événement de transmission se produise lors de rassemblements, en particulier lors de rassemblements aléatoires (Scott et coll., 2020).
- Les événements de superpropagation (ESP) ont été associés à de grands rassemblements et présentent les caractéristiques suivantes (tableau 3) :
  - Le cas index est souvent asymptomatique ou ne présente que de légers symptômes.
  - Plusieurs études ont estimé que 10 à 20 % des cas de COVID-19 provoquent environ 80 % des nouvelles infections (Adam et coll., 2020; Pozderac et coll., 2020, James et coll., 2020, Laxminara et coll., 2020).

  - Le risque de transmission dans les environnements fermés est plus élevé que dans les environnements en plein air (CR 18,7 [6,0 à 57,9] [Nishiura et coll., 2020].
  - La plupart des cas de transmission ont été attribués au nombre de contacts étroits et soutenus; les conversations, les cris et les chants forts ont tous été associés à des taux d'attaque élevés.

- Ces résultats doivent être considérés à la lumière d'autres facteurs individuels qui peuvent affecter la transmission, tels que la charge virale (Pfefferle et coll., 2020) et le fait que certaines personnes peuvent avoir un R0 plus élevé que d'autres; par exemple, les femmes ont un R) plus élevé que les hommes dans les groupes coréens (Kim & Jiang, 2020).

Vue d'ensemble des éléments de preuve

Le risque de transmission lors des rassemblements et la relation entre la taille de ces rassemblements et le risque de transmission ont été directement et indirectement explorés dans un certain nombre de modèles prédictifs. Bon nombre des modèles qui explorent plus directement cette question sont des prépublications et doivent encore être soumis au processus d'examen par les pairs. Ces modèles sont fondés sur des scénarios et sont paramétrés à partir des données d'observation sur les éclosions. La mesure dans laquelle les résultats peuvent être généralisés au contexte local est variable et doit être utilisée avec prudence.

Les études écologiques publiées estiment l'impact des rassemblements sur l'épidémie en se fondant sur l'étude des changements de trajectoire de l'épidémie après la mise en place et/ou la levée des politiques de limitation de la taille des rassemblements dans une région ou un pays. Par nature, ces études présentent un risque élevé de partialité et de sophisme écologique.

Les estimations des taux de transmission et les descriptions des ESP ou des éclosions sont obtenues à partir des données recueillies lors d'enquêtes rétrospectives sur les éclosions, qui présentent un risque de biais élevé. Ainsi, ces études sont considérées comme étant de faible qualité et il est fort probable que la conclusion changera à mesure que des preuves supplémentaires seront disponibles.

TABLE DES MATIÈRES

SEUILS À OBSERVER POUR LES RASSEMBLEMENTS

Onze modèles basés sur les agents et autres modèles de réseau explorent l'impact de différentes restrictions sur les rassemblements et la manière dont des groupes segmentés qui ont un minimum de contacts aléatoires peuvent assurer une certaine protection (Block et coll., 2020; Deforche et coll., 2020; Kain et coll., 2020; Leng et coll., 2020; Phillips et coll., 2020; Scott et coll., 2020; Sneppen et coll., 2020; St-Onge et coll., 2020; Szapudi, 2020; Weiner et coll., 2020; Zhao, 2020). Certains des modèles explorent et expliquent le concept de petits réseaux communautaires segmentés offrant une protection accrue contre l'introduction du virus et les activités qui dégradent la protection d'un réseau segmenté. Les activités classées comme des rassemblements aléatoires où se mêlent des inconnus, comme le transport, les déplacements vers un lieu de travail en dehors du réseau segmenté, les lieux sociaux tels que les bars et les restaurants, ou les événements sportifs, ont été considérées comme dégradant la protection offerte par le fait d'avoir une communauté segmentée. D'autres modèles examinent les activités de superpropagation et la façon dont le nombre de contacts dans un rassemblement peut entraîner un nombre plus élevé de cas de transmission. Peu d'études ont fourni des valeurs seuils pour les rassemblements ou même exploré les répercussions des différents seuils.

Selon une étude écologique, l'impact des restrictions sur la taille des rassemblements se traduit généralement par une réduction de 10 % du nombre infections (Esra et coll., 2020). Une autre étude a estimé une réduction de 2 % du R0 si le seuil pour les différents rassemblements était de 1000 personnes, par rapport à 21 % pour un seuil de 100 personnes et 36 % pour un seuil de 10 personnes (Brauner et coll., 2020). Deux modèles ont exploré des seuils permettant de faire chuter l'épidémie, l'un suggérant une limite de 23 personnes dans un scénario (St-Onge et coll., 2020) et l'autre suggérant une limitation des contacts à sept personnes par période de 5 jours (P. J. Zhao, 2020).

Deux évaluations des risques mesurent le risque associé à certaines activités et tentent de mettre en perspective le risque individuel. Les premières estimations du risque de transmission étaient d'environ 1 infection pour 3,836 (plage : 626 à 31 800) contacts non protégés au niveau communautaire aux États-Unis le 3 mai 2020 (Bhatia et Klausner, 2020). Une évaluation qualitative des risques réalisée en Australie décrit plusieurs lieux de rassemblement à risque élevé et estime à 200 fois la différence entre le risque relatif d'aller dîner au restaurant et celui d'aller en boîte de nuit (Dalton et coll., 2020). Parmi les autres lieux non pris en compte dans cette évaluation des risques figurent les clubs de karaoké, les gymnases, les stations de ski et les bateaux de croisière (Dalton et coll., 2020).

Étant donné que les preuves sont principalement des modèles prédictifs, des évaluations de risques et des études écologiques, on ne sait pas dans quelle mesure les estimations peuvent être généralisées au-delà des populations et des scénarios étudiés. Il convient également de noter que la plupart des études épidémiologiques sur l'impact des interventions non pharmaceutiques (INP) ne sont pas incluses dans cette revue, car elles n'isolent pas l'effet des restrictions de taille des rassemblements des autres INP qui ont été mises en œuvre presque simultanément.

Tableau 1 : Treize modèles prédictifs et évaluations des risques qui explorent l'impact des rassemblements et le risque de transmission.

Référence	Description de l'étude	Résultats pertinents
Modèles prédictifs		
(Phillips et coll., 2020) *prépublication*	Modèle basé sur les agents pour explorer le potentiel d'éclosion dans les garderies/écoles en Ontario. Ils ont étudié les différents ratios enfants-éducateurs. Les simulations ont pris en compte les ratios enseignant-enfant suivants : 2:8, 3:7, 2:15, 1:15 et 1:30.	Conclusion : Un rapport de 3:7 était le plus protecteur et le modèle 2:15 était bien moins performant. - Le fait de doubler la taille des classes de 8 élèves à 15, puis à 30 élèves a doublé la taille de l'éclosion. - Facteurs de risque accru/impact des grandes classes = • probabilité plus élevée que quelqu'un reçoive un diagnostic positif • plus d'élèves touchés lorsque la classe est mise en quarantaine • la taille de l'éclosion est plus importante en raison du nombre plus élevé de personnes exposées
(Weiner et coll., 2020) *prépublication*	Modèle fondé sur l'âge au moment de l'infection développé pour explorer l'impact des INP sur la deuxième vague potentielle en Illinois. Le modèle commence le 1er août 2020. À des fins de comparaison, l'Arizona et la Floride sont également modélisés. Les données sont empruntées à d'autres États qui connaissent déjà leur deuxième vague, par exemple le Texas.	- Dans les deux scénarios envisagés, les limites strictes imposées à l'égard des rassemblements, de la fermeture des bars et des repas en salle pour maîtriser la superpropagation (en supposant que 80 % des cas proviennent de 10 à 20 % des personnes infectées) permettent d'éviter une deuxième vague.
(Szapudi, 2020) *prépublication*	Modèle SIR avec modification utilisant un modèle de loi exponentielle qui permet l'inclusion des réseaux de connexion sociale.	- Ce modèle montre qu'en stoppant la superpropagation de cas au moyen des INP, la pandémie est considérablement ralentie.
(Kain et coll., 2020)	Modèle SEIR paramétré pour la dynamique de l'épidémie de COVID-19 en estimant un taux de transmission variable dans le temps qui intègre l'impact des INP qui changent avec le temps, dans cinq contextes épidémiologiques distincts : Los Angeles et les comtés de Santa Clara, Californie; Seattle (comté de King), Washington; Atlanta (comtés de Dekalb et Fulton), Géorgie; et Miami (comté de Miami-Dade), Floride.	- Le nombre de reproduction effectif (Re) est rapidement tombé en dessous de 1, à la suite des ordonnances de distanciation sociale à la mi-mars 2020 - Le Re a commencé à augmenter fin mai 2020 à Los Angeles, Miami et Atlanta et en juin 2020 à Santa Clara et Seattle. - Les auteurs montrent qu'il est efficace de réduire le risque de superpropagation des cas (espaces clos bondés).

(Deforche et coll., 2020)	Modèle SEIR : Données sur l'incidence et nombre de décès dans 35 pays (dont le Canada) jusqu'à la mi-mai 2020. Les auteurs étudient quels changements de mobilité pendant le confinement ont été associés de manière significative aux changements dans la transmission de la maladie.	- La réduction du nombre de personnes utilisant les transports en commun et se rendant au travail était fortement corrélée à une réduction de l'incidence de la COVID-19 dans le modèle à variables multiples. - Les changements dans le commerce de détail et les loisirs ont été les plus significatifs/fortement associés aux changements de Rt : Réduction moyenne de Rt de 0,50 (IC 95 % 0,18 à 0,81), soit une réduction moyenne de 22 % (IC 95 % 8 à 35) de la transmission. - Ainsi, d'un pays à l'autre, le paramètre commerce de détail/loisirs indique que les lieux tels que les bars, les restaurants, les centres commerciaux et les rassemblements de masse constituent des circonstances optimales pour la propagation du SRAS-CoV-2, par opposition aux facteurs individuels.
(Block et coll., 2020)	Modèle stochastique : En adoptant une approche de réseau social, les auteurs évaluent l'efficacité de trois stratégies de distanciation conçues pour maintenir la courbe plate et aider à la conformité dans un monde post-confinement. Ils démontrent qu'une réduction stratégique des contacts basée sur les réseaux sociaux renforce fortement l'efficacité des mesures de distanciation sociale tout en maintenant les risques à un niveau plus bas.	Trois approches de la définition d'un réseau de contacts fermé ont été évaluées comme étant protectrices, et toutes peuvent l'être si elles sont respectées à la lettre. - Les individus choisissent leurs interlocuteurs en fonction de la similarité d'une caractéristique individuelle prédéterminée. Cela facilite la formation de petits groupes, par exemple de quartiers ou de petites organisations. - Les individus considèrent avec qui leurs interlocuteurs interagissent et ne voient pas les gens en dehors d'un réseau de contacts défini. - Construire des bulles par des contacts répétés. Les individus décident avec qui ils veulent interagir. Cela peut également être utilisé avec les unités de travail. Il est difficile pour le virus de pénétrer dans ces microcommunautés.
(Leng et coll., 2020)	Modèle basé sur l'individu : En prenant le Royaume-Uni comme cas d'étude, un modèle mathématique a été utilisé pour évaluer l'efficacité de diverses stratégies de bulles	- En utilisant un cas de base où les magasins non essentiels et les écoles sont fermés, le taux d'attaque des ménages est de 20 %, et R0 = 0,8, un

prépublication	sociales dans le cadre d'une stratégie de sortie progressive.	certain nombre de stratégies de bulles sociales sont simulées. Les résultats montrent que dans ce scénario de base, les bulles sociales ont réduit les cas et les décès de 17 % par rapport à une augmentation non concentrée des contacts. - Le regroupement des contacts en dehors du foyer dans des bulles sociales exclusives est une stratégie efficace pour augmenter les contacts tout en limitant une partie de l'augmentation du risque d'épidémie qui y est associée (p. ex. interaction entre deux familles).
(Scott et coll., 2020)	Modèle open source australien « Covasim » basé sur les agents. Ce modèle permet des réseaux de contacts et des interactions aléatoires/classées, en particulier : les ménages, les écoles, les lieux de travail, les réseaux sociaux, les cafés et restaurants, les pubs et bars, les transports publics, les lieux de culte, le sport professionnel, le sport de proximité, les plages, les divertissements (cinémas, salles de spectacle, etc.), les parcs nationaux, les parcs publics, les grands événements (concerts, festivals, jeux sportifs, etc.), la garde d'enfants et les soins aux personnes âgées.	- Le modèle indiquait que le plus grand risque était la réouverture des bars et des restaurants, suivie des lieux de travail et des grands événements. - Les rassemblements sociaux de moins de 10 personnes étaient le type de rassemblement le moins risqué. - Le modèle suppose également qu'il pourrait falloir plus de deux mois pour détecter une augmentation des cas. - Le plus grand risque de résurgence était de permettre aux individus d'avoir de grands réseaux de contacts, en particulier lorsqu'il y a mélange d'individus qui ne se connaissent pas. - Le mélange aléatoire d'un grand nombre de personnes, lors d'événements sportifs par exemple, est risqué, car il expose le réseau plus petit et plus dense de l'individu (domicile/travail/contacts étroits) à l'introduction potentielle du virus.
(Sneppen & et coll., 2020) *prépublication*	Ce modèle basé sur les agents a exploré l'impact des événements de superpropagation. Dans le modèle de base, les événements de superpropagation ont eu peu d'effet sur l'épidémie, mais selon diverses stratégies d'intervention, le fait de limiter les contacts sociaux diffus – les événements de rassemblement aléatoire dans des lieux tels que les bars, les transports, les restaurants, les	- La limitation des événements à rassemblement aléatoire a eu un impact important sur le risque de superpropagation de cas dans ce modèle, dans le cadre de scénarios où diverses stratégies d'intervention sont mises en œuvre.

	fêtes, les concerts et les salles de conférence – est bien plus efficace que de limiter le même nombre d'événements de contact au domicile et au travail.	
(Zhao, 2020) *prépublication*	Modèle de réseau social : L'épidémie dépend de la connectivité du réseau et du temps de propagation. Ainsi, la transmission du virus est affectée par les interventions de santé publique telles que l'isolement, la quarantaine et la distanciation physique. Ce modèle de réseau social explore le niveau d'INP nécessaire pour contenir la pandémie de COVID-19. Définition du contact : un conjoint, deux enfants, un ami, un voisin, un collègue et un caissier pendant les courses.	- Sans distanciation sociale, si un seul individu est infecté par la COVID-19, la probabilité moyenne qu'une personne donnée soit infectée est de 1 sur 1,03 million. - Après la fermeture de toutes les entreprises non essentielles en Italie le 21 mars, le nombre moyen de contacts uniques par individu au cours de chaque période de génération virale devrait être de 6,6, ce qui donne un taux de reproduction prévu de 0,97. - L'épidémie aux États-Unis peut être contrôlée en limitant le nombre moyen de contacts par personne à 7 individus uniques sur chaque période de 5 jours.
(St-Onge et coll., 2020) *prépublication*	Des auteurs canadiens (de l'Université Laval) fournissent des modèles SIS/SIR utilisant un cadre scientifique de réseau pour examiner l'impact de structures telles que les rassemblements (groupes/classes/équipes sportives, etc.).	- Ils démontrent que les épidémies localisées peuvent s'effondrer si la taille du groupe ou du rassemblement reste en dessous d'un seuil. - Le seuil du régime de localisation mésoscopique, avec un taux de transmission $\beta = 0,07$ était de 23 personnes et moins.
Évaluations des risques		
(Dalton et coll., 2020)	Il s'agit d'une évaluation qualitative des risques liés à la réouverture, dans laquelle on examine les caractéristiques des situations de vente au détail et de loisirs pour déterminer si le risque de superpropagation est élevé. On suppose que jusqu'à 80 % des cas peuvent être causés par 10 à 20 % des personnes infectées et que certaines caractéristiques du milieu présentent un risque plus élevé que d'autres. Les études de cas portaient sur des salles de discothèque et de karaoké, des gymnases, des stations de ski, des bateaux de croisière, des églises et des rassemblements religieux.	- Les lieux à risque élevé ne devraient commencer à ouvrir qu'après que les lieux à faible risque aient été ouverts suffisamment longtemps pour savoir qu'il n'y a pas de pic dans les cas. - Le risque relatif associé à la fréquentation d'une boîte de nuit est 200 fois plus élevé que de manger au restaurant. - Caractéristiques de la mise en place des études de cas : Boîtes de nuit : Des centaines de personnes, la proximité, une mauvaise ventilation, des comportements sociaux. Salles de karaoké : 10 personnes, salle fermée.

		Gymnases : surfaces fréquemment touchées et risque accru de transmission de gouttelettes/aérosols >1,5 mètre. Les cours de danse/aérobie présentent un risque plus élevé lorsqu'une fréquence respiratoire et des mouvements plus importants peuvent être associés à une transmission plus poussée. Stations de ski : pas clair Bateaux de croisière : 19 navires de croisière ont eu des cas avant mars 2020. La conception et les contacts étroits contribuent à des taux d'attaque élevés. Il est peu probable que le dépistage chez les membres de l'équipage et les passagers permette d'éviter les cas de COVID-19, même dans les zones de faible transmission. Églises : Les activités comprennent des chants et le partage d'un repas. Plusieurs épidémies ont été liées à ces activités.
(Bhatia et coll., 2020)	Évaluation des risques : Quelle est la probabilité moyenne de contracter la COVID-19, d'être hospitalisé ou de mourir à la suite d'un contact non protégé au niveau communautaire aux États-Unis? Les estimations de la probabilité d'infection par la COVID-19 au niveau individuel peuvent nous éclairer sur des perceptions plus précises du risque et faciliter le réengagement dans l'activité sociale. Parmi les 100 comtés américains les plus peuplés, pour la semaine se terminant le 30 mai 2020, l'incidence quotidienne médiane des cas est de 5,92 pour 100 000 (plage de 0,65 à 35).	- La probabilité médiane de transmission de l'infection par la COVID-19 est de 1 infection pour 3836 (plage : 626 à 31 800) contacts communautaires sans protection (par exemple, sans distanciation sociale, sans port de masque, sans hygiène des mains, etc.) - Pour un individu âgé de 50 à 64 ans, la probabilité médiane d'hospitalisation est estimée à 1 hospitalisation pour 852 000 (plage : 139 000 à 7 080 000) contacts personnels au niveau communautaire et la probabilité médiane de décès est de 1 décès pour 19,1 millions (plage : 3,13 millions à 159 000 000 millions) de contacts personnels au niveau communautaire.
Études écologiques – impact des politiques de restriction des rassemblements sur l'épidémie		
(Esra et coll., 2020) *prépublication*	Étude écologique : Cadre de modèle bayésien pour estimer la transmission associée aux INP dans 26 pays et 34 États américains.	- La réduction globale estimée de l'infection associée aux différentes INP était : • 23 % (95 % IC : 18 à 27 %) associés au confinement à la maison

		• 10 % (95 % IC : 1 à 18 %) avec des limites sur le nombre de personnes dans les rassemblements • 12 % (95 % IC : 5 à 19 %) avec des fermetures d'écoles • 17 % (95 % IC : 6 à 28 %) avec des politiques sur le port du masque. - 12 % (95 % IC : 9 à 15 %) au total
(Brauner et coll., 2020) *prépublication*	Étude écologique : Modèle hiérarchique bayésien, par une liaison des dates de mise en œuvre des interventions non pharmaceutiques (INP) avec le nombre de cas et de décès au niveau national. Les données chronologiques sur les INP dans 41 pays entre janvier et mai 2020 ont été analysées. L'effet de chaque INP a une réduction multiplicative (en pourcentage) du nombre de reproduction R. Bon nombre de ces mesures ont été mises en œuvre en même temps, mais les auteurs affirment que leur modèle a permis d'estimer l'effet de l'intervention individuelle en raison de la grande quantité de données. Ils présentent une longue analyse de sensibilité. La moyenne des résultats est calculée sur l'ensemble des pays, certains pays ayant peut-être eu plus de succès que d'autres, ce qui n'est pas reflété dans cette analyse. (le Canada et les États-Unis ne sont pas étudiés)	Estimation de la réduction moyenne du R0 dans l'ensemble des pays pour huit INP : - Obligation de porter un masque dans (certains) espaces publics (2 %; 95 % IC : -14 % à 16 %) – cette INP avait été mise en œuvre après que la plupart des autres INP ont été pleinement mises en œuvre. - Limiter les rassemblements à : • 1 000 personnes ou moins (2 %; 20 % à 22 %), • 100 personnes ou moins (21 %; 1 % à 39 %), • 10 personnes ou moins (36 %; 16 % à 53 %), - Fermeture de certaines entreprises à risque élevé (31 %; - 13 % à 46 %), - Fermeture de la plupart des entreprises non essentielles (40 %; 22 % à 55 %), - Fermeture d'écoles et d'universités (39 %; 21 % à 55 %). Le modèle ne peut pas faire la distinction entre ces dernières et il peut y avoir des effets additifs tels que le fait que les parents restent à la maison, ce qui augmente l'impact de ces INP. - Émettre des ordonnances de maintien à domicile (18 %; 4 % à 31 %).

SIR = modèle « susceptible – infecté – récupéré », SEIR = « susceptible - exposé - infecté - récupéré », INP = interventions non pharmaceutiques. R0= nombre de reproduction de base, Rt= nombre de reproduction effectif.

CARACTÉRISTIQUES DES CAS DE TRANSMISSION DANS LES RASSEMBLEMENTS COMMUNAUTAIRES

Les événements de superpropagation (ESP) ou les éclosions comprennent plusieurs personnes qui contractent une infection. Les rassemblements présentent un risque d'ESP. En limitant certaines activités à risque élevé et en mettant en œuvre des mesures de santé publique, notamment en limitant la taille des rassemblements, le risque de transmission du SRAS-CoV-2 et la probabilité de superpropagation devraient être réduits.

Le tableau 2 souligne l'importance de contrôler les supertransmetteurs ou les ESP. Des analyses rétrospectives estiment qu'une grande partie des cas (80 %) sont dus à une petite proportion des personnes infectées (10 à 20 %) (Adam et coll., 2020; Pozderac et coll., 2020; James et coll., 2020b; Laxminarayan et coll., 2020). Une étude écologique du sport professionnel nord-américain a fait état d'une association entre les matchs professionnels pratiqués au début de l'épidémie et le nombre de cas et de décès par la COVID-19 dans cette ville, qui a été attribuée aux grands rassemblements associés à ce sport (Wing, Simon et Carlin, 2020).

Trois études quantifient l'impact des restrictions de taille des rassemblements et des contacts individuels (Jarvis et coll., 2020; Scire et coll., 2020; Zhang et coll., 2020). Ces études fournissent une estimation du changement de comportement et peuvent aider à paramétrer ou à estimer les changements progressifs des schémas de contact qui sont tolérables à différents moments de l'épidémie.

Tableau 2 : Estimations sur l'importance de contrôler les cas et les événements de superpropagation.

Référence	Description de l'étude	Résultats pertinents
Estimations de l'impact		
(Wing et coll., 2020) *prépublication*	Étude écologique visant à comparer le nombre de cas de COVID-19 et la mortalité entre les villes qui ont accueilli de nombreux matchs de la LNH, de la NBA et de la NCAA au cours du premier trimestre de 2020.	- Une association avec le nombre de parties a été observée : • Chaque match de la LNH ou de la NBA a entraîné 783 cas supplémentaires et 52 décès entre mars et la mi-mai 2020. - Les parties de la NCAA ont été associées à 31 cas et 2,4 décès.
(Pozderac et Skinner, 2020) *prépublication*	Modèle permettant d'estimer la variation de l'infectiosité en examinant la variation des taux de croissance précoce des nouveaux cas parmi différentes sous-populations aux États-Unis.	- Estime la dispersion de l'épidémie et signale que 88 % des cas sont probablement issus de 10 % des cas.
(A. James et coll., 2020b) *prépublication*	Analyse de l'épidémie en Nouvelle-Zélande. Cas de COVID-19 = 1 499 Les enfants de moins de 10 ans étaient sous-représentés. Les enfants infectent moins de personnes/taux d'attaque secondaire inférieur.	- La surpropagation contribue de manière significative à la dynamique de l'épidémie, avec 20 % des cas chez les adultes responsables de 65 à 85 % de la transmission.

	Les cas asymptomatiques sont transmis à moins de personnes que les cas cliniques. Intervalle de série ~5 jours	
(Laxminarayan et coll., 2020) *préublication*	Cette étude analyse les données épidémiologiques de deux États de l'Inde. Enquêtes d'identification des cas et de recherche des contacts.	- L'analyse indique que 5,4 % des cas sont responsable de 80 % des contacts infectés.
(Adam et coll., 2020) *préimpression*	Cette étude analyse les événements de superpropagation à Hong Kong dans 135 groupes.	- L'analyse a permis de déduire que 20 % des infections étaient responsables de 80 % des cas de transmission à Hong Kong. - Un groupe notable de 106 cas, attribués aux bars et aux spectacles de groupes de musique, représentait 30,4 % de la transmission locale au début de l'épidémie.
Impact des restrictions relatives aux rassemblements		
(Saidan et coll., 2020)	Cette étude calcule le R0 propre au contexte en se fondant sur des enquêtes faites sur des groupes. Ce modèle de transmission (SIR) a été développé pour ne modéliser que les groupes comparés et non la population entière.	- Estimation du R0 par type de rassemblement • Mariages/fêtes R0=5 • Rassemblements religieux R0=2,5 • Usines de transformation (viande) R0=2,0
(Scire et coll., 2020)	Suisse, du 27 février au 22 avril 2020 : Des règles strictes limitant les rassemblements à moins de 5 personnes dans les lieux publics ont été mises en place, et une quarantaine volontaire de 10 jours a été instaurée pour toute personne présentant des symptômes. À partir des données de surveillance pour le nombre de cas, le R0 a été calculé pour différentes périodes de l'épidémie. L'analyse de sensibilité indique que ce résultat n'est pas un artefact de l'intensité du test.	- Avant les restrictions relatives aux rassemblements, le R0 était compris entre 1,5 et 2. Après la mise en place des restrictions relatives aux rassemblements, le R0 est tombé entre 0,6 et 0,8 dans le premier tiers d'avril 2020.
(Jarvis et coll., 2020)	Enquête britannique sur les habitudes de contact avant et après le confinement. L'enquête a été réalisée le lendemain du confinement; elle ne peut donc pas vraiment mesurer l'adhésion à long terme.	- Réduction de 74 % du nombre de contacts quotidiens (de 10,8 contacts par jour à 2,8). - Cela devrait permettre de réduire le R0 de 2,6 à 0,62 (95 %, IC : 0,37 à 0,53) pour tous les types de contacts.
(J. Zhang et coll., 2020)	Les contacts à Wuhan et à Shanghai ont été évalués avant et après le confinement à l'aide d'une enquête menée du 1er au	- La moyenne pondérée selon l'âge des contacts quotidiens était de 14,0 à 18,8 au départ et a été réduite à 1,9 à 2,1

	10 février 2020. Le terme « contact » désigne une conversation de trois mots ou plus en présence d'une autre personne et/ou un contact direct.	pendant la période d'éclosion (p<0,001). Dans l'ensemble, les contacts qui ont eu lieu pendant l'éclosion se sont surtout produits à la maison avec des membres du ménage (94,1 % à Wuhan et 78,5 % à Shanghai). - Il était prévu que les interventions (confinement) bloquent la transmission pour un R0 avant les interventions de 6 à 7,8.

Le tableau 3 énumère les répertoires d'ESP et de foyer d'éclosion de COVID-19, les études qui examinent les caractéristiques de ces groupes, la littérature qui résume les ESP de COVID-19 associés aux rassemblements et les enquêtes épidémiologiques primaires qui impliquent des rassemblements. Cette liste n'est pas exhaustive, mais décrit un large éventail de situations dans lesquelles des événements de transmission ont été documentés. Les recherches et les ressources présentées dans cette section comportent des limites, notamment des biais qui peuvent rendre certaines ESP plus susceptibles d'être identifiées et documentées. Par exemple, les événements sociaux sont plus susceptibles d'être gardés en mémoire que les activités quotidiennes; les événements sont donc plus faciles à retracer. En outre, certains milieux peuvent être mieux représentés parce qu'ils disposent de l'infrastructure nécessaire pour surveiller et identifier les éclosions (par exemple, les prisons ou les établissements de soins de longue durée peuvent appliquer une routine de surveillance et de tests).

Des bases de données d'ESP compilées par des chercheurs et des journalistes ont été identifiées; la plus complète compte actuellement plus de 1 400 ESP documentés à partir de la littérature primaire et grise (tableau 3). Toutes comprennent des descriptions de la taille, du contexte et d'autres attributs, tels que l'activité associée à l'ESP.

Les enquêtes sur les groupes, qui permettent d'estimer le risque de transmission par une personne infectée ou l'impact du type de rassemblement sur la taille et l'étendue de l'événement de transmission, sont importantes pour aider à étayer les situations à risque élevé ou faible (tableau 3) (Kim et coll., 2020; Liu et coll., 2020; Pfefferle et coll., 2020). Ces enquêtes montrent qu'un petit nombre de cas peut être responsable de la majorité des événements de transmission et que le risque de transmission est très variable. Ces dernières études sont fondées sur des enquêtes rétrospectives de recherche de contacts, qui présentent un risque élevé de biais et peuvent ne pas représenter le spectre des événements de transmission lors de rassemblements qui ont eu lieu. La sous-déclaration des événements de transmission lors de rassemblements, en particulier les situations où les gens sont rassemblés aléatoirement comme dans les transports publics, est très probable, car ces événements seraient difficiles à étudier.

Les observations générales concernant les événements de superpropagation (ESP) qui se sont produits en dehors du ménage sont les suivantes (tableau 3) :

- Souvent, le cas index était asymptomatique ou ne présentait que de légers symptômes au moment de l'événement de transmission.
- La plupart des ESP se sont produits dans des environnements intérieurs.
- La plupart sont associés à des espaces bondés et à une période prolongée passée dans cet espace ou à un contact étroit et intense avec la personne infectée (Leclerc, Fuller, Knight, Funk et Knight, 2020; Swinkels, 2020).
    - Des activités telles que les interactions à distance rapprochée dans les maisons de soins pour personnes âgées et les événements comportant des chants, des conversations ou des cris importants ont été associées aux ESP.
- Les milieux à risque élevé sont des lieux où un grand nombre de personnes se rassemblent. Il s'agit notamment de l'hébergement de grands groupes, d'environnements de travail confinés et de rassemblements de masse. [Notez que les ménages représentent de 50 à 60 % (Swinkels, 2020)].
    - Environ 15 % des ESP sont associés aux divertissements/loisirs : restaurants, sports et conditionnement physique, fêtes, bars et boîtes de nuit.
    - Environ 5 % des ESP sont associés à des centres commerciaux intérieurs et à des supermarchés (trois ESP ont été associés à des marchés extérieurs).
    - Environ 3 % des ESP sont associés à des rassemblements religieux.
    - Environ 2 % des ESP sont associés aux écoles.
    - Les ESP dans un environnement de travail (~7 %) comprennent principalement les environnements de bureau, suivis des usines de transformation des aliments. Peu de groupes étaient associés au travail à l'extérieur.
        - Les éclosions dans les usines de transformation d'aliments se sont surtout produites dans des environnements de transformation réfrigérés plutôt que dans d'autres types d'installations. Cela peut être dû au fait que l'environnement de travail est favorable à la persistance du SRAS-CoV-2 (basse température et humidité, surfaces métalliques solides), que les lieux de travail sont achalandés, que le transport et les logements sont partagés, et que la main-d'œuvre est peu susceptible de ne pas travailler malgré les symptômes (Chong, Ng, Hori, & et coll., 2020; Durand-Moreau et coll., 2020).
    - Environ 7 % des ESP ont eu lieu dans des logements partagés tels que des dortoirs de travailleurs, des prisons et des établissements de soins de longue durée.
    - Le transport (~1 %) a également été associé à quelques groupes, notamment les bus, les vols et les trains.

Tableau 3 : Études et répertoires qui résument les caractéristiques des rassemblements associés à la transmission.

Référence	Description de l'étude	Résultats pertinents
Répertoire d'événements de transmission de la COVID-19		
(Swinkels, 2020)	Les événements de surpropagation dans le monde entier [Feuille de calcul Google]. Version mise à jour le 15 août 2020 - Les événements de transmission comptant plus de 5 cas secondaires sont inclus dans cette liste. - Les sources englobent à la fois la littérature primaire et la littérature grise. - Les détails comprennent l'emplacement, le contexte, la description, l'intérieur, le nombre de cas, la date d'index, la référence, et d'autres paramètres. - Les ESP associées à une forte vocalisation et ceux qui se produisent dans un environnement réfrigéré sont marqués.	- Le projet comprend plus de 1 400 ESP. La feuille de calcul est disponible aux fins de téléchargement et d'analyse. *Les proportions sommaires dans le texte sont issues de ce travail.* • Actuellement, 21 ESP sont répertoriés à partir du Canada.
(Institute for Investigative Journalism, Concordia, 2020)	Projet pandémie Une liste canadienne de groupes de déclarés dans tout le Canada, compilée dans le cadre d'une initiative conjointe de journalistes canadiens. *Ce site n'est pas accessible librement, mais il s'agit d'un répertoire de données qui n'est pas disponible ailleurs.*	En date du 18 août : - 58 groupes d'usines de transformation des aliments, le plus grand comptait plus de 650 cas d'infection - 53 centres de détention ont signalé des groupes
(Leclerc et coll., 2020)	Cet examen rapide et cette base de données sur les ESP ont compilé la littérature jusqu'au 7 juin 2020; par la suite, les efforts déployés n'ont pas été exhaustifs. Les détails comprennent le contexte, l'intérieur, le pays, les détails, la référence, la date, le nombre de groupes, le nombre total de cas et les taux d'attaque.	Contexte de l'ESP / COMPTE N=265 / % Chantier de construction 4 1,5 % Conférence 5 1,9 % Soins aux personnes âgées 21 7,9 % Usine de transformation des aliments 21 7,9 % Funérailles 2 0,8 % Hôpital 9 3,4 % Hôtel 3 1,1 % Ménage 38 14,3 %

		Logement partagé	30	11,3 %
		Repas	17	6,4 %
		Parti	14	5,3 %
		Prison	6	2,3 %
		Public	6	2,3 %
		Religieux	22	8,3 %
		Organisme ou établissement	11	4,2 %
		Bateau	5	1,9 %
		Chantier naval	1	0,4 %
		Achats	8	3,0 %
		Sport	22	8,3 %
		Moyen de transport	1	0,4 %
Caractéristiques des événements de transmission et leur association avec les rassemblements				
(Kuebart et Stabler, 2020)	Cet article étudie les ESP en Allemagne et examine la propagation sociospatiale du SRAS-CoV-2 et les facteurs associés à cette propagation.	- Cet article souligne l'importance du lieu, de la foule et de l'activité en tant que facilitateurs de la transmission : • Une éclosion régionale en Allemagne de l'Ouest centrée dans le district de Heinsberg (février 2020). • Les touristes qui retournent dans leur région d'origine alors qu'ils sont porteurs d'une infection. • Réseaux d'infection basés sur des lieux ou des événements spécifiques.		
(Kim et Jiang, 2020) *prépublication*	Cette étude a examiné les propriétés du réseau de cas survenant en Corée. (n=3 127 cas) - Réseau de transmission longitudinale - 147 groupes ont été identifiés - 12 comptaient 20 cas ou plus	- Les femmes avaient un R0 plus élevé que les hommes. - Les adultes plus âgés (ne bénéficiant pas de soins de longue durée) avaient un R0 plus élevé que les jeunes adultes et les adultes d'âge moyen. - Les rassemblements religieux, les gymnases, les établissements de soins de longue durée et les centres d'appel pour le service à la clientèle sont à l'origine des plus longs événements de transmission.		
(On Kwok et coll., 2020)	Analyse des données épidémiologiques jusqu'au 3 mars 2020 de Hong Kong, du Japon et de Singapour pour évaluer la	- La probabilité d'observer des groupes de cas secondaires de taille ≥ 4 varie de 10,6 % à 21,5 % des groupes.		

	présence et la probabilité de groupes ou d'événements de transmission. La taille moyenne des groupes était de 2,54 (HK), 1,92 (JP) et 3,32 (SG); tandis que les tailles maximales étaient de 16 (HK), 28 (JP) et 31 (SG).	
(Adam et coll., 2020) *prépublication*	Cette étude analyse les événements de superpropagation à Hong Kong dans 135 groupes.	- L'analyse a permis de déduire que 20 % des infections étaient responsables de 80 % des cas de transmission à Hong Kong. - Un groupe notable de 106 cas, attribués aux bars et aux spectacles de groupes de musique, représentait 30,4 % de la transmission locale au début de l'épidémie.
(Hamner et coll., 2020)	Taux élevé d'attaques par le SRAS-CoV-2 suite à une exposition lors d'une répétition de chorale – Skagit County, Washington, mars 2020	- Parmi les 61 personnes qui ont assisté à la répétition de la chorale le 10 mars 2020, le taux d'attaque secondaire était de 53 % chez les cas confirmés et de 87 % chez tous les cas potentiels. - Le chant a été attribué à la cause du taux d'attaque élevé.
(Nishiura et coll., 2020) *prépublication*	Cet article examine les données épidémiologiques sur 11 groupes de 110 cas au total qui se sont produits au Japon en date du 26 février : 4 à Tokyo et 1 dans chacune des préfectures de Aichi, Fukuoka, Hokkaido, Ishikawa, Kanagawa et Wakayama.	- Tous les groupes étaient associés à des environnements intérieurs : gymnase, restaurant, hôpital et un festival où l'on mangeait sous des tentes. - Cette étude a estimé que la probabilité de transmission dans un environnement fermé par rapport à un environnement en plein air était de CR 18,7 (95 % IC 6,0 à 57,9). Cette analyse n'a pas permis de contrôler les facteurs de confusion ou l'interaction potentielle avec d'autres prédicteurs.
(S. Zhao et coll., 2020) *prépublication*	L'analyse de l'éclosion sur le navire Diamond Cruise, février 2020.	- Le terme de dispersion (k) a été estimé à 44 (95 % IC 6 à 88), ce qui est nettement supérieur à 1 et suppose une probabilité moindre d'événements de superpropagation. En comparaison avec le SRAS et d'autres coronavirus, la COVID-19 a un potentiel de superpropagation moins élevé et un fort potentiel de persistance dans une population.

Synthèse des groupes		
(Leclerc et coll., 2020)	Revue systématique, date de recherche 31 mars 2020, qui résume 201 groupes de transmission.	- Caractéristiques des groupes : • Milieux intérieurs ou milieux intérieurs/extérieurs (21/22). • Grands groupes, comme ceux liés aux églises et aux navires, moins de 100 cas (181/201). • Plus de 100 cas ont été enregistrés dans des hôpitaux, des centres de soins pour personnes âgées, des dortoirs de travailleurs, des usines de transformation des aliments (9 groupes), des prisons, des écoles (8 groupes), des magasins et des navires. • Groupes de 50 à 100 cas : sport, bar, mariage, travail, conférence. • C'est dans les ménages que l'on a observé le plus de groupes, lesquels comptaient généralement moins de 10 personnes.
(Bouffanais et Lim, 2020)	Commentaire sur les points chauds de transmission de la COVID-19.	- 95 % des cas de Singapour se sont produits dans des dortoirs qui hébergent des travailleurs migrants (42 000 cas, soit 12,5 % des personnes vivant dans ces dortoirs).
(Prakash, 2020) *prépublication*	Cette synthèse n'a pas été réalisée selon la méthodologie standard d'examen systématique, bien qu'une recherche approfondie ait été effectuée. Ils ont identifié 20 situations qui ont donné lieu à 418 infections dans 32 cas chez 44 personnes (8 présentaient des symptômes légers, 36 étaient asymptomatiques).	- Situation (taux de transmission) : • Repas/événements familiaux, de 15,7 % à 66,7 %. • Réunions (1 heure de réunion privée, 72,7 % [43,6 à 98,0]. • Espace de travail ouvert avec mouvement des personnes [78,7 % (IC 70,3 à 85,3 %)]. • Chant [par exemple, pratique de 2 heures 86,7 % (IC 76.2 à 93,2 %)], (Hamner et coll., 2020)]. • Service de prière (a entraîné de 1 à 7 infections secondaires par personne infectée). • Voyager en voiture (environnement fermé) et parler présentait un risque élevé [100 % (IC 20 à 100 %)]. • Transports publics, port d'un masque sans parler (~0 %).

		• Hôtels 53,3 % (30,1 à 75,2 %)/bateaux de croisière 28,1 % (27,3 à 29,0 %) où l'espace est partagé pendant plusieurs jours. • Interaction directe avec un agent de vente infecté 25,0 % (10,2 à 49,5 %). • Boîte de nuit, taux d'attaque parmi les contacts directs >50 %, parmi les clients de la discothèque 6,27 % (5,15 à 7,61 %) (Adam et coll., 2020). • Taux d'attaque global dans les restaurants [9,9 % (IC : 5.3 à 17,7 %)] par rapport à celui associé à la circulation de l'air climatisé 45,0 % (25,8 à 65,8 %). - Parmi tous ces événements de superpropagation, le nombre d'infections causées dépend du nombre de contacts étroits et dans la plupart des cas, le cas index n'était pas détectable au moment de la transmission.
(Y. Liu, Eggo et Kucharski)	Cette courte communication résume 9 foyers d'éclosion ayant entraîné 48 infections secondaires chez 137 personnes à la fin du mois de janvier.	- Cela donne un taux d'attaque secondaire de 35 % (95 % : 27 à 44). • 3 foyers d'éclosion sont liés à des repas à domicile (AR : 100 %, 31 %, 44 %). • 1 repas au restaurant (21 %). • 4 repas inconnus (100 %, 87,5 %, 11,7 %, 21 %). • 1 Chalet en France (45 %).
Recherche primaire sur les groupes		
(Walker et coll., 2020)	Le premier événement de superpropagation en Allemagne.	- L'éclosion de Heinsberg associée à la participation à une activité pendant le carnaval, le 15 février 2020. - Elle a donné lieu à la première éclosion à grande échelle en Allemagne. Plus de 1 700 cas ont été retracés jusqu'à cet événement.
(Pfefferle et coll., 2020)	Cette étude a utilisé la génomique virale et l'appel de variantes pour suivre la transmission virale lors de l'éclosion initiale à Hambourg, en Allemagne. Ils fournissent des preuves de la transmission de doses virales élevées et de faibles doses virales.	- Le patient 0 a été en contact avec 132 personnes sur son lieu de travail dans les deux jours précédant l'apparition des symptômes. Ces événements de transmission sont considérés comme des événements de transmission à faible dose.

		- Un collègue de travail exposé à un risque élevé et son épouse ont reçu un diagnostic positif pour le SRAS-CoV-2. 1/33 des interactions à risque élevé et 0/98 des interactions à faible risque ont donné lieu à des cas positifs. - L'épouse était asymptomatique, mais le virus a été cultivé à partir de son prélèvement oropharyngé et sa charge virale ainsi que celle du cas index ont rapidement diminué au cours des 5 premiers jours de la maladie. - Un groupe familial présente également des preuves de variantes de séquences minoritaires, ce qui indique une exposition à une charge virale élevée par les gouttelettes.
(Ghinai et coll., 2020)	Les éclosions survenues à Chicago sont associées à une réunion de famille et à des funérailles.	- Le cas index avait récemment voyagé et était légèrement symptomatique au moment de la transmission. Les événements de transmission comprennent le partage d'un repas et la participation à l'enterrement où il y a eu plusieurs contacts (poignée de main et étreinte) - La fête d'anniversaire a eu lieu dans une maison avec 9 membres de la famille (se serrant dans les bras, partageant la nourriture). - La transmission survenue lors du service religieux découle d'une conversation entre des personnes très près l'une de l'autre, assises dans une même rangée pendant 90 minutes.
(A. James et coll., 2020a)	Éclosion dans une église de l'Arkansas en mars 2020.	- Deux personnes pré-symptomatiques ont assisté à des rassemblements à l'église et le taux d'attaque qui en a résulté était de 35/92 et au moins 26 cas supplémentaires ont été observés dans la communauté.
(Shen, Xu et coll., 2020)	La ville de Jiaxing a connu des éclosions où les rassemblements comprenaient des mariages, des fêtes d'anniversaire et des activités professionnelles.	- Le taux d'attaque secondaire (SAR) était de 0,6 % (3/473). Les cas de tests positifs ont eu un contact avec le cas index; ils ont mangé à la même table pendant le mariage, ont eu des conversations

		étroites, ont passé de longues périodes dans la même pièce. Le taux de SAR parmi les contacts proches était de 29 % (2/7).
(Breton et coll., 2020)	Premier groupe de cas en France associé à une semaine de prière à l'église du 17 au 21 février 2020, n=2 000 R0= 1,4 Intervalle de série = 4 jours.	- Le seuil épidémique a été estimé à 4 cas par jour. - La courbe d'incidence montre que l'épidémie a commencé avant qu'une alerte sanitaire ne soit donnée et que certains des participants à la semaine de prière chrétienne présentaient des symptômes avant l'événement.
(Chaw et coll., 2020; Wong, Jamaludin, Alikhan et Chaw, 2020)	Groupe de cas en Malaisie liés au rassemblement religieux de Tablighi Jamaat. 19/75 participants ont été infectés lors de l'événement, ils ont causé 52 cas secondaires. - Un modèle binomial négatif a été utilisé pour explorer les facteurs de risque.	- Le plus fort taux d'attaque (AR) a été le rassemblement : [14,8 % IC 95 % : 7,1, 27,7)]. - Les AR des ménages de cas symptomatiques étaient plus élevés (14,4 % IC 95 % : 8.8, 19.9) que les cas asymptomatiques ou présymptomatiques (5,4 % IC 95 % : 1,2, 9,6). - De faibles AR (< 1 %) ont été observés sur le lieu de travail et dans les milieux sociaux.
(Chen et coll., 2020)	Une étude rétrospective de 141 cas de COVID-19 à Chongquing en janvier-février 2020. 90 faisaient partie de groupes et 51 étaient considérés comme sporadiques.	- 82 % des cas de groupes étaient associés à une exposition lors d'une réunion familiale.
(Adam et coll., 2020) *prépublication*	Un groupe notable au début de l'épidémie à Hong Kong.	- Au début de l'épidémie, 106 cas retracés à des bars et des spectacles de groupes de musique représentaient 30,4 % de la transmission locale à Hong Kong. - On pense que cela a été causé par une série d'événements de superpropagation parmi le personnel, les groupes de musique et les clients.
(Ye et coll., 2020)	(en chinois) Une éclosion à Ningbo, associée à un rassemblement bouddhiste, dans lequel le cas index a utilisé le transport en commun (autobus).	- Le taux d'attaque global était de 37/1,283, soit 2,88 % et le taux d'infection de 48/1,008, soit 4,76 %. Cependant, le taux d'attaque dans les autobus de 33,82 % (23/68) et le taux d'infection de 38,24 % (26/68) représentaient la majeure partie de la transmission.

		- Le cas index présumé avait commencé à présenter des symptômes un jour avant de participer à l'événement.
(Y. F. Liu et coll., 2020 [en chinois]; Wu et coll., 2020; Y. Zhang et coll., 2020)	Enquête sur les groupes à Tianjin jusqu'au 22 février 2020. N=115 cas dans 33 groupes.	- 28 groupes familiaux. - 1 groupe dans un lieu de travail (le cas index a infecté >6 personnes). - 3 groupes liés au transport (2 avions, 1 train). - 1 groupe dans un grand magasin (1 vendeur infecté, 20 clients et 3 collègues).
(Correa-Martínez et coll., 2020)	Une épidémie associée à une ville où se trouve une station de ski, Ishgl, en Autriche. Reconnu par un hôpital local, l'hôpital universitaire de Münster (UKM) en Allemagne. N-19 cas.	- 36/90 cas de COVID s'étaient récemment rendus à Ischgl (39,6 %), une ville où se trouve une station de ski. Un bar d'après-ski où un barman a été déclaré positif a également été fréquenté par de nombreux cas positifs. Ce bar est considéré comme la source potentielle de l'ESP.
(Park et coll., 2020)	Ce rapport décrit une épidémie de COVID-19 dans un centre d'appel en Corée. Sur 1 143 personnes testées pour la COVID, 97 (8,5 %) ont reçu un résultat positif. La majorité de ces employés (94/97) travaillaient dans un centre d'appel du 11e étage comptant 216 employés.	- Le taux d'attaque était de 43,5 % (95 % IC : 36,9 à 50,4 %). Le taux d'attaque secondaire des ménages parmi les cas symptomatiques était de 16,2 % (IC à 95 %) : 11,6 à 22 %).
(Shen et coll., 2020) *prépublication*	La première enquête sur l'éclosion a porté sur le transport en autobus de personnes se rendant à un événement religieux. Une deuxième éclosion impliquant un atelier de 30 personnes utilisant un transport commun. L'enquête comprend la recherche de cas index et des cas secondaires, et la vérification du temps relatif passé à proximité du cas index.	- Éclosion 1 : L'autobus 2 a eu un taux d'attaque de 34,3 %, et personne dans l'autobus 1 n'a été infecté. - Lors de la deuxième éclosion, le taux d'attaque global a été de 48,3 %. - On suppose que les ventilateurs et les climatiseurs en mode recirculation ont contribué à la circulation du virus dans la pièce/autobus. Ils suggèrent que la transmission aérienne est probablement partiellement responsable des taux d'attaque élevés.
(Qian et coll., 2020) *prépublication*	Cette étude a analysé tous les foyers d'éclosion impliquant 3 cas ou plus signalés aux commissions municipales de santé en Chine du 4 janvier au 11 février 2020. 318 foyers d'éclosion intérieurs dans 120 villes sont décrits. 80 % des foyers	- 318 foyers d'éclosion intérieurs dans 120 villes impliquant la famille (129), les proches (133), les personnes socialement connectées (29) et les personnes socialement déconnectées (24) sont décrits. 80 % des foyers d'éclosion ont touché moins de 5 personnes. 83 foyers

	d'éclosion ont touché moins de 5 personnes.	d'éclosion touchaient plusieurs sites, soit un total de plus de 100 % (n=318) • 79,9 % ont eu lieu à l'intérieur d'une maison, • 34,0 % dans le transport, • 4,4 % au restaurant, • 2,2 % dans des commerces de détail • 9,7 % dans d'autres lieux.

Méthodologies

Une recension quotidienne de la littérature (publiée et prépubliée) est effectuée par le Groupe des sciences émergentes de l'ASPC. Cette recension a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver de la littérature pertinente sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont mises en correspondance avec les publications figurant sur la liste de littérature de l'OMS au sujet de la COVID, et les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de la recension sont conservés dans une base de données Refworks et une liste Excel qui peut être consultée. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour y relever des citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés sont les suivants : « social » ET (« network », « gathering », « cluster », « outbreak »), « superspread »* OU (« super spread »*). Environ 278 citations ont été examinées pour en déterminer la pertinence et d'autres foyers d'éclosion ont été tirés de la liste des documents relatifs aux foyers d'éclosion dans les précédents examens des événements de superpropagation et des événements de transmission sur le lieu de travail/à l'intérieur. Cette revue contient des recherches publiées avant le 18 août 2020.

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Emerging Evidence on COVID-19

Evidence Brief of SARS-CoV-2 Risks in Arenas

Introduction

What evidence exists for the risk of SARS-CoV-2 transmission in arenas, on and off the ice surface?

COVID-19 outbreaks related to arenas and ice sports have highlighted the need to understand how transmission is occurring and what environmental and behavioural factors may be altered to lower the risk of transmission. Professional and recreational hockey, along with other indoor ice surface sports such as curling, ringette, skating and sledge hockey exposures were considered relevant for this evidence brief. Evidence on transmission risks in ice arenas and literature specific to COVID-19 for sport or recreational participants, coaches, spectators, and arena staff was collected. Activities in different sub-environments (e.g., use of the lobby, dressing rooms and hallways before and after on-ice activities, the spectator areas and the on-ice activities) were considered when reviewing the evidence. Reviews on the effect of temperature and humidity on transmission of SARS-CoV-2 were also included in this brief as indirect evidence of SARS-CoV-2 survival under cold conditions. The use of combustion engine ice resurfacing equipment has lead to indoor ice facility air quality concerns in the past, but no connection of this research to COVID-19 risks has been documented, so it not considered. This brief summarizes review and primary literature available up to February 12, 2021.

Key Points

- This review included 13 publications: two outbreak investigations related to ice hockey (1, 2), and two related to curling bonspiels (3, 4). Two cross-sectional studies included observational data from August to October 2020 looking at risk factors for COVID-19 associated with other recreational sports in the USA (5, 6). Three reviews summarize the literature on SARS-Cov-2 under cold or low humidity environments such as those found in the arena.

Arena/Ice Sports:

- Hockey provides favourable conditions for SARS-CoV-2 transmission due to:
  - Heavy breathing on ice and on the bench due to high intensity physical activity;
  - Close proximity of players, coaches;
  - Indoor gathering;
  - Dry, cold air of the arena; and
  - Segregated air mass due to ~10 foot barriers around the ice leading to poor air circulation. (1, 2, 7).

- An investigation of a June 2020 outbreak among recreational men's hockey teams theorized that one presymptomatic individual lead to 14 symptomatic adults (12 confirmed, 2 not tested), 13 players across both teams and 1 arena employee (2). No PHMs were reported to have been in place.

- An outbreak within the Finnish U-20 hockey league was investigated and speculated to have likely been caused by one asymptomatic player, resulting in transmission to two opposing teams and tertiary transmission to senior league teams for a total of 49 confirmed COVID-19 infections (1). After the outbreak, the league implemented measures to minimize the risk COVID-19 transmission, including associating with only one team.

- Two bonspiel outbreak investigations noted social gatherings with few precautions for a prolonged period of time (3, 4). Thus, transmission risk cannot be attributed to the sport or the venue.

- When resuming both recreational and professional hockey and other indoor ice activities, strategies for reducing transmission risk include: limiting the number of individuals in the arena, lessening time in the arena, screening of individuals and increasing sanitation, cohorting players, minimizing exposure time and sharing of equipment, using masks and maintaining physical distancing (5-9).

Other Sports:

- Evidence from two cross-sectional studies describes lower risk of COVID-19 among outdoor sports compared to indoor sports, non-contact sports compared to contact sports and that for some indoor sports, wearing a mask had a significant protective association (5, 6).

Indirect Evidence:

- Evidence of the survival and transmission potential of SARS-CoV-2 in cold and low humidity level environments has not been studied well in the literature. However recent reviews that looked at experimental evidence consistently indicate lower temperatures and humidity are favorable for SARS-CoV-2 survival. Similarly, studies of weather and environment consistently indicate higher SARS-CoV-2 transmission in areas with low temperatures (0-17°C) and a significant interaction between temperature and humidity, but not humidity on its own (10-16).

Overview of the Evidence

Thirteen articles were included in this brief, six primary literature articles that provide descriptions of outbreaks related to sports, four guidance documents for resumption of hockey (two for professional hockey leagues, one for Canadian hockey and one for youth sports) and three reviews that cover transmission of SARS-CoV-2 or survival in cold temperatures. Four outbreaks, two non-professional hockey and two curling bonspiels and two cross-sectional analyses of non-arena based sports at high school and youth soccer were included. No evidence was found related to other indoor ice activities, such as skating, sledge hockey or ringette.

Outbreak investigations are retrospective collections of evidence and findings are at risk of several biases; and all identified uncertainty about where transmission occurred. Some cross-sectional studies were included, which provide a point in time dataset of a population, however they can only establish associations and not causation between an exposure and an outcome. A range of review types were included, and systematic reviews were rated by the AMSTAR-2 tool. Narrative literature reviews were considered low quality due to a high risk of bias. The limitations of the evidence include a very small number of articles in the literature related to arenas, despite many jurisdictions reporting cases or outbreaks traced to hockey teams or curling (e.g., CBC news January 16, 2021). The nature of sports makes it difficult to establish with certainty where transmission occurred, as teammates often spend time together for practice, training, game travel, meals and recreational activities. Tournaments can add more mixing opportunities and exposures between teams, as well. Lastly, all of the outbreaks currently in the literature occurred early in the pandemic, when mask use and other public health measures were not widely used.

CONTENTS

INDOOR ICE SPORT OUTBREAKS

Table 1: Transmission Linked to Indoor Ice Sports and Other Sports (n=6)

STUDY	OUTBREAK DESCRIPTION	KEY OUTCOMES
Hockey (n=2)		
Atrubin (2020) (2) Outbreak investigation United States Jun 2020	2 Teams (A & B) played a recreational hockey game June 16, 2020 (day 0) in Tampa Bay, Florida. Each team had 11 male members, aged 19-53 years. By June 21 (day 5), 15 individuals were symptomatic with suspected COVID-19. • Index patient – Team A player, who was symptomatic 1 day after the game; and tested positive on day 3. • Secondary cases – 14 symptomatic adults (12 confirmed, 2 not tested); 13 of the game players and 1 employee at the arena. • Asymptomatic contacts of the game were not tested.	Subsequent cases: • 8 of 10 teammates of the index case became symptomatic; • 5 of 11 players of opposing team became symptomatic; • 1 arena employee symptomatic; and • Asymptomatic contacts not tested: players (8 of 21), 2 referees and 1 spectator. • PHMs were not reported including wearing masks. • Game play was 60 minutes. • Locker rooms used, one for each team, 20 minutes before and after game.

		• Transmission opportunity existed only at the arena, no other contact the week prior. Authors note that hockey provides favourable conditions for SARS-CoV-2 transmission: • Heavy breathing on ice and on the bench due to high intensity physical activity; • Close proximity of players; • Indoor gathering; and • Segregated air mass due to ~10 foot barriers around the ice.
Kuituen (2021) (1) Outbreak investigation Finland Sep 2020	This descriptive report covers transmission of SARS-CoV-2 in a Finnish U-20 hockey league. Team A played team B Sept 4, 2020 (day 0) and team C Sept 5, 2020 (day 1). Some players on all 3 teams also train with senior teams. An asymptomatic player was the index case, and 49 secondary and tertiary cases were detected in 5 teams and 6 teams were quarantined (U-20 A, B and C and Senior A, B and C). • Index case – assumed to be a Team A player who was asymptomatic but infective on day 0. (Given there was a high number of asymptomatic positive test results on day 3 post the first game, the index case was not identified.) • Secondary cases (U-20 league): TEAM A - 3 players symptomatic on day 2 and tested positive. Team A all tested day 3 (28 players + staff) with 22 positive players. Team A spent 10h on a bus together travelling to and from their games.	An asymptomatic hockey player is hypothesized to have been the source of the outbreak that resulted in 49 confirmed COVID-19 infections during a 16-day follow-up. Precautions employed in league: - No guidance on face coverings (masks were not worn by players); - Teams did not shake hands in games; and - Spectators were limited so social distancing could be maintained. Transmission within a team may have occurred through travel on the team bus, the locker room or other common team gathering, transmission to team B and C players was determined to have most likely occurred during game play. Multiple close contacts and heavy breathing from high intensity activity during the game are identified as risks for on-ice transmission. As well, the dry, cold air of the arena is suggested to increase the risk of aerosolization of expelled SARS-CoV-2 droplets.

	TEAM B - 3 players tested positive on day 5; 11 more cases subsequently detected. TEAM C – 6 players test positive day 6 (exposure to team A on day 1); 10 more cases subsequently detected. • Tertiary cases (senior league): TEAM A – no detected cases. TEAM B – 2 players tested positive. TEAM C – 1 player tested positive.	This outbreak resulted in a change in the Finnish leagues, disallowing U-20 players to train or play with more than 1 team. Bubbles and continuous testing used in professional level sports are not feasible for amateur and youth hockey. A limitation of this investigation is that it is based on publically available data and authors did not interview the players or have access to their health records. This means that the index case was not identified, but assumed to be an asymptomatic player and the likely sequence of transmission is unknown (i.e., how many people were likely infected during the game vs. by their infected teammates at a later date).
Curling (n=2)		
Burak (2021) (3) Outbreak investigation Alberta, Canada Mar 2020	A curling bonspiel in Edmonton Mar 11-14, 2020 was attended by 73 individuals. This descriptive study is based on interviews of the attendees between Apr 17 and May 5. In addition to the self-reported symptoms and test results, samples were collected for serology testing from 62 of 73 participants. 58 of the 73 participants in the bonspiel were physicians, all were healthcare workers. 40 curlers tested positive for SARS-CoV-2, and 30 of these individuals had a positive serology result within 222 days after the bonspiel. 16 others who reported symptoms tested negative or were not tested (14 of these are reported as probable cases) and 7 of the probable cases had positive serology results. Asymptomatic attendees were not tested. Serology testing was negative for 12 and positive in 1 of the 17 asymptomatic curlers. 35 suspected cases of secondary	The curling event and related social activities led to a 74% attack rate for COVID-19 in participants. No index case was identified, but 10 individuals reported minor nonspecific symptoms at the time of the bonspiel. The study does not determine the activities that resulted in transmission, but does hypothesize shared meals as the source due to surveys of participants' activities.

	transmission were reported by participants due to symptoms or positive tests of household contacts after the event.	
Luethy (2020) (4) Preprint Outbreak investigation United States Mar 2020	The 2020 USA Curling Club Nationals was held Mar 7-14, 2020 in Laurel, Maryland. 88 athletes/coaches from across the US travelled to participate in the tournament, with a total attendance of 187 individuals. Traditional banquets were replaced with single use, disposable container packaged meals and increased cleaning was implemented during the tournament to mitigate SARS-CoV-2 transmission. Despite efforts, this descriptive study documents 55.6% of participants reported COVID-19 symptoms after their attendance at the tournament. Participants, volunteers and spectators were informed on Mar 18 that a person in attendance had tested positive for COVID-19. A second announcement on Mar 27 reported multiple participants had tested positive for COVID-19. A survey of players, coaches, officials, volunteers and spectators (n=187) was undertaken Sept 1-13, 2020 with an 85% (159/187) response rate and results presented in this descriptive study.	55.6% (104/187) of attendees reported symptoms consistent with COVID-19. A large difference was found between coaches/players and volunteers, of whom 77.3% (68/88) and 33.0% (29/88), respectively, reported symptoms. Testing for SARS-CoV-2 was reported by 44 individuals; 19.8% (37/187) of attendees reported positive tests for SARS-CoV-2, and 3.7% (7/187) reported negative. Serology testing of 73 individuals is reported, with 66 testing positive. Due to the large amount of mixing and length of the tournament, as well as the lack of testing available at the time of the tournament, the time and place of the transmissions cannot be determined. Similarly, no index case(s) are identified.
Non-arena based sports (n=2)		
Watson (2021) (5) Preprint Cross-sectional study United States Aug-Oct 2020	A nationwide survey of USA high school athletes that participated in fall sports included 991 schools, 152484 athletes on 5844 teams. Analyses are adjusted by state COVID-19 incidence, and school instruction type.	2565 athletes reported COVID-19 of which 69 were directly attributed to sport contact. The total rate was 24.6 per 100 000 player-days. COVID-19 incidence was lower: • Outdoor versus indoor sports (incidence rate ratio [IRR]=0.54, 95% CI=0.49-0.60, p<0.001). • Non-contact versus contact sports (IRR=0.78 [0.70-0.87], p<0.001).

		• No difference between team versus individual sports (IRR=0.96 [0.84-1.1], p=0.49). Face mask use (reported by 28% of schools) was associated with a decreased incidence in some sports: • Girls' volleyball (IRR=0.53 [0.37-0.73], p<0.001). • Boys' basketball (IRR=0.53 [0.33-0.83], p=0.008). • Girls' basketball (IRR=0.36 [0.19-0.63], p<0.001). • Football (IRR=0.79 [0.59-1.04], p=0.10). • Cheer/dance (IRR=0.75 [0.53-1.03], p=0.081). • No association was found for other sports.
Watson (2020) (6) Preprint Cross-sectional study United States Aug 2020	A survey of soccer clubs in the USA and the incidence of COVID-19 within the club in the preceding 10 weeks. 129 clubs responded to the survey, 124 had reinitiated soccer and included 91007 players for a median duration of 73 days. 119 clubs had progressed to group activities.	Among these 218 COVID-19 cases were reported among 85861 players. Youth soccer players had a lower case rate and incidence rate than the national rate for children in the US (254 v. 477 cases per 100,000; IRR = 0.511, 95% CI = [0.40-0.57], p<0.001). After adjusting for local COVID-19 incidence, there was no relationship between club COVID-19 incidence and phase of return (non-contact).

GUIDANCE FOR HOCKEY DURING COVID-19

Table 2: Guidance for hockey and youth sports (n=4)

STUDY	METHOD	KEY OUTCOMES
Scientific Literature		
DiFiori (2020) (7) Protocol United States Sep 2020	This protocol was written by physicians associated with professional sports associations in North America (NBA, MLB, NHL, MLS, NFL) and discusses resumption of professional sports during the COVID-19 epidemic.	The paper does not address hockey or arena specific issues, but the following recommendations for all professional sports are of note:

	The focus is 'phased-in-play' so resumption of spectators is not considered within the paper.	• Plan to switch the protocol rapidly if the level of disease transmission in the community changes; • Provide hand sanitizer and masks; • Consider heightened hygiene practices and preventative measure such as mask wearing for all involved in the sport at all times; • Ensure thorough and regular disinfection of the sport facility; • Increase ventilation and airflow in the sport facility; • Reduce the number of people in the facility significantly; • Conduct pre-event screening; and • Limit shared materials.
Parker (2020) (17) Guidance Document United States Oct 2020	This paper details the considerations of reopening large stadiums and arenas, specifically in the US, in the COVID-19 era.	No specific attention is given to arenas and the unique challenges the cold indoor air may present. The main focus of the paper is public health initiatives and guidance for mass gatherings and the risk points involved in the facility use.
National & Regional Guidance		
Hockey Canada (2020) (8) Online Resource Centre Canada Jun 2020	As the Canadian governing body for the sport of hockey in Canada, Hockey Canada provides a central resource for return to hockey information and updates within the country. Information regarding safety, seasonal structure, coaching, officiating, regulations and up-to-date provincial and territorial guidelines. Safety guidelines from Hockey Canada provide an overview of how to organize or participate in hockey during the COVID-19 pandemic. The common theme is checklists of what information to gather from local health authorities and facilities; and dissemination of that information to participants, families, etc.	In addition to guidance to follow local public health protocols, Hockey Canada lists common hygiene and COVID-19 prevention recommendations, such as: • Hand washing; • Hand sanitizer use; • Containing droplets when coughing or sneezing; • Physical distancing; • Individual water bottles; and • Avoid group transportation (i.e. bus) to games. Upon a positive test for COVID-19, Hockey Canada advises: • Immediate removal of household members from hockey setting; • Further action based on advice of local public health; and

	Links are provided for hockey associations within provinces and territories to provide local updates and information:
	• British Columbia & Yukon
	  • B.C. Hockey
	• Alberta
	  • Hockey Alberta
	• Saskatchewan
	  • Saskatchewan Hockey Association
	• Manitoba
	  • Hockey Manitoba
	• Ontario
	  • Hockey Northwestern Ontario
	  • Ontario Hockey Federation
	  • Hockey Eastern Ontario
	• Quebec
	  • Hockey Quebec
	• New Brunswick
	  • Hockey New Brunswick
	• Nova Scotia
	  • Hockey Nova Scotia
	• Prince Edward Island
	  • Hockey P.E.I.
	• Newfoundland & Labrador
	  • Hockey Newfoundland & Labrador
	• Northwest Territories & Nunavut
	  • Hockey North
		• Return to hockey only upon written medical authority.

CDC (2020) (9) Guidance Document United States Dec 2020	CDC provides national guidance for youth sport administrators during the COVID-19 pandemic, and advises them to consult and follow their local public health officials. Guidance on assessing the level of risk, reducing transmission, maintaining healthy environments and operations and how to prepare strategies for when a participant becomes sick are provided.	Level of risk for a sport should be assessed by considering: • Community levels of COVID-19; • Proximity of individuals during game play, practice, etc, the number of individuals exposed to one another and the duration of close proximity; • Physical intensity of activities; • Indoor vs. outdoor gathering; • Shared equipment; and • Player age and risk of severe illness. With respect to hockey, the following recommendations apply:

		• Indoor settings are higher risk than outdoor, and proper ventilation systems are needed to circulate air; • Physical distancing and mask wearing reduce risk for all participants; • High intensity activity increases risk due to increased breathing rates; • Larger teams increase potential for transmission to others; • Nonessential spectators should not be present; • Communal space (i.e. locker rooms) should have increased time between use by different groups if being utilized, and cleaning and disinfecting is required; and • Cohorting of small groups of individuals.

EFFECTS OF TEMPERATURE AND HUMIDITY

Given the lack of published research considering SARS-CoV-2 transmission dynamics and viability within indoor ice rinks/arenas, indirect evidence was also considered. Weather related associations (temperature and humidity) summarized in a recent review with evidence up to October 1, 2020 concluded the highest incidence of COVID-19 was between the temperatures of 0-17°C, humidity had mixed results and a significant interaction was reported between temperature and humidity. Few basic research studies have described experiments on SARS-CoV-2 survival in cold temperature environments. A small experiment reported survival at 4°C for 14 days.

Table 3: Reviews of the Effect of Temperature and Humidity on SARS-CoV-2 (n=3)

STUDY	METHOD	KEY OUTCOMES
McClymont (2020) (10) Review Australia 2019-Oct 2020	This review considers the effect of weather, temperature and relative humidity, on the number of COVID-19 cases. The search was limited to publications up to Oct 1, 2020; and 23 articles were included in the review after full inclusion criteria were met and a quality assessment performed.	Ecological studies found correlations with higher transmission in areas with lower temperatures and humidity early in the epidemic. Temperature was a significant climatic factor in the 20 of the 23 studies, with a negative correlation to COVID-19 cases for 13 of the studies. Humidity was reported as significant in 12 of the 16 studies considering humidity, but with mixed results of positive (n=4) or

		negative (n=6) correlations or an optimal range (n=2). It is noted that winter conditions can contribute to increased COVID-19 transmission.
Aboubakr, 2020 (11) Review United States Jul 2020	This review includes studies presenting data for the stability of coronaviruses, including SARS-CoV-2. The persistence of coronaviruses in aerosols, on surfaces, in human fluids and in water is considered within the review, as well as the influence of temperature and humidity, pH and climatic and meteorological factors.	No studies on virus survival directly for arena temperatures/humidity were presented in this review. One study extensively tested the effects of temperature on stability of SARS-CoV-2 and found it to be highly stable at 4°C (the lowest temperature within the presented experiments) (13).
Abd El-Wahab (2020) (12) Review Egypt Dec 2019 – Jul 2020	Articles concerning SARS-CoV-2 transmission from Dec 28, 2019 – July 31, 2020 were included in this review. 302 articles are included in the review, considering three main themes of transmission: 1) SARS-CoV-2 survival; 2) transmission period and transmissibility; and 3) routes of SARS-CoV-2 spread.	This review captures the same experiment as (11) of SARS-CoV-2 stability at various temperatures (13). Empirical data that 90% of COVID-19 cases before March 22, 2020 were recorded in non-tropical countries (14) and investigations of temperature and humidity found that high temperatures were associated with lower R_e of SARS-CoV-2 (15, 16).

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: hockey OR ((arena OR curling OR skating OR ringette OR (sports AND outbreak)) [TITLE]). Information on how air conditions can affect SARS-CoV-2 transmission were also sought from the daily scan database with a search of: temperature AND humidity AND review [TITLE]. This review contains research published up to February 12, 2021. Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted

into the review. Grey literature was included, specifically guidance on hockey, or sports in general, from national health agencies or hockey associations within North America.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur les risques associés au SRAS-CoV-2 dans les arénas

Introduction

Quelles preuves existe-t-il à propos du risque de transmission du SRAS-CoV-2 dans les arénas, sur la glace et à l'extérieur de celle-ci?

Les éclosions de COVID-19 associées aux arénas et aux sports sur glace ont fait ressortir la nécessité de comprendre comment se produit la transmission et quels facteurs environnementaux et comportementaux peuvent être modifiés pour réduire le risque de transmission. Le hockey professionnel et amateur, ainsi que d'autres sports intérieurs sur glace comme le curling, la ringuette, le patinage et le hockey sur luge, ont été jugés pertinents pour la présente revue. On a recueilli des données probantes sur les risques de transmission dans les patinoires et de la documentation propre à la COVID-19 en ce qui concerne les participants aux activités sportives ou récréatives, les entraîneurs, les spectateurs et le personnel de l'aréna. Les activités dans différents sous-environnements (p. ex., l'utilisation du hall d'entrée, les vestiaires et les couloirs avant et après les activités sur glace, les aires réservées aux spectateurs et les activités sur glace) ont été prises en compte lors de l'examen des preuves. Nous avons également inclus dans la revue des études sur l'effet de la température et de l'humidité sur la transmission du SRAS-CoV-2 comme preuve indirecte de la survie du SRAS-CoV-2 dans des conditions froides. L'utilisation des moteurs à combustion dans l'équipement de resurfaçage de la glace a déjà suscité des préoccupations relatives à la qualité de l'air dans les installations avec glace intérieure, mais aucun lien entre cette recherche et les risques liés à la COVID-19 n'a été documenté. Elle n'a donc pas été prise en compte. Le présent document résume tous les examens et la littérature primaire disponibles jusqu'au 12 février 2021.

Points clés

- Cette revue a porté sur 13 publications, soit deux enquêtes sur des éclosions liées au hockey sur glace (1, 2) et deux autres liés à des tournois de curling (3, 4). Deux études transversales comprenaient des données d'observation recueillies entre août et octobre 2020 et portant sur les facteurs de risque pour la COVID-19 associés à d'autres sports amateurs aux États-Unis (5, 6). Trois revues résument la documentation sur le SRAS-CoV-2 dans des environnements froids ou avec un faible niveau d'humidité comme ce que l'on trouve dans les arénas.

Aréna/sports de glace :

- Le hockey offre des conditions favorables à la transmission du SRAS-CoV-2 pour les raisons suivantes :
    - Respiration forte, tant sur la glace que sur le banc, en raison d'une activité physique intense;

  - Proximité des joueurs et des entraîneurs;
  - Rassemblement à l'intérieur;
  - Air sec et froid de l'aréna;
  - Masse d'air séparée en raison des barrières d'environ 3 mètres (10 pieds) de hauteur tout autour de la glace, ce qui cause une mauvaise circulation de l'air. (1, 2, 7).

- Une enquête sur une éclosion qui s'est produite en juin 2020 dans des équipes de hockey masculin amateur a permis de théoriser qu'une personne présymptomatique avait contaminé 14 adultes symptomatiques (12 confirmés, 2 non testés), 13 joueurs des deux équipes et 1 employé de l'aréna (2). Aucune mesure de santé publique n'a été mise en place.

- Une éclosion dans la ligue de hockey U-20 de Finlande a fait l'objet d'une enquête. On a présumé qu'elle avait probablement été causée par un joueur asymptomatique, ce qui a permis de transmettre le virus à deux équipes opposées et donné lieu à une transmission tertiaire aux équipes de la ligue senior, pour un total de 49 infections à la COVID-19 confirmées (1). Après l'éclosion, la ligue a instauré des mesures pour réduire au minimum le risque de transmission de COVID-19, y compris en ne s'associant qu'avec une seule équipe.

- Deux enquêtes sur les éclosions qui se sont produites lors d'un bonspiel ont révélé que peu de précautions avaient été prises lors de rencontres sociales ayant duré longtemps (3, 4). Le risque de transmission ne peut donc pas être attribué au sport ou au site.

- Lors de la reprise du hockey amateur et professionnel et d'autres activités sur glace, à l'intérieur, les stratégies mises en œuvre afin de réduire le risque de transmission ont inclus le fait de limiter le nombre de personnes pouvant se trouver dans l'aréna, de réduire le temps passé dans l'aréna, d'effectuer le dépistage des personnes et d'améliorer l'hygiène, de regrouper les joueurs, de minimiser le temps d'exposition et le partage du matériel, de favoriser le port de masques et d'assurer le maintien de la distanciation physique (5 à 9).

Autres sports :

- Les données probantes tirées de deux études transversales décrivent un risque plus faible d'attraper la COVID-19 lorsque l'on fait des activités sportives en plein air comparativement aux activités sportives pratiquées à l'intérieur, lorsque les sports sans contact sont pratiqués comparativement aux sports de contact et que, en ce qui concerne certains sports de plein air, le port d'un masque avait eu un effet protecteur important (5, 6).

Preuve indirecte :

- Les données probantes sur la survie et le potentiel de transmission du SRAS-CoV-2 dans des environnements froids et à faible taux d'humidité n'ont pas été étudiées de façon appropriée dans la littérature. Cependant, des études récentes qui ont examiné les preuves expérimentales indiquent

chaque fois que la baisse des températures et de l'humidité est favorable à la survie du SRAS-CoV-2. De même, les études sur les conditions météorologiques et l'environnement indiquent toujours une transmission plus élevée du SRAS-CoV-2 dans les régions où les températures sont basses (0 à 17 °C) et une interaction importante entre la température et l'humidité, mais pas l'humidité en elle-même (10 à 16).

Vue d'ensemble des éléments de preuve

Treize articles ont été inclus dans cette revue, six articles provenant de la littérature primaire qui décrivent des éclosions liées aux sports, quatre documents d'orientation en ce qui concerne la reprise du hockey (deux pour les ligues de hockey professionnel, un pour le hockey canadien et un pour les sports chez les jeunes) et trois revues qui portent sur la transmission du SRAS-CoV-2 ou la survie de ce virus par temps froid. Quatre éclosions, deux matchs de hockey et deux tournois de curling amateurs ainsi que deux analyses transversales sur des sports pratiqués hors des arénas dans des écoles secondaires et sur le soccer pour les jeunes ont été incluses. On n'a trouvé aucune preuve à propos d'autres activités sur glace à l'intérieur, comme le patinage, le hockey sur luge ou la ringuette.

Puisque les enquêtes sur les éclosions sont des collectes rétrospectives de données probantes, les constatations risquent de comporter plusieurs biais, ainsi que toutes les incertitudes en ce qui concerne l'endroit où la transmission s'est produite. Certaines des études transversales qui ont été incluses fournissent un ensemble de données chronologiques d'une population, mais ne peuvent qu'établir des associations (sans cause) entre une exposition et un résultat. Un éventail de types d'examen ont été inclus, et les examens systématiques ont été évalués avec l'outil AMSTAR-2. Les revues de la littérature narrative ont été jugées être comme de faible qualité en raison d'un risque élevé de biais. Les limites de la preuve comprennent un très petit nombre d'articles dans la littérature sur les arénas, malgré le fait que bon nombre d'administrations aient signalé des cas ou des éclosions liés à des équipes de hockey ou de curling (p. ex., CBC News, 16 janvier 2021). En raison de la nature des sports, il est difficile d'établir avec certitude l'endroit où la transmission s'est produite, puisque les coéquipiers passent souvent du temps ensemble lorsqu'ils s'exercent, s'entraînent, se déplacent pour se rendre aux différentes parties, mangent et participent à des activités récréatives. Les tournois peuvent également augmenter le nombre possible de rencontres et d'exposition entre les équipes. Enfin, toutes les éclosions actuellement mentionnées dans la revue ont eu lieu au début de la pandémie, lorsque les couvre-visages et d'autres mesures de santé publique n'étaient pas utilisés à grande échelle.

TABLE DES MATIÈRES

ÉPIDÉMIES DANS LES SPORTS SUR GLACE À L'INTÉRIEUR

Tableau 1 : Transmission liée aux sports sur place à l'intérieur et à d'autres sports (n = 6)

ANNÉE	DESCRIPTION DE L'ÉCLOSION	PRINCIPAUX RÉSULTATS
Hockey (n = 2)		
Atrubine (2020) (2) Enquête sur l'épidémie États-Unis Juin 2020	Deux équipes (A et B) ont joué un match de hockey amateur le 16 juin 2020 (jour 0) à Tampa Bay, en Floride. Chaque équipe comprenait 11 hommes âgés de 19 à 53 ans. Le 21 juin (jour 5), 15 personnes présentaient des symptômes soupçonnés de COVID-19. • Patient index – Joueur de l'équipe A, qui était symptomatique un jour après la partie et a obtenu un résultat positif le jour 3. • Cas secondaires – 14 adultes symptomatiques (12 confirmés, 2 non testés); 13 joueurs et 1 employé de l'aréna. • Les cas asymptomatiques liés à la partie n'ont pas subi de test.	Cas suivants : • 8 des 10 coéquipiers du cas index sont devenus symptomatiques; • 5 des 11 joueurs de l'équipe adverse sont devenus symptomatiques; • 1 employé de l'aréna est devenu symptomatique; • cas asymptomatiques non testés : joueurs (8 sur 21), 2 arbitres et 1 spectateur. • Aucune mesure de sécurité publique n'a été mise en œuvre, y compris le fait de porter un couvre-visage. • La partie a duré 60 minutes. • Les vestiaires ont été utilisés, un par équipe, 20 minutes avant et après la partie. • La possibilité de transmission n'existait qu'à l'aréna, aucun autre contact n'avait eu lieu la semaine précédente. Les auteurs font remarquer que le hockey offre des conditions favorables pour la transmission du SRAS-CoV-2 : • Respiration forte, tant sur la glace que sur le banc, en raison d'une activité physique intense; • Proximité des joueurs; • Rassemblement à l'intérieur; • Masse d'air séparée en raison des barrières d'environ 3 mètres (10 pieds) de hauteur tout autour de la glace.
Kuituen (2021) (1) Enquête sur l'épidémie	Ce rapport descriptif porte sur la transmission du SRAS-CoV-2 dans une ligue de hockey finlandaise, U-20.	On suppose qu'un joueur de hockey asymptomatique a été la source de l'éclosion qui a entraîné 49 infections

Finlande Septembre 2020	L'équipe A a joué contre l'équipe B le 4 septembre 2020 (jour 0) et l'équipe C le 5 septembre 2020 (jour 1). Certains joueurs des trois équipes s'entraînent également avec des équipes de niveau senior. Un joueur asymptomatique était le cas index, et 49 cas secondaires et tertiaires ont été détectés dans 5 équipes. Six équipes ont alors été mises en quarantaine (équipes A, B et C du U-20 et équipes senior A, B et C). • Cas index - on suppose qu'il s'agit d'un joueur de l'équipe A qui était asymptomatique, mais infectieux le jour 0. (Étant donné qu'il y avait un nombre élevé de résultats positifs asymptomatiques le jour 3 après la première partie, le cas index n'a pas été déterminé.) • Cas secondaires (ligue U-20) : ÉQUIPE A - 3 joueurs symptomatiques le jour 2 avec résultat positif au test. Tous les membres de l'équipe A ont passé le test le jour 3 (28 joueurs + membres du personnel) et 22 joueurs ont obtenu des résultats positifs. L'équipe A a passé 10 heures dans un autobus pour aller aux parties et en revenir. ÉQUIPE B - 3 joueurs ont obtenu un résultat positif le jour 5; 11 autres cas ont ensuite été détectés. ÉQUIPE C – 6 joueurs ont obtenu un résultat positif le jour 6 (exposition à l'équipe A le jour 1); 10 autres cas ont été détectés par la suite. • Cas tertiaires (ligue senior) : ÉQUIPE A – aucun cas détecté. ÉQUIPE B – 2 joueurs ont obtenu un résultat positif. ÉQUIPE C – un joueur a obtenu un résultat positif.	confirmées par la COVID-19 au cours d'un suivi ayant duré 16 jours. Précautions prises par la ligue : - Aucune directive en ce qui concerne le port du couvre-visage (les joueurs n'en portaient pas) - les équipes ne se sont pas serré la main pendant les parties; - Le nombre de spectateurs était limité pour assurer le maintien de distanciation sociale. La transmission au sein d'une équipe peut s'être produite lors d'un déplacement effectué dans l'autobus de l'équipe, dans le vestiaire ou lors d'un autre rassemblement d'équipe, et la transmission aux joueurs des équipes B et C a été déterminée comme ayant fort probablement eu lieu pendant la partie. Les multiples contacts rapprochés et la respiration forte résultant d'une activité intense pendant le jeu sont vus comme des risques de transmission sur glace. De plus, l'on suggère que l'air sec et froid de l'aréna augmente le risque d'aérosolisation des gouttelettes de SARS-CoV-2 expulsées. Cette éclosion a entraîné la mise en place de modifications pour les ligues finlandaises qui empêchent désormais les joueurs de la ligue U-20 de s'entraîner ou de jouer avec plus d'une équipe. L'utilisation des bulles et des tests continus dans les sports de niveau professionnel n'est pas possible pour le hockey amateur et les jeunes. Une des limites de cette enquête est le fait qu'elle est fondée sur des données accessibles au public et que les auteurs

		n'ont pas interviewé les joueurs ou n'ont pas eu accès à leur dossier de santé. Cela signifie que le cas index n'a pas été déterminé, mais l'on présume qu'il s'agit d'un joueur asymptomatique et que la séquence probable de transmission est inconnue (c.-à-d. combien de personnes ont probablement été infectées pendant la partie par rapport à leurs coéquipiers qui ont été infectés à une date ultérieure).
Curling (n = 2)		
Burak (2021) (3) Enquête sur l'épidémie Alberta, Canada Mars 2020	Du 11 au 14 mars 2020, 73 personnes ont participé à un bonspiel de curling à Edmonton. Cette étude descriptive est fondée sur des entrevues réalisées avec des participants effectuées entre le 17 avril et le 5 mai. En plus des symptômes autodéclarés et des résultats des tests, des échantillons ont été prélevés pour des tests sérologiques auprès de 62 participants sur 73. 58 des 73 participants au bonspiel étaient des médecins alors que tous étaient des travailleurs de la santé. 40 joueurs de curling ont eu un résultat positif au test de dépistage du SRAS-CoV-2, et 30 d'entre eux ont obtenu un résultat sérologique positif dans les 222 jours qui ont suivi le bonspiel. 16 autres personnes qui ont déclaré que les symptômes ont reçu un résultat négatif ou n'ont pas été testées (14 de ces cas ont été déclarés comme étant des cas probables) et 7 des cas probables ont obtenu un résultat positif à la sérologie. Les participants asymptomatiques n'ont pas été testés. Les tests sérologiques ont été négatifs pour 12 personnes et positifs pour 1 des 17 joueurs asymptomatiques. Les participants ont également signalé 35 cas soupçonnés de transmission secondaire associés à des symptômes ou	L'événement de curling et les activités sociales connexes ont donné un taux d'attaque de 74 % de la COVID-19 chez les participants. Aucun cas index n'a été déterminé, mais 10 personnes ont signalé des symptômes non spécifiques mineurs au moment du bonspiel. Même si l'étude ne permet pas de déterminer quelles activités ont entraîné la transmission, elle se fonde plutôt sur les émet plutôt l'hypothèse que les repas partagés en sont la source en raison des enquêtes sur les activités des participants.

	à des tests positifs reçus par des contacts des ménages, après l'événement.	
Luethy (2020) (4) Prépublication Enquête sur l'épidémie États-Unis Mars 2020	Les championnats nationaux de curling des États-Unis ont eu lieu du 7 au 14 mars 2020 à Laurel, au Maryland. 88 athlètes et entraîneurs de partout aux États-Unis ont participé au tournoi, auquel ont assisté 187 participants. Les banquets traditionnels ont été remplacés par des repas emballés dans des contenants jetables à usage unique et un nettoyage accru a été effectué pendant le tournoi afin d'atténuer la transmission du SRAS-CoV-2. Malgré les efforts déployés, l'étude descriptive indique que 55,6 % des participants ont signalé des symptômes de la COVID-19 après avoir pris part au tournoi. Les participants, les bénévoles et les spectateurs ont été informés le 18 mars qu'une des personnes présentes avait obtenu un résultat positif au test de dépistage de la COVID-19. Une deuxième annonce faite le 27 mars a indiqué que plusieurs participants avaient obtenu un résultat positif au test de COVID-19. Un sondage effectué auprès des joueurs, des entraîneurs, des officiels, des bénévoles et des spectateurs (n = 187) du 1er au 13 septembre 2020 a obtenu un taux de réponse de 85 % (159/187) et les résultats sont présentés dans cette étude descriptive.	55,6 % (104/187) des participants ont signalé avoir eu des symptômes correspondant à la COVID-19. On a constaté une grande différence entre les entraîneurs/joueurs et les bénévoles, dont 77,3 % (68/88) et 33,0 % (29/88), respectivement, ont déclaré des symptômes. 44 personnes ont dit avoir subi des tests de dépistage du SRAS-CoV-2. 19,8 % (37 sur 187) des participants ont déclaré avoir reçu un résultat positif au SRAS-CoV-2 alors que 3,7 % (7 sur 187) ont dit avoir reçu un résultat négatif. Des tests sérologiques ont été effectués sur 73 personnes et ont entraîné 66 résultats positifs. En raison du grand nombre de rassemblements et de la longueur du tournoi, ainsi que du manque de tests disponibles au moment du tournoi, il est impossible de déterminer l'heure et le lieu des transmissions. Aucun cas index n'a pu être déterminé.
Sports à l'extérieur des arénas (n = 2)		
Watson (2021) (5) Prépublication Étude transversale États-Unis Août à octobre 2020	Un sondage effectué à l'échelle nationale auprès d'athlètes des écoles secondaires américaines ayant participé à des sports d'automne a inclus 991 écoles et 152 484 athlètes de 5 844 équipes.	Parmi les 2 655 athlètes qui ont dit avoir eu la COVID-19, 69 cas étaient directement attribuables à des contacts dans le cadre du sport, pour un taux total de 24,6 par 100 000 jours-joueurs. L'incidence de la COVID-19 était plus faible dans les cas suivants :

	Les analyses sont ajustées selon l'incidence de la COVID-19 et selon le type d'enseignement.	• Sports pratiqués à l'extérieur c. à l'intérieur (ratio du taux d'incidence [TRI] = 0,54, IC à 95 % = 0,49 à 0,60, p < 0,001). • Sports sans contact c. sports avec contact (TRI = 0,78 [0,70 à 0,87], p < 0,001). • Aucune différence entre les sports d'équipe et les sports individuels (TRI = 0,96 [0,84 à 1,1], p = 0,49). Le port du couvre-visage (indiqué par 28 % des écoles) était associé à une diminution de l'incidence dans certains sports : • Volley-ball féminin (TRI = 0,53 [0,37 à 0,73], p < 0,001). • Basket-ball des garçons (TRI = 0,53 [0,33 à 0,83], p = 0,008). • Basket-ball féminin (TRI = 0,36 [0,19 à 0,63], p < 0,001). • Football (TRI = 0,79 [0,59 à 1,04], p = 0,10). • Cheerleading/danse (TRI = 0,75 [0,53 à 1,03], p = 0,081). • Aucune association n'a été trouvée pour les autres sports.
Watson (2020) (6) Prépublication Étude transversale États-Unis Août 2020	Une enquête sur les clubs de soccer aux États-Unis et l'incidence de la COVID-19 dans les clubs au cours des 10 semaines précédentes. 129 clubs ont répondu au sondage. De ces clubs, 124 avaient recommencé à jouer au soccer et comptaient 91 007 joueurs pour une durée médiane de 73 jours. 119 clubs sont passés à des activités de groupe.	Parmi les 85 861 joueurs, 218 cas de COVID-19 ont été signalés. Les jeunes joueurs de soccer affichaient un taux de cas et un taux d'incidence plus faibles que le taux national pour les enfants aux États-Unis (254 c. 477 cas par 100 000; TRI = 0,511, IC à 95 % = [0,40 à 0,57], p < 0,001). Après correction de l'incidence locale de la COVID-19, il n'y avait aucun lien entre l'incidence de COVID-19 du club et la phase de retour (sans contact).

ORIENTATION EN CE QUI CONCERNE LE HOCKEY EN PÉRIODE DE COVID-19

Tableau 2 : Orientation pour le hockey et les sports pratiqués par les jeunes (n = 4)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
Littérature scientifique		
DiFiori (2020) (7) Protocole États-Unis Septembre 2020	Ce protocole a été rédigé par des médecins qui collaborent avec des associations sportives professionnelles en Amérique du Nord (NBA, MLB, NHL, MLS, NFL) et traite de la reprise des sports professionnels pendant l'épidémie de COVID-19. Puisque l'accent est mis sur la « mise en œuvre progressive », le retour des spectateurs n'a pas été pris en compte dans le document.	Le document ne traite pas de questions propres au hockey ou à l'aréna, mais les recommandations suivantes portant sur l'ensemble des sports professionnels sont dignes de mention : • Prévoir de changer rapidement le protocole si le niveau de transmission de la maladie dans la collectivité change; • Fournir du désinfectant pour les mains et des couvre-visage; • Penser à mettre en place des pratiques d'hygiène plus strictes et des mesures préventives comme obliger le port en tout temps d'un couvre-visage pour ceux qui ne pratiquent pas le sport; • Assurer la désinfection complète et régulière des installations sportives; • Augmenter la ventilation et la circulation d'air dans les installations sportives; • Réduire considérablement le nombre de personnes qui se trouvent dans les installations; • Effectuer un contrôle avant l'événement; • Limiter le partage de l'équipement ou du matériel.
Parker (2020) (17) Ligne directrice États-Unis Octobre 2020	Ce document décrit en détail les éléments dont il faut tenir compte avant de rouvrir les grands stades et arénas, en particulier aux États-Unis, à cette ère de COVID-19.	Aucune attention particulière n'est accordée aux arénas ni aux défis uniques associés à l'air froid à l'intérieur des installations. Le document met principalement l'accent sur les initiatives de santé publique et l'orientation pour les rassemblements de masse et les points de risque liés à l'utilisation des installations.
Orientation nationale et régionale		
Hockey Canada (2020) (8)	En tant qu'organisme dirigeant du hockey au Canada, Hockey Canada est une ressource centrale pour le retour de	En plus des directives sur le respect des protocoles locaux de santé publique, Hockey Canada présente différentes

Centre de ressources en ligne
 	
Canada
Juin 2020
	l'information et des mises à jour sur le hockey au pays. Renseignements en ce qui concerne la sécurité, la structure saisonnière, l'entraînement, l'arbitrage, la réglementation et les dernières nouvelles provinciales et territoriales.
	
	Les Lignes directrices sur la sécurité de Hockey Canada donnent un aperçu de la manière d'organiser les parties de hockey ou d'y participer pendant la pandémie de COVID-19. Le thème commun comporte des listes de contrôle axées sur les renseignements à recueillir auprès des autorités et des établissements de santé locaux, ainsi que la diffusion de ces renseignements aux participants, aux familles, etc.
	
	Le document comporte des liens vers les associations de hockey des provinces et des territoires où obtenir des mises à jour et des renseignements locaux :
	• Colombie-Britannique et Yukon
	  • B.C. Hockey
	• Alberta
	  • Hockey Alberta
	• Saskatchewan
	  • Saskatchewan Hockey Association
	• Manitoba
	  • Manitoba Amateur Hockey Association
	• Ontario
	  • Hockey Northwestern Ontario
	  • Ontario Hockey Federation
	  • Hockey Eastern Ontario
	• Québec
	  • Hockey Québec
	• Nouveau-Brunswick
	  • Hockey Nouveau-Brunswick
	• Nouvelle-Écosse
	  • Hockey Nova Scotia
	• Île-du-Prince-Édouard
		recommandations communes en matière d'hygiène et de prévention de COVID-19, notamment :
		• Lavage des mains;
		• Utilisation du désinfectant pour les mains;
		• Blocage des gouttelettes au moment de tousser ou d'éternuer;
		• Respect de la distanciation physique;
		• Utilisation de bouteilles d'eau individuelles;
		• éviter le transport de groupe (p. ex., autobus) vers les parties.
		
		En cas de test positif à la COVID-19, Hockey Canada conseille ce qui suit :
		• Retrait immédiat de l'équipe et de son entourage de toute personne infectée;
		• Autres mesures établies en fonction des conseils de la santé publique locale;
		• ne revenir au jeu qu'après avoir l'autorisation écrite du médecin.

	• Hockey P.E.I.
	• Terre-Neuve et Labrador
	  • Hockey Newfoundland & Labrador
	• Territoires du Nord-Ouest et Nunavut
	  • Hockey North	

CDC (2020) (9) Ligne directrice États-Unis Décembre 2020	Le CDC fournit des lignes directrices destinées aux administrateurs des sports pour les jeunes pendant la pandémie de COVID-19 et leur conseille de consulter les responsables locaux de la santé publique et de suivre leurs orientations. Conseils sur l'évaluation du niveau de risque, la réduction de la transmission, le maintien d'environnements et d'opérations sains et la façon de préparer des stratégies lorsqu'un joueur est malade.	Le niveau de risque associé à un sport doit être évalué en tenant compte de ce qui suit : • Niveaux communautaires de COVID-19; • Proximité des personnes pendant la partie, la pratique, etc., le nombre d'individus exposés les uns aux autres et la durée de la proximité; • Intensité physique des activités; • Rassemblement à l'intérieur ou à l'extérieur; • Équipement partagé; et • Âge du joueur et risque de maladie grave. En ce qui concerne le hockey, les recommandations suivantes s'appliquent : • Les installations intérieures présentent un risque plus élevé que les installations extérieures, et des systèmes de ventilation appropriés sont nécessaires pour faire circuler l'air; • La distanciation physique et le port d'un couvre-visage réduisent le risque pour tous les participants; • L'activité intense augmente le risque en raison de l'augmentation de la fréquence respiratoire; • Les équipes plus grandes augmentent le potentiel de transmission aux autres; • Les spectateurs non essentiels ne doivent pas être présents; • Le temps entre l'utilisation des espaces communautaires (c.-à-d. les vestiaires) par différents groupes devrait être augmenté, et si différents groupes les utilisent, ils doivent être nettoyés et désinfectés entre chaque groupe;

		• Les personnes doivent être regroupées en petites cohortes.

EFFETS DE LA TEMPÉRATURE ET DE L'HUMIDITÉ

En raison du manque de recherches publiées sur la dynamique de transmission du SRAS-CoV-2 et sa viabilité dans les patinoires et les arénas intérieurs, des preuves indirectes ont également été prises en compte. Des liens établis avec les conditions météorologiques (température et humidité) ont été présentés dans une revue récente comprenant des preuves recueillies jusqu'au 1er octobre 2020. Ils concluaient notamment que l'incidence de COVID-19 était plus forte dans les températures entre 0 et 17 °C. Le taux d'humidité n'a donné que des résultats mitigés, mais un lien significatif a été établi entre la température et l'humidité. Peu d'études de recherche fondamentale ont décrit des expériences sur la survie du SARS-CoV-2 dans des environnements froids. Une petite expérience a cependant montré que le virus survivait à une température de 4 °C pendant 14 jours.

Tableau 3 : Examens de l'effet de la température et de l'humidité sur le SRAS-CoV-2 (n = 3)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
McClymont (2020) (10) Revue Australie 2019 à octobre 2020	Cette revue a examiné l'effet des conditions météorologiques, de la température et de l'humidité relative sur le nombre de cas de COVID-19. La recherche s'est limitée aux publications diffusées jusqu'au 1er octobre 2020, et 23 articles ont été inclus dans l'examen après que les critères d'inclusion complets ont été remplis et qu'une évaluation de la qualité a été effectuée.	Au début de l'épidémie, des études écologiques ont révélé des corrélations avec un niveau de transmission plus élevé dans les régions où les températures et l'humidité étaient plus basses. La température a été un facteur climatique important dans 20 des 23 études, avec une corrélation négative avec les cas de COVID-19 dans 13 des études. L'humidité a été signalée comme étant significative dans 12 des 16 études tenant compte de l'humidité, mais avec des résultats mixtes de corrélations positives (n = 4) ou négatives (n = 6) ou une plage optimale (n = 2). Il est à noter que les conditions hivernales peuvent contribuer à accroître la transmission de la COVID-19.

Aboubakr, 2020 (11) Revue États-Unis Juillet 2020	Cet examen comprend des études qui présentent des données sur la stabilité des coronavirus, y compris le SRAS-CoV-2. Il tient compte de la persistance des coronavirus dans les aérosols, sur les surfaces, dans les fluides humains et dans l'eau, ainsi que de l'influence de la température et de l'humidité, du pH et des facteurs climatiques et météorologiques.	Aucune étude sur la survie du virus ne portant précisément sur les températures et l'humidité dans les arénas n'a été présentée dans cette revue. Une étude a abondamment testé les effets de la température sur la stabilité du SRAS-CoV-2 et a révélé qu'il était très stable à 4 °C (la température la plus basse dans les expériences présentées) (13).
Abd El-Wahab (2020) (12) Revue Égypte Décembre 2019 à juillet 2020	Les articles portant sur la transmission du SRAS-CoV-2 du 28 décembre 2019 au 31 juillet 2020 ont été inclus dans cet examen. La revue a porté sur 302 articles et a tenu compte de trois principaux thèmes de transmission : 1) la survie du SRAS-CoV-2; 2) la période de transmission et la transmissibilité; et 3) les voies de propagation du SRAS-CoV-2.	Cette revue reprend la même expérience que (11) de stabilité du SRAS-CoV-2 à diverses températures (13). Les données empiriques selon lesquelles 90 % des cas de COVID-19 avant le 22 mars 2020 ont été enregistrés dans des pays non tropicaux (14) et les enquêtes sur la température et l'humidité ont révélé que les températures élevées étaient associées à des taux R_e plus faibles de SARS-CoV-2 (15, 16).

Méthodologie :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient : hockey OU ((arena OU curling OU skating OU ringette OU (sports ET outbreak)) [TITRE]). Des renseignements sur la manière dont les conditions atmosphériques peuvent affecter la transmission du SRAS-CoV-2 ont également fait l'objet de recherches dans la base de données de l'analyse quotidienne avec les termes temperature ET humidity ET review [TITRE]. La présente revue contient des recherches publiées jusqu'au 12 février 2021. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la

revue. De la littérature grise a été incluse, plus particulièrement des conseils sur le hockey, ou le sport en général, fournie par des agences nationales de santé ou des associations de hockey en Amérique du Nord.

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Emerging Evidence on COVID-19

Rapid Review of COVID-19 hospitalizations and length of stay

Introduction

This rapid review identifies and summarizes published and pre-published data on the proportion of COVID-19 cases hospitalized, admitted to intensive care unit (ICU) and requiring invasive mechanical ventilation as well as their average or median length of stay in hospital, ICU and duration of ventilation up to August 20, 2020. Both the scarcity of hospitalization data in the Canadian context and variability in these data across studies has lead to the on-going collection and synthesis of global results to improve and/or validate parameters in predictive models that aimed to measure the capacity of the Canadian health systems to manage the pandemic.

What's New?

- Six new studies from United States (3), United Kingdom (1), Italy (1) and China (1). The following tables were updated Proportion of patients in ICU, Proportion of ventilated patients, Length of stay in hospital, LOS in ICU, Duration of ventilation
- One study conducted in United States involved exclusively patients under 18 years of age. LOS by age-group were provided.
- Changes are highlighted.

Key Points

- The average percentage of hospitalization of COVID-19 cases varied 11%-77% over the study population. Older age groups had increasing proportion hospitalized.
- The percentage of admission to Intensive Care Unit (ICU) of COVID-19 cases varied from:
  - 1% to 32% among infected patients
  - 12% to 40% among hospitalized patients
- The percentage of patients requiring ventilation varied from:
  - 1% to 13% among infected patients
  - 5% to 19% among hospitalized (including ICU) patients
  - 28% to 94% among patients in ICU; the two recent studies were 92% and 94%
- The length of stay (LOS) for hospitalization (including ICU) of COVID-19 cases median days across studies was 4-19 days with an interquartile range (IQR) of 3 to 27 days:
  - Among survivors median LOS for hospitalization varied from 5 to 9 days with a IQR of 3 to 13

    - Among non-survivors median LOS for hospitalization varied from 4 to10 with a IQR of 3 to 16
- The median length of stay in ICU varied from 4 to 23 days with a IQR of 2 to 32 days among all patients in ICU
    - Among survivors, median LOS in ICU varied from 8 to 26 days with a IQR of 5 to 46 days
    - Among non-survivors, median LOS in ICU varied from 6 to 12 days with a range of 2 to 26 days
- Median duration of ventilation for patients who required mechanical ventilation was 6 to 13 days with a range of 5 to 22 days.
- In August 2020, MMWR published an analysis of pediatric COVID-19 hospitalization data from 14 states (L. Kim et al., 2020a). It found that although the cumulative rate of COVID-19–associated hospitalization among children (8.0 per 100,000 population) was low compared with that in adults (164.5), the hospitalization rates among Hispanic was eight times higher, and among black children was five times higher, than the rate in white children. An underlying medical condition was present in 42% of the children; obesity was the most prevalent underlying medical condition.
    - Hospitalization rate was highest for those under 2 years of age (24.8 per 100,000 population).
    - One third of hospitalized patients were admitted to the ICU (33.2%)
    - The proportion of hospitalized patients requiring invasive mechanical ventilation was 5.8%
    - The median LOS in hospital overall was 2.5 days with a range of 1 to 5 days
    - The median LOS in ICU was 2 days with a range of 1 to 5 days

Overview of the Evidence

The review identified and summarized 64 published and pre-published studies. Most of the studies were retrospective observational studies conducted at the hospital level, and do not necessarily represent the nationwide statistics. Results of studies with low sample size should be interpreted with caution.

CONTENTS

PROPORTION OF HOSPITALIZATION (OVERALL)

Table 1 presents the percentage of hospitalized COVID-19 patients overall, including patients admitted to the ICU, among COVID-19 cases.

TABLE 1: Proportion of hospitalization reported in 14 studies

Author	Country	Date	N-denominator	% Hospitalization	Notes
(Rizzo et al., 2020)	United States	20 February 2020 to 6 June 2020	<18 y: 1,767 18-29 y : 8,214 30-39 y: 11,034 40-49 y: 11,635 50-64 y: 21,606 65-74 y: 10,946 75-84 y: 6,689 >85 y: 4,926	<18 y : 10.8% 18-29 y : 9.8% 30-39 y : 12.2% 40-49 y : 16.6% 50-64 y : 22.7% 65-74 y : 30.1% 75-84 y : 37.9% >85 y : 35.8%	N hospitalized <18 y : 190 18-29 y: 802 30-39 y: 1,351 40-49 y: 1,933 50-64 y: 4,906 65-74 y : 3,298 75-84 y : 2,537 >85 y : 1,763
(McPadden et al., 2020)	United States	01 March 2020 to 04 May 2020	All=7995 18-34 y : 1,570 35-44 y : 1,321 45-54 y : 1,546 55-64 y : 1,583 65-74 y : 885 75-84 y : 565 >=85 y : 516	All=27% 18-34 y : 11% 35-44 y : 14% 45-54 y : 17% 55-64 y : 27% 65-74 y : 45% 75-84 y : 66% >=85 y : 69%	All=2154 18-34 y : 146 35-44 y : 181 45-54 y : 258 55-64 y : 435 65-74 y : 402 75-84 y : 374 >=85 y : 358
(Martín-Sánchez et al., 2020)	Spain (Madrid)	28 February 2020 to 31 March 2020	All=1,379 cases 18-44 y: 250 45-54 y: 246 55-64 y: 247 65-74 y: 237 75-84 y: 235 >=85 y: 164	All:74.6% 18-44 y: 50% 45-54 y: 61.4% 55-64 y: 71.7% 65-74y: 86.1% 75-84 y: 91.9% >=85 y: 95.1%	All=1,030 cases 18-44 y: 125 45-54 y: 151 55-64 y: 177 65-74 y: 204 75-84 y: 216 >=85 y: 156
(Hsu et al., 2020)	United States (Boston, Massachusetts)	01 March to 18 May 2020	2,729 cases	40%	N=1,088
(Soares, Mattos, & Raposo, 2020)	Brazil (Espirito Santo state)	As of 11 June 2020	10,713 cases	11%	N=1,152
(Alsofayan, Althunayyan, Khan, Hakawi, & Assiri, 2020)	Saudi Arabia	01 March to 31 March 2020	1519 cases	67%	N=513 hospitalized

Author	Country	Date	N-denominator	% Hospitalization	Notes
(Reilev et al., 2020)	Denmark	27 February 2020 to 30 April 2020	Cases All= 9,519 0-9 y:135 10-19 y: 342 20-29 y: 1,212 30-39 y: 1,234 40-49 y: 1,556 50-59 : 1,466 60-69 y: 801 70-79 y: 316 80-89 y: 260 90+ y: 227	All: 22% 0-9 y:1.8% 10-19 y: 4.6% 20-29 y: 16% 30-39 y: 17% 40-49 y: 21% 50-59 y: 20% 60-69 y: 11% 70-79 y: 4.3% 80-89 y: 3.5% 90+ y: 2.4%	N Hospitalized All=2,090 0-9 y:10 10-19 y: 12 20-29 y: 51 30-39 y: 81 40-49 y: 183 50-59 y: 310 60-69 y: 351 70-79 y: 541 80-89 y: 431 90+ y: 120
(*COVID-19, australia: Epidemiology report 13 (reporting week to 23:59 AEST 26 april 2020)*2020)	Australia	As of 26 April 2020	6,711 cases	12%	
(CDC, 2020)	United States (49 states, the District of Columbia, and three U.S. territories)	12 February to 6 March 2020	2,712 cases	All ages- 20.7 - 31.4% 0-19 y : 14.3 - 20.8% 20-44 y :21.2 - 28.3% 45-54 y : 20.5 - 30.1% 55-64 y: 28.6 - 43.5% 65-74 y: 30.5 - 58.7% 75-84 y: 30.5 - 58.7% >=85 y: 31.3 - 70.3%	-The upper bound is the % hospitalized with known hospitalization status. Lower bound is % hospitalized over the whole age group
(Tadrigo & Veltri, 2020)	Italy	As of 22 March 2020	46,638 COVID-19 cases	49%	

Author	Country	Date	N-denominator	% Hospitalization	Notes
(ECDC, 2020)	16 countries of EU/EEA and the United Kingdom.	As of 24 March 2020	43,438 COVID-19 cases	All ages 30% Median 24%, IQR: 11-41% < 10 y: 11 - 25% 10-19 y: 2 -15% 20-29 y : 9 - 13% 30-39 y : 10 -13% 40-49 y : 5 -12% 50-59 y :11 - 14% 60-69 y:17 - 23% 70-79 y: 27 – 34% >=80 y: 26 - 35%	-Data from 14 countries with >50% completeness for hospitalization -These numbers were extracted from Figure 3 of the report and therefore were approximated
(Team,COVID-National Incident Room Surveillance, 2020)	Australia	As of 22 March 2020	717 cases	26%	
(Cai et al., 2020)	China	11 January 2020 to 06 February 2020	298 cases	77%	
(Verity et al., 2020)	China	As of 08 February 2020	Cases 0 - 9 y : 13 10-19 y : 50 20-29 y: 437 30-39 y: 733 40-49 y: 743 50-59 y: 790 60-69 y: 560 70-79 y:263 80+ y: 76	0 - 9 y : 0% 10-19 y : 0.04% (0.02, 0.08) 20-29 y: 1.1% (0.62, 2.1) 30-39 y: 3.4% (2.1, 7.0) 40-49 y: 4.3% (2.5, 8.7) 50-59 y: 8.2% (4.9, 16.7) 60-69 y:11.8% (7.0, 24.0) 70-79 y:16.6% (9.9, 33.8)	-In this study from a subset of cases reported in mainland China, the authors estimate the proportion of all infections that would be hospitalized under the definition of severe cases in the UK context (in opposite to

Author	Country	Date	N-denominator	% Hospitalization	Notes
				80+ y: 18.4% (11.0, 37.6)	all infected patient in China)

PROPORTION OF PATIENTS ADMITTED TO THE ICU

Table 2 presents the percentage of patients admitted to the ICU among COVID-19 cases OR hospitalized patients.

TABLE 2: Proportion of patients in ICU in 34 studies

Author	Country	Date	N-denominator	% admitted to the ICU	Notes
(Vena et al., 2020) *new*	Italy (Genoa)	25 February to 25 March 2020	317 hospitalized	20.5%	N in ICU 65
(Turcotte et al., 2020) *new*	United States (Annapolis)	01 March to 12 April 2020	117 hospitalized	30.8%	N in ICU 36
(L. Kim et al., 2020a) {{61027;}} *new*	United States (14 States)	01 March to 25 July 2020	Patients <18 y=208 0–2 y=61 2–4 y=24 5–17 y=123	Patients <18 years=33.2% 0–2 y=31.1% 2–4 y= 37.5% 5–17 y= 33.3%	N in ICU All ages=69 0–2 y=19 2–4 y= 9 5–17 y=41
(Rizzo et al., 2020)	United States	20 February 2020 to 06 June 2020	All : 16,099 cases <18 y: 185 18-65 y: 8,958 >65 y: 6,956	Median (IQR) All: 23.4% <18 y: 16.8% 18-65 y: 19.8% >65 y: 28.1%	All : 3,768 <18 y: 31 18-65 y: 1,777 >65 y: 1,960
(Martín-Sánchez et al., 2020)	Spain (Madrid)	28 February 2020 to 31 March 2020	All=1,379 cases 18-44 y: 250 45-54 y: 246 55-64 y: 247 65-74 y: 237	All: 5.9% 18-44y: 3.2% 45-54y: 6.1% 55-64y: 12.1% 65-74y: 8.9 % 75-84y: 3.4 %	All : 82 cases 18-44 y: 8 45-54 y: 15 55-64 y: 30 65-74 y: 21 75-84 y: 8

Author	Country	Date	N-denominator	% admitted to the ICU	Notes
			75-84 y: 235 >=85 y: 164	>=85y: 0%	>=85 y: 0
(Hsu et al., 2020)	United States (Boston, Massachusetts)	01 March to 18 May 2020	1,088 hospitalized	17%	N=188
(Shah et al., 2020)	United States (Southwest Georgia)	02 March 2020 to 06 May 2020	N=522 hospitalized	23.6%	N=123
(Suleyman et al., 2020)	United States (Detroit, Michigan)	09 March to 27 March 2020	N=355 hospitalized	40%	N=141 in ICU
(Yang et al., 2020)	China (Wuhan)	13 February to 14 March	N=463 hospitalized	14%	N=66 in ICU
(Alsofayan et al., 2020)	Saudi Arabia	01 to 31 March 2020	N=1519 cases	4.7%	N=36 in ICU
(Reilev et al., 2020)	Denmark	27 February to 2020 to 30 April 2020	Cases All= 9,519 0-9 y :135 10-19 y : 342 20-29 y : 1,212 30-39 y : 1,234 40-49 y: 1,556 50-59 y : 1,466 60-69 y : 801 70-79 y : 316 80-89 y : 260 90+ y : 227	All: 3.2% 0-9 y : 0% 10-19 y : 0% 20-29 y : 2% 30-39 y : 3% 40-49 y: 9% 50-59 y : 15% 60-69 y : 27% 70-79 y : 34% 80-89 y : 11% 90+ y : 0%	N in ICU All=300 0-9 y : 0 10-19 y : 0 20-29 y : 6 30-39 y : 10 40-49 y: 161 50-59 y : 262 60-69 y : 80 70-79 y : 102 80-89 y : 32 90+ y : 0
(A. B. Docherty et al., 2020a)	United Kingdom	06 February to 19 April 2020	18,183 cases	17%	208 hospitals
(L. Kim et al., 2020b)	United States (14 States)	01 March to 02 May, 2020	2,491 cases	32%	-154 acute care hospitals

Author	Country	Date	N-denominator	% admitted to the ICU	Notes
					in 74 counties in 13 states -See appendix for the list of States
(Fletcher et al., 2020)	United Kingdom	01January 2020 to 23 April 2020	1,148 cases	10%	
(Almazeedi et al., 2020)	Kuwait	24February 2020 to 20 April 2020	1,096 cases	4%	
(Liang et al., 2020)	China	As of 31 January 2020	1,590 cases	8%	Cases from 575 hospitals in 31 provincial administrative regions
(*COVID-19, australia: Epidemiology report 13 (reporting week to 23:59 AEST 26 april 2020)*2020)	Australia	As of 26 April 2020	829 cases	18%	
(Lian et al., 2020)	China	17 January to 31 January 2020	475 cases	1%	N in ICU =5
(CDC,2020)	United States (49 states, the District of Columbia, and three U.S. territories)	12 February to 06 March 2020	2,253 cases	All ages - 4.9 - 11.5% 0-19 y :0% 20-44 y :2.0 - 4.2% 45-54 y :5.4 - 10.4% 55-64 y: 4.7 - 11.2% 65-74 y: 8.1 - 18.8% 75-84 y: 10.5 - 31.0% >=85 y: 6.3 - 29.0%	-The upper bound is the % ICU admissions with known ICU status. Lower bound is % ICU over the whole age group

Author	Country	Date	N-denominator	% admitted to the ICU	Notes
(Tradigo, Guzzi, & Veltri, 2020)	Italy	As of 22 March 2020	46,638 cases	6%	
(Cai et al., 2020)	China	11 January 2020 to 06 February 2020	298 cases	11%	
(Massonnaud, Roux, & Crépey, 2020)	France	As of 20 March 2020	2,030 cases	5%	
(ECDC, 2020)	16 countries of European Union, European Economic Area (EU/EEA) and the United Kingdom.	As of 24 March 2020	49,282 cases	4% Median 3%, IQR: 3%, 2-8%	-From 16 countries with >50% data completeness
(Castro, McCoy, & Perlis, 2020)	United States (Massachusetts)	As of June 5 2020	2,511 hospitalized	8.6%	N=215 in ICU
(Abdolahi et al., 2020)	Iran (Northeast)	24 February to 01 April 2020	427 hospitalized	19%	N=81 in ICU
(C. M. Petrilli et al., 2020a)	United stated (New York)	01 March 2020 to 08 April 2020	2,741 hospitalized	36%	
(Wang et al., 2020)	China	01 January to 28 January 2020	138-hospitalized	26%	
(Zhou et al., 2020)	China	As of 31 January 2020	191-hospitalized	26%	
(Rottoli et al., 2020)	Italy	28 February and 28	296 hospitalized	22%	

Author	Country	Date	N-denominator	% admitted to the ICU	Notes
		March 2020			
(Gold et al., 2020)	United States (Georgia)	As of 28 April 2020	Hospitalized All: 305 18-49 y: 89 50-64 y: 99 >=65 y: 117	All: 39% 18-49 y: 27% 50-64 y: 32% >=65 y: 54%	
(Cummings et al., 2020)	United States (New-York)	As of 14 April 2020	1,550-hospitalized	22%	
(A. B. Docherty et al., 2020b)	United Kingdom	As of 04 April 2020	1,914-hospitalized	17%	
(Fang et al., 2020)	China, USA, Germany, South Korea, Vietnam, Nepal, Thailand, Singapore, Canada and Italy	11 December 2019 to 14 February 2020	1,612 hospitalized	12%	-Systematic review with 72 retrospective studies (10 from outside of China and 52 from China)

PROPORTION OF PATIENTS REQUIRING MECHANICAL VENTILATION

Table 3 presents the percentage of patients who required an invasive mechanical ventilation among COVID-19 cases OR hospitalized patients OR patients admitted to the ICU.

TABLE 3: Proportion of ventilated patients

Author	Country	Date	N-denominator	% under ventilator	Notes
(Vena et al., 2020) *new*	Italy (Genoa)	25 February to 25 March 2020	65 in ICU	92%	N ventilated 60

Author	Country	Date	N-denominator	% under ventilator	Notes
(Turcotte et al., 2020) new	United States (Annapolis)	01 March to 12 April 2020	36 in ICU	94%	N ventilated 34
(L. Kim et al., 2020a) *new*	United States (14 States)	01 March to 25 July 2020	N hospitalized Patients <18 years=207 0–2 y=61 2–4 y=24 5–17 y=122	 Patients <18 years=5.8%% 0–2 y=0% 2–4 y= 16.7% 5–17 y= 6.6%	N ventilated All ages=12 0–2 y=0 2–4 y= 4 5–17 y=8
(Rizzo et al., 2020)	United States	20 February 2020 to 06 June 2020	 All : 16,099 <18 y: 185 18-65 y: 8,958 >65 y: 6,956	Median (IQR) All: 12.9% <18 y: 3.2% 18-65 y: 10.9% >65 y: 15.9%	 All: 2,085 <18 y: 6 18-65 y: 973 >65 y: 1,106
(Martín-Sánchez et al., 2020)	Spain (Madrid)	28 February 2020 to 31 March 2020	1,379 cases	6%	N=81
(Hsu et al., 2020)	United States (Boston ,Massachusetts)	01 March to 18 May 2020	N=188 in ICU	37%	N=69
(Shah et al., 2020)	United States (Southwest Georgia)	02 March 2020 to0 6 May 2020	N=123 in ICU	79%	N=97
(Suleyman et al., 2020)	United States (Detroit, Michigan)	09 March to 27 March 2020	N=141 in ICU	81%	N=114 under ventilation
(Yang et al., 2020)	China (Wuhan)	13 February to 14 March	N=66 in ICU	55%	N=36 under ventilation
(Fletcher et al., 2020)	United Kingdom	01January 2020 to 23 April 2020	1148 cases	7%	
(Lian et al., 2020)	China	17 January to 31 January 2020	475 cases	1%	N=4 under ventilation
(Castro et al., 2020)	United States (Massachusetts)	As of 05 June 2020	2,511 hospitalized	6.5%	N=164 under ventilation

Author	Country	Date	N-denominator	% under ventilator	Notes
(Casas Rojo et al., 2020)	Spain	As of 30 April 2020	6,424 hospitalized	5.6%	109 hospitals
(Garibaldi et al., 2020)	United States (Maryland DC region)	04 March to 24 April 2020	832 hospitalized	9.9%	N=74 under ventilation, 5 hospitals
(Regina et al., 2020)	Switzerland	01 March to 25 March 2020	200 hospitalized	19%	N=37 under ventilation
(C. M. Petrilli et al., 2020a)	United stated (New York)	01 March to 08 April 2020	990 patients in ICU	65%	N=647 under ventilation
(Almeshari et al., 2020)	Italy China United States		Patients in ICU	65% (95% CI: 49-80) I^2 84.37%	-Systematic review on mechanical ventilation, 5 studies included in the meta-analysis
(Mitra et al., 2020)	Canada (Vancouver)	21 February to 14 April 2020	117 patients in ICU	63.2%	N under ventilator=74
(A. B. Docherty et al., 2020a)	England, Scotland, and Wales	06 February to 19 April 2020	3,001 patients in ICU	55%	N=1,656 under ventilation 208 hospitals
(L. Kim et al., 2020b)	United States (14 States)	01 March to 02 May2020	798 patients in ICU	58%	N=462 under ventilation 154 acute care 137 hospitals in 74 counties in 14 States (see appendix for list of States)

Author	Country	Date	N-denominator	% under ventilator	Notes
(Gold et al., 2020)	United States (Georgia)	As of 28 April 2020	In ICU All: 119 18-49 y: 24 50-64 y: 32 >=65 y: 63	 All: 77% 18-49 y: 71% 50-64 y: 84% >=65 y: 76%	
(Cummings et al., 2020)	United States (New-York)	As of 14 April 2020	257 patients in ICU	78%	
(*COVID-19, australia: Epidemiology report 13 (reporting week to 23:59 AEST 26 april 2020)*2020)	Australia	As of 26 April 2020	148 patients in ICU	28%	
(Simonnet et al., 2020)	France	As of 06 April 2020	124 patients in ICU	69%	
(Zhou et al., 2020)	China	As of 31 Jan 2020	191 patients in ICU	64%	
(Cai et al., 2020)	China	11 January to 06 February 2020	32 patients in ICU	50%	

LENGTH OF STAY IN HOSPITAL (OVERALL)

Table 4 presents the median OR the mean of the overall length of stay of hospitalised patients, including patients admitted to the ICU.

TABLE 4: Length of stay in hospital in 27 studies

Author	Country	Date	N-hospitalized	LOS in hospital	Notes
(Vena et al., 2020)	Italy (Genoa)	25 February	275 hospitalized	Median (IQR) 12 days (5-19)	

Author	Country	Date	N-hospitalized	LOS in hospital	Notes
new		to 25 March 2020			
(Zhao et al., 2020) *new*	United States (New Jersey)	12 March to 08 April 2020	All=722 Non-survivors=186 Survivors=536	Median (IQR) All=7.0 days (4-13) Non-survivors=11 days (6-17) Survivors=6 days (3-11)	
(L. Kim et al., 2020a) {{61027;}} *new*	United States (14 States)	01 March to 25 July 2020	Patients <18 years =208 0–2 y=NR 2–4 y=NR 5–17 y=NR	Median (IQR) Patients <18 years =2.5 days (1—5) 0–2 y= 2 days (1—2) 2–4 y= 3 days (1—4) 5–17 y= 3 days (2—6)	NR=Not reported
(Perez-Guzman et al., 2020) *new*	United Kingdom (London)	07 March to 30 March 2020	All=614 Non-survivors=178 Survivors=381	Median (IQR) All=7 days (6-8) Non-survivors=7 days (5-8) Survivors=6 days (5-7)	
(Yu et al., 2020) *new*	China (Wuhan)	14 January to 28 February 2020	All=1663 Non-severe=799 Severe=864	Median (IQR) All=17.0 days (13.0–19.0) Non-severe=18.0 days (15.0–20.0) Severe=17.0 days (11.0–18.0)	-See definition of "severe disease" in appendix
(Gavin et al., 2020) *new*	United States (Indiana)	01 March to 31 March 2020	-All= 140 -No MV = 83 -Received MV and survived =35 -Received MV and died = 18	Mean (IQR) All= 10.7 days (4-15) No MV = 6.5 days (3-8) Received MV and survived =21.3 days (12-25) Received MV and died =12.8 days (8-16)	MV=Mechanical ventilation
(Nabavi, Javidarabshahi, Allahyari, & et al., 2020)	Iran (Mashhad)	February-April 2020	Mild/moderate=33 Severe=139 Critical=28	Mean (STD) Mild/moderate =6.48±3.94 Severe =7.27±3.39 Critical=7.56±4.74	-See definition of mild/moderate, severe and critical in appendix
(Rizzo et al., 2020)	United States	20 February	All : 16,099 <18y: 185	Median (IQR) All: 6.0 [4·0,11·0] <18y: 3.0 [2·0,5·0]	

Author	Country	Date	N-hospitalized	LOS in hospital	Notes
		to 06 June 2020	18-65y: 8,958 >65y: 6,956	18-65y: 6.0 [3·0,9·0] >65y: 7.0 [5·0,12·0]	
(Koleilat et al., 2020)	United States (New-York)	01 March, to 10 April 2020	DVT negative=117 DVT positive=18	Median (IQR) DVT negative =8.0 days (5.0-12.8) DVT positive 6.0 days (5.0-11.5) The difference was not statistically different (p=0.6)	DVT=deep venous thrombosis
(Lovinsky-Desir, 2020)	United States (New-York)	11 February to 05 July 2020	No asthma=1135 <21 y: 42 21-39y: 261 40-65y: 832 Asthma=163 <21 y: 13 21-39y: 39 40-65y: 111	Median (IQR) No asthma: 5 days (7) <21 y: 3 days (7) 21-39y: 4 days (4) 40-65y: 6 days (9) Asthma=6 days (9) <21 y: 9 days (14) 21-39y: 6 days (6) 40-65y: 6 days (9)	
(Ortiz-Brizuela et al., 2020)	Mexico (Mexico city)	26 February to 11 April	N=140	Median IQR) 5 days (3-8)	
(Shah et al., 2020)	United States (Southwest Georgia)	02 March to 06 May 2020	All=522 Non-Survivors=92 Survivors=430	Median (IQR) All= 6 days (4–11) Non-Survivors= 10 days (6-16) Survivors= 6 days (3-10)	
(Yang et al., 2020)	China (Wuhan)	13 February to 14 March 2020	N=463	Median (IQR) 19.0 days (13.0-27.0)	
(Vanhems et al., 2020)	France (Lyon)	08 February to 24 April 2020	All=412 Non-survivors=86 Survivors=326	Median (IQR) All= not reported Non survivors=10 days (6-14)	

Author	Country	Date	N-hospitalized	LOS in hospital	Notes
				Survivors=9 days (4-13)	
(Argenziano et al., 2020)	United Stated (New York)	01 March to 05 April 2020	850 hospitalized	Median (IQR) 6 days (3-14)	
(Casas Rojo et al., 2020)	Spain	As of 30 April 2020	6,424 hospitalized	Mean 10.4 days (range: 1-62 days)	109 hospitals
(Garibaldi et al., 2020)	United States (Maryland DC region)	04 March to 24 April 2020	832 hospitalized	Median (IQR) All: 6.1 days (IQR 2.6 - 10.8) Mild/moderate: 4.8 days (2.6- 8) Severe - 15 days (10.2-20.6) Dead - 6.8 days (IQR 3.3-11.2)	In 5hospitals -See definition of Mild/moderate and severe illness in appendix
(C. M. Petrilli et al., 2020a)	United stated (New York)	01 March to 08 April 2020	2,741 hospitalized	Median (IQR) 7 days IQR 3-13 Full range 0-52 days.	
(Rastad et al., 2020)	Iran	20 February and 25 March 2020	All=2,957 Non-survivors=301 Survivors=2656	Median (IQR) All: Not reported Non-survivors: 4 days (IQR 2-6) Survivors: 5 days (IQR 3-7)	
(Rees et al., 2020)	Systematic review gathering 52 studies -46 based in China and the other based in, United States, UK, Italy and whole EU region	24 December 2019 to 16 April 2020	Based on 45 studies	Median hospital LoS -China: 14 days (IQR: 10-19) -Outside China: 5 days (IQR: 3-9) outside of China	-Includes 3 pediatric studies -Includes patients with complete as well as patients with incomplete follow-up -Inclusion criteria are not always clearly specified

Author	Country	Date	N-hospitalized	LOS in hospital	Notes
					-Sample sizes varies from n=5 to n=2,936
(Gold et al., 2020)	United States (Georgia)	As of 28 April 2020	All: 305 18-49 y: 89 50-64 y: 99 >=65 y: 117	Median: All: 8.5 days (IQR 5.0–14.0) 18-49 y: 7.0 days (IQR 4.3–11.8) 50-64 y: 8.0 days (5.0–12.8) >=65 y: 10.0 days (6.0–16.0)	
(A. B. Docherty et al., 2020b)	United Kingdom	As of 04 April 2020	16,749	Median: 7 days [IQR 4,12]	
(Lv et al., 2020)	China	16 December 2019 to 21 February 2020	153	Median: -All: 15 days IQR(10-23)	Exclude patients in ICU
(Argenziano et al., 2020)	United States (New-York)	11 March to 15 April 2020	1,000	Mean: 11.4 days (5.01) n=618	
(Guan et al., 2020)	China	As of 29 January 2020	All=1,099 Severe=173 Non-severe=926	Median -All:12 days (IQR: 10-14) -Severe : 13 days (IQR: 11.5-17) -Non-severe: 11 days (10-13)	-See definition of 'severe' in appendix
(Zhou et al., 2020)	China	As of January 2020	191	Median: 11 days (IQR 7-14) days	
(Cao et al., 2020)	China	18 January to 03 February 2020	100	Median: 16 days (IQR 13-18)	

LENGTH OF STAY IN THE ICU

Table 5 presents the median OR the mean of the length of stay of all patients in the ICU. A specification is added in the notes section when the LOS is specific to sub-group such as survivors or non survivors.

TABLE 5: LOS in ICU in 24 studies

Author	Country	Date	N- in the ICU	LOS in ICU	Notes
(Vena et al., 2020) *new*	Italy (Genoa)	25 February to 25 March 2020	46 hospitalized	Median (IQR) 12 days (6.5-21.5)	
(Zhao et al., 2020) *new*	United States (New Jersey)	12 March to 08 April 2020	All=193 Non-survivors=107 Survivors=86	Median (IQR) All =8.5 days (4-14) Non-survivors =8 days (4-12.5) Survivors =10 days (4-20)	
(Turcotte et al., 2020) *new*	United States (Annapolis)	01 March to 12 April 2020	36 hospitalized	Mean (STD) 14.86 days (11.35) Confidence Interval 95% 14.35 – 22.38 days Median 20 days	N in ICU 36
(L. Kim et al., 2020a) *new*	United States (14 States)	01 March to 25 July 2020	Patients <18 y=208 0–2 y=NR 2–4 y=NR 5–17 y=NR	Median (IQR) Patients <18 y=2 days (1—5) 0–2 y= 1day (1—3) 2–4 y= 2 days (2—5) 5–17 y= 3.5 days (1—7)	NR=Not reported
(Rizzo et al., 2020)	United States	20 February 2020 to 06 June 2020	All : 3,768 <18 y: 31 18-65 y: 1,777 >65 y: 1,960	Median (IQR) All: 4.0 [1·0,10·0] <18 y: 2.0 [1·0,7·0] 18-65 y: 4.0 [1·0,10·0] >65 y: 4.0 [1·0,10·0]	
(Xu et al., 2020)	China (Wuhan)	12 January to 03 February 2020	All=239 Non-survivors=147	Median (IQR) All=17 days (10–26) Non-survivors= 12 days (8–18)	

Author	Country	Date	N- in the ICU	LOS in ICU	Notes
			Survivors=92	Survivors= 26.5 (19-46.5)	
(Suleyman et al., 2020)	United States (Detroit, Michigan)	09 March to 27 March 2020	N=141 in ICU	Median (IQR) 15 days (9-23)	
(Yang et al., 2020)	China (Wuhan)	13 February to 14 March 2020	N=66 in ICU	Median (IQR) 14.5 days (IQR 7.3-21.8)	
(Ayed et al., 2020)	Kuwait	As of May 20, 2020	All=103 in ICU Non survivors=45 Survivors (discharged)=47	Median (IQR) All=11 days (6-18.5) Non survivors =13 days (7-23) Survivors= 10 days (6-15)	Non-discharged:N=11
(Vanhems et al., 2020)	France (Lyon)	08 February to 24 April 2020	All=66 in ICU Non-survivors=30 Survivors=36	Median (IQR) All= not reported Non survivors=10.5 days (5-15.5) Survivors=12 days (9-17.2)	
(Argenziano et al., 2020)	United Stated (New York)	01 March to 05 April 2020	N-236 patients in ICU	Median (IQR) 23 days (12-32)	
(Mitra et al., 2020)	Canada (Vancouver)	21 February to 14 April 2020	117 patients in ICU	Median (IQR) Overall: 9 days (5–21) Discharged from ICU: (n = 87) 7 days (3–16)	
(C. M. Petrilli et al., 2020a)	United stated (New York)	01 March to 08 April 2020	990 patients in ICU	Median (IQR) 9 days (5-17)	
(L. Kim et al., 2020b)	United States (14 States)	01 March to 02 May 2020	798 patients in ICU	Median 6 days (range, 1-41; IQR, 2–11)	N=462 under ventilation 154 acute care 137 hospitals in

Author	Country	Date	N- in the ICU	LOS in ICU	Notes
					74 counties in 14 states -See list of states in appendix
(Rees et al., 2020)	Systematic review gathering 52 studies -46 based in China and the other based in, United States, UK, Italy and whole EU region	24 December 2019 to 16 April 2020	Based on 9 studies	Median hospital LOS -China: 8 days (IQR 5-13) days -Outside China: 7 days (IQR: 4-11) outside of China	-Includes 3 pediatric studies -Includes patients with complete as well as patients with incomplete follow-up -Inclusion criteria are not always clearly specified -Sample sizes varies from n=5 to n=2,936
(Gold et al., 2020)	United States (Georgia)	As of 28 April 2020	All: 119 18-49 y: 24 50-64 y: 32 >=65 y: 63	Median: All: 8.0 (5.0–12.0) 18-49 y: 7.0 (4.0–14.0) 50-64 y: 8.0 (6.0–11.0) >=65 y: 9.0 (5.0–12.0)	
(C. M. Petrilli et al., 2020b)	United States (New-York)	As of 07 April 2020	445	Median: -Discharged or died: 6 days (IQR 3-9) -Still in ICU 11 days (IQR 8-15)	
(Lv et al., 2020)	China	16 December 2019 to 21 February 2020	55	Median: 16 days (IQR 10-21)	
(Argenziano et al., 2020)	United States (New-York)	11 March to 15 April 2020	231	Mean: 14.6 days (SD 5.94)	
(Zhou et al., 2020)	China	As of January 2020	50	Median: 8 days (range 4–12)	
(Zhang et al., 2020)	China	02 January 2020 to 10	All=32	Median (IQR)	

Author	Country	Date	N- in the ICU	LOS in ICU	Notes
		February 2020	Non-survivors=9 Survivors=23	Non-survivors:11.0 days (4.5-14.5) Survivors: 8.0 days (range 5.0-13.0)	
(Grasselli et al., 2020)	Italy	20 February to 18 March 2020	1,591	Median: 9 days (6-13 [95% CI, 9-9])	
(Cao et al., 2020)	China	18 January to 03 February 2020	100	Median: All: 11 days (IQR 7 to 17) Survivors: 11 days (IQR 9 to 14) Non-survivors: 11 days (IQR 7 to 17)	Clinical trial: patients under standard treatment
(Cao et al., 2020)	China	18 January to 03 February 2020	99	Median: All: 6 days (IQR 2 to 11) Survivors: 9 days (IQR 5 to 44) Non survivors: 6 days (IQR 2 to 11)	Clinical trial: patients under Lopinavir-Ritonavir

DURATION OF MECHANICAL VENTILATION

Table 6 presents the median OR the mean of the duration of mechanical ventilation. A specification is added in the notes section when the LOS is specific to sub-group such as survivors or non survivors.

TABLE 6: Duration of ventilation in 9 studies

Author	Country	Date	N- under ventilation	Duration of ventilation	Notes
(Vena et al., 2020) *new*	Italy (Genoa)	25 February to 25 March 2020	60 hospitalized	Median (IQR) 9 days (IQR, 4.5-16.5)	
(Turcotte et al., 2020) *new*	United States (Annapolis)	01 March to 12 April 2020	34 hospitalized	Mean (STD) 11.74 days (8.17)	

Author	Country	Date	N- under ventilation	Duration of ventilation	Notes
				Confidence Interval 95% 8.88 – 14.59 days Median 9 days	
(Gavin et al., 2020) *new*	United States (Indiana)	01 March to 31 March 2020	-All=53 -Received MV and survived =35 -Received MV and died = 18	Mean (IQR) All= 10.9 days (6-14) Received MV and survived =11.1 days (6-14) Received MV and died =10.6 days (6-13)	MV=Mechanical ventilation
(Almeshari et al., 2020)	China United-States		2 studies N=18 N=4	Median for 2 studies (no meta-analysis performed) 10-17 days with IQR 2-19 days	-Systematic review on mechanical ventilation. Duration of ventilation based on 2 studies with one study including only 4 patients
(Mitra et al., 2020)	Canada (Vancouver)	21 February to 14 April 2020	74	Median (IQR) 13.5 days (8–22)	
(Regina et al., 2020)	Switzerland	01 March to 25 March 2020	37	Median 6 days (IQR 5·00 - 11·00)	
(Gold et al., 2020)	United States (Georgia)	As of 28 April 2020	All: 92 18-49 y: 17 50-64 y: 27 >=65 y: 48	Median: All: 9.0 (5.0–12.0) 18-49 y: 8.5 (5.0–13.3) 50-64 y: 9.0 (5.5–10.5) >=65 y: 10.0 (6.0–12.0)	
(Bhatraju et al., 2020)	United States (Seattle region)	February 24 to March 09, 2020	18	10 days (IQR 7–12)	All ventilated patients (including patients still under ventilation)

Author	Country	Date	N- under ventilation	Duration of ventilation	Notes
(Bhatraju et al., 2020)	United States (Seattle region)	24 February to 09 March 2020	15	11 days (IQR range 7–12)	Extubated patients

Methods:

A weekly scan of the literature (published and pre-published) related to hospitalization and length of stay of COVID-19 patients is conducted by the Emerging Science Group, PHAC. Searches to retrieve relevant literature are conducted in the Refworks database and an Excel Spreadsheet maintained by the Emerging Science team. The Refworks database and the Excel file gather literature related to COVID-19 since the beginning of the outbreak. The literature is retrieved from Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced, the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley.

This review contains research related to hospitalization and length of stay of COVID-19 patients published up to August 20, 2020

Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review. Research studies with large sample size are preferred. Studies with less than 100 hospitalized patients, less than 25 patients admitted in ICU, or less than 10 patients under ventilation are excluded. However, this selection criteria was not applied to systematic reviews.

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Appendix

(Guan et al., 2020)	Definition of 'severe':
	Validated definition includes either 1 major or 3 or more minor criteria
	• Minor criteria
	  ○ Respiratory rate > 30 breaths/min
	  ○ PaO2/FIO2 ratio < 250
	  ○ Multilobar infiltrates
	  ○ Confusion/disorientation
	  ○ Uremia (blood urea nitrogen level >20 mg/dl)
	  ○ Leukopenia* (white blood cell count, 4,000 cells/ml)
	  ○ Thrombocytopenia (platelet count, 100,000/ml)
	  ○ Hypothermia (core temperature , 368C)
	  ○ Hypotension requiring aggressive fluid resuscitation
	• Major criteria
	  ○ Septic shock with need for
	  ○ vasopressors
	  ○ Respiratory failure requiring mechanical

(L. Kim et al., 2020b)	-States included in the study: California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New-York, Ohio, Oregon, Tennessee, and Utah.
(Garibaldi et al., 2020)	-Definition are based on WHO classification (WHO. WHO R&D Blueprint: Novel Coronavirus. COVID-19 Therapeutic Trial Synopsis2020.) -Hospitalized, mild disease: Hospitalized, no oxygen therapy OR oxygen by mask or nasal prongs. -Hospitalized, severe disease: Non-invasive ventilation or high flow oxygen, Intubation od mechanical ventilation, ventilation + additional organ support – pressor, RRT, ECMO.
(Nabavi et al., 2020)	-Mild/Moderate: no or mild pneumonia; -Severe: with dyspnea (respiratory rate >30) or hypoxia (O2 saturation <93); Critical: with respiratory failure, shock, or multi-organ dysfunction
(Yu et al., 2020)	-Severe COVID-19 was defined if they meet one of following criteria: (1) Respiratory distress with respiratory frequency ≥30 breaths per min with shortness of breath or difficulty breathing; (2) Oxygen saturation ≤93% at rest; (3) Artery partial pressure of oxygen (PaO2)/inspired oxygen fraction (FiO2) ≤300 mmHg (1 mmHg = 0.133 kPa).

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Preuve émergente sur la COVID-19

Examen rapide des hospitalisations liées à la COVID-19 et de la durée du séjour

Introduction

Cette revue rapide a permis de cerner et de résumer les données publiées et pas encore publiées jusqu'au 20 août 2020 sur la proportion de cas de COVID-19 ayant donné lieu à des hospitalisations, à des admissions aux services de soins intensifs (SSI) et à l'utilisation d'un ventilateur mécanique invasif. Elle présente également des données sur la durée moyenne ou médiane du séjour à l'hôpital ou aux soins intensifs, ainsi que la période pendant laquelle le patient a été sous ventilateur. La rareté des données sur les hospitalisations dans le contexte canadien et la variabilité de ces données entre les études ont mené à la collecte et à la synthèse de résultats provenant de partout dans le monde afin d'améliorer ou de valider les paramètres des modèles prédictifs visant à mesurer la capacité des systèmes de santé canadiens à gérer la pandémie.

Quoi de neuf?

- Six nouvelles études ont été menées aux États-Unis (3), au Royaume-Uni (1), en Italie (1) et en Chine (1). Les tableaux suivants ont été mis à jour Proportion de patients au SERVICE **des soins intensifs**, Proportion de patients ayant **exigé un ventilateur**, Durée du séjour **à l'hôpital**, Durée du séjour **aux soins intensif**, Durée de la **ventilation**
- Une étude menée aux États-Unis a porté exclusivement sur des patients âgés de moins de 18 ans. La durée du séjour par groupe d'âge a été fournie.
- Les modifications sont mises en évidence.

Points clés

- Le pourcentage moyen d'hospitalisation de patients atteints de COVID-19 variait de 11 % à 77 % dans la population incluse dans l'étude. La proportion d'hospitalisations était cependant plus grande chez les personnes âgées.
- Les variations étaient les suivantes en ce qui concerne le pourcentage d'admissions de patients atteints de COVID-19 au service de soins intensifs :
    - Entre 1 et 32% de patients infectés;
    - Entre 12 et 40 % de patients hospitalisés.
- Le pourcentage de patients qui se sont retrouvés sous ventilateur variait ainsi :
    - Entre 1 et 13 % de patients infectés;

  - Entre 5 % et 19 % de patients hospitalisés (y compris ceux qui se sont retrouvés aux soins intensifs);
  - De 28 % à 94 % de patients aux soins intensifs, alors que deux études récentes indiquaient des pourcentages de 92 % et de 94 %.
- La durée médiane d'hospitalisation (y compris le séjour aux soins intensifs) des patients atteints de COVID-19 entre les études variait de 4 à 19 jours avec un écart interquartile (EI) de 3 à 27 jours :
  - Chez les survivants, la durée médiane de l'hospitalisation variait de 5 à 9 jours avec un EI de 3 à 13.
  - Chez les patients décédés, la durée médiane de l'hospitalisation variait de 4 à 10 jours avec un EI de 3 à 16.
- La durée médiane du séjour aux soins intensifs variait de 4 à 23 jours avec un EI de 2 à 32 jours pour tous les patients qui s'y sont retrouvés.
  - Chez les survivants, la durée médiane du séjour aux soins intensifs variait de 8 à 26 jours avec un EI de 5 à 46 jours.
  - Chez les patients décédés, la durée médiane du séjour aux soins intensifs variait de 6 à 12 jours, avec un intervalle de 2 à 26 jours.
- La durée médiane d'utilisation du ventilateur mécanique pour les patients qui en ont eu besoin était de 6 à 13 jours, avec un intervalle de 5 à 22 jours.
- En août 2020, MMWR a publié une analyse des données sur l'hospitalisation pour COVID-19 des enfants provenant de 14 États (L. Kim et al., 2020a). Cette analyse a révélé que même si le taux cumulatif d'hospitalisations associées à la COVID-19 chez les enfants (8,0 pour 100 000 habitants) était faible comparativement à celui des adultes (164,5), le taux d'hospitalisation chez les Hispaniques était huit fois plus élevé et qu'il était cinq fois plus élevé chez les enfants noirs que celui qui a été observé chez les enfants blancs. Une condition médicale sous-jacente était également présente chez 42 % des enfants, l'obésité était la plus prévalente.
  - Le taux d'hospitalisation était le plus élevé chez les enfants de moins de deux ans (24,8 pour 100 000 habitants).
  - Un tiers des patients hospitalisés ont été admis aux soins intensifs (33,2 %).
  - La proportion de patients hospitalisés qui ont exigé le recours à un ventilateur mécanique invasif était de 5,8 %.
  - La durée médiane de l'hospitalisation globale était de 2,5 jours, avec un intervalle de 1 à 5 jours.
  - La durée médiane du séjour aux soins intensifs était de 2 jours, avec un intervalle de 1 à 5 jours.

Vue d'ensemble des éléments de preuve

La revue a permis de cerner et de résumer 64 études publiées et pas encore publiées. Bon nombre des études étaient des études d'observation rétrospectives effectuées au niveau de l'hôpital. Elles ne représentent donc pas nécessairement les statistiques nationales. Il faut faire preuve de prudence au moment d'interpréter les résultats lorsque les études ne comportent qu'un échantillon de petite taille.

CONTENU

PROPORTION DES HOSPITALISATIONS (DANS L'ENSEMBLE)

Le tableau 1 présente le pourcentage de patients hospitalisés en raison de la COVID-19 dans l'ensemble, ce qui inclut les patients admis aux services de soins intensifs (SSI).

TABLEAU 1: Proportion d'hospitalisations déclarées dans 14 études

Auteur	Pays	Date	Dénominateur n	% d'hospitalisations	Remarques
(Rizzo et al., 2020)	États-Unis	Du 20 février 2020 au 6 juin 2020	<18 ans : 1 767 18 à 29 ans : 8 214 30 à 39 ans : 11 034 40 à 49 ans : 11 635 50 à 64 ans : 21 606 65 à 74 ans : 10 946 75 à 84 ans : 6 689 >85 ans : 4 926	<18 ans : 10,8 % 18 à 29 ans : 9,8 % 30 à 39 ans : 12,2 % 40 à 49 ans : 16,6 % 50 à 64 ans : 22,7 % 65 à 74 ans : 30,1 % 75 à 84 ans : 37,9 % >85 ans : 35,8 %	N hospitalisations <18 ans : 190 18 à 29 ans : 802 30 à 39 ans : 1 351 40 à 49 ans : 1 933 50 à 64 ans : 4 906 65 à 74 ans : 3 298 75 à 84 ans : 2 537 >85 ans : 1 763
(McPadden et al., 2020)	États-Unis	Du 1er mars 2020 au 4 mai 2020	Tous = 7 995 18 à 34 ans : 1 570 35 à 44 ans : 1 321 45 à 54 ans : 1 546 55 à 64 ans : 1 583 65 à 74 ans : 885 75 à 84 ans : 565 > = 85 ans : 516	Tous = 27 % 18 à 34 ans : 11 % 35 à 44 ans : 14 % 45 à 54 ans : 17 % 55 à 64 ans : 27 % 65 à 74 ans : 45 % 75 à 84 ans : 66 % > = 85 ans : 69 %	Tous = 2 154 18 à 34 ans : 146 35 à 44 ans : 181 45 à 54 ans : 258 55 à 64 ans : 435 65 à 74 ans : 402 75 à 84 ans : 374 > = 85 ans : 358
(Martín-Sánchez et al., 2020)	Espagne (Madrid)	Du 28 février 2020 au 31 mars 2020	Total = 1 379 cas 18 à 44 ans : 250 45 à 54 ans : 246 55 à 64 ans : 247 65 à 74 ans : 237 75 à 84 ans : 235 > = 85 ans : 164	Tous : 74,6 % 18 à 44 ans : 50 % 45 à 54 ans : 61,4 % 55 à 64 ans : 71,7 % 65 à 74 ans : 86,1 %	Total = 1 030 cas 18 à 44 ans : 125 45 à 54 ans : 151 55 à 64 ans : 177 65 à 74 ans : 204 75 à 84 ans : 216 > = 85 ans : 156

Auteur	Pays	Date	Dénominateur n	% d'hospitalisations	Remarques
				75 à 84 ans : 91,9 % > = 85 ans : 95,1 %	
(Hsu et al., 2020)	États-Unis (Boston, Massachusetts)	Du 1er mars au 18 mai 2020	2 729 cas	40 %	N = 1 088
(Soares, Mattos, & Raposo, 2020)	Brésil (État d'Espírito Santo)	Au 11 juin 2020	10 713 cas	11 %	N = 1 152
(Alsofayan, Althunayyan, Khan, Hakawi, & Assiri, 2020)	Arabie Saoudite	Du 1er mars au 31 mars 2020	1 519 cas	67 %	N = 513 hospitalisations
(Reilev et al., 2020)	Danemark	Du 27 février 2020 au 30 avril 2020	Cas Tous = 9 519 0 à 9 ans : 135 10 à 19 ans : 342 20 à 29 ans : 1 212 30 à 39 ans : 1 234 40 à 49 ans : 1 556 50 à 59 : 1 466 60 à 69 ans : 801 70 à 79 ans : 316 80 à 89 ans : 260 90+ ans : 227	Tous : 22 % 0 à 9 ans : 1,8 % 10 à 19 ans : 4,6 % 20 à 29 ans : 16 % 30 à 39 ans : 17 % 40 à 49 ans : 21 % 50 à 59 ans : 20 % 60 à 69 ans : 11 % 70 à 79 ans : 4,3 % 80 à 89 ans : 3,5 % 90+ ans : 2,4 %	N hospitalisations Toutes = 2 090 0 à 9 ans : 10 10 à 19 ans : 12 20 à 29 ans : 51 30 à 39 ans : 81 40 à 49 ans : 183 50 à 59 ans : 310 60 à 69 ans : 351 70 à 79 ans : 541 80 à 89 ans : 431 90+ ans : 120
(*COVID-19, australia: Epidemiology report 13 (reporting week to 23:59 AEST 26 april 2020)*2020)	Australie	Au 26 avril 2020	6 711 cas	12 %	

Auteur	Pays	Date	Dénominateur n	% d'hospitalisations	Remarques
(CDC, 2020)	États-Unis (49 États, le District de Columbia et trois territoires américains)	12 février au 6 mars 2020	2 712 cas	Tous les âges - 20,7 à 31,4 % 0 à 19 ans : 14,3 à 20,8 % 20 à 44 ans : 21,2 à 28,3 % 45 à 54 ans : 20,5 à 30,1 % 55 à 64 ans : 28,6 à 43,5 % 65 à 74 ans : 30,5 à 58,7 % 75 à 84 ans : 30,5 à 58,7 % > = 85 ans : 31,3 à 70,3 %	– La limite supérieure est le pourcentage d'hospitalisations dont le statut d'hospitalisation est connu. La valeur limite inférieure est le pourcentage d'hospitalisations pour l'ensemble de la tranche d'âge
(Tadrigo et Veltri, 2020)	Italie	Au 22 mars 2020	46 638 cas de COVID-19	49 %	
(ECDC, 2020)	16 pays de l'UE/EEE et le Royaume-Uni.	Au 24 mars 2020	43 438 cas de COVID-19	Tous les âges 30 % Médiane 24 %, EI : 11 à 41 % < 10 ans : 11 à 25 % 10 à 19 ans : 2 à 15 % 20 à 29 ans : 9 à 13 % 30 à 39 ans : 10 à 13 % 40 à 49 ans : 5 à 12 % 50 à 59 ans : 11 à 14 % 60 à 69 ans : 17 à 23 % 70 à 79 ans : 27 à 34 %	– Données provenant de 14 pays avec un taux d'exhaustivité de plus de 50 % pour l'hospitalisation – Ces chiffres ont été extraits de la figure 3 du rapport et été évalués de façon approximative

Auteur	Pays	Date	Dénominateur n	% d'hospitalisations	Remarques
				> = 80 ans : 26 à 35 %	
(Team,COVID-National Incident Room Surveillance, 2020)	Australie	Au 22 mars 2020	717 cas	26 %	
(Cai et al., 2020)	Chine	Du 11 janvier 2020 au 6 février 2020	298 cas	77 %	
(Verity et al., 2020)	Chine	Au 8 février 2020	Cas 0 à 9 ans : 13 10 à 19 ans : 50 20 à 29 ans : 437 30 à 39 ans : 733 40 à 49 ans : 743 50 à 59 ans : 790 60 à 69 ans : 560 70 à 79 ans : 263 80+ ans : 76	0 à 9 ans : 0 % 10 à 19 ans : 0,04 % (0,02, 0,08) 20 à 29 ans : 1,1 % (0,62, 2,1) 30 à 39 ans : 3,4 % (2,1, 7,0) 40 à 49 ans : 4,3 % (2,5, 8,7) 50 à 59 ans : 8,2 % (4,9, 16,7) 60 à 69 ans : 11,8 % (7,0, 24,0) 70 à 79 ans : 16,6 % (9,9, 33,8) 80+ ans : 18,4 % (11,0, 37,6)	– Dans cette étude effectuée à partir d'un sous-ensemble de cas signalés en Chine continentale, les auteurs estiment la proportion de toutes les infections pour lesquelles des patients auraient été hospitalisés selon la définition des cas graves dans le contexte du Royaume-Uni (contrairement à tous les patients infectés en Chine).

PROPORTION DE PATIENTS ADMIS AUX SOINS INTENSIFS

Le tableau 2 présente le pourcentage de patients admis aux soins intensifs parmi les cas de COVID-19 OU les patients hospitalisés.

TABLEAU 2: Proportion de patients au service des soins intensifs dans 34 études

Auteur	Pays	Date	Dénominateur n	% admis aux SSI	Remarques
(Vena et al., 2020) *nouveaux*	Italie (Gênes)	25 février au 25 mars 2020	317 hospitalisations	20,5 %	N aux SSI 65
(Turcotte et al., 2020) *nouveaux*	États-Unis (Annapolis)	Du 1er mars au 12 avril 2020	117 hospitalisations	30,8 %	N aux SSI 36
(L. Kim et al., 2020a) {{61027;}} *nouveaux*	États-Unis (14 États)	Du 1er mars au 25 juillet 2020	Patients <18 ans = 208 0 à 2 ans = 61 2 à 4 ans = 24 5 à 17 ans = 123	Patients <18 ans = 33,2 % 0 à 2 ans = 31,1 % 2 à 4 ans = 37,5 % 5 à 17 ans = 33,3%	N aux SSI Tous les âges = 69 0 à 2 ans = 19 2 à 4 ans = 9 5 à 17 ans = 41
(Rizzo et al., 2020)	États-Unis	Du 20 février 2020 au 6 juin 2020	Tous : 16 099 cas < 18 ans : 185 18 à 65 ans : 8 958 >65 ans : 6 956	Médiane (EI) Tous : 23,4 % < 18 ans : 16,8 % 18 à 65 ans : 19,8 % >65 ans : 28,1 %	Tous : 3 768 < 18 ans : 31 18 à 65 ans : 1 777 >65 ans : 1 960
(Martín-Sánchez et al., 2020)	Espagne (Madrid)	Du 28 février 2020 au 31 mars 2020	Total = 1 379 cas 18 à 44 ans : 250 45 à 54 ans : 246 55 à 64 ans : 247 65 à 74 ans : 237 75 à 84 ans : 235 > = 85 ans : 164	Tous : 5,9 % 18 à 44 ans : 3,2 % 45 à 54 ans : 6,1 % 55 à 64 ans : 12,1 % 65 à 74 ans : 8,9 % 75 à 84 ans : 3,4 %	Tous : 82 cas 18 à 44 ans : 8 45 à 54 ans : 15 55 à 64 ans : 30 65 à 74 ans : 21 75 à 84 ans : 8

Auteur	Pays	Date	Dénominateur n	% admis aux SSI	Remarques
				> = 85 ans : 0 %	> = 85 ans : 0
(Hsu et al., 2020)	États-Unis (Boston, Massachusetts)	Du 1er mars au 18 mai 2020	1 088 hospitalisations	17 %	N = 188
(Shah et al., 2020)	États-Unis (sud-ouest de la Géorgie)	Du 2 mars 2020 au 6 mai 2020	N = 522 Hospitalisations	23,6 %	N = 123
(Suleyman et al., 2020)	États-Unis (Detroit, Michigan)	Du 9 au 31 mars 2020	N = 355 hospitalisations	40 %	N = 141 aux SSI
(Yang et al., 2020)	Chine (Wuhan)	Du 13 février au 14 mars	N = 463 hospitalisations	14 %	N = 66 aux SSI
(Alsofayan et al., 2020)	Arabie Saoudite	Du 1er au 31 mars 2020	N = 1 519 cas	4,7 %	N = 36 aux SSI
(Reilev et al., 2020)	Danemark	Du 27 février 2020 au 30 avril 2020	Cas Tous = 9 519 0 à 9 ans : 135 10 à 19 ans : 342 20 à 29 ans : 1 212 30 à 39 ans : 1 234 40 à 49 ans : 1 556 50 à 59 ans : 1 466 60 à 69 ans : 801 70 à 79 ans : 316 80 à 89 ans : 260 90 ans et plus : 227	Tous : 3,2 % 0 à 9 ans : 0 % 10 à 19 ans : 0 % 20 à 29 ans : 2 % 30 à 39 ans : 3 % 40 à 49 ans : 9 % 50 à 59 ans : 15 % 60 à 69 ans : 27 % 70 à 79 ans : 34 % 80 à 89 ans : 11 % 90 ans et plus : 0 %	N aux SSI Tous = 300 0 à 9 ans : 0 10 à 19 ans : 0 20 à 29 ans : 6 30 à 39 ans : 10 40 à 49 ans : 161 50 à 59 ans : 262 60 à 69 ans : 80 70 à 79 ans : 102 80 à 89 ans : 32 90 ans et plus : 0
(A. B. Docherty et al., 2020a)	Royaume-Uni	Du 6 février au 19 avril 2020	18 183 cas	17 %	208 hôpitaux

Auteur	Pays	Date	Dénominateur n	% admis aux SSI	Remarques
(L. Kim et al., 2020b)	États-Unis (14 États)	Du 1er mars au 2 mai 2020	2 491 cas	32 %	- 154 hôpitaux de soins actifs dans 74 comtés dans 13 États – Voir l'annexe pour la liste des États
(Fletcher et al., 2020)	Royaume-Uni	Du 1er janvier 2020 au 23 avril 2020	1 148 cas	10 %	
(Almazeedi et al., 2020)	Koweït	Du 24 février 2020 au 20 avril 2020	1 096 cas	4 %	
(Liang et al., 2020)	Chine	Au 31 janvier 2020	1 590 cas	8 %	Cas provenant de 575 hôpitaux dans 31 régions administratives provinciales
(*COVID-19, australia: Epidemiology report 13 (reporting week to 23:59 AEST 26 april 2020)*2020)	Australie	Au 26 avril 2020	829 cas	18 %	
(Lian et al., 2020)	Chine	Du 17 janvier au 31 janvier 2020	475 cas	1 %	N aux SSI = 5
(CDC, 2020)	États-Unis (49 États, le District de Columbia et	Du 12 février au 6 mars 2020	2 253 cas	Tous les âges - de 4,9 à 11,5 % 0 à 19 ans : 0 %	– La limite supérieure est le pourcentage

Auteur	Pays	Date	Dénominateur n	% admis aux SSI	Remarques
	trois territoires américains)			20 à 44 ans : 2,0 à 4,2 % 45 à 54 ans : 5,4 à 10,4 % 55 à 64 ans : 4,7 à 11,2 % 65 à 74 ans : 8,1 à 18,8 % 75 à 84 ans : 10,5 à 31,0 % > = 85 ans : 6,3 à 29,0 %	d'admissions aux SSI dont l'état est connu. La valeur limite inférieure est le pourcentage d'admissions aux SSI pour toute la tranche d'âge
(Tradigo, Guzzi, & Veltri, 2020)	Italie	Au 22 mars 2020	46 638 cas	6 %	
(Cai et al., 2020)	Chine	Du 11 janvier 2020 au 6 février 2020	298 cas	11 %	
(Massonnaud, Roux, & Crépey, 2020)	France	Au 20 mars 2020	2 030 cas	5 %	
(ECDC, 2020)	16 pays de l'Union européenne, de l'Espace économique européen (UE/EEE) et du Royaume-Uni.	Au 24 mars 2020	49 282 cas	4 % Médiane 3%, EI : 3 %, 2 à 8 %	– De 16 pays dont les données sont complètes à plus de 50 %
(Castro, McCoy, & Perlis, 2020)	États-Unis (Massachusetts)	Au 5 juin 2020	2 511 hospitalisations	8,6 %	N = 215 aux SSI
(Abdolahi et al., 2020)	Iran (nord-est)	Du 24 février au 1er avril 2020	427 hospitalisations	19 %	N = 81 aux SSI
(C. M. Petrilli et al., 2020a)	États-Unis (New York)	Du 1er mars 2020 au 8 avril 2020	2 741 hospitalisations	36 %	

Auteur	Pays	Date	Dénominateur n	% admis aux SSI	Remarques
(Wang et al., 2020)	Chine	Du 1er janvier au 28 janvier 2020	138 hospitalisations	26 %	
(Zhou et al., 2020)	Chine	Au 31 janvier 2020	191 hospitalisations	26 %	
(Rottoli et al., 2020)	Italie	28 février et 28 mars 2020	296 hospitalisations	22 %	
(Gold et al., 2020)	États-Unis (Géorgie)	Au 28 avril 2020	Hospitalisations Tous : 305 18 à 49 ans : 89 50 à 64 ans : 99 > = 65 ans : 117	Tous : 39 % 18 à 49 ans : 27 % 50 à 64 ans : 32 % > = 65 ans : 54 %	
(Cummings et al., 2020)	États-Unis (New York)	Au 14 avril 2020	1 550 hospitalisations	22 %	
(A. B. Docherty et al., 2020b)	Royaume-Uni	Au 4 avril 2020	1 914 hospitalisations	17 %	
(Fang et al., 2020)	Chine, États-Unis, Allemagne, Corée du Sud, Vietnam, Népal, Thaïlande, Singapour, Canada et Italie	Du 11 décembre 2019 au 14 février 2020	1 612 hospitalisations	12 %	– Revues systématiques avec 72 études rétrospectives (10 provenant de l'extérieur de la Chine et 52 provenant de la Chine)

PROPORTION DE PATIENTS NÉCESSITANT UN VENTILATEUR MÉCANIQUE

Le tableau 3 présente le pourcentage de patients ayant nécessité un ventilateur mécanique invasif parmi les cas de COVID-19 OU les patients hospitalisés OU les patients admis aux soins intensifs.

TABLEAU 3: Proportion de patients ayant exigé un ventilateur

Auteur	Pays	Date	Dénominateur n	% sous ventilateur	Remarques
(Vena et al., 2020) *nouveaux*	Italie (Gênes)	25 février au 25 mars 2020	65 aux SSI	92 %	N sous ventilateur 60
(Turcotte et al., 2020) nouveaux	États-Unis (Annapolis)	Du 1er mars au 12 avril 2020	36 aux SSI	94 %	N sous ventilateur 34
(L. Kim et al., 2020a) *nouveaux*	États-Unis (14 États)	Du 1er mars au 25 juillet 2020	N hospitalisations Patients <18 ans = 207 0 à 2 ans = 61 2 à 4 ans = 24 5 à 17 ans = 122	Patients < 18 ans = 5,8 % 0 à 2 ans = 0% 2 à 4 ans = 16,7% 5 à 17 ans = 6,6%	N sous ventilateur Tous les âges = 12 0 à 2 ans = 0 2 à 4 ans = 4 5 à 17 ans = 8
(Rizzo et al., 2020)	États-Unis	Du 20 février 2020 au 6 juin 2020	Tous : 16 099 < 18 ans : 185 18 à 65 ans : 8 958 >65 ans : 6 956	Médiane (EI) Tous : 12,9 % < 18 ans : 3,2 % 18 à 65 ans : 10,9 % >65 ans : 15,9 %	Tous : 2 085 < 18 ans : 6 18 à 65 ans : 973 >65 ans : 1 106
(Martín-Sánchez et al., 2020)	Espagne (Madrid)	Du 28 février 2020 au 31 mars 2020	1 379 cas	6 %	N = 81
(Hsu et al., 2020)	États-Unis (Boston ,Massachusetts)	Du 1er mars au 18 mai 2020	N = 188 aux SSI	37 %	N = 69
(Shah et al., 2020)	États-Unis (sud-ouest de la Géorgie)	Du 2 mars 2020 au 6 mai 2020	N = 123 aux SSI	79 %	N = 97
(Suleyman et al., 2020)	États-Unis	Du 9 mars	N = 141 aux SSI	81 %	N = 114 sous ventilateur

Auteur	Pays	Date	Dénominateur n	% sous ventilateur	Remarques
	(Detroit, Michigan)	au 27 mars 2020			
(Yang et al., 2020)	Chine (Wuhan)	Du 13 février au 14 mars	N = 66 aux SSI	55 %	N = 36 sous ventilateur
(Fletcher et al., 2020)	Royaume-Uni	Du 1er janvier 2020 au 23 avril 2020	1 148 cas	7 %	
(Lian et al., 2020)	Chine	Du 17 janvier au 31 janvier 2020	475 cas	1 %	N = 4 sous ventilateur
(Castro et al., 2020)	États-Unis (Massachusetts)	Au 5 juin 2020	2 511 hospitalisations	6,5 %	N = 164 sous ventilateur
(Casas Rojo et al., 2020)	Espagne	Au 30 avril 2020	6 424 hospitalisations	5,6 %	109 hôpitaux
(Garibaldi et al., 2020)	États-Unis (région du Maryland, DC)	Du 4 mars au 24 avril 2020	832 hospitalisations	9,9 %	N = 74 sous ventilateur, 5 hôpitaux
(Regina et al., 2020)	Suisse	Du 1er mars au 25 mars 2020	200 hospitalisations	19 %	N = 37 sous ventilateur
(C. M. Petrilli et al., 2020a)	États-Unis (New York)	Du 1er mars au 8 avril 2020	990 patients aux SSI	65 %	N = 647 sous ventilateur
(Almeshari et al., 2020)	Italie Chine États-Unis		Patients aux SSI	65 % (49 à 80, IC de 95 %) I^2 84,37 %	– Revue systématique de la ventilation mécanique, cinq études incluses dans la méta-analyse
(Mitra et al., 2020)	Canada (Vancouver)	Du 21 février au 14 avril 2020	117 patients aux SSI	63,2 %	N sous ventilateur = 74

Auteur	Pays	Date	Dénominateur n	% sous ventilateur	Remarques
(A. B. Docherty et al., 2020a)	Angleterre, Écosse et Pays de Galles	Du 6 février au 19 avril 2020	3 001 patients aux SSI	55 %	N = 1 656 sous ventilateur 208 hôpitaux
(L. Kim et al., 2020b)	États-Unis (14 États)	Du 1er mars au 2 mai 2020	798 patients aux SSI	58 %	N = 462 sous ventilateur 154 dans des hôpitaux de soins actifs, 137 hôpitaux dans 74 comtés de 14 États (voir la liste des États en annexe)
(Gold et al., 2020)	États-Unis (Géorgie)	Au 28 avril 2020	Aux SSI Tous : 119 18 à 49 ans : 24 50 à 64 ans : 32 > = 65 ans : 63	Tous : 77 % 18 à 49 ans : 71 % 50 à 64 ans : 84 % > = 65 ans : 76 %	
(Cummings et al., 2020)	États-Unis (New York)	Au 14 avril 2020	257 patients aux SSI	78 %	
(*COVID-19, australia: Epidemiology report 13 (reporting week to 23:59 AEST 26 april 2020)*2020)	Australie	Au 26 avril 2020	148 patients aux SSI	28 %	
(Simonnet et al., 2020)	France	Au 6 avril 2020	124 patients aux SSI	69 %	

Auteur	Pays	Date	Dénominateur n	% sous ventilateur	Remarques
(Zhou et al., 2020)	Chine	Au 31 janvier 2020	191 patients aux SSI	64 %	
(Cai et al., 2020)	Chine	Du 11 janvier au 6 février 2020	32 patients aux SSI	50 %	

DURÉE DU SÉJOUR À L'HÔPITAL (DANS L'ENSEMBLE)

Le tableau 4 présente la médiane OU la moyenne du séjour total des patients hospitalisés, y compris les patients admis aux soins intensifs.

TABLEAU 4 : Durée du séjour à l'hôpital dans 27 études

Auteur	Pays	Date	N hospitalisations	Durée du séjour à l'hôpital	Remarques
(Vena et al., 2020) *nouveaux*	Italie (Gênes)	25 février au 25 mars 2020	275 hospitalisations	Médiane (EI) 12 jours (5 à 19)	
(Zhao et al., 2020) *nouveaux*	États-Unis (New Jersey)	Du 12 mars au 8 avril 2020	Tous = 722 Décédés = 186 Survivants = 536	Médiane (EI) Tous = 7,0 jours (4 à 13) Décédés = 11 jours (6 à 17) Survivants = 6 jours (3 à 11)	
(L. Kim et al., 2020a) {{61027;}} *nouveaux*	États-Unis (14 États)	Du 1er mars au 25 juillet 2020	Patients <18 ans = 208 0 à 2 ans = n.d. 2 à 4 ans = n.d. 5 à 17 ans = n.d.	Médiane (EI) Patients <18 ans = 2,5 jours (1 à 5) 0 à 2 ans = 2 jours (1 à 2) 2 à 4 ans = 3 jours (1 à 4) 5 à 17 ans = 3 jours (2 à 6)	n.d. = Non déclaré
(Perez-Guzman et al., 2020) *nouveaux*	Royaume-Uni (Londres)	Du 7 au 30 mars 2020	Tous = 614 Décédés = 178 Survivants = 381	Médiane (EI) Tous = 7 jours (6 à 8) Décédés = 7 jours (5 à 8)	

Auteur	Pays	Date	N hospitalisations	Durée du séjour à l'hôpital	Remarques
				Survivants = 6 jours (5 à 7)	
(Yu et al., 2020) *nouveaux*	Chine (Wuhan)	Du 14 janvier au 28 février 2020	Tous = 1 663 Non grave = 799 Sévère = 864	Médiane (EI) Tous = 17,0 jours (13,0 à 19,0) Peu sévère = 18,0 jours (15,0 à 20,0) Sévère = 17,0 jours (11,0 à 18,0)	– Voir la définition de « maladie sévère » en annexe
(Gavin et al., 2020) *nouveaux*	États-Unis (Indiana)	Du 1er mars au 31 mars 2020	– Tous = 140 – Aucun VM = 83 – Avec VM et a survécu = 35 – Avec VM et décédé = 18	Moyenne (EI) Tous = 10,7 jours (4 à 15) Aucun VM = 6,5 jours (3 à 8) Avec VM et a survécu = 21,3 jours (12 à 25) Avec VM et est décédé = 12,8 jours (8 à 16)	VM = ventilateur mécanique :
(Nabavi, Javidarabshahi, Allahyari, & et al., 2020)	Iran (Mashhad)	De février à avril 2020	Peu sévère/modérée = 33 Sévère = 139 Critique = 28	Moyenne (normale) Peu sévère/modérée = 6,48 ± 3,94 Sévère = 7,27 ± 3,39 Critique = 7,56 ± 4,74	– Voir la définition des termes « peu sévère/modérée », « sévère » et « critique » en annexe
(Rizzo et al., 2020)	États-Unis	Du 20 février 2020 au 6 juin 2020	Tous : 16 099 <18 ans : 185 18 à 65 ans : 8 958 >65 ans : 6 956	Médiane (EI) Tous : 6,0 [4,0 à 11,0] <18 ans : 3,0 [2,0 à 5,0] 18 à 65 ans : 6,0 [3,0 à 9,0] >65 ans : 7,0 [5,0 à 12,0]	
(Koleilat et al., 2020)	États-Unis (New York)	Du 1er mars au 10 avril 2020	Négatif à une TVP = 117 Positif à une TVP = 18	Médiane (EI) Négatif à une TVP = 8,0 jours (5,0 à 12,8) Positif à une TVP = 6,0 jours (5,0 à 11,5)	TVP = thrombose veineuse profonde

Auteur	Pays	Date	N hospitalisations	Durée du séjour à l'hôpital	Remarques
				L'écart n'était pas statistiquement différent (p = 0,6)	
(Lovinsky-Desir, 2020)	États-Unis (New York)	Du 11 février au 5 juillet 2020	Pas d'asthme = 1 135 < 21 ans : 42 21 à 39 ans : 261 40 à 65 ans : 832 Asthme = 163 < 21 ans : 13 21 à 39 ans : 39 40 à 65 ans : 111	Médiane (EI) Pas d'asthme : 5 jours (7) < 21 ans : 3 jours (7) 21 à 39 ans : 4 jours (4) 40 à 65 ans : 6 jours (9) Asthme = 6 jours (9) < 21 ans : 9 jours (14) 21 à 39 ans : 6 jours (6) 40 à 65 ans : 6 jours (9)	
(Ortiz-Brizuela et al., 2020)	Mexique (Mexico)	Du 26 février au 11 avril	N = 140	EI médian 5 jours (3 à 8)	
(Shah et al., 2020)	États-Unis (sud-ouest de la Géorgie)	Du 2 mars au 6 mai 2020	Tous = 522 Décédés = 92 Survivants = 430	Médiane (EI) Tous = 6 jours (4 à 11) Décédés = 10 jours (6 à 16) Survivants = 6 jours (3 à 10)	
(Yang et al., 2020)	Chine (Wuhan)	Du 13 février au 14 mars 2020	N = 463	Médiane (EI) 19,0 jours (13,0 à 27,0)	
(Vanhems et al., 2020)	France (Lyon)	Du 8 février au 24 avril 2020	Tous = 412 Décédés = 86 Survivants = 326	Médiane (EI) Tous = non déclaré Décédés = 10 jours (6 à 14) Survivants = 9 jours (4 à 13)	
(Argenziano et al., 2020)	États-Unis (New York)	Du 1er mars au 5 avril 2020	850 hospitalisations	Médiane (EI) 6 jours (3 à 14)	

Auteur	Pays	Date	N hospitalisations	Durée du séjour à l'hôpital	Remarques
(Casas Rojo et al., 2020)	Espagne	Au 30 avril 2020	6 424 hospitalisations	Moyenne 10,4 jours (variant 1 à 62 jours)	109 hôpitaux
(Garibaldi et al., 2020)	États-Unis (région du Maryland, DC)	Du 4 mars au 24 avril 2020	832 hospitalisations	Médiane (EI) Tous : 6,1 jours (EI 2,6 à 10,8) Peu sévère/modérée 4,8 jours (2,6 à 8) Maladies sévères 15 jours (10,2 à 20,6) Décès 6,8 jours (EI 3,3 à 11,2)	Dans cinq hôpitaux – Voir la définition des maladies « peu sévères/modérées » et « sévères » en annexe
(C. M. Petrilli et al., 2020a)	États-Unis (New York)	Du 1er mars au 8 avril 2020	2 741 hospitalisations	Médiane (EI) 7 jours ((EI 3 à 13) Intervalle complet 0 à 52 jours.	
(Rastad et al., 2020)	Iran	Du 20 février et 25 mars 2020	Tous = 2 957 Décédés = 301 Survivants = 2656	Médiane (EI) Tous : non déclaré Décédés : 4 jours (EI 2 à 6) Survivants : 5 jours (EI 3 à 7)	
(Rees et al., 2020)	Revues systématiques avec 52 études - 46 provenant de la Chine et les autres, des États-Unis, du Royaume-Uni, de l'Italie et dans toute l'UE	Du 24 décembre 2019 au 16 avril 2020	En fonction de 45 études	Durée médiane du séjour à l'hôpital – Chine : 14 jours (EI : 10 à 19) – À l'extérieur de la Chine : 5 jours (EI : 3 à 9) à l'extérieur de la Chine	– Comprend trois études pédiatriques – Comprend les patients dont le suivi est complet et incomplet – Critères d'inclusion ne sont pas toujours précisés de façon claire – Taille des échantillons

Auteur	Pays	Date	N hospitalisations	Durée du séjour à l'hôpital	Remarques
					varie de n = 5 à n = 2 936
(Gold et al., 2020)	États-Unis (Géorgie)	Au 28 avril 2020	Tous : 305 18 à 49 ans : 89 50 à 64 ans : 99 > = 65 ans : 117	Médiane : Tous : 8,5 jours (EI 5,0 à 14,0) 18 à 49 ans : 7,0 jours (EI 4,3 à 11,8) 50 à 64 ans : 8.0 jours (5,0 à 12,8) > = 65 ans : 10.0 jours (6,0 à 16,0)	
(A. B. Docherty et al., 2020b)	Royaume-Uni	Au 4 avril 2020	16 749	Médiane : 7 jours [EI 4,12]	
(Lv et al., 2020)	Chine	Du 16 décembre 2019 au 21 février 2020	153	Médiane : – Tous : 15 jours (EI 10 à 23)	Exclut les patients aux soins intensifs
(Argenziano et al., 2020)	États-Unis (New York)	Du 11 mars au 15 avril 2020	1 000	Moyenne : 11,4 jours (5,01) n = 618	
(Guan et al., 2020)	Chine	Au 29 janvier 2020	Tous = 1 099 Sévère = 173 Non grave = 926	Médiane – Tous : 12 jours (EI : 10 à 14) – Sévère : 13 jours (EI : 11,5 à 17) – Non sévère : 11 jours (10 à 13)	– Voir la définition de « sévère » en annexe
(Zhou et al., 2020)	Chine	Remarque – Les estimations des événements sont annuelles.	191	Médiane : 11 jours (EI 7 à 14) jours	
(Cao et coll., 2020)	Chine	Du 18 janvier au 3 février 2020	100	Médiane : 16 jours (EI 13 à 18)	

DURÉE DU SÉJOUR AUX SOINS INTENSIFS

Le tableau 5 présente la médiane OU la moyenne de durée du séjour de tous les patients aux soins intensifs. Une spécification est ajoutée dans la section des notes lorsque la durée du séjour est spécifique à un sous-groupe comme les survivants ou les personnes décédées.

TABLEAU 5: Durée du séjour aux soins intensif dans 24 études

Auteur	Pays	Date	N- aux soins intensifs	Durée du séjour aux soins intensifs	Remarques
(Vena et al., 2020) *nouveaux*	Italie (Gênes)	25 février au 25 mars 2020	46 hospitalisations	Médiane (EI) 12 jours (6,5 à 21,5)	
(Zhao et al., 2020) *nouveaux*	États-Unis (New Jersey)	Du 12 mars au 8 avril 2020	Tous = 193 Décédés = 107 Survivants = 86	Médiane (EI) Tous = 8,5 jours (4 à 14) Décédés = 8 jours (4 à 12,5) Survivants = 10 jours (4 à 20)	
(Turcotte et al., 2020) *nouveaux*	États-Unis (Annapolis)	Du 1er mars au 12 avril 2020	36 hospitalisations	Moyenne (normale) 14,86 jours (11,35) Intervalle de confiance de 95 % 14,35 à 22,38 jours Médiane 20 jours	N aux SSI 36
(L. Kim et al., 2020a) *nouveaux*	États-Unis (14 États)	Du 1er mars au 25 juillet 2020	Patients <18 ans = 208 0 à 2 ans = n.d. 2 à 4 ans = n.d. 5 à 17 ans = n.d.	Médiane (EI) Patients <18 ans = 2 jours (1 à 5) 0 à 2 ans = 1 jour (1 à 3) 2 à 4 ans = 2 jours (2 à 5) 5 à 17 ans = 3,5 jours (1 à 7)	n.d. = Non déclaré
(Rizzo et al., 2020)	États-Unis	Du 20 février 2020 au 6 juin 2020	Tous : 3 768 < 18 ans : 31 18 à 65 ans : 1 777 >65 ans : 1 960	Médiane (EI) Tous : 4,0 [1,0 à 10,0] < 18 ans : 2,0 [1,0 à 7,0] 18 à 65 ans : 4,0 [1,0 à 10,0]	

Auteur	Pays	Date	N- aux soins intensifs	Durée du séjour aux soins intensifs	Remarques
				>65 ans : 4,0 [1,0 à 10,0]	
(Xu et al., 2020)	Chine (Wuhan)	Du 12 janvier au 3 février 2020	Tous = 239 Décédés = 147 Survivants = 92	Médiane (EI) Tous = 17 jours (10 à 26) Décédés = 12 jours (8 à 18) Survivants = 26,5 (19 à 46,5)	
(Suleyman et al., 2020)	États-Unis (Detroit, Michigan)	Du 9 mars au 27 mars 2020	N = 141 aux SSI	Médiane (EI) 15 jours (9 à 23)	
(Yang et al., 2020)	Chine (Wuhan)	Du 13 février au 14 mars 2020	N = 66 aux SSI	Médiane (EI) 14,5 jours (EI 7,3 à 21,8)	
(Ayed et al., 2020)	Koweït	Au 20 mai 2020	Tous = 103 aux soins intensifs Décédés = 45 Survivants (congé) = 47	Médiane (EI) Tous = 11 jours (6 à 18,5) Décédés = 13 jours (7 à 23) Survivants = 10 jours (6 à 15)	Encore à l'hôpital : n = 11
(Vanhems et al., 2020)	France (Lyon)	Du 8 février au 24 avril 2020	Tous = 66 aux soins intensifs Décédés = 30 Survivants = 36	Médiane (EI) Tous = non déclaré Décédés = 10,5 jours (5 à 15,5) Survivants = 12 jours (9 à 17,2)	
(Argenziano et al., 2020)	États-Unis (New York)	Du 1er mars au 5 avril 2020	N-236 patients aux soins intensifs	Médiane (EI) 23 jours (12 à 32)	

Auteur	Pays	Date	N- aux soins intensifs	Durée du séjour aux soins intensifs	Remarques
(Mitra et al., 2020)	Canada (Vancouver)	Du 21 février au 14 avril 2020	117 patients aux soins intensifs	Médiane (EI) Globalement : 9 jours (5 à 21) Congé des soins intensifs : (n = 87) 7 jours (3 à 16)	
(C. M. Petrilli et al., 2020a)	États-Unis (New York)	Du 1er mars au 8 avril 2020	990 patients aux soins intensifs	Médiane (EI) 9 jours (5 à 17)	
(L. Kim et al., 2020b)	États-Unis (14 États)	Du 1er mars au 2 mai 2020	798 patients aux SSI	Médiane 6 jours (écart, 1 à 41; EI 2 à 11)	N = 462 sous ventilateur 154 hôpitaux de soins actifs dans 137 hôpitaux de 74 comtés dans 14 États – Voir la liste des États en annexe
(Rees et al., 2020)	Revues systématiques avec 52 études - 46 provenant de la Chine et les autres, des États-Unis, du Royaume-Uni, de l'Italie et dans toute l'UE	Du 24 décembre 2019 au 16 avril 2020	En fonction de 9 études	Durée du séjour médian à l'hôpital – Chine : 8 jours (EI 5 à 13) jours – À l'extérieur de la Chine : 7 jours (EI : 4 à 11) à l'extérieur de la Chine	– Comprend trois études pédiatriques – Comprend les patients dont le suivi est complet et incomplet – Critères d'inclusion ne sont pas toujours précisés de façon claire – Taille des échantillons varie de

Auteur	Pays	Date	N- aux soins intensifs	Durée du séjour aux soins intensifs	Remarques
					n = 5 à n = 2 936
(Gold et al., 2020)	États-Unis (Géorgie)	Au 28 avril 2020	Tous : 119 18 à 49 ans : 24 50 à 64 ans : 32 > = 65 ans : 63	Médiane : Tous : 8,0 (5,0 à 12,0) 18 à 49 ans : 7,0 (4,0 à 14,0) 50 à 64 ans : 8,0 (6,0 à 11,0) > = 65 ans : 9,0 (5,0 à 12,0)	
(C. M. Petrilli et al., 2020b)	États-Unis (New York)	Au 7 avril 2020	445	Médiane : – A reçu son congé d'hôpital ou est décédé : 6 jours (EI 3 à 9) – Toujours aux soins intensifs 11 jours (EI 8 à 15)	
(Lv et al., 2020)	Chine	Du 16 décembre 2019 au 21 février 2020	55	Médiane : 16 jours (EI 10 à 21)	
(Argenziano et al., 2020)	États-Unis (New York)	Du 11 mars au 15 avril 2020	231	Moyenne : 14,6 jours (grave 5,94)	
(Zhou et al., 2020)	Chine	Remarque – Les estimations des événements sont annuelles.	50	Médiane : 8 jours (écart 4 à 12)	
(Zhang et al., 2020)	Chine	Du 2 janvier 2020 au 10 février 2020	Tous = 32 Décédés = 9 Survivants = 23	Médiane (EI) Décédés : 11,0 jours (4,5 à 14,5) Survivants : 8,0 jours (intervalle 5,0 à 13,0)	
(Grasselli et al., 2020)	Italie	Du 20 février au 18 mars 2020	1 591	Médiane : 9 jours (6 à 13 [IC 95 %, 9 à 9])	
(Cao et al., 2020)	Chine	Du 18 janvier au 3 février 2020	100	Médiane :	Essai clinique :

Auteur	Pays	Date	N- aux soins intensifs	Durée du séjour aux soins intensifs	Remarques
				Tous : 11 jours (EI 7 à 17) Survivants : 11 jours (EI 9 à 14) Décédés : 11 jours (EI 7 à 17)	patients sous traitement standard
(Cao et al., 2020)	Chine	Du 18 janvier au 3 février 2020	99	Médiane : Tous : 6 jours (EI 2 à 11) Survivants : 9 jours (EI 5 à 44) Décédés : 6 jours (EI 2 à 11)	Essai clinique : patients sous Lopinavir-Ritonavir

DURÉE DE L'UTILISATION DU VENTILATEUR MÉCANIQUE

Le tableau 6 présente la médiane OU la moyenne de la durée du recours au ventilateur mécanique. Une spécification est ajoutée dans la section des notes lorsque la durée du séjour est spécifique à un sous-groupe comme les survivants ou les personnes décédées.

TABLEAU 6 : Durée de la ventilation dans 9 études

Auteur	Pays	Date	N sous ventilateur	Durée de la ventilation	Remarques
(Vena et al., 2020) *nouveaux*	Italie (Gênes)	25 février au 25 mars 2020	60 hospitalisations	Médiane (EI) 9 jours (EI 4,5 à 16,5)	
(Turcotte et al., 2020) *nouveaux*	États-Unis (Annapolis)	Du 1er mars au 12 avril 2020	34 hospitalisations	Moyenne (normale) 11,74 jours (8,17) Intervalle de confiance de 95 % 8,88 à 14,59 jours Médiane 9 jours	
(Gavin et al., 2020) *nouveaux*	États-Unis (Indiana)	Du 1er mars au 31 mars 2020	– Tous = 53 – Avec VM et a survécu = 35	Moyenne (EI) Tous = 10,9 jours (6 à 14)	VM = ventilateur mécanique :

Auteur	Pays	Date	N sous ventilateur	Durée de la ventilation	Remarques
			– Avec VM et décédé = 18	Avec VM et a survécu = 11,1 jours (6 à 14) Avec VM et est décédé = 10,6 jours (6 à 13)	
(Almeshari et al., 2020)	Chine États-Unis		2 études N = 18 N = 4	Médiane pour 2 études (aucune méta-analyse effectuée) 10 à 17 jours avec EI 2 à 19 jours	– Revue systématique de la ventilation mécanique. Durée du recours au ventilateur mécanique en fonction de deux études, dont une n'a porté que sur quatre patients
(Mitra et al., 2020)	Canada (Vancouver)	Du 21 février au 14 avril 2020	74	Médiane (EI) 13.5 jours (8 à 22)	
(Regina et al., 2020)	Suisse	Du 1er mars au 25 mars 2020	37	Médiane 6 jours (EI 5,00 à 11,00)	
(Gold et al., 2020)	États-Unis (Géorgie)	Au 28 avril 2020	Tous : 92 18 à 49 ans : 17 50 à 64 ans : 27 > = 65 ans : 48	Médiane : Tous : 9,0 (5,0 à 12,0) 18 à 49 ans : 8,5 (5,0 à 13,3) 50 à 64 ans : 9,0 (5,5 à 10,5) > = 65 ans : 10,0 (6,0 à 12,0)	
(Bhatraju et al., 2020)	États-Unis (région de Seattle)	Du 24 février au 9 mars 2020	18	10 jours (EI 7 à 12)	Tous les patients ayant eu recours au ventilateur (y compris les patients encore sous ventilateur)

Auteur	Pays	Date	N sous ventilateur	Durée de la ventilation	Remarques
(Bhatraju et al., 2020)	États-Unis (région de Seattle)	Du 24 février au 9 mars 2020	15	11 jours (EI 7 à 12)	Patients extubés

Méthodes :

Une analyse hebdomadaire de la littérature (publiée et prépubliée) en ce qui concerne l'hospitalisation et la durée du séjour pour les patients atteints de COVID-19 est effectuée par le groupe des sciences émergentes de l'ASPC. Les recherches pour trouver de la documentation pertinente sont effectuées dans la base de données Refworks et dans une feuille de calcul Excel gérée par le groupe des sciences émergentes. La base de données Refworks et le fichier Excel rassemblent la documentation relative à la COVID-19 depuis le début de l'épidémie. La littérature est extraite de Pubmed, de Scopus, de BioRxiv, de MedRxiv, d'ArXiv, de SSRN, de Research Square et croisée avec la liste de littérature sur la COVID de l'OMS et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley.

Cette revue contient les recherches relatives à l'hospitalisation et à la durée de séjour des patients atteints de la COVID-19 publiées jusqu'au 20 août 2020.

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites dans l'examen. Il est préférable d'utiliser des études de recherche avec un grand échantillon. Les études qui portent sur moins de 100 patients hospitalisés, moins de 25 patients admis aux soins intensifs ou moins de 10 patients sous ventilation sont exclues. Toutefois, ces critères de sélection n'ont pas été appliqués aux revues systématiques.

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Annexe

(Guan et al., 2020)	Définition de « grave » :
	La définition validée comprend soit un critère majeur, soit trois critères mineurs ou plus
	
	• Critères mineurs
	  ○ Fréquence respiratoire > 30 respirations/min
	  ○ Rapport PaO2/FiO2 < 250
	  ○ Infiltrations multilobées
	  ○ Confusion/désorientation
	  ○ Urémie (niveau d'azote uréique dans le sang >20 mg/dl)
	  ○ Leucopénie* (nombre de globules blancs, 4 000 cellules/ml)
	  ○ Thrombocytopénie (numération des plaquettes, 100 000/ml)
	  ○ Hypothermie (température centrale de 36,8 °C)
	  ○ Hypotension nécessitant une réanimation liquidienne énergique
	• Critères majeurs
	  ○ Choc septique nécessitant des vasopresseurs
	  ○
	  ○ Insuffisance respiratoire nécessitant un traitement mécanique

(L. Kim et al., 2020b)	– États inclus dans l'étude : Californie, Colorado, Connecticut, Géorgie, Iowa, Maryland, Michigan, Minnesota, Nouveau-Mexique, New York, Ohio, Oregon, Tennessee et Utah.
(Garibaldi et al., 2020)	– Les définitions sont basées sur la classification de l'OMS (OMS R&D Blueprint: Novel Coronavirus. COVID-19 Therapeutic Trial Synopsis 2020.) – Hospitalisation, maladie peu sévère : Hospitalisation, pas d'oxygénothérapie OU oxygène par masque ou pince nasale. – Hospitalisation, atteinte grave : ventilation non invasive ou oxygène à haut débit, intubation ou ventilateur mécanique, ventilation + soutien supplémentaire pour les organes - hypertenseur, transplantation rénale, OCEC.
(Nabavi et al., 2020)	– Peu sévère/modérée : aucune pneumonie ou pneumonie légère; – Sévère : avec dyspnée (fréquence respiratoire > 30) ou hypoxie (saturation en O_2 < 93); Critique : en cas d'insuffisance respiratoire, de choc ou de dysfonctionnement de plusieurs organes
(Yu et al., 2020)	– La COVID-19 sévère doit satisfaire l'un des critères suivants : (1) détresse respiratoire avec fréquence respiratoire ≥ 30 respirations par minute avec essoufflement ou difficulté à respirer; (2) saturation en oxygène ≤ 93 % au repos; (3) pression partielle artérielle de l'oxygène (PaO_2)/fraction d'oxygène inspirée (FiO_2) ≤ 300 mmHg (1 mmHg = 0,133 kPa).

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Emerging Evidence on COVID-19

Evidence Brief of COVID-19 Infectious Period in Immunosuppressed/Immunocompromised Individuals

Introduction

What is the length of the infectious period of SARS-CoV-2 in immunosuppressed and immunocompromised individuals?

The infectious period (also known as the communicability period) is defined as the time during which an infected person can transmit an infectious agent to another person. The infectious period is an important clinical and epidemiologic parameter to understand for the control of any infectious disease. Estimates of the average infectious period of SARS-CoV-2 for mild/moderately symptomatic immunocompetent cases is considered to start on average 2.5 days before developing symptoms, peak around day 4 of symptoms and decrease to low levels within 8-10 days after the start of symptoms for a total of 10-13 days (see Rapid Review on Infectious Period, Sep 2020).

In this brief, immunosuppressed and immunocompromised populations are considered. Immunosuppression may result from certain immune-mediated diseases and/or therapies (e.g. anti-cancer therapy, anti-rejection medication, etc.). Immunocompromised individuals may have an immune deficiency from infectious or genetic causes. Early case reports have documented longer periods (>14 days) during which replication-competent (i.e., culture positive) SARS-CoV-2 can be recovered in these populations and in severe cases of COVID-19. Further, immunosuppression has been shown to be associated with higher odds of persistent viral RNA shedding (>21 days) in two studies (1, 2), while another study found no significant association (3). Potential prolonged and recurrent infections in this population identified the need for further research on infectiousness and unique strategies for safe de-isolation to prevent further transmission.

This brief focuses on research conducted to document infectious period in immunosuppressed/immunocompromised cases of COVID-19 published up to February 5, 2021. They have been organized by underlying disease condition and type of study. Because of their preliminary nature, case reports were not included in this review. Infectious period estimates were determined by a combination of epidemiological and clinical investigations that together informed when an infected person could, or was likely to, no longer transmit the virus. Most studies used RT-PCR to diagnose cases of COVID-19 and to monitor viral RNA shedding over time. However, detection of viral RNA by RT-PCR does not provide proof of infectivity as this test also gives positive results when non-infectious virus particles are present. These particles are commonly shed from

infected tissue for a period of time after an infection has been cleared by the host immune system (4). Recovery of replication-competent virus has been used as an *in vitro* proxy for human-to-human infectiousness. To establish if viable virus has been isolated in a sample, replication of virus is established most reliably by cell culture. Unfortunately, few studies employed culture methods because they can be slow and expensive. Detection of subgenomic RNA has been recommended as a proxy for shedding of infectious virus (5), however there is not yet consensus on this application (6).

Key Points

- The review identified 19 studies including 1 bidirectional cohort, 1 prospective cohort, 10 retrospective cohort studies, and 7 longitudinal case series. Immunosuppressed populations included cancer (n=11) and transplant patients (n=6). Immunocompromised patients included those with HIV (n=2). Only two studies provided evidence of viable virus via cell culture while the others described the length of viral RNA shedding via RT-PCR or qRT-PCR.

Culture studies (n=2)

- Recovery of replication-competent SARS-CoV-2 has been reported in patients immunosuppressed due to hematologic cancers for at least 2 months. This is much longer than the infectious period estimated in the average immunocompetent populations (10-13 days, see Rapid Review on Infectious Period).

RT-PCR studies (n=17)

- RT-PCR conducted on respiratory samples from mildly symptomatic immunocompentent typically become negative within 14-20 days. As shown in the points below, time to viral RNA clearance was much longer in immunosuppressed/immunocomptent individuals. How long there was viral RNA shedding depended to some degree on the cause of the immunosuppression/immunocompromise.
    - In cancer patients, median time to viral RNA clearance ranged from 12-50 days with an overall range of 9-78 days. Systemic anticancer therapy (i.e., chemotherapy, hormonal therapy, targeted drugs, and immunotherapy), before or during COVID-19 positivity, was not significantly associated with viral clearance time.
    - In solid organ transplant patients undergoing immunosuppressive therapy, time to viral clearance ranged from 9-66 days. Mean viral RNA shedding was significantly

longer in kidney transplant patients than immunocompetent individuals (28.4 days vs. 12.2 days, $p<0.01$). Further, evidence from one study reported high viral loads at day 30 of infection in a group of transplant patients indicating high likelihood of SARS-CoV-2 transmission 30 days after symptom onset.

- In patients with HIV, RNA viral clearance occurred over a median of 18 days (IQR 7-28) but remained detectable in some patients >40 days post symptom onset. Severe HIV cases had a longer duration of viral RNA shedding compared to mild/moderate cases.

Overview of the Evidence

A total of 19 studies were included in this review, including cohort studies and longitudinal case series. Many of these are pre-prints and have not undergone a peer-review process. Prospective cohorts are of lower risk of bias and are considered higher quality research, but there are few of this study design contributing to this question. Case series suffer from low sample size, selection bias and recall bias (e.g., self-report symptom onset). In addition, many of the immunosuppressed/immunocompromised cases described in this review also had additional underlying chronic health conditions and it is difficult to determine if and how this affected the results. Overall, due to the risks of bias, these studies should be interpreted with caution, as results are likely to change with additional research.

Several knowledge gaps exist for the infectious period of SARS-CoV-2 in special populations. Few studies utilize cell culture and instead depend on detection of viral RNA as a proxy for potential infectious period. Such methods cannot distinguish between infectious and non-infectious viral particles, however, the relationship between viral load and probability of culture positivity has been covered in the literature. Additional research on immunity and how infectious period is impacted by immunosuppressive therapies for other immune-mediated diseases (e.g., rheumatoid arthritis, Crohn's disease, etc.) is needed. As well, further exploration into strategies for safely de-isolating these cases to prevent further transmission is warranted.

CONTENTS

INFECTIOUS PERIOD OF IMMUNO-SUPPRESSED/COMPROMISED INDIVIDUALS

Cancer/hematological disease patients (n=11):

- Only two studies provided evidence of replication-competent virus via cell culture:
    - Patients with immunosuppression due to hematologic cancers, that underwent allogenic or autologous hematopoietic cell transplantation or received cellular therapies, shed replication-competent SARS-CoV-2 for at least 2 months (7, 8). This was much longer than in immunocompetent patients (<7 days) (8).
- Many cases had additional underlying chronic health conditions (9, 10).
- Majority of cases required >14 days to achieve consecutive negative PCR results, with a median time ranging from 12-50 days and an overall range of 9-78 days (7-17).
- Anticancer therapy (i.e., chemotherapy, hormonal therapy, targeted drugs, and immunotherapy), before or during COVID-19 positivity, was not significantly associated with viral RNA clearance time (11, 12, 16).
- Severe cases had a longer duration of viral RNA shedding compared to mild/moderate cases, but this finding was not significant (13).

Solid organ transplant patients (n=6):

- The majority of patients were taking immunosuppressive therapy (18-21).
- No studies provided evidence of viable virus via cell culture.
- The majority of cases required >14 days to achieve consecutive negative PCR results, with an overall range of approximately 9-66 days (18-23).
- The mean time of SARS-CoV-2 viral RNA shedding in a group of kidney transplant patients was 28.4 ± 9.3 days, which was significantly longer than that of immunocompetent individuals (12.2 ± 4.6 days, $p<0.01$) (23).
- A study of kidney transplant recipients reported 43% of patients still had positive RT-PCR results at day 30 of follow-up with viral loads above 3 $\log^{10}$ copies per reaction, the threshold for which there is a risk of SARS-CoV-2 transmission (22).

- Severe cases had a longer duration of viral RNA shedding compared to mild/moderate cases, but this association was not statistically investigated (21).

Human immunodeficiency virus (HIV) patients (n=2):

- All patients were on antiretroviral therapy (24, 25).
- No studies provided evidence of viable virus via cell culture.
- RNA viral clearance occurred over a median of 18 days (IQR 7-28) post symptom onset (24).
- SARS-CoV-2 viral RNA may remain detectable in some HIV patients for >40 days post symptom onset (24, 25).
- Patients with longer times to viral RNA clearance had more severe disease, higher ICU admission, lower nadir CD4 cell counts, and a higher proportion of comorbidities than individuals with shorter times to viral clearance ($p<0.05$) (24).

Table 1: Studies reporting infectious period estimates in immunosuppressed and immunocompromised COVID-19 patients (n=19)

STUDY	METHOD	KEY OUTCOMES
IMMUNOSUPPRESSED PATIENTS		
Cancer patients (n=11)		
Roedl 2020 (8) *LTE* Retrospective cohort study Germany Nov 2020*	Studied patients with malignancies being treated with allogenic hematopoietic stem cell transplant (HSCT) recipients or chimeric antigen receptor T-cell (CAR-T) therapy who also required ICU treatment for COVID-19 (n=6). Outcomes were compared with COVID-19 patients without a history of malignant disease (n=18). SARS-CoV-2 was detected by RT-PCR and viral isolation was performed using cell culture. After 48–72 hours of incubation, infected Vero cells (CCL81; American Type Culture Collection) were monitored for cytopathic effect.	Bronchoalveolar and plasma samples -In patients with history of HSCT or CAR-T, viral loads remained high until end of follow-up, day 28 (in both respiratory and plasma samples). In contrast, SARS-CoV-2 RNA was below the limit of detection after 21 and 11 days in respiratory and plasma samples, respectively, in immunocompetent patients. -Infectious virus was isolated from five samples from four patients with a history of HSCT or CAR-T therapy, obtained 4-28 days post ICU admission. In immunocompetent patients, infectious virus could not be detected after Day 7.

Aydillo 2020 (7) *LTE* Longitudinal case series USA Mar-Apr 2020	Analyzed longitudinal samples collected from immunocompromised cancer patients with COVID-19 (n=20). Cell culture was used to detect viable virus and whole-genome sequencing was used to detect genetic variants. Inoculated Vero E6 cell monolayers were incubated for a week and monitored daily for cytopathic effect. Time from symptom onset to negative RT-PCR was also measured.	Nasopharyngeal and sputum swabs -There were 18 recipients of allogenic (n=6) or autologous (n=10) hematopoietic stem-cell transplants or chimeric antigen receptor (CAR) T-cell therapy (n=2). Fifteen were receiving active treatment or chemotherapy. -Viral RNA was detected up to 78 days after the onset of symptoms (IQR: 24-64 days). -Viable virus was isolated from follow-up samples from five patients for 8, 17, 25, 26, and 61 days after the onset of symptoms. -The patients with viable virus for more than 20 days had received allogeneic hematopoietic stem-cell transplants or CAR T-cell therapy within the previous 6 months and remained seronegative for antibodies to viral nucleoprotein. Two of these patients had severe COVID-19. -Whole-genome sequencing showed no major changes in the consensus sequences of the original serial specimens or cultured isolates, consistent with persistent infection.
Wong 2020 (15) Bidirectional cohort study USA Dec 2020*	Cancer patients positive for SARS-CoV-2 that had undergone cancer-directed therapy (n=26) were tested every two weeks by PCR (targeting N2 and ORF1a) until two successive negative PCR results were obtained.	Nasopharyngeal swabs -Various cancer cases were included, 15 of which (58%) had advanced stage IV disease. -Mean time to consecutive negative PCR results was 32 days. -Twenty (77%) patients required >14 days to achieve consecutive negative PCR results.
Nakamura 2020 (10) *Preprint* Retrospective cohort study Japan Jan-May 2020	Analyzed data from COVID-19 patients with a history of cancer (n=32). Measured the time between illness onset and the first of two consecutive negative SARS-CoV-2 RT-PCR results.	Nasopharyngeal swab -Twenty-five patients (78%) had solid tumors, while 7 (22%) had hematologic malignancies. Nineteen (59%) also had at least one comorbidity (e.g. hypertension, 41%). Thirteen patients (41%) received cancer treatment within the last 30 days. -The median period between illness onset and the first of two consecutive negative SARS-CoV-2 RT-PCR results was 22 days (IQR: 18–25) in survivors (n=224).
Fox 2020 (11)	Analyzed data from COVID-19 patients with a hematological disorder, mostly cancers (n=55). The duration of viral RNA	Nose and throat swabs -94% (52/55) of patients were currently on or had previously received systemic anti-cancer therapy (chemotherapy or immunotherapy).

Retrospective cohort study UK Mar-May 2020	shedding was analyzed using Kaplan-Meier methods from date of illness onset to first of consecutive negative SARS-CoV-2 RT-PCR results (targeting the N gene).	-The median duration of SARS-CoV-2 viral RNA shedding was 34 days in survivors (n=27, 95% CI, 27–47). The longest duration of shedding (still positive at the end of follow-up) was 49 days. -The duration of viral RNA shedding was not prolonged in patients treated with chemo- or immuno-therapy in the last 14 or 28 days.
Ramaswamy 2020 (16) Retrospective cohort study India Apr-Jun 2020	Cancer patients undergoing systemic therapy with laboratory confirmed COVID-19 (n=230) were tested every 3-4 days until RT-PCR negativity. Logistic regression analysis was conducted to evaluate factors affecting delayed conversion to RT-PCR negativity.	Oropharyngeal or nasopharyngeal swab -Patients had various cancer diagnoses, the most prevalent malignancies were acute leukemia (20%) and gastrointestinal malignancies (17%). -53% of patients had evidence of remission or controlled cancer status, while 14% had uncontrolled cancer status or were on active symptom control. -The median time to SARS-CoV-2 seroconversion was 17 days (IQR: 17-28). -Duration of viral RNA shedding was ≤14 days for 52 patients (30%; n=182), 52 patients (30%) tested negative between 15 and 21 days, and 50 patients (29%) were still positive >21 days of follow-up. -None of the factors evaluated, including age, gender, diabetes mellitus, hematolymphoid malignancies, uncontrolled cancer status, and nonmyelosuppressive systemic therapy were found be significantly associated with prolonged viral RNA shedding.
Infante 2020 (9) *LTE* Retrospective cohort study Spain Mar-Apr 2020	Analyzed data from COVID-19 patients with hematological malignancies (n=41). Time to viral clearance was measured by RT-PCR but start/end points were not defined.	Nasal swab -Twenty-nine (70%) of patients had a lymphoid malignancy. Twenty-one (51%) were under active treatment at the time of COVID-19. -The majority of patients (93%) had additional chronic medical conditions. -The median duration of viral RNA shedding was 32.7 days (range 10-70) in surviving patients (n=26). A patient with acute myeloid leukemia under induction therapy at the time of infection was still positive by RT-PCR after 70 days of follow-up.
Xu 2020 (12) *Preprint* Retrospective cohort study USA	Analyzed all patients at a tertiary care hospital with confirmed COVID-19, who had a cancer-related clinical visit within 3 years, and at least one follow-up SARS-CoV-2 assay (n=32). Time to viral clearance was analyzed using Kaplan-Meier methods, for which	Nasopharyngeal swab -Sixteen patients had metastatic disease, 17 were on active treatment at the time of COVID-19 diagnosis, with 8 receiving cytotoxic chemotherapy. -The median time to viral clearance was estimated at 50 days (95% CI, 33-58 days). -Using the UK-NICE guidelines, median time to clearance was 31 days (95% CI, 26-42 days).

Mar-June 2020	data was censored at the time of the last known RT-PCR assay. This method was compared with other guidelines for viral clearance: • UK-NICE guidelines: measured as time to one negative RT-PCR test. • CDC criteria: Symptom/time based strategy measured as 10 days after first positive RT-PCR and 3 days after last symptoms.	-Using a symptom/time-based strategy per CDC criteria, median time to clearance was 13 days (95% CI, 10-17 days). -Cox proportional hazards models showed symptomatic patients had longer viral RNA shedding than asymptomatic patients (HR 0.25 for negative PCR, 95% CI 0.08-0.76, p=0.01). -Anticancer therapy (chemo-, immuno-, targeted- or hormonal therapy), before or during COVID-19 positivity, was not significantly associated with viral clearance time.
Berghoff 2020 (17) Retrospective cohort study Austria Mar-May 2020	Patients with cancer (n=1,016) were routinely tested for SARS-CoV-2 RNA by RT-PCR. Measured time from first positive test to first negative RT-PCR test.	Nasal or pharyngeal swab -SARS-CoV-2 infection was confirmed in 4 of 1,016 (0.4%) patients. Cancers included stomach (n=1), sarcoma (n=1) and head and neck cancer (n=2). Two of the patients were under active anticancer therapy. -Viral clearance was achieved in three patients 14-56 days after testing positive. One patient had still not achieved viral clearance 28 days after first positive at time of this report.
Sanchez-Pina 2020 (13) Retrospective matched cohort study Spain Mar-Apr 2020	Analyzed patients with COVID-19 and haematological malignancies (n=39). Outcomes were compared to a matched control group of 53 non-cancer patients with COVID-19. Follow-up COVID-19 PCR testing was performed in a subset of the cancer patients (n=20) to measure time to viral clearance.	Nasopharyngeal swab -The most frequent haematological diseases were lymphoma (n=12), multiple myeloma (n=12), and chronic lymphocytic leukaemia (n = 6). -In the 20 follow-up cases, median time to achieve PCR negativity was 14 days. -Five patients experienced prolonged viral RNA shedding with a median duration of 23 days (range 16-31 days). -Severe cases had a longer duration of viral RNA shedding compared to mild/moderate cases (22 vs. 14 days), but this finding was not significant (p=0.441).
O'Nions 2020 (14) *Preprint* Longitudinal case series UK Apr-May 2020	Analyzed longitudinal samples from hospitalized COVID-19 patients with aggressive hematological malignancy on systemic anti-cancer treatment (n=10). Measured days from symptom onset to negative PCR result.	Nose and throat swabs -Hematological malignancies included acute myeloid leukaemia, B-lymphoblastic leukaemia, T lymphoblastic leukaemia, and diffuse large B cell lymphoma. -All patients received systemic anti-cancer treatment within 28 days of developing COVID-19. - Eight patients seroconverted and developed antibodies to the major SARS-CoV-2 antigens (S1 and N) with six producing neutralising antibody responses.

		-The median duration of PCR positivity was 12 days (IQR 24). -Days from symptom onset to negative PCR ranged from 9-62 days.
Solid organ transplant patients (n=6)		
Benotmane 2020 (18) Retrospective cohort study France Mar-Apr 2020	Studied kidney transplant recipients with COVID-19 (n=40). qRT-PCR was used to detected SARS-CoV-2 nucleic acid (targeting two regions on the RNA dependent RNA polymerase gene). Patients were followed up weekly until discharge then tested at 30, 45, and 60 days after symptom onset. Viral clearance was defined as at least 1 negative RT-PCR test.	Nasopharyngeal swabs and plasma samples -The median time after kidney transplantation was 6.6 years (IQR: 2.8-14.6 years). At the time of COVID-19 diagnosis, 35 (87.5%) patients were taking immunosuppressive therapy. -The viral load of most patients (74.4%) peaked at the time of diagnosis. -No patient showed a viral clearance before day 21. Ten patients (24.4%) showed persistent viral RNA shedding after 31 days. -Patients receiving immunosuppressive therapy tended to have more positive RNAemia, but this finding was not significant (p=0.29).
Zhu 2020 (23) Retrospective cohort study China Jan-Mar 2020	Analyzed data from renal transplant recipients with laboratory-confirmed COVID-19 pneumonia (n=10). Also collected and compared clinical data from immunocompetent family members with COVID-19 pneumonia (n=10). Time of virus shedding, defined as illness onset to negative RT-PCR test, was monitored.	Throat swabs -The mean time of virus shedding in the transplant patients was 28.4 ± 9.3 days. This was significantly longer than that of the immunocompetent family members (12.2 ± 4.6 days , p<0.01).
Caillard 2020 (22) *LTE* Longitudinal case series France Oct 2020*	Prospectively monitored kidney transplant recipients with COVID-19 (n=42). RT-PCR was used to detect SARS-CoV-2 nucleic acid (targeting two regions on the RNA dependent RNA polymerase gene).	Nasopharyngeal swab, saliva, and respiratory specimens -At day 30, 15/35 (43%) patients tested still had positive RT-PCR results, with viral loads above the threshold for which there is a risk of SARS-CoV-2 transmission (>3 log10 copies per reaction). -At day 45, 12 patients (34%) still had positive RT-PCR results. -At 60 days, 6 patients (17%) had low but still detectable SARS-CoV-2 loads.
Gaston 2020 (19) Longitudinal case series	Analyzed data from solid organ transplant recipients on maintenance immunosuppression with symptomatic COVID-19 infection (n=25). Viral positivity	Nasopharyngeal and oropharyngeal swabs -Only 5 patients had serial testing. -4/5 patients had RT-PCR results longer than 21 days post symptom onset.

USA Mar-May 2020	was assessed by RT-PCR (targeting N1 and N2 SARS-CoV-2 gene).	-Two patients were still positive ≥27 days post symptom onset. -One patients was still positive at day 38.
Christensen 2020 (20) Longitudinal case series USA Mar-May 2020	Analyzed data from symptomatic kidney/liver transplant recipients with COVID-19 (n=6). Viral positivity was assessed by qRT-PCR.	Nasopharyngeal swabs -The median time from transplant was 1.9 years (range: 0.21-9.3). All six patients had hypertension (100%) and 5 had diabetes (83%). -All patients had been on immunosuppressant medication prior to COVID-19 diagnosis. Five had their immunosuppressant medication stopped at time of hospital admission while the other patient who was managed as an outpatient had their medication reduced by 50%. -Four of 5 patients (80%) were positive for SARS-CoV-2 viral RNA, while 1 patients only had a positive SARS-CoV-2 neutralizing antibody test. -One patient had a positive RT-PCR result for 28 days of follow-up, despite presence of SARS-Cov-2 IgG.
Silvano 2021 (21) Longitudinal case series Portugal Mar-Jun 2020	Analyzed data from kidney transplant patients with COVID-19 (n=6). Duration of viral RNA shedding measured and defined as the time between the first and the last positive RT-PCR SARS-CoV-2 test.	Nasopharyngeal and oropharyngeal swabs -The median time from transplant to COVID-19 diagnosis was 161 months (range: 8-235). Only one patients had undergone transplantation in the past year. All patients were on immunosuppression therapy. -Duration of viral RNA shedding was measured for five of the patients. -For the two patients with moderate severity, the duration of viral RNA shedding was <9 days. -For the three patients with severe disease, the duration of viral RNA shedding was >40 days, persisting despite symptom resolution. Two still had positive RT-PCR swabs at the end of follow-up (>44 and >66 days).
IMMUNOCOMPROMISED PATIENTS		
People with HIV (n=2)		
Vizcarra 2020 (24) Prospective cohort study Spain	Studied consecutive HIV-infected adults who had suspected or confirmed COVID-19 as of April 30, 2020 (n=51). SARS-CoV-2 was detected by qRT-PCR.	Nasopharyngeal swabs, sputum, or lower respiratory tract aspirates -54% (19/35) of individuals with laboratory-confirmed SARS-CoV-2 infection had follow-up qRT-PCR assays conducted. -All patients were on antiretroviral therapy. -Viral clearance occurred over a median of 18 days (IQR 7-28) post symptom onset for 68% (13/19) of

May 2020*		individuals. For the other six individuals, SARS-CoV-2 remained detectable for a median of 40 days (IQR 13–45) post symptom onset. These patients had more severe disease, higher ICU admission, lower nadir CD4 cell counts are a higher proportion of comorbidities than individuals with shorter times to viral clearance ($p<0.05$).
Mondi 2020 (25) Longitudinal case series Italy Mar-May 2020	Analyzed data from HIV-positive patients hospitalized with COVID-19 (n=5). Viral clearance was defined as two consecutive negative RT-PCR tests for SARS-CoV-2 (targeting the E and RNA-dependent RNA polymerase genes).	Nasopharyngeal swab -All five patients were virologically suppressed on antiretroviral therapy. -Serial testing results were only available for two patients. For these two patients, viral clearance occurred on day 29 and 43, from symptom onset.

*Date estimated from publication date

LTE=Letter to the editor

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within the excel database to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: (immunosup* OR immunocomp* OR transplant OR cancer) AND (persist* OR prolonged OR viable OR shed* OR culture OR dynamics OR clearance). This review contains research published up to February 5, 2021. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur la période infectieuse de la COVID-19 chez les personnes immunodéprimées ou immunodéficientes

Introduction

Quelle est la durée de la période infectieuse du SRAS-CoV-2 chez les personnes immunodéprimées et immunodéficientes?

La période infectieuse (aussi appelée période de contagiosité) est définie comme la durée pendant laquelle une personne infectée peut transmettre un agent infectieux à une autre personne. Il s'agit d'un paramètre clinique et épidémiologique important à comprendre pour pouvoir contrôler quelque maladie infectieuse que ce soit. On estime que la période infectieuse moyenne du SRAS-CoV-2 pour les immunodépressifs légers/moyennement symptomatiques commence en moyenne 2,5 jours avant l'apparition des symptômes, atteint un sommet vers le jour 4 puis redescend dans un délai de 8 à 10 jours après le début des symptômes, ce qui donne environ 10 à 13 jours de contagiosité (se reporter à la Revue rapide de la période infectieuse, septembre 2020).

La présente synthèse porte sur les populations immunodéprimées et immunodéficientes. L'immunosuppression peut découler de certaines maladies ou de certains traitements d'origine immunologique (p. ex., traitement anticancéreux, médicament antirejet, etc.) alors que l'immunodéficience peut être liée à des causes infectieuses ou génétiques. Les premiers exposés de cas ont mentionné de plus longues périodes (> 14 jours) pendant lesquelles on pouvait obtenir un SRAS-CoV-2 réplicatif (c.-à-d. positif à la coproculture) dans ces populations et chez les personnes gravement atteintes de la COVID-19. Deux études (1, 2) ont aussi démontré que l'immunosuppression est associée à une probabilité plus élevée d'excrétion d'ARN viral persistant (> 21 jours) alors qu'une autre n'a révélé aucun lien significatif (3). La possibilité d'infections prolongées et récurrentes dans cette population a fait ressortir la nécessité d'effectuer d'autres recherches sur l'infectiosité et de mettre en place des stratégies uniques pour sortir ces personnes de l'isolement de façon sécuritaire tout en prévenant la transmission de la maladie.

La présente synthèse en bref porte sur la recherche effectuée et publiée jusqu'au 5 février 2021 et vise à documenter la période infectieuse chez les personnes immunodéficientes ou immunodéprimées atteintes de COVID-19. Les études présentées ont été organisées par maladie sous-jacente et type d'étude. En raison de leur nature préliminaire, les exposés de cas n'ont pas été inclus dans cette synthèse. Les estimations en ce qui concerne la période infectieuse ont été établies

en combinant des études épidémiologiques et cliniques qui ont permis de préciser le moment où une personne infectée ne pouvait plus transmettre le virus ou n'était plus susceptible de pouvoir le transmettre. La plupart des études ont utilisé le RT-PCR pour diagnostiquer les cas de COVID-19 et surveiller l'excrétion de l'ARN viral avec le temps. Même si le test RT-PCR peut être utilisé pour détecter l'ARN viral, il ne fournit aucune preuve d'infectivité puisqu'il donne également des résultats positifs lorsque des particules virales non infectieuses sont présentes. Les tissus infectés continuent généralement d'excréter ces particules pendant un certain temps après que l'infection a été éliminée par le système immunitaire hôte (4). La récupération d'un virus réplicatif a été utilisée comme substitut *in vitro* de l'infectiosité entre humains. Pour déterminer si un virus viable a été isolé dans un échantillon, la culture cellulaire est la façon la plus fiable d'en établir la réplication. Peu d'études ont malheureusement utilisé des méthodes de culture parce qu'elles peuvent être lentes et coûteuses. La détection de l'ARN subgénomique a été recommandée comme substitut pour l'excrétion du virus infectieux (5), mais il n'y a pas encore de consensus à cet effet (6).

Points clés

- Dix-neuf études ont été examinées dans cette synthèse, dont une cohorte bidirectionnelle, une cohorte prospective, dix études de cohorte rétrospectives et sept séries de cas longitudinales. Les populations immunodéprimées incluaient des personnes atteintes d'un cancer (n = 11) et des patients qui ont subi une greffe (n = 6). Des personnes atteintes du VIH figuraient parmi les personnes immunodéprimées (n = 2). Seules deux études ont fourni des preuves de la présence d'un virus viable dans la culture cellulaire, alors que les autres ont décrit la durée de l'excrétion d'ARN viral à l'aide du test RT-PCR ou qRT-PCR.

Études portant sur les cultures (n = 2)

- Deux mois après l'infection, le virus SRAS-CoV-2 réplicatif était encore présent chez des patients immunodéprimés en raison de cancers hématologiques, une période beaucoup plus longue que la période infectieuse estimée dans les populations immunocompétentes moyennes (entre 10 et 13 jours, comme indiqué dans la Revue rapide de la période infectieuse).

Études portant sur le test RT-PCR (n = 17)

- Tests RT-PCR effectués sur des échantillons respiratoires provenant d'une personne immunocompétente légèrement symptomatique deviennent généralement négatifs dans les 14 à 20 jours. Comme le montrent les points ci-dessous, la clairance de l'ARN viral était

beaucoup plus longue chez les personnes immunodéprimées ou immunocompétentes. La durée de l'excrétion de l'ARN viral dépendait dans une certaine mesure de la cause de l'immunosuppression ou de l'immunodéficience.

- Chez les patients atteints de cancer, le délai médian avant la clairance de l'ARN viral variait de 12 à 50 jours, avec une plage globale allant de 9 à 78 jours. La thérapie anticancéreuse systémique (c.-à-d. chimiothérapie, hormonothérapie, médicaments à cible définie et immunothérapie), avant ou pendant la positivité à la COVID-19, n'était pas associée de façon significative à la durée de la clairance virale.

- Chez les patients qui ont subi une greffe d'organe entier et suivent une thérapie immunosuppressive, le temps qui s'est écoulé avant la clairance virale variait entre 9 et 66 jours. L'excrétion moyenne d'ARN viral était beaucoup plus longue chez les patients ayant subi une greffe de rein que chez les personnes immunocompétentes (28,4 jours comparativement à 12,2 jours, $p < 0,01$). Les données d'une étude ont, en outre, révélé une charge virale élevée au jour 30 de l'infection chez un groupe de patients ayant subi une greffe, ce qui indique une probabilité élevée de transmission du SRAS-CoV-2 30 jours après l'apparition des symptômes.

- Chez les patients atteints de VIH, la clairance virale de l'ARN a atteint 18 jours en moyenne (EI 7 à 28), mais elle est demeurée détectable chez certains patients plus de 40 jours après l'apparition des symptômes. On a cependant vu une plus longue excrétion d'ARN viral chez les cas graves de VIH que chez les cas légers/modérés.

Vue d'ensemble des éléments de preuve

Au total, 19 études ont été incluses dans la présente synthèse, ce qui inclut des études de cohorte et des séries de cas longitudinales. Bon nombre d'entre elles sont des prépublications qui n'ont donc pas fait l'objet d'un examen par les pairs. Les cohortes prospectives présentent un risque de biais plus faible et sont vues comme des recherches de meilleure qualité, mais peu d'études portent sur cette question. Les séries de cas comprennent un petit échantillon, en plus de présenter un biais de sélection et un biais de rappel (p. ex., apparition de symptômes autodéclarés). En outre, bon nombre des cas de personnes immunodéprimées ou immunodéficientes décrits dans la présente revue présentaient également d'autres problèmes de santé chroniques sous-jacents, et il est difficile de déterminer si ces problèmes ont influé sur les résultats et si oui, de quelle façon ils ont influé sur

ceux-ci. Dans l'ensemble, en raison des risques de biais, il faut faire preuve de prudence au moment d'interpréter ces études, puisque les résultats sont susceptibles de changer si des recherches supplémentaires sont effectuées.

Il existe également plusieurs lacunes dans les connaissances sur la période infectieuse du SRAS-CoV-2 dans des clientèles ayant des besoins particuliers. Peu d'études ont utilisé la culture cellulaire et se sont plutôt tournées vers la détection de l'ARN viral comme indicateur pour la période infectieuse potentielle. De telles méthodes ne permettent pas de faire la distinction entre les particules virales infectieuses et non infectieuses, mais la relation entre la charge virale et la probabilité de positivité de la culture a été abordée dans la littérature. Il faut effectuer d'autres recherches sur l'immunité et sur l'incidence des thérapies immunosuppressive sur la période infectieuse d'autres maladies d'origine immunitaire (p. ex., arthrite rhumatoïde, maladie de Crohn, etc.). Il sera également justifié d'explorer plus à fond des stratégies pour pouvoir sortir ces personnes de l'isolement de façon sécuritaire et empêcher une transmission du virus.

TABLE DES MATIÈRES

PÉRIODE INFECTIEUSE DES PERSONNES IMMUNODÉPRIMÉES OU IMMUNODÉFICIENTES

Patients atteints d'un cancer ou d'une maladie hématologique (n = 11) :

- Seules deux études ont fourni des preuves de la capacité de réplication du virus par culture cellulaire :
    - Les patients dont l'immunosuppression est due à des cancers hématologiques, qui ont subi une greffe de cellules hématopoïétiques allogéniques ou autologues ou qui ont reçu des thérapies cellulaires, ont excrété des virus SARS-CoV-2 réplicatifs pendant au moins deux mois (7, 8), ce qui est beaucoup plus long que ce qui a été noté chez les patients immunocompétents (< 7 jours) (8).
- De nombreux patients souffraient d'autres maladies chroniques sous-jacentes (9, 10).
- Dans la majorité des cas, il a fallu plus de 14 jours pour obtenir des résultats négatifs après le test PCR avec un délai médian variant entre 12 et 50 jours et une plage globale de 9 à 78 jours (7 à 17).

- La thérapie anticancéreuse (c.-à-d. chimiothérapie, hormonothérapie, médicaments à cible définie et immunothérapie), avant ou pendant la positivité à la COVID-19, n'était pas associée de façon significative à la durée de la clairance de l'ARN viral.

- Les cas graves présentaient une durée d'élimination de l'ARN viral plus longue que les cas légers/modérés, mais cette constatation n'était cependant pas significative (13).

Patients ayant subi une greffe d'organe entier (n = 6) :

- La majorité des patients suivaient un traitement immunosuppresseur (18 à 21).

- Aucune étude n'a démontré la présence d'un virus viable obtenu par culture cellulaire.

- Dans la majorité des cas, il a fallu plus de 14 jours pour obtenir des résultats négatifs après le test PCR avec une plage globale variant entre 9 et 66 jours (18 à 23).

- Le temps moyen d'excrétion de l'ARN viral du SRAS-CoV-2 dans un groupe de patients ayant subi une greffe de rein était de 28,4 ± 9,3 jours, ce qui était considérablement plus long que pour les personnes immunocompétentes (12,2 ± 4,6 jours, $p < 0,01$) (23).

- Une étude menée auprès de receveurs de greffes du rein a révélé que 43 % des patients présentaient toujours des résultats positifs au test RT-PCR au 30^{e} jour avec une charge virale supérieure à 3 copies log^{10} par réaction, soit le seuil pour lequel il existe un risque de transmission du SRAS-CoV-2 (22).

- Les cas graves ont cependant eu une durée d'élimination de l'ARN viral plus longue que les cas légers/modérés, mais cette association n'a pas l'objet d'une enquête statistique (21).

Patients atteints du virus de l'immunodéficience humaine (VIH) (n = 2) :

- Tous les patients suivaient un traitement antirétroviral (24, 25).

- Aucune étude n'a démontré la présence d'un virus viable obtenu par culture cellulaire.

- La clairance virale de l'ARN s'est produite sur une médiane de 18 jours (EI 7 à 28) après l'apparition des symptômes (24).

- L'ARN viral du SRAS-CoV-2 a pu continuer d'être détecté chez certains patients atteints du VIH pendant plus de 40 jours après l'apparition des symptômes (24, 25).

- Les patients pour qui le temps de clairance de l'ARN viral était plus long étaient atteints d'une forme plus grave de la maladie, avaient été admis plus souvent aux soins intensifs, avaient un nadir de

compte de cellules CD4 moins élevé et une plus forte proportion de comorbidités que les personnes dont le temps de clairance virale était plus court ($p < 0,05$) (24).

Tableau 1 : Études faisant état d'estimations de la période infectieuse chez les patients immunodéprimés et immunodéficients ayant la COVID-19 (n = 19)

ANNÉE	MÉTHODE	PRINCIPAUX RÉSULTATS
PATIENTS IMMUNODÉPRIMÉS		
Patients atteints de cancer (n = 11)		
Roedl 2020 (8) *Lettre à la rédaction* Étude de cohorte rétrospective Allemagne Novembre 2020*	Étude portant sur des patients dont la tumeur maligne a été traitée par une greffe allogénique de cellules souches hématopoïétiques (GCSH) ou par un traitement avec lymphocytes T à récepteur antigénique chimérique (CAR-T) et qui ont dû être hospitalisés aux soins intensifs en raison de la COVID-19 (n = 6). Les résultats ont été comparés à ceux des patients atteints de la COVID-19 qui n'avaient aucun antécédent d'affection maligne (n = 18). Le SRAS-CoV-2 a été détecté par RT-PCR et l'isolement de virus a été effectué par culture cellulaire. Puis, après 48 à 72 heures d'incubation, l'effet cytopathique dans les cellules Vero infectées (CCL81; American Type Culture Collection) a été évalué.	Échantillons broncho-alvéolaires et de plasma -Chez les patients qui ont des antécédents de GCSH ou de CAR-T, les charges virales sont demeurées élevées jusqu'à la fin du suivi, soit jusqu'au jour 28 (tant dans les échantillons respiratoires que de plasma). En revanche, l'ARN du SRAS-CoV-2 était inférieur à la limite de détection après 21 et 11 jours dans les échantillons respiratoires et les échantillons de plasma, respectivement, chez des patients immunocompétents. -Le virus infectieux a été isolé dans cinq échantillons provenant de quatre patients ayant des antécédents de GCSH ou de thérapie CAR-T, obtenus entre 4 et 28 jours après l'admission aux soins intensifs. Chez les patients immunocompétents, le virus infectieux n'a pas pu être détecté après le jour 7.
Aydillo 2020 (7) *Lettre à la rédaction* Séries de cas longitudinales ÉTATS-UNIS Mars et avril 2020	Analyse d'échantillons longitudinaux prélevés chez des patients immunodéprimés et atteints de cancer ayant eu la COVID-19 (n = 20). La culture cellulaire a été utilisée pour détecter des virus viables et le séquençage du génome entier a été utilisé pour détecter des variantes génétiques. Les monocouches de cellules Vero E6 inoculées ont été incubées	Sécrétions rhinopharyngées prélevées par écouvillonnage et expectorations -Dix-huit personnes ont reçu une greffe allogénique (n = 6) ou autologue (n = 10) de cellules souches ou un traitement avec lymphocytes T à récepteur antigénique chimérique (CAR-T) (n = 2). Quinze recevaient un traitement ou une chimiothérapie actif. -L'ARN viral a été détecté jusqu'à 78 jours après l'apparition des symptômes (EI : 24 à 64 jours). -Un virus viable a été isolé dans les échantillons de suivi de cinq patients 8, 17, 25, 26 et 61 jours après l'apparition des symptômes.

	pendant une semaine et surveillées quotidiennement afin d'en voir l'effet cytopathique. Le temps qui s'est écoulé entre l'apparition des symptômes et le résultat négatif au test RT-PCR a également été mesuré.	-Les patients chez qui l'on a retrouvé un virus viable depuis plus de 20 jours avaient reçu des greffes allogéniques de cellules souches hématopoïétiques ou un traitement avec lymphocytes T à récepteur antigénique chimérique dans les six derniers mois et étaient demeurés séronégatifs pour les anticorps à la nucléoprotéine virale. Deux de ces patients ont eu une forme grave de la COVID-19. -Le séquençage du génome entier n'a révélé aucun changement important dans les séquences consensus des spécimens en série originaux ou des isolats en culture, ce qui correspond à une infection persistante.
Wong 2020 (15) Étude de cohorte bidirectionnelle ÉTATS-UNIS Décembre 2020*	Étude qui évalue des patients cancéreux ayant eu un résultat positif au SRAS-CoV-2 qui avaient subi un traitement anticancéreux (n = 26) et ont subi un test PCR (ciblant les gènes N2 et ORF1a) toutes les deux semaines jusqu'à ce qu'ils aient obtenu deux résultats négatifs successifs à ce test.	Sécrétions rhinopharyngées prélevées par écouvillonnage -Différents cas de cancer ont été inclus, dont 15 (58 %) présentaient une maladie au stade avancé (stade IV). -Le temps moyen avant d'obtenir des résultats négatifs au test PCR était de 32 jours. -Il a fallu plus de 14 jours à vingt (77 %) patients avant d'obtenir des résultats négatifs à des tests PCR consécutifs.
Nakamura 2020 (10) *Prépublication* Étude de cohorte rétrospective Japon Janvier à mai 2020	Analyse des données provenant de patients atteints de la COVID-19 et ayant des antécédents de cancer (n = 32). Mesure le temps qui s'est écoulé entre l'apparition de la maladie et le premier de deux résultats négatifs consécutifs au test de dépistage RT-PCR pour le SARS-CoV-2.	Sécrétions rhinopharyngées prélevées par écouvillonnage -Vingt-cinq patients (78 %) avaient des tumeurs solides, tandis que sept (22 %) avaient une hémopathie maligne. Dix-neuf (59 %) avaient aussi au moins une comorbidité (p. ex., hypertension, 41 %). Treize patients (41 %) avaient reçu un traitement contre le cancer au cours des 30 derniers jours. -La période médiane entre l'apparition de la maladie et le premier de deux résultats négatifs consécutifs au test de dépistage RT-PCR pour le SARS-CoV-2 était de 22 jours (EI : 18 à 25) chez les survivants (n = 224).
Fox 2020 (11) Étude de cohorte rétrospective Royaume-Uni	Analyse des données provenant de patients atteints de la COVID-19 et ayant des troubles hématologiques, majoritairement des cancers (n = 55). La durée de l'excrétion d'ARN viral a été analysée avec les méthodes Kaplan-Meier, de la date de l'apparition de la maladie au	Échantillon prélevé dans la gorge et dans le nez -94 % (52/55) des patients suivaient ou avaient déjà suivi un traitement anticancer systémique (chimiothérapie ou immunothérapie). -Le délai médian d'excrétion de l'ARN viral du SARS-CoV-2 était de 34 jours chez les survivants (n = 27, IC à 95 %, 27 à 47). La plus longue période d'excrétion a été de 49 jours (même si le résultat était toujours positif à la fin de la période de suivi).

Mars à mai 2020	premier de deux résultats négatifs consécutifs au test de dépistage RT-PCR pour le SARS-CoV-2 (ciblant le gène N).	-La durée de l'excrétion de l'ARN viral n'a pas été prolongée chez les patients qui ont reçu un traitement par chimiothérapie ou immunothérapie au cours des 14 ou des 28 derniers jours.
Ramaswamy 2020 (16) Étude de cohorte rétrospective Inde D'avril à juin 2020	Étude dans laquelle les patients atteints de cancer qui suivent une thérapie générale et dont la COVID-19 a été confirmée en laboratoire (n = 230) ont subi des tests de dépistage tous les 3 ou 4 jours jusqu'à ce que le résultat du test RT-PCR soit négatif. Une analyse de régression logistique a été effectuée pour évaluer les facteurs qui retardaient la conversion en RT-PCR négatif.	Écouvillonnage du rhinopharynx ou du nasopharynx -Les patients étudiés avaient reçu divers diagnostics de cancer, dont les plus malins étaient la leucémie aiguë (20 %) et les tumeurs gastro-intestinales malignes (17 %). -53 % des patients présentaient des signes de rémission ou de cancer contrôlé, alors que 14 % avaient un cancer non contrôlé ou étaient en contrôle actif de leurs symptômes. -Le délai médian avant la séroconversion du SRAS-CoV-2 était de 17 jours (EI : 17 à 28). -La durée de l'excrétion de l'ARN viral était de 14 jours pour 52 patients (30 %; n = 182), 52 patients (30 %) ont obtenu un résultat négatif après 15 à 21 jours alors que pour 50 patients (29 %), le résultat était toujours positif après plus de 21 jours de suivi. -Aucun des facteurs évalués, incluant compris l'âge, le sexe, le diabète sucré, les cancers hématolymphoïdes, le cancer non contrôlé et la thérapie systémique non myélosuppressive, n'a été associé de façon significative à l'excrétion prolongée d'ARN viral.
Infante 2020 (9) *Lettre à la rédaction* Étude de cohorte rétrospective Espagne Mars et avril 2020	Analyse des données provenant de patients atteints de la COVID-19 et ayant une hémopathie maligne (n = 41). Le temps nécessaire à la clairance virale a été mesuré avec le test RT-PCR, mais les dates de début et de fin n'ont pas été précisées.	Écouvillonnage du nez -Vingt-neuf (70 %) des patients avaient une lymphopathie maligne. Vingt et un (51 %) étaient sous traitement actif au moment où ils ont attrapé la COVID-19. -La majorité des patients (93 %) avaient d'autres problèmes de santé chroniques. -Le délai médian de l'excrétion d'ARN viral était de 32,7 jours (plage de 10 à 70 jours) chez les patients survivants (n = 26). Un patient atteint de leucémie myéloïde aiguë qui recevait un traitement d'induction au moment de l'infection a obtenu un résultat positif au test RT-PCR après 70 jours.
Xu 2020 (12) *Prépublication*	Analyse de tous les patients d'un hôpital de soins tertiaires dont la COVID-19 a été confirmée, qui ont dû consulter un médecin en raison	Sécrétions rhinopharyngées prélevées par écouvillonnage -Seize patients avaient une maladie métastatique, 17 suivaient un traitement actif au moment du

Étude de cohorte rétrospective ÉTATS-UNIS Mars à juin 2020	d'un cancer dans les trois dernières années et au moins un essai de suivi sur le SRAS-CoV-2 (n = 32). Le temps avant la clairance virale a été analysé à l'aide des méthodes Kaplan-Meier, pour lesquelles les données ont été censurées au moment du dernier essai RT-PCR connu. Cette méthode a été comparée à d'autres lignes directrices sur la clairance virale : • Lignes directrices UK-NICE : délai mesuré avant d'obtenir un résultat négatif au test RT-PCR. • Critères du CDC : Stratégie basée sur les symptômes/délai mesurés 10 jours après le premier résultat positif au test RT-PCR et 3 jours après les derniers symptômes.	diagnostic de COVID-19 et huit recevaient un traitement cytotoxique. -Le délai médian avant la clairance virale a été estimé à 50 jours (IC à 95 %, 33 à 58 jours). -Selon les lignes directrices UK-NICE, le délai médian avant la clairance était de 31 jours (IC à 95 %, 26 à 42 jours). -En fonction d'une stratégie basée sur les symptômes/délai et fondée sur les critères du CDC, le temps moyen avant la clairance était de 13 jours (IC à 95 %, 10 à 17 jours). -Les modèles des risques proportionnels de Cox ont montré que les patients symptomatiques présentaient une excrétion d'ARN viral plus longue que les patients asymptomatiques (HR 0,25 pour un résultat négatif au test PCR, IC à 95 % 0,08 à 0,76, p = 0,01). -La thérapie anticancéreuse (chimiothérapie, immunothérapie, thérapie ciblée ou hormonale), avant ou pendant la positivité à la COVID-19, n'a pas été associée de façon significative à la durée de la clairance virale.
Berghoff 2020 (17) Étude de cohorte rétrospective Autriche Mars à mai 2020	Les patients atteints de cancer (n = 1 016) étaient régulièrement soumis à des tests de dépistage RT-PCR pour l'ARN du SRAS-CoV-2. Temps entre le premier résultat positif et le premier résultat négatif.	Écouvillonnage du nez ou pharyngé -L'infection par le SRAS-CoV-2 a été confirmée chez 4 des 1 016 patients (0,4 %). Les patients touchés étaient atteints d'un cancer de l'estomac (n = 1), d'un sarcome (n = 1) et d'un cancer de la tête et du cou (n = 2). Deux des patients suivaient une thérapie anticancéreuse active. -La clairance virale a été atteinte chez trois patients entre 14 et 56 jours après avoir obtenu un résultat positif au test. Au moment de la rédaction du rapport, un patient n'avait pas encore atteint la clairance virale 28 jours après le premier résultat positif.
Sanchez-Pina 2020 (13) Étude rétrospective de cohorte appariée Espagne	Étude ayant analysé les résultats des patients atteints de COVID-19 et de cancers hématologiques (n = 39). Les résultats ont été comparés à un groupe témoin apparié comprenant 53 patients non atteints de cancer, mais ayant la COVID-19. Un test PCR de suivi pour la COVID-19 a été effectué	Sécrétions rhinopharyngées prélevées par écouvillonnage -Les cancers hématologiques les plus fréquents étaient un lymphome (n = 12), un myélome multiple (n = 12) et la leucémie lymphocytaire chronique (n = 6). -Dans les 20 cas de suivi, il a fallu un délai médian de 14 jours avant d'obtenir un résultat négatif au test de PCR.

Mars et avril 2020	chez un sous-ensemble de patients cancéreux (n = 20) pour mesurer le temps nécessaire à la clairance virale.	-Cinq patients ont subi une excrétion prolongée d'ARN viral avec un délai médian de 23 jours (plage variant entre 16 et 31 jours). -Les cas graves présentaient une durée d'excrétion de l'ARN viral plus longue que les cas légers/modérés (22 jours plutôt que 14), mais cette constatation n'était cependant pas significative (p = 0,441).
O'Nions 2020 (14) *Prépublication* Séries de cas longitudinales Royaume-Uni Avril et mai 2020	Analyse d'échantillons longitudinaux provenant de patients hospitalisés pour la COVID-19 et atteints d'une tumeur hématologique agressive suivant un traitement anticancer systémique (n = 10). Nombre de jours mesuré entre l'apparition des symptômes et le résultat négatif au test de PCR.	Échantillon prélevé dans la gorge et dans le nez -Les hémopathie maligne incluaient la leucémie myéloïde aiguë, la leucémie lymphoblastique B, la leucémie lymphoblastique T et le lymphome diffus à grandes cellules B. -Tous les patients ont reçu un traitement anticancer systémique dans les 28 jours suivant l'apparition de la COVID-19. - Huit patients ont eu une séroconversion et développé des anticorps contre les principaux antigènes du SARS-CoV-2 (S1 et N) avec six réponses d'anticorps neutralisants. -Le délai médian de la positivité évaluée par test PCR était de 12 jours (EI : 24). -Le nombre de jours entre l'apparition des symptômes et un résultat négatif au test PCR variait de 9 à 62 jours.
Patients ayant subi une greffe d'organe entier (n = 6)		
Benotmane 2020 (18) Étude de cohorte rétrospective France Mars et avril 2020	Étude ayant évalué des personnes ayant reçu une greffe de rein alors qu'elles avaient la COVID-19 (n = 40). Le procédé qRT-PCR a été utilisé pour détecter l'acide nucléique du SARS-CoV-2 (ciblant deux régions du gène polymérase de l'ARN dépendant de l'ARN). Les patients faisaient l'objet d'un suivi hebdomadaire jusqu'à leur congé, après quoi ils ont subi de nouveaux tests 30, 45 et 60 jours après l'apparition des symptômes. La clairance virale a été définie comme exigeant au moins 1 résultat négatif au test RT-PCR.	Sécrétions rhinopharyngées prélevées par écouvillonnage et échantillons de plasma -Le délai médian après une greffe de rein était de 6,6 ans (EI : entre 2,8 et 14,6 ans). Au moment du diagnostic de COVID-19, 35 (87,5 %) patients suivaient un traitement immunosuppresseur. -La charge virale de la plupart des patients (74,4 %) a atteint un sommet au moment du diagnostic. -Aucun patient n'a montré de clairance virale avant le 21e jour. Dix patients (24,4 %) montraient encore une excrétion persistante d'ARN viral après 31 jours. -Les patients qui recevaient un traitement immunosuppresseur avaient tendance à avoir une RNAémie plus positive, mais ce résultat n'était pas significatif (p = 0,29).
Zhu 2020 (23)	Données analysées provenant de personnes ayant reçu une	Prélèvements de gorge

Étude de cohorte rétrospective Chine Janvier à mars 2020	transplantation rénale et atteinte d'une pneumonie due à la COVID-19 confirmée en laboratoire (n = 10). Des données cliniques des membres immunocompétents de la famille, qui étaient aussi atteints de pneumonie due à la COVID-19 (n = 10), ont également été recueillies et comparées. Le temps avant l'excrétion du virus, défini comme l'obtention d'un résultat négatif au test RT-PCR, a été surveillé.	-La durée moyenne d'excrétion du virus chez les patients qui ont subi une greffe était de 28,4 ± 9,3 jours. Ce délai était beaucoup plus long que celui obtenu pour les membres immunocompétents de la famille (12,2 ± 4,6 jours, p < 0,01).
Caillard 2020 (22) *Lettre à la rédaction* Séries de cas longitudinales France Octobre 2020*	Étude prospective ayant évalué des personnes ayant reçu une greffe de rein et atteintes de la COVID-19 (n = 42). Le test RT-PCR a été utilisé pour détecter l'acide nucléique du SARS-CoV-2 (ciblant deux régions du gène polymérase de l'ARN dépendant de l'ARN).	Sécrétions rhinopharyngées prélevées par écouvillonnage, prélèvements de salive et respiratoires -Au jour 30, 15 patients sur les 35 (43 %) ayant été testés présentaient toujours des résultats positifs au test RT-PCR, avec des charges virales supérieures au seuil pour lesquelles il y a un risque de transmission du SRAS-CoV-2 (> 3 copies log10 par réaction). -Au jour 45, 12 patients (34 %) obtenaient encore des résultats positifs au test RT-PCR. -Au jour 60, 6 patients (17 %) présentaient des charges de SRAS-CoV-2 faibles, mais néanmoins détectables.
Gaston 2020 (19) Séries de cas longitudinales ÉTATS-UNIS Mars à mai 2020	Analyse des données de personnes ayant subi une greffe d'organes entiers qui reçoivent une immunosuppression d'entretien et ont une infection symptomatique à la COVID-19 (n = 25). La positivité virale a été évaluée à l'aide du test RT-PCR (ciblant les gènes N1 et N2 du SARS-CoV-2).	Sécrétions rhinopharyngées et oropharyngées prélevées par écouvillonnage -Seulement 5 patients ont subi des tests en série. -4 patients sur 5 ont obtenu des résultats positifs au test RT-PCR plus de 21 jours après l'apparition des symptômes. -Deux patients ont reçu des résultats positifs 27 jours après l'apparition des symptômes. -Un patient a obtenu un autre résultat positif au jour 38.
Christensen 2020 (20) Séries de cas longitudinales	Analyse des données sur des personnes ayant reçu une greffe de rein ou de foie symptomatiques pour la COVID-19 (n = 6). La positivité virale a été	Sécrétions rhinopharyngées prélevées par écouvillonnage -Le délai médian de la greffe était de 1,9 an (plage : 0,21 à 9,3). Les six patients souffraient tous de l'hypertension (100 %) et cinq étaient diabétiques (83 %).

ÉTATS-UNIS Mars à mai 2020	évaluée à l'aide du procédé qRT-PCR.	-Tous les patients avaient pris des immunosuppresseurs avant le diagnostic de COVID-19. Cinq patients ont cessé de prendre leurs immunosuppresseurs au moment de leur admission à l'hôpital, alors que l'autre patient qui a été vu en consultation externe a vu ses médicaments réduits de 50 %. -Quatre des cinq patients (80 %) ont obtenu un résultat positif pour l'ARN viral du SRAS-CoV-2, tandis qu'un seul patient a obtenu un résultat positif au test d'anticorps neutralisant du SRAS-CoV-2. -Un patient a obtenu un résultat positif au test RT-PCR pendant les 28 jours de suivi, malgré la présence d'IgG de SARS-Cov-2.
Silvano 2021 (21) Séries de cas longitudinales Portugal Mars à juin 2020	Analyse de données provenant de patients ayant subi une greffe de rein et atteints de la COVID-19 (n = 6). La durée de l'excrétion de l'ARN viral a été mesurée et définie comme le temps écoulé entre le premier et le dernier résultat positif au test RT-PCR pour le SARS-CoV-2.	Sécrétions rhinopharyngées et oropharyngées prélevées par écouvillonnage -Le délai médian entre la greffe et le diagnostic de COVID-19 était de 161 mois (plage : entre 8 et 235). Un seul patient avait subi une transplantation au cours de la dernière année. Tous les patients prenaient un traitement d'immunosuppression. -La durée de l'excrétion d'ARN viral a été mesurée pour cinq des patients. -Pour les deux patients atteints d'une forme modérée de la maladie, la durée de l'excrétion d'ARN viral était inférieure à 9 jours. -Pour les trois patients atteints d'une forme grave de la maladie, la durée de l'excrétion d'ARN viral était supérieure à 40 jours et a persisté malgré la disparition des symptômes. Deux avaient ont obtenu des écouvillons positifs au test RT-PCR à la fin du suivi (> 44 et > 66 jours).
PATIENTS IMMUNODÉPRIMÉS		
Personnes atteintes du VIH (n = 2)		
Vizcarra 2020 (24) Étude de cohorte prospective Espagne Mai 2020*	Étude portant sur des adultes infectés par le VIH et dont l'infection à la COVID-19 était soupçonnée ou confirmée au 30 avril 2020 (n = 51). Le SRAS-CoV-2 a été détecté par le procédé qRT-PCR.	Sécrétions rhinopharyngées prélevées par écouvillonnage, expectorations ou prélèvement par aspiration dans les voies respiratoires inférieures -54 % (19 sur 35) des personnes atteintes d'une infection au SRAS-CoV-2 confirmée en laboratoire ont fait l'objet de tests qrt-PCR de suivi. -Tous les patients suivaient un traitement antirétroviral. -La clairance virale s'est produite pendant une médiane de 18 jours (EI : entre 7 et 28) après

		l'apparition des symptômes chez 68 % (13/19) des personnes. Chez les six autres personnes, le SRAS-CoV-2 est demeuré détectable pendant une période médiane de 40 jours (EI : entre 13 et 45) après l'apparition des symptômes. Ces patients étaient atteints d'une forme plus grave de la maladie, avaient été admis plus souvent aux soins intensifs, avaient un nadir de compte de cellules CD4 moins élevé et une plus forte proportion de comorbidités que les personnes dont le temps de clairance virale était plus court ($p < 0,05$).
Mondi 2020 (25) Séries de cas longitudinales Italie Mars à mai 2020	Analyse des données sur des patients séropositifs hospitalisés et atteints de la COVID-19 (n = 5). La clairance virale a été définie comme deux résultats négatifs aux tests RT-PCR consécutifs pour le SRAS-CoV-2 (ciblant les gènes de la polymérase de l'ARN dépendant de l'E et de l'ARN).	Sécrétions rhinopharyngées prélevées par écouvillonnage -Les cinq patients faisaient tous l'objet d'une suppression virologique par traitement antirétroviral. -Les résultats des tests en série n'étaient disponibles que pour deux patients. Pour ces deux patients, la clairance virale a eu lieu les 29e et 43e jours après l'apparition des symptômes.

*Date estimée en fonction de la date de publication

Méthodologie :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient : (immunosup* OU immunocomp* OU transplant OU cancer) ET (persist* OU prolonged OU viable OU shed* OU culture OU dynamics OU clearance). La présente revue contient des recherches publiées jusqu'au 5 février 2021. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

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Emerging Evidence on COVID-19

Evidence Brief of Ivermectin

Introduction

Is there evidence that Ivermectin is an efficacious treatment for COVID-19?

Ivermectin is a broad-spectrum anti-parasitic agent approved in Canada to treat intestinal strongyloidiasis and onchocerciasis, tropical parasitic infections, and is considered safe at dosages <200 ug/kg (1, 2). Ivermectin has not been authorized for use in the treatment of COVID-19 by Health Canada, Food and Drug Administration of the USA, and the European Medicines Authority, and has not been recommended by the Pan American Health Organization (PAHO) or the World Health Organization (WHO) except in clinical trials (1-5). However, it has been explored for use in COVID-19 due to its antiviral activity *in vitro* against a range of viruses including SARS-CoV-2 (6, 7). The suggested mechanism of action is that ivermectin inhibits and disrupts binding of the SARS-CoV-2 S protein at the ACE-2 receptor (8). Ivermectin was not included in the WHO SOLIDARITY trial for repurposing drugs for COVID-19, some authors suggest this is because the anti-viral effects seen *in vitro* would require nine times the recommended dosage of ivermectin (6). Dosages evaluated across studies were generally <200 ug/kg with some dosing 2 – 3 times 200 ug/kg and ranged from a single dose to treatment over several days up to 14 days. This review summarises systematic reviews and new randomized controlled trials (RCTs) on the efficacy and safety of ivermectin compared to a standard of care or placebo for the prevention of infection with SARS-CoV-2 (post-exposure prophylaxis) and for use as a treatment of COVID-19 cases receiving either inpatient or outpatient care published up to July 5, 2021.

Key Points

- The WHO updated its living guidelines March 31, 2021 to include ivermectin (1) and currently does not recommend the use of ivermectin for the treatment of COVID-19 due to low certainty in the evidence and the availability of other more efficacious treatments.
- Eight systematic or rapid reviews on ivermectin as a therapeutic including two guidelines documents from WHO and PAHO that were underpinned by synthesis research are summarized below. Three systematic reviews summarized the literature on prophylactic use of ivermectin to prevent COVID-19.
- There was variability in the meta-analyses between reviews due to variability in studies included. Across meta-analyses some syntheses included randomized controlled trials (RCTs) only, others restricted to RCTs with low risk of bias, while others included observational studies of both prospective and retrospective design.
    - Moderate/high risk of bias RCTs frequently had inadequate randomization and/or allocation concealment.
    - Many of the RCTs on ivermectin have been small and thus lack power and precision in the estimates.
- There is low or very low certainty in the results for all COVID-19 outcomes, which are summarized below.

Mortality:

- Meta-analyses on the prevention of mortality with ivermectin treatment are inconsistent and had very low to moderate certainty depending on the analysis. The meta-analyses with the most restrictive inclusion criteria (e.g., RCTs of low risk of bias) did not report an association with mortality, whereas those that included RCTs of moderate/high risk of bias or non-RCTs reported an association as shown in the PAHO rapid review (2).

  No association with mortality:

  - 28-day mortality RR 0.33 (95% 0.01-8.14) from 3 RCTs/ 60 day mortality RR 2.00 (0.18-21.91) from 1 RCT (9).
  - RR 0.94 (95%CI 0.51-1.73) from 4 RCTs at low risk of bias / RR 0.32 (95%CI 0.16-0.64) from 6 RCTs at moderate/high risk of bias (2).
  - RR 0.37 (95%CI 0.12 to 1.13) from 5 RCTs, very low certainty of evidence and the subgroup analysis showed a reduction in mortality across 3 RCTs at high risk of bias (RR 0.18, 95%CI 0.07-0.49) (10).

  Reduced mortality

  - OR 0.19 (95%CI 0.09-0.36) from 7 RCTs very low certainty (1).
  - RR 0.38 (95%CI 0.19 -0.73) from 15 studies (RCT and observational studies) moderate certainty evidence, this persisted only for mild/moderate cases (RR 0.24, 95%CI 0.06-0.94) in subgroup analysis (11).
  - RR 0.31 (95%CI 0.15–0.62) from 8 RCTs that persisted only for mild/moderate COVID-19 (RR 0.15, 95%CI 0.03-0.67) in a sub-group analysis (12).
  - OR 0.39 (95%CI 0.22-0.70) from 22 studies (RCT, observational, descriptive) and very low certainty in the evidence. Clinical trials only (OR 0.32, 95%CI 0.15-0.65) had similar results and the authors note that the benefit of ivermectin treatment was only seen in mild/moderate cases (13).

Severe disease:

- Ivermectin was not shown to reduce the risk of symptomatic disease, hospitalization or mechanical ventilation, or length of stay (1, 2, 9-11, 13-15)
  - One meta-analysis reported reduced severity of COVID-19 (RR 0.43 [95% CI 0.23–0.81], I2=65%, p = 0.008, 8 RCTs, n=1638), in the subgroup analysis reduced severity was only associated with mild/moderate cases (RR 0.44, 95%CI 0.22–0.85) (12).

Time to symptom resolution:

- Conflicting results for symptom resolution or improvement were reported across analyses with many reporting no difference (1).
  - RR 1 (95%CI 0.9-1.11, I^2=30%) 2 RCTs low risk of bias and moderate certainty of evidence vs. RR 1.35 (95%CI 1.16-1.57) 6 RCTS of moderate/high risk of bias (2).

Time to PCR negative:

- Time to viral clearance was similar between ivermectin and controls in several analyses (1, 10, 15)
  - Faster time to PCR negative (HR 2.70, 95%CI 1.21- 6.04, 1 RCT) in mild cases, an outcome reported in only 1 of 18 included RCTs, very low certainty (9).
  - Higher PCR negative rate (RR 1.23, 95% CI 1.01–1.51) from 9 RCTs, low certainty and shorter time to PCR negative (mean difference [MD] −3.29, 95%CI −5.69, −0.89) from 6 studies (12).
  - Compared to Lopinavir-Ritonavir, the ivermectin treatment group had a faster time to PCR negative (HR 2.02, 95%CI 1.28-3.18) among hospitalized cases in 1 RCT (9).

Severe adverse events:

- There is no evidence that there was an association between ivermectin treatment and severe adverse events (1, 2, 9-11, 13-15).

Prophylactic use to prevent COVID-19:

- Three systematic reviews report on the RCTs and/or clinical trials on prophylaxis have shown some protective effect of ivermectin supplementation however, the certainty in this evidence is very low to low:
  - Ivermectin prophylaxis reduced COVID-19 infection by 86% (95%CI 79-91%, 3 studies, 738 participants) – low certainty of evidence (11).
  - Ivermectin alone on suspected, probable, or laboratory confirmed COVID-19 infection (159 fewer per 1000, 165 fewer to 144 fewer) remain very uncertain (16)
  - A protective effect of ivermectin supplementation to prevent symptomatic COVID-19 (RR 0.13, 95%CI 0.08-0.21, 1 RCT) or confirmed COVID-19 (RR 0.20, 95%CI 0.04-0.89, 1 RCT) very low certainty of evidence (9).

On-going ivermectin and COVID-19 research:

- On clinicaltrials.gov there are 24 trials involving ivermectin that have been completed and 48 that are registered an in various stages of execution as of July 7, 2021. Some of the registered trials are large, placebo-controlled RCTs on ivermectin that should have enough power to address some of the concerns about the existing evidence (17).

Overview of the Evidence

Systematic reviews of RCTs and RCTs published since the last SR search date were included in this evidence brief. Systematic reviews were evaluated using the AMSTAR 2 tool for systematic reviews (18).

CONTENTS

THERAPEUTIC USE

Therapeutic use of ivermectin in the treatment of COVID-19 has been studied in several clinical trials and a wide range of severities and outcomes have been reported. Several reviews report moderate/high risk of bias in many of the RCTs examining ivermectin treatment. To minimize the bias in the analyses some authors analysed low risk of bias RCTs separate from moderate/high risk of bias RCTs (2, 10) and in some analyses authors have limited analysis to RCTs (1, 12, 13), while others have included multiple study designs in one meta-analysis (11, 13, 14). There are also websites that collect and meta-analyse the literature on ivermectin without conducting a systematic review process. These were excluded from this evidence brief, but are listed in the appendix for reference.

Most RCTs on ivermectin as a therapeutic were small, which impact power and precision of the results and many were at risk of bias due to inappropriate randomization or inadequate allocation concealment. Thus, the studies included in each meta-analysis differed from one systematic review to the next and for a few outcomes (e.g., mortality) the analyses were conflicting.

Table 1: Treatment of COVID-19 with ivermectin (n=8 systematic/rapid reviews and 1 new RCT)

STUDY	METHOD	KEY OUTCOMES
Evidence-Based Guidelines		
WHO Living guideline on Therapeutics for COVID-19 (1) Mar 2021	The living guideline is underpinned by a systematic review process with GRADE certainty of evidence. 16 RCTs (2407 participants) were included and all other study designs were excluded. Many RCTs did not report on patient-important outcomes. Meta-analysis and sub-group analysis was conducted by grouping different ivermectin dosages. There are few RCTs available on ivermectin and RCTs are small with few events. Relative to alternative treatment options, there is a high degree of uncertainty in the evidence. *See figure in appendix*.	Recommendation: WHO recommends not to use ivermectin in patents with COVID-19 except in the context of a clinical trial. This recommendation applies to patients with any disease severity and any duration of symptoms. WHO recommendation: "*A recommendation to only use a drug in the setting of clinical trials is appropriate when there is very low certainty evidence and future research has a large potential for reducing uncertainty about the effects of the intervention and for doing so at reasonable cost.*" For most key outcomes, including mortality, mechanical ventilation, hospital admission, duration of hospitalization and viral clearance, the panel considered the evidence of very low certainty *(Summary of Findings table in Appendix*). Note the meta-analytic findings for mortality were significant (OR 0.19, 95%CI

		0.09-0.36, from 7 RCTs n=1419 observations), however the certainty in the evidence was rated as very low. Evidence was rated as very low certainty primarily because of very serious imprecision for most outcomes: the aggregate data had wide confidence intervals and/or very few events. There were also serious concerns related to risk of bias for some outcomes, specifically lack of blinding, lack of trial pre-registration, and lack of outcome reporting for one trial that did not report mechanical ventilation despite pre-specifying it in their protocol (publication bias). Ivermectin used to treat COVID-19, more than 66 RCTs planning to enrol more than 12 000 participants (range 24 - 2724) are registered or on-going.
Pan American Health Organization (PAHO) Living Update of COVID-19 Therapeutic Options (2) Rapid Review May 2021	The rapid review follows systematic review methodology and uses the Living OVerview of Evidence (L·OVE; https://iloveevidence.com) platform to identify studies for inclusion in this review. Studies included up to May 6, 2021. RCTs of therapeutic interventions for COVID-19 were included. The outcomes focused on were comparative effectiveness studies that provide evidence on outcomes of crucial importance to patients (mortality, invasive mechanical ventilation, symptom resolution or improvement, infection [prophylaxis studies] and severe adverse events) Meta-analysis: Random effects meta-analysis was performed. Where significant heterogeneity existed, subgroup analysis by risk of bias was performed considering: 1) Risk of bias (high/moderate vs low risk of bias), 2) Disease severity (mild, moderate, severe	28 RCTs (4837 cases, mild to severe) and most were very small RCTs with a small number of events (low power and high imprecision). • 17 did not report any clinically important outcomes. • 11 of those studies reported on clinically important outcomes. • Methodological limitations in studies that reported clinically important outcomes included inappropriate randomization or allocation concealment. Results: • Ivermectin may not significantly reduce mortality, RR 0.94 (95%CI 0.51 to 1.73 I^2 =1%); RD - 0.96% (95%CI -7.8% to 11.7%); low certainty based on 4 low risk of bias studies. High risk of bias RCTs (n=6) showed significant protection from mortality (RR 0.32, 95%CI 0.16-0.64, I^2 = 39%), 2/6 found an association within study. • It is uncertain if ivermectin affects mechanical ventilation requirements, RR 0.89 (95%CI 0.38 to 2.07); RD -1.9% (95%CI -10.7% to 18.5%); very low certainty based on 4 low risk of bias RCTs.

	or critical); and 3) Intervention's characteristics A risk of bias assessment was applied to RCTs focusing on randomization, allocation concealment, blinding, attrition, or other biases relevant to the estimates of effect. The GRADE approach was used to assess the certainty on the body of evidence for every comparison on an outcome basis.	• Ivermectin probably does not improve symptom resolution or improvement, RR 1 (95%CI 0.9-1.11, I^2=30%); RD 0% (95%CI -6%-6.6%); moderate certainty based on 2 RCTS with low risk of bias. 2/6 high risk of bias RCTs found an association symptom improvement (RR 1.35, 95%CI 1.16-1.57, I^2=60%). • It is uncertain if ivermectin affects symptomatic infection, RR 0.22 (95%CI 0.09 to 0.53); RD -13.6% (95%CI -15.8% to -8.2%); very low certainty based on 4 low risk of bias studies. • It is uncertain if ivermectin affects hospitalizations in non-severe patients, RR 0.66 (95%CI 0.69 to 2.30); RD 2.5% (95%CI -6% to 9.6%); very low certainty from 1 RCT at low risk of bias. • It is uncertain if there are severe adverse events (RR 1.04, 95%CI 0.32 – 3.38); very low certainty from 4 low risk of bias RCTs.
Synthesis Research		
COVID nma (2021) (9) Living Systematic Review June 2021* NA*	Current up to June 24, 2021. This is a living summary of RCTs on pharmacological interventions updated weekly. The outcomes considered were clinical improvement, mortality, viral negative conversion, serious adverse events, as well as time to these events. Meta-analysis is conducted for each outcome. The Cochrane Risk of Bias 2.0 tool is used assess risk of bias and GRADE is used to assess the certainty of the evidence. Results are updated weekly.	26 RCTs have investigated ivermectin. 8 high risk of bias and 18 with some concerns. Trial size was 32-476 people. No significant outcomes of treatment were reported in studies varying the dosage of ivermectin, for 4 RCTs on ivermectin vs. hydroxychloroquine or 1 RCT on Ivermectin+Doxycycline vs Hydroxychloroquine+Azithromycin Outcomes with at least one significant result: MILD CASES • 1/18 RCTs on ivermectin vs. placebo reported faster time to PCR negative (HR 2.70, 95%CI 1.21- 6.04, 1 RCT) in mild cases. No other outcomes were significant. • 1/4 RCTs on ivermectin+Doxycyclin vs.placebo showed better clinical improvement in the placebo group (RR 0.63, 95%CI 0.45-0.87) and faster time

		to clinical improvement (HR 0.51, 95%CI 0.32-0.81) in the placebo group. HOSPITALIZED CASES • 1 RCT on ivermectin+Doxycycline vs. ivermectin reported more adverse events in the ivermectin+Doxycycline group (RR 1.69, 95%CI 1.15- 2.49). • 1 RCT on ivermectin vs. Lopinavir-Ritonavir reported faster time to PCR negative (HR= 2.02, 95%CI 1.28-3.18) among hospitalized patients in the ivermectin group. GRADE for the ivermectin outcomes ranged from very low to moderate certainty.
Bryant (2021) (11) Systematic Review Jun 2021* (AMSTAR rating high)	Search date April 26, 2021. RCTs and quasi-RCTs were included. Objective was to assess the efficacy of ivermectin treatment in reducing mortality, and in chemoprophylaxis, among people with, or at high risk of, COVID-19 infection. Secondary outcomes included hospital stay, admission to hospital/ICU and adverse outcomes. Cochrane Risk of Bias 2.0 was used. GRADE was used to assess the certainty of the evidence.	24 RCTs (n=3406 participants) met the inclusion criteria- 22 studies on treatment. • Across 15 RCTs ivermectin reduced risk of death to 2.3% vs. 7.8% among hospitalized cases (RR 0.38, 95%CI 0.19 - 0.73, I^2=49%, 15 studies) – moderate certainty evidence. This was robust in a sensitivity analysis. • For moderate/mild COVID the reduced risk of mortality RR 0.24 (95%CI 0.06 -0.94) and no association for severe COVID-19 RR 0.51 (95%CI 0.22 – 1.14). • Deterioration of disease status RR 0.35 (0.19-0.65, 7 studies). • No benefit from ivermectin was identified in prevention of ICU admission or mechanical ventilation- very low /low certainty of evidence. • No association with adverse events – low certainty.
Roman (2021) (10) Systematic Review May 2021* (AMSTAR rating high)	Search conducted March 22, 2021 for Published and preprint randomized controlled trials (RCTs) assessing ivermectin treatment effects on COVID-19 adult patients. Primary outcomes were all-cause mortality, length of stay (LOS), and adverse events (AE). Secondary outcomes included viral clearance and severe AEs.	Ten RCTs (n=1173) were included. RCTs sample size ranged from 24 to 398 patients, and severity of COVID-19 disease was mild in 8 RCTs, moderate in one RCT, and mild and moderate in one RCT. • Ivermectin did not reduce all-cause mortality vs. controls (RR 0.37, 95%CI 0.12 to 1.13, I^2=16%, 5 RCTs, very low QoE-Quality of Evidence).

	Risk of bias (RoB) conducted with the Cochrane RoB 2·0 tool. Meta-analysis was conducted. Subgroup analyses by severity of disease and RoB, and sensitivity analyses by time of follow-up were conducted.	○ A significant reduction in mortality was seen across 3 RCTs at high risk of bias (RR 0.18, 95%CI 0.07-0.49; RoB p for interaction=0.1) ○ Sensitivity analyses excluding RCTs with follow up <21 days showed no difference in all-cause mortality. • Ivermectin did not reduce LOS vs. controls (MD 0.72 days, 95%CI -0.86 to 2.29, I^2=0%, 3 RCTs, very low QoE). • Severe adverse effects were similar between ivermectin and controls (RR 0.95, 95%CI 0.85 to 1.07, I^2=0%, 3 RCTs, low QoE) • Viral clearance was similar between ivermectin and controls (RR 0.96, 95%CI 0.79 to 1.16, I2 =0%, 4 RCTs low QoE)
Hariyanto (2021) (12) Systematic Review (AMSTAR rating moderate)	Search date May 10, 2021. Published RCTs on COVID-19 and ivermectin as a treatment for COVID-19 cases were included. Outcomes: severe COVID-19, mortality, negative RT-PCR test results rate, time to negative RT-PCR test results, symptoms alleviations rate, time to symptoms alleviations and time to hospital discharge. The quality of the study was assessed using Jadad scale assessment tool for clinical trial studies. Overall meta-analysis included all studies regardless of the COVID-19 severity included in the study. Sub-group analysis separating mild/moderate and severe COVID was conducted and is noted in key observations where heterogeneity was explained or only one subgroup remained significant. Several outcomes had high heterogeneity >60% that was not explained by sub-group analysis. This variability in the outcome reduces our confidence that the meta-analytic summary represents the true value, thus	19 RCTs with 2768 COVID-19 patients were included (10 open-label and 9 double blinded). Ivermectin was associated with: • Reduction in severity of COVID-19 (RR 0.43 [95% CI 0.23–0.81], I^2=65%, p = 0.008, 8 studies, n=1638). ○ Sub-group analysis was only significant for mild/moderate COVID-19: RR 0.44 [95%CI 0.22–0.85], p= 0.01, I^2= 47%, n = 1294. • Reduction of mortality (RR 0.31 [95% CI 0.15–0.62], p = 0.001, I^2=40%, 8 studies, n-1726.) ○ Sub-group analysis of mild/moderate COVID-19 only: RR 0.15 [95%CI 0.03–0.67], p = 0.01, I^2 = 0%, n = 1169 ○ Sub group analysis of severe COVID-19: RR 0.41 [95%CI 0.16–1.04], p = 0.06, I^2 = 58%, n = 377. • Higher negative RT-PCR test results rate (RR 1.23 [95% CI 1.01–1.51], p = 0.04, I^2=91%, 9 studies, n=1205). • Shorter time to negative RT-PCR test results (mean difference [MD] −3.29 [95% CI −5.69, −0.89], p = 0.007, I^2=96%, 6 studies, n=782). • Higher symptoms alleviations rate (RR 1.23 [95% CI 1.03−1.46], p = 0.02, I^2=85%, 8 studies, n=1535).

	the value would be expected to change with additional research.	• Shorter time to symptoms alleviations (MD −0.68 [95% CI −1.07,-0.29], p = 0.0007, I^2=68%, 6 studies, n=950).
		  ○ Sub-group analysis of mild/moderate COVID-19 only: MD −0.65 (95% CI −1.12, −0.18), p = 0.007, I^2 = 0%, 4 studies, n = 701.
		  ○ Sub group analysis of severe COVID-19: MD −1.00 [95% CI −1.14, −0.86), p < 0.00001, I2 = 0%, 1 study, n = 69.
		• Shorter time to hospital discharge (MD −2.66 [95%CI −4.49, -0.82], p = 0.004, I^2=98%, 7 studies, n=1032).
		Ivermectin administered to mild/moderate cases had a greater benefit of reducing severity and morality.

Karale (2021) *preprint* (13) Systematic Review May 2021* (AMSTAR rating moderate)	Search date Feb 2020 to Mar 27, 2021 Primary outcomes were overall mortality, need for intensive care unit (ICU) admission; secondary outcomes were - adverse effects, need for mechanical ventilation. Random-effects meta-analysis was conducted. Cochrane ROB and and NIH quality assessment tools were used and evidence was GRADED for certainty. 38 studies were included (n=15002) 19 RCTs, 14 observational, 6 case series; 30 included in the meta-analysis.	Mortality is reported in 22 studies: • Mortality overall: The odds of mortality in the ivermectin group were significantly lower compared to control group (OR 0.39, 95%CI 0.22-0.70, p=0.002; I^2=81%) but evidence was graded very low. • Mortality clinical trials: Subgroup analysis of 15 clinical trials (RCTs N=12, Non-RCTs N=3) and observed similar mortality benefit (OR 0.32, 95%CI 0.15-0.65, p=0.002; I^2 =65%). • Mortality benefit was not observed in severe/critical cases, thus ivermectin was only indicated as possibly beneficial to mild/moderate cases. Severity outcomes ICU admission (n=5 studies) and Mechanical ventilation (n=9) were not associated with ivermectin. Adverse events are reported in 10 studies; • Adverse events in the ivermectin treatment arms were not associated with treatment in 17 studies (245/973) vs control group (234/945). We did not find an association between ivermectin and rate of adverse events as compared to controls (OR 0.92, 95%CI 0.64- 1.33, p=0.67; I^2 =14%).
Murchu (2021) (14)	Search date January 6, 2021. Clinical trials (RCT or nRCT) were included and risk of bias assessment	One study on a combination intervention of oral ivermectin plus doxycycline, conducted in Iraq (n=96). Treatment: 200 µg/kg ivermectin

Systematic review Jun 2021* (AMSTAR rating moderate)	was conducted using the Cochrane RoB 2.0 and the certainty of evidence was assessed with GRADE. The review assessed ambulatory treatments for COVID-19. 8 RCTs were included, only one was on an ivermectin plus Doxycycline treatment.	orally daily for 2 to 3 days and 100 mg oral doxycycline twice daily for 5 to 10 days plus standard therapy. • Mean time to recovery in patients with mild/moderate disease was 6.34 days (SD = 2.4) in the intervention group compared with 13.66 days (SD = 6.4) in the control group ($P < 0.01$). • Progression to severe disease or mortality and adverse reactions did not occur in this study.
New RCTs		
Vallejos (2021) (15) RCT Aug 2020 – Feb 2021 Argentina	RCT double-blind, placebo-controlled study (n=501) "IVERCORCOVID19" ivermectin treatment to prevent hospitalization in individuals with early COVID-19 cases. Dose was according to weight: mean dose 192.37 µg/kg/day (SD ± 24.56) up to 80kg received 12mg/d for 2 days. >80kg received 18mg/d for 2 days. >110kg received 24mg/d for 2 days. Mean age was 42 years (SD ± 15.5) and the median time since symptom onset to the inclusion was 4 days [interquartile range 3-6]. ClinicalTrials.gov (NCT04529525)	• Hospitalizations: 14/250 (5.6%) ivermectin group vs. 21/251 (8.4%) placebo group (OR 0.65; 95%CI 0.32-1.31; p = 0.227). • Time to hospitalization was not statistically different between groups. • The mean time from study enrollment to invasive mechanical ventilation was 5.25 days (SD ± 1.71) in ivermectin group vs. 10 days (SD ± 2) in placebo group, (p = 0.019). • No statistically significant differences in the other secondary outcomes including polymerase chain reaction test negativity and safety outcomes.

LTE= letter to editor, * the date or location is based on citation information. QoE= quality of evidence

PROPHYLAXIS

Three systematic reviews report on the RCTs and/or clinical trials on prophylaxis have shown some protective effect of ivermectin supplementation however the certainty in this evidence is very low to low

Table 2: Prophylaxis (n=3)

Systematic review		
Bartoszko (2021) (16) Living Systematic Review	Search date Feb 2020 to Mar 27, 2021 Included randomised trials of people at risk of covid-19 who were assigned to receive prophylaxis or no prophylaxis (standard care or placebo).	There was serious risk of bias and very serious imprecision for each outcome, thus there is very low certainty in this evidence. • The effects of ivermectin combined with iota-carrageenan on laboratory confirmed

May 2021* (AMSTAR quality high)	Random effects Bayesian network meta-analysis was performed. Risk of bias was assessed by a modification of the Cochrane risk of bias 2.0 tool and GRADE was applied for the certainty of evidence.	COVID-19 (52 fewer per 1000, 58 fewer to 37 fewer). • Ivermectin alone on laboratory confirmed COVID-19 infection (50 fewer per 1000, 59 fewer to 16 fewer). • Ivermectin alone on suspected, probable, or laboratory confirmed COVID-19 infection (159 fewer per 1000, 165 fewer to 144 fewer), remains very uncertain.
Bryant (2021) (11) Systematic Review Jun 2021* (AMSTAR rating high)	Search date April 26, 2021. RCTs and quasi-RCTs were included. Objective was to assess the efficacy of ivermectin treatment in reducing mortality, and in chemoprophylaxis, among people with, or at high risk of, COVID-19 infection. Secondary outcomes included hospital stay, admission to hospital/ICU and adverse outcomes. Cochrane Risk of Bias 2.0 was used. GRADE was used to assess the certainty of the evidence.	24 RCTs (n=3406 participants) met the inclusion criteria – 3 studies on prophylaxis. • Ivermectin prophylaxis reduced COVID-19 infection by 86% (95%CI 79-91%, 3 studies, 738 participants); low certainty of evidence. .
COVID nma (2021) (9) Living Systematic Review June 2021* NA*	Current up to June 2021. This is a living summary of RCTs on pharmacological interventions. The outcomes considered were clinical improvement, mortality, viral negative conversion, serious adverse events, as well as time to these events. Meta-analysis is conducted for each outcome. The Cochrane Risk of Bias 2.0 tool is used assess risk of bias and GRADE is used to assess the certainty of the evidence. Results are updated weekly. 4 RCTs investigated ivermectin as a preventative treatment.	Ivermectin vs. placebo: 2 RCTS • A protective effect of ivermectin supplementation to prevent symptomatic COVID-19 (RR 0.13, 95%CI 0.08-0.21, 1 RCT) or confirmed COVID-19 (RR 0.20, 95%CI 0.04-0.89, 1 RCT); very low certainty of evidence. Ivermectin vs. Vitamin C: 1 RCT • No difference in incidence of symptomatic or confirmed COVID-19, adverse events, hospitalization, ICU admission or mortality. Ivermectin+Iota-Carrageenan vs. Placebo: 1 RCT • Ivermectin +Iota-Carrageenan reduced the risk of confirmed COVID-19 (RR 0.13, 95%CI 0.04-0.47), risk of symptomatic COVID-19 (RR 0.04, 95%CI 0.01-0.30), and there was no mortality in either group.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search term used included: ivermectin.
This review contains research published up to July 5, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX

Figure: WHO Living Guidelines on Therapeutics: Network meta-analysis figure indicates that the data and studies supporting the data for Ivermectin is weak.

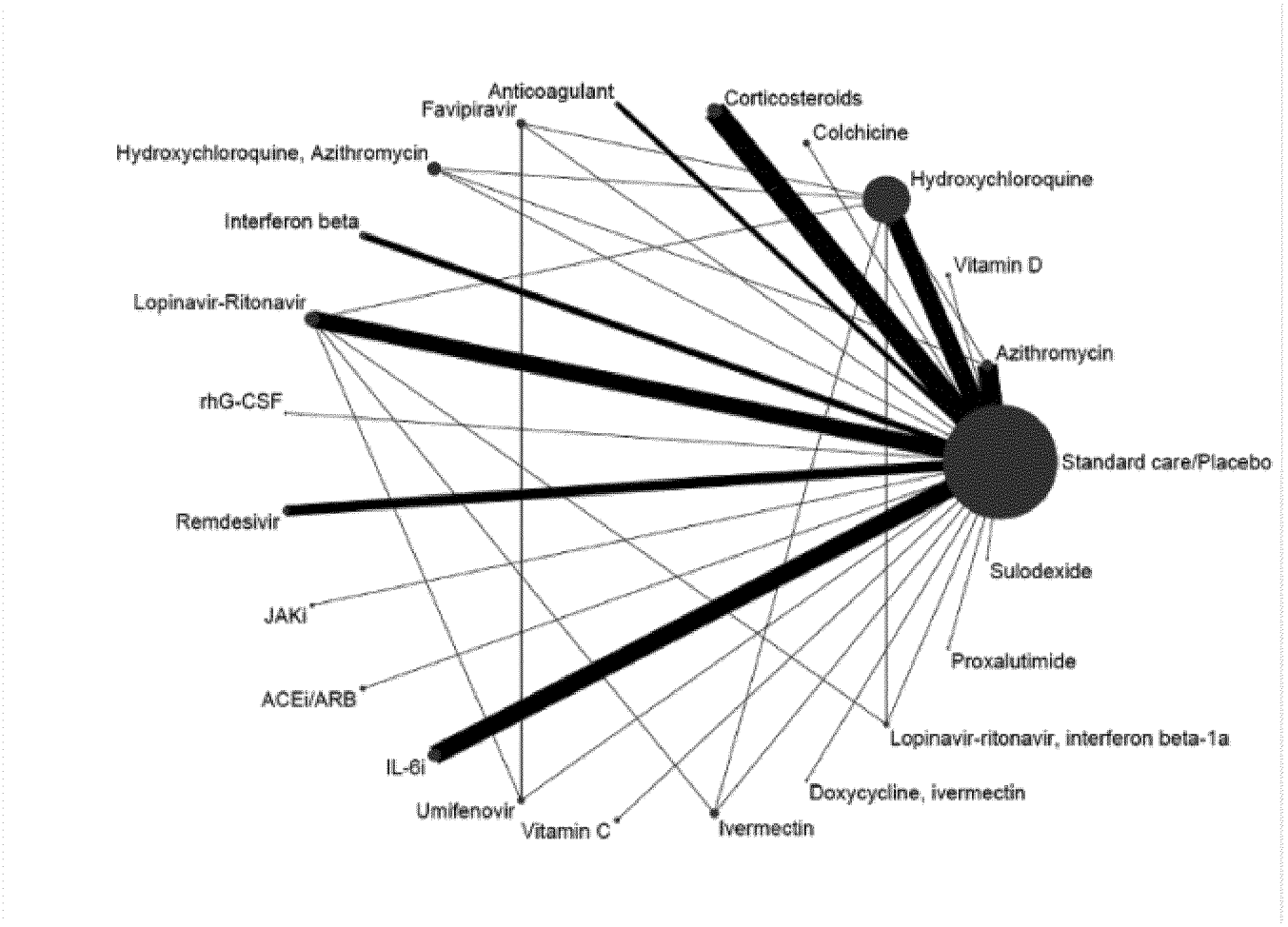

Table: WHO Living Guidelines on Therapeutics: The summary of findings analysis conducted on RCT trial on Ivermectin.

Clinical question/ PICO

Population: Patients with COVID-19 infection (all disease severities)
Intervention: Ivermectin
Comparator: Usual care

Summary

Outcome Timeframe	Study results and measurements	Absolute effect estimates Standard care	 Ivermectin	Certainty of the evidence (Quality of evidence)	Plain text summary
Mortality	Odds ratio 0.19 (CI 95% 0.09 - 0.36) Based on data from 1,419 patients in 7 studies. [1] (Randomized controlled)	70 per 1000	14 per 1000 Difference: **56 fewer** per 1000 (CI 95% 63 fewer - 44 fewer)	Very Low Due to serious risk of bias and very serious imprecision [2]	The effect of ivermectin on mortality is uncertain.
Mechanical ventilation	Odds ratio 0.51 (CI 95% 0.12 - 1.77) Based on data from 687 patients in 5 studies. (Randomized controlled)	20 per 1000	10 per 1000 Difference: **10 fewer** per 1000 (CI 95% 18 fewer - 15 more)	Very Low Due to very serious imprecision and publication bias [3]	The effect of ivermectin on mechanical ventilation is uncertain.
Viral clearance 7 days	Odds ratio 1.62 (CI 95% 0.95 - 2.86) Based on data from 625 patients in 6 studies. (Randomized controlled)	500 per 1000	618 per 1000 Difference: **118 more** per 1000 (CI 95% 13 fewer - 241 more)	Low Due to serious inconsistency and imprecision [4]	Ivermectin may increase or have no effect on viral clearance.
Hospital admission (outpatients only)	Odds ratio 0.36 (CI 95% 0.08 - 1.48) Based on data from 398 patients in 1 studies. (Randomized controlled)	50 per 1000	18 per 1000 Difference: **32 fewer** per 1000 (CI 95% 47 fewer - 23 more)	Very Low Due to extreme imprecision [5]	The effect of ivermectin on hospital admission is uncertain.
Serious adverse events	Odds ratio 3.07 (CI 95% 0.77 - 12.09) Based on data from 584 patients in 3 studies. (Randomized controlled)	9 per 1000	27 per 1000 Difference: **18 more** per 1000 (CI 95% 2 fewer - 89 more)	Low Due to very serious imprecision [6]	Ivermectin may increase the risk of serious adverse events leading to drug discontinuation.

Outcome Timeframe	Study results and measurements	Absolute effect estimates Standard care	 Ivermectin	Certainty of the evidence (Quality of evidence)	Plain text summary
Time to clinical improvement	Measured by: days Lower better Based on data from: 633 patients in 2 studies. (Randomized controlled)	11 days (Mean)	10.5 days (Mean) Difference: MD 0.5 fewer (CI 95% 1.7 fewer - 1.1 more)	Low Due to very serious imprecision [7]	Ivermectin may have little or no difference on time to clinical improvement
Duration of hospitalization	Measured by: days Lower better Based on data from: 252 patients in 3 studies. (Randomized controlled)	12.8 days (Mean)	11.7 days (Mean) Difference: MD 1.1 fewer (CI 95% 2.3 fewer - 0.1 more)	Very Low Due to serious imprecision, inconsistency and serious risk of bias [8]	The effect of ivermectin on hospital length of stay is uncertain.
Time to viral clearance	Measured by: days Lower better Based on data from: 559 patients in 4 studies. (Randomized controlled)	7.3 days (Mean)	5.7 days (Mean) Difference: MD 1.6 fewer (CI 95% 4.1 fewer - 3 more)	Very Low Due to very serious imprecision and serious risk of bias. [9]	We are uncertain whether ivermectin improves or worsen time to viral clearance

1. Systematic review (3). **Baseline/comparator:** Control arm of reference used for intervention. We elected to use the control arm of the WHO solidarity trial, reflecting usual care across countries participating in the trial.
2. **Risk of bias: Serious.** The large trial contributing most of the effect estimate was driven by studies that were not blinded.. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** The number of total events was very small.. **Publication bias: No serious.**
3. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Very few events and credible intervals that include both important benefit and harm.. **Publication bias: Serious.**
4. **Inconsistency: Serious.** The point estimates varied widely and credible intervals do not substantially overlap.. **Indirectness: No serious. Imprecision: Serious.** Credible interval includes no effect.. **Publication bias: No serious.**
5. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Credible interval includes important benefit and harm.. **Publication bias: No serious.**
6. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious.** Credible interval includes little to no difference.. **Publication bias: No serious.**
7. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious. Publication bias: No serious.**
8. **Risk of bias: Serious.** Result driven by one study that was not blinded.. **Inconsistency: Serious.** Despite overlapping confidence intervals, point estimates discrepant.. **Indirectness: No serious. Imprecision: Serious.** Credible intervals include no difference.. **Publication bias: No serious.**
9. **Risk of bias: Serious.** Concerns around risk of bias.. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Credible interval includes important benefit and important harm.. **Publication bias: No serious.**

Evidence Synthesis sources that are websites and reports that were identified, but are not summarized above due to identified limitations:

Source	Methods	Key outcomes
Ivermectin for COVID-19: real-time meta-analysis of 60 studies. https://ivmmeta.com Living Meta-analysis Accessed July 6, 2021	• Their on-going search strategy is sensitive to the identification of relevant literature. • Primary Outcome: not stated.	A list of 61 studies are included as of July 6, 2021; there are short descriptions of each study in the appendix as well as the outcomes extracted for that study. These include: - Early treatment

	• All study designs included. • No risk of bias assessment of the included studies • Meta-analysis conducted with no definition of heterogeneity. • Arbitrarily broad inclusion criteria, and no specific outcomes stated for inclusion led to a high number of RCTs identified, however few report clinically relevant outcomes and participants.	- Late treatment - Prophylaxis Several meta-analysis results are included, however meta-analyses merge together study designs and different outcomes, which is not appropriate.
Lawrie (2021) Report (not peer reviewed). Ivermectin reduces the risk of death from COVID-19 -a rapid review and meta-analysis in support of the recommendation of the Front Line COVID-19 Critical Care Alliance. Published: 5 January 2021. DOI: 10.13140/RG.2.2.27751.88486. Accessed June 25, 2021	This rapid review and meta-analysis followed many steps of conducting rapid reviews. Search strategy not specified, references taken from a website: Primary Outcome: death Study design: RCT and observational studies included. Risk of Bias: ROBINS-I for non-randomized studies of interventions and the Cochrane handbook for randomized trials. Meta-analysis methods: Random effects meta-analysis and heterogeneity was evaluated by I^2 and was assessed by visual inspection of forest plots. Study designs were pooled together (not appropriate), and no analysis by risk of bias was conducted. Studies examined were those included by Kory 2021.	15 studies (2 reported two studies), 10 randomized controlled trials and 7 controlled observational studies (6 considered low, 9 moderate and 2 high risk of bias.) Outcome RR CERTAINTY (# studies): • Mortality: RR 0.17 (95% 0.08 to 0.35) MODERATE (5 studies) • Condition improvement (mild to moderate COVID19) RR 1.34 (1.22 to 1.48) MODERATE (5 studies) • Condition improvement (severe COVID-19) RR 1.88 (1.54 to 2.30) LOW (1 study) • Condition deterioration RR 0.47 (0.29 to 0.77) MODERATE (4 studies) • Admission to ICU RR 0.11 (0.01 to 0.80) LOW (1 study) • Prophylaxis to prevent COVID-19 infection RR 0.12 (0.08 to 0.18) MODERATE (4 studies) NOTE: Lawrie excluded 12 of the 27 studies considered by Kory.

Kory (2021) Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19. American Journal of Therapeutics Review May 2021 (Journal not indexed, identified in grey literature search) Previous preprint version posted on this site: https://covid19criticalcare.com/	This is a review with meta-analysis and there are no methods. Primary Outcome: time to clinical recovery and mortality. Included study: RCT and observational studies. Published peer-reviewed studies, preprints, expert meta-analyses, and numerous epidemiological analyses of regions with Ivermectin distribution campaigns. Meta-analyses are not underpinned by a systematic review. There is no protocol, no inclusion criteria, no information on search or risk of bias assessment.	27 studies included, meta-analyses based on 18 randomized controlled treatment trials of Ivermectin in COVID-19 have found large, statistically significant reductions in mortality, time to clinical recovery, and time to viral clearance. Furthermore, results from numerous controlled prophylaxis trials report significantly reduced risks of contracting COVID-19 with the regular use of Ivermectin.

Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur l'ivermectine

Introduction

Existe-t-il des preuves que l'ivermectine est un traitement efficace contre la COVID-19?

L'ivermectine est un agent antiparasitaire à large spectre approuvé au Canada pour traiter la strongyloïdose intestinale et l'onchocercose, des infections parasitaires tropicales, et est considérée comme sûre à des doses < 200 ug/kg (1, 2). L'utilisation de l'ivermectine dans le traitement de la COVID-19 n'a pas été autorisée par Santé Canada, la Food and Drug Administration des États-Unis et l'Autorité européenne des médicaments, et n'a pas été recommandée par l'Organisation panaméricaine de la santé (OPS) ou l'Organisation mondiale de la santé (OMS), sauf dans le cadre d'essais cliniques (1 à 5). Cependant, son utilisation dans le traitement de la COVID-19 a été étudiée en raison de son activité antivirale *in vitro* contre une série de virus, dont le SRAS-CoV-2 (6, 7). Le mécanisme d'action suggéré est que l'ivermectine inhibe et perturbe la liaison de la protéine S du SRAS-CoV-2 au récepteur ACE-2 (8). L'ivermectine n'a pas été incluse dans l'essai SOLIDARITY de l'OMS pour la réorientation des médicaments vers la COVID-19, certains auteurs suggèrent que c'est parce que les effets antiviraux observés *in vitro* nécessiteraient neuf fois la dose recommandée d'ivermectine (6). Les doses évaluées dans l'ensemble des études étaient généralement < 200 ug/kg, certaines doses étant 2 à 3 fois supérieures à 200 ug/kg et allant d'une dose unique à un traitement sur plusieurs jours, voire 14 jours. Cette revue résume les revues systématiques et les nouveaux essais contrôlés randomisés (ECR) sur l'efficacité et la sécurité de l'ivermectine par rapport à une norme de soins ou un placebo pour la prévention de l'infection par le SRAS-CoV-2 (prophylaxie post-exposition) et pour l'utilisation comme traitement des cas de COVID-19 recevant des soins hospitaliers ou ambulatoires publiés jusqu'au 5 juillet 2021.

Points clés

- L'OMS a mis à jour ses lignes directrices évolutives le 31 mars 2021 pour inclure l'ivermectine (1) et ne recommande actuellement pas l'utilisation de l'ivermectine pour le traitement de la COVID-19 en raison du faible degré de certitude des preuves et de la disponibilité d'autres traitements plus efficaces.
- Huit revues systématiques ou rapides sur l'ivermectine en tant que thérapeutique, y compris deux documents de directives de l'OMS et de l'OPS, qui ont été étayés par une recherche de synthèse, sont résumés ci-dessous. Trois revues systématiques ont résumé la littérature sur l'utilisation prophylactique de l'ivermectine pour prévenir la COVID-19.
- Les méta-analyses varient d'une revue à l'autre en raison de la variabilité des études incluses. Parmi les méta-analyses, certaines ne comprenaient que des essais contrôlés randomisés (ECR), d'autres se limitaient aux ECR présentant un faible risque de biais, tandis que d'autres encore incluaient des études observationnelles de conception prospective et rétrospective.
    - Les ECR à risque modéré/élevé de biais présentaient fréquemment une randomisation et/ou une assignation secrète inadéquate.

    - Bon nombre des ECR sur l'ivermectine sont de petite taille et ne permettent donc que des estimations manquant de puissance et de précision.
- La certitude des résultats pour tous les extrants de la COVID-19 est basse, voire très basse, ce qui est résumé ci-dessous.

Mortalité :

- Les méta-analyses sur la prévention de la mortalité par le traitement à l'ivermectine sont incohérentes et présentent un degré de certitude très faible à modéré selon l'analyse. Les méta-analyses dont les critères d'inclusion étaient les plus restrictifs (par exemple, les ECR à faible risque de biais) n'ont pas fait état d'une association avec la mortalité, tandis que celles qui incluaient des ECR à risque modéré/élevé de biais ou des ECNR ont fait état d'une association, comme le montre la revue rapide de l'OPS (2).

  Aucune association avec la mortalité :

  - Mortalité à 28 jours RR 0,33 (95 % de 0,01 à 8,14) de 3 ECR/ Mortalité à 60 jours RR 2,00 (de 0,18 à 21,91) de 1 ECR (9).
  - RR 0,94 (IC à 95 % de 0,51 à 1,73) de 4 ECR à faible risque de biais / RR 0,32 (IC à 95 % de 0,16 à 0,64) de 6 ECR à risque de biais modéré/élevé (2).
  - RR 0,37 (IC à 95 % de 0,12 à 1,13) de 5 ECR, très faible certitude de preuve et l'analyse de sous-groupe a montré une réduction de la mortalité dans 3 ECR à haut risque de biais (RR 0,18, IC à 95 % de 0,07 à 0,49) (10).

  Réduction de la mortalité

  - RC 0,19 (IC à 95 % de 0,09 à 0,36) de 7 ECR à très faible certitude (1).
  - RR 0,38 (IC à 95 % de 0,19 à 0,73) à partir de 15 études (ECR et études observationnelles) preuve de certitude modérée, ceci a persisté seulement pour les cas légers/modérés (RR 0,24, IC à 95 % de 0,06 à 0,94) dans l'analyse de sous-groupe (11).
  - RR 0,31 (IC à 95 % de 0,15 à 0,62) de 8 ECR qui n'a persisté que pour la COVID-19 légère/modérée (RR 0,15, IC à 95 % de 0,03 à 0,67) dans une analyse de sous-groupe (12).
  - RC 0,39 (IC à 95 % de 0,22 à 0,70) à partir de 22 études (ECR, observationnelles, descriptives) et très faible certitude dans les preuves. Les essais cliniques uniquement (RC 0,32, IC à 95 % de 0,15 à 0,65) ont donné des résultats similaires et les auteurs notent que le bénéfice du traitement à l'ivermectine n'a été constaté que dans les cas légers/modérés (13).

Maladie sévère :

- Il n'a pas été démontré que l'ivermectine réduisait le risque de maladie symptomatique, d'hospitalisation ou de ventilation mécanique, ou la durée du séjour (1, 2, 9 à 11, 13 à 15)
  - Une méta-analyse a rapporté une réduction de la sévérité de la COVID-19 (RR 0,43 [IC à 95 % de 0,23 à 0,81], I2=65 %, p = 0,008, 8 ECR, n=1638), dans l'analyse de sous-groupe, la réduction de la sévérité n'était associée qu'aux cas légers/modérés (RR 0,44, IC à 95 % de 0,22 à 0,85) (12).

Temps pour la résolution des symptômes :

- Des résultats contradictoires concernant la résolution ou l'amélioration des symptômes ont été rapportés dans toutes les analyses, beaucoup d'entre elles ne faisant état d'aucune différence (1).
    - RR 1 (0,9 à 1,11, I^2=30 %) 2 ECR à faible risque de biais et certitude modérée des preuves comparés à RR 1,35 (IC à 95 % de 1,16 à 1,57) 6 ECR à risque modéré/élevé de biais (2).

Temps jusqu'à une PCR négative :

- Le délai de clairance virale était similaire entre l'ivermectine et les témoins dans plusieurs analyses (1, 10, 15)
    - Temps plus court pour obtenir un résultat négatif à la PCR (TR 2,70, IC à 95 % de 1,21 à 6,04, 1 ECR) dans les cas légers, un résultat rapporté dans seulement 1 des 18 ECR inclus, très faible certitude (9).
    - Taux de PCR négative plus élevé(RR 1,23, IC à 95 % de 1,01 à 1,51) selon 9 ECR, faible certitude et délai plus court pour obtenir une PCR négative (différence moyenne [DM] -3,29, IC à 95 % de -5,69 à -0,89) selon 6 études (12).
    - Comparativement au groupe Lopinavir-Ritonavir, le groupe traité à l'ivermectine a eu une PCR négative après un temps plus rapide (TR 2,02, IC à 95 % de 1,28 à 3,18) parmi les cas hospitalisés dans 1 ECR (9).

Événements indésirables graves :

- Rien ne prouve qu'il y ait eu une association entre le traitement par l'ivermectine et les événements indésirables graves (1, 2, 9 à 11, 13 à 15).

Utilisation prophylactique pour prévenir la COVID-19 :

- Trois revues systématiques rapportent que les ECR et/ou les essais cliniques sur la prophylaxie ont montré un certain effet protecteur de l'apport complémentaire en ivermectine; cependant, le degré de certitude de ces preuves est très faible à faible :
    - La prophylaxie à l'ivermectine a réduit l'infection à la COVID-19 de 86 % (IC à 95 % de 79 à 91 %, 3 études, 738 participants) – faible degré de certitude des preuves (11).
    - L'efficacité de l'ivermectine seule en cas d'infection suspectée, probable ou confirmée en laboratoire à la COVID-19 (159 de moins pour 1000, 165 de moins à 144 de moins) reste très incertaine (16)
    - Un effet protecteur de l'apport complémentaire en ivermectine pour prévenir les COVID-19 symptomatiques (RR 0,13, IC à 95 % de 0,08 à 0,21, 1 ECR) ou confirmés (RR 0,20, IC à 95 % de 0,04 à 0,89, 1 ECR) : très faible certitude de preuve (9).

Recherche en cours sur l'ivermectine et la COVID-19 :

- Sur le site clinicaltrials.gov, il y a 24 essais impliquant l'ivermectine qui sont terminés et 48 qui sont enregistrés et à différents stades d'exécution au 7 juillet 2021. Certains des essais enregistrés sont de grands ECR contrôlés par placebo sur l'ivermectine qui devraient avoir une puissance suffisante pour répondre à certaines des préoccupations concernant les preuves existantes (17).

Vue d'ensemble des éléments de preuves

Les revues systématiques d'ECR et les ECR publiés depuis la dernière date de recherche de SR ont été inclus dans cette synthèse en bref. Les revues systématiques ont été évaluées à l'aide de l'outil AMSTAR 2 pour les examens systématiques (18).

TABLE DES MATIÈRES

UTILISATION THÉRAPEUTIQUE

L'utilisation thérapeutique de l'ivermectine dans le traitement de la COVID-19 a été étudiée dans plusieurs essais cliniques et un large éventail de sévérités et de résultats a été rapporté. Plusieurs revues font état d'un risque de biais modéré/élevé dans bon nombre des ECR portant sur le traitement à l'ivermectine. Pour minimiser le biais dans les analyses, certains auteurs ont analysé les ECR à faible risque de biais séparément des ECR à risque modéré/élevé de biais (2, 10) et dans certaines analyses, les auteurs ont limité l'analyse aux ECR (1, 12, 13), tandis que d'autres ont inclus plusieurs modèles d'étude dans une méta-analyse (11, 13, 14). Il existe également des sites Web qui rassemblent et méta-analysent la littérature sur l'ivermectine sans procéder à une revue systématique. Ils ont été exclus de cette synthèse en bref, mais sont listés dans l'appendice pour référence.

La plupart des ECR sur l'ivermectine en tant que traitement sont de petite taille, ce qui a un impact sur la puissance et la précision des résultats, et beaucoup présentent un risque de biais en raison d'une randomisation inappropriée ou d'une dissimulation inadéquate de l'allocation. Ainsi, les études incluses dans chaque méta-analyse différaient d'une revue systématique à l'autre et pour quelques résultats (par exemple, la mortalité), les analyses étaient contradictoires.

Tableau 1 : Traitement de la COVID-19 avec l'ivermectine (n=8, revues systématiques/rapides et 1 nouvel ECR)

ÉTUDES	MÉTHODE	RÉSULTATS PERTINENTS
Lignes directrices fondées sur des données probantes		
QUI Ligne directrice évolutive sur la thérapeutique	La ligne directrice évolutive est étayée par un processus de revue systématique avec une certitude de preuves évaluée à l'aide de GRADE.	Recommandation : L'OMS recommande de ne pas utiliser l'ivermectine pour traiter la COVID-19 sauf dans le cadre d'un essai clinique. Cette recommandation s'applique aux patients,

pour la COVID-19 (1) Mars 2021	16 ECR (2407 participants) ont été retenus et tous les autres modèles d'étude ont été exclus. De nombreux ECR n'ont pas fait état de résultats importants pour le patient. Une méta-analyse et une analyse de sous-groupes ont été réalisées en regroupant les différents dosages d'ivermectine. Il y a peu d'ECR disponibles sur l'ivermectine et les ECR sont de petite taille avec peu d'événements. Par rapport aux autres options thérapeutiques, les données probantes présentent un degré élevé d'incertitude. *Voir la figure en annexe*.	quelles que soient la gravité de la maladie et la durée des symptômes. Recommandation de l'OMS : « *Une recommandation d'utiliser un médicament uniquement dans le cadre d'essais cliniques est appropriée lorsqu'il y a des preuves de très faible certitude, que les recherches futures ont un grand potentiel pour réduire l'incertitude sur les effets de l'intervention et que cela puisse être fait à un coût raisonnable*. » Pour la plupart des résultats clés, y compris la mortalité, la ventilation mécanique, l'admission à l'hôpital, la durée de l'hospitalisation et la clairance virale, le panel a considéré que les preuves avaient un degré de certitude très faible *(tableau de résumé des résultats dans l'appendice*). Il convient de noter que les résultats de la méta-analyse concernant la mortalité étaient significatifs (RC 0,19, IC à 95 % de 0,09 à 0,36, à partir de 7 ECR n=1419 observations), mais que le degré de certitude des preuves a été jugé très faible. La certitude des preuves a été évaluée comme étant très faible principalement en raison de l'imprécision très sérieuse de la plupart des résultats : les données agrégées ayant de larges intervalles de confiance et/ou très peu d'événements. Il y avait également de sérieuses préoccupations liées au risque de biais pour certains résultats, en particulier l'absence d'insu, l'absence de préinscription à l'essai et l'absence de rapport sur les résultats pour un essai qui n'a pas fait état de la ventilation mécanique bien qu'elle ait été spécifiée dans son protocole (biais de publication). L'ivermectine a été utilisée pour traiter la COVID-19, plus de 66 ECR prévoyant d'enrôler plus de 12 000 participants (entre 24 et 2724) sont enregistrés ou en cours.
Organisation panaméricaine de la santé (OPS) Mise à jour régulière des	La revue rapide suit une méthodologie d'examen systématique et utilise la plateforme Living OVerview of Evidence (L-OVE; https://iloveevidence.com) pour	28 ECR (4837 cas, légers à graves) et la plupart étaient de très petits ECR avec un petit nombre d'événements (faible puissance et forte imprécision).

options thérapeutiques pour la COVID-19 (2) Revue rapide Mai 2021	identifier les études à inclure dans cette revue. Études incluses jusqu'au 6 mai 2021. Les ECR d'interventions thérapeutiques pour la COVID-19 ont été inclus. Les résultats visés sont les études d'efficacité comparative qui fournissent des preuves sur des résultats d'une importance cruciale pour les patients (mortalité, ventilation mécanique invasive, résolution ou amélioration des symptômes, infections [études de prophylaxie] et événements indésirables graves) Méta-analyse : une méta-analyse à effets aléatoires a été réalisée. En cas d'hétérogénéité significative, une analyse de sous-groupe en fonction du risque de biais a été réalisée en considérant : 1) le risque de partialité (élevé/modéré comparé à faible), 2) la gravité de la maladie (légère, modérée, sévère ou critique); et 3) les caractéristiques de l'intervention Une évaluation du risque de biais a été appliquée aux ECR en se concentrant sur la randomisation, la dissimulation de l'allocation, l'insu, l'attrition ou d'autres biais pertinents pour les estimations de l'effet. L'approche GRADE a été utilisée pour évaluer la certitude de l'ensemble des preuves pour chaque comparaison sur la base des résultats.	• 17 n'ont pas rapporté de résultats cliniquement importants. • 11 de ces études ont fait état de résultats cliniquement importants. • Les limites méthodologiques des études qui ont rapporté des résultats cliniquement importants comprenaient une randomisation ou une assignation secrète inappropriée. Résultats : • L'ivermectine pourrait ne pas réduire significativement la mortalité, RR 0,94 (IC à 95 % de 0,51 à 1,73 I2 =1 %); RD – 0,96 % (IC à 95 % de -7,8 % à 11,7 %); faible certitude basée sur 4 études à faible risque de biais. Les ECR à risque élevé de biais (n=6) ont montré une protection significative contre la mortalité (RR 0,32, IC à 95 % de 0,16 à 0,64, I2 = 39 %), 2 sur 6 ont trouvé une association au sein de l'étude. • Il n'est pas certain que l'ivermectine affecte les besoins en ventilation mécanique, RR 0,89 (IC à 95 % de 0,38 à 2,07); RD -1,9 % (IC à 95 % de -10,7 % à 18,5 %); très faible certitude basée sur 4 ECR à faible risque de biais. • L'ivermectine n'améliore probablement pas la résolution ou l'amélioration des symptômes, RR 1 (IC à 95 % de 0,9 à 1,11, I2=30 %); RD 0 % (IC à 95 % de -6 % à -6,6 %); certitude modérée basée sur 2 ECT avec un faible risque de biais. 2 ECR sur 6 à haut risque de biais ont trouvé une amélioration des symptômes d'association (RR 1,35, IC à 95 % de 1,16 à 1,57, I2=60 %). • Il est incertain que l'ivermectine affecte l'infection symptomatique, RR 0,22 (IC à 95 % de 0,09 à 0,53); RD -13,6 % (IC à 95 % de -15,8 % à -8,2 %); très faible certitude basée sur 4 études à faible risque de biais. • Il n'est pas certain que l'ivermectine affecte les hospitalisations chez les patients non sévères, RR 0,66 (IC à 95 % de 0,69 à 2,30);

		RD 2,5 % (IC à 95 % de -6 % à 9,6 %); très faible certitude à partir d'un ECR à faible risque de biais. • Il n'est pas certain qu'il y ait des effets indésirables graves (RR 1,04, IC à 95 % de 0,32 à 3,38); très faible certitude à partir de 4 ECR à faible risque de biais.
Recherche de synthèse		
COVID-nma (2021) (9) Revue systématique évolutive Juin 2021* S.O.*	En vigueur jusqu'au 24 juin 2021. Il s'agit d'un résumé évolutif portant sur les ECR d'interventions pharmacologiques, mis à jour chaque semaine. Les résultats pris en compte étaient l'amélioration clinique, la mortalité, la conversion virale négative, les événements indésirables graves, ainsi que le délai d'apparition de ces événements. Une méta-analyse est effectuée pour chaque résultat. L'outil Cochrane Risk of Bias 2.0 est utilisé pour évaluer le risque de biais et l'approche GRADE est utilisée pour évaluer la certitude des preuves. Les résultats sont mis à jour chaque semaine.	26 ECR ont étudié l'ivermectine. 8 avec un risque élevé de biais et 18 avec quelques préoccupations. La taille des essais était de 32 à 476 personnes. Aucun résultat significatif du traitement n'a été rapporté dans les études faisant varier le dosage de l'ivermectine, pour 4 ECR sur l'ivermectine comparée à l'hydroxychloroquine ou 1 ECR sur l'ivermectine + la doxycycline comparées à l'hydroxychloroquine + l'azithromycine Résultats avec au moins un résultat significatif : CAS LÉGERS • 1 ECR sur 18 sur l'ivermectine par rapport au placebo a rapporté un temps plus rapide pour obtenir une PCR négative (TR 2,70, IC à 95 % de 1,21- 6,04, 1 ECR) dans des cas légers. Aucun autre résultat n'était significatif. • 1 ECR sur 4 sur l'ivermectine + la doxycyclinepar rapport au placebo ont montré une meilleure amélioration clinique dans le groupe placebo (RR 0,63, IC à 95 % de 0,45 à 0,87) et un délai plus rapide d'amélioration clinique (TR 0,51, IC à 95 % de 0,32 à 0,81) dans le groupe placebo. CAS HOSPITALISÉS • Un ECR sur l'ivermectine + la doxycycline par rapport à l'ivermectine a rapporté plus d'événements indésirables dans le groupe ivermectine + doxycycline (RR 1,69, IC à 95 % de 1,15 à 2,49).

		• Un ECR sur l'ivermectine par rapport au lopinavir-ritonavir a rapporté un temps plus rapide pour obtenir une PCR négative (TR = 2,02, IC à 95 % de 1,28 à 3,18) chez les patients hospitalisés dans le groupe ivermectine. L'évaluation GRADE des résultats obtenus avec l'ivermectine allait d'une certitude très faible à modérée.
Bryant (2021) (11) Revue systématique Juin 2021* (Cote AMSTAR élevée)	Date de recherche : 26 avril 2021. Les ECR et les quasi ECR ont été inclus. L'objectif était d'évaluer l'efficacité du traitement à l'ivermectine dans la réduction de la mortalité, et dans la chimioprophylaxie, chez les personnes atteintes ou à haut risque d'infection par la COVID-19. Les résultats secondaires comprenaient le séjour à l'hôpital, l'admission à l'hôpital ou à l'USI et les résultats indésirables. La version Cochrane Risk of Bias 2.0 a été utilisée. L'approche GRADE a été utilisée pour évaluer le degré de certitude des preuves.	24 ECR (n=3406 participants) ont répondu aux critères d'inclusion – 22 études sur le traitement. • Sur l'ensemble des 15 ECR, l'ivermectine a réduit le risque de décès à 2,3 % contre 7,8 % chez les cas hospitalisés (RR 0,38, IC à 95 % de 0,19 -0,73, I2=49 %, 15 études) - preuve de certitude modérée. L'analyse de la sensibilité a été robuste. • Pour les cas de COVID modérée/douce, la réduction du risque de mortalité est de 0,24 (IC à 95 % de 0,06 -0,94) et aucune association pour les cas de COVID-19 sévère RR 0,51 (IC à 95 % de 0,22 - 1,14). • Détérioration de l'état de la maladie RR 0,35 (0,19 à 0,65, 7 études). • Aucun avantage de l'ivermectine n'a été identifié dans la prévention de l'admission en soins intensifs ou de la ventilation mécanique - certitude très faible / faible des preuves. • Aucune association avec des événements indésirables - faible certitude.
Roman (2021) (10) Revue systématique Mai 2021* (Cote AMSTAR élevée)	Recherche effectuée le 22 mars 2021 pour les essais contrôlés randomisés (ECR) publiés et prépubliés évaluant les effets du traitement à l'ivermectine sur les patients adultes atteints de la COVID-19. Les principaux résultats étaient la mortalité toutes causes confondues, la durée du séjour (DS) et les événements indésirables (EI). Les résultats secondaires comprenaient la clairance virale et les effets indésirables graves.	Dix ECR (n=1173) ont été inclus. La taille de l'échantillon des ECR varie de 24 à 398 patients, et la gravité de la maladie COVID-19 était légère dans 8 ECR, modérée dans un ECR, et légère et modérée dans un ECR. • L'ivermectine n'a pas réduit la mortalité toutes causes confondues par rapport aux groupes témoins (RR 0,37, IC à 95 % de 0,12 à 1,13, I2=16 %, 5 ECR, qualité des preuves (QP) très faible). ○ Une réduction significative de la mortalité a été observée dans 3 ECR à

	Le risque de biais a été évalué avec l'outil Cochrane RoB 2.0. Une méta-analyse a été réalisée. Des analyses de sous-groupes en fonction de la gravité de la maladie et du risque de biais, ainsi que des analyses de sensibilité en fonction de la durée du suivi ont été réalisées.	haut risque de biais (RR 0,18, IC à 95 % de 0,07 à 0,49; risque de biais pour interaction=0,1) ○ Les analyses de sensibilité excluant les ECR avec un suivi < 21 jours n'ont montré aucune différence dans la mortalité toutes causes confondues. • L'ivermectine n'a pas réduit la durée de séjour par rapport aux groupes témoins (DM 0,72 jours, IC à 95 % de -0,86 à 2,29, I2=0 %, 3 ECR, QP très faible). • Les effets indésirables graves étaient similaires entre les patients traités à l'ivermectine et les groupes témoins (RR 0,95, IC à 95 % de 0,85 à 1,07, I2=0 %, 3 ECR, QP faible) • La clairance virale était similaire entre les patients traités à l'ivermectine et les groupes témoins (RR 0,96, IC à 95 % de 0,79 à 1,16, I2 =0 %, 4 ECR à QP faible)
Hariyanto (2021) (12) Revue systématique (cote AMSTAR modérée)	Date de recherche : 10 mai 2021. Les ECR publiés sur la COVID-19 et l'ivermectine comme traitement des cas de COVID-19 ont été inclus. Résultats : COVID-19 sévère, mortalité, taux de résultats négatifs au test RT-PCR, temps jusqu'à l'obtention de résultats négatifs au test RT-PCR, taux de soulagement des symptômes, temps jusqu'au soulagement des symptômes et temps jusqu'à la sortie de l'hôpital. La qualité de l'étude a été évaluée à l'aide de l'outil d'évaluation d'échelle Jadad pour les études d'essais cliniques. La méta-analyse globale a inclus toutes les études, quelle que soit la sévérité de la COVID-19 incluse dans l'étude. Une analyse de sous-groupe séparant la COVID léger/modéré et sévère a été menée et est notée dans les observations clés où l'hétérogénéité a été expliquée ou un seul sous-groupe est resté significatif. Plusieurs résultats présentaient une hétérogénéité élevée	19 ECR avec 2768 patients atteints de la COVID-19 ont été inclus (10 ouverts et 9 à double insu). L'ivermectine a été associée aux faits suivants : • Réduction de la sévérité de la COVID-19 (RR 0,43 [IC à 95 % de 0,23 à 0,81], I2=65 %, p = 0,008, 8 études, n=1638). ○ L'analyse des sous-groupes n'était significative que pour les cas de COVID-19 légers/modérés : RR 0,44 [IC à 95 % de 0,22 à 0,85], p= 0,01, I2= 47 %, n = 1294. • Réduction de la mortalité (RR 0,31 [IC à 95 % de 0,15 à 0,62], p = 0,001, I2=40 %, 8 études, n-1726) ○ Analyse du sous-groupe des cas de COVID-19 légers/modérés uniquement : RR 0,15 [IC à 95 % de 0,03 à 0,67], p = 0,01, I2 = 0 %, n = 1169 ○ Analyse des sous-groupes des cas de COVID-19 sévères : RR 0,41 [IC à 95 % de 0,16 à 1,04], p = 0,06, I2 = 58 %, n = 377.

	>60 % qui n'était pas expliquée par l'analyse des sous-groupes. Cette variabilité des résultats réduit notre confiance dans le fait que le résumé méta-analytique représente la valeur réelle, et on peut donc s'attendre à ce que la valeur change avec des recherches supplémentaires.	• Taux plus élevé de résultats négatifs au test RT-PCR (RR 1,23 [IC à 95 % de 1,01 à 1,51], *p* = 0,04, I2=91 %, 9 études, n=1205).
		• Temps plus court pour obtenir des résultats négatifs au test RT-PCR (différence moyenne [DM] -3,29 [IC à 95 % de -5,69 à -0,89], *p* = 0,007, I2=96 %, 6 études, n=782).
		• Taux plus élevé de soulagement des symptômes (RR 1,23 [IC à 95 % de 1,03 à 1,46], *p* = 0,02, I2=85 %, 8 études, n=1535).
		• Temps plus court jusqu'au soulagement des symptômes (DM -0,68 [IC à 95 % de -1,07 à -0,29], *p* = 0,0007, I2=68 %, 6 études, n=950).
		  ○ Analyse du sous-groupe des cas de COVID-19 légers/modérés uniquement : DM -0,65 (IC à 95 % de -1,12 à -0,18), *p* = 0,007, I2 = 0 %, 4 études, *n* = 701.
		  ○ Analyse des sous-groupes des cas de COVID-19 sévères : DM -1,00 [IC à 95 % de -1,14 à -0,86], p < 0,00001, I2 = 0 %, 1 étude, n = 69.
		• Temps plus court jusqu'à la sortie de l'hôpital (DM -2,66 [IC à 95 % de -4,49 à -0,82], *p* = 0,004, I2=98 %, 7 études, n=1032).
		L'ivermectine administrée aux cas légers/modérés a permis de réduire davantage la gravité et la moralité.

Karale (2021) *prépublication* (13) Revue systématique Mai 2021* (Cote AMSTAR modérée)	Date de recherche : de février 2020 au 27 mars 2021 Les résultats primaires étaient la mortalité globale, la nécessité d'une admission en unité de soins intensifs (USI); les résultats secondaires étaient les effets indésirables, la nécessité d'une ventilation mécanique. Une méta-analyse à effets aléatoires a été réalisée. Les outils d'évaluation de la qualité Cochrane ROB et du NIH ont été utilisés et les preuves ont été notées en fonction de leur degré de certitude.	La mortalité est rapportée dans 22 études : • Mortalité globale : Les chances de mortalité dans le groupe traité à l'ivermectine étaient significativement plus faibles que dans le groupe témoin (RC 0,39, IC à 95 % de 0,22 à 0,70, p=0,002; I2=81 %), mais les preuves ont été catégorisées comme très faibles. • Essais cliniques sur la mortalité : Analyse en sous-groupe de 15 essais cliniques (ECR N=12, ECNR N=3) et observation d'un bénéfice similaire en termes de mortalité (RC 0,32, IC à 95 % de 0,15 à 0,65, p=0,002; I2 =65 %). • Aucun avantage en termes de mortalité n'a été observé dans les cas graves/critiques, et

	38 études ont été incluses (n=15002) 19 ECR, 14 études d'observation, 6 séries de cas; 30 ont été incluses dans la méta-analyse.	l'ivermectine n'a donc été indiquée que comme pouvant être bénéfique pour les cas légers/modérés. Les résultats de la sévérité de l'admission en USI (n=5 études) et de la ventilation mécanique (n=9) n'étaient pas associés à l'ivermectine. Des événements indésirables sont rapportés dans 10 études. • Les événements indésirables dans les bras utilisés pour administrer le traitement à l'ivermectine n'étaient pas associés au traitement dans 17 études (245 sur 973) par rapport au groupe témoin (234 sur 945). Nous n'avons pas trouvé d'association entre l'ivermectine et le taux d'événements indésirables par rapport aux groupes témoins (RC 0,92, IC à 95 % de 0,64 à 1,33, p=0,67; I2 =14 %).
Murchu (2021) (14) Revue systématique Juin 2021* (Cote AMSTAR modérée)	Date de recherche : 6 janvier 2021. Les essais cliniques (ECR ou ECNR) ont été inclus et l'évaluation du risque de biais a été réalisée à l'aide du Cochrane RoB 2.0 et la certitude des preuves a été évaluée avec GRADE. La revue a évalué les traitements ambulatoires pour la COVID-19. 8 ECR ont été inclus, un seul portait sur un traitement à base d'ivermectine et de doxycycline.	Une étude sur une intervention combinant l'ivermectine orale et la doxycycline, menée en Irak (n=96). Traitement : 200 µg/kg d'ivermectine par voie orale par jour pendant 2 à 3 jours et 100 mg de doxycycline par voie orale deux fois par jour pendant 5 à 10 jours en plus du traitement standard. • Le temps moyen de récupération chez les patients atteints d'une maladie légère/modérée était de 6,34 jours (ET = 2,4) dans le groupe d'intervention, contre 13,66 jours (ET = 6,4) dans le groupe témoin *(P* < 0,01). • Il n'y a pas eu de progression vers une maladie grave, ni de mortalité, ni d'effets indésirables dans cette étude.
Nouveaux ECR		
Vallejos (2021) (15) ECR D'août 2020 à février 2021 Argentine	ECR étude à double insu, contrôlée par placebo (n=501) « IVERCORCOVID19 » Traitement à l'ivermectine pour prévenir l'hospitalisation chez les personnes présentant des cas précoces de COVID-19. La dose était fonction du poids : dose moyenne de 192,37 µg/kg/jour (ET ± 24,56)	• Hospitalisations : 14 sur 250 (5,6 %) dans le groupe traité à l'ivermectine contre 21 sur 251 (8,4 %) dans le groupe placebo (RC 0,65; IC à 95 % de 0,32 à 1,31; p = 0.227). • Le délai d'hospitalisation n'était pas statistiquement différent entre les groupes. • Le délai moyen entre l'inscription à l'étude et la ventilation mécanique invasive était de 5,25 jours (ET ± 1,71) dans le groupe traité à

	Jusqu'à 80 kg : 12 mg/j administrés pendant 2 jours. > 80 kg : 18 mg/j administrés pendant 2 jours. > 110 kg : 24 mg/j administrés pendant 2 jours. L'âge moyen était de 42 ans (ET ± 15.5) et le temps médian depuis l'apparition des symptômes jusqu'à l'inclusion était de 4 jours [intervalle interquartile 3-6]. ClinicalTrials.gov (NCT04529525)	l'ivermectine contre 10 jours (ET ± 2) dans le groupe placebo (p = 0,019). • Aucune différence statistiquement significative dans les autres résultats secondaires, y compris la négativité du test de réaction en chaîne par polymérase et les résultats de sécurité.

LAE= lettre à l'éditeur, * la date ou le lieu est fonction des informations de la citation. QP= qualité des preuves

PROPHYLAXIE

Trois revues systématiques font état d'ECR et/ou d'essais cliniques sur la prophylaxie qui ont montré un certain effet protecteur de l'apport complémentaire en ivermectine, mais le degré de certitude de ces preuves est très faible à faible

Tableau 2 : Prophylaxie (n=3)

Revue systématique		
Bartoszko (2021) (16) Revue systématique évolutive Mai 2021* (qualité AMSTAR élevée)	Date de recherche : de février 2020 au 27 mars 2021 Comprend des essais randomisés portant sur des personnes à risque de Covid-19 qui ont été assignées à recevoir une prophylaxie ou aucune prophylaxie (soins standard ou placebo). Une méta-analyse en réseau bayésienne à effets aléatoires a été réalisée. Le risque de biais a été évalué à l'aide d'une modification de l'outil Cochrane Risk of bias 2.0 et l'approche GRADE a été appliquée pour évaluer la certitude des preuves.	Vu le risque sérieux de biais et l'imprécision très sérieuse de chaque résultat, cette preuve présentait une très faible certitude. • Les effets de l'ivermectine associée à l'iota-carraghénane sur les cas de COVID-19 confirmés en laboratoire (52 en moins pour 1000, 58 en moins à 37 en moins). • L'ivermectine seule contre les infections à la COVID-19 confirmée en laboratoire (50 en moins pour 1000, 59 en moins à 16 en moins). • L'efficacité de l'ivermectine seule contre une infection suspectée, probable ou confirmée en laboratoire à la COVID-19 (159 en moins pour 1000, 165 en moins à 144 en moins) reste très incertaine.
Bryant (2021) (11) Revue systématique Juin 2021*	Date de recherche : 26 avril 2021. Les ECR et les quasi ECR ont été inclus. L'objectif était d'évaluer l'efficacité du traitement à l'ivermectine dans la réduction de la mortalité, et dans la chimioprophylaxie, chez les personnes atteintes ou à haut risque d'infection par	24 ECR (n=3406 participants) répondaient aux critères d'inclusion – 3 études sur la prophylaxie. • La prophylaxie à l'ivermectine a réduit l'infection à la COVID-19 de 86 % (IC à 95 % de 79 à 91 %, 3 études, 738

(Cote AMSTAR élevée)	la COVID-19. Les résultats secondaires comprenaient le séjour à l'hôpital, l'admission à l'hôpital ou à l'USI et les résultats indésirables. La version Cochrane Risk of Bias 2.0 a été utilisée. L'approche GRADE a été utilisée pour évaluer le degré de certitude des preuves.	participants); faible certitude des preuves. .
COVID-nma (2021) (9) Revue systématique évolutive Juin 2021* S.O.*	En cours jusqu'en juin 2021. Il s'agit d'un résumé vivant des ECR d'interventions pharmacologiques. Les résultats pris en compte étaient l'amélioration clinique, la mortalité, la conversion virale négative, les événements indésirables graves, ainsi que le délai d'apparition de ces événements. Une méta-analyse est effectuée pour chaque résultat. L'outil Cochrane Risk of Bias 2.0 est utilisé pour évaluer le risque de biais et l'approche GRADE est utilisée pour évaluer la certitude des preuves. Les résultats sont mis à jour chaque semaine. 4 ECR ont étudié l'ivermectine comme traitement préventif.	ivermectine contre placebo : 2 ECR • Un effet protecteur de la supplémentation en ivermectine pour prévenir les COVID-19 symptomatiques (RR 0,13, IC à 95 % de 0,08 à 0,21, 1 ECR) ou confirmés (RR 0,20, IC à 95 % de 0,04 à 0,89, 1 ECR) : très faible certitude de preuve. ivermectine contre vitamine C : 1 ECR • Pas de différence dans l'incidence de COVID-19 symptomatique ou confirmé, d'événements indésirables, d'hospitalisation, d'admission en soins intensifs ou de mortalité. ivermectine+iota-carraghénane c. placebo : 1 ECR • L'ivermectine + iota-carraghénane a réduit le risque de COVID-19 confirmé (RR 0,13, IC à 95 % de 0,04 à 0,47), le risque de COVID-19 symptomatique (RR 0,04, IC à 95 % de 0,01 à 0,30), et il n'y a pas eu de mortalité dans les deux groupes.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets des analyses sont conservés dans une base de données RefWorks et dans une liste Excel qui peut être consultée. Une recherche ciblée par mot clé

est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-COV-2. Les termes de recherche utilisés comprennent : ivermectine.
Cette revue contient des recherches publiées jusqu'au 5 juillet 2021.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites pour être incluses dans la revue.

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

Préparé par : Lisa Waddell, LNM, Groupe des sciences émergentes, ASPC.

Connaissances mobilisées par le Bureau de la Conseillère scientifique en chef : phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca

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APPENDICE

Figure : Lignes directrices évolutives de l'OMS sur la thérapeutique : La figure de la méta-analyse en réseau indique que les données et les études à l'appui des données pour l'ivermectine sont faibles.

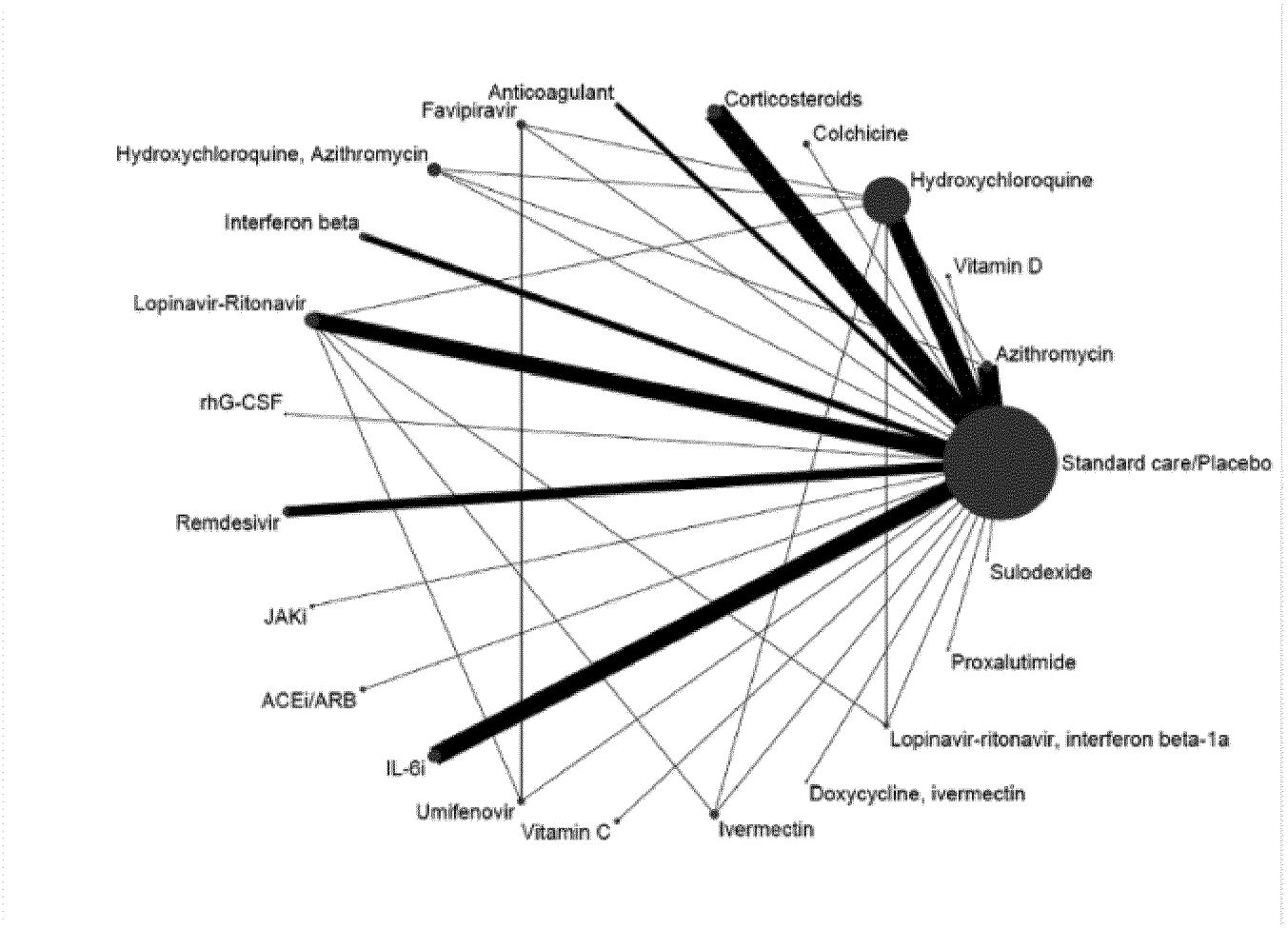

Tableau : Lignes directrices évolutives de l'OMS sur la thérapeutique : Le résumé des résultats de l'analyse menée sur l'essai ECR sur l'ivermectine.

Clinical question/ PICO

Population: Patients with COVID-19 infection (all disease severities)
Intervention: Ivermectin
Comparator: Usual care

Summary

Outcome Timeframe	Study results and measurements	Absolute effect estimates Standard care	 Ivermectin	Certainty of the evidence (Quality of evidence)	Plain text summary
Mortality	Odds ratio 0.19 (CI 95% 0.09 - 0.36) Based on data from 1,419 patients in 7 studies. [1] (Randomized controlled)	70 per 1000	14 per 1000 Difference: **56 fewer** per 1000 (CI 95% 63 fewer - 44 fewer)	Very Low Due to serious risk of bias and very serious imprecision [2]	The effect of ivermectin on mortality is uncertain.
Mechanical ventilation	Odds ratio 0.51 (CI 95% 0.12 - 1.77) Based on data from 687 patients in 5 studies. (Randomized controlled)	20 per 1000	10 per 1000 Difference: **10 fewer** per 1000 (CI 95% 18 fewer - 15 more)	Very Low Due to very serious imprecision and publication bias [3]	The effect of ivermectin on mechanical ventilation is uncertain.
Viral clearance 7 days	Odds ratio 1.62 (CI 95% 0.95 - 2.86) Based on data from 625 patients in 6 studies. (Randomized controlled)	500 per 1000	618 per 1000 Difference: **118 more** per 1000 (CI 95% 13 fewer - 241 more)	Low Due to serious inconsistency and imprecision [4]	Ivermectin may increase or have no effect on viral clearance.
Hospital admission (outpatients only)	Odds ratio 0.36 (CI 95% 0.08 - 1.48) Based on data from 398 patients in 1 studies. (Randomized controlled)	50 per 1000	18 per 1000 Difference: **32 fewer** per 1000 (CI 95% 47 fewer - 23 more)	Very Low Due to extreme imprecision [5]	The effect of ivermectin on hospital admission is uncertain.
Serious adverse events	Odds ratio 3.07 (CI 95% 0.77 - 12.09) Based on data from 584 patients in 3 studies. (Randomized controlled)	9 per 1000	27 per 1000 Difference: **18 more** per 1000 (CI 95% 2 fewer - 89 more)	Low Due to very serious imprecision [6]	Ivermectin may increase the risk of serious adverse events leading to drug discontinuation.

Outcome Timeframe	Study results and measurements	Absolute effect estimates Standard care	 Ivermectin	Certainty of the evidence (Quality of evidence)	Plain text summary
Time to clinical improvement	Measured by: days Lower better Based on data from: 633 patients in 2 studies. (Randomized controlled)	11 days (Mean)	10.5 days (Mean) Difference: MD 0.5 fewer (CI 95% 1.7 fewer - 1.1 more)	Low Due to very serious imprecision [7]	Ivermectin may have little or no difference on time to clinical improvement
Duration of hospitalization	Measured by: days Lower better Based on data from: 252 patients in 3 studies. (Randomized controlled)	12.8 days (Mean)	11.7 days (Mean) Difference: MD 1.1 fewer (CI 95% 2.3 fewer - 0.1 more)	Very Low Due to serious imprecision, inconsistency and serious risk of bias [8]	The effect of ivermectin on hospital length of stay is uncertain.
Time to viral clearance	Measured by: days Lower better Based on data from: 559 patients in 4 studies. (Randomized controlled)	7.3 days (Mean)	5.7 days (Mean) Difference: MD 1.6 fewer (CI 95% 4.1 fewer - 3 more)	Very Low Due to very serious imprecision and serious risk of bias. [9]	We are uncertain whether ivermectin improves or worsen time to viral clearance

1. Systematic review (3). **Baseline/comparator:** Control arm of reference used for intervention. We elected to use the control arm of the WHO solidarity trial, reflecting usual care across countries participating in the trial.
2. **Risk of bias: Serious.** The large trial contributing most of the effect estimate was driven by studies that were not blinded.. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** The number of total events was very small.. **Publication bias: No serious.**
3. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Very few events and credible intervals that include both important benefit and harm.. **Publication bias: Serious.**
4. **Inconsistency: Serious.** The point estimates varied widely and credible intervals do not substantially overlap.. **Indirectness: No serious. Imprecision: Serious.** Credible interval includes no effect.. **Publication bias: No serious.**
5. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Credible interval includes important benefit and harm.. **Publication bias: No serious.**
6. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious.** Credible interval includes little to no difference.. **Publication bias: No serious.**
7. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious. Publication bias: No serious.**
8. **Risk of bias: Serious.** Result driven by one study that was not blinded.. **Inconsistency: Serious.** Despite overlapping confidence intervals, point estimates discrepant.. **Indirectness: No serious. Imprecision: Serious.** Credible intervals include no difference.. **Publication bias: No serious.**
9. **Risk of bias: Serious.** Concerns around risk of bias.. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Credible interval includes important benefit and important harm.. **Publication bias: No serious.**

Sources de synthèse des preuves qui sont des sites Web et des rapports qui ont été identifiés, mais qui ne sont pas résumés ci-dessus en raison des limitations identifiées :

Source	Méthodologies	Résultats pertinents
Ivermectine pour la COVID-19 : méta-analyse en temps réel de 60 études https://ivmmeta.com Méta-analyse évolutive Consulté le 6 juillet 2021	• Leur stratégie de recherche continue est sensible à l'identification de la littérature pertinente. • Résultat primaire : non indiqué.	Une liste de 61 études est incluse à la date du 6 juillet 2021; l'annexe contient une brève description de chaque étude ainsi que les résultats extraits pour cette étude. Les voici :

	• Tous les modèles d'étude ont été inclus. • Aucune évaluation du risque de biais dans les études incluses • Méta-analyse réalisée sans définition de l'hétérogénéité. • Des critères d'inclusion arbitrairement larges et l'absence de résultats spécifiques déterminant l'inclusion ont conduit à l'identification d'un nombre élevé d'ECR, mais peu d'entre eux font état de résultats et de participants cliniquement pertinents.	- Traitement précoce - Traitement tardif - Prophylaxie Plusieurs résultats de méta-analyses sont inclus, mais les méta-analyses fusionnent des plans d'études et des résultats différents, ce qui n'est pas approprié.
Lawrie (2021) Rapport (non examiné par les pairs). L'ivermectine réduit le risque de décès dû à la COVID-19 – une revue rapide et une méta-analyse à l'appui de la recommandation de la Front Line COVID-19 Critical Care Alliance. Publié : 5 janvier 2021. DOI: 10.13140/RG.2.2.27751.88486. Consulté le 25 juin 2021	Cette revue rapide et cette méta-analyse ont suivi de nombreuses étapes de la réalisation de revues rapides. Stratégie de recherche non spécifiée, références prises sur un site Web : Résultat primaire : décès Plan d'étude : ECR et études d'observation inclus. Risque de biais : ROBINS-I pour les études non randomisées des interventions et le manuel Cochrane pour les essais randomisés. Méthodes de méta-analyse : La méta-analyse à effets aléatoires et l'hétérogénéité ont été évaluées par I^2 et ont été évaluées par inspection visuelle des graphiques en forêt. Les modèles d'étude ont été regroupés (ce qui n'est pas approprié), et aucune	15 études (2 ont rapporté deux études), 10 essais contrôlés randomisés et 7 études observationnelles contrôlées (6 considérées comme présentant un risque de biais faible, 9 un risque modéré et 2 un risque élevé) Résultat de la CERTITUDE RR (nombre d'études) : • Mortalité : RR 0,17 (95 % de 0,08 à 0,35) MODÉRÉ (5 études) • Amélioration de l'état (COVID 19 légère à modérée) – RR 1,34 (1,22 à 1,48) MODÉRÉ (5 études) • Amélioration de l'état (COVID-19 sévère) – RR 1,88 (1,54 à 2,30) FAIBLE (1 étude) • Détérioration de l'état – RR 0,47 (0,29 à 0,77) MODÉRÉ (4 études) • Admission en USI – RR 0,11 (0,01 à 0,80) FAIBLE (1 étude) • Prophylaxie pour prévenir l'infection par la COVID-19 – RR 0,12 (0,08 à 0,18) MODÉRÉ (4 études) REMARQUE : Lawrie a exclu 12 des 27 études prises en compte par Kory.

	analyse par risque de biais n'a été effectuée. Les études examinées sont celles incluses par Kory 2021.	
Kory (2021) Revue des nouvelles données démontrant l'efficacité de l'ivermectine dans la prophylaxie et le traitement de la COVID-19. American Journal of Therapeutics Revue Mai 2021 (Journal non indexé, identifié dans une recherche de littérature grise) Version précédente de prépublication a été publiée sur ce site : https://covid19criticalcare.com/	Il s'agit d'une revue avec méta-analyse sans méthode. Résultat primaire : temps de récupération clinique et mortalité. Étude incluse : ECR et études observationnelles. Publication d'études évaluées par des pairs, prépublications, méta-analyses d'experts et nombreuses analyses épidémiologiques de régions ayant fait l'objet de campagnes de distribution d'ivermectine. Les méta-analyses ne sont pas étayées par une revue systématique. Il n'y a pas de protocole, pas de critères d'inclusion, pas d'informations sur la recherche ou l'évaluation du risque de biais.	27 études incluses, les méta-analyses basées sur 18 essais de traitement contrôlés et randomisés de l'ivermectine dans la COVID-19 ont trouvé des réductions importantes et statistiquement significatives de la mortalité, du temps de récupération clinique et du temps de clairance virale. En outre, les résultats de nombreux essais contrôlés de prophylaxie font état d'une réduction significative des risques de contracter la COVID-19 avec l'utilisation régulière de l'ivermectine.

July 5, 2021

Evidence Snapshot:

Therapeutic or Prophylactic Use of Ivermectin for COVID-19

Context

Ivermectin is a broad-spectrum anti-parasitic agent approved in Canada to treat intestinal strongyloidiasis and onchocerciases infections. Ivermectin is not authorized for use in the treatment of COVID-19 by Health Canada, Food and Drug Administration or the European Medicines Authority. It is also not recommended by the World Health Organization (WHO) or Pan American Health Organization who are maintaining living guidelines on COVID-19 therapeutics. Due to antiviral activity seen in *in vitro* studies, several clinical trials have been conducted to evaluate the therapeutic or prophylactic use of ivermectin for COVID-19.

Key Findings

This evidence brief summarizes systematic reviews and new randomized controlled trials (RCTs) on ivermectin treatment (n=9) or prophylactic use (n=3) in COVID-19 up to July 5, 2021.
The key findings were:

- The WHO living guideline does not recommend the use of ivermectin for treatment of COVID-19 due to low certainty in the evidence and availability of more efficacious treatments.
- Ivermectin trials have been small with very few events reported per trial, thus precision from individual trials was very low. Risk of bias in the majority of trials was moderate or high due to inappropriate randomization or allocation concealment. Taken together the overall certainty in the evidence is low to very low for each outcome.
- Several meta-analyses reported a protective association with ivermectin treatment and mortality, however this was only seen when RCTs of moderate or high-risk bias or non-RCTs were included in the analysis. There was very low certainty in this outcome.
- Only a couple meta-analyses reported an association with reduced severity in the ivermectin treatment group, others reported no association with hospitalization, mechanical ventilation or length of stay.
- There were conflicting results on whether ivermectin decreased the time to viral clearance or symptom resolution.
- There was no evidence for an association with severe adverse effects of ivermectin treatments which ranged from <200ug/kg (safe dosage) to 2-3 times higher across trials.
- Across meta-analyses a protective effect of prophylactic was observed, however the certainty of this evidence was very low to low.

Considerations

There are over 48 registered on-going trials and over 24 completed, some of which are not yet published. Among the on-going trials are larger, placebo-controlled RCTs on ivermectin that may have enough power to address some of the concerns about the existing evidence.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evidence Brief of Ivermectin. July 5, 2021. Full report available from: **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Aperçu des éléments de preuve : **Utilisation thérapeutique ou prophylactique de l'ivermectine pour traiter la COVID-19**

Contexte

L'ivermectine est un agent antiparasitaire à large spectre approuvé au Canada pour traiter les infections intestinales de strongyloïdose et d'onchocercose. L'ivermectine n'est pas autorisée pour le traitement de la COVID-19 par Santé Canada, la Food and Drug Administration ou l'Autorité européenne des médicaments. Elle n'est pas non plus recommandée par l'Organisation mondiale de la santé (OMS) ou l'Organisation panaméricaine de la santé qui maintiennent des lignes directrices évolutives sur la thérapeutique de la COVID-19. En raison de l'activité antivirale observée dans les études *in vitro*, plusieurs essais cliniques ont été menés afin d'évaluer l'utilisation thérapeutique ou prophylactique de l'ivermectine pour traiter la COVID-19.

Principales constatations

Cette note de synthèse résume les revues systématiques et les nouveaux essais contrôlés randomisés (ECR) sur le traitement à l'ivermectine (n=9) ou l'utilisation prophylactique (n=3) contre la COVID-19 jusqu'au 5 juillet 2021.

Les principales conclusions sont les suivantes :

- La ligne directrice évolutive de l'OMS ne recommande pas l'utilisation de l'ivermectine pour le traitement de la COVID-19 en raison de la faible certitude des preuves et de la disponibilité de traitements plus efficaces.
- Les essais sur l'ivermectine ont été de petite taille avec très peu d'événements rapportés par essai, la précision des essais individuels était donc très faible. Le risque de biais dans la majorité des essais était modéré ou élevé en raison d'une randomisation ou d'une assignation secrète inappropriée. Dans l'ensemble, la certitude globale des preuves est faible à très faible pour chaque résultat.
- Plusieurs méta-analyses ont fait état d'une association protectrice entre le traitement à l'ivermectine et la mortalité, mais cette association n'a été observée que lorsque des ECR présentant un risque de biais modéré ou élevé ou des ECNR ont été inclus dans l'analyse. La certitude de ce résultat était très faible.
- Seules quelques méta-analyses ont rapporté une association avec une réduction de la gravité dans le groupe traité à l'ivermectine, d'autres n'ont rapporté aucune association avec l'hospitalisation, la ventilation mécanique ou la durée du séjour.
- Les résultats étaient contradictoires quant à savoir si l'ivermectine diminuait le délai de clairance virale ou de résolution des symptômes.
- Rien ne prouve l'existence d'une association avec les effets indésirables graves des traitements à l'ivermectine, qui varient de < 200 ug/kg (dose sûre) à 2 à 3 fois plus selon les essais.

- Dans toutes les méta-analyses, un effet protecteur de la prophylaxie a été observé, mais le degré de certitude de cette preuve était très faible à faible.

Facteurs dont il faut tenir compte

Il existe plus de 48 essais enregistrés en cours et plus de 24 essais terminés, dont certains ne sont pas encore publiés. Parmi les essais en cours, il y a des ECR de plus grande envergure, avec des placebos comme témoin, sur l'ivermectine qui pourraient avoir une puissance suffisante pour répondre à certaines des préoccupations concernant les preuves existantes.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Synthèse en bref sur l'ivermectine. 5 juillet 2021. Rapport complet disponible auprès de : **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Emerging Evidence on COVID-19

Rapid Review on the Characteristics of Effective Non-Medical Face Masks in Reducing the Risk of SARS-CoV-2 Transmission

Introduction

What is the evidence on the characteristics (e.g., design, material, fit) and efficacy of non-medical face masks in reducing SARS-CoV-2 transmission? (i.e., prevention of the spread of SARS-CoV-2 if worn by an infectious person or protection afforded to the wearer from inhaling SARS-CoV-2.)

Many public health organizations globally such as the World Health Organization recommend the use of face masks in public spaces to protect against COVID-19. Non-medical face masks (i.e. homemade or manufactured) are not regulated as personal protective equipment as they are not tested according to a set of standardized test methods (e.g., NIOSH, ASTM F2100 or EN 14683) like medical masks are (e.g., N95 respirators and surgical masks). Thus, they are not recommended for use by healthcare professionals and those with an increased risk of infection in situations where physical distancing is not possible (1).

The focus of this review was on the efficacy of non-medical masks for use in the general population during the COVID-19 pandemic. As such, articles that only evaluated respirators or surgical masks were not included in this review. Articles that compare the performance of respirators or surgical masks to non-medical masks are included and benchmarking outcomes were of interest to understand how the performance of different non-medical masks contrasts to the performance of medical masks. This rapid review summarizes literature until December 2, 2020 on evidence of the characteristics of non-medical face masks including the material, design and fit that make masks effective at filtering SARS-CoV-2 while maintaining an appropriate level of breathability. In the context of the COVID-19 pandemic and this review, studies examined masks both as a form of source control (i.e. preventing the spread of SARS-CoV-2 if worn by an infectious person) as well as protection they afford to the wearer from inhaling SARS-CoV-2. There is a synergistic effect when both the virus receiver and spreader wear masks (2).

Key Points

- Fifty-four primary research articles were identified, which included 22 studies investigating the prevention of the spread of SARS-CoV-2 by non-medical masks if worn by an infectious person (source control) and 37 studies investigating the protection provided by non-medical masks to a non-infected individual from inhaling SARS-CoV-2. Studies were conducted utilizing human volunteers (n=15), manikins (n=15), filter-holders (n=34) and animal models (n=1).

- Experimental simulation studies have found that non-medical masks are more effective for source control (Table 1) than protection of uninfected individuals (Table 2). There is a synergistic effect when both the uninfected person and the infected person wear masks (2).
- A face mask can significantly limit the distance respiratory droplets travel during indoor talking, coughing and sneezing, however, the efficacy of non-medical masks depends on three characteristics: 1) filtration efficiency 2) breathability and 3) fit.
- Filtration efficiency depends on the type, size, and velocity of the respiratory droplets and is dependent on the fabric quality (tightness of the weave, fibre or thread diameter) and inherent characteristics of the fabric (e.g., electrostatic charge and hydrophobicity).
- When made of high quality fabrics with multiple layers that fit snuggly around the mouth and nose, non-medical face masks can reduce the risk of spreading or being exposed to SARS-CoV-2, although to a lesser extent than medical masks.
    - Tight-fitting, double-layered masks comprising different material types (e.g., combed cotton and polyester) or masks made from one type of material but with greater than 2 layers exhibited similar outward blocking efficiencies as medical masks (>90%) while still maintaining comparable breathability.
    - Masks that do not fit tightly against the skin were shown to significantly reduce the mask effectiveness and in some studies the reduction was more than 50% in filtration effectiveness.
- A diverse range of non-medical face masks and materials were evaluated for filtration efficiency in 42 studies and a wide range of filtration efficiency results were reported (<10% to >95%).
    - Multiple layers for cloth masks improve filtration efficiency, however breathability decreases with additional layers. Research shows that greater than three layers significantly reduces breathability. Some samples fabricated with three layers were able to reach filtration efficiencies >90%.
    - Filtration efficiencies of most household materials were higher for larger droplets and droplets expelled at lower velocity.
- Studies show the type of fabric and use of mixed fabrics improve the filterability, breathability and longevity (i.e. reusability).
    - Materials used for masks should be a fine or tightly woven fabric. Some fabrics are hydrophobic (e.g., polyester, spunbound polypropylene, or polyaramid) or can capture charged particles via a form of static electricity (e.g., polyester or silk), while others may have hydrophilic properties to enhance comfort and longevity (e.g., cotton).
    - Multiple studies found a triple-layered mask made of a hydrophobic exterior, blended non-woven fabric middle, and hydrophilic interior was found to be an ideal combination to

maximize both the transmission-reducing potential and protection capacity of non-medical masks.

- Some fabrics are not recommended for use in non-medical face masks.
    - Vacuum cleaner bags have been shown to have filtration efficiencies comparable to medical masks, however they are not certified clinical products and may contain unhealthy ingredients and harmful fibers.
    - Loosely folded face masks, bandana-style face masks, and single-layered neck gaiters do a poor job at blocking respiratory droplets and offer little protection. The evidence is highly variable for neck gaiters, several studies showed no protection by neck gaiters, one showed enhanced production of aerosols, while another study reported blocking efficiencies similar to a cotton face mask.
    - Respirators with an exhalation valve can protect the wearer from SARS-CoV-2 but do not prevent virus dispersion by the wearer, and thus are not effective for source control.

Overview of the Evidence

There were 54 primary research articles pertaining to the characteristics and effectiveness of non-medical face masks in reducing the risk of SARS-CoV-2 transmission identified and included in this review. The focus of the review was on the efficacy of non-medical masks for use in the general population. As such, articles that only evaluated respirators or surgical masks were not included in this review. Articles that compare the performance of respirators or surgical masks to non-medical masks are included and benchmarking outcomes were of interest to understand how the performance of different non-medical masks contrasts to the performance of medical masks that are regulated. A rapid review on the use of face masks to prevent COVID-19 in community settings has been conducted and is available through the Emerging Science Secretariat.

The majority of studies included in this review were quasi- and simulation experiments that investigated the blocking/filtration efficiency, breathability and fit (i.e. a measure of how well the mask conforms to the face leaving minimal space or gaps between the mask and the skin) of various non-medical mask materials and styles utilizing human volunteers, manikins, animal models, and/or fabric filter holders. These experiments are an approximation of a real situation and are subject to the limitations of the models used. Manikins do not perfectly mimic human face shapes, movement (i.e. impacting fit) or respiratory activities, so extrapolation of these results to humans should be done with caution. Similarly, experiments using filter holders overestimate mask efficacy as they only evaluate the filterability of the fabric and not the fit of a mask on a person, thus the efficiency of a mask on volunteers or manikins would be expected to be lower due to leakage around the mask. None of the studies identified evaluate how effective specific types of non-medical masks are in real world settings, thus the results of this review only represent the efficacy of different masks evaluated under controlled experimental conditions. Further, while it was possible to compare and rank different

designs/materials/fit within studies, differing methodologies and material combinations made comparisons across studies difficult.

A SARS-CoV-2 virion is 0.1 µm in diameter, but is usually transported within other particles such as respiratory particles that come in a continuum of sizes ranging in size from <1 µm to >5 µm. Please request the review on aerosol transmission for further information. Particle sizes and velocities were not consistent between studies and filtration of different particle sizes varied across fabrics, thus filtration efficiencies are difficult to compare/synthesize. Many studies did not use real respiratory droplets or virus laden particles and instead utilized aerosol dispersion of alternative particles (e.g., NaCl, starch, bacteria, latex, silicon dioxide). The existing research on how effective non-medical masks are is of low quality and results will likely change with additional research.

CONTENTS

NON-MEDICAL MASKS FOR SOURCE CONTROL

Human and manikin studies (n=15):

The effectiveness of non-pharmaceutical interventions, such as social distancing, can be increased by reducing the level of infectious droplets/aerosols in the air of shared spaces (3). In light of the fact that people infected with COVID-19 can be asymptomatic or pre-symptomatic, universal masking in public areas is recommended as a means of source control to reduce exhalation particle dispersion, velocity and potential transmission.

Studies on human volunteers (n=10) and manikins (n=7) have been conducted. Manikins do not perfectly mimic human skin and movement (i.e. impacting fit) or respiratory activities as the air typically travels in only one direction (4).

Non-medical masks are better at source control (blocking viral droplets/aerosols (i.e. limiting transmission from an infected individual) (Table 1) than providing protection to uninfected people (Table 2) (2, 4, 5).

- Fabric masks, such as those made from cotton, are not as effective as medical masks at reducing outward droplet/aerosol dispersal (6, 7). This is likely due to the fabric used in the mask as well as increased air leakage resulting from a looser fit (6, 8).

- Compared to no mask, having a mask reduced the outward droplet/aerosol dispersal, however the magnitude of the reduction varied by the composition of the mask and specific attributes of the experiment (Table 1):
    - A cloth mask (fabric/composition not reported) was effective in reducing the respiratory jet distance while breathing and coughing from beyond the experimental field of view at 562mm (no face mask) to 150mm (similar to a surgical mask) (6).
    - A mask made from quilting cotton reduced the respiratory jet distance from 8ft to 2.5in (8).
    - A person standing 2m from someone coughing without a mask was exposed to over 1000 times more respiratory droplets than from someone standing 5 cm away wearing a basic single layer mask (9).
- Tightly-fitted surgical style masks made with multiple layers that included 100% cotton fabric and middle layers of non-woven polypropylene is very effective in reducing droplet dispersal (3, 10). Duckbill mask designs also demonstrated satisfactory fit and blocking efficiency (11). Breathability was not assessed in these studies. Examples of these styles are provided in the Appendix.
- Double-layered masks perform better at blocking droplets/aerosols during speaking, coughing, and sneezing than a single layer cloth face mask (12).
- A triple-layered cotton mask was found to be just as effective as a surgical mask at supressing respiratory droplet dispersion (86.4% and 99.9%, $p>0.05$, respectively) (13).
- Adding a filter layer such as a kitchen paper towel could significantly reduce the transmission potential (14).
- Loosely folded face masks and bandana-style coverings do a poor job at blocking respiratory droplets (8). When used as a single-layered face covering, polyester neck gaiters are not effective in preventing droplet/aerosol dispersion (14, 15), however, when double-layered, they provide blocking efficiencies similar to that of cloth face masks (16).
- Respirators with a valve do not prevent virus dispersion by the wearer (6, 15).

Filter holder studies (n=7):

Filter holder studies use fabric samples mounted in place by a filter holder and do not take fit of a human face into account, and thus may over-estimate the efficacy of face masks.

- Double-layered masks exhibited better blocking efficiencies than single-layered masks (17-19). Further, double-layered masks comprising different material types (e.g., combed cotton and polyester) or masks made from one type of tightly woven material (e.g., cotton), but with more than 2 layers

exhibited similar blocking efficiencies as medical masks (>90%) while still maintaining comparable breathability to surgical masks (20-23).

- Blocking efficiency is much higher for low-velocity droplets (e.g., generated by speaking) than high velocity droplets (e.g., generating by sneezing) (21).
- Fabric compositions that performed best included hydrophilic materials such as terry cloth, quilting cotton or flannel in combination with a hydrophobic barrier layer comprising nonwoven polypropylene, polyester or polyaramid which prevents more aerosols from getting through the mask (20).
- N95 standards are set using a particle size range of 0.1-0.3 µm. The majority of studies on non-medical masks have also used a similar size range in their experiments. Filtration efficiency for medical masks and many household fabrics was shown to be lower for smaller particles compared to larger droplets. One experiment on ultrafine particles (<0.1 µm) reported N95 respirators and surgical masks had 52.5% and 47.5% filtration efficiencies, respectively (19). In comparison, felted wool (35.87%), quilting cotton (34.54%) and cotton flannel (28.50%) had lower filtration efficiencies for these very small particles (19).
- Layered silk had a 94% filtration efficiency against small aerosol-sized particles (0.75 µm), likely because of its electrostatic charge (18). Silk did not perform as well for larger particles.
- Layered materials, including a hydrophobic outer layer (e.g., polyester, spunbound polypropylene, or polyaramid), an inner layer of high quality cotton fabric, and a middle layer of non-woven or electrostatically charged materials (e.g., natural silk, chiffon, or polyester) would be an ideal combination to maximize both the protection capacity and transmission-reducing potential of non-medical masks.
- A wide range of materials were investigated across studies, some of which may not be safe to use as a mask. Vacuum bags for example were shown to be effective at filtering in more than one study, however, they may have component materials that are unsafe to inhale or come into close contact with the face (19).

Table 1: Studies that investigate source control characteristics of non-medical masks (n=22)

STUDY*	METHOD	KEY OUTCOMES
Experiments conducted with human volunteer(s) and manikins (n=15)		
Ho 2020 (13) Quasi-experiment China	Assessment of the filtration efficiency of a 3-layer cotton mask and a surgical mask worn by adult patients (n=211) with confirmed influenza (n=208) and suspected cases of COVID-19 (n=6) compared with no mask and the background particles in the unoccupied	- The filtration efficiency of the triple-layered cotton mask was 86.4% and the surgical mask was 99.9%. - In both the bedroom and an air-conditioned car, the mean particle concentration for volunteers wearing no mask was significantly higher than in those wearing a surgical mask

Sep 2020	space, in two settings: a bedroom and a car with air conditioning. Four repeat measurements of 1-hr were taken with a particle counter located within 1m of the infected patient. Measurements: the filtration efficiency at 5.5cm/s. Temperature, humidity and cough/sneeze counts were also recorded. Paired t-tests were used for within-group comparisons.	or a cotton mask (p-value < 0.05 in both settings). - The concentration of particles did not significantly differ between a triple-layered cotton mask and a surgical mask in either setting.
Asadi 2020 (7) Quasi-experiment USA Sep 2020	To assess the efficacy of unvented KN95 respirators, vented N95 respirators, surgical masks, homemade single layer paper towel, homemade single layer and double layer t-shirt cotton masks at reducing aerosol particle emission rates from breathing, speaking and coughing by healthy individuals (n=10), study participants were asked to sit with their mouths positioned in front of a funnel attached to an aerodynamic particle sizer (particle counter). They then performed different expiratory activities while wearing or not wearing masks.	- Compared to no mask, both surgical masks and non-fit tested unvented KN95 respirators, reduced the average outward particle emission rates during speaking by 90% and during coughing by 74%. - Cotton masks were difficult to assess. Shedding of non-expiratory micron-scale particulates from fibers in homemade cotton-fabric masks confounded explicit determination of their efficacy as measured particle emission rate for the double-layered mask was not statistically different than no mask at all and single-layered cotton mask was much higher than that of no mask at all.
Fischer 2020 (15) Quasi-experiment USA Sep 2020	Used a simple optical measurement method to evaluate the efficacy of masks to reduce the transmission of respiratory droplets during speech. One human volunteer wore a face mask and spoke into the direction of an expanded laser beam inside a dark enclosure. A cell phone camera recorded droplets that propagated through the laser beam scatter light. A simple computer algorithm was used to then count the droplets. Masks tested included: surgical, valved N95, knitted, polypropylene, Poly/cotton, Maxima AT,	- The fitted N95 mask performed the best with a droplet transmission fraction of 0.1%> surgical > cotton/polypropylene/cotton, 2 layer polypropylene > mask material+ polypropylene swath (loose fit) > 4 different double layer cotton masks, valved N95 > MAxAT, single layer cotton > knitted > bandana > none > neck gaiter. - The neck gaiter performed the worst with a droplet transmission fraction of 110% as the fabric broke larger droplets into a multitude of smaller droplets. - This study has an extremely small sample size and should be used with caution.

	four double-layered cotton masks, one single-layered cotton mask, a neck gaiter, bandana and a fitted N95 (no valve).	
Swain 2020 (14) Quasi-experiment United Kingdom Jul 2020	Humidity was used as a quantitative approximation of viral shedding. At measured distances from a sensor, 4 healthcare staff wearing a mask or no mask were assessed for the change in relative humidity and oxygen saturation, in 3 scenarios over 2 minutes: 1) Hard breathing 65mm 2) Quiet breathing 20cm 3) Hard breathing 20cm The masks tested included a prototype mask from AngelMed (no valve), a standard NHS clinical mask and a FFP2V mask (one-way valve). Homemade masks materials tested included a t-shirt, a double-layered Buff, sock masks (both with and without paper filters, and a homemade mask designed to enable lip-reading (made from a thick material surrounding a clear window).	- Compared to no mask, the AngelMed mask, standard NHS clinical mask and FFP2V mask all significantly prevented a change in humidity. - The t-shirt and double-layered buff were the same as no mask change in humidity for hard breathing @ 65mm scenario (5.4% and 5.1%, respectively). - A two-layer sock mask performed better than a single-layered sock (15.3% vs 9.5%). - The home-made lip-reading mask prevented any increase in relative humidity. However, this mask restricted breathing and was found to reduce oxygen saturation in participants. - Findings are preliminary and caution should be taken when interpreting the results.
Viola 2020 (6) *Preprint* Quasi-experiment United Kingdom May 2020	To compare the air flow ejected by a person wearing no or 7 different face covers while quietly and heavily breathing or coughing, using a Background Oriented Schlieren technique. A human volunteer (n=1) and a manikin were used in the study. Five face masks were studied: FFP1, FFP2, respirator, surgical mask, hand-made mask and two face shields.	- With no face mask, the air jet extended beyond the boundary of the field of view at 562 mm from the mouth after breathing or coughing. - The FFP2 mask was the most effective in reducing all exhaled air dispersal. When not properly sealed to the nose, leakage was observed towards the crown. - The respirator had a valve system that did not stop the displacement of the front through flow, thus offering no prevention of virus dispersion from the wearer.

		- The handmade mask (composition not described) was the least effective in stopping air leakage, and the surgical mask was the least effective in preventing backward jet flow. - Findings are preliminary and caution should be taken when interpreting the results.
Bandiera 2020 (9) *Preprint* Quasi experiment United Kingdom Aug 2020	Assessed effectiveness of surgical masks and single layer cotton masks at mitigating large respiratory droplet dispersion with speaking and coughing simulations in manikins. The number of droplets from the manikin/air compressor were quantified using laser sheet illumination and UV-light for those that had landed at table height at up to 2m. For human volunteers (n=6) wearing surgical masks during speaking and coughing, expiratory droplets were caught on a microscope slide 5cm from the mouth.	- Estimated that a person standing 2m from someone coughing without a mask is exposed to over 1000 times more respiratory droplets than from someone standing 5cm away wearing a basic single layer mask. - Face coverings show consistent efficacy at blocking respiratory droplets of 20-30µm for speaking and coughing simulations ($p<0.05$). - No statistically significant difference in droplet deposition was seen between the surgical mask and the single layer cotton mask. - No droplet deposition occurred with wearing a surgical mask by the volunteers.
Stubington 2020 (11) Quasi experiment United Kingdom Aug 2020	A single volunteer wore several masks and was filmed exhaling visible water vapour, to test the trajectory of exhaled material from a masked individual.	- Flexible pleated and solid FFP masks directed exhaled material downwards, exceeding 25cm. - Duckbill masks directed exhaled material laterally, producing a smaller plume. - Wearing a visor provided no reduction in plume size of exhaled vapour for any mask type. - Fluid repellent material reduced the exhaled material traveling downwards.
Rodriguez-Palacios 2020 (10) Quasi Experiment	The effectiveness of cotton masks in retaining/reducing the risk of environmental contamination by oral/saliva droplets produced by one of the investigators (a healthy volunteer) during a speech trial (counting from 1	- The same cotton mask on a human volunteer, demonstrated even a single layer of the material reduced the risk of environmental contamination by oral/saliva droplets compared to no mask.

USA Aug 2020	to 100 in English) conducted at 30cm over a sterile TSA agar plate. (Table 2 has the protective effect animal model experiment).	
Bahl 2020 (12) Quasi Experiment Australia Jul 2020	This study evaluated the effectiveness of the Centers for Disease Control and Prevention (CDC) recommended one- and two-layer cloth face covering against a three-ply surgical mask. The single-layer covering was made using 'quick cut T-shirt face covering (no-sew method)' and the two-layer covering was prepared using a no sew method recommended by CDC. To provide visual evidence of the efficacy of face coverings, a tailored LED lighting system along with a high-speed camera were used to capture the light scattered by droplets and aerosols expelled during speaking, coughing and sneezing by a single volunteer.	- Based on visualizations (photos in the paper and no analysis) of speaking, coughing and sneezing, a single-layer cloth face mask reduced the droplet spread, a double-layer covering performed significantly better with very little visible droplets upon sneezing only, and the surgical mask performed best by preventing droplet spread from any respiratory emission.
Pan 2020 (4) *Preprint* Simulation experiment USA Nov 2020	Evaluated the effectiveness of 11 face masks in a manikin model for material filtration, inward and outward protection across broad aerosol size range 0.04-135µm. Challenge particles were generated from a 2% NaCl solution. They evaluated both inward and outward protection efficiency of face masks using two manikins mounted on opposite sides of a 57-L acrylic chamber. The "exhaling" manikin was connected to a nebulizer and the "inhaling" manikin was connected to a vacuum. A mask was worn by the inhaling manikin and then the exhaling manikin, to measure the number of	- Filtration efficiency increased with increasing particle size and prevented droplets larger than 20µm from spreading 33 cm away. - Particles 2µm had >90% efficiency using the vacuum bag, microfiber cloth, surgical mask, and MERV 12 filter. - The vacuum bag and microfiber had the highest filtration efficiencies, with a range of 60-90%, surgical masks ~50-75%, coffee filter 10-75% over particle sizes (0.04-1µm). - The thin cotton mask and bandana (2 ply), had low efficiencies (30-50%), with even lower efficiencies (5-40%) for submicron particles.

	particles that passed through the mask, respectively. Face mask: Vacuum bag, surgical mask, MERV 12 filter, Bandana, 200-thread count cotton pillowcase, cotton t-shirt, microfiber cloth, coffee filter, thin cotton, thin acrylic and a plastic face shield.	- Inward protection efficiency and outward protection efficiency were similar for most of the masks. - Loose fitting masks (e.g., the bandana) did not perform as well for source control. - The thin acrylic mask performed the worst. - The combined effects of reduced gaps and reduced air velocity resulted in a high outward protection efficiency for the CDC non-sewn mask made from a 200-thread count cotton pillowcase.
Lindsley 2020 (16) *Preprint* Simulation experiment USA Nov 2020	A cough aerosol simulator with a pliable skin manikin headform was used to propel small aerosol particles (<0.6 to 7 µm) into a N95 respirator, a medical grade procedure mask, a 3-layered cotton cloth mask, a polyester neck gaiter and a face shield. The simulated cough aerosol was generated by nebulizing a solution of 14% KCl and 0.4% sodium fluorescein. Fit tests were conducted using a PortaCount.	- All face masks significantly reduced the aerosol released into the environment ($p<0.0001$), except for the face shield. - The N95 respiratory blocked 99% of aerosols, the medical procedure mask blocked 59%, the cloth mask blocked 51%, the single-layer gaiter blocked 47%, the double-layer gaiter blocked 60% and the face shield only blocked 2%. - Blocking efficiencies for all masks increased with increasing particle size. - The N95 respirator had the best fit, followed by the medical procedure mask, the double-layer gaiter, the single-layer gaiter and the cloth mask.
Kähler 2020 (5) Simulation experiment Germany Oct 2020	Quantitative particle image velocimetry measurements helped determine the spread of exhaled air, the velocity of the exhaled droplets and the turbulence properties of the flow. A single human volunteer was used to observe the flow field generated by coughing without and with a surgical mask using smoke to demonstrate the effect of the gap around the mask edge (surgical and FFP2 masks).	- A surgical mask limited the spread of air and aerosol when speaking or coughing. - Mouth-and-nose covers and surgical masks did not fit tightly enough on the face to protect against droplet infection, as demonstrated by photographic evidence of droplets passing unhindered through the mask. - Masks made from toilet paper with 4 layers, paper towel, coffee filters, fleece and microfiber cloth had low filtration.

	The filtering performance of the different materials on small aerosols (0.3–2µm) was observed with a digital camera in front of and behind the filter material.	- Vacuum cleaner bags with fine dust filters demonstrated comparable filtering effect to FFP2/N95/KN95 masks, but are not suitable for use.
Ueki 2020 (2) Simulation experiment Japan Oct 2020	This study describes an airborne transmission simulator of infectious SARS-CoV-2-containing droplets/aerosols produced by human respiration and coughs. It is used to assess the transmissibility of the infectious droplets/aerosols and the ability of various types of face masks to block the transmission. A test chamber utilized 2 manikin heads placed facing each other connected to a customized compressor nebulizer. Cotton masks, surgical masks and N95 masks were evaluated.	- The N95 mask had the highest protective efficacy (reduced exposure to infectious particles by 80-90%). - Surgical masks and N95 masks were not able to completely block the transmission of virus droplets/aerosols even when completely sealed. The viral load passing through a fitted N95 mask when worn by the spreader was 0.3 $\log_{10}$ copies and when worn by the receiver was 10 $\log_{10}$ copies. - A cotton mask (no description of composition) led to a 20-40% reduction in virus uptake compared to no mask. - Cotton and surgical masks were better at blocking virus dispersion by the wearer (>50%) (i.e., as a form of source control) than protection. - There was a synergistic effect when both the virus receiver and virus spreader wore masks (cotton masks or surgical masks). For example, when the receiver wore a cotton mask the viral load passing through the mask was 63 $\log_{10}$ copies, when the spreader wore a mask the viral load passing through was 42 $\log_{10}$ copies and when both the receiver and spreader wore a mask the viral load was the lowest at 33 $\log_{10}$ copies. See graphs in paper.
Edwards 2020 (3) *Preprint*	This randomized effectiveness study used a 10% NaCl nebulized polydisperse particle solution (0.3 µm up to 10 µm in size) delivered by an exhalation simulator and manikins to conduct 94 experiment runs with	- Non-medical grade mask designs or fabric combinations are statistically significant in reducing airborne dispersion of particles from exhalation compared to no mask. - Fabric, mask design and the interaction of fabric and exhalation breath level have a

Simulation experiment USA Aug 2020	combinations of 8 different fabrics, 5 mask designs and airflows for both talking and coughing. Two novel metrics of Filtration Efficiency Indicator (FEI) and Expiratory Flow Dispersion Factor (EDF) are established in this study to present quantitative values that give relative indicators to the dispersion control performance of non-medical masks. Higher values in both these metrics indicates better filtration and performance with more reduction in particle velocities, respectively.	significant effect on filtration efficiency of exhaled particles. - The best overall performing mask design was a surgical style with internal non-woven layers. - The best overall fabric depends on a reduction in velocity, change in direction or increased filtration performance. - The FEI values for various materials from best to worst were: Bath towel > Sweat pant > T-shirt > Bandana > Microfiber towel > Pillow case > Mover blanket > Dress shirt. - The EDF values for various materials from best to worst were: Pillow case > Microfiber towel > Sweat pant > Bath towel > T-shirt > Dress shirt > Mover blanket > Bandana.
Verma 2020 (8) Simulation experiment USA Jun 2020	This study uses qualitative visualizations of emulated coughs and sneezes using a manikin head to examine how material- and design-choices impact the extent to which droplet-laden respiratory jets are blocked.	- Loosely folded face masks and bandana-style coverings provide minimal stopping-capability for the smallest aerosolized respiratory droplets. - Well-fitted homemade masks with multiple layers of quilting fabric, and off-the-shelf cone style masks, proved to be the most effective in reducing droplet dispersal. These masks did have some leakage through the mask material and from small gaps along the edges.
Filter holder studies to assess source control characteristics of mask materials (n=7)		
Aydin 2020 (21) Simulation experiment USA Jul 2020	This study investigated the performance of 11 household fabrics reducing droplet dispersion, using a commercial medical mask as a benchmark. Also assessed was their breathability (air permeability), texture, fiber composition and water absorption properties. Filtration efficiency of large, high-velocity droplets was assessed by	- Most single-layered fabrics had a relatively high droplet blocking efficiency (median values>70%) when challenged with high velocity droplets representative of sneezing, coughing or speaking. - The medical mask had a blocking efficiency of 98.5%. - Two or 3 layers of fabric, such as T-shirt cloth, blocked droplets with an efficacy similar to

	placing the fabrics 25mm in front of the nozzle of an inhaler, loaded with a suspension of 100nm fluorescent beads. Low-momentum droplets were assessed by placing the fabric 300mm from the inhaler. Air permeability was assessed using a plug flow tube experiment. Test fabrics included: polypropylene medical mask, 100% cotton t-shirts, 100% cotton quilt cloth, cotton and polyester blend t-shirts, polyester bed sheet, polyester and polyamide blend dishcloth, and silk shirts.	that of medical masks (>94%), while still maintaining comparable breathability. - Blocking efficiency by T-shirt fabric is much higher for low-velocity droplets than high velocity droplets. - Less breathable fabrics are more effective in blocking droplets.
Xiao 2020 (18) Simulation experiment Japan Jun 2020	Efficiency of surgical masks, gauze masks, gauze, cotton, silk, linen and tissue paper on blocking micro-droplet sized starch particles (average 8.2µm) and latex microspheres (0.75µm) with a velocity of 44.4m/s (high-velocity sneeze conditions) created by centrifugation was qualitatively analyzed using imaging-based analysis.	- The cotton gauze mask was the most efficient at blocking starch particles (90.4% blocking efficiency), followed by 2 layers of cotton (89.0%). Other materials ranged from 76.4%-87.9% efficiencies, while 8 layers of gauze performed very poorly (36.7%). The surgical mask blocked 78.2% of particles. - When latex microspheres were used to mimic aerosol-sized particles, materials with the best blocking efficiencies were the 4 layers of silk (93.8%), likely because of electrostatic charge, the gauze mask (78.5%) and the 2 layers of cotton (74.6%). - Multi-layered linen performed significantly better than a single layer (66.5% vs. 53.2%).
O'Kelly 2020 (19) Simulation experiment USA	In this study, 20 commonly available fabrics and materials were evaluated for their ability to reduce air concentrations of ultrafine particles (0.1µm and smaller in diameter) at a face velocity of 16.5m/s (coughing velocity). Further assessment was made on the filtration ability of select fabrics while damp and of fabric combinations which might be	- Ultrafine particles used in this study lead to a low 'baseline' for filtration efficiency. - The N95 mask (52.47%), surgical mask (47.46%), and disposable HEPA vacuum (60.86%) had had the highest filtration efficiencies.

Jun 2020	used to construct homemade masks. Breathing resistance was estimated based on qualitative feedback. In this study, filtration efficiency represents the percent of particles a filter medium can block. Fabrics tested included: Felt, Lycra, washable vacuum bags, and quilt batting/wadding and various weaves of cotton commonly available, including quilting cotton, shirting cotton and cotton jersey knit.	- Denim jeans (45.94%) and windbreaker fabric (47.12%) were efficient, but lacked breathability. - High filtration efficiency and low breathing resistance materials included felted wool (35.87%), quilting cotton (34.54%), and cotton flannel (28.50%). - Common fabrics were able to achieve much higher levels of ultrafine particle filtration when layered (60%), but were less breathable. - Vacuum bags were effective, but are unsafe for use.
Foschini 2020 (17) *Preprint* Simulation experiment Brazil May 2020	This study compares the relative efficiencies of commercial respiratory masks (medical masks) and homemade fabric masks. A nebulizer was used to create the aerosol from distilled water. For the optical scattering measurements 2 different techniques were used simultaneously to compare the intensity of light dispersion by the droplets between the windows before and after the sample.	- The N95 respirator and surgical mask (99.7%) had the highest blocking efficiencies. - The coffee filter also had high blocking efficiency (99.6%) but low breathability and degraded with increasing humidity, making paper products a poor choice for mask material. - Confectioner masks (51.0%), do not have as many layers as surgical masks, thus reducing their efficiency. - Conventional fabrics with a higher cotton content were the most effective of the household fabrics (1-layer: 46.5%). Double layering increased the blocking efficiency (2-layers: 66%).
Lustig 2020 (20) Simulation experiment USA May 2020	In this study, over 70 different common fabric combinations and masks were evaluated under steady-state, forced convection air flux with pulsed aerosols that simulate forceful respiration.	- Effective materials (lower fractional transmission estimates) comprise both absorbent, hydrophilic layers and barrier, hydrophobic layers. - Effective designs are noted with absorbent layers (double-layered) comprising terry cloth towel, quilting cotton, and flannel. These commonly available mask materials exhibit

		fractional transmissions within 10% of the five-layer N95 respirator. - Effective designs had barrier layers comprising nonwoven polypropylene, polyester and polyaramid. - Many masks made from either a single-layer or one type of fabric exhibited higher fractional transmissions than the N95 respirator.
Rodriguez-Palacios 2020 (22) Simulation experiment USA May 2020	This study assessed household textiles to quantify their potential as effective environmental droplet barriers. They used a bacterial-suspension spray simulation model of droplet ejection (mimicking a sneeze) to quantify the extent to household clothing fabrics reduce the dispersion of droplets onto surface within 1.8m (the minimum distance recommended for COVID-19 "social distancing"). Textiles tested included: 100% combed cotton (T-shirt material), 100% polyester microfiber 300-thread count fabric (pillow case), 2 loosely woven "homespun" 100% cotton fabrics, and "dry technology" 100% polyester common in sport jerseys. These textiles were compared to no "mask", and medical/surgical mask material.	- When no mask was used, a simulated sneeze could transport bacteria-carrying droplets farther than 1.8m. - All single-layered textiles were able to significantly reduce the ejection of macro-droplets and micro-droplets to <25.5-34cm. - Double-layered textiles (of 100%-combed cotton and 100% polyester) completely prevented the ejection of large macro-droplets, and reduced the ejection of micro-droplets by 97.2% (P<0.020) vs. single-layers and dispersion to <10cm. Even the least effective single-layered textile (loosely woven homespun 100% cotton) achieved a 90-99% droplet retention improvement when double-layered. - Double-layered textiles were as effective as medical/surgical mask material for preventing droplet dispersion.
Amendola 2020 (23) Simulation experiment Italy	The experiment simulated respiratory action measuring the distribution of aqueous-based aerosol particles. The average filtration efficiency was reported taking into account the particles with diameters greater than 0.28µm. The face masks were tested in both the inhalation and exhalation direction.	- The medical face mask demonstrated filtration efficiencies higher than 97%. - Only the face masks fabricated with 3 layers mainly constituted by non-woven fabric material were able to reach values higher than 95% including triple-layer TNT, TNT-cotton-TNT mask.

May 2020	TNT= A non-woven material made of fabric-based polypropylene and viscose	

*Location or date of study was estimated based on author affiliations and / or publication date.

NON-MEDICAL MASKS FOR PROTECTION FROM INHALING SARS-COV-2

Human, manikin and animal model studies (n=17):

Studies on human volunteers (n=7), manikins (n=10) and experimental germ-free mice (n=1) have been conducted. Manikins do not perfectly mimic humans (i.e. impacting fit) or respiratory activities as the air travels in only one direction (4). Thus, caution should be used when extrapolating the manikin results to human face mask wearers.

While non-medical masks have been shown to function better as a form of source control (i.e. limiting transmission from infected individuals) (2, 4, 5), they have also been shown to offer some protection to the wearer (Table 2). The most effective transmission-reducing scenario is one when everyone (both healthy and infected) wears a face mask (2).

- Proper fitting N95 respirators offer the highest degree of protection (>95%) (2, 24-31). Improper fitting N95 respirator offer a range of protection, in some cases comparable to surgical and cloth masks (24, 30).
- Surgical masks have better filtration efficiencies than non-medical masks (range: 19.94%->95%) (4, 25-28).
- Cloth masks generally had lower filtration efficiencies compared to medical masks although certain fabrics and layers performed comparably to medical masks (4, 25, 27, 28).
    - Mask performance (filtration of respiratory droplets, minimal air leakage) was higher for tighter fitting masks (5, 24-26, 30, 32) and for multi-layered masks (29, 31, 33). Filtration efficiency was higher for larger particles (4).
- Silk was found to be very hydrophobic and effective at impeding penetration of water droplets during spray tests (34).
- Bandana's and single-layered cotton fabrics were found to fit and perform poorly (<15-30% efficiency) (4, 27-29, 31).
- Surgical-style non-medical cloth masks did not perform as well as cone or duckbill shaped masks (26, 35).
- In an animal model study, when protected by two layers 100% combed cotton, all mice were 100% protected from becoming contaminated by the bacteria contained in the microdroplets (10).

Filter holder studies (n=20):

Under experimental conditions (i.e. measurements taken while fabric was sealed to a holder) the filtration efficiencies were higher compared to the studies cited above where masks were tested while on a wearer (36-42). Thus, these experimental simulations overestimate the efficacy of household fabrics in protecting potential wearers from SARS-CoV-2 because they do not directly assess breathability or fit, but they do help to understand the relative filtration efficiency of one fabric compared to another.

- Increasing the number of layers increases the filtration efficiency, but increases air resistance (and therefore lowers breathability). Non-medical masks should have an air resistance <40 Pa/cm2) (41-49). All samples tested with <four layers had breathability values below the maximum NIOSH recommendations set for medical masks (50). Samples fabricated with three or more layers were able to reach filtration efficiencies >90% (23, 37, 40, 42-44, 50, 51).
- Simulated leaks in the fabric (to indirectly measure the effect of fit) have been shown to strongly impact filtration efficiency (44, 52). Thus, fit is very important for adequate protection.
- Non-medical masks did not perform as well as medical masks. However, the addition of an activated carbon filter as a middle layer in a cotton mask significantly improved the filtration efficiency (46, 53). One study found that treating household materials with a NaCl solution may be useful in increasing the filtration ability of non-medical masks (54).
- Huge filtration efficiency differences were found between house-hold materials and for different particle sizes, ranging from <10% to >95%. Filtration efficiencies were higher for slower-moving particles produced during talking vs. faster moving particles produced during coughing or sneezing (46).
- Quality of fabric (i.e. tight weave, low porosity) was just as important as the number of layers (43, 44, 46).
- Some fabrics have electrostatic charges that attract and bind nanometer-sized particles, resulting in increased filtration efficiency (44, 52, 55). Combining layers and leveraging mechanical and electrostatic filtering may be effective in maximizing filtration efficiency in a non-medical mask (44, 52). Layered materials, including a hydrophobic outer layer (e.g., polyester, spunbound polypropylene, or polyaramid), an inner layer of high quality cotton fabric and a middle layer of non-woven or electrostatically charged materials (e.g., natural silk, chiffon or polyester) would be an ideal combination to maximize both the transmission-reducing potential and protection capacity of non-medical masks.
- While vacuum cleaner bags have been shown to have filtration efficiencies comparable to medical masks (4, 5, 40, 42, 46, 50), they are not certified clinical products and may contain unhealthy ingredients and harmful fibers. It is not recommended to use the material for homemade masks (5).

Table 2: Studies that assess the protective characteristics of non-medical masks (n=37)

STUDY*	METHOD	KEY OUTCOMES
Experiments conducted with a human volunteer(s), manikins, or animal models (n=17)		
Park 2020 (31) Quasi-experiment USA Aug 2020	In this mask development study, 10 different samples of various material configurations were evaluated for air permeability, particle size filtration efficiency and pressure drop, to arrive at a mask design with optimal comfort and barrier efficacy. One human subject wore the test mask for extended periods of time simulating a typical workday and assessed its performance. Air permeability was assessed with method ASTM D737-96, and filtration and pressure drop were assessed with ASTM F2299-03 with particle sizes 0.2-1µm and air flow of 8.7cm/s.	- Medical masks had the highest filtration efficiency while handkerchief fabric was found to perform the worst (highest air permeability and a filtration efficiency of only 19% even with 4 layers). - The barrier configuration deemed optimal was 'Filter 2 (Pile Up)' between two 100% polyester barrier layers. This mask performed better for filtration and permeability than the commercial double-layer knitted mask evaluated. - Filtration efficiency was better for larger challenge particles than smaller particles.
O'Kelly 2020 (24) *Preprint* Quasi-experiment USA Aug 2020	Seven human volunteers were used to quantitatively evaluate the level of fit offered by various types of masks (N95 masks, a KN95 mask, a surgical mask and fabric masks), and most importantly, assess the accuracy of implementing fit checks by comparing fit check results to quantitative fit testing results. Quantitative fit testing simultaneously assesses the number of particles inside and outside a mask Fit factor scores were derived from the number of particles filtered by the mask.	- N95 masks offered the highest degree of protection. Averaged fit scores across different models ranged from 13.2-72.3. - Poorly fit N95 masks offered a range of protection, in some cases comparable with surgical and cloth masks. - The KN95 and surgical mask showed an average fit score of 3.2 and 2.2., respectively. - The fabric face masks tested produced similar fit scores to KN95 masks and surgical masks. - Improved design coupled with the use of better materials would likely raise the effectiveness of these masks.

	Each participant completed one quantitative fit test and one subjective fit-check per mask.	
Mueller 2020 (26) Quasi-experiment USA May 2020	Quantified the efficacy of community- and commercially-produced fabric masks as personal protective equipment with the use of two particle counter that concurrently sampled ambient air and air inside different types of masks worn by a single volunteer. Mask performance was then evaluated by mean particle (size < 0.3µm) removal efficiency and statistical variability when worn as designed and with a nylon over layer, to independently assess fit and material.	- The properly fitted N95 mask had the greatest mean removal efficiency (99%) and a high fit factor. - When a poor fitting N95 mask was used, the removal efficiency and fit factor decreased to 90.6% and 10.6, respectively. - Standard surgical masks and 4 layer masks with a charcoal layer had a mean removal efficiency of 50-75%. - Cloth mask particle removal efficiencies ranged from <30% to 90%. The best performing cloth masks were cone shaped and included a layer of melt blown filter fabric between fabric cover layers. - Surgical-style cloth masks did not perform as well as cone shaped masks, but were enhanced by a nylon over layer. - A nylon over layer did not provide significant filtration efficiency, but improved the snugness of the fit of the mask underneath.
Ueki 2020 (2) Quasi experiment Japan Oct 2020	This study describes an airborne transmission simulator of infectious SARS-CoV-2-containing droplets/aerosols produced by human respiration and coughs. It is used to assess the transmissibility of the infectious droplets/aerosols and the ability of various types of face masks to block the transmission. A test chamber utilized 2 manikin heads placed facing each other connected to a customized compressor nebulizer.	- The N95 mask had the highest protective efficacy (reduced exposure to infectious particles by 80-90%). - Surgical masks and N95 masks were not able to completely block the transmission of virus droplets/aerosols even when completely sealed. The viral load passing through a fitted N95 mask when worn by the spreader was 0.3 $\log_{10}$ copies and when worn by the receiver was 10 $\log_{10}$ copies. - A cotton mask led to a 20-40% reduction in virus uptake compared to no mask. - Cotton and surgical masks performed much better at blocking virus dispersion by the

		wearer (>50%) (i.e. as a form of source control) than protection. - There was a synergistic effect when both the virus receiver and virus spreader wore masks (cotton masks or surgical masks). For example, when the receiver wore a cotton mask the viral load passing through the mask was 63 log_{10} copies, when the spreader wore a mask the viral load passing through was 42 log_{10} copies and when both the receiver and spreader wore a mask the viral load was the lowest at 33 log_{10} copies. See graphs in paper.
Teesing 2020 (35) Quasi experiment Netherlands Oct 2020	A closed particle chamber was built to test potential filter materials found to be recommended by governments for homemade masks. Materials were tested alone, as well as between 2 layers of cotton, simulating a homemade mask. Various mask designs were tested: folded, pleated, round, flat and duckbill shapes. Mask fit was tested with an AccuFIT 9000 Respirator Fit Test apparatus and a human volunteer. A pressure test was conducted to quantify breathability of designs and materials for those passing the fit test.	- Particle testing of materials was compared to N95/FFP2/KN95 masks; and the best performing material was ePM_1 85%, while from readily available materials top performance came from leather, followed by a folded coffee filter between cotton layers, a folded paper towel between cotton and microfiber fabric. - None of the cotton masks with an inserted filter passed the fit test conducted. The duckbill model was found to have a satisfactory fit. - The duckbill design pressure drop was tested and the single and folded tea towel showed comparable breathability to the 3M reference mask.
Mboowa 2020 (41) *Preprint* Quasi experiment Uganda	Eight commercially available masks were tested for filtration efficiency breathability, microbial cleanliness, and re-usability. Mycobacterium smegmatis was aerosolized by a hand-held sprayer and directed at sections of filter-	- The filterability was best in surgical face masks > local double-layered face mask > double-layered cloth masks. - Treatment with 70% ethanol decreased fitness and re-usability. - Double-layered masks had the best fit as evidenced by the saccharine taste test. It took

Sep 2020	holder mounted face masks. The filtered air was inoculated on agar media. Volunteers wearing face masks were challenged with saccharine (taste test) to evaluate mask fit. Tests were repeated after washing or 70% ethanol treatment to assess re-usability. Masks tested included: polypropylene, "thick" material, kitengi (inside)/cotton (outside), cloth, surgical and face scrub cloth.	more sprays for the volunteer to taste the saccharine when wearing double-layered mask than a single-layered masks. - Caution should be used in interpreting these results, the methodology is unclear.
Rodriguez-Palacios 2020 (10) Quasi experiment USA Aug 2020	This study reported an *in vivo* experiment with bacteria-carrying microdroplets (probiotic-cultured dairy product bacteria) to determine to what extent double-layered 100% combed cotton (common T-shirt material) prevented contamination of germ-free mice using a spray simulation method. Two different fabric densities were tested: 120 and 200 g/m2. (Table 1 reports on the source control experiment)	- When protected by 2 layers 100% combed cotton, all mice were 100% protected from becoming contaminated by the bacteria contained in the microdroplets (2mL spray). - When exposed to 10x the spray volume (20mL) textile barriers still protected all mice (even with low textile density; heavy vs. light fabric, paired t-test, p = 0.002) against high droplet doses. - The same experiments on partly covered cages resulted in microbial contamination of all mice.
Pan 2020 (4) *Preprint* Simulation experiment USA Nov 2020	Evaluated the filtration efficacy of 11 face masks in a manikin model for inward and outward protection across a broad range of aerosols 0.04-135 µm. Challenge particles were generated from a 2% NaCl solution. Two manikins mounted on opposite sides of a 57-L acrylic chamber were used. The "exhaling" manikin was connected to a	- Filtration efficiency increased with increasing particle size and prevented droplets larger than 20µm from spreading 33cm away Particles 2µm had >90% efficiency using the vacuum bag, microfiber cloth, surgical mask and MERV 12 filter - The vacuum bag and microfiber had the highest filtration efficiencies, with a range of 60-90%, surgical masks ~50-75%, coffee filter 10-75% over particle sizes (0.04-1 µm).

	nebulizer and the "inhaling" manikin was connected to a vacuum. A mask was worn by the inhaling manikin and then the exhaling manikin, to measure the number of particles that passed through the mask, respectively. Face masks: Vacuum bag, surgical mask, MERV 12 filter, Bandana, 200-thread count cotton pillowcase, cotton t-shirt, microfiber cloth, coffee filter, thin cotton, thin acrylic and a plastic face shield.	- The thin cotton mask and bandana (2-ply), had low efficiencies (30-50%), with even lower efficiencies (5-40%) for submicron particles. - Inward protection efficiency and outward protection efficiency were similar for most of the masks. - Loose fitting masks (e.g., the bandana) did not perform as well for source control. - The thin acrylic mask performed the worst. - The combined effects of reduced gaps and reduced air velocity resulted in a high outward protection efficiency for the CDC non-sewn mask made from a 200-thread count cotton pillowcase.
Kähler 2020 (5) Simulation experiment Germany Oct 2020	Quantitative particle image velocimetry measurements helped determine the spread of exhaled air, the velocity of the exhaled droplets and the turbulence properties of the flow. A single human volunteer was used to observe the flow field generated by coughing with and without a surgical mask using smoke to demonstrate the effect of the gap around the mask edge (surgical and FFP2 masks). The filtering performance of the different materials on small aerosols (0.3–2µm) was observed with a digital camera in front of and behind the filter material.	- A surgical mask limited the spread of air and aerosol when speaking or coughing. - Mouth-and-nose covers and surgical masks did not fit tightly enough on the face to protect against droplet infection, as demonstrated by photographic evidence of droplets passing unhindered through the mask. - Masks made from toilet paper with 4 layers, paper towel, coffee filters, fleece and microfiber cloth had low filtration. - Vacuum cleaner bags with fine dust filters demonstrated comparable filtering effect to FFP2/N95/KN95 masks, but are not suitable for use.
Hill 2020 (30)	Masks are tested to compare efficiency of a material itself (baseline) with the filtration	- Baseline filtration found a single layer of 500 thread count cotton to have the lowest filtration efficiency (26.2% and 17.4% for 60

Simulation experiment USA Sep 2020	efficiency observed for a mask being worn. Silicon dioxide nanoaerosol was created with media diameter of 40nm and added to a stainless steel enclosure. Baseline filtration efficiency was tested with material clamped (no tension) and an airflow of 0.0465 LPM/cm^2. Masks were fitted to a manikin with intake flow fitted to the nose. Particles of 60 and 125nm were sampled at 1 per second for 180 seconds.	and 125nm droplets, respectively). Dust mask, coffee filter, 2 layer cotton and shop towel performed slightly better. - Particulate respirators (KN95, 3M 8511 and FTF467 ULPA) had filtration efficiencies above 98%. - Significant drop in filtration efficiency seen for all materials when tested as a worn mask, compared to material baseline. The addition of a filter layer between a 2 layer cotton mask did not significantly improve filtration due to leakage around the mask. - The filtration efficiency of a poorly fitted or loose mask can drop by more than 60% compared to the filtration efficiency of the material.
Realmuto 2020 (32) Simulation experiment USA Sep 2020	Mask fabrication that requires no sewing by folding a square piece of cloth into a duck-billed style mask is presented and tested using various materials and compared to commercially available N95 and surgical masks. A manikin fit test simulator was used for filtration, breathability and leakage testing. The manikin head with a breathing tube simulator was placed in a chamber with a mixing fan and set testing valves, while salt concentration particles of 50-700 nm were introduced to the chamber. Materials tested: Non-woven polypropylene (NWPP), "Filti" mask material (Polypropylene/ Nanofiber/ Polyester composite filter media), MERV filters, muslin cotton, reusable wipes, oil towel.	- Filtration efficiencies for masks tested, from best to worst: N95 > surgical > 3 layer polypropylene/filti/polypropylene mask > three layer polypropylene/MERV13 or 8/polypropylene> inner ply Halyad H600, 1 ply Filti. - Double-layered masks had higher filtration efficiencies than single-layered. - Experiments showed mask leakage greatly reduces mask efficiency. - Ear loops did not prevent leakage as well as head straps because gaps between the mask and skin could be reduced more easily with head straps.

Parlin 2020 (34) Simulation experiment USA Sep 2020	Various materials (cotton, polyester, silk, paper towel) were compared to surgical masks under laboratory conditions for their hydrophobicity and breathability before and after cleaning. Laboratory-based tests were done as face coverings on manikins.	- Silk is a hydrophobic material that impedes droplets and performed well to impede droplet absorption similar to a single use surgical mask and maintained its breathability better than hydrophilic materials such as cotton. Silk performed well after cleaning. - When challenged with aerosolized droplets in spray tests, silk, cotton and polyester did not differ in their ability to prevent aerosol droplet penetration when the fabric barriers had 1 or 2 layers.
Bhimaraju 2020 (28) *Preprint* Simulation experiment USA Aug 2020	The filtration efficacy of particulate matter below 2.5µm was assessed with an inhalation system and manikin. Masks tested included: N95 respirators, surgical masks, cloth masks, cloth masks with activated carbon air filters, cloth masks with HVAC air filters, lightly starch-enhanced cloth masks and heavily-starched cloth masks.	- Activated carbon masks and HVAC air filter masks were nearly as effective as N95 respirators, followed by surgical masks>heavy starch cloth masks>light starch cloth masks. - Regular cloth masks provided very little filtration for particles <2.5um compared to the other masks.
Shahane-Kapse 2020 (29) *Preprint* Simulation experiment India Aug 2020	This study described a mask made from 2 layers of cotton with a layer of polypropylene coated with polyurethane applied to the outside layer in the middle half of the mask so it is in front of the mouth and nose, N95 respirator, triple-layer surgical masks and a single-layer cotton mask and a face shield. The amount and degree of droplet and aerosol to each mask was evaluated when worn by a manikin with no gas exchange (i.e. breathing). Fluorescent dyes were	- The fluorescent dye did not penetrate to the inner layer of the triple-layered surgical masks or N95. - The triple-layered mask made from 2 layers of cotton with a polypropylene outer layer blocked the fluorescent dye where the impermeable cloth was, however on the lateral sides of the polypropylene, few spots were visible on the outer cotton layer, but they did not penetrate through to the inner cotton layer. - The fluorescent dye penetrated through the single layer cotton mask to the manikin.

	sprayed from a distance of 1 and 2m at 180km/hr.	
Dhanraj 2020 (33) *Preprint* Simulation experiment USA Jul 2020	The objective of this study was to report the characterization results for Swiffer as an alternate filter media material and evaluate the size-dependent filtration efficiency. Two systems were used: one as 47 mm punches in a filter holder assembly systems, and second in a chamber-based system where the home-made mask (Bandana type) with Swiffer material layered between pillowcase fabrics was placed on a manikin.	- The Swiffer material was very efficient in filtering ultra-fine particles (<0.08µm). - The highest filtration efficiencies were seen when two layers of Swiffer material were stacked in between two layers of pillowcase fabric. The efficiency ranged from 45–62% for particle sizes between 0.1–0.5µm from 30-45% with a single Swiffer.
Joshi 2020 (25) *Preprint* Simulation experiment India Jun 2020	Mask efficiency and pressure drop was measured by mounting the face mask to a glass pipe and measuring the particles upstream and downstream across the test sample. The testing parameters include the particle capture efficiency of the mask material, pressure drop and the fit factor (leakage). Experiments were conducted with atomized NaCl test aerosols, on 3 types of face masks: commercial N-95, surgical mask and cloth mask (no info on specific material).	- The average filtration efficiencies for 0.3µm particles for the N-95 respirator, surgical mask, and cloth mask were 96.19%, 40.08% and 14.22%, respectively. - Filtration efficiency for particle sizes small than 0.3µm were did not change for N95 and cloth masks, surgical masks may have better filtration efficiency. - Tighter mask fits had higher filtration efficiencies: N95, surgical mask and cloth mask were 95.60%, 41.65% and 13.79%, respectively; compared to 95.08%, 19.94% and 11.67% when fit was not as tight, respectively.
Sheets 2020 (27) *Preprint* Simulation experiment USA	To quantify breathability, filtration efficiency and sensitivity to fit for a set of proposed filter and mask designs, a steady flow of aerosolized air was directed at a fit tester manikin and a clamp-style materials tester. Protection against water aerosols >0.3µm was	- N95 masks had the highest filtration efficiencies (>95%). - A woven bandana provided little protection (<15%) but had high breathability. - The surgical mask has twice as good filterability as a bandana with similar breathability.

Jun 2020	measured using off-the-shelf particulate, flow and pressure sensors, permitting rapid comparative evaluation of these 3 properties.	- Sterilization wrap (a non-woven material used by healthcare professionals for packaging surgical instruments) has a higher filtration efficiency compared to a surgical mask but is less breathable. - Filtration of aerosols through the KN95 mask fitted as received and properly fitted demonstrated that a proper fit decreased the number of aerosols that passed through the mask from >50% to <20% when fitted properly.
Filter holder studies to assess protective characteristics of mask materials (n=20)		
Bayersdorfer 2020 (48) Simulation experiment USA Dec 2020	Eight mask prototypes were developed and laboratory tested; 4 for bacterial filtration efficiency (BFE) and pressure drop; and the other 4 for particle filtration efficiency (PFE).	- BFE results of 83.0% to 97.7% in one ply masks and 96.3% to 98.1% in two ply masks. - PFE results ranged from 92.3% to 97.7% for 1 and 2 ply masks.
Li 2020 (36) Simulation experiment China Nov 2020	In this study, filtration efficiency of (a 3-layered mask made from 2 pieces of kitchen towels and a piece of 4-ply tissue paper compared to medical masks were tested under laminar flow within a scaled air duct system using nebulised NaCl aerosols sized 6–220nm.	- The filtration efficiency of the home-made masks was similar to that of medical masks at 6–200nm (84.54% vs 86.94%, P = 0.102).
Maher 2020 (47) Simulation experiment USA	Filtration efficacy of 14 common materials was tested by measuring the concentration of aerosol droplets, the pressure difference across each material and the air-flow characteristics.	- Aerosol concentration results indicated the materials broke large particles into multiple smaller particles. - Multiple layers of fabrics increased the filtering efficiency 4-15%, compared to a single layer of the same fabric; but this decreased breathability with a 3-4x increase

Oct 2020		in pressure difference and three layer masks were 2-2.5x higher pressure difference compared to two-layers. - All tested multi-layer materials had a filtration efficiency > 95% for aerosols 1µm to 4.7µm.
Wang 2020 (51) Simulation experiment China Oct 2020	Referring to the national standard for the "Surgical Mask" of China, 17 materials were tested for pressure difference, particle filtration efficiency, bacterial filtration efficiency and resistance to surface wetting. Material tested included: T-shirt, fleece sweater, outdoor jacket, down jacket, sun-protective clothing, jeans, hairy tea towel, granular tea towel, non-woven shopping bag, vacuum cleaner bag, diaper, sanitary pad, pillowcases, medical non-woven fabric, medical gauze.	- Eleven single-layer materials met the standard of pressure difference (≤49 Pa), of which 3 met the standard of resistance to surface wetting (≥3), 1 met the standard of particle filtration efficiency (≥30%), but none met the standard of bacterial filtration efficiency (≥95%). - Three double-layer materials including double-layer medical non-woven fabric, medical non-woven fabric plus non-woven shopping bag, and medical non-woven fabric plus granular tea towel were close to the standard of the bacterial filtration efficiency.
Long 2020 (50) Simulation experiment USA Oct 2020	This study describes the conversion of standard equipment used to fit-test respirators in hospital and industrial settings into a setup that measures quantitative filtration efficiencies of materials based on NIOSH N95 guidelines, and subsequently measure filtration efficiencies of materials found in healthcare and consumer spaces.	- Filtration efficiencies for single-layered materials ranged between 35 and 53%. Two materials (coffee filter and cotton cloth) had the lowest filtration efficiencies while the vacuum bag, which is not safe for use, had the highest with a filtration efficiency of 82%. - Filtration efficiencies up to 90.37% were reported for multi-layered combinations of materials. - All materials had Δp values below the maximum NIOSH-allowed resistance for respirators (35mmH2O).
Whiley 2020 (40)	This study used a standard mask testing method (ASTM F2101-14) and bacteriophage MS2 to test the viral filtration efficiency (VFE) of	- All the fabric masks had a VFE of at least 50% for 6.0 µm aerosols. This improved to 63% against 2.6µm aerosols.

Simulation experiment Australia Sep 2020	fabric masks (purchased form on online retail website) compared with commercially available disposable, surgical, and N95 masks. The masks were challenged with 2 differenent sized aerosols (6µm and 2.6µm) The conduct and measurements in this study are not standardized. Caution should be used in interpreting these results.	- The N95 and surgical masks had >99% filtration efficiency. - A cotton mask with a filter added and a reusable shopping bag/cotton mask performed just as well as the medical masks (~99% VFE). - A triple-layered hemp/poly-membrane/cheesecloth mask also performed well (>89% VFE).
Maurer 2020 (43) Simulation experiment Germany Sep 2020	In this study, community masks of major manufacturers were tested. The filtration efficiency was determined using radioactive aerosol particles. Air resistance (i.e. breathability) was measured using a pneumotachograph.	- Filtration efficiencies (%) for investigated materials from best to worst were as follows: - Triple-layered masks: Medical membrane according to EN > Outside layer of knitted polypropylene/polyamid, midlayer of microfilament fleece, and inside layer of polyester/polyamid > 100% cotton - Double-layered masks: 100% bio-cotton > cotton/polyester > 100% cotton > polyamide/elastan > polyester and fleece polypropylene - Single layer masks: Texlyte Nano > polyester/carbon > 100% cotton > multifilament yarn > 100% polyester - None of the community face masks met the requirements for medical face mask European standards (filtration efficacy >99% and air resistance <40 Pa/cm2). - Triple-layered masks showed the highest filtration efficiencies but (lower breathability. - When it comes to filtration efficacy, the quality of the fabric seems to be more important than the number of layers (1 vs. 2).
Pei, 2020 (55)	This study evaluated commercial respirators and masks, and common household materials for	- Electret masks (filter with electrostatic charges) filtration efficiencies were 70–85%, with efficiencies increasing with particle size.

Simulation experiment USA Sep 2020	filtration efficiency and breathing resistance (pressure drop). All samples were cut to fit the filter holder. They measured the fractional efficiency with monodisperse NaCl particles (0.03-1µm).	- The N95 and KN95 mask had efficiencies above 90%. - The non-electret media masks filtration efficiencies were significantly lower than that of the electret media mask (as low as 20% for particles 0.3–0.4µm, but increased to 40% for 1 µm. - All respirators and masks tested had acceptable breathing resistance. - Vacuum filters had better filtration efficiencies than even the N95 respirator, but 10x the breathing resistance and thus, impractical as a mask material. - Of the common household materials, 2-layer Thinsulate, 5-layer bed sheets, T-shirts, and Swiffer Sweeper had approximately 50% efficiency for particles around 0.3µm. Their efficiency could be further improved by adding more layers. Breathing resistance was high compared to a procedural mask. - Two-layers of coffee filter has the worst filtration efficiency and breathing resistance.
Schilling 2020 (38) Simulation experiment USA Aug 2020	This study examines both aerosol filtration and breathability of 47 "non-regulation masks" by the use of a polydisperse aerosol and assess filtrations efficiencies of 6 N95 respirators and a number of non-regulation masks. Filtration was assessed by particle sizes ranging (0.2–1µm) and a velocity of 10 cm/s and breathability by measuring the pressure drop (in mm H_2O) across a 40mm disk of mask filter material.	- The filtration efficiencies of the 6 N95 respirators tested ranged from 98-99%. - Some "non-regulation" masks had filtration efficiencies similar to the N95 mask for 0.2µm and above, and others had poor filtration efficiencies (i.e. <80%). - All masks were below the NIOSH threshold of 0.0247-mm H_2O/(cm3/s) for breathability.
Hao 2020 (46)	To evaluate the filtration of non-medical materials under different velocities. Breathability was	- The filtration efficiencies from best to worst were: N95 and KN95 respirators > surgical mask > air filters > vacuum bag > activated

Simulation experiment USA Aug 2020	measured via the flow resistance across the materials. Filtration efficiencies were compared against medical masks: N95, KN95 and surgical masks. To simulate different breathing conditions, nebulizer dispersed NaCl-water aerosols were directed into materials under face velocities of 23.2, 15.3, and 9.2 cm s−1.	carbon filter > 1000 thread count pillowcase > Coffee filter > 600 thread count pillowcase > Four layers of scarf > 400 thread count pillowcase > bandana. - Fabrics with denser weaving patterns were able to provide a higher filtration efficiency Filtration efficiency was inversely related to breathability and increasing velocity of particles.
Drewnick 2020 (52) Simulation experiment Germany Aug 2020	To assess particle-size dependent filtration efficiencies for 44 samples of household materials and several medical masks by using a nebulizer generated NaCl aerosol and counting the particles.	- Huge filtration efficiency differences were found between materials and for different particle sizes, ranging from <10% to almost 100%. - Household materials such as French terry, fleece, microfiber cloth, felt, muslin or velour showed high filtration efficiencies, while materials like poplin, surgical gown or silk showed lower filtration efficiencies. - Reasonable filtration efficiency can be achieved by layers but leaks of just 1-2% can strongly impact filtration efficiency.
Carnino 2020 (54) Simulation experiment USA Aug 2020	To enhance the filtration ability of kitchen paper towel, laboratory paper towel and the middle filter layer of a standard surgical mask pretreated with a salt-based solution (which was then dried). After treatment with fluorescent nanoparticles similar in size to the COVID-19 virus, particle penetration was measured via a microscope.	- When untreated, household materials did a poor job at filtering out nanoparticles. - When household materials were presoaked in a NaCl (+/- TWEEN20) solution the penetration of nanoparticles was blocked after just 10 minutes of treatment. - Bacterial inhibition was also noted.
Loupa 2020 (53) *Preprint*	Eight commercially available masks were tested for filterability of aerosols diameters of 0.006µm to 10µm. A velocity equal to human breathing rate was used.	- Simple cloth masks (with 2 layers of cotton) had the lowest filtration efficiency.

Simulation experiment Greece Jul 2020	Five of the masks were triple-layer masks, 1 was a KN95 mask with a "one way valve", and 2 were fabric masks.	- The addition of activated carbon in a cotton mask significantly improved the filtration efficiency. - Apart from the KN95 mask, all other masks were permeable to aerosols in the range of 0.25-0.5µm (<90% filtration efficiency).
Lammers 2020 (49) Simulation experiment USA Jul 2020	Surgical sterilization wrap was assessed by the TSI 8130 automated filter testing, as required for the N95 respirator mask. Single and double layers of the wrap were tested and compared to the penetrance assessment of the N95.	- Filtration efficacy of the wrap was 64.5% and 78.3% for single and double-ply, respectively. This failed to meet the standard testing requirements for an N95 respirator.
Varallyay 2020 (42) Simulation experiment USA Jul 2020	In this study, common household fabrics were tested for filtration efficiency using a fit testing setup with a standard 40nm median diameter particle generator and airflow resistance with pressure gauge setup. Three different levels of layering (1, 2, and 4) were tested.	- Polyester felt demonstrated the highest filtration efficiency ($p<0.0001$), higher than all tested 100% cotton materials as well as surgical masks ($P<0.05$). - Layering increased filtration efficiency and airflow resistance ($p<0.0001$ and $p<0.01$, respectively). - Filtration efficiencies of various woven and knitted materials were from best to worst were: microfiber cloth > tea towel > hospital scrubs > thick fleece > Buff headwear > T-shirt > pillowcase > non-elastic woven fabric > scarf. - Filtration efficiencies of various non-woven materials from best to worst were: N95 respirator > vacuum cleaner bag > surgical mask > felt > paper kitchen towel > surgical gown > paper facial tissue. - Washing plus drying did not alter filtration performance significantly.
Zhao 2020 (39)	To evaluate the filtration properties of natural and synthetic	- The filtration efficiencies for various medical masks and non-medical materials from best

Simulation experiment USA Jun 2020	materials using an Automated Filter Tester with a flow rate of 32 L/min (similar to human breathing). The filtration efficiency is the percentage of NaCl particles filtered by the material and the pressure drop is the air resistance across the filter material. The higher the pressure drop the less breathable the material. Authors note that their results differ from recent work and this may arise from differences in instrumentation, testing method and source of material.	to worst were: N95 respirator > cotton sweater > exercise pants > T-shirt > tissue paper > polyester toddler wrap > paper towel > polypropylene interfacing material > pillow cover > napkin. - Some of the cotton materials had filtration efficiencies comparable to medical face masks (e.g., cotton sweater and T-shirt). - Paper products may be suitable to use as a disposable media in some homemade facial coverings, but their performance in high humidity environments remains to be examined.
Zangmeister 2020 (45) Simulation experiment USA Jun 2020	To assess filtration efficiency, differential pressure (ΔP), quality factor, and construction parameters for 32 cloth materials including multilayered and mixed-material samples of natural, synthetic or natural-synthetic blends. Materials were microimaged and tested against size selected NaCl aerosols with particle mobility diameters between 50 and 825nm. Particles were charge neutralized.	- Woven 100% cotton with high to moderate yarn counts, and 2 woven synthetic fabrics of moderate yarn count performed the best. - The filtration efficiency of 2 layers of a high performing cloth (32%) was lower than high-density medical-grade wraps (86%), and the N95 mask (>99.9%), and the HEPA vacuum bag (94%). - The fabric with the lowest filtration efficiency was polyester (lightweight chiffon), followed by cotton (muslin), polyester (knit), rayon and 65% polyester/35% cotton blend. - Filtration efficiency and ΔP increased with the number of cloth layers; 4 layers exceeded the recommended ΔP (breathability).
Amendola 2020 (23) Simulation experiment Italy	The experiment simulated respiratory action measuring the distribution of aqueous-based aerosol particles. The average filtration efficiency was reported taking into account the particles with diameters greater than 0.28μm. The face masks were	- The medical face mask demonstrated filtration efficiencies higher than 97%. - Only the face masks fabricated with three layers mainly constituted by non-woven fabric material were able to reach values higher than 95% including triple layer TNT, TNT-cotton-TNT mask.

May 2020	tested in both the inhalation and exhalation direction. TNT= A non-woven material made of fabric-based polypropylene and viscose	
Konda 2020 (44) Simulation experiment USA Apr 2020	To assess filtration efficiencies of several common fabrics including cotton, silk, chiffon, flannel, various synthetics and their combinations as a function of polydispersed NaCl aerosol particulate sizes 10nm-10µm. To simulate fit, holes were drilled in the connecting tube onto which the fabric was mounted resulting in openings of area ~0.5–2% of the active sample area.	- The ranges below represent the filtration efficiency for small particle sizes (<300nm) to larger particle size (>300nm). - A moderate thread count cotton fabric (80 threads per inch) demonstrated inferior efficiency (5-55%) compared to a high thread count cotton fabric (65->90%). - A quilt, with a fibrous cotton batting, provided excellent filtration efficiency (80->90%). - In contrast to the cotton fabrics, the 3 fabrics expected to possess electrostatic charges, silk, chiffon, and flannel, performed better for smaller particles (<300nm) than larger particles (>300nm). - Increasing the number of layers increased filtration efficiency. - Three hybrid combinations were tested: 1 layer 600 TPI cotton with 2 layers of silk, 2 layers of chiffon, and 1 layer of flannel. All combinations performed well, with filtration efficiencies 80%->90%, comparable to that of N95 masks. - In tests where the effect of "leakage" was tested, the openings resulted in up to a 60% drop in filtration efficiency.
Ma 2020 (37) Simulation experiment	The efficacy of 3 types of masks was evaluated using the avian influenza virus to mock the coronavirus. A nebulizer was used to produce aerosols <5.0 um.	- Compared with 1 layer of polyester cloth, the N95 mask blocked 99.98% of the virus, the surgical mask blocked 97.14%, and the homemade mask blocked 95.15%.

China Mar 2020	The top parts of 60mL syringes were removed and then wrapped with the tested masks: 1 layer polyester cloth, a homemade mask made of 1 layer polyester cloth plus 4 layers of kitchen paper, a surgical mask and an N95 mask. A sponge was set inside the syringe behind the mask to collect the virus that passed through the masks.	

*Location or date of study was estimated based on author affiliations and / or publication date.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Knowledge Synthesis team in the Emerging Science Group, Public Health Agency of Canada. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The cumulative scan results are maintained in a Refworks database and an excel list that can be searched. Details on this search strategy are available upon request. From this database and excel list, article titles and summaries were systematically searched for the following key words: mask* OR (face AND cover*). Each potentially relevant primary research reference was analyzed to confirm its relevance and data was extracted into the review. Several reviews and synthesis research of variable quality were identified that covered mask composition to some degree, however most included pre-pandemic research only and thus were excluded from this summary as they were missing recent research. This review contains primary research published up until December 2, 2020.

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Appendix

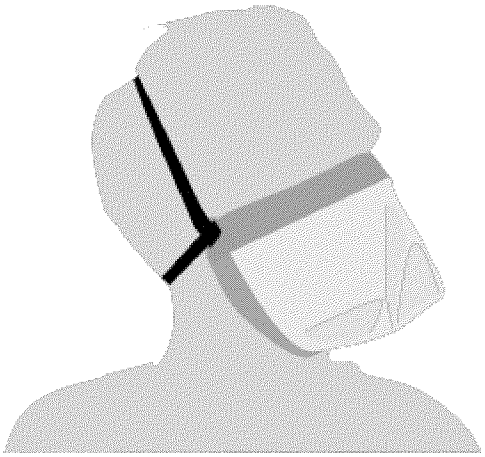

Figure 1. Duck-billed shaped mask design. Source: (32)

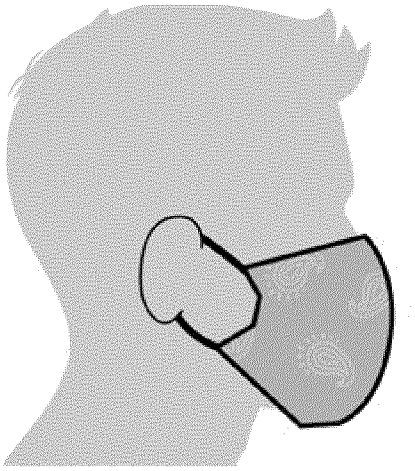

Figure 2. Surgical-style shaped mask design. Source: (56)

Nouveaux éléments de preuve sur la COVID-19

Revue rapide sur les caractéristiques des masques non médicaux ou des couvre-visages efficaces pour réduire le risque de transmission du SRAS-CoV-2

Introduction

Quelles sont les données probantes en ce qui concerne les caractéristiques (par exemple, conception, matériau, ajustement) et l'efficacité des masques non médicaux ou des couvre-visage pour réduire la transmission du SRAS-CoV-2? (En un mot, à quel point sont-ils efficaces pour prévenir la propagation du SRAS-CoV-2 lorsqu'ils sont portés par une personne confirmée contagieuse ou quel type de protection offrent-ils contre l'inhalation du SRAS-CoV-2 à la personne qui les porte)

De nombreuses organisations de santé publique dans le monde, incluant l'Organisation mondiale de la santé, recommandent le port du masque ou du couvre-visage dans les espaces publics pour se protéger contre la COVID-19. Les masques non médicaux ou couvre-visages (qu'ils soient faits maison ou aient été fabriqués) ne sont pas réglementés comme équipement de protection individuelle, car ils n'ont pas été testés à l'aide d'un ensemble de méthodes de test normalisées (par exemple, NIOSH, ASTM F2100 ou EN 14683) comme le sont les masques médicaux (par exemple, les masques N95 et les masques chirurgicaux). Il n'est donc pas recommandé aux professionnels de la santé et aux personnes présentant un risque accru d'infection de les porter dans les situations où le respect de la distanciation physique n'est pas possible (1).

Cette revue rapide a donc porté sur l'efficacité des masques non médicaux ou des couvre-visages portés par la population en général pendant la pandémie de COVID-19. Ainsi, les articles qui n'évaluaient que des masques comme les N95 ou des masques chirurgicaux n'ont pas été inclus dans la présente revue. Ceux qui comparaient le rendement des masques N95 ou des masques chirurgicaux à celui des masques non médicaux ou des couvre-visages sont inclus et l'analyse comparative de ces différents masques ou couvre-visage a permis de comprendre le contraste entre différents masques non médicaux ou couvre-visages et les masques médicaux. La présente revue rapide contient des recherches publiées jusqu'au 2 décembre 2020 portant sur les caractéristiques des masques non médicaux ou des couvre-visages, ce qui inclut le matériau, la conception et l'ajustement qui permettent aux masques ou aux couvre-visage de filtrer efficacement le SRAS-CoV-2 tout en conservant un niveau approprié de respirabilité. Dans le contexte de la pandémie COVID-19 et de la présente revue, les études ont examiné les masques ou couvre-visages tant comme forme de contrôle à la source (c'est-à-dire pour empêcher la propagation du SRAS-CoV-2 s'ils sont portés par une personne confirmée contagieuse) que comme protection contre l'inhalation du SRAS-CoV-2. Il y a un effet synergique lorsque le récepteur et le propagateur du virus portent tous deux un masque ou couvre-visage (2).

Points clés

- Parmi les cinquante-quatre articles de recherche originale sélectionnés, 22 études portaient sur la prévention de la propagation du SRAS-CoV-2 par des masques non médicaux ou des couvre-visages portés par une personne confirmée contagieuse (contrôle à la source) alors que 37 autres portaient sur la protection qu'offrent les masques non médicaux ou couvre-visages à une personne non infectée contre l'inhalation du SRAS-CoV-2. Les études ont été effectuées sur des volontaires humains (n = 15), des mannequins (n = 15), des porte-filtres (n = 34) et des modèles animaux (n = 1).
- Des études expérimentales de simulation ont montré que les masques non médicaux ou couvre-visages sont plus efficaces comme méthode de contrôle à la source (tableau 1) que pour protéger les personnes non infectées (tableau 2). Il y a un effet synergique lorsque tant la personne non infectée que la personne infectée portent un masque (2).
- Un masque ou couvre-visage peut limiter de manière significative la distance que parcourent les gouttelettes de salive pendant l'élocution, la toux ou les éternuements à l'intérieur, mais l'efficacité de ces masques non médicaux dépend de trois caractéristiques : 1) l'efficacité de filtration, 2) la respirabilité, et 3) l'ajustement.
- L'efficacité de filtration dépend du type, de la taille et de la vitesse des gouttelettes de salive et de la qualité du tissu (étanchéité du tissage, diamètre de la fibre ou du fil) et des caractéristiques inhérentes au tissu (par exemple, charge électrostatique et hydrophobie).
- Lorsqu'ils sont faits en tissu de haute qualité à plusieurs épaisseurs qui s'adaptent parfaitement à la bouche et au nez, les masques non médicaux ou couvre-visages peuvent réduire le risque de propagation ou d'exposition au SRAS-CoV-2, même si cette réduction est inférieure à celle qu'offrent les masques médicaux.
    - Les masques double épaisseur bien ajustés et en différents types de matériaux (par exemple, coton peigné et polyester) ou les masques comportant un seul type de matériau, mais avec plus de deux épaisseurs, présentaient une efficacité en blocage vers l'extérieur semblable à celle des masques médicaux (> 90 %) tout en conservant une respirabilité comparable.
    - Il a été démontré que le fait de ne pas bien ajuster le masque ou couvre-visage sur la peau en réduit considérablement l'efficacité, réduction qui a atteint plus de 50 % dans l'efficacité de filtration.
- L'efficacité de filtration de divers masques non médicaux et de différents matériaux a été évaluée dans 42 études et a permis d'obtenir un vaste éventail de résultats (< 10 % à > 95 %)</10 %>.
    - Le fait que les masques ou couvre-visages en tissu comportent de multiples épaisseurs augmente l'efficacité de filtration, mais le nombre d'épaisseurs entraîne également une diminution de la respirabilité. Ainsi, les recherches montrent que le fait d'avoir plus de trois

épaisseurs de tissu réduit considérablement la respirabilité. Certains échantillons comportant trois épaisseurs ont cependant permis d'atteindre une efficacité de filtration supérieure à 90 %.

- Le niveau d'efficacité de filtration de la plupart des textiles de maison était plus grand pour les grosses gouttelettes et pour les gouttelettes expulsées à plus basse vitesse.

- Des études montrent que le type de tissu et le fait d'utiliser un mélange de tissus améliorent la filtrabilité, la respirabilité et la longévité (c'est-à-dire la capacité à réutiliser le masque ou couvre-visage).
    - Les masques ou couvre-visages devraient être faits d'un tissu fin ou tissé serré. Certains tissus sont hydrophobes (par exemple, le polyester, le polypropylène lacé par filage ou le polyaramide) ou peuvent capturer des particules chargées électriquement grâce à une certaine forme d'électricité statique (par exemple, le polyester ou la soie), alors que d'autres peuvent avoir des propriétés hydrophiles qui en améliorent le confort et la longévité (par exemple, le coton).
    - De multiples études ont montré qu'un masque ou couvre-visage trois épaisseurs, composé d'une couche externe hydrophobe, d'une couche centrale en tissu mélangé non-tissé et d'une couche intérieure hydrophile, était la combinaison idéale pour optimiser tant le potentiel de réduction de transmission que la capacité de protection offerte par les masques non médicaux ou couvre-visages.
- Certains tissus ne sont cependant pas recommandés comme masques non médicaux ou couvre-visages.
    - Il a ainsi été démontré que les sacs pour aspirateur ont une efficacité de filtration comparable à celle des masques médicaux, mais il ne s'agit cependant pas de produits cliniques certifiés et peuvent contenir des ingrédients malsains et des fibres nocives.
    - Les masques ou couvre-visages pliés, mais non ajustés, les masques ou couvre-visage de type bandana et les guêtres simple épaisseur pour le cou bloquent mal les gouttelettes de salive et offrent donc peu de protection. Les données probantes sont très variables en ce qui concerne les guêtres de cou. En fait, plusieurs études ont montré qu'elles n'offraient aucune protection, une a montré une plus grande production d'aérosols alors qu'une autre étude a indiqué des efficacités de blocage similaires à celles d'un masque ou d'un couvre-visage en coton.
    - Les masques ou respirateurs munis d'une soupape ou d'un évent expiratoire peuvent protéger la personne qui les porte contre le SRAS-CoV-2, mais n'empêcheront cependant pas la dispersion du virus et ne sont donc pas efficaces pour le contrôle à la source.

Vue d'ensemble des éléments de preuve

Cette revue rapide comprenait donc 54 articles de recherche originale portant sur les caractéristiques et l'efficacité des masques non médicaux ou des couvre-visage afin de réduire le risque de transmission du SRAS-CoV-2. Elle portait principalement sur l'efficacité des masques non médicaux ou des couvre-visages portés par la population en général. Ainsi, les articles qui n'évaluaient que des masques comme les N95 ou des masques chirurgicaux n'ont pas été inclus dans la présente revue. Les articles qui comparaient le rendement des masques N95 ou des masques chirurgicaux à ceux des masques non médicaux ou des couvre-visages sont inclus. L'analyse comparative de ces différents masques ou couvre-visages a permis de comparer différents masques non médicaux ou couvre-visages aux masques médicaux réglementés. Une revue rapide sur le port des masques ou des couvre-visage pour prévenir la COVID-19 dans les milieux communautaires a été réalisée et est disponible auprès du Secrétariat des sciences émergentes.

La majorité des études incluses dans cette revue rapide étaient des quasi-expériences et des expériences de simulation visant à étudier l'efficacité de blocage et de filtration, la respirabilité et l'ajustement (c'est-à-dire une mesure de la façon dont le masque s'adapte au visage et laisse un minimum d'espace entre le masque ou couvre-visage et la peau) des masques non médicaux ou des couvre-visages en différents matériaux et avec différents styles en utilisant pour ce faire des volontaires humains, des mannequins, des modèles animaux et des porte-filtres en tissu. Ces expériences sont donc une approximation d'une situation réelle et sont soumises aux limites des modèles utilisés. Les mannequins n'imitent pas parfaitement les formes d'un visage humain, les mouvements (c'est-à-dire l'incidence qu'ils peuvent avoir sur l'ajustement) ou les activités respiratoires, ce qui veut dire qu'il faut faire preuve de prudence au moment d'extrapoler ces résultats aux humains. De même, les expériences effectuées avec des porte-filtres surestiment l'efficacité des masques, puisqu'elles n'évaluent que la filtrabilité du tissu et non l'ajustement d'un masque ou d'un couvre-visage sur une personne. Ainsi, l'efficacité d'un masque ou couvre-visage porté par des volontaires ou des mannequins devrait être plus faible en raison des fuites tout autour du masque. Aucune des études recensées n'évalue l'efficacité des types spécifiques de masques non médicaux ou de couvre-visage dans le monde réel. Les résultats de la présente revue rapide ne présentent donc que des données sur l'efficacité de différents masques évalués dans des conditions expérimentales contrôlées. En outre, s'il était possible de comparer et de classer différents modèles, matériaux et ajustements dans les diverses études, les différences dans les méthodologies et les combinaisons de matériaux auraient rendu difficiles les comparaisons entre les différentes études.

Un virion du SRAS-CoV-2 a un diamètre de 0,1 µm, mais il est généralement transporté par d'autres particules comme les particules respirables qui ont un continuum de tailles allant de < 1 µm à > 5 µm. Veuillez demander la revue sur la transmission des aérosols pour plus d'information à cet égard. La taille et la vitesse des particules n'étaient pas cohérentes d'une étude à l'autre alors que la filtration des particules de tailles différentes variait d'un tissu à l'autre, ce qui rend les efficacités de filtration difficiles à comparer ou à synthétiser. Bon nombre d'études n'ont pas utilisé de véritables gouttelettes de salive ou particules chargées de virus et ont plutôt utilisé la dispersion en aérosol de particules alternatives (par exemple, NaCl, amidon,

bactéries, latex, dioxyde de silicium). Les recherches actuelles sur l'efficacité des masques non médicaux ou des couvre-visages sont donc de qualité médiocre et les résultats changeront probablement après des recherches supplémentaires.

TABLE DES MATIÈRES

MASQUES NON MÉDICAUX OU COUVRE-VISAGE POUR LE CONTRÔLE À LA SOURCE

Études sur les humains et les mannequins (n = 15) :

L'efficacité des interventions non pharmaceutiques, telles que la distanciation sociale, peut être augmentée en réduisant le niveau de gouttelettes ou d'aérosols infectieux qui circule dans l'air des espaces communs (3). Compte tenu du fait que les personnes infectées par la COVID-19 peuvent être asymptomatiques ou présymptomatiques, le fait de toujours porter un masque ou couvre-visage dans les lieux publics est recommandé comme moyen de contrôle à la source pour réduire la dispersion, la vitesse et la transmission potentielle des particules expirées.

Des études ont été menées sur des volontaires humains (n = 10) et des mannequins (n = 7). Les mannequins n'imitent cependant pas parfaitement la peau humaine ni les mouvements (c'est-à-dire l'incidence sur l'ajustement du masque ou du couvre-visage) ou les activités respiratoires, puisque l'air ne se déplace généralement que dans une seule direction (4).

Les masques non médicaux ou couvre-visages sont plus efficaces pour le contrôle à la source (blocage des gouttelettes ou des aérosols viraux, c'est-à-dire qu'ils limitent la transmission à partir d'une personne infectée) (tableau 1) que pour la protection des personnes non infectées (tableau 2) (2, 4, 5).

- Les masques ou couvre-visages en tissu, comme ceux en coton, ne sont pas aussi efficaces que les masques médicaux pour réduire la dispersion des gouttelettes ou des aérosols vers l'extérieur (6, 7). Cela est probablement dû au tissu utilisé pour fabriquer le masque ainsi qu'à l'augmentation des fuites d'air résultant d'un ajustement moins serré (6, 8).

- Comparativement aux données obtenues sans masque ou couvre-visage, le fait de porter un masque réduit la dispersion des gouttelettes ou aérosols vers l'extérieur, mais l'importance de la réduction varie cependant selon la composition du masque et les caractéristiques spécifiques de l'expérience (tableau 1) :

  - un masque ou couvre-visage en tissu (tissu/composition non indiquée) a permis de réduire la distance du jet respiratoire lors de la respiration et de la toux d'un champ de vision expérimental de 562 mm (sans masque ou couvre-visage) à 150 mm (similaire à un masque chirurgical) (6);

  - un masque en coton matelassé a, quant à lui, réduit la distance du jet respiratoire de 243,84 cm (8 pi) à 5,08 cm (2,5 po) (8);

  - une personne qui se tient à 2 mètres d'une personne qui tousse sans masque sera exposée à plus de 1 000 fois plus de gouttelettes de salive qu'une personne qui se tiendrait à 5 cm de distance et porterait un masque simple épaisseur (9).

- Les masques chirurgicaux bien ajustés (composés de plusieurs couches dont du tissu 100 % coton et des couches intermédiaires en polypropylène non-tissé) sont très efficaces pour réduire la dispersion des gouttelettes (3, 10). Les masques en bec de canard ont, quant à eux, démontré un ajustement satisfaisant et une efficacité de blocage (11). Les études n'ont pas évalué la respirabilité de ces masques. Des exemples des différents styles de masques sont présentés en annexe.

- Les masques ou couvre-visages double épaisseur bloquent mieux les gouttelettes ou aérosols en cas d'élocution, de toux ou d'éternuement que les masques ou couvre-visages faits d'une seule couche de tissu (12).

- Un masque en coton trois épaisseurs s'est révélé tout aussi efficace qu'un masque chirurgical pour supprimer la dispersion des gouttelettes de salive (86,4 % et 99,9 %, $p > 0,05$, respectivement) (13).

- L'ajout d'une couche filtrante comme un essuie-tout pourrait réduire considérablement le potentiel de transmission (14).

- Les masques ou couvre-visages pliés non ajustés et les masques ou couvre-visages de type bandana ne bloquent pas bien les gouttelettes de salive (8). Quant aux guêtres de cou en polyester, lorsqu'elles sont utilisées comme couvre-visage simple épaisseur, elles ne sont pas efficaces pour empêcher la dispersion des gouttelettes ou des aérosols (14, 15). Cependant, lorsqu'elles sont utilisées en double épaisseur, elles offrent une efficacité de blocage similaire à celle des masques ou des couvre-visage en tissu (16).

- Les respirateurs munis d'un évent n'empêchent pas la dispersion du virus par la personne qui le porte (6, 15).

Études sur les porte-filtres (n = 7) :

Les études sur les porte-filtres ont utilisé des échantillons de tissu maintenus en place par un porte-filtre et ne tiennent donc pas compte de l'ajustement d'un visage humain, ce qui veut dire qu'elles peuvent surestimer l'efficacité des masques ou des couvre-visage.

- Les masques double épaisseur ont démonté une plus grande efficacité de blocage que les masques simple épaisseur (17 à 19). En outre, les masques double épaisseur faits de différents types de matériaux (par exemple, coton peigné et polyester) ou les masques comportant un seul type de matériau tissé serré (par exemple, coton), mais avec plus de deux épaisseurs, ont démontré une efficacité en blocage similaire à celle des masques médicaux (> 90 %) tout en conservant un niveau de respirabilité comparable (20 à 23).
- L'efficacité de blocage est beaucoup plus élevée pour les gouttelettes à faible vitesse (par exemple, créées lors de la parole) que pour les gouttelettes à grande vitesse (par exemple, générées par les éternuements) (21).
- Les compositions de tissu qui ont donné les meilleurs résultats comprenaient des matériaux hydrophiles comme le tissu éponge, le coton piqué ou la flanelle utilisés en combinaison avec une couche barrière hydrophobe faite de polypropylène non-tissé, de polyester ou de polyaramide qui empêchera davantage d'aérosols de passer à travers le masque (20).
- Les normes N95 sont établies en fonction d'une fourchette de taille des particules allant de 0,1 à 0,3 µm. La majorité des études sur les masques non médicaux ou couvre-visages ont également utilisé un éventail de tailles de particules similaires dans leurs expériences. L'efficacité de filtration des masques médicaux et de bon nombre de textiles de maison s'est révélée plus faible pour les petites particules que pour les grosses gouttelettes. Une expérience réalisée sur les particules ultrafines (< 0,1 µm) a montré que les masques N95 et les masques chirurgicaux obtenaient une efficacité de filtration de 52,5 % et de 47,5 %, respectivement (19). En comparaison, la laine feutrée (35,87 %), le piqué de coton (34,54 %) et la flanelle de coton (28,50 %) avaient des rendements de filtration inférieurs pour les très petites particules (19).
- Un masque ou couvre-visage fait de plusieurs couches de soie a obtenu une efficacité de filtration de 94 % contre les petites particules de la taille d'un aérosol (0,75 µm), probablement en raison de sa charge électrostatique (18). La soie n'était cependant pas aussi performante pour les plus grosses particules.
- Une combinaison de plusieurs épaisseurs de matériaux, avec une couche externe hydrophobe (par exemple, du polyester, du polypropylène lacé par filage ou de la polyaramide), une couche intérieure en tissu de coton de haute qualité et une couche intermédiaire faite de matériaux non-tissés ou chargés électrostatiquement (par exemple, soie naturelle, mousseline ou polyester), serait donc idéale pour optimiser tant la capacité de protection que le potentiel de réduction de transmission des masques non médicaux ou des couvre-visages.

- Un vaste éventail de matériaux a été étudié dans différentes études, dont certains ne peuvent cependant pas être utilisés de façon sécuritaire comme masque ou couvre-visage. Les sacs pour aspirateurs, par exemple, se sont avérés efficaces pour filtrer dans plus d'une étude, mais ils peuvent inclure des composants qui ne sont pas sécuritaires lorsque vient le moment d'inhaler ou s'ils entrent en contact étroit avec le visage (19).

Tableau 1 : Études qui examinent les caractéristiques du contrôle à la source des masques non médicaux ou des couvre-visages (n = 22)

ÉTUDE*	MÉTHODE	PRINCIPAUX RÉSULTATS
Expériences effectuées avec des volontaires humains et des mannequins (n = 15)		
Ho 2020 (13) Quasi-expérience Chine Septembre 2020	Évaluation de l'efficacité de filtration des masques en coton trois épaisseurs et des masques chirurgicaux portés par des patients adultes (n = 211) avec grippe confirmée (n = 208) et infection possible à la COVID-19 (n = 6) dans deux milieux climatisés, soit une chambre et une voiture. Les résultats ont ensuite été comparés à ceux obtenus lorsque des personnes sans masque ont été exposées à une concentration de fond dans un espace inoccupé. Un compteur de particules installé à moins de 1 m de chaque patient infecté a réalisé quatre mesures en une heure. Mesure obtenue : efficacité de filtration à 5,5 cm/s. La température, l'humidité, ainsi que le nombre d'éternuements et de toux ont également été enregistrés. Des tests t pour échantillons appariés ont été utilisés pour effectuer les comparaisons dans les groupes.	- L'efficacité de filtration du masque en coton trois épaisseurs a atteint 86,4 % alors qu'avec le masque chirurgical, elle était plutôt de 99,9 %. - Dans les espaces climatisés, soit dans la chambre à coucher et dans la voiture, la concentration moyenne de particules chez les volontaires qui ne portaient pas de masque était considérablement plus élevée que chez ceux qui portaient un masque chirurgical ou un masque en coton (valeur p < 0,05 dans les deux cas). - La concentration de particules obtenue avec un masque en coton trois épaisseurs et un masque chirurgical dans les deux milieux était sensiblement la même.
Asadi 2020 (7) Quasi-expérience	Évaluation de l'efficacité des masques KN95 sans évent respiratoire, des masques N95 avec évent, des masques chirurgicaux, des couvre-visage faits maison avec une épaisseur	- Comparativement à l'absence de masque, les masques chirurgicaux et les masques KN95 sans évent ont réduit de 90 % le taux moyen d'émission de particules vers l'extérieur

États-Unis Septembre 2020	d'essuie-tout comme filtre et des masques faits maison à l'aide d'un t-shirt en coton simple épaisseur et double épaisseur à réduire les taux d'émission de particules d'aérosol lorsque des personnes en bonne santé (n = 10) respirent, parlent et toussent. On a demandé aux participants à l'étude de s'asseoir et de mettre leur bouche devant un entonnoir fixé à un mesureur de particules aérodynamiques (compteur de particules). Ils devaient ensuite effectuer différentes activités expiratoires avec ou sans masque.	lorsque la personne parlait et cette réduction a atteint 74 % lorsqu'elle toussait. - Il a été difficile d'évaluer l'efficacité des masques en coton. La dispersion des particules autres qu'expiratoires à l'échelle du micron dans les fibres des masques en coton faits maison a cependant brouillé la détermination explicite de leur efficacité, car les taux d'émission de particules mesurés avec un masque double épaisseur et sans masque n'étaient pas statistiquement différents alors que le taux était beaucoup plus élevé chez les participants qui ont porté un masque simple épaisseur en coton comparativement à ceux qui n'en portaient pas.
Fischer 2020 (15) Quasi-expérience États-Unis Septembre 2020	Évaluation de l'efficacité des masques à réduire la transmission des gouttelettes de salive lors de l'élocution grâce à une méthode de mesure optique simple. Un volontaire humain qui portait un masque ou couvre-visage a parlé dans la direction d'un faisceau laser étendu dans une enceinte sombre. Une caméra de téléphone cellulaire a été utilisée pour enregistrer la propagation des gouttelettes dans le faisceau de lumière laser diffusée. Puis, un algorithme informatique simple a permis de compter les gouttelettes. Les masques testés comprenaient des masques chirurgicaux, des masques N95 avec évent, des masques en tricot, en polypropylène, en polypropylène et en coton, des masques Maxima AT, quatre masques en coton double épaisseur, un masque en coton simple épaisseur, une	- Le masque N95 ajusté est celui qui a donné les meilleurs résultats avec une transmission fractionnelle des gouttelettes de 0,1 %, suivi du masque chirurgical, du masque en mélange de coton et de polypropylène, du masque en polypropylène double épaisseur, du masque avec matériel et spica (non ajusté), des quatre différents types de masques en coton double épaisseur, du masque N95 avec évent, du masque Maxima AT, du masque en coton simple épaisseur, du masque en tricot, du bandana, de l'absence de masque et de la guêtre de cou. - La guêtre de cou a donné les pires résultats avec une transmission fractionnelle de gouttelettes de 110 %, résultat obtenu parce que le tissu a brisé les plus grosses gouttelettes en une multitude de plus petites. - Puisque cette étude comprenait un échantillon extrêmement petit, elle devrait donc être utilisée avec prudence.

	guêtre de cou, un bandana et un masque N95 ajusté (sans évent).	
Swain 2020 (14) Quasi-expérience Royaume-Uni Juillet 2020	Utilisation de l'humidité comme méthode pour évaluer l'excrétion virale. Un capteur a été utilisé pour mesurer à des distances précises tout changement dans l'humidité relative et la saturation en oxygène qui se sont produits chez quatre membres du personnel médical qui portaient ou non un masque pendant trois scénarios qui duraient chacun deux minutes : 1) Respiration forte, 65 mm 2) Respiration normale, 20 cm 3) Respiration forte, 20 cm Les masques testés comprenaient un prototype fourni par AngelMed (sans évent), un masque clinique standard approuvé par NHS et un masque FFP2V (évent unidirectionnel). Les masques faits maison testés se composaient de différents tissus, soit t-shirt, chaussettes (avec et sans filtre en papier), masque double épaisseur avec chamois ainsi qu'un masque fait maison conçu pour permettre la lecture sur les lèvres (fait d'un matériau épais avec fenêtre transparente).	- Comparativement aux résultats obtenus lorsqu'aucun masque n'était porté, le masque AngelMed, le masque clinique standard approuvé par NHS et le masque FFP2V ont tous empêché de manière significative les variations dans l'humidité. - Le masque en t-shirt et le masque double épaisseur avec chamois ont donné les mêmes résultats puisqu'ils n'ont entraîné aucune variation dans le niveau d'humidité lors du test avec respiration forte à 65 mm (5,4 % et 5,1 % respectivement). - Le masque double épaisseur fait avec des chaussettes a donné de meilleurs résultats qu'un masque simple épaisseur fait du même tissu (15,3 % contre 9,5 %). - Le masque conçu pour permettre la lecture sur les lèvres a, quant à lui, empêché toute augmentation du niveau d'humidité relative. Il limitait cependant la respiration et on a également constaté qu'il réduisait la saturation en oxygène des participants. - Les conclusions de cette étude sont préliminaires et il faut donc faire preuve de prudence dans l'interprétation des résultats.
Viola 2020 (6) *Prépublication* Quasi-expérience Royaume-Uni	Utilisation de la technique Schlieren orientée vers l'arrière-plan pour comparer la quantité d'air expulsée par un participant portant sept types différents de masques et de couvre-visages, dans des situations où il toussait, respirait fort et respirait normalement. La même évaluation a également été effectuée par le même participant, cette fois-ci, sans masque.	- Lorsque le participant toussait ou respirait sans masque, on a pu voir que la quantité d'air expulsée atteignait une distance supérieure à la limite du champ d'exploration fixée à 562 mm de sa bouche. - Le masque FFP2 a été le plus efficace pour réduire la dispersion de l'air expiré. On pouvait cependant voir des fuites d'air près du nez lorsqu'il n'était pas bien ajusté.

Mai 2020	Un volontaire humain (n = 1) et un mannequin ont été utilisés dans cette étude. Cinq masques ou couvre-visage ont été évalués, soit un masque FFP1, un FFP2, un respirateur, un masque chirurgical, un masque fait maison et deux écrans faciaux.	- Comme le respirateur comportait un évent et n'était donc pas conçu pour arrêter le déplacement de l'air vers l'avant, il ne pouvait donc pas empêcher la dispersion du virus. - Le masque fait maison (dont la composition n'a pas été précisée) a celui qui a été le moins efficace pour arrêter les fuites d'air alors que le masque chirurgical a été le moins efficace pour empêcher l'air de fuir vers l'arrière du masque. - Les conclusions de cette étude sont préliminaires et il faut donc faire preuve de prudence dans l'interprétation des résultats.
Bandiera 2020 (9) *Prépublication* Quasi-expérience Royaume-Uni Août 2020	Évaluation de l'efficacité des masques chirurgicaux et des masques en coton simple épaisseur à atténuer la dispersion des grosses gouttelettes de salive lors de simulations d'élocution et de toux avec des mannequins. L'étude a utilisé un faisceau laser pour quantifier le nombre de gouttelettes émis par le mannequin ou le compresseur d'air alors que la lumière UV a servi à évaluer la quantité de gouttelettes ayant atterri à la hauteur d'une table, soit à un maximum de deux mètres. En ce qui concerne les volontaires humains (n = 6) qui ont parlé et toussé alors qu'ils portaient un masque chirurgical, une lame de microscope a été installée à 5 cm de leur bouche pour récupérer les gouttelettes expiratoires.	- On estime qu'une personne qui se trouve à 2 m d'une personne qui tousse sans masque sera exposée à au moins 1 000 fois plus de gouttelettes de salive qu'une personne qui se trouve à 5 m de celle-ci et qui porte un masque simple épaisseur de base. - Les masques ou couvre-visages se sont toujours révélés efficaces pour bloquer les gouttelettes de salive de 20 à 30 µm dans les simulations d'élocution et de toux ($p < 0,05$). - Aucune différence statistiquement significative dans la quantité de gouttelettes se trouvant sur le masque n'a été observée entre le masque chirurgical et le masque en coton simple épaisseur. - Aucune gouttelette ne s'est cependant déposée sur les masques chirurgicaux portés par les volontaires.
Stubington 2020 (11) Quasi-expérience	Examen de la trajectoire que prennent les particules expirées par une personne qui porte un masque. Cette étude a filmé un seul volontaire expirant de la vapeur d'eau visible alors qu'il portait différents masques ou couvre-visages.	- Les masques FFP souples, plissés et solides envoient les particules expirées vers le bas, à une distance supérieure à 25 cm. - Les masques en bec de canard dirigent, quant à eux, les particules expirées vers le côté, ce qui produit un panache plus petit.

Royaume-Uni Août 2020		- Le port d'une visière ne réduit aucunement la taille du panache de vapeur expiré, quel que soit le type de masque utilisé. - Les matériaux hydrofuges réduisent, quant à eux, le mouvement vers le bas des particules expirées.
Rodriguez-Palacios 2020 (10) Quasi-expérience États-Unis Août 2020	Évaluation de l'efficacité des masques ou des couvre-visage en coton à réduire le risque de contamination de l'environnement associé aux gouttelettes de salive ou aux goulettes orales produites par une personne ou retenir ces gouttelettes. Cette évaluation exige que l'un des enquêteurs (un volontaire sain) compte de 1 à 100 alors qu'il se trouve à 30 cm d'une plaque de gélose TSA stérile. (Le tableau 2 présente l'expérience portant sur l'effet de protection effectuée sur un modèle animal).	- Le même masque en coton porté par un volontaire humain a démontré que, comparativement à l'absence de masque, même une seule épaisseur de matériau réduisait le risque de contamination de l'environnement par les gouttelettes de salive.
Bahl 2020 (12) Quasi-expérience Australie Juillet 2020	Comparaison entre l'efficacité des masques simple et double épaisseur en tissu recommandés par le Center for Disease Control and Prevention (CDC) et les masques chirurgicaux trois épaisseurs. Les masques ou couvre-visages simple épaisseur ont été fabriqués selon la méthode qui permettait de « créer un masque ou couvre-visage rapidement, simplement en coupant un t-shirt (méthode sans couture) » alors que le masque double épaisseur a été fabriqué selon une méthode sans couture recommandée par le CDC. Afin d'avoir des preuves visuelles de l'efficacité des différents masques, un système d'éclairage à DEL sur mesure et une caméra haute vitesse	- Grâce aux visualisations obtenues (photos sur le papier, aucune analyse) pour la parole, la toux et l'éternuement, l'étude a pu démontrer que le port d'un masque en tissu simple épaisseur permettait de réduire la propagation des gouttelettes et qu'il suffisait de mettre un masque double épaisseur pour obtenir des résultats encore meilleurs, avec un très faible nombre de goulettes et que seules celles qui étaient associées aux éternuements étaient visibles. Quant au masque chirurgical, c'est celui qui a permis d'obtenir les meilleurs résultats puisqu'il a pu empêcher la propagation des gouttelettes, quel que soit le type d'émission examiné.

	ont été utilisés pour capter la lumière diffusée par les gouttelettes et les aérosols expulsés par un seul volontaire alors qu'il parlait, toussait et éternuait.	
Pan 2020 (4) *Prépublication* Expérience de simulation États-Unis Novembre 2020	Évaluation de l'efficacité de 11 masques ou couvre-visage sur un mannequin afin de connaître le niveau de filtration de chacun des matériaux et le niveau de protection lors de l'inspiration et de l'expiration pour une vaste gamme d'aérosols dont la taille variait de 0,04 à 135 µm. Les particules utilisées dans l'étude provenaient d'une solution de NaCl à 2 %. L'étude visait à évaluer l'efficacité de la protection des masques ou des couvre-visages lors de l'inspiration et de l'expiration à l'aide de deux mannequins installés des côtés opposés d'une chambre en acrylique de 57 litres. Le mannequin qui « expirait » était relié à un nébuliseur alors que celui qui « inhalait » était relié à un aspirateur. Un masque était d'abord porté par le mannequin qui inhalait, puis par le mannequin qui expirait, afin de mesurer le nombre de particules qui traversaient le masque dans chacun des cas. Masque ou couvre-visage utilisé : sac pour aspirateur, masque chirurgical, filtre MERV 12, bandana, taie d'oreiller en coton 200 fils au pouce, t-shirt en coton, chiffon en microfibre, filtre à café, coton mince, acrylique mince et écran facial en plastique.	- L'efficacité de filtration a augmenté avec la taille des particules et a ainsi empêché les gouttelettes de plus de 20µm de parcourir plus de 33 cm. - Le sac pour aspirateur, le chiffon en microfibre, le masque chirurgical et le filtre MERV 12 ont été les plus efficaces pour bloquer les particules de 2 µm avec un taux d'efficacité supérieur à 90 %. - Le sac pour aspirateur et le chiffon en microfibre sont ceux qui ont obtenu l'efficacité de filtration la plus élevée avec une plage de 60 à 90 %, alors que ce niveau variait entre 50 et 75 % pour les masques chirurgicaux. Le filtre à café a, quant à lui, obtenu une efficacité de filtration qui variait entre 10 et 75 % pour des particules de 0,04 à 1 µm. - Le masque en coton mince et le bandana (double épaisseur) avaient un faible niveau d'efficacité (30 à 50 %) et ce niveau était encore plus bas (5 à 40 %) pour les particules submicroniques. - L'efficacité de la protection lors de l'inspiration et de l'expiration était semblable pour la plupart des masques. - Les masques mal ajustés (p. ex., le bandana) n'ont pas donné d'aussi bons résultats en ce qui concerne le contrôle à la source. - L'écran en acrylique mince est celui qui a donné les plus mauvais résultats. - Le fait d'avoir pu réduire le jeu entre la peau et le masque et la vitesse de l'air a permis de

		grandement améliorer la protection en expiration du masque sans couture mentionné par le CDC et fabriqué à l'aide d'une taie d'oreiller en coton de 200 fils au pouce.
Lindsley 2020 (16) *Prépublication* Expérience de simulation États-Unis Novembre 2020	Étude qui combine un simulateur capable de générer des aérosols semblables à ceux de la toux afin de propulser de petites particules d'aérosol (< 0,6 à 7 µm) sur une fausse tête de mannequin souple et pliable portant différents masques, soit un masque N95, un masque de procédure de qualité médicale, un masque en coton trois épaisseurs, une guêtre en polyester et un écran facial. Les aérosols associés à la toux simulée ont été générés par la nébulisation d'une solution avec KCl à 14 % et fluorescéine sodique à 0,4 %. Les tests d'ajustement ont été effectués à l'aide d'un PortaCount.	- Tous les masques ou couvre-visages, à l'exception de l'écran facial, ont considérablement réduit les aérosols rejetés dans l'environnement ($p < 0,0001$). - Le masque N95 a bloqué 99 % des aérosols, le masque de procédure de qualité médicale en a bloqué 59 %, le masque en tissu en a bloqué 51 %, la guêtre simple épaisseur en a bloqué 47 % et la guêtre double épaisseur en a bloqué 60 % alors que l'écran facial n'en a bloqué que 2 %. - Lorsque la taille des particules augmentait, l'efficacité de blocage de tous les masques augmentait aussi. - Le masque N95 est celui qui a offert le meilleur ajustement, suivi du masque de procédure médicale, de la guêtre double épaisseur, de la guêtre simple épaisseur et du masque en tissu.
Kähler 2020 (5) Expérience de simulation Allemagne Octobre 2020	Utilisation des mesures vélocimétriques associées à l'image quantitative des particules pour évaluer la propagation de l'air expiré, la vitesse des gouttelettes expirées et les propriétés de turbulence du flux d'air. Dans cette étude, un seul volontaire humain a été utilisé pour examiner le champ d'écoulement associé à la toux. Les tests ont été effectués avec et sans masque chirurgical et ont utilisé de la fumée pour démontrer l'effet de l'espace qui se crée entre la peau et la bordure du masque lorsqu'un masque	- Le masque chirurgical limite la propagation de l'air et des aérosols lors de l'élocution ou de la toux. - Les masques ou couvre-visages qui recouvrent la bouche et le nez et les masques chirurgicaux n'étaient pas suffisamment ajustés sur le visage pour protéger contre l'infection par gouttelettes, comme le démontrent les preuves photographiques dans lesquelles les gouttelettes passent facilement à travers le masque. - Les masques faits avec du papier hygiénique quatre épaisseur, des essuie-tout, des filtres à

	est mal ajusté (masques chirurgicaux et FFP2). Une caméra numérique installée devant et derrière le matériau filtrant a été utilisée pour déterminer la capacité de filtration des différents matériaux sur les petits aérosols (0,3 à 2µm).	café, du molleton et du tissu en microfibre présentaient tous un bas niveau de filtration. - Les sacs pour aspirateur avec filtre pour poussière fine ont démontré un effet de filtrage comparable aux masques FFP2/N95/KN95, mais ils ne sont pas conçus pour une telle utilisation.
Ueki 2020 (2) Expérience de simulation Japon Octobre 2020	Description d'une simulation dans laquelle des gouttelettes et des aérosols contenant le virus infectieux SRAS-CoV-2 produits par la respiration humaine et la toux sont transmis dans l'air. Le simulateur a été utilisé pour évaluer la transmissibilité des gouttelettes et des aérosols infectieux et la capacité de différents types de masques à bloquer cette transmission. La simulation, qui utilise deux têtes de mannequin installées face à face et connectées à un nébuliseur de compresseur sur mesure, a permis d'évaluer différents masques, dont des masques en coton, des masques chirurgicaux et des masques N95.	- Le masque N95 présente l'efficacité de protection la plus élevée (il entraîne une réduction de l'exposition aux particules infectieuses variant entre 80 et 90 %). - Les masques chirurgicaux et les masques N95 n'ont, quant à eux, pas pu bloquer complètement la transmission des gouttelettes de virus et des aérosols, même lorsqu'ils étaient absolument étanches. La charge virale qui traverse un masque N95 ajusté, porté par le propagateur, était de 0,3 copie $\log_{10}$ alors qu'elle était de 10 copies $\log_{10}$ lorsque ce même masque était porté par le récepteur. - Comparativement à l'absence de masque ou de couvre-visage, un masque ou couvre-visage en coton (sans description de la composition) a entraîné une réduction de 20 à 40 % de l'absorption du virus. - Les résultats de l'étude indiquent que les masques ou couvre-visages en coton et les masques chirurgicaux conviennent mieux pour bloquer la dispersion du virus que pour protéger la personne qui les porte (> 50 %) (c.-à-d. comme forme de contrôle de la source). - Il y avait un effet synergique lorsque le récepteur et le propagateur du virus portaient tous deux des masques ou des couvre-visages (masques de coton ou masques chirurgicaux). Par exemple, lorsque le récepteur portait un masque ou couvre-

		visage en coton, la charge virale qui traversait le masque était de 63 copies log_{10} alors que lorsque le propagateur portait un masque, la charge virale qui traversait le masque était de 42 copies log_{10}. Quand, tant le receveur que le propagateur portaient un masque, la charge virale était plus faible, soit à 33 copies log_{10}. Voir les graphiques dans le document.
Edwards 2020 (3) *Prépublication* Expérience de simulation États-Unis Août 2020	Étude d'efficacité randomisée ayant utilisé une solution de particules polydispersées nébulisées de NaCl à 10 % (de 0,3 µm à 10 µm) administrée par un simulateur d'expiration ainsi que des mannequins pour effectuer 94 tests avec élocution et toux sur huit types de tissus différents, cinq types de masques différents et différents débit d'air. L'étude a également permis de créer deux nouvelles mesures associées à l'indicateur d'efficacité de la filtration (EEF) et au facteur de dispersion du débit expiratoire (FDDE) qui seront utilisées pour présenter des valeurs quantitatives ou indicateurs pour le rendement des masques non médicaux dans le contrôle de dispersion. Des valeurs plus élevées pour ces deux mesures indiquent une meilleure filtration et un meilleur rendement, ainsi qu'une plus grande réduction de la vitesse des particules, respectivement.	- Par rapport à l'absence de masque, les masques de qualité non médicale ou les combinaisons de tissus ont permis une réduction statistiquement significative de la dispersion atmosphérique des particules après l'expiration. - Le tissu, la conception du masque et l'interaction entre le tissu et le niveau de l'expiration ont des incidences majeures sur l'efficacité de la filtration des particules expirées. - Le masque chirurgical avec couches internes non-tissées est celui qui a été le plus performant. - L'évaluation qui permet de trouver le meilleur matériau doit, quant à elle, dépend de plusieurs éléments, à savoir quel matériau réussit à réduire la vitesse des particules, lequel force les particules à changer de direction ou encore, lequel offre un rendement accru en matière de filtration. - Voici donc les valeurs EEF pour différents matériaux, du meilleur au pire : Serviette de bain > Pantalon en molleton > t-shirt > Bandana > Serviette en microfibre > Taie d'oreiller > Couverture de déménageur > Chemise habillée. - Quant aux valeurs FDDE pour divers matériaux, en voici la liste, du meilleur au

		pire : Taie d'oreiller > Serviette en microfibre > Pantalon en molleton > Serviette de bain > t-shirt > Chemise habillée > Couverture de déménageur > Bandana.
Verma 2020 (8) Expérience de simulation États-Unis Juin 2020	Étude qui utilise des visualisations qualitatives pour la toux et les éternuements émulés avec une tête de mannequin pour examiner de quelle manière les choix de matériaux et de conception influent sur la mesure dans laquelle les jets respiratoires chargés de gouttelettes sont bloqués.	- Les masques ou couvre-visages masques pliés et non ajustés ainsi que les masques ou couvre-visages de style bandana offrent une capacité de blocage minimale pour les plus petites gouttelettes aérosolisées. - Une fois bien ajustés, les masques faits maison dans lesquels on retrouve plusieurs épaisseurs d'étoffe matelassée et les masques de type cône que l'on peut acheter en magasin se sont avérés les plus efficaces pour réduire la dispersion des gouttelettes. Ces masques ont cependant généré certaines fuites tant parce que les particules réussissent à traverser le matériau qu'en raison des petits jeux que l'on retrouve entre le bord du masque ou couvre-visage et la peau.
Études sur les porte-filtres utilisés pour évaluer les caractéristiques de contrôle à la source des matériaux utilisés dans la fabrication des masques (n = 7)		
Aydin 2020 (21) Expérience de simulation États-Unis Juillet 2020	Examen de l'efficacité de 11 types de textiles de maison pour réduire la dispersion des gouttelettes, en utilisant comme référence un masque médical commercial. L'étude a également évalué la respirabilité (perméabilité à l'air), la texture, la composition des fibres et les propriétés en matière d'absorption d'eau de ces textiles. L'efficacité de filtration des grosses gouttelettes à grande vitesse a été évaluée en plaçant les tissus à une distance de 25 mm de la buse d'un inhalateur dans lequel se trouvait une suspension de billes fluorescentes de	- En ce qui concerne les gouttelettes à haute vitesse (comme celles que l'on retrouve dans l'élocution, la toux ou les éternuements), la plupart des tissus ont obtenu une efficacité de blocage des gouttelettes relativement élevée (valeurs médianes > 70 %). - Le masque médical avait une efficacité de blocage de 98,5 %. - Deux ou trois épaisseurs de matériau, comme dans le cas du tissu pour t-shirt, permettent de bloquer les gouttelettes avec une efficacité similaire à celle des masques médicaux (>94 %), tout en conservant une respirabilité comparable.

	100 nm. Les gouttelettes à faible vitesse ont, quant à elles, été évaluées en installant le tissu à 300 mm de l'inhalateur. La perméabilité à l'air a été évaluée à l'aide d'un tube d'écoulement par bouchon. Un masque médical en polypropylène, des t-shirts 100 % coton, un tissu matelassé 100 % coton, des t-shirts en mélange de coton et de polyester, un drap en polyester, un linge à vaisselle en polyester et en mélange de polyamide, ainsi que des chemises en soie ont tous été testés.	- L'efficacité de blocage du tissu pour t-shirt est beaucoup plus élevée pour les gouttelettes à faible vitesse que pour les gouttelettes à grande vitesse. - Les tissus moins perméables à l'air sont plus efficaces pour bloquer les gouttelettes.
Xiao 2020 (18) Expérience de simulation Japon Juin 2020	Étude qui a utilisé l'analyse par imagerie pour effectuer analyser qualitativement l'efficacité des masques chirurgicaux, des masques de gaze, de la gaze, du coton, de la soie, du lin et des mouchoirs de papier face à des particules d'amidon dont la taille correspond à celle des microgouttelettes (moyenne de 8,2µm) et des microsphères de latex (0,75µm) lancés sur les masques à une vitesse de 44,4 m/s (conditions d'éternuements à grande vitesse) créée par centrifugation.	- Le masque de gaze de coton a été le plus efficace pour bloquer les particules d'amidon (90,4 % d'efficacité de blocage), suivi par le masque de coton double épaisseur (89,0 %). Le rendement des autres matériaux variait de 76,4 % à 87,9 %, alors que le rendement des huit épaisseurs de gaze était très bas (36,7 %). Le masque chirurgical a, quant à lui, bloqué 78,2 % des particules. - Lorsque des microsphères de latex ont été utilisées pour imiter des particules de la taille des aérosols, les matériaux qui ont offert la meilleure efficacité de blocage étaient les quatre épaisseurs de soie (93,8 %) (probablement en raison de leur charge électrostatique), le masque de gaze (78,5 %) et le coton double épaisseur (74,6 %). - Les masques faits de plusieurs épaisseurs de lin ont donné de bien meilleurs résultats que lorsqu'une seule épaisseur était utilisée (66,5 % contre 53,2 %).
O'Kelly 2020 (19)	Évaluation de la capacité de 20 tissus et matériaux faciles à trouver à réduire les concentrations atmosphériques de	- Les particules ultrafines utilisées dans cette étude ont entraîné une « base de référence »

Expérience de simulation États-Unis Juin 2020	particules ultrafines (0,1 µm et diamètre inférieur) à une vitesse nominale de 16,5 m/s (vitesse de la toux). Une évaluation plus poussée a été effectuée afin de connaître la capacité de filtration de certains tissus humides et de combinaisons de tissus qui pourraient être utilisées pour fabriquer des masques faits maison. La résistance respiratoire a été estimée à partir des commentaires qualitatifs. Dans cette étude, l'efficacité de filtration représente le pourcentage de particules qu'un milieu filtrant peut bloquer. Les tissus testés comprenaient : feutre, Lycra, sacs pour aspirateur lavables, ouatine matelassée/ouate à piquer et divers types de tissage de coton faciles à trouver comme l'étoffe matelassée, le coton pour chemise et le tricot pour chandail de coton.	faible en ce qui concerne l'efficacité de filtration. - Le masque N95 (52,47 %), le masque chirurgical (47,46 %) et le sac pour aspirateur HEPA jetable (60,86 %) ont obtenu les meilleurs rendements en ce qui concerne la filtration. - Les jeans en denim (45,94 %) et le tissu pour coupe-vent (47,12 %) étaient efficaces, mais manquaient de respirabilité. - Les matériaux à haute efficacité de filtration et à faible résistance respiratoire incluaient la laine feutrée (35,87 %), l'étoffe matelassée (34,54 %) et la flanelle de coton (28,50 %). - Les tissus utilisés de façon courante pouvaient atteindre des niveaux beaucoup plus élevés de filtration des particules ultrafines lorsqu'ils étaient utilisés en couches (60 %), mais ils étaient alors moins perméables à l'air. - Les sacs pour aspirateur étaient efficaces, mais leur utilisation n'est pas sécuritaire.
Foschini 2020 (17) *Prépublication* Expérience de simulation Brésil Mai 2020	Comparaison de l'efficacité relative des masques commerciaux (masques médicaux) et des masques en tissu faits maison. Un nébuliseur a été utilisé pour créer des aérosols composés d'eau distillée. En ce qui concerne les mesures de diffusion optique, deux techniques différentes ont été utilisées simultanément pour comparer l'intensité de la dispersion de la lumière par les gouttelettes entre les fenêtres avant et après l'échantillon.	- Le masque N95 et le masque chirurgical (99,7 %) sont ceux qui ont obtenu la plus grande efficacité de blocage. - Alors que le filtre à café a aussi obtenu une grande efficacité de blocage (99,6 %), il comportait cependant une faible respirabilité et s'est rapidement dégradé avec l'augmentation du niveau d'humidité, ce qui n'en fait pas un bon choix comme matériau dans un masque. - Comme les masques faits maison (51,0 %) ne comportaient pas autant d'épaisseurs que les masques chirurgicaux, cela a réduit leur efficacité.

		- Les tissus conventionnels à plus forte teneur en coton étaient les plus efficaces parmi les textiles de maison ayant été étudiés (une épaisseur : 46,5 %). Ajouter une deuxième épaisseur a cependant permis d'augmenter l'efficacité de blocage (double épaisseur : 66 %).
Lustig 2020 (20) Expérience de simulation États-Unis Mai 2020	Évaluation de plus de 70 combinaisons différentes de tissus et de masques dans un débit d'air permanent forcé par convexion avec aérosols pulsés simulant une respiration forcée.	- Parmi les matériaux efficaces (estimations plus basses en ce qui concerne la transmission fractionnelle), on trouvait tant des couches absorbantes hydrophiles que des couches barrière hydrophobes. - Les conceptions efficaces indiquées dans l'étude comportaient toutes des couches absorbantes (deux épaisseurs), soit des serviettes en éponge, du coton pour courtepointe et de la flanelle. Ces différents matériaux faciles à trouver ont tous permis d'obtenir une transmission fractionnelle à moins de 10 % de celle qu'offre le masque N95 à cinq épaisseurs. - Les conceptions efficaces comprenaient des couches barrières en polypropylène non-tissé, en polyester et en polyaramide. - De nombreux masques simple épaisseur ou faits d'un seul type de tissu présentaient des transmissions fractionnelles plus élevées que celles du masque N95.
Rodriguez-Palacios 2020 (22) Expérience de simulation États-Unis	Évaluation de différents textiles de maison pour en quantifier le potentiel comme barrières environnementales efficaces. Les auteurs ont utilisé un modèle de simulation qui pulvérise des gouttelettes avec suspension bactérienne (imitant un éternuement) pour quantifier la mesure dans laquelle les textiles domestiques utilisés pour fabriquer des vêtements réduisent la	- Lorsqu'aucun masque n'était porté, un éternuement simulé pouvait envoyer des gouttelettes porteuses de bactéries à plus de 1,8 m. - Tous les textiles simple épaisseur ont permis de réduire considérablement la distance parcourue par les macro-gouttelettes et les microgouttelettes, soit un maximum de 25,5 à 34 cm.

Mai 2020	dispersion des gouttelettes sur une surface se trouvant à moins de 1,8 m (la distance minimale recommandée pour la « distanciation sociale » selon de COVID-19). Les textiles testés comprenaient un tissu fait uniquement de coton peigné (tissu pour t-shirt), un tissu en microfibre 300 fils au pouce 100 % polyester (taie d'oreiller), deux tissus 100 % coton à tissage non serré filé à la main et un tissu de type « technologie qui garde au sec » 100 % polyester que l'on trouve souvent dans les maillots de sport. L'efficacité de ces textiles a été comparée au résultat obtenu avec un masque médical/chirurgical et sans masque.	- Les textiles deux épaisseurs (100 % coton peigné et 100 % polyester) ont bloqué complètement l'éjection des grosses macrogouttelettes et réduit de 97,2 % (P < 0,020) le déplacement des microgouttelettes par rapport aux tissus simple épaisseur et ont ainsi permis d'obtenir une dispersion inférieure à 10 cm. Même le tissu simple épaisseur le moins efficace (le tissu 100 % coton à tissage non serré filé à la main) a réussi à retenir de 90 à 99 % des gouttelettes lorsque deux épaisseurs étaient utilisées. - Les textiles double épaisseur étaient aussi efficaces que les masques médicaux et chirurgicaux pour prévenir la dispersion des gouttelettes.
Amendola 2020 (23) Expérience de simulation Italie Mai 2020	Expérience qui a simulé l'action respiratoire en mesurant la distribution des particules d'aérosol à base aqueuse. L'efficacité de filtration moyenne indiquée tenait compte des particules ayant un diamètre supérieur à 0,28 µm. Les masques ou couvre-visages ont été testés tant pour l'inhalation que l'expiration. TNT= matériau non-tissé fait de polypropylène et de viscose à base de tissu	- Le masque médical a démontré une efficacité de filtration supérieure à 97 %. - Seuls les masques faciaux triple épaisseur comprenant principalement du tissu non-tissé ont pu atteindre des valeurs supérieures à 95 %, y compris le TNT triple épaisseur et le TNT-coton-TNT.

*Le lieu ou la date de l'étude a été estimé en fonction des affiliations des auteurs et/ou de la date de publication.

MASQUES NON MÉDICAUX UTILISÉS POUR EMPÊCHER L'INHALATION DU SRAS-COV-2

Études de modélisation sur les humains, les mannequins et les animaux (n = 17) :

Des études ont été menées sur des volontaires humains (n = 7), des mannequins (n = 10) et des souris axéniques expérimentales (n = 1). Les mannequins ne reproduisent pas parfaitement les mimiques des humains (c.-à-d. incidence sur l'ajustement) ou les activités respiratoires puisque l'air ne se déplace que dans une seule direction (4). Par conséquent, il faut faire preuve de prudence lorsqu'on extrapole aux humains les résultats obtenus avec des mannequins pour les masques ou couvre-visages.

Bien qu'il ait été démontré que les masques non médicaux ou couvre-visages donnent de meilleurs résultats comme forme de contrôle à la source (c.-à-d. en limitant la transmission des personnes infectées) (2, 4, 5), il a également été démontré qu'ils offrent une certaine protection à la personne qui les porte (tableau 2). Le scénario de réduction de la transmission le plus efficace est celui dans lequel tout le monde (tant les gens sains qu'infectés) porte un masque ou couvre-visage (2).

- Les masques N95 bien ajustés offrent le plus haut degré de protection (>95 %) (2, 24-31). Un masque N95 mal ajusté offre différents niveaux de protection, dans certains cas, des niveaux comparables à ceux qu'offrent les masques chirurgicaux et les masques en tissu (24, 30).
- Les masques chirurgicaux ont une meilleure efficacité de filtration que les masques non médicaux (plage : 19,94 % à 95 %) (4, 25 à 28).
- Les masques en tissu avaient généralement une efficacité de filtration inférieure à celle des masques médicaux, bien que certains tissus et épaisseurs obtiennent un rendement comparable à celui des masques médicaux (4, 25, 27, 28).
    - Le rendement du masque (filtration des gouttelettes de salive, fuite d'air minimale) était plus élevé pour les masques plus ajustés (5, 24-26, 30, 32) et pour les masques multicouche (29, 31, 33). L'efficacité de filtration était plus élevée pour les grosses particules (4).
- On a constaté que la soie était très hydrophobe et efficace pour empêcher la pénétration des gouttelettes d'eau pendant les tests de pulvérisation (34).
- On a également constaté que le bandana et les tissus de coton simple épaisseur s'ajustaient mal et donnaient de mauvais résultats (efficacité inférieure à 15 à 30 %) (4, 27-29, 31).
- Les masques en tissu non médical de style chirurgical n'étaient pas aussi efficaces que les masques en forme de cône ou en bec de canard (26, 35).
- Dans une étude de modélisation avec des animaux, lorsqu'elles étaient protégées par deux couches de coton peigné à 100 %, toutes les souris étaient protégées à 100 % contre la contamination par les bactéries contenues dans les microgouttelettes (10).

Études des porte-filtres (n = 20) :

Dans des conditions expérimentales (c'est-à-dire lorsque les mesures étaient prises alors que le tissu était scellé sur un support), les efficacités de filtration étaient plus élevées que dans les études citées ci-dessus dans lesquelles les masques étaient testés alors qu'ils étaient portés par une personne (36 à 42). Par conséquent, ces simulations expérimentales surestiment l'efficacité des textiles de maison en ce qui concerne la protection potentielle contre le SRAS-CoV-2 des personnes qui les portent parce qu'elles n'évaluent pas directement la respirabilité ou l'ajustement, mais elles aident cependant à comprendre l'efficacité relative de filtration d'un tissu par rapport à un autre.

- L'augmentation du nombre d'épaisseurs augmente l'efficacité de filtration, mais augmente également la résistance à l'air (et réduit la respirabilité). Les masques non médicaux doivent avoir une résistance à l'air inférieure à 40 Pa/cm^2 (41 à 49). Les valeurs de perméabilité à l'air de tous les échantillons comprenant moins de quatre épaisseurs qui ont été analysés étaient inférieures aux valeurs maximales recommandées par le NIOSH pour les masques médicaux (50). Les échantillons comprenant trois épaisseurs ou plus ont réussi à obtenir une efficacité de filtration supérieure à 90 % (23, 37, 40, 42-44, 50, 51).
- Il a été démontré que les fuites simulées dans le tissu (visant à mesurer indirectement l'effet de l'ajustement) ont une grande incidence sur l'efficacité de filtration (44, 52). L'ajustement est donc très important pour assurer une protection adéquate.
- Les masques non médicaux ne donnaient pas d'aussi bons résultats que les masques médicaux. Cependant, l'ajout d'un filtre à charbon actif comme couche intermédiaire dans un masque de coton a considérablement amélioré l'efficacité de filtration (46, 53). Une étude a révélé que le fait de traiter les textiles de maison avec une solution de NaCl pouvait permettre d'accroître la capacité de filtration des masques non médicaux (54).
- D'énormes différences dans l'efficacité de filtration ont été observées tant entre les textiles de maison qu'en raison des tailles de particules, avec un écart allant d'un taux inférieur à 10 % à un taux supérieur à 95 %. L'efficacité de filtration était plus élevée pour les particules à déplacement plus lent produites pendant l'élocution que pour les particules à déplacement plus rapide produites pendant la toux ou l'éternuement (46).
- La qualité du tissu (c.-à-d. tissage serré, faible porosité) était tout aussi importante que le nombre d'épaisseurs (43, 44, 46).
- Certains tissus comportent des charges électrostatiques qui attirent et lient des particules de la taille d'un nanomètre, ce qui augmente l'efficacité de filtration (44, 52, 55). Combiner différentes épaisseurs de tissu et optimiser le filtrage mécanique et électrostatique peut être efficace pour maximiser l'efficacité de filtration dans un masque non médical (44, 52). Une combinaison de plusieurs épaisseurs de matériaux, avec une couche externe hydrophobe (par exemple, du polyester, du polypropylène lacé par filage ou de la polyaramide), une couche intérieure en tissu de coton de haute qualité et une

couche intermédiaire faite de matériaux non-tissés ou chargés électrostatiquement (par exemple, soie naturelle, mousseline ou polyester) serait donc idéale pour optimiser tant la capacité de protection que le potentiel de réduction de transmission des masques non médicaux ou des couvre-visages.

- Bien qu'il ait été démontré que les sacs pour aspirateur ont une efficacité de filtration comparable à celle des masques médicaux (4, 5, 40, 42, 46, 50), ce ne sont pas des produits cliniques certifiés, ce qui signifie qu'ils peuvent donc contenir des ingrédients malsains et des fibres nocives. Il n'est donc pas recommandé de les utiliser dans les masques faits maison (5).

Tableau 2 : Études qui évaluent les caractéristiques de protection des masques non médicaux ou des couvre-visage (n = 37)

ÉTUDE*	MÉTHODE	PRINCIPAUX RÉSULTATS
Expériences menées avec un ou plusieurs volontaires humains, des mannequins ou des modèles animaux (n = 17)		
Park 2020 (31) Quasi-expérience États-Unis Août 2020	Étude sur le développement de masques qui a évalué 10 échantillons différents de diverses configurations de matériaux afin d'en déterminer la perméabilité à l'air, l'efficacité de filtration selon la taille des particules et la chute de pression, pour en arriver à une conception de masque offrant un confort optimal et une efficacité barrière optimale. Un sujet humain a porté le masque à l'essai pendant de longues périodes alors qu'il simulait une journée de travail type, puis en a évalué le rendement. La perméabilité à l'air a été évaluée à l'aide de la méthode ASTM D737-96 alors que la filtration et la chute de pression ont été évaluées avec la méthode ASTM F2299-03 avec des particules de 0,2 à 1 µm et un débit d'air de 8,7 cm/s.	- Les masques médicaux ont obtenu la plus grande efficacité de filtration, alors que le tissu utilisé pour faire des mouchoirs était le moins performant (perméabilité à l'air la plus élevée, mais avec une efficacité de filtration de seulement 19 % même avec quatre épaisseurs). - La configuration de blocage jugée optimale était « filtre 2 (superposition) » entre deux couches de tissu barrière 100 % polyester. Ce masque a obtenu de meilleurs résultats en ce qui concerne la filtration et la perméabilité que le masque commercial en tricot double épaisseur évalué. - L'efficacité de filtration était meilleure pour les particules de plus grande taille que pour les particules plus petites.

O'Kelly 2020 (24) *Prépublication* Quasi-expérience États-Unis Août 2020	Sept volontaires humains ont été utilisés pour évaluer quantitativement le niveau d'ajustement de divers types de masques (masques N95, masques KN95, masques chirurgicaux et masques en tissu), et surtout, pour examiner l'exactitude des vérifications d'ajustement effectuées en comparant les résultats des vérifications d'ajustement aux résultats quantitatifs des essais d'ajustement. Les tests d'ajustement quantitatifs évaluent simultanément le nombre de particules qui se trouvent à l'intérieur et à l'extérieur d'un masque. Les notes indiquées pour le facteur d'ajustement proviennent du nombre de particules filtrées par le masque. Chaque participant a effectué un test quantitatif d'ajustement et une vérification subjective de l'ajustement pour chacun des masques.	- Les masques N95 offraient le plus haut degré de protection avec des notes moyennes pour l'ajustement des différents modèles variant entre 13,2 et 72,3. - Les masques N95 mal ajustés offraient différents niveaux de protection, dans certains cas comparables aux masques chirurgicaux et aux masques en tissu. - Le KN95 et le masque chirurgical ont obtenu une note d'ajustement moyenne de 3,2 et de 2,2, respectivement. - Les masques ou couvre-visages en tissu ont quant à eux donné des résultats semblables à ceux des masques KN95 et des masques chirurgicaux. - Une conception améliorée combinée à l'utilisation de meilleurs matériaux accroîtrait probablement l'efficacité de ces masques.
Mueller 2020 (26) Quasi-expérience États-Unis Mai 2020	Quantification de l'efficacité des masques en tissu produits dans la collectivité et dans le commerce comme équipement de protection individuelle grâce à deux compteurs de particules qui échantillonnent simultanément l'air ambiant et l'air à l'intérieur de différents types de masques portés par un seul volontaire. Le rendement du masque a ensuite	- Un masque N95 bien ajusté présentait l'efficacité d'élimination moyenne la plus élevée (99 %), ainsi qu'un facteur d'ajustement élevé. - Lorsqu'un masque N95 mal ajusté a été utilisé, l'efficacité d'élimination des particules et le facteur d'ajustement ont diminué pour atteindre 90,6 % et 10,6, respectivement. - Les masques chirurgicaux standards et les masques quatre épaisseurs avec une couche de charbon de bois avaient une efficacité

	été évalué selon l'efficacité d'élimination des particules (taille inférieure à 0,3 µm) et la variabilité statistique lorsqu'il est porté comme prévu, ainsi qu'avec une épaisseur de nylon, pour ainsi en évaluer de façon indépendante l'ajustement et le matériau.	moyenne d'élimination variant entre 50 et 75 %. - L'efficacité d'élimination des particules du masque en tissu variait entre une valeur inférieure à 30 % et 90 %. Les masques en tissu les plus performants étaient en forme de cône et comprenaient une couche de tissu filtrant soufflé par fusion entre les couches de tissu. - Les masques en tissu de style chirurgical n'étaient pas aussi efficaces que les masques en forme de cône, mais ils étaient rehaussés d'une épaisseur de nylon. - L'épaisseur de nylon n'a pas eu une efficacité de filtration significative, mais a amélioré l'ajustement du masque en dessous.
Ueki 2020 (2) Quasi-expérience Japon Octobre 2020	Description d'une simulation dans laquelle des gouttelettes et des aérosols contenant le virus infectieux SRAS-CoV-2 produits par la respiration humaine et la toux sont transmis dans l'air. Le simulateur a été utilisé pour évaluer la transmissibilité des gouttelettes et des aérosols infectieux et la capacité de différents types de masques à bloquer cette transmission. Ce simulateur comprend deux têtes de mannequin installées l'une face à l'autre et reliées à un nébuliseur de compresseur sur mesure.	- Le masque N95 présente l'efficacité de protection la plus élevée (il entraîne une réduction de l'exposition aux particules infectieuses variant entre 80 et 90 %). - Les masques chirurgicaux et les masques N95 n'ont, quant à eux, pas pu bloquer complètement la transmission des gouttelettes de virus et des aérosols, même lorsqu'ils étaient absolument étanches. La charge virale qui traverse un masque N95 ajusté, porté par le propagateur, était de 0,3 copie $\log_{10}$ alors qu'elle était de 10 copies $\log_{10}$ lorsque ce même masque était porté par le récepteur. - Comparativement à l'absence de masque ou de couvre-visage, un masque ou couvre-visage en coton a entraîné une réduction de 20 à 40 % de l'absorption du virus. - Les masques ou couvre-visages en coton et les masques chirurgicaux conviennent beaucoup mieux pour bloquer la dispersion du virus que pour protéger la personne qui

		les porte (> 50 %) (c.-à-d. comme forme de contrôle de la source). - Il y avait un effet synergique lorsque le récepteur et le propagateur du virus portaient tous deux des masques ou des couvre-visages (masques de coton ou masques chirurgicaux). Par exemple, lorsque le récepteur portait un masque ou couvre-visage en coton, la charge virale qui traversait le masque était de 63 copies $\log_{10}$ alors que lorsque le propagateur portait un masque, la charge virale qui traversait le masque était de 42 copies $\log_{10}$. Quand, tant le récepteur que le propagateur portaient un masque, la charge virale était la plus faible à 33 copies $\log_{10}$. Voir les graphiques dans le document.
Teesing 2020 (35) Quasi-expérience Pays-Bas Octobre 2020	Étude qui a utilisé chambre à particules fermée construite pour tester les matériaux filtrants potentiels recommandés par les gouvernements pour les masques faits maison. Les matériaux ont été testés seuls, ainsi qu'entre deux couches de coton, comme dans un masque fait maison. Divers modèles de masques ont été testés, soit des masques pliés, plissés, ronds, plats et en bec de canard. L'ajustement du masque a été testé avec un appareil AccuFIT 9000 pour ajustement de masque et un volontaire humain. Un test de pression a été effectué pour quantifier la perméabilité à l'air des différents matériaux et	- Les résultats des tests avec particules effectués sur les différents matériaux ont été comparés à ceux obtenus avec les masques N95/FFP2/KN95, et le matériau le plus performant était l'ePM$_1$ avec un résultat de 85 %. Certains autres matériaux facilement disponibles qui ont obtenu de bons rendements incluaient le cuir, un filtre à café plié entre des épaisseurs de coton, ainsi qu'un essuie-tout plié entre du coton et le tissu en microfibre. - Aucun des masques en coton avec filtre n'a réussi l'essai d'ajustement effectué. Le modèle en bec de canard a été jugé satisfaisant. - La chute de pression associée au masque en bec de canard a été testée et le linge à vaisselle simple épaisseur plié a démontré une respirabilité comparable à celle du masque 3M de référence.

	conceptions après un test d'ajustement réussi.	
Mboowa 2020 (41) *Prépublication* Quasi-expérience Ouganda Septembre 2020	Étude qui a testé huit masques offerts sur le marché afin d'en connaître l'efficacité de filtration, la propreté microbienne et la capacité de réutilisation. Du *Mycobacterium smegmatis* a été aérosolisé par un pulvérisateur portatif et envoyé sur des sections de masques installés sur des porte-filtres. L'air filtré a ensuite été inoculé sur de la gélose. De la saccharine (test de goût) a été utilisée pour évaluer l'ajustement du masque des volontaires. Après un lavage ou un traitement avec éthanol à 70 %, ces mêmes tests ont été refaits afin d'évaluer la réutilisabilité des masques ou couvre-visage. Des masques chirurgicaux, ainsi que des masques en polypropylène, faits d'un tissu « épais », en kitengi (intérieur)/coton (extérieur), en chiffon et faits avec une débarbouillette ont également été testés.	- Les masques chirurgicaux, suivis des masques double épaisseur en tissu local et des masques double épaisseur en tissu ont obtenu la meilleure filtrabilité. - L'ajout du traitement avec éthanol à 70 % a réduit tant l'ajustement que la capacité de réutilisation du masque. - Comme l'a montré le test de goût avec la saccharine, les masques double épaisseur étaient les mieux ajustés puisqu'il a fallu un plus grand nombre de pulvérisations, comparativement au masque simple épaisseur, pour que le bénévole qui le portait goûte la saccharine. - Il faut cependant interpréter ces résultats avec prudence, car la méthodologie utilisée n'est pas claire.
Rodriguez-Palacios 2020 (10) Quasi-expérience États-Unis Août 2020	Étude qui a fait état d'une expérience *in vivo* utilisant une méthode avec pulvérisation simulée de microgouttelettes porteuses de bactéries (bactéries de produits laitiers avec probiotiques) pour déterminer dans quelle mesure le tissu 100 % coton peigné double épaisseur (un	- Lorsque deux épaisseurs de tissu 100 % coton peigné ont été utilisées pour protéger les souris, aucune d'entre elles n'a été contaminée par les bactéries contenues dans les microgouttelettes (vaporisation de 2 ml). - Une fois exposées à 10 fois le volume de pulvérisation (20 ml), les barrières textiles ont continué à protéger toutes les souris (même avec un textile de faible densité; tissu épais

	tissu pour t-shirt couramment utilisé) a empêché la contamination chez des souris axéniques. Deux densités de tissu différentes ont été testées, soit 120 et 200 g/m^2. (Le tableau 1 présente l'expérience avec contrôle à la source)	ou mince, tests t pour échantillons appariés, p = 0,002) contre des doses élevées de gouttelettes. - Lorsque les mêmes expériences ont été effectuées sur des cages partiellement couvertes, toutes les souris ont été contaminées.
Pan 2020 (4) *Prépublication* Expérience de simulation États-Unis Novembre 2020	Évaluation de l'efficacité de filtration de 11 masques ou couvre-visages sur des mannequins pour connaître le niveau de protection de chacun lors de l'inspiration et de l'expiration. Ce test a été réalisé avec une vaste gamme d'aérosols allant de 0,04 à 135 µm. Les particules utilisées dans l'étude provenaient d'une solution de NaCl à 2 %. Deux mannequins installés sur des côtés opposés d'une chambre en acrylique de 57 L ont été utilisés. Le mannequin qui « expirait » était relié à un nébuliseur alors que celui qui « inhalait » était relié à un aspirateur. Un masque était d'abord porté par le mannequin qui inhalait, puis par le mannequin qui expirait, afin de mesurer le nombre de particules qui traversaient le masque dans chacun des cas. masques ou couvre-visage testés : sac pour aspirateur, masque chirurgical, filtre MERV 12, bandana, taie d'oreiller en coton 200 fils au pouce, t-shirt en coton,	- Comme l'efficacité de filtration augmentait lorsque la taille des particules augmentait, ce qui a empêché les gouttelettes de plus de 20µm d'aller à plus de 33 cm. Le sac pour aspirateur, le chiffon en microfibre, le masque chirurgical et le filtre MERV 12 ont été les plus efficaces pour bloquer les particules de 2 µm avec une efficacité supérieure à 90 %. - Le sac pour aspirateur et le chiffon en microfibre sont ceux qui ont obtenu l'efficacité de filtration la plus élevée avec une plage de 60 à 90 %, alors que ce niveau variait entre 50 et 75 % pour les masques chirurgicaux. Le filtre à café a, quant à lui, obtenu une efficacité de filtration qui variait entre 10 et 75 % pour des particules de 0,04 à 1 µm. - Le masque en coton mince et le bandana (double épaisseur) avaient un bas niveau d'efficacité (30 à 50 %) qui a encore descendu (5 à 40 %) avec les particules submicroniques. - L'efficacité de la protection lors de l'inspiration et de l'expiration était semblable pour la plupart des masques. - Les masques mal ajustés (p. ex., le bandana) n'ont pas donné d'aussi bons résultats en matière de contrôle à la source.

	tissu en microfibre, filtre à café, coton mince, acrylique mince et écran facial en plastique.	- L'écran en acrylique mince est celui qui a donné les plus mauvais résultats. - Le fait d'avoir pu réduire le jeu entre la peau et le masque et la vitesse de l'air a permis d'améliorer grandement la protection en expiration du masque sans couture mentionné par le CDC et fabriqué avec une taie d'oreiller en coton de 200 fils au pouce.
Kähler 2020 (5) Expérience de simulation Allemagne Octobre 2020	Utilisation des mesures vélocimétriques associées à l'image quantitative des particules pour évaluer la propagation de l'air expiré, la vitesse des gouttelettes expirées et les propriétés de turbulence du flux d'air. Dans cette étude, un seul volontaire humain a été utilisé pour examiner le champ d'écoulement associé à la toux. Les tests ont été effectués avec et sans masque chirurgical et ont utilisé de la fumée pour démontrer l'effet de l'espace qui se crée entre la peau et la bordure du masque lorsqu'un masque est mal ajusté (masques chirurgicaux et FFP2). Une caméra numérique installée devant et derrière le matériau filtrant a été utilisée pour déterminer la capacité de filtration des différents matériaux sur les petits aérosols (0,3 à 2 µm).	- Le masque chirurgical limite la propagation de l'air et des aérosols lors de l'élocution ou de la toux. - Les masques ou couvre-visages qui recouvrent la bouche et le nez et les masques chirurgicaux n'étaient pas suffisamment ajustés sur le visage pour protéger contre l'infection par gouttelettes, comme le démontrent les preuves photographiques dans lesquelles les gouttelettes passent facilement à travers le masque. - Les masques faits avec du papier hygiénique quatre épaisseur, des essuie-tout, des filtres à café, du molleton et du tissu en microfibre présentaient tous un bas niveau de filtration. - Les sacs pour aspirateur avec filtre pour poussière fine ont démontré un effet de filtrage comparable aux masques FFP2/N95/KN95, mais ils ne sont pas conçus pour une telle utilisation.
Colline 2020 (30) Expérience de simulation	Étude qui a testé des masques afin de comparer l'efficacité d'un matériau neuf (référence) et l'efficacité de filtration de ce même matériau, une fois le masque déjà porté.	- La filtration de référence a révélé qu'une seule épaisseur de coton 500 fils par pouce avait l'efficacité de filtration la plus faible (26,2 % et 17,4 % pour les gouttelettes de 60 et de 125 nm, respectivement). Le masque protecteur contre la poussière, le filtre à café,

États-Unis Septembre 2020	Un nanoaérosol avec dioxyde de silicium d'un diamètre moyen de 40 nm a ensuite été ajouté à une enceinte en acier inoxydable. L'efficacité de filtration de base a été testée avec un matériau attaché (sans tension) et un débit d'air de 0,0465 LPM/cm^2. Des masques ont ensuite été installés sur un mannequin auquel un débit d'admission était installé sur le nez. Des particules de 60 et de 125 nm ont été échantillonnées à raison de 1 par seconde pendant 180 secondes.	le coton double épaisseur et la serviette d'atelier ont donné des résultats un peu meilleurs. - Les appareils de protection respiratoire à filtres à particules (KN95, 3M 8511 et FTF467 ULPA) avaient une efficacité de filtration supérieure à 98 %. - Comparativement aux matériaux de référence, on a noté une importante baisse de l'efficacité de filtration pour tous les matériaux testés comme lorsque ce même masque avait déjà été porté. L'ajout d'une couche filtrante dans un masque en coton double épaisseur n'a pas permis d'améliorer considérablement la filtration en raison des fuites autour du masque. - L'efficacité de filtration d'un masque mal ajusté ou non serré peut donc chuter de plus de 60 % par rapport à l'efficacité de filtration du matériau.
Realmuto 2020 (32) Expérience de simulation États-Unis Septembre 2020	Étude qui a comparé des tests effectués sur un masque en bec de canard (masque sans couture obtenu simplement en pliant un morceau de tissu carré pour former un masque) faits de différents matériaux aux masques chirurgicaux et aux masques N95 disponibles dans le commerce. Un simulateur d'essai d'ajustement sur mannequin a été utilisé pour les tests de filtration, de perméabilité à l'air et de fuite. La tête du mannequin sur laquelle un simulateur de tube respiratoire a été installé a ensuite été mise dans une chambre avec un ventilateur de mélange et des valves d'essai	- Efficacité de filtration des masques testés, du meilleur au pire : masque N95 > chirurgical > triple épaisseur en polypropylène/Filti/polypropylène > triple épaisseur en polypropylène/MERV 13 ou huit/polypropylène> couche intérieure en Halyad H600, Filti simple épaisseur. - Les masques double épaisseur avaient une plus grande efficacité de filtration que les masques simple épaisseur. - Les expériences ont montré que les fuites dans les masques réduisaient considérablement l'efficacité de ce dernier. - Les résultats obtenus avec les sangles de tête étaient meilleurs que ceux obtenus avec les boucles d'attache dernière les oreilles, car l'espace entre le masque et la peau était plus facile à réduire avec ce type de sangle.

	alors que des particules avec une concentration de sel variant entre 50 et 700 nm étaient introduites dans la chambre. Matériaux testés : polypropylène non-tissé, matériau de masque « Filti » (polypropylène/nanofibre/matériau filtrant en polyester composite), filtres MERV, mousseline de coton, lingettes réutilisables, serviettes d'atelier pour l'huile.	
Parlin 2020 (34) Expérience de simulation États-Unis Septembre 2020	Comparaison de divers matériaux (coton, polyester, soie, essuie-tout) à des masques chirurgicaux dans des conditions de laboratoire afin d'en évaluer l'hydrophobie et la respirabilité avant et après un nettoyage. Des tests en laboratoire ont été effectués avec des masques installés sur des mannequins.	- La soie est un matériau hydrophobe qui bloque les gouttelettes et qui a réussi à empêcher l'absorption des gouttelettes comme le fait un masque chirurgical à usage unique, en plus de mieux conserver sa respirabilité que les matériaux hydrophiles comme le coton. La soie a également donné de bons résultats après avoir été nettoyée. - Lorsque la soie, le coton et le polyester ont été soumis à des tests de pulvérisation avec gouttelettes aérosolisées, la capacité de bloquer la pénétration des goulettes dans les aérosols n'a pas varié, que la barrière utilisée ait été simple ou double épaisseur.
Bhimaraju 2020 (28) *Prépublication* Expérience de simulation États-Unis Août 2020	Étude qui a utilisé un mannequin et un système d'inhalation pour évaluer l'efficacité de filtration des particules de moins de 2,5 µm. Les masques testés comprenaient : masques N95, masques chirurgicaux, masques en tissu, masques en tissu avec filtres à air au charbon actif, masques en tissu avec filtres à air de type CVCA, masques en tissu légèrement	- Les masques au charbon actif et les masques avec filtre à air de type CVCA étaient presque aussi efficaces que les masques N95, suivis des masques chirurgicaux, des masques en tissu fortement amidonnés et des masques en tissu légèrement revêtus d'amidon. - Le niveau de filtration des masques ordinaires en tissu pour les particules < 2,5 um était très bas par rapport aux autres masques.

	revêtus d'amidon et masques en tissu fortement amidonnés.	
Shahane-Kapse 2020 (29) *Prépublication* Expérience de simulation Inde Août 2020	Comparaison entre un masque double épaisseur en coton avec une couche de polypropylène enduit de polyuréthane appliqué sur l'extérieur du masque au centre du masque (afin qu'elle recouvre la bouche et le nez), un masque N95, des masques chirurgicaux triple épaisseur, un masque ou couvre-visage en coton et un écran facial. La quantité et le degré de gouttelettes et d'aérosols dans chacun des masques ont été évalués lorsque ceux-ci étaient portés par un mannequin, mais cette étude ne comportait cependant aucun échange gazeux (c.-à-d. respiration). Des colorants fluorescents ont été pulvérisés d'une distance de 1 et de 2 m à 180 km/h.	- Le colorant fluorescent n'a pas pénétré la couche intérieure des masques chirurgicaux trois épaisseurs ou des N95. - Le masque trois épaisseurs composé de deux couches de coton et d'une couche extérieure en polypropylène a bloqué le colorant fluorescent aux endroits où le tissu était imperméable. On pouvait cependant voir quelques taches sur la couche extérieure en coton sur les côtés du polypropylène, mais le colorant n'a cependant pas pénétré la couche de coton intérieure. - Le colorant fluorescent a cependant pénétré le masque en coton simple épaisseur et s'est retrouvé sur le mannequin.
Dhanraj 2020 (33) *Prépublication* Expérience de simulation États-Unis Juillet 2020	Étude visant à présenter les résultats de la caractérisation du Swiffer comme matériau filtrant de rechange et à évaluer l'efficacité de filtration de ce matériau selon la taille des particules. Deux systèmes ont été utilisés. Dans l'un, des confettis ronds de 47 mm étaient envoyés sur un système avec porte-filtre alors que dans l'autre, un masque (de type bandana) fait maison avec des Swiffer intercalés entre du tissu de taie d'oreiller, a été placé sur un mannequin dans une chambre.	- Le Swiffer a été très efficace pour filtrer les particules ultrafines (< 0,08 µm). - On a observé de plus grandes efficacités de filtration lorsque deux épaisseurs de Swiffer étaient intercalées entre deux couches de tissu de taie d'oreiller. Ainsi, avec deux épaisseurs de Swiffer, l'efficacité variait entre 45 et 62 % pour les particules de 0,1 à 0,5 µm alors qu'elle atteignait 30 à 45 % avec un seul Swiffer.

Joshi 2020 (25) *Prépublication* Expérience de simulation Inde Juin 2020	Étude qui a mesuré l'efficacité et la chute de pression du masque en installant le masque ou couvre-visage sur un tuyau en verre et en mesurant les particules en amont et en aval présentes dans l'échantillon. Les paramètres du test incluaient l'efficacité de capture des particules du matériau du masque, la chute de pression et le facteur d'ajustement (fuite). Des expériences ont été menées avec des aérosols faits de NaCl atomisé sur trois types de masques, soit le N95 commercial, le masque chirurgical et le masque en tissu (aucune information sur un matériau particulier utilisé).	- L'efficacité de filtration moyenne pour les particules de 0,3 µm pour le masque N95, le masque chirurgical et le masque en tissu était de 96,19 %, de 40,08 % et de 14,22 % respectivement. - L'efficacité de filtration pour les particules de moins de 0,3 µm n'a pas changé pour le N95 et les masques en tissu, mais les masques chirurgicaux pourraient, quant à eux, avoir une meilleure efficacité de filtration. - Les masques plus serrés avaient une plus grande efficacité de filtration. Ainsi, le N95, le masque chirurgical et le masque en tissu ont obtenu 95,60 %, 41,65 % et 13,79 %, comparativement à 95,08 %, 19,94 % et 11,67 %, respectivement, lorsque l'ajustement n'était pas aussi serré.
Sheets 2020 (27) *Prépublication* Expérience de simulation États-Unis Juin 2020	Étude qui utilise un débit constant d'air aérosolisé envoyé vers un mannequin test pour l'ajustement des masques et vers un essayeur de matériaux à pince afin de quantifier la perméabilité à l'air, l'efficacité de filtration et la sensibilité de l'ajustement d'un ensemble particulier de types de conceptions de masques et de filtres. Des capteurs de particules, de débit et de pression disponibles dans le commerce ont été utilisés pour mesurer la protection contre les aérosols aqueux d'une taille supérieure à 0,3 µm, ce qui a permis d'évaluer rapidement ces trois propriétés.	- Les masques N95 présentaient l'efficacité de filtration la plus élevée (> 95 %). - Le bandana tissé offrait peu de protection (< 15 %), mais avait une grande respirabilité. - Le masque chirurgical a une filtrabilité deux fois plus élevée qu'un bandana ayant la même respirabilité. - L'emballage pour stérilisation (un matériau non-tissé utilisé par les professionnels de la santé pour emballer les instruments chirurgicaux) a une plus grande efficacité de filtration que le masque chirurgical, mais est moins perméable à l'air. - La filtration des aérosols à travers le masque KN95 installé tel que reçu et correctement ajusté a démontré qu'un ajustement correct a réduit le nombre d'aérosols qui traversaient le masque de > 50 % à < 20 % lorsqu'il était bien ajusté.

Études sur les porte-filtres utilisés pour évaluer les caractéristiques de protection des matériaux utilisés dans la fabrication des masques (n = 20)		
Bayersdorfer 2020 (48) Expérience de simulation États-Unis Décembre 2020	Huit prototypes de masque ont été mis au point et testés en laboratoire. De ceux-ci, quatre ont été utilisés pour évaluer l'efficacité de filtration bactérienne (EFB) et la chute de pression alors que les l'efficacité de filtration des particules (EFP) a été évaluée avec les quatre autres.	- Les résultats en ce qui concerne l'EFB sont de 83,0 % à 97,7 % pour les masques simple épaisseur et de 96,3 % à 98,1 % pour les masques double épaisseur. - Les résultats pour l'EFP variaient de 92,3 % à 97,7 % pour les masques simple et double épaisseur.
Li 2020 (36) Expérience de simulation Chine Novembre 2020	Étude qui a évalué l'efficacité de filtration d'un masque triple épaisseur (fait avec deux serviettes de cuisine et des mouchoirs en papier quatre épaisseurs) comparativement à celle des masques médicaux sous flux laminaire dans un système de conduits d'air à plusieurs niveaux avec des aérosols de NaCl nébulisés de 6 à 220 nm.	- L'efficacité de filtration des masques faits maison était semblable à celle des masques médicaux pour les particules de 6 à 200 nm (84,54 % contre 86,94 %, P = 0,102).
Maher 2020 (47) Expérience de simulation États-Unis Octobre 2020	Étude qui a utilisé la concentration des gouttelettes d'aérosol, la différence de pression entre chaque matériau et les caractéristiques du débit d'air pour mesurer l'efficacité de filtration de 14 matériaux courants.	- Les résultats obtenus en ce qui concerne la concentration en aérosols ont indiqué que les matériaux divisaient les grosses particules en plusieurs particules plus petites. - Les couches multiples de tissu augmentaient l'efficacité du filtrage de 4 à 15 %, comparativement à une seule épaisseur du même tissu, mais cela diminuait la perméabilité à l'air et augmentait de 3 à 4 fois la différence de pression. Les masques triple épaisseur ont donc obtenu une pression 2 à 2,5 fois plus élevée que les masques double épaisseur.

		- Tous les matériaux multicouche testés avaient une efficacité de filtration > 95 % pour les aérosols de 1 µm à 4,7 µm.
Wang 2020 (51) Expérience de simulation Chine Octobre 2020	Étude réalisée en conformité avec la norme nationale chinoise qui oblige le port du « masque chirurgical » et a testé 17 matériaux pour en évaluer la différence de pression, l'efficacité de filtration des particules, l'efficacité de filtration bactérienne et la résistance à l'humidité de surface. Les matériaux testés comprenaient : t-shirt, chandail en molleton, manteau d'extérieur, manteau en duvet, vêtements de protection solaire, jeans, linge à vaisselle pelucheux, linge à vaisselle à texture granuleuse, sac à provisions non-tissé, sac pour aspirateur, couche, serviette hygiénique, taies d'oreiller, tissu médical non-tissé, gaze médicale.	- Parmi les onze matériaux simple épaisseur ont satisfait la norme de différence de pression (≥ 49 Pa), trois correspondaient à la norme de résistance à l'humidité de surface (≥ 3), un a satisfait la norme d'efficacité de filtration des particules (≥ 30 %), mais aucun ne répondait à la norme d'efficacité de filtration bactérienne (≥ 95 %). - Trois matériaux double épaisseur, y compris un tissu médical non-tissé, un tissu médical non-tissé et un sac à provisions non-tissé, et un tissu médical non-tissé et une serviette à thé à texture granuleuse, ont cependant obtenu des résultats proches de la norme d'efficacité de filtration bactérienne.
Long 2020 (50) Expérience de simulation États-Unis Octobre 2020	Étude qui décrit la conversion de l'équipement standard utilisé pour effectuer les tests d'ajustement des respirateurs en milieu hospitalier et industriel en une installation qui mesure l'efficacité de filtration quantitative des matériaux en fonction des lignes directrices du NIOSH pour les masques N95, ainsi que l'efficacité de filtration des matériaux que l'on retrouve dans le secteur des soins de santé et de consommation générique.	- L'efficacité de filtration des matériaux simple épaisseur variait entre 35 et 53 %. Deux matériaux (filtre à café et chiffon en coton) présentaient les plus faibles efficacités de filtration, tandis que le sac pour aspirateur, dont l'utilisation comme masque n'est pas sécuritaire, affichait la plus grande efficacité avec une efficacité de filtration de 82 %. - Des efficacités de filtration pouvant atteindre 90,37 % ont été déclarées pour les combinaisons de matériaux multicouche. - Tous les matériaux présentaient des valeurs Δp inférieures à la résistance maximale

		autorisée par le NIOSH pour les respirateurs (35 mm H_2O).
Whiley 2020 (40) Expérience de simulation Australie Septembre 2020	Étude qui a utilisé une méthode standard d'essai pour les masques (ASTM F2101-14) et la méthode avec bactériophage MS2 pour tester l'efficacité de filtration virale (EFV) des masques en tissu (achetés sur un site Web de vente au détail en ligne) comparativement aux masques jetables, chirurgicaux et N95 disponibles dans le commerce. Deux types d'aérosols de taille différente, soit 6 µm et 2,6 µm, ont été utilisés pour tester les masques. Ni le déroulement de cette étude ni les mesures qui y sont présentées ne sont normalisés. Il faut donc interpréter ces résultats avec prudence.	- Tous les masques en tissu présentaient une EFV d'au moins 50 % pour les aérosols de 6,0 µm. Ce taux est passé à 63 % pour les aérosols de 2,6 µm. - Les masques N95 et chirurgicaux avaient une efficacité de filtration supérieure à 99 %. - Un masque en coton avec filtre ajouté et un sac à provisions/masque en coton réutilisable ont obtenu des résultats aussi bons que ceux obtenus avec les masques médicaux (EFV d'environ 99 %). - Un masque triple épaisseur en chanvre, en polymembrane et en coton a également donné de bons résultats (EFV supérieure à 89 %).
Maurer 2020 (43) Expérience de simulation Allemagne Septembre 2020	Étude qui a évalué des masques de type communautaire fournis par de grands fabricants. L'efficacité de filtration a été déterminée avec des particules aérosol radioactives. La résistance à l'air (c.-à-d. la perméabilité à l'air) a été mesurée avec un pneumotachographe.	- Les efficacités de filtration (%) des matériaux étudiés, de la meilleure à la pire, étaient les suivantes : - Masques triple épaisseur : membrane médicale selon EN > Couche extérieure en tricot de polypropylène/polyamide, couche médiane en microfilaments de molleton et couche intérieure en polyester/polyamide > 100 % coton - Masques double épaisseur : 100 % coton biologique > coton/polyester > 100 % coton > polyamide/élasthanne > polyester et polypropylène avec molleton - Masques simple épaisseur : Texlyte Nano > polyester/carbone > 100 % coton > fil multifilament > 100 % polyester

		- Aucun des masques ou des couvre-visage de type communautaire n'était conforme aux normes européennes pour les masques médicaux (efficacité de filtration supérieure à 99 % et résistance de l'air inférieure à 40 Pa/cm^2). - Les masques triple épaisseur présentaient l'efficacité de filtration la plus élevée, mais avaient une respirabilité réduite. - En ce qui concerne l'efficacité de filtration, la qualité du tissu semble plus importante que le nombre d'épaisseurs (simple et double).
Pei, 2020 (55) Expérience de simulation États-Unis Septembre 2020	Étude qui visait à évaluer l'efficacité de filtration et la résistance à la respiration (chute de pression) des respirateurs et des masques commerciaux, ainsi que des matériaux domestiques courants. Tous les échantillons ont été coupés pour s'adapter au porte-filtre. L'efficacité fractionnelle a été mesurée avec des particules monodispersées de NaCl (entre 0,03 et 1 µm).	- Les masques électrets (filtre à charges électrostatiques) ont une efficacité de filtration de 70 à 85 % et l'efficacité augmente avec la taille des particules. - Les masques N95 et KN95 avaient une efficacité supérieure à 90 %. - L'efficacité de filtration des masques avec filtre non-électret était nettement inférieure à celle du masque avec filtre électret (aussi faible que 20 % pour les particules de 0,3 à 0,4 µm, mais qui augmente à 40 % pour 1 µm). - Tous les respirateurs et masques testés avaient une résistance respiratoire acceptable. - Les filtres pour aspirateur avaient une meilleure efficacité de filtration que le respirateur N95, mais ils avaient une résistance respiratoire 10 fois supérieure et se sont donc révélés peu pratiques comme matériau pour fabriquer des masques. - Parmi les textiles de maison courants, le Thinsulate double épaisseur, les draps cinq épaisseurs, les t-shirts et le Swiffer Sweeper avaient une efficacité d'environ 50 % pour les particules d'environ 0,3 µm. Leur efficacité

		pourrait être améliorée en ajoutant d'autres épaisseurs. La résistance à la respiration était élevée comparativement à un masque de procédure. - Deux épaisseurs de filtre à café offrent la pire efficacité de filtration et la pire résistance à la respiration.
Schilling 2020 (38) Expérience de simulation États-Unis Août 2020	Étude qui a examiné la filtration des aérosols et la respirabilité de 47 « masques non réglementaires » en utilisant des aérosols polydispersés. Elle a également évalué l'efficacité de filtration de six masques N95 et d'un certain nombre de masques non réglementaires. La filtration a été évaluée en fonction de la taille des particules (0,2 à 1 µm) à une vitesse de 10 cm/s et de la perméabilité à l'air en mesurant pour ce faire la chute de pression (en mm H_2O) sur un disque de 40 mm conçu avec le même matériau que celui du masque.	- L'efficacité de filtration des six masques N95 testés variait de 98 à 99 %. - Certains masques « non réglementaires » ont obtenu des efficacités de filtration semblables à celles du masque N95 pour les particules de 0,2µm et plus, alors que d'autres avaient des efficacités de filtration médiocres (c.-à-d. < 80 %). - Tous les masques étaient sous le seuil établi par le NIOSH pour la respirabilité, soit de 0,0247 mm $H_2O/(cm^3/s)$.
Hao 2020 (46) Expérience de simulation États-Unis Août 2020	Étude qui a évalué la filtration de matériaux non médicaux à des vitesses différentes. La perméabilité à l'air a été mesurée par la résistance à l'écoulement des matériaux. L'efficacité de filtration a été comparée à celle des masques médicaux, soit les masques N95, KN95 et chirurgicaux. Pour simuler différentes conditions respiratoires, des aérosols d'eau avec NaCl dispersés par nébuliseur ont été dirigés vers des matériaux	- L'efficacité de filtration du meilleur au pire était la suivante : masques N95 et KN95 > masque chirurgical > filtres à air > sacs pour aspirateur > filtre à charbon actif > taie d'oreiller 1 000 fils au pouce > filtre à café > taie d'oreiller 600 fils au pouce > quatre épaisseurs de foulard > taie d'oreiller à 400 fils au pouce > bandana. - Les tissus qui avaient des motifs de tissage plus denses ont offert une plus grande efficacité de filtration. Cette efficacité était cependant inversement liée à la respirabilité et à la vitesse croissante des particules.

	à des vitesses de 23,2, de 15,3 et de 9,2 cm/s-1.	
Drewnick 2020 (52) Expérience de simulation Allemagne Août 2020	Étude qui a évalué l'efficacité de filtration selon la taille des particules de 44 échantillons de textiles de maison et de plusieurs masques médicaux avec un nébuliseur produisant un aérosol de NaCl et avec un compteur de particules.	- D'énormes différences dans l'efficacité de filtration ont été observées tant entre les textiles de maison qu'en raison des tailles de particules, avec un écart allant de < 10 % à > 100 %. - Les matériaux ménagers comme le jersey bouclette, le molleton, la microfibre, le feutre, la mousseline ou le velours ont montré une efficacité de filtration élevée, tandis que des matériaux comme la popeline, la blouse de chirurgie ou la soie ont montré une efficacité de filtration moindre. - Une efficacité de filtration raisonnable peut être obtenue en empilant plusieurs épaisseurs, mais des fuites de seulement 1 à 2 % peuvent avoir un impact important sur l'efficacité de filtration.
Carnino 2020 (54) Expérience de simulation États-Unis Août 2020	Étude qui a évalué si un prétraitement à base de sel sur des tissus qui ont ensuite été asséchés permettait d'augmenter la capacité de filtration de l'essuie-tout de cuisine, de l'essuie-tout de laboratoire et de la couche filtrante centrale d'un masque chirurgical standard. Après un traitement avec des nanoparticules fluorescentes de taille similaire à celle du virus COVID-19, la pénétration des particules a été mesurée au microscope.	- En l'absence de traitement, les textiles de maison ont mal filtré les nanoparticules. - Lorsque ces textiles ont été trempés dans une solution de NaCl (+/- TWEEN20), la pénétration des nanoparticules était bloquée après seulement 10 minutes de traitement. - L'inhibition bactérienne a également été mentionnée.
Loupa 2020 (53) *Prépublication*	Étude qui a évalué huit masques disponibles dans le commerce afin d'en vérifier la filtrabilité à des aérosols d'un diamètre compris entre 0,006 µm et 10 µm. On a	- Les masques ou couvre-visages en tissu simples (avec deux épaisseurs de coton) ont obtenu l'efficacité de filtration la plus faible.

Expérience de simulation Grèce Juillet 2020	utilisé une vitesse égale à la fréquence respiratoire humaine. Cinq des masques avaient trois épaisseurs, un était un masque KN95 avec un « évent antiretour » et deux étaient des masques ou des couvre-visages en tissu.	- L'ajout de charbon actif dans un masque en coton a considérablement amélioré l'efficacité de filtration. - Mis à part le masque KN95, tous les autres masques étaient perméables aux aérosols de l'ordre de 0,25 à 0,5 µm (< 90 % d'efficacité de filtration).
Lammers 2020 (49) Expérience de simulation États-Unis Juillet 2020	Étude qui a évalué l'emballage chirurgical pour stérilisation dans un test automatisé pour filtre TSI 8130, comme cela est exigé pour le masque N95. Des couches simples et doubles de l'emballage ont été testées et comparées à l'évaluation d'imprégnation du masque N95.	- L'efficacité de filtration de l'emballage était de 64,5 % et de 78,3 % pour les épaisseurs simple et double, respectivement. Cela ne respectait pas les exigences d'essai standard pour un masque N95.
Varallyay 2020 (42) Expérience de simulation États-Unis Juillet 2020	Étude qui a évalué l'efficacité de filtration des textiles de maison courants avec une configuration de test d'ajustement et générateur de particules standard de diamètre médian (40 nm) et résistance du débit d'air avec un manomètre. Trois niveaux différents de superposition (1, 2 et 4) ont été testés.	- Le feutre de polyester a démontré la plus grande efficacité de filtration ($p < 0,0001$), supérieure à tous les matériaux 100 % coton testés, ainsi qu'aux masques chirurgicaux ($P < 0,05$). - La superposition a augmenté l'efficacité de filtration et la résistance au débit d'air ($p < 0,0001$ et $p < 0,01$, respectivement). - L'efficacité de filtration de divers matériaux tissés et de tricot variait. Elle est indiquée ici, de la plus grande à la plus faible, soit tissu en microfibre > linge à vaisselle > uniforme d'hôpital > molleton épais > chapeau en chamois > t-shirt > taie d'oreiller > matériel tissé sans plastique > foulard. - L'efficacité de filtration de divers matériaux non-tissés a également varié et figure ici, de la plus grande à la plus faible : masque N95 > sac pour aspirateur > masque chirurgical > feutre > essuie-tout de cuisine > blouse chirurgicale > mouchoirs en papier.

		- Le lavage et le séchage n'ont pas modifié de façon significative les performances de filtration.
Zhao 2020 (39) Expérience de simulation États-Unis Juin 2020	Étude qui a évalué les propriétés de filtration des matériaux naturels et synthétiques à l'aide d'un testeur de filtre automatisé à un débit de 32 L/min (semblable à la respiration humaine). L'efficacité de filtration est le pourcentage de particules de NaCl filtrées par le matériau alors que la chute de pression est la résistance de l'air à travers le matériau filtrant. Plus la pression est élevée, moins le matériau est perméable à l'air. Les auteurs font remarquer que leurs résultats diffèrent des travaux récents et que cela peut découler de différences dans l'instrumentation, la méthode d'essai et la source du matériel.	- Voici l'efficacité de filtration pour divers masques médicaux et textiles non médicaux, du meilleur au pire : masque N95 > chandail en coton > pantalon de sport > t-shirt > mouchoirs en papier > cache-couche en polyester > essuie-tout > matériau d'interface en polypropylène > housse d'oreiller > serviette en papier. - Certains des matériaux en coton présentaient des efficacités de filtration comparables à celles des masques médicaux ou des couvre-visages (p. ex., chandail et t-shirt en coton). - Les produits en papier peuvent être utilisés comme support jetable dans certains masques ou couvre-visage maison, mais leur performance dans des environnements très humides reste à examiner.
Zangmeister 2020 (45) Expérience de simulation États-Unis Juin 2020	Étude qui a évalué l'efficacité de filtration, la pression différentielle (ΔP), le facteur de qualité et les paramètres de fabrication de 32 tissus, y compris des échantillons multicouches et mixtes faits de mélanges naturels, synthétiques ou synthétiques naturels. Les matériaux ont fait l'objet de microimages et de tests avec des aérosols de NaCl de taille choisie, avec des diamètres de mobilité des particules variant entre 50 et 825 nm. La charge des particules a été neutralisée.	- Les tissus 100 % coton à teneur élevée ou modérée en fils et deux tissus synthétiques à teneur moyenne en fils sont ceux qui ont donné les meilleurs résultats. - L'efficacité de filtration de deux couches d'un tissu très performant (32 %) était inférieure à celle des emballages de qualité médicale à haute densité (86 %), du masque N95 (> 99,9 %) et du sac pour aspirateur HEPA (94 %). - Le tissu le moins filtrant était le polyester (chiffon léger), suivi du coton (mousseline), du polyester (tricot), de la rayonne et du mélange 65 % polyester/35 % coton. - L'efficacité de filtration et la ΔP augmentaient avec le nombre d'épaisseurs de tissu. Ainsi,

		les masques quatre épaisseurs ont dépassé la ΔP recommandée (perméabilité à l'air).
Amendola 2020 (23) Expérience de simulation Italie Mai 2020	Expérience qui a simulé l'action respiratoire en mesurant la distribution des particules d'aérosol à base aqueuse. L'efficacité de filtration moyenne indiquée tenait compte des particules ayant un diamètre supérieur à 0,28 µm. Les masques ou couvre-visages ont été testés tant pour l'inhalation que l'expiration. TNT= matériau non-tissé fait de polypropylène et de viscose à base de tissu	- Le masque médical a démontré une efficacité de filtration supérieure à 97 %. - Seuls les masques faciaux fabriqués avec trois épaisseurs constituées principalement de tissu non-tissé ont pu atteindre des valeurs supérieures à 95 %, y compris le TNT triple épaisseur et le TNT-coton-TNT.
Konda 2020 (44) Expérience de simulation États-Unis Avril 2020	Évaluation de l'efficacité de filtration de plusieurs tissus courants, y compris le coton, la soie, le chiffon, la flanelle, divers tissus synthétiques et leurs combinaisons à l'aide de particules d'aérosols de NaCl polydispersées dont la taille variait entre 10 nm et 10 µm. Pour simuler l'ajustement, on a percé des trous dans le tube de raccordement sur lequel le tissu était installé, ce qui a entraîné des ouvertures de ~0,5 à 2 % dans la zone d'échantillonnage active.	- Les plages ci-dessous représentent l'efficacité de filtration pour les particules de petite taille (< 300 nm) à plus grande taille (> 300 nm). - Un tissu de coton à contexture modérée (80 fils au pouce) a démontré une efficacité inférieure (entre 5 et 55 %) comparativement à un tissu de coton à contexture élevée (entre 65 et 90 %). - Une courtepointe, avec de la ouate de coton fibreuse, a offert une excellente efficacité de filtration (entre 80 et 90 %). - Contrairement aux tissus de coton, les trois tissus qui devraient posséder des charges électrostatiques, soit la soie, le chiffon et la flanelle, ont obtenu un meilleur rendement pour les plus petites particules (< 300 nm) que pour les plus grandes particules (> 300 nm). - L'augmentation du nombre de couches a augmenté l'efficacité de filtration.

		- Trois combinaisons hybrides ont été testées, soit une épaisseur de coton TPI 600 avec deux épaisseurs de soie, deux épaisseurs de chiffon et une épaisseur de flanelle. Toutes les combinaisons ont donné de bons résultats, avec une efficacité de filtration variant entre 80 % et 90 %, comparable à celle des masques N95. - Dans les tests où l'effet de « fuite » a été testé, les ouvertures ont réduit l'efficacité de filtration de 60 %.
Ma 2020 (37) Expérience de simulation Chine Mars 2020	Évaluation de l'efficacité de trois types de masques en utilisant le virus de la grippe aviaire pour simuler le coronavirus. Un nébuliseur a été utilisé pour produire des aérosols de taille inférieure à 5,0 um. Les parties supérieures des seringues de 60 ml ont été retirées, puis enveloppées dans des masques testés, soit une épaisseur de tissu de polyester, un masque maison fait d'une épaisseur de polyester et de quatre épaisseurs d'essuie-tout de cuisine, un masque chirurgical et un masque N95. Une éponge a été insérée dans la seringue derrière le masque pour recueillir les virus qui passaient à travers les masques.	- Comparativement au polyester simple épaisseur, le masque N95 a bloqué 99,98 % du virus, le masque chirurgical en a bloqué 97,14 % et le masque fait maison en a bloqué 95,15 %.

*Le lieu ou la date de l'étude a été estimé en fonction des affiliations des auteurs et/ou de la date de publication.

Méthodologie :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et dans les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Les résultats cumulatifs de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Des détails sur cette stratégie de recherche sont disponibles sur demande. Une recherche ciblée par mot-clé dans les titres et les résumés des articles a été effectuée dans ces bases de données et dans la liste en Excel. Les termes de recherche utilisés comprenaient : mask* OU (face ET cover*). Chaque référence de recherche originale potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue. Parmi les examens et synthèses de recherche de qualité variable portant sur la composition des masques ou des couvre-visages qui ont été sélectionnés, la plupart n'incluaient que la recherche pré-pandémique et ont donc été exclus de ce résumé car ils manquaient de recherches récentes. La présente revue contient des recherches originales publiées jusqu'au 2 décembre 2020.

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Annexe

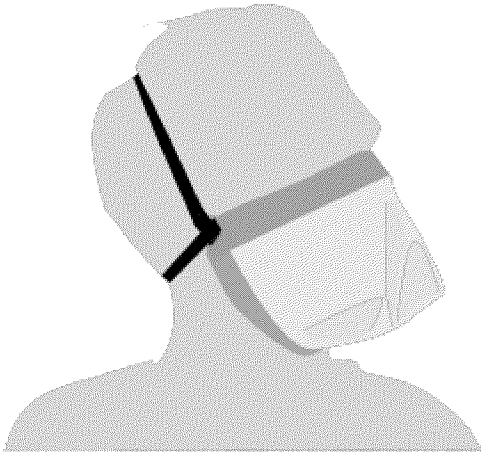

Figure 1. Conception d'un masque en forme de bec de canard. Source : (32)

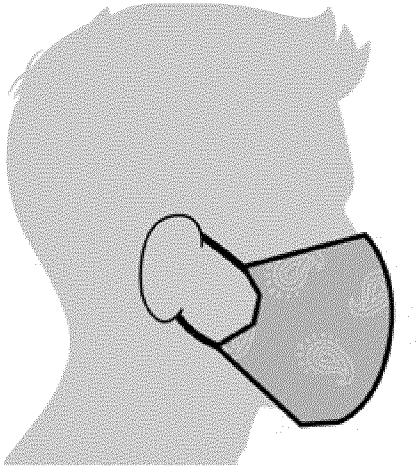

Figure 2. Conception d'un masque de style chirurgical. Source : (56)

Don't have Emerging Evidence on COVID-19

Evidence Brief of Multisystem Inflammatory Syndrome in Adults (MIS-A)

Introduction

What are the epidemiological and clinical characteristics of multisystem inflammatory syndrome in adults (MIS-A)?

Numerous cases of Multisystem Inflammatory Syndrome in Children (MIS-C) have been described worldwide since the beginning of the COVID-19 pandemic. More recently, clinical features similar to MIS-C have been described in adults. A definition for Multisystem Inflammatory Syndrome in Adults (MIS-A) does not exist; therefore, case selection has been based on the definition of MIS-C excluding the age criteria.

There are at least four definitions of MIS-C. The World Health Organisation (WHO) (1) definition of MIS-C includes children and adolescents below the age of 19, a positive COVID-19 test or likely contact with COVID-19 positive individuals and several signs and symptoms, which include fever lasting for more than 3 days and two of the following:

- Rash
- Bilateral non-purulent conjunctivitis
- Signs of muco-cutaneous inflammation signs (in the mouth or on the hands or feet)
- Hypotension or shock
- Myocardial dysfunction, pericarditis, valvulitis or coronary abnormalities (including echocardiogram findings or elevated Troponin/NT-proBNP)
- Coagulopathy (increased prothrombin time, activated partial thromboplastin time, elevated D-Dimers)
- Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

There must be laboratory evidence of inflammation, such as an elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), or procalcitonin, and other obvious microbial causes of inflammation such as bacterial sepsis, staphylococcal or streptococcal shock syndromes must be excluded as a plausible diagnosis.

The Centers for Disease Control (CDC) (2) Health Advisory defines an MIS-C case as an individual below the age of 21 presenting with fever lasting for more than 24 hours and laboratory evidence of inflammation such as an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin. The patient must also have an evidence of clinically severe illness requiring hospitalization, with multisystem organ involvement and no alternative plausible diagnoses. The patient must be positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or must have been exposed to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

According to the Royal College of Paediatrics and Child Health (RCPCH) (3) a case MIS-C is a child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopaenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with persistent fever over 38.5 °C, most of the time, oxygen requirement, hypotension, and other additional features. The laboratory tests must show abnormal fibrinogen, absence of potential causative organisms (other than SARS-CoV-2), high CRP, high D-Dimers, high ferritin, hypoalbuminaemia, and/or lymphopenia. This may include children fulfilling full or partial criteria for Kawasaki disease. Any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus must be excluded. The SARS-CoV-2 PCR testing may be positive or negative.

Finally, the Canadian Pediatric Society (CPS) (4) defines MIS-C as the presence of high and persistent fever (≥3 days) unexplained by other causes. Fever together with laboratory evidence of marked systemic inflammation and temporal association with COVID-19 having been present in the community should raise the index of suspicion for MIS-C. The clinical presentations described to date have included fever with hyperinflammation; a Kawasaki-like syndrome; and shock or toxic shock-like states, with signs of hypotension and poor perfusion related to severe myocardial dysfunction. GI distress, that may or may not occur with neurological signs such as neck stiffness, altered mental status, or lethargy.

This review describes the first reported cases of MIS-A in order to identify common features of the disease and raise the awareness of clinicians regarding the appropriate management of cases. It summarizes literature until November 13, 2020.

Key Points

Demographic characteristics, COVID status, and comorbidities

- All nine MIS-A cases described were relatively young adults, with a median age of 31 years and IQR [25-45]. Six cases (67%) were male (5-10) and three cases (33%) were female (11-13). Six out of nine studies reported ethnicity. Three cases (33%) had African origins (5,7,12), two cases (22%) were of Hispanic origin (10,13) one (11%) was Caucasian (9). In the three remaining cases (33%) ethnicity was not reported.
- All nine cases underwent a RT-PCR test. Five cases (56%) had negative RT-PCR results, but positive serology tests (5-7,9,13). One case (11%) had a negative PCR result with a history of a positive RT-PCR result a few days earlier (12). Results of RT-PCR swab test and serology were both positive in one case (11%)(11). The two remaining cases (22%) had a positive RT-PCR test but did not undergo serology test (8,10).These findings suggested that MIS-A generally occurred (n=6; 67%) during viral clearance.
- Seven out of nine studies reported on comorbidity. Two cases (22%) had both hypertension and obesity (5,12) of which one of them also had diabetes (12). Five cases (56%) had no known comorbidity (8,10,13) and in two (22%) the comorbidity status was not reported.

Clinical and laboratory findings

- All cases had fever; seven cases had fever for 5-7 days prior to hospital admission; two cases did not report on the duration of fever (4,11).
- The majority of cases (n=8; 89%) had digestive symptoms upon admission. The most common digestive symptom was diarrhea (n=6; 67%) followed by vomiting (n=4; 44%), rash (n=4; 44%) and neck pain (n=4; 44%) with or without lymphadenopathy. One case (11%) had bilaterally enlarged parotid glands.
- All cases had multi-organ involvement. Cardiovascular system involvement was the most common (n=7; 78%)(5,6,8-11,13), represented via echocardiography by acute myocardial dysfunction with left ventricular systolic dysfunction and pericardial effusion (n=4, 44%), ventricular fibrillation, dilated inferior vena cava (n=2; 22%) with overloaded right ventricular pressure and mild enlargement of the main pulmonary artery and hyperkinetic left ventricle (n=1; 11%).
- All cases had elevated inflammatory markers. The most common elevated inflammatory marker was C-reactive-protein CRP (n=8; 89%) (5,6,8-11), followed by D-dimers (n=6; 67%) (6,8,10-13) and troponin (n=6; 67%) (5-10). Lymphopenia was also common (n=6; 67%) (7-11).

Treatment and outcome

- Intravenous immunoglobulin (n=3; 33%) (7,10,11), prednisolone (n=3; 33%) (7,8,13) and aspirin (n=3; 33%) (6,11,13) were the most common treatments given. Immunoglobulin was not given in one case because the patient responded well to aspirin. In another case, prednisolone was not given because the patient had a concomitant tracheal aspiration positive for *Enterobacter aerogenes* that was then treated with Trimethoprim Sulfamethoxazole (5). One patient did not receive any specific treatment; as she died while being evaluated for admission and could not be resuscitated (12).
- Seven cases (77%) survived hospitalization. Three cases (33%) had severe symptoms, requiring admission to the ICU but recovered (5,6,11). Two cases (22%) presented with hypotension and tachycardia upon admission but did not require admission to intensive care unit (ICU) and recovered (9,10,13). One case (11%) presented with vasoplegic shock upon admission, had a length of stay (LOS) in hospital of 8 days and recovered under treatment (9). One case (11%) did not demonstrate shock-like signs and recovered under treatment (8). One case died in hospital (11%). The case that died had been previously hospitalized for COVID-19 and discharged 12 days earlier, upon readmission she presented with rapid onset of fever and developed hemodynamic instability and ventricular fibrillation and could not be resuscitated. The outcome of one patient (11%) was not reported (7).

Overview of the Evidence

Nine case reports of MIS-A were identified in the literature. Five cases were identified in the United-States, two in France and two in the United Kingdom. The case descriptions revealed similarities in clinical features such as occurrence after viral clearance, fever, digestive symptoms, cardiac involvement and elevated inflammatory markers. All cases where hospitalized, two required admission to the ICU and one died. The most common treatments were intravenous immunoglobulin, prednisolone and aspirin. The findings suggest early recognition of MIS-A may improve outcome.

Limitations

Only case reports were identified in this review. Although case reports can help in the identification of new trends or diseases, they have a number of limitations. They are difficult to compare since cases have different backgrounds and are not representative of a population. Therefore these findings are very preliminary; as more studies become available we will learn more about the common epidemiological and clinical characteristics of this condition.

Data gaps

It appears MIS-A is a rare complication of COVID-19 disease. Studies to date include a total of 9 MIS-A cases and were limited to three countries, United-States, France and the United-Kingdom. There is no definition of MIS-A; using the MIS-C case definition (minus age) has challenges as there are at least 4 definitions and in the cases reviewed, how they met the case definition was not always clear. For example, the authors did not always specify how they excluded all other potential causes of the multi system inflammatory syndrome and the duration of fever or presence of comorbidities were not always reported. More systematic description of ethnicity and Severity of the disease is needed. For example, when hypotension was identified, the presence or not of shock-like syndrome was not always specified.

A case definition for MIS-A is needed to help standardize reporting. Future studies of MIS-A are also indicated to learn more about this disease and the effectiveness of treatment.

Table: Summary of case reports on Multisystem Inflammatory Syndrome in Adults (MIS-A) (n=9)

STUDY	METHOD	KEY OUTCOMES
Case reports (n=9)		
Boudhabhay (2020) (5) Case report France 16 Sept 2020*	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met only RCPCH definition, since the duration of the fever was not specified.	*Demographic characteristics and past medical history* • The patient was a 46 years old male of African descent. • History of hypertension and obesity *MIS-A characteristics* Fever and other signs and symptoms • Admitted for hypertensive emergency (189/123 mmHg) and fever (duration not reported). Evidence of coagulopathy and renal involvement • Acute kidney injury (AKI): Serum creatinine (sCr) level was 169µmol/L associated with 1g per day proteinuria, aseptic pyuria, no hematuria and low natriuresis (< 20mmol/L) • Renal biopsy light microscopy revealed typical lesions of thrombotic micro angiopathy TMA including fibrin thrombi within glomeruli and myxoid intimal alterations of arterioles and small-to-medium sized renal arteries • On day four the patient presented evanescent facial erythema and developed acute myocardial dysfunction with reduced left ventricular ejection fraction to 40%, pericardial effusion. On day five the patient presented a neurological impairment. Abnormal supratentorial periventricular MRI signals responsible for a restriction of the diffusion due to an acute vasculitis. PCR and serology for SARS-CoV-2 • RT-PCR negative, IgM negative and IgG positive (no previous COVID-19 symptoms were reported) Inflammatory markers • C-Reactive protein (CRP) level was 312 mg/L • Thrombocytopenia: neutrophil count was 18.7 G/L • High sensitive Troponin (hsTroponin) elevation

		Treatment • No immunosuppressive treatment was introduced because of concomitant tracheal aspiration positive for *Enterobacter aerogenes* treated with trimethoprim sulfamethoxazole. • Dobutamine and renal replacement therapy (RRT). • Specific complement inhibition with Eculizumab therapy (900mg) *Severity and outcome* • On day 5 hospitalization neurological impairment appeared with coma leading to intubation and mechanical ventilation. • The patient was discharged after 30 days in hospital.
Chowdhary (2020) (6) Case report United Kingdom Sept 2020*	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met RCPCH, CDC, CPS and WHO definitions.	*Demographic characteristics and past medical history* • 26 years old male • Ethnicity was not reported. • The presence or absence of comorbidity was not reported. • Exposure to SARS-CoV-2 was reported. *MIS-A characteristics* Fever and other signs and symptoms • Patient was admitted after five days of fever • Dry cough, myalgia, diarrhoea, vomiting, and abdominal pain • Patient was hypotensive and hypoxic upon admission One or more organ involved (pulmonary, cardiac, digestive) • Computed tomography (CT) showed bilateral pulmonary basal ground-glass changes and bowel oedema • Initial transthoracic echocardiography demonstrated severe left ventricular (LV) systolic dysfunction with pericardial effusion. • CT of the abdomen demonstrating mesenteric lymphadenopathy and small bowel oedema PCR and serology for SARS-CoV-2 • RT-PCR negative, IgG and IgM positive serology Inflammatory markers • C-reactive protein (CRP) 419 mg/L • Ferritin 3275 lg/L (<322 µg/L)

		• Procalcitonin 164 lg/L (<50 µg/L) • Troponin I 2030 ng/L (<57 ng/L) • D-dimer 2722 ng/mL (<220 ng/mL) Treatment • Vasopressor therapy, high-dose aspirin, and broad-spectrum antibiotics in intensive care • Immunomodulatory therapy was not given due to the good response to aspirin. *Severity and outcome* • The case was admitted to ICU and recovered over 10 days.
Fox (2020) (12) Case report United States July 2020*	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met only RCPCH definition, since the duration of the fever was not specified.	*Demographic characteristics and past medical history* • The patient was a 31 years old African American female. • Comorbidities: hypertension with lisinopril, diabetes with poor adherence to metformin and glizide, and obesity (BMI=36.1 kg/m^2) • She had been discharged 12 days earlier after a hospitalization for COVID-19 disease with a positive RT-PCR. *MIS-A characteristics* • Admitted for sudden fever 39.8 °C (duration not specified), tachycardia 120 beats/min, left-sided neck pain, nausea and vomiting Inflammatory markers • D-dimer level of 2.48 nmol/L • C-reactive protein levels 165 mg/L then 580 mg/L • Ferritin level, 114.2 µg/L • Lactic acid level, 3.1 mmol/L • Lymphopenia One or more organ involved (pulmonary, cardiac, parotids, renal) • Computed tomography scan of her neck showed bilaterally enlarged parotid glands and swelling in the posterior nasopharynx to oropharynx. • Computed tomography scan of her chest showed interval improvement of bibasilar ground-glass opacities, with cervical and anterior mediastinal lymphadenopathy

		• Creatinine level 202.44 µmol/L; glomerular filtration rate 32 mL/min/1.73 m^2 PCR and serology for SARS-CoV-2 • RT-PCR was positive 12 days prior to re-admission MISC-A, RT-PCR was negative at re-admission and serology was not performed *Treatment, severity and outcome* • Patient developed hemodynamic instability and ventricular fibrillation during evaluation for hospital admission and died.
Jones (2020)(7) Case report United Kingdom The date the study was conducted was not reported Sept 2020*	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met RCPCH, CDC, CPS and WHO definitions.	*Demographic characteristics and past medical history* • The case was a 21 years old male of African descent. • The presence or absence of comorbidity was not reported. *MIS-A characteristics* Fever and other signs or symptoms • 6 days of fever • Admitted for abdominal pain associated with constipation, anorexia • Transient maculopapular palmar rash 4 days into illness • Non-exudative conjunctivitis, • Cervical lymphadenopathy, • Cracked lips, and prominent lingual papillae PCR and serology for SARS-CoV-2 • RT-PCR negative and serology was strongly positive, suggesting recent exposure to SARS-CoV-2 One organ or more involved • Rash • Conjunctivitis • Cervical lymphadenopathy • Cracked lips, and prominent lingual papillae Inflammatory markers • Lymphopenia • Elevated inflammatory and elevated troponin T • Other infective and inflammatory conditions were excluded

		Treatment • Intravenous immunoglobulin • Methylprednisolone *Severity and outcome* • The patient was discharged after a length of stay in hospital of 8 days.
Kofman(2020) (11) Case report United States The date the study was conducted was not reported Sept 2020*	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met RCPCH, CDC, CPS and WHO definitions.	*Demographic characteristics and past medical history* • The case was a 25 years old female. • Ethnicity was not reported. • She was non-smoker, not a drug user, no medications, no known allergies. • She had taken ibuprofen and acetaminophen over the prior week for symptomatic relief. *MIS-A characteristics* Fever and other signs and symptoms • One week of low grade fever, weakness, dyspnea, fatigue • Also developed mild cough, sore throat, vomiting, diarrhea, and lymph node swelling • Upon admission o She was afebrile, with mild hypotension (blood pressure 98/56 mmHg) o Oxygen saturation was normal on room air. o She appeared ill, with tender cervical lymphadenopathy o Significant conjunctival injection without perilimbal sparing; injected, erythematous, and cracked lips o Tenderness to palpation in the left lower abdominal quadrant One or more organ involved (renal, cardiac, digestive, ocular) • Acute kidney injury: Creatinine 7.74 mg/dL (Normal: 0.5 -1.2 mg/dL) and leukocytosis • Point-of-care echocardiogram revealed a dilated inferior vena cava andoverloaded right ventricular pressure • CT angiogram of the chest showed mild enlargement of the main pulmonary artery • CT abdomen/pelvis demonstrated mild peripancreatic fat stranding, felt to possibly represent acute uncomplicated

		pancreatitis, as well as nonspecific bilateral perinephric fat stranding • Conjunctivitis PCR and serology for SARS-CoV-2 • Positive RT-PCR and IgG serology Inflammatory markers • C-reactive protein 90 mg/L (Normal: 0-10 mg/L) • D-dimer 960 mg/L (Normal : 0-574 mg/L) • Ferritin 798 ng/ml (Normal : 11-307 ng/ml) • Lymphocytes 3% (Normal: 19-53) Treatment: • Aggressive fluid resuscitation and vasopressor • Intravenous immunoglobulin (IVIG), 2 g/kg split equally between hospital days 2 and 3 • Aspirin 325 mg daily for 7 days • Patient was offered remdesivir under an Emergency Use Authorization (EUA) basis, but declined • At discharge she was prescribed a 7-day course of apixaban for COVID-19-associated coagulopathy per Emory University Hospital COVID-19 treatment guidelines Severity and outcome • The patient was admitted to ICU twice during her hospital stay and was discharged day 5.
Lidder (2020) (8) Case report United States May 2020	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met RCPCH, CDC, CPS and WHO definitions.	*Demographic characteristics and past medical history* • The case was a 45 years old male with no comorbidities. • Ethnicity was not reported. *MIS-A characteristics* Fever and other signs and symptoms • He had fever for 5 days, sore throat, diarrhea, eye redness, eyelid swelling, and a diffuse rash including bilateral upper and lower eyelids. One or more organ involved (renal, cardiac, digestive, ophthalmological)

		• A transthoracic echocardiogram demonstrated global hypokinesis and a reduced ejection fraction of 40%.
		• CT imaging showed unilateral cervical lymphadenopathy with a lymph node measuring 1.8 cm.
		• Photophobia and swollen eyelids. No vision changes including blurry vision and eye pain.
		• Uncorrected near visual acuity was 20/20 bilaterally
		  ○ Bilateral superficial punctate keratitis, symmetric anterior chamber (AC) inflammation with 10–15 cells per high power field, and normal intraocular pressure. Dilated fundus exam was notable only for one small peripheral cotton wool spot in each eye.
		• Punch biopsy of his erythema multiforme-like rash
		  ○ Showed sparse superficial perivascular infiltrate of lymphocytes with neutrophils and scattered eosinophils, suggestive of toxic shock syndrome.
		
		Excluding other cause
		• Testing for myositis and HIV was negative.
		• An exhaustive rheumatologic workup including ANA, RF, anti-CCP, anti-Smith, anti-dsDNA, p-ANCA/MPO, c-ANCA/PR3 was also negative.
		• Blood cultures were negative.
		
		PCR and serology for SARS-CoV-2
		• Positive RT-PCR
		
		Inflammatory markers
		• Lymphopenia
		• Ferritin, CRP, ESR, D-dimer and troponin were elevated
		
		Treatment:
		• Ophthalmic lubricating therapy in addition to prednisolone acetate 1% eye drops four times daily for his photophobia in the setting of AC inflammation
		• IVIG and an IL-6 inhibitor (tocilizumab) in addition to using a topical triamcinolone ointment for his diffuse rash

		Severity and outcome • The length of stay in hospital was not reported but the patient did not demonstrate shock-like signs.

Moghadam (2020) (9)
 	
Case report
 	
France
 	
The date the study was conducted was not reported
 	
July 2020*
	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome.
	
	The case met RCPCH, CDC and WHO definitions.
		Demographic characteristics and past medical history
		• The case was a 21 years old Caucasian male.
		• The presence or absence of comorbidity was not reported.
		
		MIS-A characteristics
		Fever and other signs and symptoms
		• He had fever and non-bloody watery diarrhea lasting for 7 days.
		• Asymptomatic rash over his trunk and palms, consisting of erythematous round-shaped macules with a darker and raised rim, 1-3 cm in diameter
		• Bilateral conjunctivitis
		• Blood pressure 80/40 mmHg
		• Respiratory rate was 38 breaths/min, and oxygen saturation was 97% on ambient air
		
		One or more organ involved (cardiac, digestive, pleural)
		• Electrocardiogram showed diffuse negative T waves, and echocardiography displayed hyperkinetic left ventricle with normal ejection fraction, normal right cavities, and dilated non-compressible inferior vena cava.
		• Thoraco-abdominal computed tomography (CT) scan did show
		  ○ Signs of congestive heart failure
		  ○ Bilateral pleural effusion
		  ○ Wall thickening of the right colon
		• Respiratory function deterioration
		
		PCR and serology for SARS-CoV-2
		• Negative RT-PCR and IgG positive serology
		
		Inflammatory markers
		• Lymphocytes of 900/mm3
		• C-reactive protein 365 mg/L
		• Procalcitonin was 3.4 ng/mL
		• Ferritin was 1282 mg/L (normal <30)
		• Lactate 2.4 mmol/L (normal <1.6)

		• Troponin level was 550 ng/L (normal <34) • Cutaneous biopsy showed a slightly inflammatory infiltrate in upper dermis, and direct cutaneous immunofluorescence was negative. Exclusion of other causes • Patient denied any drug intake • He did not smoke tobacco, or use illicit drugs • Extensive infectious inquiry and search for antinuclear antibodies were negative • The rash was particular and diagnosis of erythema multiforma and subacute lupus erythematosus were ruled out. Treatment: • Volume resuscitation • Noradrenaline • Antibiotics (ie, ceftriaxone and amikacin) • High-flow nasal oxygenation Severity and outcome • The length of stay in ICU was 8 days.
Sokolovsky(2020) (13) Case report United States The date the study was conducted was not reported June 2020*	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met RCPCH, CDC, CPS and WHO definitions.	*Demographic characteristics and past medical history* • The case was a 36 years old Hispanic female. • She had no known comorbidity. *MIS-A characteristics* Fever and other signs and symptoms • One week of fever, abdominal pain, vomiting, and diarrhea • Two days of a diffuse rash and arthralgias • Tachycardia, tachypnea, hypotensive • Classic phenotype of complete Kawasaki's Disease: bilateral nonexudative conjunctivitis mucositis wit cracked lips, edema of the bilateral hands and feet; a diffuse maculopapular rash and cervical lymphadenopathy One or more organ involved (cardiac, digestive) • CT angiogram of the chest: normal lung parenchyma and a trace right pleural effusion

		• CT abdomen/pelvis illustrated mild circumferential gallbladder wall thickening and a small area of colitis • Echocardiogram after treatment with ○ IVIG revealed an EF of 65% with moderate tricuspid valve regurgitation. Subsequent CTA coronaries was normal except for a trace pericardial effusion. PCR and serology for SARS-CoV-2 • Negative RT-PCR and IgG positive serology Inflammatory markers • CRP: 30 mg/dL (0.0–0.9) • D-dimer: 652 ng/mL (<318) Exclusion of other cause • Anti-dsDNA, anti-smith, anti-RNP, SSB, RF, CCP, ANCA, ASO, and anti-Jo-1 antibodies were negative • HIV and hepatitis panels were negative Treatment: • Fluid resuscitation for shock • A single dose of aspirin 650 mg • IVIG 2 g/kg • Methylprednisolone 2 mg/kg for 5 days followed by a prednisone taper Severity and outcome • She stayed at least 6 days in hospital.
Shaigany (2020) (10) Case report United States The date the study was conducted was not reported	A case of MIS-A was described, including clinical and laboratory characteristics, treatment and outcome. The case met RCPCH, CDC,	*Demographic characteristics and past medical history* • The case was a 45 years old Hispanic male. • He had no known comorbidity. *MIS-A characteristics* Fever and other signs and symptoms • Six days of fever, sore throat, diarrhoea, bilateral lower extremity pain, conjunctivitis, and diffuse exanthema • Exposure to SARS-CoV-2 infection 2 weeks earlier • Respiratory rate was 25–33 breaths per min • Hypotension (systolic blood pressure 80–90 mm Hg)

July 2020	CPS and WHO definitions.	• Tachycardia with episodes of atrial fibrillation with rapid ventricular response
		• Bilateral, nonexudative conjunctival injection,
		• Tender left neck swelling with palpable lymphadenopathy, periorbital oedema with overlying erythema, lip cheilitis, and targetoid erythematous papules and plaques with central duskiness involving the back, palms, neck, scalp, anterior trunk, and upper thighs
		
		One or more organ involved (renal, cardiac, digestive, ophthalmological)
		• CT of the neck revealed inflammation and oedema involving the bilateral lower eyelid and pre-septal space, as well as sub-occipital reactive lymphadenopathy.
		• Electrocardiogram demonstrated:
		  ○ ST elevations in the anterolateral leads,
		  ○ Global hypokinesis of the left ventricular wall with a mild to moderately reduced ejection fraction of 40%
		• Diffuse conjunctivitis with chemosis, as well as the presence of inflammatory cells within the anterior chamber, indicative of uveitis
		• A 4-mm punch biopsy of the skin was performed on a papule on the back, with histology revealing rare intraepithelial collections of neutrophils with necrotic keratinocytes and a sparse interstitial, mixed-cell dermal infiltrate with vacuolar interface changes.
		
		PCR and serology for SARS-CoV-2
		• Positive RT-PCR
		
		Inflammatory markers
		• Lymphopenia (0–700 lymphocytes per µL)
		• Erythrocyte sedimentation rate of 120 mm/hr
		• Ferritin of 21 196 ng/mL
		• C-reactive protein of 546·7 mg/L
		• D-dimer of 2977 ng/mL
		• Procalcitonin of 31·79 ng/mL
		• Interleukin-6 (IL-6) 117 pg/mL
		• Troponin 8·05 g/mL)

		Exclusion of other causes • HIV-1 and HIV-2 antibodies were negative • Bacterial blood cultures were negative Treatment: • Therapeutic dose low molecular weight heparin • Intravenous immunoglobulin (2 g/kg) over 2 days • A single intravenous dose of the IL-6 inhibitor tocilizumab (400 mg) Severity and outcome • The patient was 8 days in hospital and did not require vasopressor support or intensive care unit level of care.

*The date was based on the publication date as the date the case occurred was not reported

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: "MIS-A", "Kawasaki", "multisystem inflame", "multi-system inflam", "inflammatory multisystem", "inflammatory multi-system", and "inflammatory disease" , "Kawasaki-like", "COVID-19 linked disease. This review contains research published up to November 13, 2020.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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Nouveaux éléments de preuve sur la COVID-19

Sommaire des éléments de preuve sur le syndrome inflammatoire multisystémique chez l'adulte (MIS-A)

Introduction

Quelles sont les caractéristiques épidémiologiques et cliniques du syndrome inflammatoire multisystémique chez l'adulte (MIS-A) ?

Depuis le début de la pandémie de COVID-19, de nombreux cas de syndrome inflammatoire multisystémique chez les enfants (MIS-C) à l'échelle mondiale ont été décrits. Plus récemment, des caractéristiques cliniques similaires à celles du MIS-C ont été signalées chez les adultes. Comme il n'existe aucune définition du syndrome inflammatoire multisystémique chez l'adulte (MIS-A); la sélection des cas a donc été basée sur la définition du MIS-C, en excluant les critères d'âge.

Il existe au moins quatre définitions du MIS-C. La définition du MIS-C selon l'Organisation mondiale de la santé (OMS) (1) comprend les enfants et les adolescents de moins de 19 ans, un test COVID-19 positif ou un contact probable avec des personnes positives à la COVID-19, ainsi que plusieurs signes et symptômes, dont une fièvre qui dure plus de 3 jours et deux des éléments suivants :

- Éruption
- Conjonctivite bilatérale non purulente
- Signes d'inflammation muco-cutanée (dans la bouche ou sur les mains ou les pieds)
- Hypotension ou choc
- Dysfonctionnement du myocarde, péricardite, valvulite ou anomalies coronariennes (notamment constatation suite à un échocardiogramme ou niveau élevé de troponine/NT-proBNP)
- Coagulopathie (augmentation du temps de prothrombine, temps de thromboplastine partielle activée, D-dimères élevés)
- Troubles gastro-intestinaux aigus (diarrhées, vomissements ou douleurs abdominales).

Il est nécessaire de disposer de résultats de laboratoire indiquant une inflammation, tels qu'une augmentation de la vitesse de sédimentation des érythrocytes (VS), du taux de protéine C réactive (CRP) ou de la procalcitonine, et d'exclure les autres causes microbiennes évidentes d'inflammation telles que la septicémie bactérienne, les syndromes de choc staphylococcique ou streptococcique, comme diagnostic plausible.

Un avis de santé publique émis par les centres de contrôle des maladies (CDC) (2) définit un cas de MIS-C comme étant un individu de moins de 21 ans présentant une fièvre de plus de 24 heures accompagnée de signes inflammatoires attestés par des résultats de laboratoire tels qu'une augmentation du taux de protéine C-réactive (CRP), de la vitesse de sédimentation des érythrocytes (VS), du taux de fibrinogène, de la procalcitonine, des D-dimères, de la ferritine, de l'acide lactique déshydrogénase (LDH) ou de l'interleukine 6

(IL-6), ainsi qu'une hausse du nombre de neutrophiles, des lymphocytes réduits et une faible teneur en albumine. Le patient doit également présenter les signes d'une maladie cliniquement grave nécessitant une hospitalisation, avec une atteinte multisystémique des organes et sans autre diagnostic plausible. La contamination actuelle ou récente du patient par le CoV-2 - SRAS doit avoir été établie par RT-PCR, sérologie ou test d'antigène; ou le patient doit avoir été exposé à un cas suspecté ou confirmé de COVID-19 dans les 4 semaines précédant l'apparition des symptômes.

Selon le Royal College of Paediatrics and Child Health (RCPCH) (3), un cas de MIS-C est un enfant présentant une fièvre persistante, une inflammation (neutrophilie, CRP élevée et lymphopénie) ainsi que des signes de dysfonctionnement d'un ou de plusieurs organes (choc, trouble cardiaque, respiratoire, rénal, gastro-intestinal ou neurologique) avec le plus souvent, une fièvre persistante supérieure à 38,5 °C, un besoin en oxygène, une hypotension et d'autres caractéristiques. Les tests de laboratoire doivent indiquer un taux de fibrinogène anormal, une absence d'organismes potentiellement responsables (autres que le SRAS-CoV-2), une augmentation de la CRP élevée, des D-dimères, de la ferritine, une hypoalbuminémie et/ou une lymphopénie. Cela peut concerner des enfants qui remplissent tous ou certains des critères de la maladie de Kawasaki. Toute autre cause microbienne, notamment la septicémie bactérienne, les syndromes de choc staphylococcique ou streptococcique, les infections associées à la myocardite telles que l'entérovirus doivent être exclues. Le test PCR pour le SRAS-CoV-2 peut être positif ou négatif.

Enfin, la Société canadienne de pédiatrie (SCP) (4) définit la MIS-C comme caractérisée par une fièvre élevée et persistante (≥3 jours) inexpliquée par d'autres causes. La fièvre associée à des résultats de laboratoire attestant d'une inflammation systémique marquée et à un lien temporel avec la présence de COVID-19 dans la communauté sont des indices qui doivent orienter le diagnostic vers un éventuel MIS-C. Les cas cliniques décrits à ce jour comprennent de la fièvre associée à une hyperinflammation, un syndrome de Kawasaki et des états de choc ou de choc toxique, avec des signes d'hypotension et de mauvaise perfusion liés à un dysfonctionnement myocardique grave. Les troubles gastro-intestinaux, susceptibles ou non de se manifester, peuvent être accompagnés de symptômes neurologiques tels qu'une raideur de la nuque, une altération de l'état mental ou une léthargie.

Cette étude décrit les premiers cas de MIS-A signalés afin d'identifier les caractéristiques communes de la maladie et de sensibiliser les cliniciens à la gestion appropriée des cas. Il résume la littérature jusqu'au 13 novembre 2020.

Points clés

Caractéristiques démographiques, COVID et facteurs de comorbidité

- Les neuf cas de MIS-A décrits concernaient tous des adultes relativement jeunes, dont l'âge médian était de 31 ans et l'EI était [25-45]. Six cas (67 %) étaient des hommes (5-10) et trois cas (33 %) étaient des femmes (11-13). Six études sur neuf faisaient état de l'ethnicité. Trois cas (33 %) étaient d'origine

africaine (5,7,12) deux cas (22 %) étaient d'origine hispanique (10,13) un cas (11 %) était de type caucasien (9). Pour les trois autres cas (33 %), l'appartenance ethnique n'a pas été signalée.

- Les neuf cas ont été soumis à un test RT-PCR. Le test RT-PCR était négatif pour cinq cas (56 %), mais leurs tests sérologiques étaient positifs (5-7,9,13). Un cas (11 %) a obtenu un résultat PCR négatif associé à un historique de résultat RT-PCR positif quelques jours plus tôt (12). Les résultats du test RT-PCR et de la sérologie étaient positifs pour un cas (11 %)(11). Les deux cas restants (22 %) ont obtenu un test RT-PCR positif, mais n'ont pas été soumis à un test sérologique (8,10) ■ Ces résultats suggèrent que le MIS-A s'est globalement déclaré (n=6; 67 %) pendant la clairance virale.
- Sept études sur neuf ont rapporté l'existence de facteurs de comorbidité. Deux cas (22 %) présentaient à la fois de l'hypertension et des problèmes d'obésité (5,12) et l'un d'entre eux était également diabétique (12). Cinq cas (56 %) ne présentaient aucun facteur de comorbidité connu (8,10,13) et dans deux cas (22 %), la présence de facteurs de comorbidité n'a pas été indiquée.

Résultats cliniques et de laboratoire

- Tous les cas présentaient de la fièvre; pour sept cas la fièvre a duré de 5 à 7 jours avant leur admission à l'hôpital; deux cas n'ont pas indiqué la durée de la fièvre (4,11).
- La majorité des cas (n=8; 89 %) présentaient des symptômes digestifs à l'admission. Le symptôme digestif le plus fréquent était la diarrhée (n=6; 67 %), suivi par des vomissements (n=4; 44 %), des éruptions cutanées (n=4; 44 %) et des douleurs cervicales (n=4; 44 %) avec ou sans lymphadénopathie. Un cas (11 %) présentait une hypertrophie bilatérale des glandes parotides.
- Tous les cas impliquaient plusieurs organes. L'atteinte du système cardiovasculaire était la plus fréquente (n=7; 78 %)(5,6,8-11,13), elle était représentée par échocardiographie et caractérisée par un dysfonctionnement myocardique aigu avec dysfonctionnement systolique du ventricule gauche et épanchement péricardique (n=4, 44 %), fibrillation ventriculaire, veine cave inférieure dilatée (n=2; 22 %) avec pression ventriculaire droite surchargée et léger élargissement de l'artère pulmonaire principale et ventricule gauche hyperkinétique (n=1; 11 %).
- Tous les cas présentaient un niveau élevé des marqueurs inflammatoires. Le marqueur inflammatoire élevé le plus courant était la protéine C-réactive CRP (n=8; 89 %) (5,6,8-11), suivi par les D-dimères (n=6; 67 %) (6,8,10-13) et la troponine (n=6; 67 %) (5-10). La lymphopénie était également fréquente (n=6; 67 %) (7-11).

Traitement et résultats

- L'immunoglobuline par intraveineuse (n=3; 33 %) (7,10,11), la prednisolone (n=3; 33 %) (7,8,13) et l'aspirine (n=3; 33 %) (6,11,13) ont été les traitements les plus couramment administrés. Dans un cas,

l'immunoglobuline n'a pas été administrée, car le patient a bien répondu à l'aspirine. Dans un autre cas, la prednisolone n'a pas été administrée, car le patient était sous aspiration trachéale concomitante en raison de la contamination par *Enterobacter aerogenes* qui a ensuite été traitée avec du Triméthoprime Sulfaméthoxazole (5). Une patiente n'a pas reçu de traitement spécifique, car elle est décédée pendant l'évaluation en vue de son admission et n'a pas pu être réanimée (12).

- Sept cas (77 %) ont survécu à l'hospitalisation. Trois cas (33 %) présentaient des symptômes graves, nécessitant une admission en soins intensifs, mais ils se sont rétablis (5,6,11). Deux cas (22 %) présentaient une hypotension et une tachycardie à l'admission, mais n'ont pas nécessité d'être admis en unité de soins intensifs (USI) et se sont rétablis (9,10,13). Un cas (11 %) présentait un choc vasoplégique à l'admission, son séjour à l'hôpital a duré 8 jours et il s'est rétabli sous traitement (9). Un cas (11 %) ne présentait aucun signe de choc et s'est rétabli sous traitement (8). Un cas est mort à l'hôpital (11 %). Le patient décédé avait été hospitalisé pour la COVID-19 et avait quitté l'hôpital 12 jours plus tôt. Lors de sa réadmission, il a subi une brusque poussée de fièvre puis a développé une instabilité hémodynamique et une fibrillation ventriculaire, il n'a pas pu être réanimé. L'issue de l'état de santé d'un patient (11 %) n'a pas été communiquée (7).

Vue d'ensemble des éléments de preuve

Neuf cas de MIS-A ont été identifiés dans la littérature. Cinq cas ont été identifiés aux États-Unis, deux en France et deux au Royaume-Uni. Les descriptions des cas ont révélé des similitudes dans les caractéristiques cliniques telles que la déclaration du syndrome après la clairance virale, de la fièvre, des troubles digestifs, l'atteinte cardiaque et un niveau anormalement élevé des marqueurs inflammatoires. Tous les cas ont été hospitalisés, deux ont nécessité une admission en soins intensifs et un est décédé. Les traitements les plus couramment administrés ont été l'immunoglobuline par intraveineuse, la prednisolone et l'aspirine. Les résultats indiquent qu'une reconnaissance précoce du MIS-A pourrait améliorer les chances des patients.

Limites

Seuls des rapports de cas ont été identifiés dans le cadre de cette étude. Bien qu'ils puissent contribuer à identifier de nouvelles tendances ou maladies, les rapports de cas présentent un certain nombre de limites. Il est difficile d'établir une comparaison, car les origines des cas sont différentes et ils ne sont pas représentatifs d'une population. Ces résultats sont donc très préliminaires; à mesure que d'autres études seront disponibles, nous en apprendrons davantage sur les caractéristiques épidémiologiques et cliniques communes de cette maladie.

Lacunes dans les données

Il semble que le MIS-A soit une complication rare de la maladie COVID-19. Les études menées à ce jour portent sur un total de 9 cas de MIS-A et ont été limitées à trois pays, les États-Unis, la France et le Royaume-Uni. Il n'existe aucune définition du MIS-A; l'utilisation de la définition des cas de MIS-C (sans tenir compte de l'âge)

est problématique, car il existe au moins 4 définitions et dans les cas examinés, la manière dont ils ont répondu à la définition de cas n'était pas toujours claire. Par exemple, les auteurs n'ont pas toujours précisé la manière dont ils excluaient toutes les autres causes potentielles du syndrome inflammatoire multisystémique, et la durée de la fièvre ou la présence de facteurs de comorbidité n'étaient pas toujours signalées. Une description plus systématique de l'ethnicité et de la gravité de la maladie est nécessaire. Par exemple, lorsque l'hypotension a été identifiée, la présence ou non d'un syndrome de choc n'a pas toujours été précisée.

Une définition de cas du MIS-A est nécessaire pour contribuer à normaliser le signalement. Il est également indiqué que de futures études portent sur le MIS-A pour en savoir plus sur cette maladie et sur l'efficacité du traitement.

Tableau : Résumé des rapports de cas sur le syndrome inflammatoire multisystémique chez l'adulte (MIS-A) (n=9)

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Rapports de cas (n=9)		
Boudhabhay (2020) (5) Rapport de cas France 16 Sept 2020*	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait uniquement à la définition du RCPCH, puisque la durée de la fièvre n'était pas précisée.	*Caractéristiques démographiques et antécédents médicaux* • Le patient était un homme de 46 ans, d'origine africaine. • Antécédents d'hypertension et d'obésité *Caractéristiques du MIS-A* Fièvre et autres signes et symptômes • Admis pour une urgence hypertensive (189/123 mmHg) et de la fièvre (durée non précisée). Coagulopathie et atteinte rénale établies • Lésion rénale aiguë (AKI) : le taux de créatinine sérique (sCr) était de 169 µmol/L associé à 1 g par jour de protéinurie, pyurie aseptique, absence d'hématurie et faible natriurèse (< 20 mmol/L) • La biopsie rénale au microscope optique a révélé des lésions typiques de la microangiopathie thrombotique (MAT), notamment des thrombus de fibrine dans les glomérules et des altérations de l'intimité myxoïde des artérioles et des artères rénales de petite et moyenne taille • Le quatrième jour, le patient a présenté un érythème facial évanescent et a développé un dysfonctionnement myocardique aigu avec une diminution de 40 % de la fraction d'éjection ventriculaire gauche, un épanchement péricardique. Le cinquième jour, le patient a développé une déficience neurologique. Signaux d'IRM périventriculaires supratentoriels anormaux responsables d'une restriction de la diffusion due à une vascularite aiguë. PCR et sérologie pour le SRAS-CoV-2 • Test RT-PCR négatif, test IgM négatif et test IgG positif (aucun symptôme antérieur de la COVID-19 n'a été signalé) Marqueurs inflammatoires • Le niveau de protéine C réactive (CRP) était de 312 mg/L • Thrombocytopénie : le nombre de neutrophiles était de 18,7 G/L

		• Augmentation du dosage de troponine hautement sensible (hsTroponine) *Traitement* • Aucun traitement immunosuppresseur n'a été administré en raison d'une aspiration trachéale concomitante positive pour une contamination par *Enterobacter aerogenes* traitée avec du triméthoprime sulfaméthoxazole. • Dobutamine et thérapie de remplacement rénal (TRR). • Inhibition du complément spécifique avec thérapie à l'Eculizumab (900 mg) *Gravité et résultats* • Au cinquième jour de l'hospitalisation, une atteinte neurologique est apparue avec un coma entraînant une intubation et une ventilation mécanique. • Le patient a reçu son congé au bout de 30 jours d'hospitalisation.
Chowdhary (2020) (6) Rapport de cas Royaume-Uni Sept 2020*	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait uniquement aux définitions du RCPCH, des CDC, du CPS et de l'OMS.	*Caractéristiques démographiques et antécédents médicaux* • Homme de 26 ans • L'origine ethnique n'a pas été indiquée. • La présence ou l'absence de facteurs de comorbidité n'a pas été communiquée. • Une exposition au SRAS-CoV-2 a été signalée. *Caractéristiques du MIS-A* Fièvre et autres signes et symptômes • Le patient a été admis après cinq jours de fièvre • Toux sèche, myalgie, diarrhée, vomissements et douleurs abdominales • Au moment de son admission, le patient était hypotendu et hypoxique Un ou plusieurs organes étaient atteints (système pulmonaire, cardiaque, digestif) • La tomographie informatisée a indiqué la présence de plages de verre dépoli bilatérales basales et un œdème intestinal

		• L'échocardiographie transthoracique initiale a mis en évidence un dysfonctionnement systolique grave du ventricule gauche (VG) avec épanchement péricardique. • Le CT de l'abdomen a révélé une lymphadénopathie mésentérique et un œdème de l'intestin grêle PCR et sérologie pour le SRAS-CoV-2 • Sérologie RT-PCR négative, IgG et IgM positive Marqueurs inflammatoires • Protéine C-réactive (CRP), 419 mg/L • Ferritine, 3 275 lg/L (<322 µg/L) • Procalcitonine, 164 lg/L (<50 µg/L) • Troponine I, 2 030 ng/L (<57 ng/L) • D-dimères, 2 722 ng/mL (<220 ng/mL) Traitement • Thérapie vasopressive, aspirine à forte dose et antibiotiques à large spectre en soins intensifs • La thérapie immunomodulatoire n'a pas été administrée en raison de la bonne réaction à l'aspirine. *Gravité et résultats* • Le cas a été admis en USI et a été récupéré en 10 jours.
Fox (2020) (12) Rapport de cas États-Unis Juillet 2020*	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait uniquement à la définition du RCPCH, puisque la durée de la	*Caractéristiques démographiques et antécédents médicaux* • La patiente était une Afro-Américaine de 31 ans. • Facteurs de comorbidité : hypertension avec lisinopril, diabète avec mauvaise adhérence à la metformine et au glizide, et obésité (IMC = 36,1 kg/m2) • Elle avait reçu son congé 12 jours plus tôt, après une hospitalisation pour maladie de COVID-19 avec un RT-PCR positif. *Caractéristiques du MIS-A* • Admis pour fièvre soudaine 39,8 °C (durée non précisée), tachycardie 120 battements/min, douleur au cou du côté gauche, nausées et vomissements Marqueurs inflammatoires

	fièvre n'était pas précisée.	• Dosage des D dimères, 2,48 nmol/L • Taux de protéine C réactive, 165 mg/L, puis 580 mg/L • Niveau de ferritine, 114,2 µg/L • Niveau d'acide lactique, 3,1 mmol/L • Lymphopénie Un ou plusieurs organes atteints (système pulmonaire, cardiaque, parotidien, rénal) • La tomographie informatisée de son cou a révélé une hypertrophie bilatérale des glandes parotides et un gonflement du nasopharynx postérieur à l'oropharynx. • La tomographie informatisée de sa poitrine a indiqué une amélioration de l'intervalle des plages de verre dépoli bilatérales basales, avec une lymphadénopathie médiastinale cervicale et antérieure • Taux de créatinine 202,44 µmol/L; taux de filtration glomérulaire 32 mL/min/1,73 m^2 PCR et sérologie pour le SRAS-CoV-2 • La RT-PCR était positive 12 jours avant la réadmission pour MISC-A, la RT-PCR était négative à la réadmission et la sérologie n'a pas été effectuée *Traitement, gravité et résultats* • La patiente a développé une instabilité hémodynamique et une fibrillation ventriculaire pendant l'évaluation en vue de son admission à l'hôpital et elle est décédée.
Jones (2020)(7) Rapport de cas Royaume-Uni La date à laquelle l'étude a été menée n'a pas été communiquée	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait uniquement aux	*Caractéristiques démographiques et antécédents médicaux* • Le cas concernait un homme de 21 ans d'origine africaine. • La présence ou l'absence de facteurs de comorbidité n'a pas été communiquée. *Caractéristiques du MIS-A* Fièvre et autres signes ou symptômes • 6 jours de fièvre • Admis pour des douleurs abdominales associées à une constipation, de l'anorexie • Éruption palmaire maculopapuleuse transitoire 4 jours après le début de la maladie

Sept 2020*	définitions du RCPCH, des CDC, du CPS et de l'OMS.	• Conjonctivite non exsudative, • Lymphadénopathie cervicale, • Lèvres fendues et papilles linguales proéminentes PCR et sérologie pour le SRAS-CoV-2 • RT-PCR négative et sérologie fortement positive, ce qui suggère une exposition récente au SARS-CoV-2 Un ou plusieurs organes atteints • Éruption • Conjonctivite • Lymphadénopathie cervicale • Lèvres fendues et papilles linguales proéminentes Marqueurs inflammatoires • Lymphopénie • Niveau élevé des marqueurs inflammatoires et de la troponine T • Les autres causes infectieuses et inflammatoires ont été exclues Traitement • Immunoglobuline en intraveineuse • Méthylprednisolone *Gravité et résultats* • Le patient a reçu son congé de l'hôpital au bout de 8 jours.
Kofman(2020) (11) Rapport de cas États-Unis La date à laquelle l'étude a été menée n'a pas été communiquée	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait uniquement aux définitions du	*Caractéristiques démographiques et antécédents médicaux* • Le cas comprenait une femme de 25 ans. • L'origine ethnique n'a pas été indiquée. • Elle ne fumait pas, ne se droguait pas, ne prenait pas de médicaments et n'avait pas d'allergies connues. • Elle avait pris de l'ibuprofène et de l'acétaminophène au cours de la semaine précédente pour soulager ses symptômes. *Caractéristiques du MIS-A* Fièvre et autres signes et symptômes • Une semaine de fièvre légère, accompagnée de faiblesse, dyspnée et fatigue

Sept 2020*	RCPCH, des CDC, du CPS et de l'OMS.	• Elle a également développé une légère toux, un mal de gorge, des vomissements, de la diarrhée et un gonflement des ganglions lymphatiques
		• Lors de l'admission
		  ○ Elle était fébrile, avec une légère hypotension (pression sanguine 98/56 mmHg)
		  ○ La saturation en oxygène était normale dans l'air ambiant.
		  ○ Elle semblait malade et présentait une lymphadénopathie cervicale sensible
		  ○ Injection conjonctivale importante sans épargner le périlimbe; lèvres injectées, érythémateuses et fissurées
		  ○ Sensibilité à la palpation dans le quadrant inférieur gauche de l'abdomen
		
		Un ou plusieurs organes étaient atteints (système rénal, cardiaque, digestif, oculaire)
		• Lésion rénale aiguë : Créatinine, 7,74 mg/dL (normal : 0,5 - 1,2 mg/dL) et leucocytose
		• L'échocardiogramme au point de service a révélé une dilatation de la veine cave inférieure et une surcharge de la pression ventriculaire droite
		• L'angiographie CT du thorax a indiqué une légère hypertrophie de l'artère pulmonaire principale
		• Le scanner de l'abdomen et du bassin a mis en évidence une légère infiltration de graisse péripancréatique, qui pourrait représenter une pancréatite aiguë sans complication, ainsi qu'une infiltration de graisse périnéphrétique bilatérale non spécifique
		• Conjonctivite
		
		PCR et sérologie pour le SRAS-CoV-2
		• Sérologie RT-PCR et IgG positive
		
		Marqueurs inflammatoires
		• Protéine C-réactive, 90 mg/L (normal : 0-10 mg/L)
		• D-dimères,960 mg/L (normal : 0-574 mg/L)
		• Ferritine, 798 ng/ml (normal : 11-307 ng/ml)
		• Lymphocytes, 3 % (normal : 19-53)

		Traitement : • Réanimation liquidienne énergique et vasopresseur • Immunoglobuline en intraveineuse (IVIG), 2 g/kg répartis à parts égales entre les jours d'hospitalisation 2 et 3 • Aspirine, 325 mg par jour pendant 7 jours • La patiente s'est vu proposer le remdesivir dans le cadre d'une autorisation d'utilisation d'urgence (AUE), mais a refusé • À sa sortie, on lui a prescrit un traitement de 7 jours d'apixaban pour la coagulopathie associée à la COVID-19, conformément aux directives de traitement de la COVID-19 de l'hôpital universitaire Emory Gravité et résultats • La patiente a été admise deux fois en soins intensifs pendant son séjour à l'hôpital et a reçu son congé le cinquième jour.
Lidder (2020) (8) Rapport de cas États-Unis Mai 2020	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait uniquement aux définitions du RCPCH, des CDC, du CPS et de l'OMS.	*Caractéristiques démographiques et antécédents médicaux* • Le cas concernait un homme de 45 ans sans facteurs de comorbidité. • L'origine ethnique n'a pas été indiquée. *Caractéristiques du MIS-A* Fièvre et autres signes et symptômes • Il a eu de la fièvre pendant 5 jours, un mal de gorge, de la diarrhée, une rougeur des yeux, un gonflement des paupières et une éruption diffuse comprenant les paupières supérieures et inférieures bilatérales. Un ou plusieurs organes atteints (système rénal, cardiaque, digestif, ophtalmologique) • Un échocardiogramme transthoracique a révélé une hypokinésie globale et une diminution de 40 % de la fraction d'éjection. • La tomodensitométrie a indiqué une lymphadénopathie cervicale unilatérale avec un ganglion lymphatique de 1,8 cm. • Photophobie et gonflement des paupières. Aucune modification de la vision, y compris vision floue et douleurs oculaires.

		• L'acuité visuelle de près non corrigée était de 20/20 des deux côtés
		  ○ Kératite ponctuée superficielle bilatérale, inflammation symétrique de la chambre antérieure (CA) avec 10-15 cellules par champ de haute puissance, et pression intraoculaire normale. L'examen du fond d'œil dilaté notable uniquement pour une petite tâche périphérique d'ouate dans chaque œil.
		• Biopsie par perforation de son érythème polymorphe
		  ○ Présence d'un infiltrat périvasculaire superficiel épars lymphocitaire avec dispersion de neutrophiles et d'éosinophiles, suggérant un syndrome de choc toxique.
		
		À l'exclusion de toute autre cause
		• Les tests de dépistage de la myosite et du VIH étaient négatifs.
		• Le bilan rhumatologique exhaustif incluant les ANA, RF, anti-CCP, anti-Smith, anti-ADN, p-ANCA/MPO, c-ANCA/PR3 était également négatif.
		• Les hémocultures étaient négatives.
		
		PCR et sérologie pour le SRAS-CoV-2
		• Test RT-PCR positif
		
		Marqueurs inflammatoires
		• Lymphopénie
		• Dosage élevé de ferritine, CRP, ESR, D-dimères et troponine
		
		Traitement :
		• Thérapie ophtalmique lubrifiante en plus de l'acétate de prednisolone 1 % en gouttes oculaires quatre fois par jour pour sa photophobie dans le cadre de l'inflammation AC
		• IVIG et un inhibiteur de l'IL-6 (tocilizumab) en plus de l'utilisation d'une pommade topique à base de triamcinolone pour son éruption diffuse
		
		Gravité et résultats

		• La durée du séjour à l'hôpital n'a pas été communiquée, mais le patient n'a présenté aucun signe de choc.
Moghadam (2020) (9) Rapport de cas France La date à laquelle l'étude a été menée n'a pas été communiquée Juillet 2020*	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait aux définitions du RCPCH, des CDC et de l'OMS.	*Caractéristiques démographiques et antécédents médicaux* • Le cas concernait un homme caucasien de 21 ans. • La présence ou l'absence de facteurs de comorbidité n'a pas été communiquée. *Caractéristiques du MIS-A* Fièvre et autres signes et symptômes • Il a eu de la fièvre et une diarrhée aqueuse non sanglante pendant 7 jours. • Éruption asymptomatique sur le tronc et les paumes des mains, consistant en macules érythémateuses de forme ronde avec un bord plus foncé et surélevé, de 1 à 3 cm de diamètre • Conjonctivite bilatérale • Tension artérielle 80/40 mmHg • La fréquence respiratoire était de 38 respirations/min, et la saturation en oxygène était de 97 % dans l'air ambiant Un ou plusieurs organes étaient atteints (système cardiaque, digestif, pleural) • L'électrocardiogramme a révélé des ondes T négatives diffuses, et l'échocardiographie a indiqué un ventricule gauche hyperkinétique avec une fraction d'éjection normale, des cavités droites normales et une veine cave inférieure dilatée et non compressible. • La tomodensitométrie thoraco-abdominale (CT) a indiqué o Des signes d'insuffisance cardiaque congestive o Un épanchement pleural bilatéral o Un épaississement de la paroi du côlon droit • Détérioration de la fonction respiratoire PCR et sérologie pour le SRAS-CoV-2 • Sérologie RT-PCR négative et IgG positive Marqueurs inflammatoires • Lymphocytes de 900/mm3 • Protéine C réactive, 365 mg/L • La procalcitonine était de 3,4 ng/mL

		• La ferritine était de 1 282 mg/L (normale <30) • Lactate, 2,4 mmol/L (normal <1,6) • Le taux de troponine était de 550 ng/L (normal <34) • La biopsie cutanée a révélé un infiltrat légèrement inflammatoire dans le derme supérieur, et l'immunofluorescence cutanée directe était négative. Exclusion d'autres causes • Le patient s'est vu refuser toute prise de médicament • Il ne fumait pas de tabac et ne consommait pas de drogues illicites • L'analyse infectieuse approfondie et la recherche d'anticorps antinucléaires n'ont donné aucun résultat • L'éruption était particulière et le diagnostic d'érythème polymorphe et de lupus érythémateux subaigu a été écarté. Traitement : • Volume réanimation • Noradrénaline • Antibiotiques (ceftriaxone et amikacine) • Oxygénation nasale à haut débit Gravité et résultats • Le séjour en USI a duré 8 jours.
Sokolovsky(2020) (13) Rapport de cas États-Unis La date à laquelle l'étude a été menée n'a pas été communiquée Juin 2020*	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le traitement et le résultat. Le cas satisfaisait uniquement aux définitions du RCPCH, des	*Caractéristiques démographiques et antécédents médicaux* • Le cas concernait une femme hispanique de 36 ans. • Elle ne présentait aucun facteur de comorbidité connu. *Caractéristiques du MIS-A* Fièvre et autres signes et symptômes • Une semaine de fièvre, de douleurs abdominales, de vomissements et de diarrhée • Deux jours d'éruption diffuse et d'arthralgies • Tachycardie, tachypnée, hypotension • Phénotype classique de la maladie de Kawasaki complète : conjonctivite mucosite bilatérale non exsudative avec lèvres fissurées, œdème bilatéral des mains et des pieds; éruption maculopapuleuse diffuse et lymphadénopathie cervicale

	CDC, du CPS et de l'OMS.	Un ou plusieurs organes étaient atteints (système cardiaque, digestif) • Angiographie CT du thorax : parenchyme pulmonaire normal et trace d'épanchement pleural droit • Le scanner de l'abdomen et du bassin a révélé un léger épaississement de la paroi circonférentielle de la vésicule biliaire et une petite zone de colite • Échocardiogramme après traitement par o IVIG a révélé une FE de 65 % avec une régurgitation modérée de la valve tricuspide. Les coronaires CTA subséquents étaient normaux, à l'exception d'une trace d'épanchement péricardique. PCR et sérologie pour le SRAS-CoV-2 • Sérologie RT-PCR négative et IgG positive Marqueurs inflammatoires • CRP : 30 mg/dL (0,0-0,9) • D-dimères : 652 ng/mL (<318) Exclusion d'une autre cause • Le dosage des anticorps anti-ADNdb, anti-Smith, anti-RNP, SSB, RF, CCP, ANCA, ASO et anti-Jo-1 était négatif • Les panels de VIH et hépatite étaient négatifs Traitement : • Réanimation liquidienne pour choc • Une dose unique d'aspirine 650 mg • IVIG 2 g/kg • Méthylprednisolone 2 mg/kg pendant 5 jours, suivi d'une cure de prednisone Gravité et résultats • Elle est restée au moins 6 jours à l'hôpital.
Shaigany (2020) (10) Rapport de cas États-Unis	Un cas de MIS-A a été décrit, il comprenait les caractéristiques cliniques et de laboratoire, le	*Caractéristiques démographiques et antécédents médicaux* • Le cas concernait un homme hispanique de 45 ans. • Il ne présentait aucun facteur de comorbidité connu. *Caractéristiques du MIS-A* Fièvre et autres signes et symptômes

La date à laquelle l'étude a été menée n'a pas été communiquée Juillet 2020	traitement et le résultat. Le cas satisfaisait uniquement aux définitions du RCPCH, des CDC, du CPS et de l'OMS.	• Six jours de fièvre, de maux de gorge, de diarrhée, de douleurs bilatérales aux membres inférieurs, de conjonctivite et d'exanthème diffus • Exposition à l'infection par le SRAS-CoV-2 2 semaines plus tôt • La fréquence respiratoire était de 25-33 respirations par minute • Hypotension (pression artérielle systolique 80-90 mm Hg) • Tachycardie avec épisodes de fibrillation auriculaire et réponse ventriculaire rapide • Injection conjonctivale bilatérale, non exsudative, • Gonflement sensible de la partie gauche du cou avec lymphadénopathie palpable, œdème périorbitaire avec érythème sus-jacent, chéilite labiale et papules et plaques érythémateuses ciblées avec crépuscule central touchant le dos, les paumes, le cou, le cuir chevelu, le tronc antérieur et le haut des cuisses Un ou plusieurs organes étaient atteints (système rénal, cardiaque, digestif, ophtalmologique) • Le scanner du cou a révélé une inflammation et un œdème impliquant les deux paupières inférieures et l'espace pré-septal, ainsi qu'une lymphadénopathie réactive sous-occipitale. • L'électrocardiogramme a révélé : o Élévations ST dans les voies antérolatérales, o Hypokinésie globale de la paroi ventriculaire gauche avec une diminution légère à modérée de 40 % de la fraction d'éjection • Conjonctivite diffuse avec chimiose et présence de cellules inflammatoires dans la chambre antérieure, indiquant une uvéite • Une biopsie cutanée à l'aide d'un poinçon de 4 mm a été réalisée sur une papule dans le dos, l'histologie a révélé de rares collections intraépithéliales de neutrophiles avec des kératinocytes nécrosés et un infiltrat cutané interstitiel peu abondant à cellules mixtes avec des modifications de l'interface vacuolaire. PCR et sérologie pour le SRAS-CoV-2

		• Test RT-PCR positif Marqueurs inflammatoires • Lymphopénie (0-700 lymphocytes par µL) • Vitesse de sédimentation des érythrocytes de 120 mm/h • Ferritine de 21 196 ng/mL • Protéine C-réactive de 546-7 mg/L • D-dimères de 2 977 ng/mL • Procalcitonine de 31-79 ng/mL • Interleukine-6 (IL-6) 117 pg/mL • Troponine 8-05 g/mL) Exclusion d'autres causes • Le dosage des anticorps du VIH-1 et du VIH-2 était négatif • Les hémocultures bactériennes étaient négatives Traitement : • Héparine de faible poids moléculaire à dose thérapeutique • Immunoglobuline en intraveineuse (2 g/kg) sur 2 jours • Une dose unique de tocilizumab en intraveineuse, un inhibiteur de l'IL-6 (400 mg) Gravité et résultats • Le patient a été hospitalisé pendant 8 jours et n'a pas eu besoin de soutien vasopresseur ou de niveau de soins d'unité de soins intensifs.

*La date est basée sur la date de publication, car la date à laquelle le cas s'est déclaré n'a pas été communiquée

Méthodes :

Un balayage quotidien de la littérature (publiée et pré-publiée) est effectué par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont effectuées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et croisées avec les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste excel qui peut être consultée. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur COVID-19 et SARS-COV-2. Les termes de recherche utilisés comprenaient : « MIS-A »,

« Kawasaki », « multisystem inflame », « multi-system inflam », « inflammatory multisystem », « inflammatory multi-system », et « inflammatory disease », « Kawasaki-like », « COVID-19 linked disease ». Cette étude contient les recherches publiées jusqu'au 13 novembre 2020.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle contenait des données pertinentes et les données pertinentes sont extraites dans l'étude.

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Nouvelles données probantes sur la COVID-19

Examen rapide du syndrome inflammatoire multisystémique chez les enfants (MIS-C)

INTRODUCTION

Quelles sont les caractéristiques épidémiologiques du syndrome inflammatoire multisystémique chez les enfants?

L'objectif de cet examen est de résumer les caractéristiques épidémiologiques du syndrome inflammatoire multisystémique chez les enfants, également appelé le Paediatric Inflammatory Multisystem Syndrome (PIMS). Le syndrome inflammatoire multisystémique chez les enfants est une maladie émergente qui a été identifiée lors de la pandémie de COVID-19. Des cas d'enfants présentant des signes de la maladie de Kawasaki suite à un résultat positif à un test de dépistage de la COVID-19 ont été signalés pour la première fois au Royaume-Uni le 27 avril 2020 (1). Des définitions de cas ont depuis été publiées par l'Organisation mondiale de la santé (2), les Centres de contrôle et de prévention des maladies des États-Unis (3) et le Royal College of Paediatrics and Child Health au Royaume-Uni (4). Comme l'illustre l'annexe, les trois définitions de cas sont similaires, mais pas identiques.

Dans cet examen, le nom syndrome inflammatoire multisystémique chez les enfants (MIS-C) est utilisé pour des raisons de cohérence, mais il désigne globalement le syndrome connu sous le nom de PIMS. Il n'existe pas de test de diagnostic définitif pour le MIS-C. Il est considéré comme un syndrome distinct, mais apparenté à la forme complète, incomplète ou atypique de la maladie de Kawasaki, au Kawasaki disease shock syndrome (KDSS), au syndrome de choc toxique (SCT) et au syndrome d'activation macrophagique, avec de nombreuses caractéristiques qui se chevauchent (5). L'examen comprend des données probantes provenant d'articles où l'une des trois définitions a été appliquée, ou la maladie de Kawasaki ou un syndrome inflammatoire lié à la COVID-19 a été diagnostiqué.

La grande majorité des articles sur le MIS-C étaient des rapports de cas et des études par cohorte. Pour donner une indication approximative de la solidité des données probantes, les articles ont ensuite été organisés en trois catégories : important, moyen et petit, en fonction du nombre de patients atteints du MIS-C présentés dans l'article ≥50, 6-49 et ≤5, respectivement. Les résultats liés à l'épidémiologie du MIS-C ont été résumés, notamment : les données démographiques des patients atteints de MIS-C (âge, sexe, origine ethnique/race et comorbidités), les résultats de gravité commune (admission en unité de soins intensifs [USI], ventilation mécanique et utilisation de l'oxygénation extracorporelle), la mortalité liée au MIS-C et le moment par rapport à la forme grave de la COVID-19. Notez que des cas similaires de syndrome inflammatoire multisystémique ont été signalés chez les adultes (connu sous le nom de MIS-A), qui font l'objet d'un examen séparé disponible sur demande : phac.evidence-donnees.probantes.aspc@canada.ca

POINTS CLÉS

Il y a eu 102 articles recensés. Onze articles étaient des vastes études de cohortes, décrivant chacune plus de 50 cas de MIS-C. Quarante-trois articles étaient de taille moyenne, décrivant chacun 6 à 49 cas de MIS-C. Quarante-huit articles étaient des rapports de cas où le nombre de cas de MIS-C décrits allait de un à cinq.

Prévalence parmi les cas de COVID-19 chez les enfants

Une vaste étude internationale menée sur plusieurs emplacements a estimé que le MIS-C touchait entre 0,5 % et 3,1 % de tous les enfants ayant un diagnostic de COVID-19 et entre 0,9 % et 7,6 % des enfants atteints de la COVID-19 hospitalisés et âgés de moins de 18 ans (6). Trois autres articles ont examiné la fréquence du MIS-C parmi les cas de COVID-19 chez les enfants hospitalisés, avec des estimations variant de 6 % au Pérou (7) à 9 % et 11 % aux États-Unis (8,9).

Âge

Le MIS-C peut toucher les enfants de tout âge, comme l'indiquent les intervalles entre les articles. Cependant, l'âge médian des cas était de 7 à 11 ans. Cela a été constant avec les articles importants, moyens et petits.

Sexe

Dans les articles importants, moyens et petits, de 57 à 58 % des cas étaient de sexe masculin.

Comorbidités

Dans les articles qui ont fait état de comorbidités, la définition de la comorbidité était incohérente. La comorbidité la plus souvent signalée est l'obésité. Les taux d'obésité étaient cohérents, mais plus faibles dans les petits articles (8 %) que dans les articles moyens (22 %) et importants (24-29 %). Une autre comorbidité courante était l'asthme (6 à 18 %). Les patients présentant au moins une comorbidité allaient de 19 % lorsque l'obésité était exclue à 29 % lorsque l'obésité était incluse. Peu d'articles ont comparé les taux d'une comorbidité donnée à la prévalence de cette comorbidité dans la population pédiatrique générale. Un article a révélé que la proportion de patients atteints du MIS-C et obèses est légèrement plus élevée que celle rapportée dans la population avec des problèmes sous-jacents (10).

Aucun article n'a tenté de démêler la relation entre une condition donnée, l'infection à la COVID-19 et le développement du MIS-C. Par exemple, les enfants obèses ou asthmatiques pourraient être plus susceptibles de contracter la COVID-19, et seraient donc surreprésentés dans les cas de MIS-C, sans être spécifiquement prédisposés au MIS-C. Cette relation est largement inexplorée et doit être étudiée davantage.

Origine ethnique

Bien que certains articles aient traité de l'origine ethnique ou de la race, peu d'entre eux ont fourni des comparaisons avec la composition de la population avec des problèmes sous-jacents. Cependant, dans 14 articles de taille moyenne des États-Unis, les enfants noirs et hispaniques représentaient la plus grande partie des patients, avec respectivement 36 % et 29 %. Un important article des États-Unis fait état de

données démographiques similaires (33 % hispaniques et 27 % noirs) (10). Les Centres de contrôle et de prévention des maladies des États-Unis indiquent que, par rapport aux Blancs, les Noirs ont 2,6 fois plus de risques et les Hispaniques 2,8 fois plus de risques d'être infectés par la COVID-19 (11). Cela peut expliquer en partie ou en totalité les taux disproportionnellement élevés de MIS-C parmi ces populations. Cette relation complexe doit être étudiée davantage.

Déclenchement du MIS-C par rapport à l'infection par le SRAS-CoV-2

Les données de cas cliniques suggèrent qu'il y a un retard dans l'apparition du MIS-C après une infection grave causée par le SRAS-CoV-2. Dans trois articles qui ont documenté le moment de l'infection de la forme grave de la COVID-19 pour chaque patient du MIS-C, l'apparition du MIS-C est survenue de 15 à 24 jours après l'apparition des symptômes de la forme grave de la COVID-19. Une poignée d'articles (n=6) ont déterminé que le délai entre le pic des cas de MIS-C était d'environ deux à cinq semaines après le pic des cas de COVID-19 à l'échelle de l'état ou du pays. Le retard dans l'apparition des symptômes est encore renforcé par les faibles taux de positivité (<50 %) avec le modèle RT-PCR par rapport au test sérologique d'anticorps IgG (>75 %). Cela suggère que le MIS-C est souvent un syndrome après-infection, ayant une apparition retardée après la forme grave de la COVID-19.

Résultats de la gravité

Les données probantes suggèrent que les patients atteints de MIS-C ont souvent besoin de soins intensifs, mais que le taux de survie global est élevé. Huit importants articles ont fait état d'un taux d'admission aux soins intensifs de 21 à 80 %, ce qui correspond à un taux de 65 % pour les articles de taille moyenne et de 74 % pour les petits articles. En outre, entre 25 et 40 % des cas de MIS-C ont été intubés et de 5 à 11 % ont nécessité une oxygénation extracorporelle. Dans les articles importants, le taux de mortalité variait de 0 à 2,2 % des patients hospitalisés et 2,6 % des patients atteints du MIS-C admis aux soins intensifs. Cela correspond aux articles de taille moyenne qui font état d'un taux de mortalité de 2 %, mais qui est inférieur au taux de 7 % de mortalité signalés dans les petits articles. Il se peut que des cas et des décès en double soient inclus dans ces totaux, mais le nombre de décès pourrait également être une sous-estimation, car tous les cas n'ont pas été résolus au moment de la publication des documents.

VUE D'ENSEMBLE DES DONNÉES PROBANTES

Lors d'une recherche documentaire effectuée jusqu'au 10 novembre 2020, 102 articles contenant des renseignements sur les caractéristiques épidémiologiques du MIS-C ont été trouvés. Presque tous ces articles étaient des rapports de cas ou des études de cohortes rétrospectives.

Il y avait 11 importants articles qui étaient pour la plupart des études de cohortes rétrospectives. Notamment deux études de plusieurs pays, quatre articles des États-Unis, trois du Royaume-Uni et deux du continent européen (tableau 1).

Il y avait 43 articles de taille moyenne (avec un total de 861 cas de MIS-C) qui ont été inclus dans cet examen. Il s'agissait de séries de cas et d'études de cohortes rétrospectives. Au total, 18 provenaient des États-Unis (379 cas), 13 d'Europe (314 cas), quatre d'Amérique du Sud (50 cas), deux du Moyen-Orient (53 cas), deux de l'Inde (42 cas) et un d'Afrique du Sud (23 cas) (tableau 2).

Les rapports de cas ont tendance à être publiés lorsqu'une nouvelle maladie est identifiée. Ils sont bons pour générer des hypothèses, mais sont généralement considérés comme des données probantes faibles. Ces 48 rapports de cas s'inscrivent dans cette tendance puisqu'ils reprennent certains des rapports de cas antérieurs du MIS-C, avant la reconnaissance officielle du syndrome et pour mettre en évidence l'éventail des pays qui ont signalé des cas de MIS-C : 20 provenaient des États-Unis, 13 d'Europe, et le reste de l'Inde (6 articles), du Moyen-Orient (5 articles), de l'Amérique du Sud (2 articles), de l'Afrique (1 article) et du Canada (1 article) (tableau 3).

Limites

- La majorité des articles de cet examen proviennent des États-Unis et d'Europe. En revanche, seuls deux articles proviennent d'Afrique, et seule une partie d'un examen a tiré des données en Asie. Il n'y a qu'un seul rapport de cas en provenance du Canada.
- Il y a un problème de double comptage des patients, car certains articles provenaient des mêmes hôpitaux, régions ou sources de données. Cela pourrait fausser les résultats. Lorsque signalé par l'auteur, il est inscrit dans les tableaux ci-dessous. Afin d'éviter un double comptage important, les examens systématiques et autres types n'ont pas été inclus.
- De nombreux articles comportaient des données incomplètes, en particulier des données sur la comorbidité et l'origine ethnique, qui n'étaient souvent recueillies que pour une partie des cas.
- Comme il s'agit d'un syndrome émergent, les définitions de cas et les critères d'inclusion ont évolué au fil du temps. Chaque cas peut ou non répondre à l'une des trois définitions de cas standard, ou aux exigences relatives à la maladie de Kawasaki.
- Aucun des articles ne prévoit de suivi des patients après leur rétablissement du MIC-C grave. Par conséquent, les séquelles ou les complications ultérieures sont encore inconnues.

TABLE DES MATIÈRES

Pour chaque étude incluse dans les tableaux des données probantes ci-dessous, les renseignements suivants sur le MIS-C sont fournis lorsqu'ils sont disponibles : Âge, sexe, origine ethnique/race, comorbidités, résultats

de la gravité (admission en USI, intubation, oxygénation extracorporelle et décès), résultats des tests PCR et sérologique pour le SRAS-CoV-2, et intervalle entre la forme grave de la COVID-19 et l'apparition du MIS-C. Ces variables ne sont pas incluses lorsqu'elles n'ont pas été déclarées.

ARTICLES IMPORTANTS

Tableau 1 : Articles décrivant 50 cas ou plus de MIS-C, par ordre décroissant de taille

Étude	Méthode	Principales conclusions
Godfred-Cato (2020) (10) Étude de cohorte rétrospective États-Unis Mars-juillet 2020	Les données relatives à 570 cas de MIS-C ont été recueillies auprès de 40 départements de la santé des États du District de Columbia et de la ville de New York	- Âge médian = 8 ans (fourchette = 2 semaines - 20 ans) - 316/570 (55 %) de sexe masculin - 187 (33 %) étaient hispaniques, 153 (27 %) noirs, 61 (11 %) blancs, 13 (2 %) asiatiques, 48 (8 %) d'une autre origine ethnique et 108 (19 %) d'une origine ethnique inconnue. Cette étude révèle que la proportion de patients hispaniques, noirs et blancs atteints du MIS-C et obèses est légèrement plus élevée que celle rapportée dans la population. - 146 (26 %) étaient obèses, 48 (8 %) étaient atteints d'une maladie pulmonaire chronique. - 364 (64 %) admis aux soins intensifs, 69 (12 %) nécessitant une ventilation mécanique. - 10 (2 %) décès. - Tous sauf 5 ont été testés positifs pour la COVID-19 par l'un ou l'autre ou les deux tests PCR ou sérologique et les 5 autres avaient un lien épidémiologique avec un cas connu de COVID-19.
Feldstein (2020) (12) Étude de cohorte rétrospective États-Unis Mars-mai 2020	Surveillance prospective et rétrospective de 186 patients atteints de MIS-C admis dans les centres de santé participants dans 26 États des États-Unis.	- Âge médian = 8,3 ans (EI = 3,3-12,5 ans) - 115/186 (62 %) de sexe masculin - 57 (31 %) étaient hispaniques, 46 (25 %) noirs, 35 (19 %) asiatiques, 9 (5 %) d'une autre origine ethnique et 41 (22 %) d'une origine ethnique inconnue. - 45 (24 %) étaient obèses. De plus, 51 (27 %) présentaient une comorbidité, dont 33 (18 %) avec des maladies respiratoires, 5 (3 %) avec des maladies cardiaques, 10 (5 %) avec des maladies liées au système immunitaire et 20 (11 %) avec d'autres maladies.

		- 148 (80 %) admis aux soins intensifs, 37 (20 %) nécessitant une ventilation mécanique, 8 (4 %) nécessitant une oxygénation extracorporelle. - Quatre (2 %) décès. - 131 personnes ont obtenu un résultat positif pour la COVID-19 par l'un ou l'autre, ou les deux tests, PCR ou sérologique et les 5 autres avaient un lien épidémiologique avec un cas connu de COVID-19. - Les cas de MIS-C sont survenus en moyenne 25 jours (intervalle = 6-51 jours) après la forme grave de la COVID-19.
Deep (2020) (13) Étude de cohorte rétrospective Royaume-Uni Mars-mai 2020 Remarque : 78 des enfants de cette étude avaient déjà fait partie d'un rapport.	116 enfants admis dans 24 unités de soins intensifs au Royaume-Uni ont été traités pour une insuffisance rénale aiguë. Les patients atteints de maladie du rein existante ont été exclus.	- Âge médian = 11 ans (EI = 7-14 ans) - 76/116 (66 %) de sexe masculin - 51 (45 %) étaient noirs, 29 (26 %) asiatiques, 24 (21 %) blancs, 9 (8 %) d'autres origines ethniques. - 20 (17 %) avaient une comorbidité, dont 5 (4 %) asthmatiques, 3 (3 %) atteints de fibrose kystique, 1 (1 %) d'une maladie pulmonaire chronique, 1 (1 %) autiste, 10 (9 %) atteints d'une autre maladie. - 116 (100 %) admis en soins intensifs (selon le modèle d'étude), 41 (35 %) nécessitant une ventilation mécanique, 3 (3 %) nécessitant une oxygénation extracorporelle. - Deux (2 %) décès.
Belot (2020) (14) Étude de cohorte rétrospective France Mars-mai 2020	Tous les services de pédiatrie en France ont déclaré 108 cas de MIS-C diagnostiqués après le 1er mars 2020, pour estimer la charge de cette affection en France.	- Âge médian = 8 ans (EI = 5-11 ans) - 53/108 (49 %) de sexe masculin - 72 (67 %) admis aux soins intensifs, 46 (43 %) nécessitant une ventilation mécanique. - Un (1 %) décès. - Un total de 79 personnes ont obtenu un résultat positif pour la COVID-19 par l'un ou l'autre, ou les deux tests, PCR ou sérologique. 16 ont eu un contact avéré avec des cas de COVID-19 et 13 ont été suspectés d'avoir eu la COVID-19 sur la base des symptômes et des antécédents.

		- Les cas de MIS-C ont atteint un pic 4 à 5 semaines après le pic des cas locaux de COVID-19.
Dufort (2020) (15) Étude de cohorte rétrospective États-Unis Mars-mai 2020	Les hôpitaux de l'État de New York qui fournissent des soins pédiatriques ont signalé 99 cas potentiels de MIS-C.	- Des catégories d'âge ont été données : 31 (31 %) étaient âgés de 0 à 5 ans, 42 (42 %) de 6 à 12 ans et 26 (26 %) de 3 à 20 ans. - 53/99 (54 %) de sexe masculin. - 31 (31 %) étaient hispaniques, 29 (29 %) blancs, 4 (4 %) asiatiques, 14 (14 %) d'une autre origine ethnique et 21 (21 %) d'une origine ethnique inconnue. - 36 (36 %) avaient une comorbidité, dont 29 (29 %) étaient obèses et 14 (14 %) étaient atteints d'une maladie pulmonaire chronique. - 79 (80 %) admis en soins intensifs, 10 (10 %) nécessitant une ventilation mécanique, 1 (1 %) nécessitant une oxygénation extracorporelle. - Deux (2 %) décès. - 76/77 (99 %) ont obtenu un résultat positif au test sérologique et 50/99 (56 %) ont obtenu un résultat positif au test PCR. - Les cas de MIS-C ont atteint un pic 31 jours après le pic des cas locaux de COVID-19.
Antunez-Montes (2020) (16) Cohorte ambidirectionnelle Mexique, Colombie, Pérou, Costa Rica et Brésil Juillet-août, 2020	Un groupe de médecins d'Amérique centrale et du Sud a recueilli 95 cas de MIS-C parmi 409 cas pédiatriques confirmés. Infections par le SRAS-CoV-2	- 95 cas de MIS-C ont été identifiés parmi 409 enfants admis à l'hôpital avec un résultat positif de la COVID-19 (23 %). - Âge médian = 7 ans (intervalle = 1 mois - 17 ans). Les patients atteints du MIS-C étaient nettement plus âgés que les enfants non atteints du MIS-C admis à l'hôpital avec la COVID-19. - 52/95 (55 %) de sexe masculin. - 11 (12 %) présentaient des comorbidités et avaient un statut socioéconomique nettement inférieur à celui des enfants admis avec la forme grave de la COVID-19. - 20 (21 %) admis aux soins intensifs, 9 (9 %) nécessitant une ventilation mécanique. - Deux (2 %) décès.

		- Tous ont obtenu un résultat positif pour la COVID-19 par l'un ou l'autre, ou les deux tests, PCR ou sérologique.
Davies (2020) (17) Étude de cohorte rétrospective Royaume-Uni Avril-mai 2020 Remarque : Huit des enfants inclus dans cette étude avaient déjà fait partie d'un rapport.	Une description de 78 cas de PIMS, âgés de 17 ans et moins, admis dans les unités de soins intensifs au Royaume-Uni	- Avant l'arrivée de la COVID-19, les données historiques concernant des maladies inflammatoires similaires faisaient état d'une admission moyenne aux soins intensifs par semaine (IC à 95 %; 0,85 à 1,22). En comparaison, il y avait une moyenne de 14 cas par semaine pour le PIMS, et un pic de 32 admissions par semaine pendant la période d'étude. - Âge médian = 11 ans (EI = 8-14 ans) - 52/78 (67 %) de sexe masculin. - 37 (47 %) étaient noirs, 22 (28 %) asiatiques, 17 (22 %) blancs, 2 (3 %) d'autres origines ethniques. - 17 (22 %) présentaient des comorbidités, dont 2 (3 %) avec des maladies graves préexistantes. - 78 (100 %) admis en soins intensifs (requis pour faire partie de l'étude), 36 (46 %) nécessitant une ventilation mécanique, 3 (4 %) nécessitant une oxygénation extracorporelle. - Deux (3 %) décès. - 33/35 (94 %) ont obtenu un résultat positif au test sérologique et 17/78 (22 %) ont obtenu un résultat positif au test PCR.
Jonat (2020) (18) Étude de cohorte rétrospective États-Unis Mars-juin 2020	Une description des 54 cas de MIS-C identifiés dans un seul hôpital dans la période donnée.	- Âge médian = 7 ans (intervalle = 10 mois - 20 ans) - 25/54 (46 %) de sexe masculin. - 19 (35 %) étaient blancs, 10 (19 %) noirs, 8 (15 %) d'une autre origine ethnique, 17 (31 %) d'une origine ethnique inconnue. - Sept avaient des conditions préexistantes (à l'exclusion de l'obésité). - 31 (57 %) ont été admis aux soins intensifs. Aucun patient n'a eu besoin de ventilation mécanique ou d'oxygénation extracorporelle. - Aucun décès.

		- 41/54 (97 %) ont obtenu un résultat positif au test sérologique et 20/54 (34 %) ont obtenu un résultat positif au test PCR.
Cattalini (2020) (19) *(préimpression)* Étude de cohorte rétrospective Italie Février-mai 2020	Un sondage envoyé à la société italienne de pédiatrie; 53 patients avaient les caractéristiques d'un diagnostic de « KawaCOVID » (équivalent du MIS-C).	- L'âge médian des cas de KawaCOVID = 7 ans (EI : 4,5-11 ans), alors que l'âge médian des cas de Kawasaki = 2 ans (EI : 1-4 ans). L'âge médian est significativement différent (p<0,0001). - Il n'y a pas eu de différence significative dans le sex-ratio de KawaCOVID par rapport à la maladie de Kawasaki. - L'admission aux soins intensifs était plus fréquente dans les cas de KawaCOVID que dans ceux de la maladie de Kawasaki (23,1 % par rapport à 1,1 %; p<0,0001) - Les cas de KawaCOVID présentaient une atteinte cardiaque plus grave que les cas de Kawasaki - myocardite (60,4 % par rapport à 3,1 %; p<0,0001), péricardite (26,4 % par rapport à 7,3 %; p=0-0013), insuffisance cardiaque (35,8 % par rapport à 1 %; p<0,00001) et autres. - Tous les patients atteints de KawaCOVID ont obtenu un résultat positif pour la COVID-19 par PCR ou par un test sérologique, ou les deux (31 ont été obtenu un résultat positif au test sérologique et 14 par PCR). - Aucun décès.
Whittaker (2020) (20) Étude de cohorte rétrospective Royaume-Uni Mars-mai 2020 Remarque : Huit des enfants inclus dans cette étude avaient déjà fait partie d'un rapport.	Un sondage en ligne avec des données sur 58 enfants qui ont été admis dans huit hôpitaux en Angleterre avec le PIMS (MIS-C).	- Âge médian = 9 ans (EI = 5,7-14 ans, intervalle = 3 mois - 17 ans) - 38/58 (66 %) de sexe masculin. - Sept (12 %) présentaient des comorbidités, dont 3 (5 %) asthmatiques, et 1 chacun (2 %) avec un trouble du développement neurologique, de l'épilepsie, le trait drépanocytaire et l'alopécie. - 29 (50 %) des patients admis aux soins intensifs, 25 (43 %) nécessitant une ventilation mécanique, 2 (3 %) nécessitant une oxygénation extracorporelle. - Un (2 %) décès. - 40/46 (87 %) ont obtenu un résultat positif au test sérologique et 15/58 (26 %) ont obtenu un résultat positif au test PCR.

Duarte-Salles (2020) (6) *(préimpression)* Étude de cohorte rétrospective États-Unis, Espagne, France, Allemagne et Corée du Sud Janvier-juin 2020	Sur la base des dossiers médicaux, des données de facturation des hôpitaux et des données relatives aux demandes d'assurance aux États-Unis, en Europe et en Asie, les enfants diagnostiqués ou hospitalisés avec la COVID-19 ont été comparés à une précédente cohorte de grippe saisonnière.	- Cette étude porte sur 55 270 enfants et adolescents atteints de la COVID-19, dont 3 693 ont été hospitalisés avec la COVID-19 et ont été comparés à une cohorte historique de 1 952 693 enfants atteints de la grippe. - Le MIS-C était relativement peu fréquent, touchant entre 0,5 % et 3,1 % des patients atteints de la COVID-19, et entre 0,9 % et 7,6 % des patients hospitalisés avec la COVID-19. - On pensait que le MIS-C était lié à la COVID-19, car des syndromes similaires sont beaucoup moins fréquents dans la cohorte historique de la grippe.

ARTICLES DE TAILLE MOYENNE

Tableau 2 : Articles décrivant de 6 à 49 cas de MIS-C, par ordre décroissant de taille

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Mamishi (2020) (21) Étude de cohorte rétrospective Iran Mars-juin 2020	45 cas de MIS-C sont décrits.	- Âge médian = 7 ans (intervalle = 10 mois - 17 ans) - 24/45 (46 %) de sexe masculin. - Six (13 %) avaient des maladies préexistantes - Cinq (11 %) décès - quatre d'entre eux avaient des maladies sous-jacentes (leucémie aiguë lymphoblastique, néphropathie chronique, paralysie cérébrale et syndrome de Budd-Chiari). - 35 tests sérologiques positifs, 10 tests PCR positifs
Miller (2020) (22) Étude de cohorte rétrospective États-Unis Avril-mai 2020	44 cas de MIS-C sont décrits.	- Âge médian = 7,3 ans (EI = 4,98 ans, intervalle = 7 mois - 20 ans) - 20/44 (45 %) de sexe masculin. - 15 (34 %) étaient hispaniques, 9 (20 %) noirs, 9 (20 %) blancs, 11 (25 %) origines ethniques inconnues.

		- 16 (36 %) étaient en surpoids. - Un (2 %) a nécessité de la ventilation mécanique. - Aucun décès. - 31/32 ont été testés positifs avec un test sérologique et 15/44 avec un test PCR.
Belhadjer (2020) (23) Étude de cohorte rétrospective France Mars-avril 2020	35 cas de MIS-C ayant eu une implication cardiaque et nécessitant une admission en soins intensifs sont décrits.	- Âge médian = 10 ans (intervalle = 2-16 ans) - 18/35 (51 %) de sexe masculin. - Six (17 %) étaient en surpoids, 3 (9 %) asthmatiques, 1 (3 %) atteint de lupus. - 35 (100 %) admis aux soins intensifs, 22 (63 %) nécessitant une ventilation mécanique, 10 (29 %) nécessitant une oxygénation extracorporelle. - Aucun décès. - 14 ont eu un résultat positif au test PCR, tandis que 30 patients ont eu un résultat positif au test sérologique (28 positifs pour les anticorps IgG et 2 positifs pour les anticorps IgM).
Hameed (2020) (24) Étude de cohorte rétrospective Royaume-Uni Avril-mai 2020 Remarque : Huit patients ont fait partie d'autres études.	35 cas de MIS-C de moins de 17 ans sont décrits.	- Âge médian = 11 ans (EI = 8 ans) - 27/35 (77 %) de sexe masculin. - 24 (69 %) admis aux soins intensifs, 7 (20 %) nécessitant une ventilation mécanique, 2 (6 %) nécessitant une oxygénation extracorporelle. - Un (3 %) décès. - 25 ont été testés positifs pour les anticorps IgG et 23 pour les anticorps IgM.
Sethuraman (2020) (25) Étude de cohorte rétrospective États-Unis Avril-juillet 2020	34 cas de MIS-C sont décrits.	- Âge médian = 6 ans (EI = 8 ans) - 16/34 (47 %) de sexe masculin. - 23 (68 %) étaient noirs, autre origine ethnique/race non déclarée. - Deux (6 %) étaient obèses et 9 (26 %) étaient asthmatiques. 24 (71 %) admis aux soins intensifs, 8 (24 %) nécessitant une ventilation mécanique, 2 (6 %) nécessitant une oxygénation extracorporelle.

		- Aucun décès. - 18/25 testés positifs pour les anticorps IgG, 8/34 testés positifs au test PCR. - Les cas de MIS-C ont atteint un pic 3 semaines après le pic des cas locaux de COVID-19.
Minocha (2020) (26) Étude de cohorte rétrospective États-Unis Mars-juin 2020	33 cas de MIS-C sont décrits.	- Âge médian = 2,8 ans (EI = 1,4-9 ans) - 19/33 (56 %) de sexe masculin. - 12 (36 %) hispaniques, 10 (30 %) blancs, 7 (21 %) noirs, 4 (12 %) asiatiques. - Sept (21 %) étaient obèses, 5 (15 %) étaient asthmatiques, 1 (3 %) est né prématurément. - 11 (33 %) ont été admis aux soins intensifs. - Aucun décès. - 14/23 testés positifs pour les anticorps IgG, 11/33 testés positifs au test PCR.
Kaushik, Aydin, (2020) (27) Étude de cohorte rétrospective États-Unis Avril-mai 2020 Remarque : Quatre patients ont fait partie d'autres études.	33 cas de MIS-C qui ont été admis aux soins intensifs sont décrits.	- Âge médian = 10 ans (EI = 6-13 ans) - 20/33 (61 %) de sexe masculin. - 15 (45 %) étaient hispaniques, 13 (39 %) noirs, 3 (9 %) blancs, 1 (3 %) asiatique, 1 (3 %) d'une autre origine ethnique. - 16 (48 %) des patients présentaient des comorbidités - 4 (12 %) étaient obèses, 2 (6 %) étaient en surpoids, 5 (15 %) étaient asthmatiques, 3 (9 %) avaient des allergies/eczémas, 2 (6 %) avaient des problèmes cardiaques, 2 (6 %) avaient des problèmes hématologiques - 33 (100 %) admis aux soins intensifs, 5 (15 %) nécessitant une ventilation mécanique, 1 (3 %) nécessitant une oxygénation extracorporelle. - Un (3 %) décès. - 11 tests PCR positifs et 27 tests sérologiques positifs.
Capone (2020) (28) Étude de cohorte rétrospective États-Unis	33 cas de MIS-C sont décrits.	- Âge médian = 8,6 ans (EI = 5,5-12,6 ans) - 20/33 (61 %) de sexe masculin. - Huit (24 %) étaient noirs, 3 (9 %) blancs, 3 (9 %) asiatiques, 19 (58 %) autres origines ethniques ou

Avril-mai 2020		inconnues. Les taux de l'ethnicité dans les cas de MIS-C étaient similaires aux taux de l'ethnicité de la population hospitalisée. - 12 (36 %) étaient obèses, 2 (6 %) étaient en surpoids. Le taux d'obésité infantile dans la région est de 18 %, les patients obèses sont donc surreprésentés dans les cas de MIS-C dans cette étude. - 26 (79 %) admis aux soins intensifs, 6 (18 %) nécessitant une ventilation mécanique. - Aucun décès. - 30 personnes testées positives pour les anticorps IgG. - Les cas de MIS-C ont atteint un pic 5 semaines après le pic d'hospitalisation local de la COVID-19.
Moraleda (2020) (29) Étude de cohorte rétrospective Espagne Mars-juin 2020	31 cas de MIS-C sont décrits.	- Âge médian = 7,6 ans (EI = 4,5-11,5 ans) - 18/31 (58 %) de sexe masculin. - Trois (10 %) étaient obèses, 4 (13 %) étaient asthmatiques et 1 chacun (3 %) était atteint d'une maladie cardiaque chronique, d'une maladie hématologique et d'un cancer. - 20 (65 %) admis aux soins intensifs, 6 (19 %) nécessitant une ventilation mécanique. - Un (3 %) décès. - 17 ont été positifs au test PCR, 10 tests positifs pour les anticorps IgM et 19 tests positifs pour les anticorps IgG. - Les cas de MIS-C ont atteint un pic un mois après le pic d'hospitalisation local de la COVID-19.
Aulnes (2020) (30) Étude de cohorte rétrospective Royaume-Uni Mars-mai 2020	31 cas de MIS-C sont décrits.	- Âge médian = 10,1 ans (intervalle = 8,7-13,9 ans) - 21/31 (68 %) de sexe masculin. - 14 (45 %) étaient noirs, 9 (29 %) asiatiques, 4 (13 %) blancs, 3 (10 %) d'origine mixte, 1 (3 %) d'origine ethnique inconnue. - Cinq (16 %) étaient en surpoids et 7 (23 %) étaient obèses - 14 (45 %) nécessitant une ventilation mécanique, 1 (3 %) nécessitant une oxygénation extracorporelle. - Aucun décès.

		- 20 tests PCR positifs et 28 tests sérologiques positifs.
Felsenstein (2020) (31) Étude de cohorte rétrospective Royaume-Uni Mars-juin 2020	29 cas de MIS-C sont décrits.	- Âge médian = 6 ans (EI = 3,8-9,9 ans) - 20/29 (69 %) de sexe masculin. - 12 (41 %) étaient blancs, 6 (21 %) d'Asie du Sud-Est, 4 (14 %) noirs, 2 (7 %) d'Asie de l'Est, 5 (17 %) d'origine ethnique inconnue. - Aucun décès. - 14 tests sérologiques positifs, 3 tests PCR positifs. - Les cas de MIS-C ont atteint un pic 4 semaines après le pic des cas locaux de COVID-19.
Lee (2020) (32) Étude de cohorte rétrospective États-Unis Mars-juin 2020	28 cas de MIS-C sont décrits.	- Âge médian = 9 ans (échelle = 1 mois - 17 ans) - 16/28 (57 %) de sexe masculin. - 12 (43 %) étaient hispaniques, 10 (36 %) blancs, 5 (18 %) noirs. - 14 (50 %) présentaient des comorbidités; 4 (14 %) étaient obèses, 3 (11 %) étaient asthmatiques et 1 chacun (4 %) était atteint de cardiopathie congénitale, de drépanocytose et de trouble mitochondrial. - 17 (61 %) ont été admis aux soins intensifs, aucun n'a nécessité de ventilation mécanique ou d'oxygénation extracorporelle. - Aucun décès. - 17 tests PCR positifs et 18 tests sérologiques positifs.
Matsubara (2020) (33) Étude de cohorte rétrospective États-Unis Avril-juin 2020	28 cas de MIS-C sont décrits.	- Âge médian = 11,4 ans (EI = 8-13, 7 ans) - 14/28 (50 %) de sexe masculin. - 13 (46 %) étaient noirs, 7 (25 %) blancs, 4 (14 %) hispaniques, 1 (4 %) asiatique, 3 (11 %) d'origine ethnique inconnue. - Huit personnes testées positives pour les anticorps IgG.
Torres (2020) (34) Étude de cohorte rétrospective Chili Mai-juin 2020	27 cas de MIS-C chez des enfants de jusqu'à 14 ans sont décrits.	- Âge médian = 6 ans (intervalle = 0-14 ans) - 14/27 (52 %) de sexe masculin. - 23 (85 %) des parents étaient chiliens, 2 (7 %) vénézuéliens, 1 (4 %) haïtien, 1 (4 %) péruvien. - Quatre (15 %) étaient en surpoids ou obèses, 1 (4 %) était asthmatique, 1 (4 %) était immunodéprimé.

		- 16 (59 %) admis aux soins intensifs, 12 (44 %) nécessitant une ventilation mécanique. - Aucun décès. - 14 tests PCR positifs et 10 tests sérologiques positifs.
Carter (2020) (35) Étude de cohorte prospective Royaume-Uni Avril-mai 2020	25 cas de MIS-C sont décrits.	- Âge médian = 12,5 ans (intervalle = 7,7-14,4 ans) - 15/25 (60 %) de sexe masculin. - 10 (40 %) étaient blancs, 9 (36 %) noirs, 5 (20 %) asiatiques, 1 (4 %) d'une autre origine ethnique. - Cinq (20 %) présentaient des comorbidités, dont 2 (8 %) asthmatiques (1 également autiste et 1 avec de l'eczéma), 1 (4 %) avec une allergie alimentaire, 1 (4 %) porteur du trait de l'hémoglobine C, et 1 (4 %) atteint d'anémie aplastique et immunodéprimé. - 21 (84 %) admis aux soins intensifs, 2 (8 %) nécessitant une ventilation mécanique. - Aucun décès. - 18 tests sérologiques positifs et 1 test PCR positif.
Dionne (2020) (36) Étude de cohorte rétrospective États-Unis Mars-mai 2020	25 cas de MIS-C sont décrits.	- Âge médian = 9,7 ans (EI = 2,7-15,0 ans) - 15/25 (60 %) de sexe masculin. - Quatre (16 %) étaient obèses, 4 (16 %) étaient asthmatiques et 1 chacun (4 %) atteint de drépanocytose, de trouble mitochondrial, de prématurité ou d'insuffisance respiratoire. - 14 (56 %) admis aux soins intensifs, 1 (4 %) nécessitant une ventilation mécanique. - Aucun décès. - 15 tests PCR positifs et 13 tests sérologiques positifs.
Jain (2020) (37) Étude de cohorte rétrospective Inde Mai-juillet 2020	23 cas de MIS-C sont décrits.	- Âge médian = 7,2 ans (intervalle = 0,8-14 ans) - 11/23 (48 %) de sexe masculin. - Neuf (39 %) ont nécessité de la ventilation mécanique. - Un décès (4 %). - Sept tests sérologiques positifs, 9 tests PCR positifs. - Les cas de MIS-C ont atteint un pic 2 à 4 semaines après le pic des cas locaux de COVID-19.

Webb (2020) (38) Étude de cohorte rétrospective Afrique du Sud Juin-juillet 2020	23 cas suspects de MIS-C sont décrits dans une zone où les tests de dépistage pour la COVID-19 sont limités.	- Âge moyen = 6,6 ans (IC à 95 %; 4,8-8,4 ans) - 17/23 (74 %) de sexe masculin. - 18 (78 %) étaient noirs, 5 (22 %) étaient noirs et d'origine sud-africaine. - Deux (9 %) étaient obèses, 4 (17 %) ont été exposés au VIH avant la naissance, mais séronégatifs, 1 (4 %) était asthmatique, 1 (4 %) était atteint de leucémie. - 12 (52 %) admis aux soins intensifs, 6 (26 %) nécessitant une ventilation mécanique. - Aucun décès. - Quatre tests PCR positifs. - En moyenne, les cas de MIS-C sont survenus 24 jours après la forme grave de COVID-19 (IC à 95 %; 9-39 jours).
Toubiana (2020) (39) Cohorte ambidirectionnelle France Avril-mai 2020	21 cas de MIS-C sont décrits.	- 21 cas de MIS-C sont décrits. - Âge médian = 7,9 ans (intervalle = 3,7-16,6 ans) - 24 (57 %) des parents étaient noirs, 12 (29 %) blancs, 4 (10 %) asiatiques, 2 (5 %) du Moyen-Orient. - 24 % des patients avaient un poids dépassant le 75^{e} percentile. - 17 (81 %) admis aux soins intensifs, 11 (53 %) nécessitant une ventilation mécanique. - Aucun décès. - 19 testés positifs pour les anticorps IgG, 34 tests positifs au test PCR.
Grimaud (2020) (40) Étude de cohorte rétrospective France Avril 2020	20 cas de MIS-C admis aux soins intensifs sont décrits.	- Âge médian = 10 ans (intervalle = 2,9-15 ans) - 10/20 (50 %) de sexe masculin. - 20 (100 %) admis aux soins intensifs, 8 (40 %) nécessitant une ventilation mécanique, aucun ne nécessitant l'oxygénation extracorporelle. - Aucun décès. - 15 tests sérologiques positifs, 10 tests PCR positifs.
Dhanalakshmi (2020) (41)	19 cas de MIS-C sont décrits.	- Âge médian = 6 ans (intervalle = 13 mois - 16 ans) - 8/19 (42 %) de sexe masculin. - Un (5 %) a connu des retards de développement.

Étude de cohorte rétrospective Inde Mai-juillet 2020		- 12 (63 %) ont été admis aux soins intensifs, aucun n'a nécessité de ventilation mécanique ni oxygénation extracorporelle. - Aucun décès. - Huit tests sérologiques positifs, 4 tests PCR positifs.
Blumfield & Levin (42) Étude de cohorte rétrospective États-Unis Février-mars 2020	19 cas de MIS-C sont décrits.	- Âge médian = 8 ans (intervalle = 2 mois - 18 ans) - 10/19 (53 %) de sexe masculin. - Trois (16 %) étaient obèses, 5 (26 %) présentaient des troubles neurologiques et 1 chacun (5 %) était atteint de cardiopathie congénitale, de cardiomyopathie, de cancer, d'asthme, d'hypertension, de drépanocytose, du syndrome de l'X fragile et un a connu des événements thromboemboliques antérieurs. - 14 (74 %) admis aux soins intensifs, 8 (42 %) nécessitant une ventilation mécanique. - Deux décès (11 %) - les deux avaient des comorbidités. - 18 tests PCR positifs.
Yonker (2020) (8) Étude de cohorte rétrospective États-Unis Août 2020*	18 cas de MIS-C sont décrits sur un total de 192 cas pédiatriques de COVID-19 hospitalisés.	- 18/192 (9 %) enfants se présentant à l'urgence ou hospitalisés en lien avec la COVID-19 étaient atteints du MIS-C. - Âge moyen = 7,7 ans (ET = 7 ans) - 14/18 (78 %) de sexe masculin. - Neuf (50 %) étaient blancs, 6 (33 %) hispaniques, 2 (11 %) blancs et 1 (6 %) asiatique. - Deux (11 %) étaient obèses, 1 chacun (6 %) était atteint d'une maladie inflammatoire chronique de l'intestin, de TDAH et d'autisme.
Cheung (2020) (43) Étude de cohorte rétrospective États-Unis Avril-mai 2020	17 cas de MIS-C sont décrits.	- Âge médian = 8 ans (intervalle = 1,8-16 ans) - 8/17 (47 %) de sexe masculin. - Trois (18 %) étaient asthmatiques. - Un (6 %) ont été admis aux soins intensifs, aucun n'a nécessité de ventilation mécanique ni oxygénation extracorporelle. - Aucun décès.

		- Neuf ont été testés positifs avec un test sérologique et 44 avec un test PCR.
Pouletty (2020) (44) Étude de cohorte rétrospective France Avril 2020	16 cas de MIS-C sont décrits.	- Âge médian = 12 ans (intervalle = 4,7-12,5 ans) - 8/16 (50 %) de sexe masculin. - Quatre (25 %) étaient en surpoids, 2 (13 %) étaient asthmatiques. - Sept (44 %) admis aux soins intensifs, 2 (13 %) nécessitant une ventilation mécanique, aucun ne nécessitant l'oxygénation extracorporelle. - Aucun décès. - 7/8 testés positifs pour les anticorps IgG, 11/16 testés positifs au test PCR.
Ramcharan (2020) (45) Étude de cohorte rétrospective Royaume-Uni Avril-mai 2020	15 cas de MIS-C sont décrits.	- Âge médian = 8,8 ans (EI = 6,4-11,2 ans) - 11/15 (73 %) de sexe masculin. - Six (40 %) étaient noirs, 6 (40 %) sud-asiatiques, 3 (20 %) d'autres origines ethniques. - Quatre (27 %) ont nécessité une ventilation mécanique, aucun n'a nécessité l'oxygénation extracorporelle. - Aucun décès. - 12 tests sérologiques positifs, 2 tests PCR positifs.
Riollano-Cruz (2020) (46) Étude de cohorte rétrospective États-Unis Avril-juin 2020	15 cas de MIS-C sont décrits.	- Âge médian = 12 ans (intervalle = 3-20 ans) - 11/15 (73 %) de sexe masculin. - 10 (67 %) étaient hispaniques, 2 (13 %) noirs, 2 (13 %) blancs et 1 (7 %) d'origine ethnique inconnue. - Deux (13 %) étaient obèses, 2 (13 %) étaient en surpoids, 4 (27 %) étaient asthmatiques et 1 (7 %) était atteint d'hypothyroïdie. - 15 (100 %) admis aux soins intensifs, 3 (20 %) nécessitant une ventilation mécanique, 1 (7 %) nécessitant une oxygénation extracorporelle. - Un (7 %) décès. - 15 ont été testés positifs avec un test sérologique et 9 avec un test PCR. - L'apparition du MIS-C a commencé 21 jours après la forme grave de COVID-19 (EI = 21-24 jours).

Rosat Consiglio (2020) (47) Étude de cohorte rétrospective Italie, Suède Mars-mai 2020	13 cas de MIS-C sont décrits.	- Âge médian = 106 mois (EI = 71-165 mois). - 8/11 (73 %) de sexe masculin (2 manquants). - 3/4 (75 %) ont été testés positifs pour les anticorps IgG.
Gaitonde (2020) (48) Étude cas/témoins États-Unis Mars-juin 2020	12 cas de MIS-C sont décrits.	- Âge médian = 8 ans (EI = 5,5-11,5 ans). - 9/12 (75 %) de sexe masculin. - Huit (80 %) étaient noirs, 3 (30 %) blancs, 1 (10 %) d'une autre origine ethnique. - Aucun décès.
de Farias (2020) (49) Étude de cohorte prospective Brésil Avril-juin 2020	11 cas de MIS-C sont décrits.	- Âge médian = 4 ans (intervalle = 7 mois - 11 ans) - 9/11 (82 %) de sexe masculin. - Deux (18 %) souffraient de malnutrition, 3 (27 %) étaient obèses, 3 (27 %) étaient en surpoids. - 11 admis aux soins intensifs - requis pour l'inclusion (100 %), 3 (27 %) ont nécessité une ventilation mécanique. - Deux (18 %) décès - tous deux souffraient de malnutrition. - Neuf tests sérologiques positifs, 2 tests PCR positifs. - L'apparition du MIS-C a commencé 15 jours après la forme grave de COVID-19 (intervalle = 21-60 jours).
Ouldali (2020) (50) Essai accidentel France Décembre 2005-mai 2021	10 cas de MIS-C sont décrits après le début de la pandémie de COVID-19, et comparés aux cas de Kawasaki avant avril 2020.	- Avant avril 2020, le taux d'hospitalisation pour la maladie de Kawasaki était de 1,2 cas par mois. En avril 2020, ce chiffre est passé à 6 cas par mois (soit une augmentation de 497 %). Un autre pic en décembre 2009 a atteint 6 cas par mois (soit une augmentation de 365 %) au moment de la pandémie de grippe A H1N1. - Âge médian = 11,5 ans (intervalle = 1-15 ans) - 4/10 (40 %) de sexe masculin. - Six (60 %) ont été admis aux soins intensifs, aucun n'a nécessité de ventilation mécanique ni oxygénation extracorporelle. - Aucun décès.

		- 5/10 testés positifs pour les anticorps IgG, 5/9 testés positifs au test PCR. - Les cas de MIS-C ont atteint un pic 2 semaines après le pic des cas locaux de COVID-19.
Verdoni (2020) (51) Essai accidentel Italie Février-avril 2020	10 cas de MIS-C sont décrits après le début de la pandémie de COVID-19, et comparés aux cas de Kawasaki avant février 2020.	- Il s'agit d'une étude précoce qui a permis de comparer les taux de la maladie de Kawasaki entre le 1er janvier 2015 et le 17 février 2020 (19 patients) avec ceux entre le 18 février 2020 et le 20 avril 2020 (10 patients). L'étude a révélé une multiplication par 30 de la maladie de Kawasaki au début de 2020 en Italie. - Âge médian = 7,5 ans (ET = 3,5 ans). - 7/10 (70 %) de sexe masculin. - Huit testés positifs pour les anticorps IgG, 2 testés positifs pour les anticorps IgM, 2 positifs au test PCR.
Rostad (2020) (52) Cohorte ambidirectionnelle États-Unis Mars-mai 2020	10 cas de MIS-C sont décrits.	- Âge médian = 106 mois (intervalle = 71-165 mois). - 6/10 (60 %) de sexe masculin. - 6 (60 %) étaient noirs, 3 (30 %) blancs, 1 (10 %) d'une autre origine ethnique. - 3 (30 %) étaient atteints de maladies respiratoires sous-jacentes. - 10 (100 %) ont été admis aux soins intensifs. - Tous testés positifs pour les anticorps IgG et IgM, 2 tests PCR positifs.
Gruber (2020) (53) Étude de cohorte rétrospective États-Unis Avril-juin 2020	9 cas de MIS-C sont décrits.	- Âge médian = 11,5 ans. - 4/9 (44 %) de sexe masculin. - Six (67 %) étaient hispaniques, 2 (22 %) noirs, 1 (11 %) d'origine ethnique inconnue. - Deux (22 %) étaient asthmatiques, 1 (11 %) atteint de TSPT. - Aucun décès. - Neuf tests sérologiques positifs, 3 tests PCR positifs.
Kim (2020) (9) Étude de cohorte rétrospective États-Unis	9 cas de MIS-C sont décrits sur un total de 83 cas pédiatriques de	- Sur 83 enfants hospitalisés pour la COVID-19, 9 ont eu un diagnostic de MIS-C (11 % des enfants hospitalisés avec la COVID-19). - Âge : 0-2 ans (1), 2-4 ans (5), 5-17 ans (3).

Mars-juillet 2020	COVID-19 hospitalisés.	
Khan & Ullah (2020) (54) Étude de série de cas Pakistan Août 2020*	8 cas de MIS-C sont décrits avec des données issues de rapports.	- Intervalle d'âges = 5-15 ans. - Tous les tests sérologiques étaient positifs.
Riphagen (2020) (55) Étude de cohorte rétrospective Royaume-Uni Avril 2020	8 cas de MIS-C sont décrits.	- Âge médian = 8 ans (intervalle = 4-14 ans) - 5/8 (63 %) de sexe masculin. - Six (75 %) étaient noirs, 1 (13 %) asiatique, 1 (13 %) du Moyen-Orient. - Deux (25 %) étaient obèses, 1 (13 %) en surpoids, 1 (13 %) autiste, 1 (13 %) avait le rhume des foins. - 8 (100 %) admis aux soins intensifs, 5 (63 %) nécessitant une ventilation mécanique, 1 (13 %) nécessitant une oxygénation extracorporelle. - Un décès (13 %).
Perez-Toledo (2020) (56) *(préimpression)* Étude de cohorte rétrospective Royaume-Uni Avril-mai 2020	8 cas de MIS-C sont décrits, où les patients ont eu un résultat négatif au test PCR, mais un test sérologique positif.	- Âge médian = 9 ans (intervalle 7-14 ans). - 5/8 (63 %) de sexe masculin. - Six (75 %) ont été admis aux soins intensifs. - Aucun décès.
Syrimi (2020) (57) *(préimpression)* Étude de cohorte rétrospective Royaume-Uni Avril-mai 2020	7 cas de MIS-C sont décrits.	- Âges : <5 ans (1), 5-10 ans (3), 10-15 ans (3). - 4/7 (57 %) de sexe masculin. - Quatre (57 %) étaient noirs, 2 (29 %) asiatiques, 1 (14 %) blanc. - Six (86 %) ont été admis aux soins intensifs.
Pereira (2020) (58) Étude de cohorte rétrospective Brésil	6 cas de MIS-C sont décrits à partir d'un groupe de 66 cas pédiatriques de	- Sur 66 enfants hospitalisés pour la COVID-19, 6 ont eu un diagnostic de MIS-C (9 % des enfants hospitalisés avec la COVID-19). - Âge médian = 7,8 ans (intervalle = 0,01-17,6 ans)

Avril-juin 2020	COVID-19 hospitalisés.	- 5/6 (83 %) de sexe masculin. - Cinq (83 %) avaient une maladie sous-jacente, 4 étaient immunodéprimés, 3 étaient atteints d'un cancer, 1 était atteint d'une néphropathie chronique. - Six (100 %) admis aux soins intensifs, 5 (83 %) nécessitant une ventilation mécanique. - Quatre (67 %) décès.
Chiara-Chilet (2020) (7) *(préimpression)* Étude de cohorte rétrospective Pérou Mars-juillet 2020	6 cas de MIS-C sont décrits sur un total de 91 cas pédiatriques de COVID-19 hospitalisés.	- Sur 91 enfants hospitalisés pour la COVID-19, 6 ont eu un diagnostic de MIS-C (7 % des enfants hospitalisés avec la COVID-19). - Deux (33 %) ont été admis aux soins intensifs.
Chiotos (2020) (59) Étude de série de cas États-Unis Mai 2020*	6 cas de MIS-C qui ont été admis aux soins intensifs sont décrits.	- Âge médian = 7,5 ans (intervalle = 5-14 ans) - 1/6 (17 %) de sexe masculin. - Deux (33 %) étaient noirs, 2 (33 %) blancs, 2 (33 %) d'origine ethnique inconnue. - Six (100 %) admis aux soins intensifs, 3 (50 %) nécessitant une ventilation mécanique, et aucun ne nécessitant l'oxygénation extracorporelle. - Aucun décès. - Cinq testés positifs pour les anticorps IgG, 2 testés positifs au test PCR.
Diorio (2020) (60) Étude de cohorte prospective États-Unis Avril-mai 2020	6 cas de MIS-C sont décrits.	- Âge médian = 6 ans (EI = 5-7 ans). - 2/6 (33 %) de sexe masculin. - Quatre (66 %) étaient blancs, 1 (17 %) noir, 1 (17 %) d'une autre origine ethnique. - Cinq (83 %) admis aux soins intensifs, 2 (33 %) nécessitant une ventilation mécanique, et aucun ne nécessitant l'oxygénation extracorporelle. - Aucun décès.

* Date de publication de l'article parce que les dates des cas ne sont pas disponibles.

PETITS ARTICLES

Tableau 3 : Articles décrivant de un à cinq cas de MIS-C, par pays et par taille d'étude

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
ÉTUDE DE SÉRIE DE CAS		
Blondiaux (2020) (61) Étude de série de cas France Avril 2020	Étude de série de cas descriptive de quatre patients atteints du MIS-C.	- Trois filles de 6, 8 et 11 ans; un garçon de 12 ans. - Les quatre ont été admis aux soins intensifs, un a été intubé, aucun n'a été placé sous oxygénation extracorporelle. - Aucun décès. - Tous les tests PCR étaient négatifs et positifs pour les anticorps IgG, 1 test positif pour les anticorps IgM.
Labé (2020) (62) Étude de série de cas France Mai 2020*	Étude de série de cas descriptive de deux patients atteints du MIS-C.	- Deux garçons de 3 et 6 ans. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - Aucun décès. - Un test PCR positif, aucun résultat de test sérologique.
Licciardi (2020) (63) Étude de série de cas Italie Avril 2020	Étude de série de cas descriptive de deux patients atteints du MIS-C.	- Deux garçons, âgés de 7 et 12 ans, aucun n'ayant de comorbidités. - Les deux ont été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Aucun décès. - Les deux ont eu un résultat négatif au test PCR, mais les tests étaient positifs pour les anticorps IgG et IgM.
Pang (2020) (64) Étude de série de cas Royaume-Uni Mars-mai 2020	Étude de série de cas descriptive de cinq patients atteints du MIS-C.	- Trois garçons de 8, 12 et 14 ans; deux filles de 5 et 15 ans. - Deux étaient asiatiques, un noir, un blanc et un métis. - Deux étaient atteints d'épilepsie. - Quatre ont été admis en soins intensifs et intubés. - Aucun décès. - Tous ont eu un résultat positif au test PCR, aucun résultat de test sérologique.
Ng (2020) (65) Étude de série de cas Royaume-Uni Avril-mai 2020	Étude de série de cas descriptive de trois patients atteints du MIS-C.	- Deux garçons de 13 et 17 ans; une fille de 16 ans. - Deux étaient noirs, un était asiatique. - Un était obèse. - Tous les trois ont été admis aux soins intensifs; un a été intubé; aucune oxygénation extracorporelle. - Aucun décès.

		- Les trois ont eu un résultat positif pour les anticorps IgG, un a eu un résultat positif au test PCR.
Del Greco (2020) (66) Étude de série de cas États-Unis Octobre 2020*	Étude de série de cas descriptive de quatre patients atteints du MIS-C.	- Trois filles de 4, 10 et 16 ans; un garçon de 13 ans. - Un était asthmatique, les autres n'avaient pas de comorbidité. - Deux ont été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Aucun décès. - Les quatre tests sérologiques étaient positifs, un résultat positif au test PCR.
Rogo (2020) (67) Étude de série de cas États-Unis Avril-mai 2020	Étude de série de cas descriptive de quatre patients atteints du MIS-C.	- Trois garçons de 5, 17 et 20 ans; une fille de 3 ans. - Quatre admis aux soins intensifs, deux ont été intubés, un a nécessité de l'oxygénation extracorporelle. - Un décès. - Quatre résultats négatifs au test PCR et les résultats pour les anticorps IgG étaient positifs.
Waltuch (2020) (68) Étude de série de cas États-Unis Mai 2020	Étude de série de cas descriptive de quatre patients atteints du MIS-C.	- Trois garçons de 5, 10 et 13 ans; une fille de 12 ans. - Un était atteint d'hypothyroïdie, un autre était asthmatique. - Quatre ont été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Aucun décès. - Les quatre tests sérologiques étaient positifs, un résultat positif au test PCR.
Heidemann (2020) (69) Étude de série de cas États-Unis Août 2020*	Étude de série de cas descriptive de trois patients atteints du MIS-C.	- Deux garçons de 5 et 7 ans; une fille de 6 ans, sans comorbidité. - Deux admis aux soins intensifs et intubés, un a nécessité de l'oxygénation extracorporelle. - Un décès. - Un test PCR positif et trois tests sérologiques positifs.
Schupper (2020) (70) Étude de série de cas États-Unis Juin 2020*	Étude de série de cas descriptive de deux patients atteints du MIS-C.	- Deux garçons âgés de 2 mois, 5 ans - Un atteint de trachéomalacie. - Les deux ont été admis aux soins intensifs, intubés et ont nécessité de l'oxygénation extracorporelle. - Un décès. - Un test sérologique positif, aucun résultat de test PCR.
Spencer (2020) (71) Étude de série de cas États-Unis	Étude de série de cas descriptive de	- Une fille de 7 ans; un garçon de 11 ans. - Un patient a eu une crise d'épilepsie.

Septembre 2020*	deux patients atteints du MIS-C.	- Un a été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Aucun décès. - Les deux ont eu un résultat positif au test PCR, aucun résultat sérologique.
ÉTUDE DE CAS		
Khesrani (2020) (72) Étude de cas Algérie Août 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 9 ans atteinte d'aphasie médullaire idiopathique. - A été admise aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - La patiente est décédée. - La patiente a eu un résultat positif au test PCR, aucun résultat de test sérologique.
De Paulis (2020) (73) Étude de cas Brésil Mai 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 4 ans sans comorbidité. - A été admise aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat négatif au PCR, un résultat négatif pour les anticorps IgM, mais un résultat positif pour les anticorps IgG.
Tam (2020) (74) Étude de cas Canada Septembre 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 10 ans sans comorbidité. - A été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, mais un test sérologique positif.
Klocperk (2020) (75) Étude de cas Tchéquie Juillet 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 8 ans sans comorbidité. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat positif au PCR et un résultat positif pour les anticorps IgG.
Acharyya (2020) (76) *(préimpression)* Étude de cas Inde Mai 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 4 mois sans comorbidité. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat positif au test PCR, aucun résultat de test sérologique.

Balasubramanian (2020) (77) Étude de cas Inde Juillet 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 8 ans sans comorbidité. - A été admis aux soins intensifs; aucune intubation; aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Gupta (2020) (78) *(préimpression)* Étude de cas Inde Septembre 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 2 ans. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au PCR, mais ses parents ont eu un résultat positif pour les anticorps parents IgG.
Rauf (2020) (79) Étude de cas Inde Avril 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 5 ans sans comorbidité. - A été admis aux soins intensifs; aucune intubation; aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR et pour les tests sérologiques.
Singhi (2020) (80) Étude de cas Inde Octobre 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 8 ans. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat négatif au test PCR, mais un test sérologique positif.
Tiwari (2020) (81) Étude de cas Inde Octobre 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 9 ans. - A été admise aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat négatif au test PCR, mais un test sérologique positif.
Bahrami (2020) (82) Étude de cas Iran Juillet 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 5 ans sans comorbidité. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat négatif au test PCR, mais un test sérologique positif.
Parvaneh & Rahmani (2020) (83)	Étude de cas descriptive d'un	- Garçon de 7 ans. - Le patient a survécu.

(préimpression) Étude de cas Iran Mai 2020	patient atteint du MIS-C.	- Le patient a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Regev (2020) (84) Étude de cas Israël Août 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 16 ans sans comorbidité. - A été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat positif au test PCR et un résultat positif pour les anticorps IgG.
Schnapp (2020) (85) Étude de cas Israël Juin 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 16 ans sans comorbidité. - A été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, mais un résultat positif pour les anticorps IgG.
Buonsenso (2020) (86) Étude de cas Italie Avril 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 11 ans. - La patiente a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Giannattasio (2020) (87) Étude de cas Italie Juin 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 9 ans. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, mais un résultat positif pour les anticorps IgG et IgM.
Yáñez (2020) (88) Étude de cas Pérou Juin 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 3 ans. - Aucune autre information fournie.
Tracewski (2020) (89) Étude de cas Pologne Mai 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 2 ans. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, un résultat négatif pour les anticorps IgM, mais un résultat positif pour les anticorps IgG.
Rodriguez-Gonzalez (2020) (90)	Étude de cas descriptive d'un	- Garçon de 6 mois atteint du syndrome de l'intestin court.

Étude de cas Espagne Juin 2020*	patient atteint du MIS-C.	- A été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, mais un résultat positif pour les anticorps IgG.
Bapst (2020) (91) Étude de cas Suisse Avril 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 13 ans sans comorbidité. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, mais un test sérologique positif.
Yozgat (2020) (92) *(préimpression)* Étude de cas Turquie Juillet 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 3 ans. - La patiente a survécu. - La patiente a eu un résultat négatif au test PCR, aucun résultat de test sérologique.
Domico (2020) (93) Étude de cas Royaume-Uni Avril 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 11 ans sans comorbidité. - A été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, un résultat négatif pour les anticorps IgM, mais un résultat positif pour les anticorps IgG.
Chiu (2020) (94) Étude de cas États-Unis Juin 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 10 ans sans comorbidité. - A été admis aux soins intensifs. - Le patient a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Choi (2020) (95) Étude de cas États-Unis Août 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Homme hispanique de 19 ans obèse et atteint d'apnée du sommeil. - A été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Clouser (2020) (96) Étude de cas États-Unis Mai 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille noire de 11 ans obèse. - A été admise aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - La patiente a survécu.

		- La patiente a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Dasgupta (2020) (97) Étude de cas États-Unis Juin 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille métisse de 8 ans sans comorbidité. - A été admise aux soins intensifs. - La patiente a survécu. - La patiente a eu un résultat négatif au test PCR et pour les anticorps IgG.
Deza Leon (2020) (98) Étude de cas États-Unis Mai 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 6 ans sans comorbidité. - A été admise aux soins intensifs, intubée et a nécessité de l'oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Dolhnikoff (2020) (99) Étude de cas États-Unis Août 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille noire de 11 ans sans comorbidité - A été admise aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - La patiente est décédée. - La patiente a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Dolinger (2020) (100) Étude de cas États-Unis Mai 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Un garçon de 14 ans atteint de la maladie de Crohn. - Le patient a survécu. - Le patient a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Greene (2020) (101) Étude de cas États-Unis Juin 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 11 ans sans comorbidité. - A été admise aux soins intensifs; aucune intubation; aucune oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Jones (2020) (102) Étude de cas États-Unis Juin 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 6 mois sans comorbidité. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Kaushik, Ahluwalia, (2020) (103) Étude de cas États-Unis	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 5 ans sans comorbidité. - A été admis aux soins intensifs, intubé et a nécessité de l'oxygénation extracorporelle. - Le patient est décédé.

Septembre 2020*		- Le patient a eu un résultat négatif au test PCR, mais un test sérologique positif.
Nelson (2020) (104) Étude de cas États-Unis Octobre 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 15 ans sans comorbidité. - Aucune admission aux soins intensifs, aucune intubation ni oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat négatif au test PCR, aucun résultat de test sérologique.
Rivera-Figueroa (2020) (105) Étude de cas États-Unis Juillet 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon noir de 5 ans sans comorbidité. - A été admis aux soins intensifs; aucune intubation; aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat positif au test PCR, aucun résultat de test sérologique.
Stevens (2020) (106) Étude de cas États-Unis Avril 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille noire de 10 ans asthmatique. - A été admise aux soins intensifs; aucune intubation; aucune oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat négatif au PCR, mais un résultat positif pour les anticorps IgG.
Vari (2020) (107) Étude de cas États-Unis Avril 2020	Étude de cas descriptive d'un patient atteint du MIS-C.	- Garçon de 14 ans. - A été admis aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - Le patient a survécu. - Le patient a eu un résultat négatif au test PCR, mais un résultat positif pour les anticorps IgG.
Verkuil (2020) (108) Étude de cas États-Unis Août 2020*	Étude de cas descriptive d'un patient atteint du MIS-C.	- Fille de 14 ans sans comorbidité. - A été admise aux soins intensifs; aucune intubation, aucune oxygénation extracorporelle. - La patiente a survécu. - La patiente a eu un résultat négatif au test PCR, mais un résultat positif pour les anticorps IgG.

* Date de publication de l'article parce que les dates des cas ne sont pas disponibles.

Méthodes

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable.

Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour trouver les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprennent : MIS-C, PIMS, Kawasaki, inflammation multisystémique, syndrome inflammatoire multisystémique, inflammation multi-système.

382 articles ont été recensés sur le thème du MIS-C, après élimination des doublons. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites de l'examen. 102 études recensées comme pertinentes pour le sujet de l'étude. Cet examen contient les recherches publiées jusqu'au 10 novembre 2020.

Préparé par Megan Striha. Déclaration des incidents en laboratoire du Canada, ASPC. phac.evidence-donnees.probantes.aspc@canada.ca

ANNEXE

Définition de cas de MIS-C publiée par les Centres de contrôle et de prévention des maladies des États-Unis (CDC) (3) :

- Un individu âgé de <21 ans présentant de la fièvre (>38 °C pendant ≥24 heures, ou un rapport de fièvre subjective durant ≥24 heures), des preuves en laboratoire d'une inflammation et des preuves d'une maladie cliniquement grave nécessitant une hospitalisation, avec une atteinte de plusieurs (>2) organes (cardiaque, rénal, respiratoire, hématologique, gastro-intestinal, dermatologique ou neurologique);

ET

- Pas d'autres diagnostics plausibles;

ET

- Résultat positif pour une infection actuelle ou récente par le SRAS-CoV-2 à un test RT-PCR, sérologique ou test antigénique; ou exposition à un cas suspecté ou confirmé de COVID-19 dans les quatre semaines précédant l'apparition des symptômes.

Définition du MIS-C publiée par l'Organisation mondiale de la santé (OMS) (2) :

- Enfants et adolescents de 0 à 19 ans ayant de la fièvre > 3 jours;

ET

- deux des éléments suivants :
    - Éruption cutanée ou conjonctivite bilatérale non purulente ou signes d'inflammation cutanéo-muqueux (buccale, mains ou pieds).
    - Hypotension ou choc.
    - Caractéristiques du dysfonctionnement myocardique, de la péricardite, de la valvulite ou des anomalies coronariennes (y compris les anomalies lors d'une échographie ou les taux élevés de troponine/NT-proBNP);
    - Preuve de coagulopathie (par PT, PTT, taux élevés de d-Dimères).
    - Problèmes gastro-intestinaux aigus (diarrhées, vomissements ou douleurs abdominales).

ET

- Des marqueurs d'inflammation élevés comme l'ESR, la protéine C-réactive ou la procalcitonine.

ET

- Aucune autre cause microbienne évidente d'inflammation, y compris la septicémie bactérienne, les syndromes de choc staphylococcique ou streptococcique.

ET

- Preuve de COVID-19 (RT-PCR, résultat positif à un test antigénique ou sérologique), ou contact probable avec des patients atteints de la COVID-19.

Définition du PIMS publiée par le Royal College of Paediatrics and Child Health (RCPCH) du Royaume-Uni (4) :

- Enfant présentant une fièvre persistante, une inflammation (neutrophilie, CRP élevée et lymphopénie) et des signes de dysfonctionnement d'un seul ou de plusieurs organes (choc, trouble cardiaque, respiratoire, rénal, gastro-intestinal ou neurologique) avec des caractéristiques supplémentaires. Il peut s'agir d'enfants qui répondent à tous les critères de la maladie de Kawasaki ou à une partie de ceux-ci.

ET

- Exclusion de toute autre cause microbienne, y compris la septicémie bactérienne, le syndrome de choc toxique staphylococcique ou le syndrome de choc toxique streptococcique, les infections associées à la myocardite comme l'entérovirus (l'attente des résultats de ces investigations ne devrait pas retarder la recherche d'un avis d'expert).

ET

- Le test PCR du SRAS-CoV-2 peut être positif ou négatif.

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Emerging Evidence on COVID-19

Evidence Brief of COVID-19 quarantine length reduction strategies and effectiveness, Update 1

Introduction

What is the effectiveness of shortened quarantine with and without testing for SARS-CoV-2?

This evidence brief identifies and summarizes published and pre-published data on alternative quarantine strategies (e.g. combinations of RT-PCR testing and quarantine) to explore the potential trade offs compared to the 14-day quarantine currently used. Studies up to December 3, 2020 are included.

Quarantine was one of several public health interventions adopted early in the COVID-19 pandemic by many jurisdictions. Quarantine period in this brief refers to the length of time that must elapse before a person potentially exposed to SARS-CoV-2 can be considered incapable of developing or transmitting COVID-19. The practice may be applied for incoming travellers to a region, suspected cases and/or known contacts of an index case. While many studies have explored the effectiveness of quarantine in reducing COVID-19 transmission, here we focus on the effectiveness of reduced quarantine length with and without testing. Countries have been managing the COVID-19 pandemic for roughly 10 months, and are now looking for effective interventions to reduce transmission while also limiting the negative impact of quarantine on the individual, society and the economy.

It is estimated that the current incubation period for SARS-CoV-2, the time from exposure to symptom onset averages five days (with a range of 1-14 days). It is also estimated that the infectious period may start 1-2 days before symptom onset and continue in mild cases for approximately 8-10 days (1). Exposed contacts may have knowledge of when they were most likely exposed to a known COVID-19 case, if identified by contact tracing. Travellers entering a country may be at any point in their infection from recently exposed to late in an infection at arrival. Quarantine strategies for case contacts and travellers will likely differ in their approach, but the goal is similar, to prevent transmission of SARS-CoV-2 from infected individuals.

An active SARS-CoV-2 infection is most commonly established by RT-PCR testing of a nasopharyngeal or other respiratory mucous membrane swab. The sensitivity of the RT-PCR test depends on many factors including virus load in the sample. Early in an infection the virus load may be very low and there is a high likelihood of a false negative result, which decreases as virus load increases; an example from a meta-analysis indicates false negative results are ~100% on days 1-3, 67% on day 4, 38% on day 5 (symptom onset) and 20% on day 8 post exposure (2, 3). Models included in this review consider a distribution for the sensitivity of the RT-PCR from exposure through infectious period with sensitivity increasing rapidly two days before infection to over 80% and remains high for eight or more days after symptom onset (4). Usually as infection progresses the viral load will increase, studies show variability in peak viral load timing from just before to up

to five days after symptom onset and gradually decreasing as the infection is cleared. Rapid antigen detection tests (RADT) have also started to emerge as a diagnostic tool for COVID-19 (5). RADT tests are cheaper, quicker and easier to perform than the RT-PCR, but likely suffer from lower sensitivity (5). The field performance of RADTs are less certain than RT-PCR, thus models that explored the use of RADTs as a testing option frequently cited a dearth of data on RADT performance (5). Within this review, the test modelled is mainly RT-PCR with the exception of the most recent models which look at scenarios with RT-PCR separately from RADTs.

Key Points

- Since the first version of this evidence brief, one pre-published model was updated, and one rapid review and thirteen models have been released, eleven of which are prepublications that have not completed a peer review process. The rapid review confirms that there was very little research prior to June 26 on the efficacy of quarantine for SARS-CoV-2 as well as SARS-CoV-1 and MERS. The publications in Table 1 and 2 have been issued since the review was conducted and include eight studies that focus on effective quarantine period strategies in the community for contacts of cases and fourteen studies focus on quarantine strategies for travellers to reduce the risk of importation of SARS-CoV-2.
- Two epidemiological studies in Table 1 and 2 and the rapid review in Table 3 describe observed data about the effectiveness of the 14-day quarantine period for both case contacts and travellers. These studies indicate that the 14-day quarantine was effective and the addition of an RT-PCR improved the effectiveness of the quarantine strategy.
- Quantitative models (n=17) concur the 14-day quarantine strategy is effective and explore several alternative scenarios for quarantine and test strategies in the community (Table 1) and for travellers (Table 2).
    - Shorter quarantines (seven or more days) with at least one test completed near the end of the quarantine were fairly equivalent to 14 days with no test (Table 1 & 2). Scenarios where quarantine was less than seven days were consistently less effective compared to longer quarantine.
    - Without the addition of a test, effectiveness increased over time from seven days (50-60% median range) to ten days (68-84%) compared to fourteen days.
    - Testing travellers on arrival and not quarantining those with a negative result was significantly less effective (~40%) than quarantine strategies of one week or longer with various testing strategies.
    - Testing close to the end of the quarantine period was the most effective time point in most scenarios, because individuals initially in the incubation period have a longer time for virus load to increase and thus be detected. This was particularly true to all quarantine scenarios less

than seven days. For quarantines seven days and longer, a test at seven days was just as effective as a test performed later.

  - Testing multiple times during the quarantine period resulted in minimal reduction in the risk of releasing an infectious person into the community compared to testing one time close to the end of quarantine.

- Evidence from quantitative models suggests that testing and quarantine strategies for community contacts and travellers are similar when considering testing at quarantine lengths greater than one week. For strategies less than one week, test and quarantine strategies are less effective in the community because case contacts may be early in their incubation period and test results would have a high false negative rate. This is less of an issue for travellers that may be at any point in their infection, but there is still a risk of releasing travellers early in their incubation period.
- For both community contacts and travellers, the models captured have started to look at quarantine strategies that use RT-PCR or RADTs. The RADT sensitivity is predicted in most of the models to lag behind the RT-PCR, which translated to optimal test and quarantine model results suggesting that doing an RT-PCR on day five of quarantine or the RADT on day six was equivalent. However, depending on the turn around time for the RT-PCR test (reported to be 24 to 96 hours), the RADT would shorten the quarantine period because results would be obtained on day six assuming there is minimal wait for RADT results.
- Adherence to quarantine was also discussed and modelled in several studies. All studies concluded that adherence is higher with shorter quarantines and the impact of quarantine in real life is likely much lower than reflected in the models due to a lack of compliance.

Overview of the Evidence

The review identified and summarized twenty published and pre-published studies. The limited research focused on quarantine to reduce transmission among case contacts in the community and by traveller introduction of COVID-19.
Seventeen quantitative models and risk assessments were included. These do not identify actual outcomes of strategies that have been tested, but rather present a range of plausible outcomes within theoretical scenarios being studied. Their results are useful to compare different options as part of a decision-making process, however the results should be interpreted with caution as the models will vary on their assumptions, input values based on the epidemic period and region specific parameters used.

Two epidemiological investigations, related to contact tracing or quarantine and surveillance of passengers arriving at the airport were identified. These observational studies have a moderate to high risk of bias due to selection, reporting and follow-up biases.

A single rapid review was conducted, it is considered of moderate quality by AMSTAR because only on person assessed and extracted data from each study. Within this review six additional epidemiological investigations and one model were identified for SARS-CoV-2 with similar biases as noted above.

Important knowledge gaps were identified. The knowledge base on quarantine scenarios is largely supported by models, thus there is a lack of empirical evidence on the impact quarantine has on the epidemic, particularly in a local context. Additional information on adherence to quarantine could help with future decision making on this issue. It was also noted that little performance data exists for new diagnostic tools such as RADTs, thus testing and quarantine scenarios for RADTs may change as data becomes available.

CONTENTS

QUARANTINE EFFECTIVENESS: CASE CONTACTS

Table 1 presents nine studies that examined quarantine within the community. An epidemiological account of the epidemic in Macao is presented that implemented a 14-day quarantine with a test on day 13 which successfully prevented known onward transmission (6). Seven modelling studies and one risk assessment explored the role of quarantine in controlling the epidemic. One model looked at how contact tracing (or delays in contract tracing) and adherence affect the effectiveness of different quarantine strategies ranging from no quarantine with symptom based isolation to 7, 10 or 14 day quarantines with or without one to two RT-PCR tests and concluded a 7-day quarantine with a test was equivalent to a 14-day quarantine (7). Quarantine and test strategies from quantitative models suggests that testing and quarantine strategies for community contacts and travellers is similar when considering testing quarantine lengths greater than one week. However, strategies less than one week, test and quarantine strategies are less effective in the community because case contacts may be early in their incubation period.

Other important considerations, particularly in the most recent studies, were type of test and adherence to quarantine. Models have started to look at quarantine strategies that use RT-PCR or a RADTs and strategy optimization findings were test dependent. Adherence to quarantine was examined and results suggest that adherence is higher with shorter quarantines and the impact of quarantine is likely much lower than reflected in the models due to a lack of compliance.

Table 1: Epidemiologic and modelling studies on quarantine of suspected symptomatic and/or potentially exposed individuals in the community. (n=9)

STUDY	METHOD	KEY OUTCOMES
Epidemiological studies		
Lio (2020) (6) Case investigations Macao Jan-Apr 2020	This paper describes successful quarantine (14 days) of individuals who developed symptoms of COVID-19 or were identified as possibly exposed through contact tracing in Macao, a special administration region of China January 22 through April 8, 2020. A 14-day quarantine with an RT-PCR test on day 13 to confirm negative status was implemented in Macao.	Based on surveillance data no, infectious cases were released from quarantine, two people tested positive on the day 13 RT-PCR test. The total number of people quarantined was not reported.
Modelling studies		
Quilty (2020) (7) *preprint updated* Modelling study UK* 2020*	An agent-based model was developed to simulate different quarantine scenarios for identified contacts of a confirmed index case of COVID-19. The model accounts for the time of identification and contact tracing (average is 4 days) as well as the risk of releasing an infected person from quarantine.	This study explored quarantine scenarios from 3-15 days (in graphs) and effectiveness of quarantine based on adherence. Key outcomes for prevention of onward transmission: • Self isolation based on symptoms (no quarantine) prevents 39% (95%UI; 34 – 45%) onward transmission. • 14-day quarantine prevents 70% (95%UI: 39 – 90%) onward transmission. • A negative RT-PCR upon being traced as a contact (~4 days post exposure) prevents 62% (95%UI: 40 - 84%) onward transmission. • A negative RT-PCR 7 days post exposure prevents 68% (95%UI: 40 - 88%) onward transmission. 10 days 69% (95%UI: 41-90%) and 14 days 70% (95%UI: 40-91%).

		• The 7-day quarantine with 1 test was equivalent to the 14-day quarantine with no test. • Testing upon contact tracing and at the end of quarantine had minimal gains in preventing transmission. • A delay of notifying a contact of exposure of 4 days is estimated to result in transmission potential of 26% (95%UI: 7 - 56%) and halving that to 2 days would decrease the transmission potential to 14% (95%UI: 5 - 42%).
Lewis (2020) (8) *preprint* Risk Assessment USA* 2020*	Using the 14-day quarantine as the benchmark for acceptable risk of a COVID-19 case being released from quarantine (estimated to be 0.5%), the authors use this benchmark to quantitatively explore other quarantine strategies. In this risk assessment the outcome is presented as the likelihood of being infectious given a person was symptom-free in quarantine for *x* days.	• A non-symptomatic person with a negative COVID-19 test at day 7-8 would have a lower risk of being infectious (0.4%) than someone completing a 14-day quarantine. This relationship was robust regardless of someone's initial exposure risk. Type of test received was not explored. • Shorter quarantine would improve compliance, decrease economic burden and may better identify asymptomatic infected individuals.
Peng (2020) (9) *preprint* Modelling study USA* 2020*	Simulations (individual-based forward-time simulation method) of quarantine strategies were used to explore the efficacy of strategies that include one or more tests administered during quarantine. The statistical models developed estimate the transmissibility and viral loads of SARS-CoV-2 infections, and the sensitivities of available SARS-CoV-2 testing methods.	Optimal alternative strategies to the 14-day strategy with no test included: RT-PCR • 10-day quarantine with 1 test 1-2 days before the end of quarantine (90% sensitivity RT-PCR) • 8-day quarantine with 2 tests (day 6-7 and day 8). (both RT-PCRs) • 6-day quarantine with 3 tests (days 4, 5, 6), (95% sensitivity RT-PCR) Antigen • 9-day quarantine with 2 tests (days 7 & 8)

	Tests: They model RT-PCR with 95% and 90% sensitivity and an antigen test with a 1 hour turnaround time.	• 11-day quarantine with 2 tests (days 9 & 10) • Note: Additional strategies presented in Table 2 of the paper
Van der Toorn (2020) (5) *preprint* Modelling study Germany 2020*	This paper describes a model (stochastic transit compartment model) and software interface developed to calculate the reduction in the transmissibility of COVID-19 through quarantine or isolation policies with or without testing strategies. The user chooses between three different modi (i) isolation of infected individuals *(not relevant to this review)*, (ii) management of potentially infected contacts and (iii) quarantine of incoming travelers *(see Table 2).* The user customizes the strategy. The model accounts for infection time, temporal changes in test sensitivity (Antigen test assumed to be 85% sensitivity of RT-PCR due to lack of data), incubation and infectious periods and time to symptom onset.	Outcome is a fold risk reduction (ie: x times less risk). Data is provided for each day of quarantine and test type, however only the strategies that were equivalent to a 14-day quarantine and those associated with a 10-day quarantine are reported below. Contact management with symptom screening: • 14-day quarantine 12.22 (7.88 – 22.13) • 8-day quarantine + RT-PCR test 14.48 (13.39 – 15.80) • 10-day quarantine + RDT test 14.51 (11.89-19.92) • 10-day quarantine with RT-PCR test day 5= 23.20 (19.02-31.50) • 10-day quarantine = 4.65 (3.80 – 6.46) The 14-day quarantine was equal to an 8-day with PCR test or 10 day with an antigen test. Benefits to testing include identification of asymptomatic cases and reduction of uncertainty of the quarantine strategy.
Ashcroft (2020) (10) *preprint* Modelling study Switzerland* Oct 2020*	A mathematical model was developed to explore the impact of quarantine strategies to reduce transmission of COVID-19 based on the empirical data of incubation period, infectivity and generation time. Quarantine strategies explored are for close contacts of a confirmed case that has been traced and	Results are largely presented in graphs: • Optimal duration of quarantine is 6 to 8 days, depending on the delay from exposure to quarantine (estimated to be 0-4 days). • Requiring a negative test result before release on day *n* improves transmission prevention, compared to standard release after *n* days. • Efficacy of test-and-release increases with the time from starting quarantine to testing.

	placed in quarantine for *n* days after their exposure to the case (Traveller quarantine strategies, see Table 2). Scenarios investigated: i) Test-and-release. ii) Release upon negative test with reinforced hygiene.	• Rapid testing reduces quarantine by one day, with equivalent efficacy to RT-PCR testing. For example: Day 6 rapid test (efficacy 80.5%) is equivalent to day 5 RT-PCR test with result obtained day 7 (efficacy 82.4%). • Adherence to quarantine has a large impact on efficacy.
Eilersen (2020) (11) Modelling study Denmark* Oct 2020*	Contact tracing and quarantine strategies within the community are explored to facilitate planning the lifting of a lockdown. To do this, an agent-based SEIR model was developed to simulate a society divided into families, workplace and social groups, with noted connections.	The model shows that quarantine periods longer than 5 days have limited effect on the peak infected fraction throughout the epidemic (figure 3d).
Pak (2020) (12) Modelling study Korea* Sept 2020*	Authors evaluate reasons for variability in incubation period and how that may affect quarantine periods. The authors develop a model for incubation period based on epidemiological data (n=312 cases) reported in the literature. They examined the influence of patient demographics on incubation period of documented cases.	Patients > 42 years of age had, on average, longer incubation periods than patients ≤ 42 years old. Analysis indicates that age-specific quarantine may allow for reduced quarantine duration for those less than 42 years old, without increasing the risk of releasing an infected individual from quarantine. Outcome: risk of infection to others before symptom onset: • 14-day quarantine ≤ 42 years, 8.4% > 42 years. 17.1% • 21-day quarantine ≤ 42 years, 2.2% > 42 years. 5.8% Outcome: quarantine duration required for 90% of cases to manifest symptoms before release: • ≤ 42 years, 13.1 days

		• > 42 years, 17.4 days
Wells (2020) (13) *preprint* Modelling study USA* 2020*	A mathematical model was developed to explore various quarantine scenarios: 1) Quarantine for travel, initiated at random times across the infectious course (see Table 2); 2) Quarantine prompted by contact-tracing and therefore initiated early in the infectious course; Quarantine when the time of exposure is known.	The outcome is the epidemiological equivalence to the standard 14 day quarantine to reduce the probability of post-quarantine transmission (PQT): Scenario (1 &) 2 • Testing on initiation of and exit from quarantine could reduce quarantine time by 50% • Testing at initiation only could reduce quarantine time by one day. • 7 day quarantine with testing on exit from quarantine and 6 day quarantine with testing on initiation and exit was equal to 14 day quarantine • testing during quarantine consistently outperformed testing upon tracing • optimal timing for test was one day prior to end of quarantine for periods < 7 days and on day 7 for longer periods of quarantine Scenario 3 • If testing one day post exposure, an additional test on day 6 was optimal. If entering quarantine >6 days after exposure, testing on day of entry was optimal.

*The location or timing of the study was estimated from the author affiliations and publication date respectively. UI= 95% Uncertainty Interval for super spreading events,

QUARANTINE EFFECTIVENESS: TRAVELLERS

Table 2 presents two epidemiological and twelve models related to quarantine strategies for travellers. The epidemiological studies report on the results of the quarantine program for incoming travellers which was 14 days and incorporated RT-PCR testing. In these studies there were no known infective cases released from quarantine in the reported studies.

Twelve modelling studies explore traveller quarantine lengths from zero through 14 days, with various testing strategies. Compared to a 14-day quarantine period, testing around day 5-7 and being released upon a negative test was shown to be equivalent in six models that examined this scenario. Similarly testing earlier than seven days with quarantine shorter than seven days was generally less protective than 14-day quarantine. Testing as close to the end of quarantine as possible in the less than seven day scenarios was most effective. Testing and releasing negative passengers with no quarantine was not effective.

Having multiple tests within a quarantine period resulted in marginal gains to the predicted efficacy of the quarantine scenario. In scenarios with no testing, a seven day quarantine was shown to be between 50-60% effective. A ten day quarantine was better than seven, but not as effective as fourteen.

Other important considerations, particularly in the most recent studies, were type of test and adherence to quarantine. Models have started to look at quarantine strategies that use RT-PCR or a RADTs and strategy optimization was test dependent. Adherence to quarantine was examined and results suggest that adherence is higher with shorter quarantines and the impact of quarantine is likely much lower than reflected in the models due to a lack of compliance.

TABLE 2: Epidemiologic and modelling studies of quarantine length and testing strategies for travellers (n=14)

STUDY	METHOD	KEY OUTCOMES
Epidemiologic studies		
Laiger (2020) (14) Case investigations France 2020	Repatriated travellers from Wuhan, China (n=337). A 14-day quarantine was observed with RT-PCR testing on arrival and day 5.	0/328 repatriated travellers were positive or developed COVID-19. The other 9 travellers: 1 traveller refused to be tested and 8 were only tested on arrival and had a negative result.
Lio (2020) (6) Case investigations Macao Jan-Apr 2020	This paper describes successful quarantine (14 days) of travellers (n=4347) arriving to Macao, a special administration region of China, January 22 through April 8, 2020. A 14-day quarantine with an RT-PCR test on day 13 to confirm negative status was implemented in Macao.	43/4347 travellers were identified to be infected and successfully isolated. Based on surveillance data no infectious cases were released from quarantine.
Modelling studies		

Clifford (2020) (15) *preprint* Modelling study UK* 2020*	A simulation model (generalized additive model with binomial likelihood and P-spline) of air travellers arriving to the UK from the EU or USA was developed to explore four levels of quarantine stringency: 1) Low - no mandatory quarantine, with and without arrival testing; 2) Moderate - mandatory 3, 5 or 7 day quarantine, with and without a test at end of quarantine; 3) High - mandatory quarantine until two negative tests (taken day 0-2 and 2-6 days after first), or 14 days after a positive test; 4) Maximum - mandatory 14-day quarantine with and without a single test at the end of quarantine. The outcome of the model was the number of infectious individuals who enter the country while infectious in each scenario. That result is converted into the proportion of cases prevented from entering the community due to the quarantine scenarios.	1) All scenarios are compared to no quarantine which in mid-July was predicted to be approximately 23 cases from the USA per week and 12 from the EU per week into the UK. Outcome= the proportion of cases prevented from entering the community due to the quarantine scenarios 2) 7 days, no test = 80% 6 days, test day 5 = 88% 8 days, test day 7= 94% 3) Results not extractable 4) 14 days, no test = 99% 15 days, test day 14= 99% (95%UI 97 – 100%) • There was limited utility of pre-departure testing when testing after arrival was in place. • Testing more than one time had limited benefit. Although the uncertainty interval is not presented in the paper, the figures presented in this paper show that quarantines as short as 8 days with testing on day 7 were almost equivalent to the results of a 14 day quarantine.
Dickens (2020) (4) Modelling study Singapore* 2020*	Six scenarios are simulated for preventing importation of COVID-19 cases into a country using a data-driven framework with information from 153 affected countries. Strategies explored include an arrival test and quarantine positive travellers or prohibit entry vs. quarantine only for 7 or 14 days.	Outcome= the reduction in imported cases. Quarantine scenario: • 7 days – no test = 55.4% • 14 days- no test = 91.2% • 0 days- arrival test and positives denied entry = 77.2%

	This model does not account for varying RT-PCR sensitivity through infection.	• 7 days if positive test on arrival and day 7 test = 90.2% • 14 days if positive test on arrival and test on day 14 = 91.7% 14-day quarantine of all passengers is most effective, but also the highest negative impact to travellers.
Steyn (2020) (3) *preprint* Modelling study New Zealand 2020*	A continuous time branching process model for COVID-19 transmission that includes a time-dependent probability of a false-negative test is used to simulate New Zealand's quarantine facility and each simulation is seeded with a case infected up to 14 days prior to arrival. New Zealand has a 14-day quarantine for all international arrivals that includes a minimum of two tests. The model explores 14-day quarantine without testing, 5-day quarantine with test on day 3 and pre-departure and post-arrival testing as different strategies.	Outcome: the percentage of infected travellers prevented from entering the community assuming no transmission in the quarantine facility. • 14 days, tests on day 3 & 12 = 99.9% • 14 days, no tests = 96% • 14 days, chance of early release on day 7 due to a negative test on day 3 or 8 = 99.9% • 5 days, test on arrival and day 3 = 75% • 0 days, negative test pre-departure and on arrival, positives denied entry = 50% If transmission within the quarantine facility should occur, the effectiveness of quarantine goes down and the importance of multiple tests during quarantine increases to both prevent transmission in the facility and to identify newly infected individuals.
Wells (2020) (13) *preprint* Modelling study USA* 2020*	A mathematical model was developed to explore various quarantine scenarios: 1) Quarantine for travel, initiated at random times across the infectious course; 2) Quarantine prompted by contact-tracing and therefore initiated early in the infectious course (*see Table 1)*,	The outcome is the epidemiological equivalence to the standard 14-day quarantine to reduce the probability of post-quarantine transmission (PQT): Scenario 1 & 2 • Testing on arrival and exit from quarantine could reduce quarantine time by 50%. • Testing on arrival only could reduce quarantine time by one day.

	3) Quarantine when the time of exposure is known (*see Table 1)*.	• 7-day quarantine with testing on exit from quarantine and 6-day quarantine with testing on arrival and exit was equal to 14-day quarantine. • Testing during quarantine consistently outperformed testing on arrival. • Optimal timing for test was one day prior to end of quarantine for periods < 7 days and on day 7 for longer periods of quarantine. Example of oil rig workers: • This was applied to an oil rig screening program with both arrival and exit from quarantine testing. 47/4040 employees were positive by this strategy, 16 would have been missed by entry only testing and could have lead to 9 different outbreaks. No infected worker went unidentified.
Russell (2020) (16) *preprint* Modelling study USA* 2020*	A mathematical model was developed to evaluate quarantine and testing strategies. Web application is accessible. Quarantine length examined in days: 0, 2, 5, 7, 14. Testing scenarios: no test, on arrival, 24 hours before the end of quarantine or both. Outcome is days at risk of community transmission assuming 1/10000 travellers are infected and a transmission risk of 0.5 per person-day at risk of transmission.	• Testing during quarantine consistently outperformed testing on arrival (if quarantine compliance is high). • Testing benefits diminished the longer the quarantine period; median reduction of 0.30, 0.10, and 0.004 days at risk for 2, 7, and 14-day quarantine, respectively. • The benefit of quarantine was highly sensitive to compliance where 40% compliance resulted in 1.7-2.1 days at risk, 100% compliance reduced this to 0.00-0.05 days at risk.
Johansson (2020) (17) *preprint*	A mathematical model was developed to analyze the expected effectiveness of symptom monitoring, testing, and quarantine strategies under different	Outcome: reduction in risk of transmission: • Testing on the day of departure could reduce the transmission risk while

Modelling study USA* 2020*	estimates of the infectious period, test-positivity relative to time of infection, and test sensitivity to reduce the risk of transmission from infected travelers during and after travel.	travelling by 37-61%, but 3 days before was a 5-9% reduction. • Testing and no quarantine 0-77% depending on the day of infectious period the test was performed. • Pre and post arrival test 40-66%. • Testing at arrival and 3-4 days later = 45-70%. • Isolation based on symptom monitoring = 36-52%. • 14-day quarantine = 97-100%. • 10-day quarantine = 84-100%. • 7-day quarantine = 65-95% • 7-day quarantine with a test on day 3-4 = 95-99%.
Taylor (2020) (18) *preprint* Modelling study UK Aug 2020	This study estimated that 895 (95%CI 834-958) infectious travellers were arriving in the UK in a single week in August 2020, 87% were on the UK quarantine list, and no quarantine is required for travellers from destinations not on the list. The quarantine is a 14 day self isolation (assumed to be ~80% effective due to compliance), alternative strategies were explored. They considered symptom screening at airports, self isolation for 7, 10 or 14 days and the addition of RT-PCR tests (a 48h turnaround is assumed on test results). A model was created to estimate different quarantine scenarios, but the methods section of the manuscript has been omitted from the prepublication documents, so it cannot be assessed.	• 14-day self isolation is estimated to be 78% effective (95%CI 74.4-81.6). • Thermal scanners detect 1/128 infectious travellers. • Arrival test is 39.6% effective (95%CI 35.2-43.7) – detects 2/5 infectious travellers. • 6-day quarantine with test at 4 days after arrival is 64.3% effective (95%CI 60.0-68.3). • 6-day quarantine with test at arrival and 4 days is 68.9% effective (95%CI: 64.9-73.0). • 7-day quarantine 51.3% effective (95%CI 47.2 – 55.7). • 10-day quarantine 68.8% effective (95%CI 65.1-72.9). • 9-day quarantine with test on day 7 is 74.3% effective (95%CI: 70.0-78.0).

		• 9-day quarantine with test at arrival and on day 7 is 75.9% effective (95%CI: 72.3-79.6). Strategies with testing on day 7 to clear a traveller were almost as effective as the 14-day quarantine.

Van der Toorn (2020) (5)
preprint
Modelling study
Germany
2020*
	This paper describes a model (stochastic transit compartment model) and software interface developed to calculate the reduction in the transmissibility through quarantine or isolation policies with or without testing strategies.
	
	The user chooses between three different modi
	
	(i) isolation of infected individuals *(not relevant to this review);*
	
	(ii) management of potentially infected contacts *(see Table 1);* and
	(iii) quarantine of incoming travelers.
	
	The user customizes the strategy.
	
	The model accounts for infection time, temporal changes in test sensitivity (Antigen test assumed to be 85% sensitivity of RT-PCR due to lack of data), incubation and infectious periods and time to symptom onset.
		Outcome is a fold risk reduction. (ie: x times less risk)
		
		Travellers with symptom screening:
		
		• Symptom screening and testing at arrival
		  ○ RT-PCR = 4.69 (4.19 – 4.83)
		  ○ rapid test (RDT 87% sensitivity) = 3.59 (3.22-3.69)
		• 14-day quarantine = 43.09 (21.82-94.40)
		• 10-day quarantine = 15.66 (9.77- 27.44)
		• 8-day quarantine + RT-PCR test = 47.56 (33.27-73.34)
		• 10-day quarantine + RDT test = 49.92 (30.54 – 85.67)
		• 10-day quarantine with RT-PCR test day 5 = 78.27 (48.87 – 136.94)
		
		Data is provided for each day of quarantine by test type. The 14-day quarantine was equal to an 8-day with PCR test or 10 day with an antigen test.

Ashcroft (2020) (10) *preprint* Predictive Model Switzerland* Oct 2020*	A mathematical model was developed to explore the impact of quarantine strategies to reduce transmission of COVID-19 based on the empirical data of incubation period, infectivity and generation time. Quarantine strategies explored are for travellers that has been placed in	Results are largely presented in graphs. Outcome: fraction of local transmission prevented: • Quarantine of 10 days upon arrival prevents nearly 100% of local transmission. • Testing on arrival is a poor strategy for limiting transmission: testing upon return

	quarantine for *x* days after their arrival. *(Case contacts, see Table 1).* Scenarios investigated: I. Test-and-release. II. Release upon negative test with reinforced hygiene.	at day zero only prevents 54.1% of local transmission, but testing on day five and releasing on day seven prevents 98.5% of local transmission. • Rapid testing reduces quarantine by one day, with minimal loss to efficacy compared to RT-PCR testing.
Arino (2020) (19) *preprint* Modelling study Canada* Dec 2020*	A stochastic model was developed to simulate a small population, homogeneously mixing, and the potential transmission chains that result after a case importation. Efficacy of quarantine is compared to duration of post-arrival quarantine, including how strictly quarantine is observed. Scenarios of 7, 10 and 14-day quarantines are analyzed.	Probability of preventing local transmission from an imported case increased with duration of quarantine and detection of cases from testing. • The efficacy for 7, 10, and 14-day quarantines are shown graphically (figure 7). • If 10% of cases are undetected, 14-day quarantine efficacy is 90%. • Increasing undetected cases to 90%, 14-day quarantine efficacy is 70%.
Matsinos (2020) (20) *preprint* Modelling study USA* Oct 2020*	A Monte-Carlo model is applied to the effect of quarantine length for travellers returning from high-risk COVID-19 regions. Model distributions: -Travel duration: beta(1-21 days, avg 12) -Infection timing : random -Infection probability: i) constant during travel ii) increasing with time, linear iii) increasing with time, logarithmic The model was run nine times, each simulating one million traveller scenarios.	Outcome: Probability of new infections resulting from infectious travellers being released from quarantine: • 8-day quarantine= 5% • 12-day quarantine= 1% • 16-day quarantine= 0.1% The model results do not support a reduction of quarantine from the current 10-14 day requirement of European countries.
Wilson (2020) (21) *preprint* Modelling study	A stochastic SEIR model was developed to explore the impact of various control measures upon likelihood that an infectious traveller would cause an outbreak when coming from a low	Outcome: average time between outbreaks due to travel into a COVID-19 free country: • No intervention = 1.7 years.

New Zealand* Jun 2020*	prevalence area (Australia) to a COVID-19 free area (New Zealand). Quarantine standard of 14 days and reduced 7 days were modelled as well as utilizing a test-and-release policy.	• 14-day quarantine = 34.5 years or more for all scenarios considered. • 7-day quarantine = 5.8 years. • PCR testing on days 3 & 12, release if both negative = 29.6 years

*The location or timing of the study was estimated from the author affiliations and publication date respectively. UK= United Kingdom, USA= United States of America, EU= European Union. UI = uncertainty interval, 95%CI= confidence interval

QUARANTINE EFFECTIVENESS SYNTHESIS RESEARCH

A single rapid review was identified that covered travel-related control measures. Quarantine was a component of this review and included research from SARS-CoV-1, MERS and SARS-CoV-2 up to June 26, 2020. Based on this rapid review there was very little relevant research up to June on quarantine strategies for travellers at the time of the search.

Table 3: Synthesis research related to quarantine length and testing

STUDY	METHOD	KEY OUTCOMES
Burns (2020) (22) Rapid Review Germany* 2020	Rapid review conducted by Cochrane (AMSTAR =moderate quality due to single reviewer) includes 36 studies on travel-related control measures to contain a pandemic. Search up to June 26, 2020 and included relevant studies on SARS-CoV-2 as direct evidence and SARS-CoV-1 and MERS as indirect evidence. The review includes 17 modelling studies, 7 observational screening studies and one observational ecological study on COVID-19, four modelling and six observational studies on SARS, and one modelling study on SARS and MERS, covering a variety of settings and epidemic stages.	For quarantine outcomes: • 1 COVID-19 study was included and concluded that 14-day quarantines reduced the risk of transmission from imported cases and the effectiveness of the quarantine depended on compliance (very low certainty of evidence) (Table 7). • 4 studies on SARS-1 or MERS were reported, however these looked at the impact of quarantine as a public health intervention and did not explore different quarantine strategies (Table 7). • Six COVID-19 observational studies are described particularly for repatriation flights where travellers were quarantined for 14 days and both symptom and

	None appear to have looked at different quarantine strategies, but some speak to the impact and effectiveness of the 14-day quarantine with symptom based screening or testing.	testing during quarantine was conducted. The results generally indicate that the 14 days alone or based on symptoms is not as sensitive as the use of an RT-PCR test during quarantine (no inference about shortening quarantine can be drawn from these studies) (Table 6). Other outcomes covered, but not summarized here: entry/exit symptom screening, border closures, and border restrictions.

*The location or timing of the study was estimated from the author affiliations and publication date respectively.

Methods:

A daily scan of the literature (published and pre-published) related to COVID-19 is conducted by the Emerging Science Group, PHAC; and has been ongoing since the beginning of the outbreak. The literature is retrieved from Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced, the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. A search to retrieve relevant literature for this evidence summary was conducted in the Refworks database. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. The search algorithms used isolation AND length, quarantine AND length, quarantine AND testing AND (reduce OR travel). 414 citations were screened for relevance and data was extracted from relevant articles into the review. This review contains research related to quarantine, and testing as a means to reduce quarantine duration, published up to December 3, 2020.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur les stratégies visant à réduire la durée de la quarantaine associée à la COVID-19 et leur efficacité, mise à jour 1

Introduction

Quelle est l'efficacité d'une quarantaine plus courte avec et sans test de dépistage pour le SRAS-CoV-2?

Cette synthèse des données probantes détermine et résume les données publiées et prépubliées sur différentes stratégies de rechange à la quarantaine (p. ex., combinaison de test RT-PCR et de quarantaine) afin d'explorer les solutions pouvant être mises en œuvre plutôt que la mise en quarantaine de 14 jours actuellement utilisée. Les études publiées et prépubliées jusqu'au 3 décembre 2020 ont été incluses dans cette synthèse.

La quarantaine a été l'une des nombreuses interventions en santé publique adoptées par de nombreuses administrations au début de la pandémie de COVID-19. Dans la présente synthèse, le terme « quarantaine » fait référence au temps qui doit s'écouler avant qu'une personne potentiellement exposée au SRAS-CoV-2 puisse être jugée incapable de développer ou de transmettre la COVID-19. La quarantaine peut être utilisée pour les voyageurs qui arrivent dans une région, les cas soupçonnés de COVID-19 ou les contacts connus d'un cas de référence. Bien que de nombreuses études aient examiné l'efficacité de la quarantaine pour réduire la transmission de la COVID-19, la présente synthèse porte spécifiquement sur l'efficacité de la réduction de la durée de la quarantaine avec et sans test de dépistage. Comme les pays gèrent la pandémie de COVID-19 depuis environ dix mois, ils cherchent désormais des moyens d'intervention efficaces qui pourront permettre de réduire la transmission tout en limitant les répercussions négatives de la quarantaine sur les personnes, la société et l'économie.

On estime que la période d'incubation actuelle du SRAS-CoV-2, c'est-à-dire le temps entre l'exposition au virus et l'apparition des symptômes, est de 5 jours en moyenne (elle varie cependant entre 1 et 14 jours). On estime également que la période infectieuse peut commencer un à deux jours avant l'apparition des symptômes et se poursuivre pendant environ 8 à 10 jours (1) dans les cas légers. Si elles sont identifiées par une recherche des contacts, les personnes qui ont été en contact avec le virus pourront ainsi savoir à quel moment elles ont été le plus susceptibles d'avoir été exposées à un cas connu de COVID-19. Il ne faut pas non plus oublier que tout voyageur qui arrive dans un pays peut avoir été exposé à l'infection et que cette exposition peut être récente ou remonter à quelques jours. De ce fait, même si les stratégies de mise en quarantaine pour les contacts et les voyageurs utiliseront probablement des approches différentes, elles ont cependant toutes deux le même objectif, soit prévenir la transmission du SRAS-CoV-2 par les personnes infectées.

Une infection active au SRAS-CoV-2 est le plus souvent confirmée par le test RT-PCR, soit un test de prélèvement par écouvillonnage nasopharyngé et oropharyngé qui permet d'obtenir des muqueuses respiratoires. La sensibilité du test RT-PCR dépend cependant de nombreux facteurs, dont la charge virale de l'échantillon. Puisque cette charge virale peut être très faible en début d'infection, il est fort probable qu'une personne qui passerait un test de dépistage au début de l'infection obtiendrait un résultat faussement négatif, probabilité qui diminue cependant lorsque la charge virale augmente. Un exemple tiré d'une méta-analyse indique les pourcentages suivants de faux négatifs, soit 100 % pendant les jours 1 à 3, 67 % le jour 4, 38 % le jour 5 (apparition des symptômes) et 20 % le jour 8 suivant l'exposition (2, 3). Les modèles inclus dans cette revue tiennent compte d'une répartition établie en fonction de la sensibilité du test RT-PCR établie entre le moment où une personne est exposée au virus et la fin de la période infectieuse, sachant que la sensibilité augmente rapidement deux jours avant l'infection pour atteindre plus de 80 % et reste à un niveau élevé pendant huit jours ou plus après l'apparition des symptômes (4). De façon générale, au fur et à mesure que l'infection s'étend, la charge virale augmente. Les études montrent cependant une variabilité dans le pic de la charge virale qui va du moment qui précède l'apparition des symptômes jusqu'à cinq jours après celle-ci, suivi d'une diminution graduelle à mesure que l'infection disparaît. Les tests de détection rapide d'antigènes (RADT) ont également commencé à être utilisés comme outil de diagnostic pour la COVID-19 (5). Bien que ces tests soient moins chers, plus rapides et plus faciles à réaliser que les tests RT-PCR, ils sont probablement moins sensibles que ces derniers (5). Le rendement des RADT sur le terrain est plus incertain que celui des RT-PCR et les modèles qui ont examiné l'utilisation des RADT comme option de test ont souvent mentionné le manque de données sur le rendement de ces tests (5). La présente revue porte principalement sur l'utilisation du RT-PCR, sauf en ce qui concerne les modèles les plus récents qui font une distinction entre les scénarios avec RT-PCR et les scénarios avec RADT.

Points clés

- Depuis la diffusion de la première version de cette revue rapide, une revue rapide a été publiée et un modèle prépublié a été mis à jour. Treize modèles ont également été diffusés dont onze sont des prépublications pour lesquelles aucun processus d'examen par les pairs n'a été effectué. La revue rapide confirme que très peu de recherches ont été effectuées avant le 26 juin sur l'efficacité de la quarantaine pour le SRAS-CoV-2 ainsi que pour le SRAS-CoV-1 et le MERS. Les tableaux 1 et 2 comprennent donc les publications diffusées depuis la publication de cette revue rapide, ce qui inclut huit études qui mettent l'accent sur des stratégies efficaces de quarantaine dans la collectivité pour les contacts avec les cas et quatorze autres qui portent plutôt sur les stratégies de mise en quarantaine des voyageurs afin de réduire le risque d'importation du SRAS-CoV-2.
- Les deux études épidémiologiques qui figurent dans les tableaux 1 et 2 et la revue rapide incluse dans le tableau 3 décrivent les données observées sur l'efficacité de la période de quarantaine de 14 jours pour les voyageurs et pour les personnes ayant été en contact avec des cas. Elles montrent que la quarantaine de 14 jours a été efficace et que l'ajout du test RT-PCR a permis d'augmenter l'efficacité de la stratégie de mise en quarantaine.

- Les modèles quantitatifs (n = 17) conviennent également que la stratégie de quarantaine de 14 jours est efficace, en plus d'explorer plusieurs scénarios de rechange combinant quarantaine et test, tant dans la communauté (tableau 1) que pour les voyageurs (tableau 2).
    - Une quarantaine plus courte (sept jours ou plus) combinée à au moins un test effectué vers la fin de la quarantaine a permis d'obtenir des résultats à peu près équivalents à 14 jours de quarantaine sans test (tableaux 1 et 2). Les scénarios dans lesquels la quarantaine durait moins de sept jours se sont tous révélés moins efficaces que les scénarios dans lesquels une quarantaine plus longue était respectée.
    - Sans l'ajout d'un test, l'efficacité a augmenté avec le temps de sept jours (plage médiane de 50 à 60 %) à dix jours (68 à 84 %) comparativement à quatorze jours.
    - Le fait de soumettre les voyageurs à des tests à l'arrivée et de ne pas mettre en quarantaine ceux dont le résultat était négatif s'est cependant révélé beaucoup moins efficace (~40 %) que les stratégies avec quarantaine d'une semaine ou plus combinées à différentes stratégies de dépistage.
    - La plupart des scénarios indiquent que le moment le plus approprié pour effectuer les tests de dépistage se situe vers la fin de la période de quarantaine puisque ce confinement a permis à la charge virale d'augmenter, ce qui permet de la détecter chez les personnes qui se trouvaient en période d'incubation au moment de leur mise en quarantaine. Cela était particulièrement vrai pour tous les scénarios avec quarantaine durant moins de sept jours. Lorsque la quarantaine dure sept jours et plus, un test effectué après sept jours était tout aussi efficace qu'un test effectué par la suite.
    - Le fait d'effectuer plusieurs tests pendant la quarantaine, plutôt qu'un seul test vers la fin de la quarantaine, a permis de réduire au minimum le risque de contagion dans la collectivité lorsqu'une personne terminait sa quarantaine.
- Les données probantes tirées des modèles quantitatifs indiquent que les stratégies de dépistage et de mise en quarantaine pour les contacts dans la collectivité et les voyageurs sont semblables lorsqu'on envisage d'effectuer des tests et que la quarantaine dure plus d'une semaine. En ce qui concerne les stratégies qui comportent une quarantaine durant moins d'une semaine, les stratégies avec test et quarantaine se sont révélées moins efficaces dans la collectivité parce que les personnes pouvaient être au début de leur période d'incubation et que les résultats des tests entraîneraient alors un taux élevé de faux négatifs. Cela est cependant moins problématique pour les voyageurs qui peuvent en être à quelque phase que ce soit de l'infection, mais il y a toujours un risque associé à la levée de la quarantaine pour ces voyageurs, puisqu'ils pourraient encore être au début de la période d'incubation.
- Tant pour les contacts dans la collectivité que pour les voyageurs, les modèles ont commencé à examiner les stratégies de mise en quarantaine combinée aux tests RT-PCR ou RADT. La plupart des modèles ont prédit que la sensibilité du RADT serait inférieure à celle des tests RT-PCR, ce qui s'est

traduit par des résultats optimaux pour le modèle avec test et quarantaine selon lequel le fait d'effectuer un test RT-PCR le cinquième jour de la quarantaine ou un RADT le sixième jour aurait le même effet. Toutefois, en raison du délai d'exécution du test RT-PCR (entre 24 et 96 heures), le RADT permettrait de réduire la période de quarantaine puisque l'on obtiendrait les résultats le sixième jour, si l'on présume suppose une attente minimale avant d'obtenir ces résultats.

- Le respect de la quarantaine a également été abordé et modélisé dans plusieurs études. Les études ont toutes conclu que le niveau de respect est plus élevé lorsque les quarantaines sont plus courtes et qu'en raison d'un manque de conformité, les répercussions de la quarantaine dans la vie réelle sont probablement beaucoup moins importantes que ce qu'indiquent les modèles.

Vue d'ensemble des éléments de preuve

La revue a permis de cerner et de résumer vingt études publiées et non encore publiées. La recherche, bien que limitée, a donc porté sur le rôle de la quarantaine pour réduire la transmission lors des contacts avec des cas dans la collectivité et à la transmission de la COVID-19 par les voyageurs.
Dix-sept modèles quantitatifs et évaluations du risque ont été inclus. Même si ces modèles n'ont pas permis de déterminer les résultats réels des stratégies mises à l'essai, ils offrent un éventail de résultats plausibles en ce qui concerne les scénarios théoriques à l'étude. Bien que ces résultats soient utiles pour comparer différentes options dans le cadre d'un processus décisionnel, il faut cependant faire preuve de prudence au moment de les interpréter, puisque ces modèles ont utilisé différentes hypothèses de base ainsi que des valeurs variables, notamment la période et les paramètres propres aux régions.

Deux enquêtes épidémiologiques, liées à la recherche des contacts ou à la mise en quarantaine et à la surveillance des passagers qui arrivent dans les aéroports, ont aussi été utilisées. Ces études d'observation présentent un risque modéré à élevé de biais en raison de la méthode de sélection, de la façon de présenter les résultats et du suivi utilisés.

Une seule revue rapide a été effectuée et est jugée être de qualité moyenne par AMSTAR puisqu'une seule personne a évalué et extrait les données utilisées dans chacune des études. Dans le cadre de cette revue, six enquêtes épidémiologiques supplémentaires et un modèle avec des biais semblables à ceux qui sont indiqués ci-dessus ont été utilisés pour le SRAS-CoV-2.

Des lacunes importantes dans les connaissances ont cependant été relevées. La base de connaissances sur les scénarios de quarantaine est largement appuyée par différents modèles, ce qui veut dire qu'il n'y a pas suffisamment de données empiriques sur les répercussions de la quarantaine sur l'épidémie, en particulier dans un contexte local. Des renseignements supplémentaires sur le respect de la quarantaine pourraient permettre de prendre des décisions à l'avenir en ce qui concerne cette question. Il a également été mentionné qu'il existait peu de données sur le rendement pour les nouveaux outils de diagnostic comme les tests RADT, ce qui veut dire que les scénarios de test et de quarantaine pour le RADT pourront changer à mesure que les données deviendront disponibles.

TABLE DES MATIÈRES

EFFICACITÉ DE LA QUARANTAINE : CONTACTS AVEC DES CAS

Le tableau 1 présente neuf études portant sur la quarantaine dans la collectivité. Un compte rendu épidémiologique de l'épidémie à Macao est également présenté. Il comprenait une quarantaine de 14 jours avec test effectué le jour 13 qui a permis d'empêcher la transmission subséquente (6). Sept études de modélisation et une évaluation du risque ont exploré le rôle de la quarantaine dans le contrôle de l'épidémie. Un modèle a notamment examiné la façon dont la recherche des contacts (ou les retards dans cette recherche) et le respect de la quarantaine influent sur l'efficacité des différentes stratégies en matière de quarantaine, ce qui incluait l'absence de quarantaine avec isolement fondée sur les symptômes à des quarantaines de 7, de 10 ou de 14 jours avec ou sans un ou deux tests RT-PCR. Il a conclu qu'une quarantaine de 7 jours avec test équivalait à une quarantaine de 14 jours (7). Les stratégies avec quarantaine et test tirées des modèles quantitatifs indiquent que les stratégies de dépistage et de mise en quarantaine pour les contacts dans la collectivité et les voyageurs sont semblables lorsqu'on prévoit effectuer des tests et que la quarantaine dure plus d'une semaine. Cependant, les stratégies qui s'accompagnent d'une quarantaine durant moins d'une semaine et d'un test combiné à une quarantaine se sont révélées moins efficaces dans la collectivité parce que les contacts avec les cas pouvaient encore être au début de leur période d'incubation.

D'autres éléments importants, particulièrement dans les études les plus récentes, incluaient le type de test et le respect de la quarantaine. Les modèles ont commencé à examiner les stratégies de quarantaine qui utilisent les tests RT-PCR ou RADT et les résultats de l'optimisation de la stratégie dépendaient directement des tests. Le respect de la quarantaine a alors été examiné et les résultats suggèrent que le taux de respect est plus élevé lorsque les quarantaines sont plus courtes et qu'en raison d'un manque de conformité, les répercussions de la quarantaine dans la vie réelle sont probablement beaucoup moins importantes que ce qu'indiquent les modèles.

Tableau 1 : Études épidémiologiques et de modélisation sur la mise en quarantaine dans la collectivité de personnes soupçonnées d'être symptomatiques ou d'avoir été potentiellement exposées au virus. (n = 9)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Études épidémiologiques		
Lio (2020) (6) Enquêtes sur les cas Macao Entre janvier et avril 2020	Ce document décrit la mise en quarantaine réussie (14 jours) des personnes qui ont développé des symptômes de COVID-19 ou qui ont été jugées comme ayant été possiblement exposées à la suite d'une recherche de contacts à Macao, une région administrative spéciale de la Chine, entre le 22 janvier et le 8 avril 2020. Une quarantaine de 14 jours avec test RT-PCR effectué le jour 13 pour confirmer le statut négatif a été mise en œuvre à Macao.	Selon les données de surveillance, la quarantaine n'a pas été levée pour aucune personne infectée et deux personnes ont obtenu un résultat positif au test RT-PCR effectué le jour 13. Le nombre total de personnes mises en quarantaine n'a cependant pas été déclaré.
Études de modélisation		
Quilty (2020) (7) *préimpression mise à jour* Étude de modélisation R.-U.* 2020*	Un modèle fondé sur des agents a été développé pour simuler différents scénarios de mise en quarantaine pour les contacts identifiés après un cas de référence confirmé de COVID-19. Le modèle tient compte du moment où la détermination des cas et la recherche des contacts ont été effectuées (la moyenne étant de 4 jours) ainsi que du risque qu'une personne infectée puisse circuler, après la levée de la quarantaine.	Cette étude a examiné différents scénarios dans lesquels la quarantaine variait de 3 à 15 jours (dans les graphiques), ainsi que l'efficacité de la quarantaine en fonction du respect de la quarantaine. Principaux résultats en ce qui concerne la prévention de la transmission subséquente : • L'auto-isolement fondé sur les symptômes (aucune mise en quarantaine) empêche 39 % (II à 95 %, de 34 à 45 %) de la transmission subséquente. • Une quarantaine de 14 jours empêche 70 % (II à 95 %, de 39 à 90 %) de la transmission subséquente.

		• Un résultat négatif au test RT-PCR après recherche de contacts (environ 4 jours après l'exposition) empêche 62 % (II à 95 % : de 40 à 84 %) de la transmission subséquente. • Un résultat négatif au test RT-PCR 7 jours après l'exposition empêche 68 % (II à 95 % : de 40 à 88 %) de la transmission subséquente. Le pourcentage atteint 69 % (II à 95 % : de 41 à 90 %) pour 10 jours et 70 % (II à 95 % : de 40 à 91 %) pour 14 jours. • La quarantaine de 7 jours avec 1 test équivalait à la quarantaine de 14 jours sans test. • Les tests effectués lors de la recherche des contacts et à la fin de la quarantaine ont permis de réduire au minimum la transmission. • On estime qu'un retard de 4 jours avant d'aviser un contact de toute exposition entraîne un potentiel de transmission de 26 % (II à 95 % : de 7 à 56 %) et que le fait de réduire cette période de moitié (soit 2 jours) réduirait à 14 % (II à 95 % : de 5 à 42 %) le potentiel de transmission.
Lewis (2020) (8) *préimpression* Évaluation du risque É.-U.* 2020*	Les auteurs ont utilisé la quarantaine de 14 jours comme point de référence pour définir le niveau de risque acceptable de levée de la quarantaine pour un cas de COVID-19 (estimé à 0,5 %) et explorer quantitativement d'autres stratégies en ce qui concerne la quarantaine. Dans cette évaluation du risque, le résultat est présenté comme la probabilité que le cas soit infectieux lorsqu'une personne n'a pas eu de	• Une personne non symptomatique dont le résultat du test pour la COVID-19 effectué les jours 7 ou 8 présente un risque d'infection inférieur (0,4 %) à celui d'une personne qui termine une quarantaine de 14 jours. Le lien était solide, quel que soit le risque d'exposition initial d'une personne. Le type de test effectué n'a pas été examiné. • Une quarantaine plus courte permettrait donc d'augmenter la conformité et de réduire le fardeau économique, en plus de

	symptômes pendant les *x* jours de sa quarantaine.	permettre de mieux déterminer les personnes infectées et asymptomatiques.
Peng (2020) (9) *préimpression* Étude de modélisation É.-U.* 2020*	Des simulations (méthode individuelle de simulation prospective) de stratégies de quarantaine ont été utilisées pour évaluer l'efficacité des différentes stratégies comprenant un ou plusieurs tests effectués pendant la quarantaine. Les modèles statistiques ont permis d'estimer la transmissibilité et la charge virale des infections par le SRAS-CoV-2, ainsi que la sensibilité des méthodes de dépistage du SRAS-CoV-2 disponibles. Tests : Les auteurs ont modélisé le test RT-PCR avec une sensibilité de 95 % et de 90 % et un test antigénique avec un délai d'exécution d'une heure.	Les stratégies de rechange optimales à la stratégie de 14 jours sans test comprenaient : RT-PCR • Quarantaine de 10 jours avec 1 test 1 à 2 jours avant la fin de la quarantaine (RT-PCR avec sensibilité de 90 %) • Quarantaine de 8 jours avec 2 tests (jour 6 ou 7 et jour 8). (deux RT-PCR) • Quarantaine de 6 jours avec 3 tests (jours 4, 5, 6) (RT-PCR avec sensibilité de 95 %) Antigène • Quarantaine de 9 jours avec 2 tests (jours 7 et 8) • Quarantaine de 11 jours avec 2 tests (jours 9 et 10) • Remarque : Stratégies supplémentaires présentées dans le tableau 2 du document
Van der Toorn (2020) (5) *préimpression* Étude de modélisation Allemagne 2020*	Ce document décrit un modèle (modèle de compartimentation de la transmission) et une interface logicielle conçus pour calculer la réduction dans la transmissibilité de la COVID-19 grâce à des politiques de mise en quarantaine ou d'isolement avec ou sans test. L'utilisateur a le choix entre trois modes différents : (i) isolement des personnes infectées (*non pertinent pour cette revue*), (ii) gestion des contacts potentiellement infectés, et (iii) mise en quarantaine des	Il en résulte une réduction du risque multiplié (c.-à-d. x fois moins de risque). Les données sont fournies pour chaque jour de quarantaine et chaque type de test, mais seules les stratégies qui équivalaient à une quarantaine de 14 jours et celles associées à une quarantaine de 10 jours sont mentionnées ci-dessous. Gestion des contacts avec dépistage des symptômes : • Quarantaine de 14 jours 12,22 (entre 7,88 et 22,13) • Quarantaine de 8 jours + test RT-PCR 14,48 (entre 13,39 et 15,80)

	voyageurs qui arrivent au pays *(voir le tableau 2).* L'utilisateur personnalise ensuite la stratégie. Le modèle tient compte de la durée de l'infection, des changements temporels dans la sensibilité du test (on présume que le test antigénique a une sensibilité de 85 % par rapport au test RT-PCR en raison du manque de données), des périodes d'incubation et d'infection et du temps écoulé avant l'apparition des symptômes.	• Quarantaine de 10 jours + test RDTA 14,51 (entre 11,89 et 19,92) • Quarantaine de 10 jours avec test RT-PCR le jour 5 = 23,20 (de 19,02 à 31,50) • Quarantaine de 10 jours = 4,65 (de 3,80 à 6,46) La quarantaine de 14 jours équivalait à une quarantaine de 8 jours avec test PCR ou à une quarantaine de 10 jours avec test antigénique. Les avantages des tests comprennent la détermination des cas asymptomatiques et la réduction de l'incertitude de la stratégie de quarantaine.
Ashcroft (2020) (10) *préimpression* Étude de modélisation Suisse* Octobre 2020*	Un modèle mathématique a été élaboré pour explorer les répercussions des stratégies de quarantaine visant à réduire la transmission de la COVID-19 en fonction des données empiriques sur la période d'incubation, l'infectiosité et le temps de génération. Les stratégies de quarantaine explorées portent sur les contacts étroits d'un cas confirmé ayant été cherché et mis en quarantaine pendant *n* jours après l'exposition au cas (stratégies de quarantaine pour les voyageurs, voir le tableau 2). Scénarios étudiés : i) test et levée de la quarantaine.	Les résultats sont en grande partie présentés sous forme de graphiques : • La durée optimale de la quarantaine est de 6 à 8 jours, durée établie en fonction du délai entre l'exposition et la quarantaine (estimé entre 0 et 4 jours). • Le fait d'exiger un résultat négatif au test avant la levée de la quarantaine le jour *n* augmente la prévention de la transmission, comparativement à la levée de la quarantaine standard après *n* jours. • L'efficacité des tests et de la levée de la quarantaine augmente avec le temps qui s'est écoulé entre le début de la quarantaine et les tests. • Les tests rapides réduisent la quarantaine d'un jour, avec une efficacité équivalente aux tests RT-PCR. Par exemple : Le test rapide effectué le jour 6 (efficacité de 80,5 %) est équivalent au test RT-PCR effectué le jour 5 lorsque l'on obtient le résultat le jour 7 (efficacité de 82,4 %).

	ii) Levée de la quarantaine après test négatif avec renforcement de l'hygiène.	• Le respect de la quarantaine a une grande incidence sur l'efficacité.
Eilersen (2020) (11) Étude de modélisation Danemark* Octobre 2020*	Les stratégies de recherche des contacts et de quarantaine dans la collectivité sont explorées pour faciliter la planification de la levée du confinement. Pour ce faire, un modèle SEIR (susceptible, exposé, infectieux, éliminé) basé sur les agents a été élaboré pour simuler une société divisée en familles, en milieux de travail et en groupes sociaux, dont les liens entre chaque personne étaient indiqués.	Le modèle montre que les périodes de quarantaine de plus de 5 jours ont un effet limité sur la fraction de crête des infections pendant toute la durée de l'épidémie (figure 3d).
Pak (2020) (12) Étude de modélisation Corée* Septembre 2020*	Les auteurs évaluent les raisons de la variabilité de la période d'incubation et son incidence sur les périodes de quarantaine. Les auteurs ont élaboré un modèle pour la période d'incubation fondé sur des données épidémiologiques (n = 312 cas) mentionnées dans la documentation. Ils ont examiné l'influence des données démographiques des patients sur la période d'incubation dans les cas documentés.	Les patients de plus de 42 ans avaient, en moyenne, des périodes d'incubation plus longues que les patients de 42 ans et moins. L'analyse indique que la durée de la quarantaine établie selon l'âge peut permettre de réduire la durée de la quarantaine pour les personnes de moins de 42 ans, sans augmenter le risque de levée de la quarantaine pour une personne infectée. Résultat : risque d'infection avant l'apparition des symptômes • Quarantaine de 14 jours ≤ 42 ans, 8,4 % > 42 ans. 17,1 % • Quarantaine de 21 jours ≤ 42 ans, 2,2 % > 42 ans. 5,8 % Résultat : durée de quarantaine requise dans 90 % des cas avant l'apparition des symptômes et levée de la quarantaine : • ≤ 42 ans, 13,1 jours

		• > 42 ans, 17,4 jours
Wells (2020) (13) *préimpression* Étude de modélisation É.-U.* 2020*	Un modèle mathématique a été élaboré pour explorer divers scénarios en ce qui concerne la quarantaine : 1) Mise en quarantaine pour les voyages, amorcée à différents moments établis de façon aléatoire pendant toute la phase d'infection (voir le tableau 2); 2) Mise en quarantaine motivée par la recherche des contacts et, par conséquent, amorcée au début de la phase d'infection; Mise en quarantaine lorsque le moment de l'exposition est connu.	Le résultat est l'équivalence épidémiologique avec mise en quarantaine standard de 14 jours afin de réduire la probabilité de transmission après la mise en quarantaine : Scénario (1 et) 2 • Les tests sur la date de début de la quarantaine et la levée de celle-ci pourraient réduire de 50 % la durée de la quarantaine. • Seuls les tests effectués au début de la quarantaine pourraient réduire d'une journée la durée de celle-ci. • Une quarantaine de 7 jours avec test avant la levée de la quarantaine et une quarantaine de 6 jours avec test au début et à la fin équivaut à 14 jours de quarantaine avec tests en fin de quarantaine et à une quarantaine de 6 jours avec tests au début et à la fin équivaut à une quarantaine de 14 jours. • Les tests effectués pendant la quarantaine ont toujours donné des résultats supérieurs aux tests effectués après la recherche • Le moment optimal pour effectuer le test était une journée avant la fin de la quarantaine pour les périodes < 7 jours et le jour 7 pour les périodes de quarantaine plus longues Scénario 3 • Si le test a eu lieu une journée après l'exposition, un autre test effectué le jour 6 était optimal. Si la personne avait été mise en quarantaine plus de 6 jours après l'exposition, les tests effectués le jour de l'entrée en quarantaine étaient optimaux.

*Le lieu ou le moment de l'étude a été estimé à partir des affiliations des auteurs et de la date de publication, respectivement. II= Intervalle d'incertitude à 95 % pour les événements de super propagation

EFFICACITÉ DE LA QUARANTAINE : VOYAGEURS

Le tableau 2 présente deux modèles épidémiologiques et douze modèles portant sur les stratégies de quarantaine pour les voyageurs. Les études épidémiologiques font état des résultats du programme de quarantaine pour les voyageurs qui arrivent au Canada, programme qui comprend 14 jours de quarantaine et des tests RT-PCR. Ces études n'ont relevé aucune personne contagieuse après que la quarantaine ait été levée.

Douze études de modélisation explorent la durée de la quarantaine des voyageurs. Cette durée allait de zéro à 14 jours, avec diverses stratégies de test. Comparativement à une période de quarantaine de 14 jours, les tests effectués autour des jours 5 à 7 et la levée de la quarantaine après un test négatif se sont révélés équivalents dans les six modèles examinés dans ce scénario. De même, les tests effectués avant sept jours lors d'une quarantaine de moins de sept jours offraient généralement une protection moindre que la quarantaine de 14 jours. Les tests les plus efficaces ont été effectués le plus près possible de la fin de la quarantaine dans les scénarios avec quarantaine de moins de sept jours. Il n'a pas été efficace de tester les passagers négatifs qui ne se sont pas mis en quarantaine et pour qui la quarantaine a été levée.

Le fait d'avoir effectué plusieurs tests au cours d'une période de quarantaine a entraîné des gains marginaux dans l'efficacité prévue du scénario de quarantaine. Dans les scénarios sans test, il a été démontré qu'une quarantaine de sept jours avait une efficacité variant entre 50 et 60 %. Une quarantaine de dix jours était préférable à sept jours, mais pas aussi efficace qu'une quarantaine de quatorze jours.

D'autres éléments importants, particulièrement dans les études les plus récentes, incluaient le type de test et le respect de la quarantaine. Les modèles ont commencé à examiner les stratégies de quarantaine qui utilisent les tests RT-PCR ou RADT et établi que l'optimisation de la stratégie dépendait directement des tests. Le respect de la quarantaine a alors été examiné et les résultats suggèrent que le taux de respect est plus élevé lorsque les quarantaines sont plus courtes et qu'en raison d'un manque de conformité, les répercussions de la quarantaine dans la vie réelle sont probablement beaucoup moins importantes que ce qu'indiquent les modèles.

TABLEAU 2 : Études épidémiologiques et de modélisation de la durée de la quarantaine et stratégies de dépistage pour les voyageurs (n = 14)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Études épidémiologiques		
Laiger (2020) (14) Enquêtes sur les cas France 2020	Voyageurs rapatriés de Wuhan, Chine (n = 337). Les voyageurs ont dû se soumettre à une quarantaine de 14 jours avec des tests RT-PCR à l'arrivée et au jour 5.	Parmi les 328 voyageurs rapatriés, aucun n'était positif pour la COVID-10 ou avait développé la maladie. En ce qui concerne les neuf autres voyageurs : Un voyageur a refusé de se soumettre à un test et les huit autres n'ont été soumis à un test qu'à leur arrivée et ont obtenu un résultat négatif.
Lio (2020) (6) Enquêtes sur les cas Macao Entre janvier et avril 2020	Ce document décrit la mise en quarantaine réussie (14 jours) de voyageurs (n = 4 347) qui sont arrivés à Macao, une région chinoise sous administration spéciale, entre le 22 janvier et le 8 avril 2020. Une quarantaine de 14 jours avec test RT-PCR effectué le jour 13 pour confirmer le statut négatif a été mise en œuvre à Macao.	43/4 347 voyageurs ont été jugés infectés et ont alors été isolés avec succès. Selon les données de surveillance, lorsque la quarantaine a été levée, aucun cas n'était encore infecté.
Études de modélisation		
Clifford (2020) (15) *préimpression* Étude de modélisation R.-U.* 2020*	Un modèle de simulation (modèle additif généralisé avec probabilité binomiale et courbe splinée avec pénalité) pour les voyageurs aériens qui sont arrivés au Royaume-Uni en provenance de l'Union européenne ou des États-Unis a été élaboré afin d'explorer quatre niveaux de rigueur en matière de quarantaine : 1) Faible - aucune quarantaine obligatoire, avec et sans test à l'arrivée;	1) Tous les scénarios sont comparés à l'absence de quarantaine qui, à la mi-juillet, devait être d'environ 23 cas par semaine à partir des É.-U. vers le R.-U. et de 12 par semaine de l'UE au R.-U. Résultat = la proportion des cas qui ne peuvent ensuite se retrouver dans la collectivité en raison des scénarios de quarantaine 2) 7 jours, aucun test = 80 % 6 jours, test le jour 5 = 88 %

	2) Modérée - mise en quarantaine obligatoire de 3, de 5 ou de 7 jours, avec et sans test à la fin de la quarantaine; 3) Élevée - mise en quarantaine obligatoire jusqu'à ce que deux résultats négatifs aient été obtenus aux tests (les jours 0 à 2 et 2 à 6 après le premier test), ou 14 jours après un résultat positif; 4) Maximum - quarantaine obligatoire de 14 jours avec et sans un seul test à la fin de la quarantaine. Le modèle a indiqué le nombre de personnes contagieuses qui arrivent au pays alors qu'elles sont contagieuses dans chacun des scénarios. Ce résultat est ensuite converti en proportion des cas qui ne peuvent ensuite se retrouver dans la collectivité en raison des scénarios de quarantaine.	8 jours, test le jour 7 = 94 % 3) Résultats non extractibles 4) 14 jours, aucun test = 99 % 15 jours, test le jour 14 = 99 % (II à 95 %, de 97 à 100 %) • L'utilité des tests avant le départ était limitée lorsque des tests étaient effectués après l'arrivée. • Les tests effectués à plus d'une reprise ont eu des avantages limités. Bien que l'intervalle d'incertitude ne soit pas présenté dans le document, les chiffres présentés montrent qu'une quarantaine aussi courte que 8 jours avec test effectué le jour 7 donne des résultats presque équivalents à ceux obtenus après une quarantaine de 14 jours.
Dickens (2020) (4) Étude de modélisation Singapour* 2020*	Six scénarios sont simulés pour empêcher l'importation de cas de COVID-19 dans un pays grâce à un cadre axé sur des données contenant des renseignements provenant de 153 pays touchés. Les stratégies explorées comprennent un test à l'arrivée et la mise en quarantaine des voyageurs déclarés positifs ou l'interdiction d'entrer au pays ou la mise en quarantaine seulement pendant 7 ou 14 jours. Ce modèle ne tient cependant pas compte de la sensibilité du test RT-PCR qui varie selon l'infection.	Résultat = réduction du nombre de cas importés. Scénario de quarantaine : • 7 jours - aucun test = 55,4 % • 14 jours - aucun test = 91,2 % • 0 jour - test à l'arrivée et entrée refusée à ceux dont le résultat était positif = 77,2 % • 7 jours si le résultat du test était positif à l'arrivée et test le jour 7 = 90,2 % • 14 jours si le résultat du test était positif à l'arrivée et test le jour 14 = 91,7 % La mise en quarantaine de 14 jours de tous les passagers était la plus efficace, mais était également celle qui avait le plus de répercussions négatives sur les voyageurs.
Steyn (2020)	Un modèle de processus arborescent chronologique continu pour la	Résultat : le pourcentage de voyageurs infectés qui n'ont pas pu entrer dans la

(3) *préimpression* Étude de modélisation Nouvelle-Zélande 2020*	transmission de la COVID-19 qui comprend une probabilité à dépendance temporelle avec test faussement négatif pour une simulation réalisée dans l'endroit où s'effectue la quarantaine en Nouvelle-Zélande et une simulation dans laquelle on retrouve un cas ayant été infecté jusqu'à 14 jours avant son arrivée au pays. La Nouvelle-Zélande a instauré une quarantaine de 14 jours avec un minimum de deux tests pour tous les voyageurs internationaux qui entrent au pays. Le modèle explore une quarantaine de 14 jours sans test, une quarantaine de 5 jours avec test effectué le jour 3 et des tests avant le départ et après l'arrivée comme autres stratégies.	collectivité en supposant qu'il n'y ait pas de transmission dans l'endroit où s'effectue la quarantaine. • 14 jours, tests les jours 3 et 12 = 99,9 % • 14 jours, aucun test = 96 % • 14 jours, possibilité de levée anticipée de la quarantaine le jour 7 en raison d'un test négatif effectué le jour 3 ou 8 = 99,9 % • 5 jours, test à l'arrivée et le jour 3 = 75 % • 0 jour, test négatif avant le départ et à l'arrivée et entrée refusée à ceux dont le résultat était positif = 50 % Si la transmission devait se faire dans l'endroit où s'effectue la quarantaine, l'efficacité de la quarantaine diminuerait alors et l'importance des tests multiples pendant la quarantaine augmenterait tant pour prévenir la transmission dans l'établissement utilisé à des fins de confinement que pour identifier les personnes nouvellement infectées.
Wells (2020) (13) *préimpression* Étude de modélisation É.-U.* 2020*	Un modèle mathématique a été élaboré pour explorer divers scénarios en ce qui concerne la quarantaine : 1) Mise en quarantaine pour les voyages, amorcée à différents moments établis de façon aléatoire pendant toute la phase d'infection; 2) Mise en quarantaine motivée par la recherche des contacts et, par conséquent, amorcée au début de la phase d'infection (*voir le tableau 1*), 3) Mise en quarantaine lorsque le moment de l'exposition est connu (*voir le tableau 1*).	Le résultat est l'équivalence épidémiologique avec mise en quarantaine standard de 14 jours afin de réduire la probabilité de transmission après la mise en quarantaine : Scénario 1 et 2 • Les tests effectués au début de la quarantaine et à la levée de celle-ci pourraient réduire de 50 % la durée de la quarantaine. • Les tests effectués seulement au début de la quarantaine pourraient réduire d'une journée la durée de celle-ci. • Une quarantaine de 7 jours avec test avant la levée de la quarantaine et une

		quarantaine de 6 jours avec test au début et à la fin équivaut à 14 jours de quarantaine. • Les tests effectués pendant la quarantaine ont toujours donné des résultats supérieurs aux tests effectués au début de la quarantaine. • Le moment optimal pour effectuer le test était une journée avant la fin de la quarantaine pour les périodes de moins de 7 jours et le jour 7 pour les périodes de quarantaine plus longues. Exemple des travailleurs sur les plates-formes pétrolières : • Ce modèle a été appliqué à un programme de contrôle des plates-formes pétrolières avec test et mis en quarantaine à l'arrivée et avant le départ. 47 employés sur 4 040 avaient un avis positif en ce qui concerne cette stratégie, 16 auraient été oubliés si seuls des tests à l'arrivée avaient été effectués, ce qui aurait pu entraîner 9 éclosions différentes. Aucun travailleur infecté n'est passé inaperçu.
Russell (2020) (16) *préimpression* Étude de modélisation É.-U.* 2020*	Un modèle mathématique a été élaboré pour évaluer les stratégies de quarantaine et de test. L'application web est accessible. Durée de la quarantaine examinée, en jours : 0, 2, 5, 7, 14. Scénarios de test : aucun test, à l'arrivée, 24 heures avant la fin de la quarantaine ou les deux. Le résultat est le nombre de jours de risque de transmission dans la collectivité en supposant qu'un voyageur sur	• Les tests effectués pendant la quarantaine ont toujours donné des résultats supérieurs aux tests effectués au début de la quarantaine (lorsque le niveau de respect de la quarantaine est élevé). • Les avantages des tests ont réduit la plus longue durée de la période de quarantaine : réduction médiane de 0,30, de 0,10 et de 0,004 jour à risque pour une quarantaine de 2, de 7 et de 14 jours, respectivement.

	10 000 est infecté et que le risque de transmission est de 0,5 par jour-personne de risque de transmission.	• L'avantage associé à la quarantaine était directement lié à la conformité, puisqu'une conformité de 40 % a entraîné un risque variant entre 1,7 et 2,1 jours alors qu'une conformité de 100 % a réduit ce risque à un maximum de 0,05 jour.
Johansson (2020) (17) *préimpression* Étude de modélisation É.-U.* 2020*	Un modèle mathématique a été élaboré pour analyser l'efficacité prévue du suivi des symptômes, des tests et des stratégies de mise en quarantaine selon les différentes estimations de la période infectieuse et de la positivité des tests par rapport au moment de l'infection, ainsi que pour tester la sensibilité afin de réduire le risque de transmission des voyageurs infectés pendant et après le voyage.	Résultat : réduction du risque de transmission • Les tests effectués le jour du départ pourraient réduire de 37 à 61 % le risque de transmission pendant les voyages, alors que les tests effectués trois jours auparavant ne représentaient qu'une réduction de 5 à 9 %. • Test et aucune mise en quarantaine, entre 0 et 77 % selon le jour de la période infectieuse où le test a été effectué. • Test avant et après l'arrivée, varie entre 40 et 66 %. • Test à l'arrivée et 3 ou 4 jours plus tard = entre 45 et 70 %. • Isolement basé sur la surveillance des symptômes = entre 36 et 52 %. • Quarantaine de 14 jours = entre 97 et 100 %. • Quarantaine de 10 jours = entre 84 et 100 %. • Quarantaine de 7 jours = entre 65 et 95 % • Quarantaine de 7 jours avec test les jours 3 ou 4 = entre 95 et 99 %.

Taylor (2020) (18) *préimpression* Étude de modélisation R.-U. Août 2020	Selon cette étude, 895 voyageurs infectieux (IC à 95 %, de 834 à 958) sont arrivés au Royaume-Uni pendant une seule semaine en août 2020. De ces voyageurs, 87 % figuraient sur la liste de quarantaine du Royaume-Uni, et aucune quarantaine n'est requise pour les voyageurs en provenance de destinations qui ne figurent pas sur la liste. La quarantaine est un auto-isolement de 14 jours (on suppose qu'elle est efficace à environ 80 % en raison de la conformité); d'autres stratégies ont été explorées. Les auteurs ont examiné le dépistage des symptômes dans les aéroports, l'auto-isolement pendant 7, 10 ou 14 jours et l'ajout de tests RT-PCR (un délai de 48 heures est présumé avant d'obtenir les résultats des tests). Un modèle a été créé pour estimer différents scénarios de quarantaine, mais la section sur les méthodes du manuscrit a été omise des documents de prépublication, ce qui empêche de l'évaluer.	• On estime que l'auto-isolement de 14 jours est efficace à 78 % (IC à 95 %, 74,4 à 81,6). • Les thermomètres thermiques détectent 1 voyageur infectieux sur 128. • Le test à l'arrivée est efficace à 39,6 % (IC à 95 %, 35,2 à 43,7) puisqu'il détecte deux voyageurs infectieux sur cinq. • La quarantaine de 6 jours avec test effectué 4 jours après l'arrivée est efficace à 64,3 % (IC à 95 %, 60,0 à 68,3). • La quarantaine de 6 jours avec test à l'arrivée et après 4 jours est efficace à 68,9 % (IC à 95 % : 64,9 à 73,0). • La quarantaine de 7 jours est efficace à 51,3 % (IC à 95 %, 47,2 à 55,7). • La quarantaine de 10 jours est efficace à 68,8 % (IC à 95 %, 65,1 à 72,9). • La quarantaine de 9 jours avec test le jour 7 est efficace à 74,3 % (IC à 95 % : 70,0 à 78,0). • La quarantaine de 9 jours avec test à l'arrivée et le jour 7 est efficace à 75,9 % (IC à 95 % : 72,3 à 79,6). Les stratégies de dépistage utilisées le jour 7 pour permettre à un voyageur de sortir de quarantaine étaient presque aussi efficaces que la quarantaine de 14 jours.
Van der Toorn (2020) (5) *préimpression* Étude de modélisation Allemagne	Ce document décrit un modèle (modèle stochastique de compartiment de transit) avec interface logicielle développé pour calculer la réduction de la transmissibilité par des politiques de quarantaine ou d'isolement avec ou sans stratégies de test.	Il en résulte une réduction du risque multiplié (c.-à-d. x fois moins de risque). Voyageurs avec dépistage des symptômes : • Dépistage des symptômes et tests à l'arrivée ○ RT-PCR = 4,69 (4,19 à 4,83)

2020*	L'utilisateur a le choix entre trois modes différents : (i) isolement des personnes infectées (*non pertinent pour cette revue*); (ii) gestion des contacts potentiellement infectés (*voir le tableau 1)* et (iii) mise en quarantaine des voyageurs qui arrivent au pays. L'utilisateur personnalise ensuite la stratégie. Le modèle tient compte de la durée de l'infection, des changements temporels dans la sensibilité du test (on présume que le test antigénique a une sensibilité de 85 % par rapport au test RT-PCR en raison du manque de données), des périodes d'incubation et d'infection et du temps écoulé avant l'apparition des symptômes.	○ test rapide (sensibilité de 87 % RDT) = 3,59 (3,22 à 3,69) • Quarantaine de 14 jours = 43,09 (21,82 à 94,40) • Quarantaine de 10 jours = 15,66 (9,77 à 27,44) • Quarantaine de 8 jours + test RT-PCR = 47,56 (33,27 à 73,34) • Quarantaine de 10 jours + test RDT = 49,92 (30,54 à 85,67) • Quarantaine de 10 jours avec test RT-PCR le jour 5 = 78,27 (48,87 à 136,94) Les données sont fournies pour chaque jour de quarantaine et chaque type de test. La quarantaine de 14 jours équivalait à une quarantaine de 8 jours avec test PCR ou à une quarantaine de 10 jours avec test antigénique.
Ashcroft (2020) (10) *prépublication* Modèle prédictif Suisse* Octobre 2020*	Un modèle mathématique a été élaboré pour explorer les répercussions des stratégies de quarantaine visant à réduire la transmission de la COVID-19 en fonction des données empiriques sur la période d'incubation, l'infectiosité et le temps de génération. Les stratégies de quarantaine explorées portent sur les voyageurs qui ont été mis en quarantaine pendant *x* jours après leur arrivée. *(Contacts de cas, voir le tableau 1).* Scénarios étudiés : I. test et levée de la quarantaine.	Les résultats sont en grande partie présentés sous forme de graphiques. Résultat : une fraction de la transmission locale a été évitée : • La quarantaine de 10 jours à l'arrivée empêche presque 100 % de la transmission locale. • Le dépistage à l'arrivée est une mauvaise stratégie pour limiter la transmission. Le dépistage au retour au jour 0 n'empêche que 54,1 % de la transmission locale alors que le dépistage au jour 5 et la levée de la quarantaine au jour 7 empêchent 98,5 % de la transmission locale.

	II. Levée de la quarantaine après test négatif avec renforcement de l'hygiène.	• Les tests rapides réduisent la quarantaine d'une journée, avec une perte minimale d'efficacité comparée aux tests RT-PCR.
Arino (2020) (19) *préimpression* Étude de modélisation Canada* Décembre 2020*	Un modèle stochastique a été mis au point pour simuler une petite population formée d'un mélange homogène et les chaînes de transmission potentielles qui résultent de l'importation d'un cas. L'efficacité de la quarantaine est comparée à la durée de la quarantaine après l'arrivée, y compris la façon dont la quarantaine est strictement observée. Les scénarios avec quarantaines d'une durée de 7, de 10 et de 14 jours ont été analysés.	La probabilité d'empêcher la transmission locale à partir d'un cas importé augmente avec la durée de la mise en quarantaine et la détection des cas obtenue grâce aux tests. • L'efficacité des quarantaines d'une durée de 7, de 10 et de 14 jours est illustrée sur un graphique (figure 7). • Si 10 % des cas ne sont pas détectés, une quarantaine de 14 jours a une efficacité de 90 %. • Lorsque le nombre de cas non détectés augmente et atteint 90 %, une quarantaine de 14 jours sera efficace à 70 %.
Matsinos (2020) (20) *préimpression* Étude de modélisation É.-U.* Octobre 2020*	Le modèle de simulation de Monte-Carlo est appliqué à l'effet de la durée de la quarantaine pour les voyageurs qui reviennent de régions dont le risque de COVID-19 est élevé. Distributions dans le modèle : -Durée du voyage : bêta (entre 1 et 21 jours, moyenne de 12) -Moment de l'infection : aléatoire -Probabilité d'infection : i) est constante pendant le voyage ii) augmente avec le temps, de façon linéaire iii) augmente avec le temps, de façon logarithmique Le modèle a été exécuté neuf fois, simulant chacun un million de scénarios avec voyageurs.	Résultat Probabilité de nouvelles infections découlant de voyageurs encore infectieux après la levée de la quarantaine : • Quarantaine de 8 jours = 5 % • Quarantaine de 12 jours = 1 % • Quarantaine de 16 jours = 0,1 % Les résultats du modèle n'appuient pas la réduction de la quarantaine par rapport à l'exigence actuelle qui varie entre 10 et 14 jours dans les pays européens.

Wilson (2020) (21) *préimpression* Étude de modélisation Nouvelle Zélande* Juin 2020*	Un modèle SEIR stochastique a été élaboré pour explorer l'incidence de diverses mesures de contrôle sur la probabilité qu'un voyageur infectieux entraîne une éclosion lorsqu'il vient d'une zone à faible prévalence (Australie) vers une zone exempte de COVID-19 (Nouvelle-Zélande). La mise en quarantaine standard de 14 jours et la quarantaine réduite à 7 jours ont été modélisées, tout comme l'utilisation d'une politique avec test et levée de la quarantaine.	Résultat : temps moyen qui s'est écoulé entre les éclosions à la suite d'un voyage dans un pays sans COVID-19 : • Aucune intervention = 1,7 an. • Quarantaine de 14 jours = 34,5 ans ou plus pour tous les scénarios envisagés. • Quarantaine de 7 jours = 5,8 ans. • Test PCR les jours 3 et 12, levée de la quarantaine si les deux sont négatifs = 29,6 ans

*Le lieu ou le moment de l'étude a été estimé à partir des affiliations des auteurs et de la date de publication, respectivement. R.-U. = Royaume-Uni, É.-U. = États-Unis d'Amérique, UE = Union européenne. II = intervalle d'incertitude, IC à 95 % = intervalle de confiance

RECHERCHE DE SYNTHÈSE SUR L'EFFICACITÉ DE LA QUARANTAINE

Une seule revue rapide portant sur les mesures de contrôle des voyages a été cernée. La quarantaine est l'un des éléments examinés dans cette revue qui comprenait des recherches sur le SRAS-CoV-1, le MERS et le SRAS-CoV-2 jusqu'au 26 juin 2020. Selon cette revue rapide, très peu de recherche pertinente portant sur les stratégies de quarantaine pour les voyageurs avait été effectuée jusqu'en juin, au moment de l'examen des documents disponibles.

Tableau 3 : Recherche de synthèse portant sur la durée de la quarantaine et les tests

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Burns (2020) (22) Revue rapide Allemagne* 2020	L'examen rapide effectué par Cochrane (AMSTAR = qualité modérée en raison d'un seul examinateur) comprend 36 études portant sur des mesures de contrôle pour les voyages visant à contenir la pandémie. Recherche effectuée jusqu'au 26 juin 2020 comprenant des études pertinentes sur le SRAS-CoV-2 comme preuve directe et le SRAS-CoV-1 et le MERS comme preuve indirecte. La revue comprend 17 études de modélisation, 7 études de dépistage par observation et une étude d'observation écologique sur la COVID-19, quatre études de modélisation et six études d'observation sur le SRAS, ainsi qu'une étude de modélisation sur le SRAS et le MERS, couvrant divers contextes et stades de l'épidémie. Aucune revue ne semble avoir examiné différentes stratégies de quarantaine, mais certaines parlent des répercussions et de l'efficacité d'une quarantaine de 14 jours avec test de dépistage ou tests en fonction des symptômes.	En ce qui concerne les résultats de la quarantaine : • Une étude sur la COVID-19 a été incluse et a conclu que la quarantaine de 14 jours réduisait le risque de transmission des cas importés et que l'efficacité de la quarantaine dépendait de la conformité (très faible certitude de la preuve) (tableau 7). • Quatre études sur le SRAS-1 ou le MERS ont été mentionnées, mais elles examinent les répercussions de la quarantaine comme intervention de santé publique sans explorer d'autres stratégies de quarantaine différentes (tableau 7). • Six études d'observation de la COVID-19 sont décrites et portent plus particulièrement sur les vols de rapatriement dans lesquels les voyageurs ont été mis en quarantaine pendant 14 jours et où les symptômes ont été surveillés et des tests effectués pendant la quarantaine. Les résultats indiquent généralement que la quarantaine de 14 jours, prise seule ou en fonction des symptômes, n'est pas aussi sensible que l'utilisation d'un test RT-PCR pendant la quarantaine (aucune inférence sur la réduction de la durée de la quarantaine ne peut être tirée de ces études) (tableau 6). D'autres résultats ont été abordés, mais ne sont pas résumés ici. Ils portaient notamment

		sur le dépistage des symptômes à l'arrivée au pays et au départ du pays, la fermeture de la frontière et les restrictions imposées aux frontières.

*Le lieu ou le moment de l'étude a été estimé à partir des affiliations des auteurs et de la date de publication, respectivement.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) liée à la COVID-19 est effectuée par le Groupe des sciences émergentes de l'ASPC et se continue depuis le début de l'éclosion. La littérature est extraite de Pubmed, de Scopus, de BioRxiv, de MedRxiv, d'ArXiv, de SSRN, de Research Square et croisée avec la liste de littérature sur la COVID de l'OMS et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Une recherche visant à extraire la documentation pertinente pour inclusion dans cette synthèse a été effectuée dans la base de données Refworks. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les algorithmes de recherche ont utilisé isolement ET durée, quarantaine ET durée, quarantaine ET tests ET (réduction OU voyages). La pertinence de 414 citations a été évaluée, et des données ont été tirées d'articles pertinents dans le cadre de cette revue. Cette synthèse contient des recherches liées à la mise en quarantaine et aux tests comme moyen de réduire la durée de la mise en quarantaine, publiées jusqu'au 3 décembre 2020.

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Emerging Evidence on COVID-19

Rapid Review on the use of Face Masks to Prevent the Spread of COVID-19 in Community Settings: Update 1

Introduction

What is the evidence on face mask use to prevent COVID-19 in community settings?

Of all the public health measures (PHM) that have been used during the COVID-19 pandemic, the use of face masks in the community is a technically simple one that has had little impact on the economy (1). But is it effective? This rapid review summarizes the empirical evidence on the effectiveness of masks to prevent COVID-19 cases in community settings. It is an update to the earlier *Evidence Brief on the use of Face Masks to Prevent COVID-19 in Community Settings, July 2020* (2). This review does not include experimental data on the filterability of different types of non-medical masks, materials or combinations of materials, as this is being covered as a separate review. It also does not include predictive models that estimate the mitigation effects of wearing a face mask alone or in combination with other public health interventions. This review summarizes literature until November 19, 2020.

Key Points

- Forty nine studies were identified on the effectiveness of face masks to prevent COVID-19 in community settings. There was one experimental study, 15 observational studies, 27 ecological studies and six reviews.
- The majority of studies demonstrate that community masking in observational studies and community mask policy implementation in ecological studies is protective against COVID-19, however the magnitude of this effect varied. Variability could be due to when the study was conducted, confounders, and adherence rates.
- Key findings from individual level observational studies (n=15) and a randomized control trial (n=1) include:
    - In seven observational studies, wearing a face mask was associated with a 7.0-79% decrease in COVID-19 infections.
    - A large randomized control trial (DANMASK-19) in Denmark reported insignificant results for mask usage (OR 0.82, 95% CI: 0.54-1.23, P= 0.33), although this trial suffered from low adherence in the mask group likely due to low levels of community masking during the study (3).
    - Cluster and outbreak investigations consistently reported fewer secondary cases when index cases and/or their contacts wore masks.

  - No evidence was found related to differences in effectiveness of masks between adults and children.

- Twenty-six ecological studies demonstrated that face mask policies were associated with a decrease in COVID-19 infections and deaths. There was some variability in the type of face mask policy implemented, most were universal in public spaces, and three were specific to mask policies for employees.
  - In nine studies the effect of universal face mask policies was calculated and the decrease in COVID-19 infections attributed to the policy ranged from 3.2-48%. There was some variability in the type of face mask policy implemented, most were universal in public spaces, and three were specific to mask policies for employees.
  - One study in Canada was identified, which demonstrated that mask policies in Ontario invoked in Jun-Jul resulted in a 25-31% weekly reduction in COVID-19 cases starting two weeks after implementation (4).
  - A study of COVID-19 case reductions the first month after a universal mask policy in New York demonstrated age-related differences. There was a 20.8% reduction in cases for both 65-74 year olds and 75+ year-olds in the first month, whereas 25-44 and 45-64 year-olds were associated with a 4.5% and 8.1% reduction, respectively (5).
  - Three studies of face mask policies that mandated masks for all employees at all workplaces in an area (county or state) found a decrease in COVID-19 infections and deaths (1, 6, 7), although the results were not consistent in magnitude or statistical significance across different models (1).
  - A USA study found that both early and late mask policies were effective in reducing COVID-19 infections (8).
  - The only study that did not show a significant impact with a mask policy was under lock down conditions -1% (95% CI: -13 to 8%) (9).
  - One study found that countries that had a pre-existing norm that all sick people wear masks, had a lower daily growth rate of COVID-19 cases and deaths compared to countries with no pre-existing mask norm (10).
- Implementing a community mask policy instead of only recommending people wear masks has a significant impact on adherence to mask use in public settings. The study from Ontario indicated there was a 30% increase in mask use after mask policies were implemented (4). A similar study in Australia found a mask policy increased mask use by almost 50% (11). In contrast, a study from the USA showed mask recommendations consistently did not have an impact on COVID-19 fatality rates (1).

Overview of the Evidence

Forty-nine articles pertaining to the effectiveness of face masks to prevent COVID-19 in community settings were identified and included in this review. Of these, 23 are preprints or reports and have not completed the peer-review process. The publications reporting on the effectiveness of face masks include a randomized control trial (n=1), longitudinal studies (n=2), cohort studies (n=2), a natural experiment (n=1), a case-control study (n=1), cross-sectional studies (n=5), cluster and outbreak investigations (n=4), ecological studies (n=27), and systematic or rapid reviews (n=6).

Studies where the inference can be made to the individual include randomized control trials that are the gold standard for measuring the impact of an intervention as the randomization process controls for confounding variables and assuming the sample is representative of the population, by design the RCT should isolate the effect of the intervention. The RCT included in this review was done in a community without a universal mask policy and suffered from lack of adherence to mask wearing in the treatment group, missing data, and lack of blinding. Thus this RCT has some risk of bias that decreases confidence that future research will not change the conclusions.

The 15 observational studies assessed individual level data. Cohort studies, natural experiments, longitudinal studies, and case-control studies can have moderate to high risk of bias depending on whether the sampling strategy is able to obtain a representative sample of the target population. Cross-sectional studies provide a single point in time snap shot of an issue, but cannot establish causation, therefore these studies provide low quality evidence. Retrospective cluster and outbreak investigations are at high risk of bias. In many studies outcomes and risk factors were self-reported so may have recall and social desirability bias. In general observational studies cannot establish causation, but can be useful in developing hypotheses or understanding observed factors for transmission.

The 27 ecological studies assessed population level data. These types of study are inexpensive to conduct and can be done quickly as they largely capitalize on publicly available data. They are at high risk of bias due to the use of disparate population level data and are prone to ecological fallacy (what is true at a population level may not apply at an individual level).

The six reviews were evaluated by the AMSTAR tool for systematic reviews to assess whether the conduct of a review minimized bias. The rapid and systematic reviews ranged from low to high quality, depending on the number of reporting and conduct issues in the study. Despite this, there was good agreement in the results across the review literature.

The literature on COVID-19 is rapidly evolving and with time studies with low risk of bias can be conducted to close existing knowledge gaps. An important knowledge gap is a lack of studies where the inference can be made to an individuals' mask compliance (both adherence and proper use) on SARS-CoV-2 infection in community settings. There is also minimal evidence on effectiveness of wearing a face mask or face mask policies for employees, and in school settings.

CONTENTS

EXPERIMENTAL AND OBSERVATIONAL STUDIES ASSESSING PREVENTION

There were 16 studies identified that assessed the effectiveness of face masks to prevent COVID-19 spread in community settings using individual level data (Table 1). This included one experimental study and 15 observational studies.

- The experimental study was a large randomized control trial (DANMASK-19) from Denmark. It showed that when no face mask policy was in place in the community, recommending mask use was not effective. Although those who wore a mask were 18% less likely be become infected with SARS-CoV-2 compared with those who did not wear a mask, these results were not significant (OR 0.82, 95% CI: 0.54-1.23, P= 0.33). Major limitations to this study were variable adherence to mask wearing, missing data, and a lack of blinding (3).
- The 15 observational studies included two longitudinal studies, two cohort studies, one case-control study, five cross-sectional studies, four cluster and outbreak investigations, and one natural experiment. The majority of studies demonstrated that wearing a face mask was protective against COVID-19, however the magnitude varied across studies.
    - A longitudinal study across 24 countries shows that widespread mask-wearing by 100% of individuals in a country to be associated with a 7% (95% CI: 3.94-9.99%) decline in the daily active cases of COVID-19. Over a 30 day period, this accumulated to an 88.5% (95% CI: 68.7-89.2%) decline in active cases (12).
    - A 7.0-7.9% decrease in COVID-19 cases associated with the use of face masks was also found in three cross-sectional, two cohort, one longitudinal, and one case-control study (12-18).
    - A case-control study in Thailand showed that wearing a mask all of the time versus never wearing a mask was associated with decreased risk for SARS-CoV-2 infection (aOR 0.23, 95% CI: 0.09-0.60), whereas inconsistent use was not associated with decreased risk (aOR 0.87, 95% CI: 0.41-1.84) (18).
    - Four cluster and outbreak investigations consistently reported fewer secondary cases when index cases and/or their contacts wore masks (19-22).

Table 1. Experimental and observational studies on the effectiveness of face masks to protect against COVID-19 in community settings (n=16)

STUDY	METHODS	KEY OUTCOMES
Randomized control trials (n=1)		
Bundgaard (2020) (3) Randomized control trial Denmark Apr-May 2020	This RCT assessed whether surgical mask use outside the home reduced the risk for SARS-CoV-2 infection. The study was conducted in a community where masks were uncommon and recommended by public health. 4862 participants were included (3030 were randomly assigned to wear masks and 2994 were assigned not wear a face mask). Study limitations: missing data, variable adherence to mask wearing, patient-reported findings on home tests, no blinding, and no assessment of whether masks could decrease disease transmission from mask wearers to others.	• Infection with SARS-CoV-2 occurred in 42 participants recommended to wear masks (1.8%) and 53 control participants (2.1%). • The between-group difference was 0.3 percentage point (95% CI: 1.2-0.4 percentage point, p=0.38) (OR 0.82, 95% CI: 0.54-1.23, p=0.33). • Adherence to mask wearing was self-reported. Based on the lowest adherence reported during follow-up, 46% of participants wore the mask as recommended, 47% predominantly as recommended, and 7% not as recommended.
Longitudinal studies (n=2)		
Aravindakshan (2020) *preprint* (12) Longitudinal study Global Feb-Jul 2020	A reduced form model econometric analysis was applied to measure associations between reported face mask use and SARS-CoV-2 spread in 24 countries. A longitudinal survey was conducted every 7 days to collect information on NPIs and adherence across 24 countries.	• Widespread mask-wearing by 100% of individuals in a country was associated with a 7% (95% CI: 3.94-9.99%) decline in the daily active cases of COVID-19. Over a 30 day period this accumulated to an 88.5% (95%CI: 68.7-89.2%) decline in active cases.
Rader (2020) *preprint* (23) Longitudinal study USA	Serial surveys were conducted Jun 3- Jul 27 across the USA (N=378,207) to gather data on community mask and social distancing behaviours in different communities. These data were	• There was a significant association between the proportion of people reporting wearing a mask and community transmission control (Rt<1): OR = 1.14 (95% CI: 1.07-1.20).

Jun-Jul 2020	combined with the local Rt, mobility data and information on implemented policies. The data was analysed using multivariate regression analyses to explore factors associated with community SARS-CoV-2 transmission control in the USA.	• The odds of transmission control (Rt<1) increased (OR 3.53, 95% CI: 2.03-6.43) for each 10% increase in community mask wearing reported in the survey. • Mask wearing was a robust protective factor towards community transmission control across all analyses. • Community transmission control was predicted to be highest with both high mask wearing and social distancing in place. Where social distancing was low despite high mask use community transmission control dropped to 35%. • The analysis did not find a significant increase in mask usage following mask mandate policy, possible reasons for this were not discussed. • Adherence to mask wearing was highest among women, elderly, non-white or Hispanic ethnic groups and lower income respondents. • Mask wearing was highest along the coast, southern border and in urban areas of the USA.
Cohort studies (n=2)		
Kwon (2020) *preprint* (15) Prospective cohort study USA Mar-Jul 2020	This prospective cohort "COVID symptom study" included participants in the USA using an app from March 29- July 16. Participants provided baseline and health information and were prompted to record health and COVID related information daily. 139,690 participants provided information for the association between self-reported use of a face mask and predicted risk of COVID-19.	• Individuals who reported using a mask in the community (sometimes, most of the time, or always) had an adjusted HR for predicted COVID-19 of 0.35 (95% CI: 0.30-0.42) compared to those that never wore a face mask. • Self-reported masking was associated with a 69%, 71%, and 63% reduced risk of predicted COVID-19 among individuals living in communities with excellent, fair, and poor social distancing, respectively. • The findings provide support for the efficacy of mask-wearing in reducing

	The study used predicted COVID-19 as a proxy for a positive COVID-19 test due to the small number of COVID-19 test positive app users during the study period. Survival analysis adjusted for age, sex, ethnicity, state, smoking, frontline workers and comorbidities.	COVID-19 transmission even in settings of poor social distancing.
Wang (2020) (17) Retrospective cohort study China Feb-Mar 2020	This retrospective cohort study consisted of 335 people in 124 families with at least one laboratory confirmed COVID-19 case in Beijing from Feb 28 - Mar 27, 2020.	• The secondary attack rate in families was 23.0% (77/335). • Face mask use by the primary case and family contacts before the primary case developed symptoms was 79% effective in reducing transmission (OR=0.21, 95% CI: 0.06 to 0.79). • However, wearing a mask after illness onset of the primary case was not significantly protective.
Case-control studies (n=1)		
Doung-ngern (2020) (18) Case-control study Thailand Mar 2020	This retrospective case-control study used contact tracing records in Thailand to establish their sample. 1,050 contacts of COVID-19 patients from Mar 1-31, 2020 were retrospectively interviewed. Cases (n=211) were defined as asymptomatic contacts of COVID-19 patients who later tested positive for SARS-CoV-2 infection and controls (n=839) were asymptomatic contacts who never tested positive.	• Wearing a mask at all times (aOR 0.23, 95% CI: 0.09-0.60) was independently associated with lower risk of COVID-19 infection compared to not wearing masks. However, wearing a mask sometimes (aOR 0.87, 95% CI: 0.41-1.84) was not. • Those that wore masks all the time were more likely to wash hands and practice social distancing.
Cross-sectional studies (n=5)		
Lopez (2020) *preprint* (14) Cross-sectional study	In this study, the SARS-CoV-2 seroprevalence of 753 public school staff was determined and correlations between seropositivity and self-reported histories (e.g.	• The seroprevalence was estimated to be 1.7% (90% CI: 0.27- 3.3). • After controlling for six confounders, the results of the multivariate analysis reveal that self-reported mask-wearing history

USA Jul 2020	mask wearing) and demographics were analyzed.	reduces the risk of being seropositive (RR 0.83, 95% CI: 0.18-3.8).
Rodríguez-Barranco (2020) (24) Cross-sectional study Spain Apr-May 2020	This study looked at possible routes of exposure to SARS-CoV-2, risk factors, and the effectiveness of the recommended hygiene measures. Self-reported information was collected from 2086 individuals via online survey.	• 73.4% of individuals wore a mask when they left confinement (34.9% FFP2/FFP3 face mask, 64.4% surgical, and 0.7% homemade mask). • The estimated prevalence of COVID-19 was 4.7% (49 confirmed and 50 suspected cases). • Not taking any other variable into consideration, there was no association between COVID-19 status and mask use (p=0.205): 3.9%, 5.7%, 0%, 3.1%, 5.8% reported having confirmed or suspected COVID-19 of individuals who self-reported wearing an FFP2/FFP3 mask, surgical mask, homemade mask, no mask, and reported not leaving the house respectively.
Payne (2020) (13) Cross-sectional study USA Mar-Apr 2020	A survey of US Navy service members (convenience sample, n=382) linked to a COVID-19 outbreak in an aircraft carrier was conducted to collect information on self-reported face mask use and other protective measures (e.g. avoiding common areas, social distancing). The results were analyzed to determine associations with infection risk. 284 individuals within the sample were found to be positive for SARS-CoV-2 priori to or at the time of serum testing.	• Participants that self-reported wearing a mask (55.8%) had a lower odds of COVID-19 (OR 0.3, 95% CI: 0.2–0.5) compared to those who reported not wearing a mask (80.8%).

Clipman (2020) (16) Cross-sectional study USA Jun 2020	Associations with self-reported SARS-CoV-2 positivity and adoption of NPIs was analyzed using an online survey of 1030 residents in Maryland. Logistic regression was used to identify variables associated with ever testing positive for SARS-CoV-2.	• Of the study sample, 5% (n=55) self reported ever testing positive for SARS-CoV-2. • 53% of participants reported always wearing a mask in indoor and outdoor settings. • A small association between mask wearing (always) and testing positive for SARS-CoV-2 was identified, aOR 0.63 (95% CI: 0.36-1.09).
van den Broek (2020) *preprint* (25) Cross-sectional study USA Apr-Jun 2020	In this study, community residents were surveyed and respondents (n=454) were offered RT-PCR and serological SARS-CoV-2 testing. Multivariate analysis using probit models was conducted to identify associations.	• 2.2% (95% CI: 0.8-3.6%) of the study sample were found to be SARS-CoV-2 positive by serology testing. • Mask wearing outside of work was not statistically different between those that tested positive (0.5%, SE 0.189) vs. negative (0.7%, SE 0.230) for COVID-19.
Cluster and outbreak investigations (n=4)		
Hendrix (2020) (19) Cluster investigation USA May 2020	This retrospective epidemiological investigation analyzed 139 clients that were exposed to 2 hair stylists in Missouri, USA who were infected with SARS-CoV-2. Both clients and hair stylists were wearing face masks.	• Of the 139 clients who were exposed, 67 were tested. • There were no symptomatic secondary cases reported, which was most likely due to the use of face masks.
Cheng (2020) (20) Cluster investigation Hong Kong Jan-Apr 2020	This study describes the findings of cluster investigations in Hong Kong during the first 100 days of the pandemic. The number of COVID-19 clusters involving wearing a mask and not wearing a mask were compared. Hong Kong had initiated a mandatory face mask use policy	• Up to day 100 of the epidemic, 961 cases of COVID-19 cases were confirmed in Hong Kong. Among these cases, 11 clusters of 113 persons were directly engaged in mask-off activities such as dining and drinking in a restaurant or bar, singing at karaoke, and exercise in fitness clubs compared to 3 clusters involving 11

	and adherence was estimated to be 96.6% (95% CI: 95.7 – 97.2%).	persons engaged in mask-on settings at the workplace (Chi square p=0.036).
Hong (2020) (22) Cluster investigation China Jan-Mar 2020	Clinical and epidemiological data were retrospectively retrieved from electronic medical records and valid individual questionnaires from Jan 23-Mar 1, 2020 of 127 patients with COVID-19 in Zhejiang, China.	• Before they were diagnosed, 41 COVID-19 pre-symptomatic patients had close contact with local residents. • 28/41 were wearing masks and had close contact with 123 residents, leading to 10 secondary SARS-CoV-2 infections. • The other 13 who did not wear masks had close contact with 74 residents, leading to 14 secondary SARS-CoV-2 infections. • The percentage of local residents infected with SARS-CoV-2 was significantly lower in the group who came into contact with infected individuals wearing a mask than those who came into contact with infected individuals not wearing a mask (8.1% vs. 19.0%; p < 0.001).
Liu (2020) (21) Outbreak investigation China 2020	This was a retrospective epidemiological investigation of SARS-CoV-2 exposure on public transportation. It described two bus trips in quick succession by an infected and symptomatic individual from Chongqing, the first without a face mask, and the second with a face mask.	• On the bus trip that the infected individual wore a mask, there were no others infected (14 passengers). • On the bus trip that the infected individual did not wear a mask, 5/39 people were infected.
Natural experiment (n=1)		
Pletz (2020) *preprint* (26) Natural experiment Germany Apr 2020	The effects of universal face masks in public settings was compared between two cities close together that had a similar size and community structure. In the implementation of NPIs the city of Jena implemented a face mask policy at the beginning of a 4 week lockdown and Erfurt issued the face	• No new cases of SARS-CoV-2 were observed in Jena 5 days after the implementation of a mandatory face cover policy. • In Erfurt, infections continued to spread within the community during the lockdown period, until community masking was imposed alongside lockdown phase lifting.

	mask policy at the end of lockdown. Note: both cloth masks and scarfs were acceptable if mouth and nose were covered.	• The observations may have been caused by other things so conclusions are limited, but it was a unique opportunity to look at the impact of a face mask policy between two similar communities.

CI = confidence interval, HR = hazard ratio, NPI = non-pharmaceutical intervention, OR = odds ratio, Rt = effective reproduction number

ECOLOGICAL STUDIES ASSESSING IMPACT OF POLICIES AND SOCIETAL NORMS

Twenty-seven ecological studies were identified on the impact of face mask recommendations and policies to prevent COVID-19 in community settings (Table 2). All of these studies analyzed aggregate population level data to estimate the impact of face mask polices on reducing COVID-19. A variety of approaches and sensitivity analyses were used across studies and are not detailed here; readers are encouraged to refer to the individual studies for more on their methodology.

- The majority (n=26) of these ecological studies demonstrated that face mask polices were protective against COVID-19, however the magnitude varied across studies.
    - Nine studies associated implementation of community face mask polices showed a range from 3.2-48% decrease in COVID-19 infections (4-7, 9, 27-30).
    - Five studies showed a 17-23% reduction in Rt after the implementation of mask policies. (11, 29, 31-33).
    - In an Ontario study, mask policies resulted in a 25-31% weekly reduction in COVID-19 cases two weeks after implementation (4).
    - Early and late mask policies were both effective in reducing COVID-19 infections as demonstrated in a study from the USA (8).
    - One study that compared mask effectiveness in countries with pre-existing norms compared to countries with no pre-existing mask norm found that in countries where all sick people normally wear masks, there was a lower daily growth rate of COVID-19 cases and deaths (10).
- The only study that did not show the mask policy had a significant impact was one during lock down conditions -1% (95% CI: -13 to 8%) (9).
- One study assessed effectiveness of a universal mask policy by age. Age related COVID-19 case reduction associated with a universal mask policy in New York demonstrated a 20.8% reduction in cases for both 65-74 year olds and 75+ year-olds in the first month, whereas 25-44 and 45-64 year-olds were associated with 4.5% and 8.1%, respectively (5).

- Employee face mask policies were associated with a decrease in COVID-19 infections and deaths across three studies (1, 6, 7). However, this association was not as strong or as consistent across analyses as universal mask policies (7).
- Recommendations for mask use in the community is not as effective as mask policies (1). Implementation of mask policies was shown in two studies to increase mask use by 30-54% (4, 11)
- Adherence to any of the NPIs is critical to success, one study suggested a 75% adherence rate was needed for community mask wearing to be effective and that if adherence was over 85%, social distancing policies had no additional effect on further mitigating the number of COVID-19 cases (34).

Table 2. Ecological studies on the effectiveness of face mask policies and/or societal norms to protect against COVID-19 in community settings (n=27)

STUDY	METHODS	KEY OUTCOMES
Global (n=8)		
Haug (2020) (32) Ecological study Global Mar-Aug 2020	This study aimed to assess the effectiveness of NPIs to mitigate the spread of SARS-CoV-2. Using a coded dataset of 6,068 NPIs implemented in Mar – Apr 2020 in 79 territories, the impact of government interventions on Rt was conducted using four different statistical approaches. Findings were validated using two external datasets recording 42,151 additional NPIs from 226 countries.	• Wearing a mask was associated with a significant impact on Rt by three different methods (ΔRt between −0.018 and –0.12). • Results indicate that a suitable combination of NPIs are necessary to curb the spread of the virus.
Miyazawa (2020) *preprint* (35) Ecological study 22 countries Mar-May 2020	The study aimed to identify the association between mask wearing rate and the cumulative number of deaths caused by COVID-19 across countries. Mask wearing rates were calculated from survey responses during March 9–18 and April 26 – May 1, 2020, respectively.	• In March, the face mask non-wearing rate was positively associated with the cumulative number of deaths (β 0.0048, SE 0.011, adjusted R2 0.680), but not in Apr–May (β 0.0020, SE 0.011, adjusted R2 0.466). • The regression models explained 69% of the variation in the cumulative number of deaths per million among 22 countries and identified the face mask wearing rate in March as an important predictor.
Brauner (2020) *preprint* (9)	In this study, the effectiveness of eight NPIs in 41 countries was	• Under lock down conditions some masking in public did not have a large

Ecological study Global Jan-May 2020	estimated with a Bayesian hierarchical model by linking NPI implementation dates to national case and death counts. They explored mandating mask policies, limiting gatherings <1000 or <100, or <10, closing high-risk businesses, closing non-essential businesses, closing schools and universities and stay at home orders.	impact. The mean proportion reduction with mandating mask-wearing in (some) public places was -1% (95% CI: -13 to 8%). • In this study, mandatory masking policies were implemented after all the other social distancing and school and business closures and the study ended before lifting of these restrictions.
Esra (2020) *preprint* (29) Ecological study Global Jan-May 2020	Using globally reported SARS-CoV-2 cases to fit a Bayesian model framework, this study aimed to estimate transmission associated with NPIs in 26 countries and 34 USA states. NPIs examined include stay home mandates, gathering limits, school closures, and mask policies.	• The mean reduction in Rt in SARS-CoV-2 infections was 17% (95% CI: 6-28%) with mask policies.
Zhang (2020) (36) Ecological study China, Italy, USA Jan-May 2020	This analysis of daily SARS-CoV-2 infection trends Jan 23- May 9 that specifically look at the linear trajectory of COVID-19 cases and changes that occurred after face mask policies were implemented in Italy and NYC.	• Face mask use was estimated to have avoided >75 000 in Italy (from Apr 6 – May 9) and >66 000 infections in NYC (from Apr 17 - May 9). • While other areas of the world show a linear increase, this study showed that the implementation of the mask policies in Italy and NYC reduced the spread of COVID-19.
Leffler (2020) (37) Ecological study 196 countries Jan-May 2020	The impact of masks on per-capita COVID-19 related mortality was investigated using mortality data from 196 countries up to May 9, 2020.	• Duration of mask-wearing by the public had a negative independent association with mortality (all p<0.001). • In countries with cultural norms or government policies supporting public mask-wearing, per-capita coronavirus mortality increased on average by just 16.2% each week, compared with 61.9% each week in remaining countries.

Abaluck (2020) *preprint* (10) Ecological study Global Feb-Mar 2020	This study analyzes the impact of face masks by considering the relationship between norms of face mask use and COVID-19 spread at the country level. Countries with pre-existing norms that all sick people wear masks were compared to countries that do not, but later required masks for infected individuals, and countries with no mask norm and no official mask recommendation. Countries with at least 5 million people with at least 8 days of data available after the first day with 100 reported cases were included.	• Countries with pre-existing norms that sick people should wear masks (South Korea, Japan, Hong Kong, and Taiwan) have been among the most effective countries in containing the spread of the epidemic. • The average daily growth rate of confirmed cases is 18% in countries with no pre-existing mask norms and 10% in countries with such pre-existing norms. • The average daily growth rate of deaths is 21% in countries with no pre-existing mask norms and 11% in countries with such pre-existing norms. • After adjusting for concurrent interventions, the impact of mask norms (β [SE]) was −0.076 [0.030], p<0.05 for cases, and −0.107 [0.024], p<0.01 for deaths.
Kenyon (2020) *preprint* (38) Ecological study 49 countries Jan-Mar 2020	The association between COVID-19 cases and the national promotion of face masks in public was analyzed, controlling for the age of the epidemic and testing intensity. Only countries with at least 500 cumulative cases and whose first case was reported before Mar 7, 2020 were included. 8/49 countries advocated wearing face masks in public (China, Czechia, Hong Kong, Japan, Singapore, South Korea, Thailand, and Malaysia).	• Results of multivariate analysis show face mask use in public had a negative association with the number of COVID-19 cases/inhabitant (β -326, 95% CI: -601 to -51, P=0.021).
North America (n=13)		
Karaivanov (2020) *preprint* (4)	The impact of NPIs was assessed using publically available data on mask policies in Ontario, other NPIs	• After a 2 week lag, mask policies resulted in a 25-31% weekly reduction in COVID-19 cases.

Ecological study Canada Jul-Aug 2020	in Canada, and the number of COVID-19 cases.	• Mask policies increased mask usage by 30%.
Spiegel (2020) *preprint* (1) Ecological study USA Mar-Oct 2020	This regression analysis looked at the fatality growth due to COVID-19 and the impact of mandatory mask policies across every county in the USA from March to October.	• Mandatory mask policies equate to a 1% lower 4 week and 6 week fatality growth rate compared to no mask policy, $p<0.01$. • Mask policies were effective in every specification of the model and are accompanied by relatively low economic and social costs. This result was both statistically significant and important in magnitude. • Employee mask policies were not consistently protective across all analyses. • Mask recommendations consistently did not have a protective effect on the fatality growth rate.
Shacham (2020) *preprint* (28) Ecological study USA Jun-Sep 2020	This study analyzed the impact of a mask policy implemented in 2 counties of a 5-county metropolitan region on COVID-19 cases over a 3-month period of time.	• County-level mask policies were associated with significantly lower COVID-19 case growth over time compared to neighboring counties that did not implement a mask policy. • Crude modeling with a difference-in-difference indicator showed that after three weeks of mask policy implementation, counties with a mask policy had a daily percent COVID-19 growth rate that was 1.32 times lower (32% decrease) compared to counties without a mask policy. • At 12 weeks post-mask policy implementation, the average daily COVID-19 case growth among counties without a mask policy was 2.42% (±1.92), and was significantly higher than the average daily

		COVID-19 case growth among counties with a mask policy (1.36% (±0.96%)) ($p<0.001$).
Yilmazuday (2020) *preprint* (34) Ecological study USA Feb-Aug 2020	Using a difference in-difference design, county-level data on changes in COVID-19 cases or deaths were analyzed using social interactions measured by Google mobility. Counties were categorized as mask-wearing vs. non-mask-wearing by using Mask-Wearing Survey Data. The impact of mask wearing on the causal relationship between COVID-19 cases and social interactions was subsequently analyzed.	• Adherence to wearing a face mask in the community needs to exceed 75% to reduce COVID-19 cases and deaths. The effects of social interaction on COVID-19 were statistically eliminated when more than 85% of people in a county "always" wore a face mask in public settings.
Matzinger (2020) *preprint* (8) Ecological study USA Mar-Jul 2020	A regression analysis was conducted to assess the impact of NPIs on COVID-19 cases, hospitalizations, and deaths. Mask policies were implemented between Mar-Jul, allowing for an opportunity to evaluate both early and late policies.	• Regression analysis showed that closing schools, closing bars, and wearing masks had major effects on infections, hospitalizations and death rates in the US during the COVID-19 pandemic. • For four states (IL, NJ, MA, MD), a drop in the rates of infections were observed after implementing a mask policy. Decreased rates were followed by a 2-fold drop in hospitalizations and deaths. • Across the dataset, the mask policies occurred at different times and the authors show the rate reductions followed in a predictable manner. Later policies correlated to later inflection points. This supports the evidence that these rate reductions were due to wearing masks as opposed to other potential changes in mobility or behavior. • The early and late mask policies were both effective in reducing COVID-19 infections.

		• The lag time between the implementation of mask policies to a reduction in COVID-19 infections was between 16-23 days. • One exception to the effect of early mask policies was shown in the data from NY which mandated masks after it had already turned its rapidly rising infection numbers into declining ones. The mask policy had no further suppressive effect on infections. However, when NY later opened its economy and infections began to rise, the increase was remarkably lower than those of states that opened without mask policies in place. This suggests continuing the mask policy had an effect when lifting other NPIs.
Kaufman (2020) (39) Ecological study USA Jan-Jul 2020	This study estimated the excess COVID-19 burden in USA states that had an evidence-based reopening strategy, defined as reopening indoor dining rooms after implementing a statewide masking policy, compared to states that lacked an evidence-based reopening strategy, defined as reopening indoor dining rooms before implementing a statewide masking policy.	• An estimated > 50,000 excess deaths were prevented within 6 weeks in 13 states that implemented mask policies prior to reopening. • In states reopening without mask policies, the number of excess cases per 100,000 residents is ten times the number in states with mask policies 8 weeks after reopening (643.1 cases; 95% CI: 406.9-879.2 vs. 62.9 cases; 95% CI: 12.6-113.1). • Excess cases after 6 weeks could have been reduced by 90% from 576,371 to 63,062 and excess deaths reduced by 80% from 22,851 to 4858 had states implemented mask policies prior to reopening.
Yang (2020) *preprint* (31) Ecological study	This study analyzed county level Rt values over time using a mechanistic meta-population model and associated these with county-level characteristics and NPIs such as school closures,	• The estimated impacts of individual interventions were measured during layered intervention strategies and do not estimate the potential impact if done alone.

USA Jan-Jul 2020	daycare closures, banning nursing home visits, stay home orders, and wearing a face mask. With the exception of the mask policy, the closures were confounded by workplace presence which also decreased at the same time as the closures.	• Face mask policies were associated with an 18% reduction in Rt (95% CI: 16-20%).
Chernozhukov (2020) (6) Ecological study USA Mar-Jun 2020	This study uses case data and information on changes to NPIs to assess the impact on the growth rates of confirmed COVID-19 cases and deaths. The face mask policy in this study is mandating face masks for employees. NPIs examined included stay at home orders, business closures, and school closures.	• The results attribute a 9% reduction in the weekly growth rate and a 15% reduction in the weekly death rate with a 14 day lag time to mandating employees wearing masks, $p<0.01$. This was stable across several types of analysis.
Maloney (2020) *preprint* (40) Ecological study USA Mar-Jun 2020	This study used a non-parametric machine learning algorithm to test the hypothesis that mask policies were associated with reductions in new COVID-19 cases. Data on new COVID-19 cases in 38 USA states was analysed in the month before and after the mask policy implementation date.	• All state analysis: The mean overall number of new COVID-19 cases before vs. after the mask policy was 654 (N=1138, SD=1357) vs. 639 (N=1177, SD=975), respectively. 13 states had higher mean case numbers pre vs. post mask policy. • State-wise analysis: With the exception of Georgia and Wyoming, the states with a greater mean pre vs post mask policy achieved statistical significance: strongly to moderately supporting a reduction in COVID-19 cases after implementation of the mask policy in eleven states. • Societal cohesion and close social ties was shown to best predict states where mask policies were successful. They suggest that this represents compliance across different states.
Li (2020) (30)	Analysis of the total infections and daily infections in the top 15	• The analysis finds that despite stay at home orders most states experienced an

Ecological study USA Mar-May 2020	infected USA states was conducted to investigate the impact of NPIs: such as social distancing, stay at home orders and face mask policies (6 states had no face mask orders, 9 states had face mask policies) March 1 to May 18, 2020. Changes in the regression slopes after the implementation of NPIs were measured and compared across states.	upward trend in daily new infections. Eight states experienced a reversed downward trend or slowing trend after face mask policies were introduced. • In contrast, in states where face masks were not mandated the upward trend in cases extended for up to two additional months. • The analysis estimates ~252,000 infections have been avoided across 7 states that introduced mandatory face mask policies with a projected proportion of cases prevented ranging from 3.2% to 48% up to May 18.
Lyu (2020) (7) Ecological study USA Mar-May 2020	This study measured the effects of state government policies for face mask use in the public issued by 15 states (and DC) from Apr 8-May 15, 2020. County-level case data was used from March 31 (seven days before the first state signed a face cover policy) through May 22. Between Apr 17-May 9, 2020, the impact of 20 states mandating that certain employees wear face masks was also assessed.	• There was a significant decline in daily COVID-19 growth rate after mandating face masks in public with the effect increasing over time. • There was a decline in the daily COVID-19 growth rate by 0.9, 1.1, 1.4, 1.7, and 2.0% in 1–5, 6–10, 11–15, 16–20, and 21+ days after implementation of mandatory face mask policies, respectively. • It was estimated that 230,000–450,000 cases may have been averted due to these policies by May 22. • The impact of employee-mandated face mask use was small and not statistically significant.
Yang (2020) *preprint* (5) Ecological study USA	This study used a linear regression accounting for mobility data in NYC to estimate the effectiveness of NPIs for the entire population and by age group.	• Face covering policies resulted in a 6.6% (95% CI: 0.8 - 12.4%) reduction in cases in the first month and a 3.4% reduction (95% CI: -1.9 - 8.6%) across the entire eight weeks of lockdown. • This effect varied by age: 20.8% (95% CI: -0.1-41.6%) for 65-74 year olds and 20.8% (95% CI: -0.9 – 42.5%) for 75+ year olds

Apr 2020		during the first month and remained at similar levels afterwards. For 25-44 and 45-64 year olds the effectiveness was 4.5% (95% CI: -0.6 – 9.7%) and 8.1% (95% CI: -0.1 – 16.1%) in the first month, respectively; however, it reduced substantially afterwards, likely due to reversed risk behavior.
Xu (2020) (41) Ecological study USA Mar-Apr 2020	In this study, the associations of stay-at-home order (SAHO) and face masking recommendation with COVID-19 epidemics were analyzed. The temporal trends in daily new cases and deaths COVID-19 cases and Rt were modeled. The CDC recommended the use of face masks on Apr 3, 2020.	• The overall slope change of daily new deaths face-masking were −0.13 (95% CI: −0.25 to −0.07). • The overall slope change of daily new cases attributable to face-masking were −0.10 (95% CI: −0.18 to −0.08).
Australia (n=1)		
Scott (2020) *preprint* (11) Ecological study Australia Jul-Aug 2020	Due to a resurgence of COVID-19 in Melbourne, a mandatory mask policy was implemented on Jul 22 creating a natural experiment to assess the impact of the policy on the epidemic growth rate as the policy introduction occurred in the absence of other changes to restrictions.	• The introduction of a mandatory mask policy was associated with an estimated 23% reduction in Rt, from 1.18 to 0.91. • The shift in epidemic growth was observed eight days after the policy was introduced which is consistent with the incubation time of COVID-19 plus the time needed to test and report new cases. • Analysis of images of people in public spaces showed mask usage rose from approximately 43% to 97% and survey data found that before policy introduction, 44% of participants reported "often" or "always" wearing a mask; and after, 100% reported "always" doing so.
Europe (n=4)		
Sruthi (2020) *preprint* (33) Ecological study	This study aimed to develop a systematic relation between the degrees of NPIs implemented by the 26 cantons in Switzerland and	• The mask wearing policy on public transport and in secondary schools contributed to a 0.025 (CI: 0.018-0.03)

Switzerland Mar-Sep 2020	their respective contributions to Rt. The mask wearing policy was only on public transportation and in secondary schools.	reduction in Rt compared to baseline with no policies. • When analyzed separately, a reduction of Rt 0.011 (CI: 0.008-0.0127) and 0.0139 (CI: 0.0132-0.0144) was estimated for the use of masks in secondary school and on public transport, respectively. • Some places added mandatory masks in shops, but no further reduction in Rt was detected.
Mergel (2020) *preprint* (42) Ecological study Germany Apr-Jul 2020	In this study, the impact of a face mask policy on the daily COVID-19 Rt and fatality rate was investigated. The study also looked at the implementation/lifting of NPIs (mass gathering prohibited, public life restricted, private contacts restricted, face masks in public spaces and easing of lockdown).	• In this study mask wearing was implemented April 27 after all the other restrictions. • It was not possible to separate the potential positive effect of spring and summer on the trajectory of the pandemic from the mask wearing policy that was implemented. • They did not detect an impact on Rt attributable to the mask policy. • During the time the mask policy was implemented, cases became less lethal from 7% on Apr 27 to 1% in July.
Pedersen (2020) *preprint* (43) Ecological study Italy Feb-Jul 2020	To determine which public health measures altered disease dynamics, change points in COVID-19 dynamics were estimated using regional and national data. A change point is an identified time point where there is a shift in the number of daily confirmed cases from the introduction of a public intervention 7–11 days prior.	• In Veneto, a change point was identified on Apr 21 (95% CI: 14 - 28), which corresponds to the policy of mandatory face mask use on Apr 14. • In Tuscany, a change point was identified on Apr 16 (95% CI: 8 – 24), which corresponds to face mask distribution on Apr 7. • The change points in regional COVID-19 cases correlate well with face mask policies.
Mitze (2020) *unpublished* (27)	Using epidemic data from Germany, a synthetic control method was used to assess the	• Ten days after masks became compulsory in Germany, the cumulative number of

Ecological study Germany Jan-May 2020	effect of face masks on the spread of COVID-19. The city of Jena implemented a mandatory face mask policy on Apr 6, 2020. Jena was compared to a synthetic control area that closely followed the COVID-19 trend before the introduction of mandatory masks in Jena.	registered COVID-19 cases were reduced between 2.3-13%. • After the face mask policy, the daily growth rate of reported infections decreased by 18.94%. After taking the treatment effect for larger cities into account, authors conclude there was a reduction in the growth rate of infections by around 40%.
Middle East (n=1)		
Saki (2020) *preprint* (44) Ecological study Iran Jun-Jul 2020	This study investigated the effects of implementing a social distancing policy, and the impact of its lifting, as well as the effects of face mask policies on the temporal trend of new COVID-19 cases. Data was collected both two weeks before and after the implementation of each policy.	• Prior to the implementation of the policy of wearing masks in the community, there were approximately 2491.97 new daily confirmed cases and an upward slope ($p<0.001$). • With the implementation of the face mask policy, the trend in the number of daily confirmed cases decreased that caused a change in the slope of the epidemic curve -25.84 ($p<0.001$).

CI = confidence interval, HR = hazard ratio, NPI = non-pharmaceutical intervention, NYC = New York City, OR = odds ratio, Rt = effective reproduction number, SE = standard error

SYNTHESIS RESEARCH ASSESSING EFFECTIVENESS

Six synthesis research reviews were identified on the protective effect of the use of face masks in community settings, including four systematic reviews and two rapid reviews (Table 3). The earliest review was conducted in April 2020. Two of the later reviews included studies published up to early October. A progression of evidence from April to October is discernable in these reviews. Many of the studies in the reviews are considered relevant to this rapid review and are also included in the evidence tables above.

Table 3. Synthesis research on the use of face masks to prevent COVID-19 in community settings (n=6)

STUDY	METHODS	KEY OUTCOMES
Systematic reviews (n=4)		
Li (2020) *preprint* (45) Systematic review and meta-analysis	The purpose of this review was to evaluate the effectiveness of using face masks to protect from SARS-CoV-2 infection. Six case-control studies were included, five on	• Overall, wearing a mask significantly reduced the risk of SARS-CoV-2 infection (MA OR 0.38, 95% CI: 0.21-0.69, I^2= 54.1%).

China, India, Thailand, USA Oct 2020	healthcare workers and one on the general population. Review contains literature up until Oct 2020. AMSTAR: high quality Note: Meta-analysis (MA) was conducted. Where I^2, a measure of between study heterogeneity, was > 50% a random effects model was used, otherwise a fixed-effect model was used.	• In a subgroup analysis, healthcare workers wearing a mask had a reduced risk of COVID-19 by ~70% (MA OR 0.29, 95% CI: 0.18-0.44, I^2=11%). • For the single study on the general population, wearing a mask reduced the risk of SARS-CoV-2 infection by ~28% (OR 0.72, 95% CI: 0.46-1.12) and after adjusting for confounders (aOR 0.23, 95% CI: 0.09-0.59) (18). • Studies in China showed a higher protective effect than other countries: China MA OR 0.21, 95% CI: 0.09-0.53, I^2 =26.1% vs. other countries MA OR 0.55, 95% CI: 0.32-0.95, I^2 = 39.3%.
Coclite (2020) (46) Systematic review and meta-analysis China, Hong Kong, Iran, Israel, Italy, Japan, Malaysia, Netherlands, Saudi Arabia, South Korea, Taiwan, UK, USA Apr 2020	This review aimed to summarize the evidence on the effectiveness of face mask use in the community to reduce the spread of disease. Thirty-five studies were included (3 RCTs, 13 predictive models, 10 observation studies, and 9 laboratory experiments). Seven predictive models and one laboratory study were specific to SARS-CoV-2. Review contains literature up until Apr 22, 2020. AMSTAR: high quality	• No observational studies on wearing face masks in the community for reducing the spread of COVID-19 were identified. • Mathematical models indicated a decrease in mortality when the population mask coverage was near-universal, regardless of mask efficacy. • All types of masks might reduce aerosol exposure. However, personal respirators were more efficient than surgical masks, which were more efficient than home-made masks. • RCTs showed a trend towards the protective effect of wearing face masks versus no mask (aOR 0.90, 95% CI: 0.78-1.05), however these results were not significant. Similar findings were reported in observational studies.
Chou (2020) (47) Chou (2020) (update 1) (48)	The effectiveness of N95, surgical, and cloth masks in community and health care settings for preventing respiratory virus infections was	• In the first version and second update of this review, no studies evaluating masks for preventions of SARS-CoV-2 infections in community settings were identified.

Chou (2020) (update 2) (49) Chou (2020) (update 3) (50) Living systematic review China, Thailand, USA Oct 2020	assessed in this living systematic review. Search dates: Original search: 2002 – Jun 2, 2020 Update 1: Jun 2 – July 2, 2020 Update 2: July 3 – Aug 2, 2020 Update 3: Aug 3 – Oct 2, 2020 AMSTAR: moderate-high quality (no *a priori* protocol, quality assessment was not conducted with a formal instrument, sub-optimal reporting e.g. unsure if double reviewers for quality assessment).	• The first update identified a cohort study of 124 households with an index SARS-CoV-2 case and 355 uninfected household contacts. In households where masks were used by at least one family member (including the index case) before the development of symptoms were associated with decreased risk for incident infections (aOR 0.21, 95% CI: 0.06-0.79). There was no association between mask use after illness onset in the index case and risk for SARS-CoV-2 infections in family members (17). • The third update identified a case control study in Thailand. Wearing a mask all of the time versus no use was associated with decreased risk for SARS-CoV-2 infection (aOR 0.23, 95% CI: 0.09-0.60), whereas inconsistent use was not associated with decreased risk (aOR 0.87, 95% CI: 0.41-1.84). Mask type (medical mask only, nonmedical mask only, or both) was not independently associated with risk for SARS-CoV-2 infection (p = 0.54) (18).
Chaabna (2020) (51) Systematic review and meta-analysis Australia, China, France, Germany, Hong Kong, Thailand, USA May 2020	The evidence on the effectiveness of cloth and medical face masks for preventing transmission of respiratory infections in community settings was assessed in this review. Twelve studies were included, only one on SARS-CoV-2. Review contains literature up until May 12, 2020. AMSTAR: low quality (missing an *a priori* protocol, double reviewers, only searched two databases, no formal quality assessment).	• No primary studies on cloth face mask effectiveness to prevent respiratory infection transmission were identified. • The meta-analysis identified that medical face mask use significantly reduced the risk of transmitting respiratory infections (pooled OR=0.66, 95% CI: 0.54-0.81). • One study specific to SARS-CoV-2 was identified. This retrospective cohort study demonstrated medical face masks are effective in reducing SARS-CoV-2 transmission when used before those infected develop symptoms (17).

Rapid reviews (n=2)		
Warkentin (2020) *unpublished* (52) Rapid Review Canada, China, Germany, Israel, Japan, South Africa, Thailand, Uganda, UK, USA Aug 2020	This rapid review aimed to assess the evidence on the impact of community mask use on the susceptibility to and transmission of COVID-19, and how mask use compliance affects mask effectiveness. Thirty-one studies were included (21 primary and 10 models on the effectiveness of masks and 5 on mask compliance). Of the 17 primary studies on the effectiveness of masks, there were 9 ecological studies, 1 cohort study, 1 case-control study, and 6 case report/epi investigations. Literature search included Dec 2019 – Aug 2020. AMSTAR: low quality (missing an *a priori* protocol, double reviewers, and quality assessment).	• There was insufficient evidence to quantify the effectiveness of face mask use. • Overall, mask use within the community reduced the number of COVID-19 cases within a population. • Case reports consistently reported fewer secondary cases when index cases and/or their contacts wore masks. • Modelling studies found that wearing a mask, in conjunction with other mitigation strategies, had the potential to reduce mortality due to COVID-19 and avert a resurgence of cases in places where lockdown measures had already reduced the number of cases. • There were no studies that investigated the impact of face mask use in schools.
The Royal Society (2020) *unpublished* (53) Rapid Review China Jun 2020	This rapid review aimed to evaluate the effectiveness of cloth masks and face coverings for the general public and in health-care settings. This included an international comparison of the timing and introduction of face mask policies in relation to COVID-19. Only one study on SARS-CoV-2 was included. Review contains literature up until Jun 26, 2020. AMSTAR rating: low quality (there are little details on the process of conducting the review: search, screening, assessment or extraction of data/analysis).	• Results revealed that no systematic review and meta-analysis has yet been conducted on the effectiveness of other types of cloth masks beyond surgical masks and N95 respirators. • Empirical and experimental evidence on community mask wearing and/or cloth masks is limited. • One study specific to SARS-CoV-2 was identified. This retrospective cohort study demonstrated medical face masks are effective in reducing SARS-CoV-2 transmission when used before those infected develop symptoms (17). • The meta-analysis was based on non-SARS-CoV-2 literature in the healthcare setting indicated protection afforded by

		gauze or cloth masks (RR=0.46; 95% CI: 0.22-0.97; N=746) and paper masks (RR=0.61; 95% CI: 0.41- 0.90; N=166) compared to no mask.

aOR = adjusted odds ratio, CI = confidence interval, MA = meta analysis, RCT = randomized control trial

Methods

A daily scan of the literature (published and pre-published) is conducted by the Knowledge Synthesis team in the Emerging Science Group, Public Health Agency of Canada. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square, and COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The cumulative scan results are maintained in a Refworks database and an excel list that can be searched. Details on this search strategy are available upon request. From this database and excel list, article titles and summaries will be systematically searched for the following key words: mask* OR (face AND cover*). Each potentially relevant reference was analyzed to confirm its relevance and data was extracted into the review. This review contains research published up until November 19, 2020.

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Preuve émergente sur la COVID-19

Revue rapide sur les effets physiologiques du port du couvre-visage

Introduction

Quelles sont les données probantes sur les changements physiologiques associés au port d'un couvre-visage? Y a-t-il des preuves que le port d'un couvre-visage peut avoir des effets néfastes sur les personnes ayant des problèmes médicaux?

De nombreux organismes de santé publique à l'échelle mondiale, comme l'Organisation mondiale de la Santé, recommandent le port d'un couvre-visage dans les espaces publics pour se protéger contre la COVID-19. Des préoccupations ont été soulevées au sujet du port du couvre-visage dans certains contextes ou par des personnes ayant certains problèmes de santé. La revue rapide porte donc sur les effets physiologiques du port d'un couvre-visage sur les systèmes respiratoire et cardiovasculaire, et inclut les différences statistiquement significatives signalées. Les réactions dermatologiques et psychologiques au port d'un couvre-visage ne sont pas incluses dans cette revue. Elles pourraient cependant être traitées comme un sujet distinct, puisqu'il s'agit d'effets liés au port d'un couvre-visage (1). Cette revue rapide résume la documentation disponible jusqu'au 2 décembre 2020 sur les changements physiologiques principalement liés aux systèmes respiratoires et cardiovasculaires découlant du port d'un couvre-visage, effets qui peuvent se produire tant dans les populations en santé que chez celles qui ont des problèmes médicaux.

Points clés

- Vingt articles ont été recensés, dont quinze études sur les réactions physiologiques associées au port du couvre-visage, une revue et quatre documents d'orientation. La majorité des études ont comparé les effets physiologiques associés au port d'un masque N95 ou d'un masque chirurgical. Seules deux études ont inclus des masques non médicaux (voir l'annexe pour obtenir des renseignements sur les types de masques). Ces sujets ont été étudiés dans différentes populations, soit des volontaires sains (n = 8), des travailleurs de la santé (n = 2), des femmes enceintes (n = 2) et des personnes ayant des problèmes de santé (n = 3).
- Huit études ont évalué le port d'un couvre-visage chez des volontaires en santé. Deux études portaient uniquement sur des activités sédentaires, cinq comprenaient une gamme d'activités allant des exercices légers (p. ex., marcher à un MET de 3 à 5) à intenses, alors qu'une autre a évalué les répercussions du port du couvre-visage pour des pilotes volant à une altitude de 1 524 m (5 000 pi).

  Limites :

  - Les huit études sur les volontaires sains comportaient des échantillons de petite taille, avec une moyenne de 12 participants (83 volontaires sains au total et 32 pilotes). Ces études comprenaient des

groupes de participants homogènes, p. ex., des étudiants de niveau collégial ou uniquement des hommes. Leur durée était souvent courte et ne reflétait donc pas l'incidence potentiellement associée au port d'un couvre-visage pendant une longue période. La plupart des études ont effectué des analyses pour établir la signification statistique de deux mesures ou plus, mesures qui sont indiquées dans le rapport comme des résultats significatifs. Comme les auteurs ont rarement discuté de la signification clinique des résultats présentés, les résultats des études inclus dans cette revue sont donc préliminaires. Il faudra effectuer plus de recherches avec de plus grands échantillons et des échantillons plus représentatifs pour évaluer la possibilité de généraliser ces résultats.

Masques N95 :

- Six études réalisées sur des volontaires sains indiquent que comparativement à l'absence de masque, les masques N95 ont grandement augmenté la résistance respiratoire, réduit le volume d'échange d'air, provoqué une augmentation de la fréquence cardiaque et une réduction du CO_2 en fin d'expiration et diminué la saturation en oxygène. Les symptômes associés à ces changements physiologiques incluaient une dyspnée (difficulté à respirer), des étourdissements et de la difficulté à se concentrer.
- Cinq études ont examiné l'effet du masque chez des volontaires sains qui effectuaient des exercices légers à intenses. Lorsque le port d'un masque N95 augmentait l'intensité de l'exercice, cela a eu de plus grandes répercussions sur certains paramètres physiologiques, notamment une augmentation du CO_2 en fin d'expiration, ainsi qu'une diminution du débit ventilatoire et du VO_{2max} global que lorsque les exercices étaient faits sans masque.
- Une étude a évalué les répercussions physiologiques globales des différents types de masques et classé ainsi les masques, des répercussions les plus fortes aux plus faibles : KN95 > masques chirurgicaux > masques médicaux, masques avec éponge et masques civils jetables > gaze et aucun masque.
- Quatre études ont comparé les répercussions des masques N95 et des masques chirurgicaux et déterminé que les répercussions physiologiques les plus importantes étaient associées aux masques N95. Une étude n'a pas jugé que ces différences étaient significatives, deux études les ont vues comme étant significatives pour certains paramètres, soit la fréquence cardiaque (n = une étude sur deux), le débit ventilatoire et le VO_{2max} (n = une étude sur deux), sans cependant les indiquer, alors que la quatrième présentait des données brutes et des résumés graphiques.

Masques chirurgicaux :

- Quatre études (n = 63 observations) ont examiné les effets des masques chirurgicaux comparativement à l'absence de masque et indiquent que ces masques entraînent différentes répercussions, soit une fréquence cardiaque élevée (n = 3) et une baisse de la saturation du sang en oxygène (n = 1) comparativement aux données obtenues en l'absence de masque, tant au repos que pendant l'exercice. Les masques chirurgicaux ont considérablement réduit le débit ventilatoire, mais pas le VO_{2max} À la fin d'une séance d'entraînement intense, le CO_2 de fin d'expiration avait

statistiquement augmenté avec un masque chirurgical comparativement au résultat obtenu sans masque. Le niveau d'effort perçu était également plus élevé chez les personnes qui portaient un masque chirurgical (n = 2). Les symptômes n'ont pas été mentionnés aussi fréquemment pour les masques chirurgicaux que pour les masques N95, mais incluaient tout de même de la dyspnée, des vertiges et des difficultés de concentration.

- Des pilotes qui portaient un masque en tissu chirurgical ou non médical et ont pris part à un exercice de simulation de 90 minutes à 1 524 m (5 000 pi) n'ont vu aucune différence dans leur rythme cardiaque, leur CO_2 de fin d'expiration, leur fréquence respiratoire ou leurs niveaux d'oxygène (2).

Masques non médicaux :

- Deux études ont porté sur des couvre-visages non médicaux en tissu, en éponge, en gaze ou décrits comme des masques civils jetables. Dans ces études, les répercussions physiologiques des différents matériaux composant les masques n'étaient pas significativement différentes de celles des masques chirurgicaux (2, 3).

- Des études sur les travailleurs de la santé (n = 2) ont été menées afin de comprendre l'incidence du port d'un masque N95 ou chirurgical lors de l'exécution de différentes tâches dans le cadre de leur profession.
  - Une enquête menée auprès de 250 travailleurs de la santé portant des masques chirurgicaux ou N95 plus de quatre heures par jour a révélé que 58,2 % d'entre eux ($P < 0,01$) avaient de la difficulté à respirer à l'effort. Parmi les autres symptômes, citons une transpiration excessive autour de la bouche (67,6 %), une irritation de la peau (39 %) et une douleur derrière l'oreille (45,2 %).
  - Les changements hémodynamiques cérébraux associés au port d'un masque N95 ont été évalués chez 154 travailleurs de la santé qui ont déclaré avoir des maux de tête découlant du port d'un masque N95. Cinq minutes après avoir mis le masque N95, on a remarqué une augmentation importante du débit moyen et du CO_2 en fin d'expiration. L'ajout d'un appareil de protection respiratoire à épuration d'air motorisé (APR) a cependant permis de ramener ces mesures à des niveaux normaux.
- Des femmes enceintes, saines, qui en étaient entre 13 et 35 semaines de gestation, ont également pris part à deux études (n = 2) afin de connaître l'incidence du port du masque N95.
  - Les masques N95 portés par 42 femmes enceintes effectuant un travail physique de routine (équivalent à un METS de 3) ont entraîné une diminution importante de l'air courant, du débit ventilatoire et de la consommation d'oxygène, une augmentation de la pression partielle transcutanée en raison du CO_2, ainsi que des résultats contradictoires pour la fréquence respiratoire. Aucune des deux études n'a cependant indiqué de changement dans la fréquence cardiaque maternelle, la fréquence cardiaque fœtale ou la saturation en oxygène comparativement à l'absence de masque.
  - Comparer les résultats des femmes enceintes et des femmes non enceintes n'a pas permis de voir de différences dans les répercussions physiologiques associées du port d'un masque N95 (4).

- Trois études ont évalué certains problèmes médicaux, y compris la maladie pulmonaire obstructive chronique (MPOC) (n = 2), l'asthme (n = 2) et la rhinite chronique (n = 1). Les informations portant sur d'autres conditions médicales n'ont pas été mentionnées.
    - Dans une étude sur 97 patients atteints de MPOC qui ont porté des masques N95, 7 % n'ont pas pu le garder en raison de dyspnée, de maux de tête et d'étourdissements. Il s'agissait en général de personnes atteintes d'un MPOC plus grave. Pour les patients qui ont pu terminer l'étude, les résultats indiquaient une augmentation de la fréquence respiratoire, du rythme cardiaque, de la pCO_2 en fin d'expiration et une diminution de la saturation en oxygène comparativement aux données obtenues au repos, sans masque. Les différences observées entre les résultats obtenus avec un masque N95 et sans masque se sont également accentuées pendant un exercice léger (marche). Une deuxième étude portant sur 14 patients atteints d'une MPOC légère a fait état d'une diminution du volume ventilatoire et d'un pourcentage de VEMS inférieur au volume prédit lorsque les patients portaient un masque N95 ou un demi-masque.
    - Les 42 personnes atteintes d'asthme ont, quant à elles, vu une diminution du volume respiratoire et un pourcentage de VEMS inférieur à celui qui avait été prédit avec un masque N95 ou un demi-masque, le demi-masque ayant eu une incidence légèrement moins importante. De même, la capacité respiratoire maximale a été considérablement réduite chez trois asthmatiques qui portaient un masque chirurgical.
    - Parmi les 17 personnes atteintes de rhinite chronique, les répercussions du port d'un masque N95 ou d'un demi-masque étaient similaires à celles observées chez les volontaires sains.
- Les personnes qui portent un masque doivent être conscientes de leur effort et de leur fréquence cardiaque, puisque les études montrent que le port d'un masque augmente la charge cardio-respiratoire et que les répercussions liées au masque augmentent avec l'exercice. Elles doivent s'assurer que leur fréquence cardiaque reste inférieure à 150 battements/min ou à 70 % de la fréquence cardiaque maximale selon leur âge.
- Les documents d'orientation établis par le Canada, les États-Unis et l'Organisation mondiale de la Santé (OMS) sur l'utilisation des masques non médicaux dans la collectivité recommandent que les personnes incapables de retirer leur masque sans aide n'en portent pas en raison du risque de suffocation. Cela inclut les enfants de moins de deux ans et toute personne inconsciente, handicapée ou qui a de la difficulté à respirer. Les lignes directrices de l'OMS précisent également que les masques ne doivent pas être portés à des fins de contrôle à la source pour empêcher la transmission des virus provenant d'un enfant de moins de 5 ans atteint de la COVID-19.
- La Société canadienne de thoracologie et Asthme Canada indiquent que les personnes atteintes d'un problème pulmonaire sous-jacent devraient être capables de porter un couvre-visage non médical, mais devraient consulter un professionnel de la santé si cela leur pose des problèmes.
- Les lignes directrices actuelles de l'OMS sur le port de couvre-visage dans la collectivité indiquent que ceux-ci devraient pouvoir être retirés par toute personne qui a de la difficulté à respirer.

Vue d'ensemble des éléments de preuve

Quinze articles portant sur les changements physiologiques respiratoires et cardiovasculaires associés au port d'un masque ont été recensés et inclus dans cette revue rapide. La plupart étaient des rapports d'études quasi expérimentales utilisant un modèle en chassé-croisé dans lequel les personnes exerçaient un autocontrôle. Bon nombre des études portaient sur des populations saines et comportaient de petits échantillons formés de populations homogènes (p. ex., des étudiants de niveau collégial ou uniquement des hommes), alors que d'autres incluaient des travailleurs de la santé (n = 1) et des femmes enceintes (n = 2). Il n'y a eu que trois études portant spécifiquement sur le port du masque par des personnes ayant des problèmes médicaux, soit la MPOC (n = 2) et l'asthme (n = 2). Bien que ces études aient été bien exécutées et qu'elles aient utilisé des mesures objectives pour établir leurs résultats, elles comportaient de petits échantillons et des échantillons homogènes. Il est donc probable qu'elles comportent un biais dans la sélection, mais cela n'a pas pu être évalué dans la plupart des études. Les résultats de ces études ne devraient donc pas être généralisés sans recherches supplémentaires. Une étude portant sur les travailleurs de la santé comportait une enquête transversale axée sur les répercussions autodéclarées des masques et des couvre-visage. Même si elle comprenait un échantillon de grande taille formé de travailleurs de la santé œuvrant dans un hôpital et a utilisé un questionnaire fondé sur des recherches formatives, la nature autodéclarée des résultats risque fort d'entraîner de nombreux biais.

Il faudrait donc que d'autres recherches soient effectuées avec de plus grands échantillons, qu'elles portent sur tous les types de masques et incluent également l'utilisation prolongée des masques ou des couvre-visages. De futures recherches pourraient changer notre compréhension des répercussions associées au port à court et à long terme du masque ou du couvre-visage et nous permettre de savoir précisément quelles personnes ne devraient pas en porter.

TABLE DES MATIÈRES

ÉLÉMENTS PROBANTS SUR LES EFFETS PHYSIOLOGIQUES DU PORT DU MASQUE

La réaction physiologique au port du masque a été évaluée dans 15 études portant sur différentes populations, soit des bénévoles sains, des travailleurs de la santé, des femmes enceintes, des pilotes instructeurs et des personnes atteintes de MPOC, d'asthme ou de rhinite chronique (tableau 1). Un seul

examen, jugé de très basse qualité selon AMSTAR, porte sur la réponse physiologique à l'obstruction du débit d'air causée par le port d'un masque et inclut une interprétation de ces répercussions (5). Les résultats physiologiques évalués pour chacune des études variaient d'une étude à l'autre et sont présentés dans le tableau lorsqu'ils ont été évalués. Il s'agit notamment des paramètres respiratoires (p. ex., volume total inhalé/expiré, fréquence respiratoire), de la fonction respiratoire (p. ex., niveaux d'oxygène et de CO_2), de la fréquence cardiaque, de la tension artérielle et des changements hémodynamiques cérébraux.

Parmi les huit études portant sur des volontaires sains, deux incluaient uniquement des activités sédentaires alors que cinq comprenaient une gamme d'activités allant des exercices légers (p. ex., marcher à un MET de 3 à 5) à des exercices intenses. Ces études ont donc examiné les résultats de 83 volontaires sains (taille moyenne de l'étude : 12). Une seule étude a évalué les répercussions du port du masque chez les pilotes (n = 32) lors d'une simulation de vol à 1 524 m (5 000 pi).

Six études réalisées sur des volontaires sains ont évalué le port des masques N95. Les résultats obtenus indiquaient notamment que comparativement à l'absence de masque, ce type de masque avait grandement augmenté la résistance respiratoire et réduit le volume d'échange d'air, en plus d'avoir provoqué une augmentation de la fréquence cardiaque et une réduction du CO_2 en fin d'expiration, ainsi qu'une diminution de la saturation en oxygène. Les symptômes associés aux changements physiologiques signalés comprenaient de la dyspnée (difficulté à respirer), des étourdissements et de la difficulté à se concentrer. Cinq études ont également examiné les répercussions lorsque les volontaires faisaient des exercices légers à intenses avec un masque. Les résultats ont démontré de plus grandes répercussions sur certains paramètres physiologiques, y compris une augmentation du CO_2 en fin d'expiration et une diminution du débit ventilatoire et du VO_{2max} global que lorsque ces exercices étaient faits sans masque.

Comparant les répercussions physiologiques globales de différents types de masques ou couvre-visage chez des volontaires sains, une étude a évalué les répercussions physiologiques globales de différents types de masques et classé ainsi les masques (des répercussions les plus fortes aux plus faibles) : KN95 > masques chirurgicaux > masques médicaux, masques avec éponge et masques civils jetables > gaze et aucun masque. Quatre autres études ont comparé les masques N95 aux masques chirurgicaux. L'une d'elles a notamment indiqué des répercussions moins fortes même si les différences physiologiques n'étaient pas statistiquement différentes, alors que deux autres ont mentionné que ces différences étaient significatives pour certains paramètres, soit la fréquence cardiaque (n = une étude sur deux), le débit ventilatoire et le VO_{2max} (n = une étude sur deux), mais sans les indiquer, alors que la quatrième présentait des données brutes et des résumés graphiques.

Comparativement à l'absence de masque, le port d'un masque chirurgical par des volontaires (n = 4) a révélé une fréquence cardiaque élevée (n = 3) et une baisse de la saturation en oxygène du sang (n = 1) au repos ou à l'effort. Les masques chirurgicaux ont considérablement réduit le débit ventilatoire, mais pas le VO_{2max} À la fin d'une séance d'entraînement intense, le CO_2 de fin d'expiration avait augmenté de manière importante avec un masque chirurgical comparativement au niveau observé sans masque. Le niveau d'effort perçu était également plus élevé avec un masque chirurgical (n = 2) que sans masque. Des symptômes comme de la

dyspnée, des étourdissements et de la difficulté à se concentrer ont cependant été signalés moins fréquemment avec les masques chirurgicaux qu'avec pour les masques N95.

Les masques non médicaux n'ont été examinés que dans deux études réalisées sur des volontaires sains. Ainsi, dans une étude, des pilotes qui portaient un masque en tissu chirurgical ou non médical et ont pris part à un exercice de simulation de 90 minutes à 1 524 m (5 000 pi) n'ont vu aucune différence dans leur rythme cardiaque, leur CO_2 de fin d'expiration, leur fréquence respiratoire ou leurs niveaux d'oxygène (2). La deuxième étude a, quant à elle, comparé des masques non médicaux faits d'éponge ou de gaze ou décrits comme des masques civils jetables. Les résultats sont présentés dans des graphiques et les répercussions du port de ces masques se trouvent entre les résultats associés au port du masque chirurgical et à ceux qui ont été obtenus sans masque (3).

Des études portant sur les travailleurs de la santé visaient à comprendre l'incidence du port d'un masque N95 ou chirurgical lors de l'exécution de différentes tâches dans le cadre de leur profession. Ainsi, une enquête menée auprès de 250 travailleurs de la santé portant des masques chirurgicaux ou N95 plus de quatre heures par jour a révélé que 58,2 % d'entre eux ($P < 0,01$) avaient de la difficulté à respirer à l'effort. Parmi les autres symptômes, citons une transpiration excessive autour de la bouche (67,6 %), une irritation de la peau (39 %) et une douleur derrière l'oreille (45,2 %). Une deuxième étude portait sur les changements hémodynamiques cérébraux associés au port d'un masque N95 chez les travailleurs de la santé qui ont signalé des maux de tête associés à l'utilisation d'un masque. On a remarqué une augmentation importante du débit moyen et du CO_2 en fin d'expiration cinq minutes après que les travailleurs aient mis leur masque N95. L'ajout d'un appareil de protection respiratoire à épuration d'air motorisé a cependant permis de ramener ces mesures à des niveaux normaux.

Des femmes enceintes, saines, entre 13 et 35 semaines de gestation ont également été évaluées afin de connaître l'incidence du port du masque N95. Les deux études qui ont porté sur cet échantillon ont évalué les répercussions du port du masque N95 lorsque ces femmes effectuaient un travail physique de routine (équivalent à un METS de 3). Les résultats obtenus ont indiqué une diminution importante de l'air courant, du débit ventilatoire et de la consommation d'oxygène, une augmentation de la pression partielle transcutanée en raison du CO2, ainsi que des résultats contradictoires pour la fréquence respiratoire. Aucune des études n'a cependant indiqué de changement dans la fréquence cardiaque maternelle, la fréquence cardiaque fœtale ou la saturation en oxygène. Une des études qui comparait les résultats des femmes enceintes à ceux des femmes non enceintes n'a pas trouvé de différences dans les répercussions physiologiques associées du port d'un masque N95 (4).

Trois études ont évalué certains problèmes médicaux, y compris la maladie pulmonaire obstructive chronique (MPOC) ($n = 2$), l'asthme ($n = 2$) et la rhinite chronique ($n = 1$). Les informations portant sur d'autres conditions médicales n'ont pas été mentionnées. Une étude a également évalué le port du masque N95 par 97 patients atteints de MPOC. Parmi les personnes évaluées, 7 % ont été incapables de le garder en raison de dyspnée, de maux de tête et d'étourdissements. Il s'agissait en général de personnes atteintes d'un MPOC plus grave. Les patients qui ont pu terminer l'étude ont, quant à eux, vu une augmentation de la fréquence respiratoire, du rythme cardiaque, de la pCO_2 en fin d'expiration et une diminution de la saturation en

oxygène. L'exercice léger (la marche) a également eu des répercussions sur ces différents paramètres. Une deuxième étude portant sur des patients atteints d'une MPOC légère a fait état d'une diminution du volume ventilatoire et d'un pourcentage de VEMS inférieur à celui obtenu sans masque et avec un masque N95 ou un demi-masque. Les personnes atteintes d'asthme ont, quant à elles, vu une diminution du volume respiratoire et un pourcentage de VEMS inférieur à celui qui avait été prédit avec un masque N95 ou un demi-masque, le demi-masque ayant eu des répercussions légèrement moins importantes. De même, la capacité respiratoire maximale a été considérablement réduite chez les asthmatiques qui portaient un masque chirurgical. Le port du masque N95 ou du demi-masque n'a eu, quant à lui, aucun effet significatif pour les personnes atteintes de rhinite chronique.

Les faiblesses globales en ce qui concerne les preuves présentées incluent la petite taille des échantillons, la diversité limitée des échantillons et le fait que les évaluations physiologiques aient uniquement été effectuées après une courte période de temps avec le masque. Ces différents éléments limitent la généralisabilité des conclusions et empêchent de les extrapoler aux situations dans lesquelles le masque doit être porté pendant plus de quatre heures. Puisque les auteurs ont rarement discuté de l'importance clinique des résultats déclarés, même si ces résultats ont permis d'obtenir une certaine importance statistique, l'importance clinique qui en découle pourrait différer.

Tableau 1. Preuves des effets physiologiques associées au port de masques N95, de masques chirurgicaux ou de couvre-visage non médicaux (n = 15)

RÉFÉRENCE	DESCRIPTION DE L'ÉTUDE	RÉSULTATS PERTINENTS
Volontaires sains (n = 8)		
Liu 2020 (3) Étude quasi-expérimentale Chine Mai 2020	Douze étudiants sains ont reçu un masque chirurgical, un masque médical KN95, un masque avec éponge, un masque en gaze ou un masque civil jetable qu'ils devaient porter pendant une centaine de minutes alors qu'ils étaient assis et lisaient. Ils ont ensuite rempli un questionnaire et différentes mesures physiologiques ont été prises.	• Deux éléments ont ensuite été utilisés et ont permis d'obtenir différents résultats, y compris des votes de sensation thermique et des symptômes comme des étourdissements, de la difficulté à se concentrer ou à réfléchir, l'évanouissement et la difficulté à respirer, ainsi que la peau et la bouche sèches. Les effets ressentis qu'ont ressentis les étudiants qui portaient un masque N95 étaient plus prononcés que chez ceux qui avaient un masque chirurgical ou non chirurgical, mais tous ont obtenu des résultats plus élevés ($p < 0,05$) que s'ils n'avaient pas porté de masque. • Le port du masque a également eu différentes répercussions, y compris une augmentation de la fréquence cardiaque

		(p = 0,04), une diminution de la saturation en oxygène du sang (p = 0,048) et une augmentation de la température cutanée moyenne (p < 0,01). • Comparativement aux résultats obtenus sans masque, les masques KN95 sont ceux qui ont provoqué les changements les plus importants dans ces paramètres, suivi des masques chirurgicaux, des masques médicaux, des masques avec éponge et des masques civils jetables et de la gaze. Les résultats de ces analyses sont présentés dans des graphiques. • Il n'y a pas eu de changement significatif de la tension artérielle (changement systolique < 4 %, p = 0,915, changement diastolique < 3 %, p = 0,529). • Cette étude ne peut donc pas être généralisée en raison de la petite taille et de l'homogénéité de l'échantillon.
Epstein 2020 (6) Étude quasi-expérimentale Israël Septembre 2020	Dans cette étude, 16 volontaires sains de sexe masculin ont effectué de multiples essais autocontrôlés en chassé-croisé sur des bicyclettes ergométriques dans le cadre d'un protocole d'épreuve d'effort. Ces essais d'effort maximal ont été effectués sans masque, avec un masque chirurgical et avec un masque N95. Les paramètres physiologiques et le temps de performance jusqu'à l'épuisement ont ensuite été comparés. Les éléments mesurés incluaient la fréquence cardiaque (FC), la saturation en oxygène (SO_2), la fréquence respiratoire (FR), le dioxyde de carbone en fin	• La fréquence cardiaque, la fréquence respiratoire, la tension artérielle, la saturation en oxygène et le temps de performance jusqu'à l'épuisement ne différaient pas de façon significative entre les différents types de masques. Cependant, lorsqu'on compare les données obtenues sans masque au repos, les résultats de chacune des étapes de l'essai d'effort, on peut voir que le masque N95 a chaque fois été associé à une augmentation importante du CO_2 en fin d'expiration. La différence était plus prononcée lorsque la charge augmentait (intensité de l'exercice). En ce qui concerne les masques chirurgicaux, les résultats n'ont indiqué de différence significative dans le

	d'expiration ($EtCO_2$) et la pression artérielle.	CO_2 de fin d'expiration calculé que dans la dernière phase de l'entraînement. • Cette étude ne peut donc pas être généralisée en raison de la petite taille et de l'homogénéité de l'échantillon.
Fikenzer 2020 (7) Étude quasi-expérimentale Allemagne Juillet 2020	Cette étude en chassé-croisé qui a porté sur 12 hommes sains visait à mesurer les résultats de trois tests d'effort incrémentiels effectués sans masque, avec un masque chirurgical ou avec un masque N95 (FFP2). Les essais d'effort ont été effectués sur un ergomètre semi-couché à une vitesse constante de 60 à 70 tours par minute. La charge de travail a augmenté jusqu'à l'épuisement volontaire, puis a été suivie d'une période de récupération de 10 minutes. Le débit cardiaque (DC), le volume d'éjection systolique (ES), la fréquence cardiaque (FC), la consommation maximale d'oxygène (VO_{2max}) et le débit ventilatoire (DV) ont été surveillés en continu lorsque les participants étaient au repos, pendant le test d'effort et pendant la récupération.	• Le volume d'éjection systolique, le débit cardiaque et le bilan cardiaque ne différaient pas de manière significative, que les participants portent ou non un masque ou qu'ils aient porté un masque chirurgical ou un masque N95 ($p > 0,05$). • On a cependant pu observer un effet marqué sur les paramètres pulmonaires puisque, comparativement aux mesures obtenues sans masque, le débit ventilatoire a été réduit de -12,0 ± 12,6 % avec un masque chirurgical et de -23,1 ± 13,6 % avec un masque N95. • Le VO_{2max} était considérablement plus bas avec le masque N95 comparativement aux données obtenues avec un masque chirurgical ou sans masque. La différence entre les données obtenues avec le masque chirurgical et l'absence de masque était cependant limite. • Cette étude ne peut donc pas être généralisée en raison de la petite taille et de l'homogénéité de l'échantillon.
Li 2005 (8) Étude quasi-expérimentale Hong Kong Mai 2005	Cet essai en chassé-croisé comprenait 10 participants sains qui ont fait des exercices intermittents (à trois niveaux, de faible à modéré) sur un tapis roulant dans une chambre climatique avec un masque N95 ou un masque chirurgical avec et sans traitement nanofonctionnel	• Les différences entre les masques N95 avec ou sans nanotraitement et les masques chirurgicaux n'étaient pas significatives. • La fréquence cardiaque moyenne était beaucoup plus élevée chez ceux qui portaient un masque N95 que chez ceux qui portaient un masque chirurgical.

	(traitement utilisé pour repousser l'eau et inactiver les bactéries). La température, la fréquence cardiaque et la tension artérielle ont été mesurées.	• Plus les exercices étaient intenses, plus on voyait de différence dans la fréquence cardiaque avec les différents types de masques. • L'humidité et la température à l'intérieur des masques chirurgicaux avec ou sans nanotraitement étaient inférieures à celles observées dans les masques N95 (P = 0,000). • Les symptômes de fatigue, de dyspnée et d'inconfort général étaient beaucoup plus importants avec les masques N95. • Cette étude ne peut donc pas être généralisée en raison de la petite taille et de l'homogénéité de l'échantillon.
Wong 2020 (9) Étude quasi-expérimentale Hong Kong Octobre 2020	Vingt-trois bénévoles sains provenant de différents milieux sportifs ont participé à un essai en chassé-croisé dans lequel ils ont marché à une vitesse de 4 km/h pendant six minutes avec et sans masque chirurgical sur un tapis roulant dont l'inclinaison augmentait graduellement pour étudier l'effet physiologique (fréquence cardiaque et effort perçu mesurés sur une échelle de 6 à 20) du port du masque pendant un exercice modéré.	• Par rapport aux résultats obtenus sans masque, les masques chirurgicaux ont entraîné une accélération de la fréquence cardiaque (128,4 ± 13,2 contre 124,4 ± 12,8 battements par minute) et les participants ont déclaré un niveau d'effort perçu plus élevé après 3 minutes d'exercice (12,7 ± 2,1 contre 10,8 ± 2,2). Les résultats présentés ont été établis après six minutes d'exercice. • L'auteur laisse entendre que faire de l'exercice avec un masque à un niveau sous-maximal induirait des réponses physiologiques plus fortes. Cette différence peut cependant être due à une ventilation limitée, à une respiration plus lourde et à différentes réactions sympathiques. • Puisque l'augmentation de la charge cardio-respiratoire est directement liée au fait d'avoir effectué un exercice avec un masque, les auteurs suggèrent que les personnes qui portent des masques

		doivent être conscientes des efforts qu'elles font et de leur fréquence cardiaque pour s'assurer de ne pas dépasser les 150 battements/minute ou 70 % de leur fréquence cardiaque maximale prévue selon leur âge. • Cette étude ne peut donc pas être généralisée en raison de la petite taille de l'échantillon.
Morris (2020) (10) Étude quasi-expérimentale Danemark* 2020*	Un essai en chassé-croisé comprenant 8 participants masculins a été effectué pour évaluer les répercussions du fait d'effectuer un exercice léger (5 METS) pendant 45 minutes avec un masque KN95 à une température de 40 °C avec 20 % d'humidité. Les performances cognitives et motrices fines ont été évaluées à l'aide de tests qui ont déjà démontré leur fiabilité et leur grande sensibilité pour détecter les diminutions dans la performance cognitive associée à la chaleur, y compris la déshydratation et le rayonnement. La dyspnée a, quant à elle, été mesurée à l'aide de l'échelle de dyspnée de Borg.	• Il n'y avait pas de différence significative au repos en ce qui concerne la dyspnée, mais pendant l'exercice, on a pu observer beaucoup plus de dyspnée dans le groupe dont les membres portaient un KN95 (51,3 % [27,6]) que dans le groupe sans masque (21,4 % [14,5], < 0,001). • Les résultats en ce qui concerne la mesure de la température corporelle n'étaient pas significativement différents, que le participant ait ou non porté un masque KN95. • Les autres résultats cognitifs et moteurs fins n'étaient pas non plus significativement différents, que le participant ait ou non porté un masque KN95. • Cette étude ne peut donc pas être généralisée en raison de la petite taille et de l'homogénéité de l'échantillon.
Dattel 2020 (2) Étude quasi-expérimentale États-Unis Juillet 2020	Cette étude a exploré les effets des masques en tissu (sans détails sur la composition) ou des masques chirurgicaux. On a étudié les répercussions des masques en tissu ou des masques chirurgicaux sur 32 pilotes	• Les pilotes instructeurs ont signalé des problèmes de confort et de fatigue, ainsi qu'en raison des restrictions de mouvement associées au port du masque. • Aucune différence dans le CO_2, la fréquence cardiaque, la fréquence respiratoire ou le niveau d'oxygène n'a été

	instructeurs qui se trouvaient dans une chambre de pilotage à pression normale. Des mesures du CO_2, de la fréquence cardiaque, de la fréquence respiratoire et de la saturation en oxygène ont été prises pendant 90 minutes.	constatée entre les pilotes qui portaient un masque en tissu et ceux qui portaient un masque chirurgical après un vol simulé de 90 minutes à une altitude de 1 524 m (5 000 pi). • Cette étude ne peut donc pas être généralisée en raison de la petite taille de l'échantillon.
Lee 2011 (11) Étude quasi-expérimentale Singapour 2010*	Cette étude portait sur la résistance respiratoire causée par les masques N95 (3M 8210) portés par 14 adultes sains. La résistance respiratoire a été mesurée pour l'inspiration et l'expiration, et le volume total (l en 30 s) a été mesuré avec et sans masque N95.	• Avec un masque N95, la résistance respiratoire atteignait en moyenne 126 % du débit inspiratoire et 122 % du débit expiratoire. • Il y a donc eu une réduction moyenne de 37 % du volume d'échanges gazeux lorsque les participants portaient un masque N95. • Cette étude ne peut donc pas être généralisée en raison de la petite taille de l'échantillon.
Travailleurs de la santé (n = 2)		
Purushothaman 2020 (12) Étude transversale Inde Juillet 2020	Un sondage a été effectué auprès de 250 travailleurs de la santé sans comorbidité dans un hôpital tertiaire. Ces travailleurs portaient chaque jour des masques chirurgicaux ou des masques N95 pendant au moins quatre heures. Les données ont été recueillies dans un questionnaire d'auto-évaluation élaboré à l'aide de recherches formatives, mais n'ayant pas été prétesté.	Cette étude ne fait pas de distinction entre les résultats associés aux masques chirurgicaux ou aux masques N95. • 58,2 % des travailleurs de la santé ont indiqué avoir de la difficulté à respirer à l'effort ($p < 0,001$). Aucun renseignement supplémentaire sur ce qu'on entend par « effort » n'a été fourni. • Les participants ont indiqué un vaste éventail d'éléments d'inconfort, dont les plus fréquents incluaient une sudation excessive autour de la bouche (67,6 %), de l'acné (56,0 %), une irritation de la peau (39 %) et une douleur derrière l'oreille (45,2 %).

Bharatendu 2020 (13) Étude quasi-expérimentale Singapour Février à avril 2020	Cette étude a porté sur 154 travailleurs de la santé qui ont demandé des soins médicaux en raison de maux de tête liés à l'utilisation d'ÉPI. De ce nombre, 25 % avaient des migraines et 80 % ont dit avoir eu de nouveaux maux de tête après avoir porté un masque N95. La surveillance par Doppler transcrânien de l'artère cérébrale moyenne a été effectuée à l'aide de deux mesures validées de la vitesse moyenne d'écoulement, de l'index de pulsatilité et de la pression associée au dioxyde de carbone ($ETCO_2$) en fin d'expiration, qui ont été enregistrées avant le port du masque N95 et cinq minutes après l'avoir enlevé. L'évaluation a été effectuée pour un masque N95 (masque 3M® N95) avec et sans appareil de protection respiratoire à épuration d'air motorisé (APR, 3M® Versaflo® série TR-300).	• Comparativement aux mesures obtenues sans masque, le fait de porter un masque N95 a entraîné une augmentation importante du volume de débit moyen, une variation relative de 12,3 % (ET 29,8, $p < 0,001$), une diminution de la variation relative de l'index de pulsatilité de 13,3 % (ET 11,3, $p < 0,001$) et des niveaux très élevés de dioxyde de carbone en fin d'expiration soit une augmentation de 3,1 mmHg (ET 1,2). • Quant aux vingt-quatre participants qui ont utilisé un APR, les résultats n'ont montré aucune différence dans le volume de débit moyen, l'index de pulsatilité ou les niveaux de dioxyde de carbone en fin d'expiration dans les cinq minutes qui ont suivi l'utilisation du masque avec les mesures obtenues sans masque. Le respirateur à adduction d'air rétablit donc les changements hémodynamiques cérébraux causés par le masque N95. • Étant donné que les mesures ont été prises après cinq minutes, il est impossible de savoir si ces changements se sont maintenus ou ont été corrigés par autorégulation.
Femmes enceintes (n = 2)		
Tong 2015 (14) Étude quasi-expérimentale Singapour Septembre 2011	La phase I a permis d'évaluer le volume d'absorption d'O_2 (VO_2) de huit travailleuses enceintes qui exécutaient des tâches d'infirmières lors d'une simulation. La phase 2 a comparé les données associées à l'utilisation ou non d'un masque N95 chez 20 femmes enceintes (27 à 32 semaines de	Le fait de respirer à travers un masque N95 comparativement à l'absence de masque a entraîné ce qui suit : • Un volume d'air courant significativement plus bas de -0,15 L (IC à 95 %, -0,23 à -0,08 L) au repos et de -0,21 L (-0,32 à -0,10 L) pendant l'exercice, soit une diminution globale d'environ 23 %.

	gestation) pendant deux cycles d'exercices d'une durée de 15 minutes sur un tapis roulant à 3 METS (ce qui équivaut au travail modéré normal qu'effectue un travailleur de la santé [données provenant de la phase 1]). Dans ces deux phases, les femmes portaient un masque respiratoire Hans Rudolph bien ajusté avec valve anti-asphyxie ouverte ou recouverte par le matériel utilisé pour fabriquer les masques N95. Les mesures effectuées incluaient notamment le volume d'oxygène (VO_2) et de dioxyde de carbone (VCO_2), le débit ventilatoire (DV), l'expiration forcée d'O_2 (FeO_2) et les concentrations de CO_2.	• Un débit ventilatoire (DV) fortement réduit (5,55 L [IC à 95 %, 7,58 % à 3,51 %], soit environ 25,8 %. • Aucun changement significatif dans la fréquence respiratoire avec le masque N95. • Une réduction importante de la concentration d'O_2 à l'expiration forcée (FeO_2) pendant l'exercice (-0,54 % [-0,70 à -0,38]). • Des augmentations importantes de la concentration de CO_2 expirée ($FeCO_2$) tant pendant l'exercice que dans les périodes qui ont précédé et suivi l'exercice (0,30 % [0,18 à 0,42]). • Une baisse significative de VO_2 de 13,8 % et de VCO_2 de 17,7 % a été déclarée en ce qui concerne les échanges gazeux pulmonaires. • Aucune différence n'a été observée pour le rythme cardiaque, la saturation en oxygène ou le taux d'effort perçu pour la mère ou le fœtus avec le masque N95. • Cette étude ne peut donc pas être généralisée en raison de la petite taille et de la courte durée de l'exercice.
Roberge 2014 (4) Essai contrôlé États-Unis Octobre 2014	Étude contrôlée réalisée avec 22 femmes saines enceintes (de 13 à 35 semaines de gestation) et 22 femmes saines non enceintes afin de déterminer s'il y a une différence entre les effets physiologiques et subjectifs du port d'un masque N95 (appareil respiratoire filtrant pour le visage, APR). Les éléments qui ont été évalués incluaient la fréquence respiratoire,	• Dans l'ensemble, l'utilisation du masque N95 a réduit considérablement la fréquence respiratoire, a entraîné une différence mineure comparativement à la moyenne de 0,94 (IC à 95 %, de 0,1 à 2,2) de respirations par minute, alors que la pression partielle transcutanée du dioxyde de carbone ($PtcCO_2$) a augmenté pendant l'exercice pour toutes les femmes en raison de la réinspiration des niveaux de CO_2 plus élevés générés pendant l'exercice.

	la température cutanée sur la paroi de la cage thoracique, la fréquence cardiaque maternelle et fœtale, ainsi que la saturation en oxygène déduite du pouls (SpO_2). L'échelle Borg de perception de l'effort 6 à 20 a aussi été utilisée. Des mesures ont été prises avec et sans masque N95 pendant des exercices et des activités sédentaires posturales sur une période d'une heure.	• Il n'y a cependant pas eu de différences significatives dans les réponses physiologiques et subjectives mesurées chez les femmes enceintes comparativement aux femmes non enceintes lorsque celles-ci ont porté un masque N95 pendant une heure, tant pendant les exercices que lorsqu'elles étaient sédentaires. • Il n'y a pas eu d'effet significatif sur la fréquence cardiaque fœtale. • Cette étude ne peut donc pas être généralisée en raison de la petite taille de l'échantillon.
Personnes atteintes de maladies chroniques (n = 3)		
Kyung 2020 (15) Étude quasi-expérimentale Corée du Sud Mars à mai 2015	Dans cette étude, 97 patients atteints de MPOC de gravité variable ont fait l'objet d'un suivi afin d'évaluer leurs symptômes et différentes variables physiologiques lorsqu'ils portaient un masque N95. Ces mesures ont été prises pendant une période de repos de 10 minutes et pendant un test de marche de 6 minutes. Les patients étaient âgés entre 19 à 80 ans, pouvaient marcher sans aide, n'étaient pas sous oxygénothérapie à long terme et n'avaient pas d'antécédents d'hospitalisation récente. Les mesures utilisées incluaient la fréquence respiratoire, la dyspnée, la fréquence cardiaque, la SpO_2, la tension artérielle et un questionnaire sur les symptômes avec une échelle modifiée sur la	• 7 sujets sur 97 n'ont pas pu porter le masque N95 pendant tout le test. Un score de ≥ 3 sur l'échelle de dyspnée modifié par le Conseil de recherches médicales (RC 167, IC à 95 %, de 8,4 à > 999,9; $P = 0,008$) ou un VEMS < 30 % (RC 163, IC à 95 %, de 7,4 à > 999,9; $P = 0,001$) était associé à une incapacité de continuer à porter le masque N95. Les symptômes dans ce groupe étaient plus prononcés et incluaient la dyspnée, des étourdissements et des maux de tête. Chez les membres du groupe qui ont terminé le test : • Même lorsqu'ils étaient au repos, leur fréquence respiratoire a augmenté avec un masque N95 (20,7 respirations/min) alors qu'elle était de 19,7 lorsqu'ils ne portaient pas de masque. • Le PCO_2 en fin d'expiration a atteint 25,7 mm Hg lorsqu'ils portaient un

	dyspnée établie par le Conseil de recherches médicales. La gravité de l'obstruction du débit d'air associé à la MPOC a été mesurée en utilisant le VEMS post-bronchodilatateur. Parmi tous les sujets, 31 avaient un VEMS supérieur à 50 % comme niveau de référence.	masque N95 alors qu'il était de 24,8 lorsqu'ils ne portaient pas de masque. • Les niveaux de SpO_2 étaient plus faibles avec un masque N95 (96,0 %) que lorsqu'ils ne portaient pas de masque (96,4 %). • Après 6 minutes de marche, on a constaté des différences significatives dans la fréquence cardiaque (92,4 comparativement à 87,7), la fréquence respiratoire (25,7 comparativement à 23,3 respirations/min), le PCO_2 de fin d'expiration était plus élevé (35,5 au lieu de 34,0 mm Hg) alors que les niveaux de SpO_2 (93,0 comparativement à 93,8 %) étaient plus bas chez les personnes qui portaient un masque N95 que chez celles qui n'en avaient pas. • Les auteurs ont déclaré qu'il faut avertir les patients atteints de MPOC de retirer immédiatement le masque N95 en cas de dyspnée, de maux de tête ou d'étourdissements.
Harber 2010 (16) Essai contrôlé États-Unis 2010	Cet essai visait à évaluer les effets respiratoires des demi-masques à double cartouche ou des masques N95 lorsque 97 personnes, 42 asthmatiques, 14 personnes atteintes de MPOC légère, 17 personnes atteintes de rhinite chronique et 24 personnes saines effectuaient certaines tâches. Les résultats respiratoires comprenaient le volume courant, le débit ventilatoire, le temps d'inspiration/expiration, le cycle inspiratoire et expiratoire et le débit d'écoulement de l'air.	• Comparativement aux données obtenues en portant un masque N95, le volume courant, le débit ventilatoire et la fréquence respiratoire étaient légèrement inférieurs avec un demi-masque, mais l'on ne sait pas quelle importance ces données pourraient avoir au niveau clinique. Aucun effet cohérent n'a été observé pour les volumes dans les cas de MPOC ou d'asthme. • Les personnes atteintes de MPOC ont mis plus de temps pour atteindre leur débit expiratoire maximal.

		• Les personnes atteintes de rhinite ont obtenu un meilleur rendement que celles qui étaient atteintes de MPOC et d'asthme. • L'âge n'était pas un facteur. • Les personnes atteintes d'asthme ou d'une MPOC légère présentaient un pourcentage de VEMS inférieur aux prévisions, associé au volume du masque. • Cette étude ne peut donc pas être généralisée en raison de la petite taille de l'échantillon.
Ciocan 2020 (17) Étude quasi-expérimentale Italie Octobre 2020	Dix travailleurs de la santé, dont trois souffrant d'asthme et trois fumeurs, ont été inclus dans cet essai croisé. Ils ont porté un masque chirurgical à quatre couches (AFLUID) pendant quatre heures lorsqu'ils effectuaient des activités normales, de niveau calme à modéré, dans le cadre de leur travail. Leur fonction respiratoire a été surveillée pendant ce temps. Un test de fonction respiratoire a été effectué à trois moments distincts et des échantillons de sanguin artériel ont été prélevés pour effectuer une gazométrie avant les premiers et troisièmes tests de fonction respiratoire.	• Comparativement à ceux qui ne portaient pas de masque, la ventilation volontaire maximale (VVM) était réduite avec un masque chirurgical à quatre couches ($p = 0,002$) et est demeurée basse même pendant l'activité ($p = 0,041$). • Aucune variation significative des paramètres RFT et ABG observés n'a été signalée, bien que l'étude n'ait pas permis de détecter les différences. • Cette étude ne peut donc pas être généralisée en raison de la petite taille de l'échantillon.

* L'emplacement ou la date de l'étude a été estimé en fonction des affiliations des auteurs ou de la date de publication.

CONSEILS SUR L'UTILISATION DES COUVRE-VISAGES DANS LA POPULATION EN GÉNÉRAL

Des directives clés émises par le Canada, les États-Unis et l'OMS ont été déterminées et examinées afin de formuler des recommandations sur le port du couvre-visage pour les personnes qui ont des problèmes médicaux chroniques, ainsi que sur le port générique du couvre-visage dans la collectivité (tableau 2).

- La Société canadienne de thoracologie et Asthme Canada indiquent que les personnes atteintes d'un problème pulmonaire sous-jacent devraient être capables de porter un couvre-visage non médical. Cependant, pour celles qui ont de la difficulté à porter un couvre-visage, il est suggéré de travailler en collaboration avec un prestataire de soins de santé pour trouver une solution ou éviter, dans la mesure du possible, les situations dans lesquelles elles doivent porter un couvre-visage pour minimiser le risque (18).
- Les plus récentes lignes directrices de l'OMS précisent que les masques ne doivent pas être portés à des fins de contrôle à la source pour empêcher la transmission des virus provenant d'un enfant de moins de 5 ans atteint de la COVID-19 (19). Elles ne précisent pas si les enfants de 2 à 5 ans doivent porter un masque pour se protéger, mais indiquent cependant toutes que les enfants de moins de 2 ans ne doivent pas porter de couvre-visage.

Les lignes directrices diffusées par le Canada (20), les États-Unis (21) et l'OMS (19) mentionnent que les couvre-visages ne devraient pas être requis pour toute personne incapable d'enlever son couvre-visage sans aide, ce qui inclut les enfants de moins de deux ans, et pour toute personne qui a de la difficulté à respirer, est inconsciente ou est frappée d'incapacité en raison du risque de suffocation.

- Il est également suggéré que les personnes ayant certains handicaps ou de jeunes enfants pourraient être incapables de porter leur couvre-visage correctement et ne devraient donc pas en avoir (20, 21).

Tableau 2. Conseils sur le port du couvre-visage pour les personnes atteintes de maladies et pour le grand public (n = 5)

RÉFÉRENCE	DESCRIPTION DE L'ÉTUDE	RÉSULTATS PERTINENTS
Organisation mondiale de la Santé (19) Document d'orientation Suisse Décembre 2020	Il s'agit d'une mise à jour du guide de l'OMS en date du 5 juin axé sur le port des masques et des couvre-visages : • gestion des masques; • transmission du SRAS-CoV-2; • port du couvre-visage dans les zones des établissements de santé où l'on retrouve des	• Le port du couvre-visage devrait s'inscrire dans le cadre d'une approche à plusieurs niveaux faisant partie des interventions de santé publique. • Les couvre-visages peuvent être destinés à la protection ou au contrôle des sources. (Portez un masque médical si vous pensez avoir la COVID-19).

	grappes de personnes et une transmission sporadique; • port de couvre-visage par le public dans les zones de transmission communautaire et les grappes; • solutions de rechange aux couvre-visages non médicaux pour le public; • soupape d'expiration sur les masques médicaux et couvre-visages non médicaux; • port d'un couvre-visage pendant une activité physique dont l'intensité est élevée; • paramètres essentiels dont il faut tenir compte lors de la fabrication de couvre-visages non médicaux (Annexe).	• Des lignes directrices sur l'utilisation, le rangement et le nettoyage appropriés sont présentées. • Les enfants de moins de 5 ans ne doivent pas porter de couvre-visage à des fins de contrôle à la source. L'utilisation de couvre-visage chez les enfants plus âgés varie selon des facteurs locaux et les enfants de plus de 12 ans doivent suivre les directives pour les adultes. • La fabrication de couvre-visages non médicaux doit respecter les principes suivants : trois couches avec une couche interne hydrophile, une couche externe hydrophobe et une couche intermédiaire hydrophobe qui améliore la filtration. • Les soupapes d'expiration sont déconseillées.
Canada.ca (20) Document d'orientation Canada Novembre 2020	Conseils sur l'utilisation des masques non médicaux pour prévenir la propagation de COVID-19 dans la communauté. • Ordonnances en ce qui concerne le port des masques et des couvre-visages. • Composition des masques non médicaux. • Utilisation des filtres dans les couvre-visage. • Mise en place, nettoyage et rangement. • Enfants. • Sécurité.	• Les couvre-visages non médicaux protègent la personne qui les porte et les autres contre la propagation de la COVID-19. • Des politiques sur le port obligatoire des masques et des couvre-visage sont mises en place en fonction de la transmission locale de la COVID-19. • Les masques non médicaux doivent être faits d'au moins trois couches, soit deux couches de tissu serré et une troisième couche (centrale) en tissu filtrant, comme un tissu de polypropylène non tissé. Ils doivent être bien ajustés au visage et recouvrir le nez et la bouche, mais être encore perméables à l'air.

	• Personnes malentendantes. • Écrans faciaux, cache-cou (réchauffeurs du cou), soupapes d'expiration.	• Du tissu en polypropylène non tissé (p. ex., tissu utilisé pour l'artisanat, pour les sacs à provisions réutilisables) peut être utilisé comme filtre, tout comme des filtres jetables. • Les enfants de moins de deux ans ne doivent pas porter de couvre-visage et il faut s'assurer de bien surveiller tout enfant de 2 à 5 ans qui porte un masque ou un couvre-visage. • Il faut éviter la stigmatisation des personnes qui ne peuvent porter de couvre-visage en raison d'une maladie ou d'un handicap.
Centers for Disease Control and Prevention 2020 (21) Document d'orientation États-Unis Novembre 2020	Des considérations relatives au port du masque, sans préciser de type, sont fournies pour aider à ralentir la propagation de la COVID-19. Sujets abordés : 1) Preuves de l'efficacité des masques 2) Qui doit et ne doit pas porter de masque ou de couvre-visage 3) Différence entre les types de masques ou de couvre-visages 4) Autres types de protection faciale	• Les masques ou couvre-visages ne doivent pas être portés par des enfants de moins de deux ans, par des personnes qui ont de la difficulté à respirer et par des personnes inconscientes, frappées d'incapacité ou incapables de retirer leur masque sans aide. • Les personnes ayant certains handicaps ou les enfants qui ne peuvent pas porter de masque ou de couvre-visage correctement ne devraient pas en porter. • La plupart des personnes atteintes de troubles médicaux sous-jacents peuvent et doivent porter un masque ou un couvre-visage. Si elles ont des préoccupations à cet égard, elles doivent en discuter avec leur fournisseur de soins de santé. • Le port d'un masque en tissu n'augmente pas le niveau de dioxyde de carbone (CO_2) dans l'air respiré.

		• Les masques médicaux et les masques N-95 ne doivent pas être utilisés, car ils doivent être réservés aux travailleurs de la santé. • Les écrans faciaux ou les lunettes de protection ne remplacent pas les masque ou couvre-visage. • Les masques ou les couvre-visages en tissu les plus efficaces sont perméables à l'air, comportent deux ou trois couches et sont faits de tissus serrés comme du coton et des mélanges de coton. • Les personnes qui se fient à la lecture des lèvres pour communiquer (personnes sourdes, malentendantes ou qui prennent soin de personnes ayant une déficience auditive) pourraient être incapables de porter des masques ou de couvre-visages en tissu. Le CDC recommande un masque ou couvre-visage transparent, une communication écrite ou une réduction du bruit de fond pendant la communication.
Bhoutani (2020) (18) Document d'orientation Canada Juillet 2020	Il s'agit d'une directive et d'un énoncé de position de la Société canadienne de thoracologie sur l'utilisation des masques par le public pendant la pandémie de SRAS-CoV-2.	• La Société canadienne de thoracologie appuie la recommandation de l'Agence de la santé publique du Canada de porter un masque ou couvre-visage non médical dans la collectivité lorsqu'il n'est pas possible de maintenir la distanciation physique de deux mètres. • Rien n'indique que le port d'un masque ou d'un couvre-visage non médical aggravera un problème pulmonaire sous-jacent. • Le port d'un masque ou d'un couvre-visage ne préviendra pas la propagation

		de la COVID-19 et devrait s'ajouter à d'autres mesures de santé publique recommandées, comme l'amélioration de l'hygiène des mains et la distanciation physique. • L'on recommande aux personnes qui éprouvent de la difficulté à porter un masque ou couvre-visage à parler à leur prestataire de soins de santé afin d'élaborer des stratégies pour pouvoir en porter un. Si, malgré tous les efforts, le port d'un masque ou d'un couvre-visage n'est pas possible, les personnes doivent éviter ou minimiser les circonstances dans lesquelles le respect de la distanciation physique n'est pas possible.
Asthme Canada (22) Document d'orientation Canada 2020	Asthma Canada a publié ces conseils destinés aux personnes asthmatiques afin de répondre aux préoccupations liées au port de masque ou couvre-visage et à la COVID-19.	Recommandations pour les personnes atteintes d'asthme : • Les masques sont offerts en différents styles et matériaux; choisissez le masque ou couvre-visage qui vous convient le mieux. • Testez le masque à la maison pour vous habituer à la façon dont vous vous sentez quand vous le portez. • Si vous ne pouvez pas porter de masque ou de couvre-visage puisque cela entraîne des problèmes respiratoires, n'en portez pas. Respectez plutôt la distanciation de deux mètres et réduisez au minimum le temps passé autour des personnes à l'extérieur de votre ménage. • Consultez votre professionnel de la santé pour revoir votre plan d'action contre l'asthme et explorer d'autres options pour vous protéger.

Méthodologie

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et dans les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Les résultats cumulatifs de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Des détails sur cette stratégie de recherche sont disponibles sur demande. Une recherche ciblée par mot-clé dans les titres et les résumés des articles a été effectuée dans ces bases de données et dans la liste en Excel. Les termes de recherche utilisés comprenaient : mask* OU (face ET cover*). Une recherche supplémentaire de documents d'orientation et de preuves à l'appui sur les personnes qui ne devraient pas porter de masque ou couvre-visage a été effectuée en se concentrant sur le Canada et les principaux organismes de santé, en utilisant une technique de boule de neige et en ciblant les sites web des pays. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue. La présente revue contient des recherches publiées jusqu'au 2 décembre 2020.

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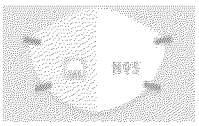
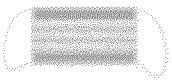
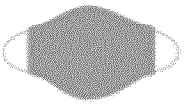
ANNEXE : TYPES DE COUVRE-VISAGE

Le blogue du NCCEH a publié un article sur le port du couvre-visage pendant la pandémie de COVID-19 (27 octobre 2020) qui décrit les différents types de couvre-visages et comprend le tableau suivant, sur les types de couvre-visages.

	Respirator	Surgical or procedure mask	Non-medical cloth mask
			
Types	N95, 99, 100 (US, Canada), FFP2 or FFP3 (EU). Various styles including cup, flat-fold and duckbill. May also include an exhalation valve.	Typically a 3-layer laminate structure that can include a combination of non-woven air-laid paper and polypropylene.[3]	Wide variability in fabric, number of layers and design with 2-layer cotton being a common design.
Use	For use in environments where exposure to aerosols is likely. Protect against most particles (e.g., N95 block 95% of particles and provide some splash and spray protection). Medical grade N95s are tested for resistance to fluids including blood, but commercial grade are not.	For use in routine care to reduce inward and outward transfer of respiratory droplets. Filter particles > 20 µm diameter and some finer droplet nuclei.[4] Block blood and infectious materials from contact with oral, nasal and skin area. Effective against splash and sprays.	For use by the public in non-healthcare settings as source control to reduce respiratory emissions from the wearer and to reduce exposure to respiratory emissions of others.[3,5]
Approval	U.S. National Institute for Occupational Safety and Health (NIOSH) for N95 or similar and EU standards for FFP equivalents.[6] The Government of Canada lists other approved alternatives to N95s.	FDA with grading based on the level of resistance to splashing (e.g., ASTM 1 – venous pressure; ASTM 2 – arterial pressure; ASTM 3 – high velocity splash).	Not approved for use in any healthcare setting; not tested to any standard of effectiveness. **Note:** Many procedure-type masks found in retail outlets may not be assessed to any approval standards, and would also be considered non-medical masks.
Advantages	Medical grade respirators can be effective against aerosol penetration. Can be reused and disinfected with precautions.	Some protection against contact transmission, are disposable and inexpensive. Fit testing is not required.	Inexpensive and can be made from household materials. Can act as a reminder to not touch face.[5] Can be reused and laundered.[7]
Disadvantages	Filtration efficiency for aerosols is only effective if properly fit tested. Some users may experience some reduction in comfort/breathability. Expensive and may be in short supply.	Less effective against smaller particles (e.g., 0.4-1.3 µm), looser fit than N95 respirators, and therefore more penetration via leaks.[8] Not recommended for reuse or disinfection for use in healthcare environments.	Variable performance for respiratory protection and breathability depending on the material and design.[9] They do not replace other protective measures (e.g., hand hygiene and distancing).[5,10]

Emerging Evidence on COVID-19

Rapid Review on the Physiological Effects of Wearing Face Masks

Introduction

What is the evidence on the physiological changes from mask use? Is there evidence that mask use may adversely affect those with medical conditions?

Many public health organizations globally such as the World Health Organization recommend the use of face masks in public spaces to protect against COVID-19. Concerns about wearing a face mask in some settings or among people with certain medical conditions have been raised. The review focuses on the physiological effects of wearing a mask on the respiratory and cardiovascular systems and highlights were statistically significant differences were reported. The dermatological and psychological reactions to mask use are not included in this review; they may be covered as a separate topic given these are also impacts of wearing a mask (1). This rapid review summarizes literature until December 2, 2020 on the physiological changes mainly related to respiratory and cardiovascular systems from mask use that may occur in healthy populations and those with medical conditions.

Key Points

- Twenty articles were identified, which included fifteen studies investigating physiological responses arising from wearing masks, one review and four guidance documents. The majority of the studies compared the physiological effects of an N95 respirator and/or a surgical mask; only two studies included non-medical masks, see appendix for information on mask types. These were studied in different populations: healthy volunteers (n=8), health care workers (HCW) (n=2), pregnant women (n=2) and people with medical conditions (n=3).
- Healthy volunteer face mask use was assessed in eight studies. Two studies included sedentary activities only, five had a range of activity from light exercise (e.g. walking at MET 3-5) to strenuous exercise and one study evaluated the impact of wearing masks among pilots flying at 5000ft.

  Limitations:

  - The eight studies on healthy volunteers were small, a median study size of 12 (83 total healthy volunteers and 32 pilots). Studies included homogeneous groups of participants e.g. college students and/or all male. The period of study was often short and as such would not reflect the potential impact of wearing a mask for prolonged periods of time. Most studies conducted analyses to establish statistical significance between two or more measurements, these are highlighted throughout the report as significant results. The clinical significance of the reported results were rarely discussed by

the authors. The findings of studies in this review are preliminary. More research is needed with larger and more representative samples to assess the generalizability of these findings.

N95 masks:

- Across six studies of healthy volunteers, N95 masks significantly increased breathing resistance and reduced air exchange volume, they caused increased heart rate and end tidal CO_2 and decreased oxygen saturation compared to no mask. Symptoms associated with these physiological changes included dyspnea (difficulty breathing), dizziness, and trouble concentrating.
- Five studies examined light to strenuous exercise in healthy volunteers. When wearing an N95 mask increased exercise intensity resulted in a more pronounced impact on some physiological parameters including increased end-tidal CO_2, and decreased minute ventilation and overall VO_{2max} compared to wearing no mask.
- One study looked at several different masks and indicated the overall physiological impact was highest for the KN95 > surgical masks > medical masks, sponge and civilian disposable masks> gauze and wearing no mask.
- In four studies, comparing the effects of N95 vs. surgical masks there was a greater physiological impact associated with N95 masks. These differences were not significant in one study, were significant for some parameters in two studies: heart rate (n=1/2 studies), minute ventilation and VO_{2max} (n=1/2) and were not reported although raw data and graphical summaries were available in the fourth study.

Surgical masks:

- Four studies (n= 63 observations) looked at surgical masks compared to no mask and they report elevated heart rate (n=3) and decreased blood oxygen saturation (n=1) compared to no mask when at rest or exercising. Surgical masks significantly reduced minute ventilation, but not VO_{2max}. At the end of the strenuous workout, end-tidal CO_2 was statistically increased with surgical mask use compared to no mask. Perceived level of exertion was higher in those who wore a surgical mask (n=2). Symptoms were not as frequently reported for surgical masks compared to N95 masks, but included dyspnea, dizziness and difficulty concentrating.
- Pilots, wearing either a surgical or non-medical cloth mask, who underwent a 90 minute 5000ft simulation exercise were found to have no difference in heart rate, end tidal CO_2, respiration rate or oxygen levels (2).

Non-medical face masks

- Two studies included non-medical face masks made of cloth, sponge, gauze or described as a civilian disposable masks. The physiological impact of different mask composition was not significantly different than surgical masks in these studies (2, 3).

- HCW studies (n=2) were conducted to understand the impact of wearing an N95 or surgical mask when executing duties related to their occupation.
    - A survey of 250 HCWs who wore surgical or N95 masks >4 hours/day reported 58.2% ($P<0.01$) had trouble breathing on exertion. Other symptoms included excessive sweating around the mouth (67.6%), skin irritation (39%) and pain behind the ear (45.2%).
    - The cerebral hemodynamic changes of donning an N95 mask were evaluated among 154 HCWs who reported headaches in association with N95 mask use. Five minutes after donning the N95 mask a significant increase in mean flow volume and end-tidal CO_2 were reported. Adding a powered air-purifying respirator (PAPR) restored these measures to normal levels.
- Pregnant women, healthy and between 13-35 weeks in gestation were studied (n=2) for the impact of N95 mask use.
    - N95 masks worn by 42 pregnant women during routine physical work (equivalent to 3 MET) showed significantly decreased tidal volume, minute ventilation and oxygen consumption, an increase in transcutaneous partial pressure CO_2, conflicting results for respiratory rate and no change in maternal heart rate, fetal heart rate or oxygen saturation compared to no mask in both studies.
    - Comparing pregnant and not pregnant women, there were no differences in the physiological impact of wearing an N95 mask (4).
- Medical conditions were assessed in three studies and included chronic obstructive pulmonary disease (COPD) (n=2), asthma (n=2) and chronic rhinitis (n=1). Information on other medical conditions was not identified.
    - In a study of 97 COPD patients using N95 masks, 7% were unable to wear the mask due to dyspnea, headache and dizziness; these tended to be individuals with more severe COPD. Those who completed the study were studied at rest and experienced increased respiratory rate, heart rate, end-tidal pCO_2 and decreased oxygen saturation compared to no mask. These differences between N95 and no mask became greater with light exercise (walking). A second study of 14 mild COPD patients reported decreased ventilatory volumes and lower FEV_1 percentage of predicted with N95 or half face mask use.
    - Among 42 people with asthma there was decreased ventilatory volumes and lower FEV_1 percentage of predicted with N95 or half face mask, the half face mask had a slightly lower impact. Similarly, the maximal voluntary ventilation was significantly reduced in three asthmatics when using a surgical mask.
    - Among 17 people with chronic rhinitis, the impact of N95 or half face mask was similar to healthy volunteers.
- Mask wearers should be cognisant of their exertion and heart rate given the studies show an increased cardio-respiratory burden of wearing any face mask and the impact increases with exercise. Heart rate should be maintained below 150 beats/min or 70% of their age max heart rate.

- Guidance Documents from Canada, United States (USA) and World Health Organization (WHO) on non-medical mask use in the community recommend that masks should not be worn by anyone who is unable to remove their mask without assistance due to risk of suffocation. This includes children under 2 years of age, and anyone who is unconscious, incapacitated, or who has trouble breathing. WHO guidelines also note masks should not be worn for source control to prevent transmission from a child under 5 with COVID-19.
- The Canadian Thoracic Society and Asthma Canada both indicate people with an underlying lung condition should be able to wear a non-medical face mask and to consult with a health care professional if this poses difficulties
- Current WHO guidelines for mask use in the community identify that masks should be removed by those who are having trouble breathing.

Overview of the Evidence

Fifteen articles pertaining to respiratory and cardiovascular physiological changes from mask use were identified and included in this review. Most were reports of quasi-experimental studies using a cross-over design where individuals acted as their own control. Most studies were in healthy populations, had small sample sizes and included homogenous populations (e.g. college students and/or male only); others included HCWs (n=1) and pregnant women (n=2). There were only three studies that specifically investigated face mask use among individuals with medical conditions: COPD (n=2), asthma (n=2). Although these studies were well-executed and had objective outcome measurements, they had low sample sizes and homogenous samples, selection bias is likely present, but could not be assessed in most studies and the findings should not be generalized without additional research. One study of HCWs was a cross-sectional survey of the self-reported impact of mask usage, the study represented HCW staff in a hospital, had a large sample size and used a questionnaire informed by formative research, however the self reported nature of results is at risk of many biases.

More research with larger sample sizes is needed for all mask types, research on the prolonged use of face masks is also needed. Thus, future research could change our understanding of the short and long term impact of wearing a face mask and who should not wear a face mask.

CONTENTS

EVIDENCE ON THE PHYSIOLOGICAL EFFECTS OF WEARING FACE MASKS

The physiological response to wearing face masks was assessed in fifteen studies on various populations: healthy volunteers, HCWs, pregnant women, instructor pilots, and persons with COPD, asthma or chronic rhinitis (Table 1). A single review, assessed to be of very low quality by AMSTAR, covers the physiological response to impeded airflow caused by face mask use and interprets this impact (5). Physiological outcomes assessed for each study were variable from study to study and are presented in the table if they were assessed. These include breathing parameters (e.g. total volume inhaled/ exhaled, breathing rate), respiratory function (e.g. oxygen and CO_2 levels), heart rate, blood pressure, and cerebral hemodynamic changes.

Eight studies using healthy volunteers included two studies on mask wearing when sedentary only, five on a range of activity from light exercise (e.g. walking at MET3-5) to strenuous exercise and included a total of 83 healthy volunteers (median study size was 12). A single study evaluated the impact of wearing masks among pilots (n=32) in a simulated flying exercise at 5000ft.

N95 masks were assessed in six studies on healthy volunteers, the masks significantly increased breathing resistance, reduced air exchange volume, heart rate and end tidal CO_2 and decreased oxygen saturation compared to no mask. Symptoms associated with the physiological changes included dyspnea (difficulty breathing), dizziness, and trouble concentrating. Five studies examined light to strenuous exercise and showed higher exercise intensity resulted in a more pronounced impact on some physiological parameters including increased end-tidal CO_2, and decreased minute ventilation and overall VO_{2max} compared to no mask.

Comparing the overall physiological impact of different masks in healthy volunteers, one study showed the impact was highest for the KN95 followed by surgical masks > medical masks, sponge and civilian disposable masks> gauze and wearing no mask. Four additional studies compared N95 to surgical masks and reported a smaller magnitude of impact where physiological outcomes were not significantly different in one study; were significant for some parameters in two studies: heart rate (1/2 studies), minute ventilation and VO_{2max} (1/2 studies) and were not reported although raw data and graphical summaries were available in the forth study.

Surgical mask use in healthy volunteers compared to no mask (n=4) report elevated heart rate (n=3) and decreased blood oxygen saturation (n=1) when at rest or exercising. Surgical masks significantly reduced minute ventilation, but not VO_{2max}. At the end of a strenuous workout end-tidal CO_2 was significantly increased with surgical masks compared to no mask. Perceived level of exertion was higher with a surgical mask (n=2) compared to no mask. Symptoms such as dyspnea, dizziness and difficulty concentrating were less frequently reported for surgical masks than N95 masks.

Non-medical face masks were only used in two studies on healthy volunteers. Pilots, wearing either a surgical or non-medical cloth mask, who underwent a 90 minute 5000ft simulation exercise were found to have no difference in heart rate, end tidal CO_2, respiration rate or oxygen levels (2). The second study compared non-

medical masks made of sponge, gauze or described as a civilian disposable masks, results are only in graphs and the impact of these masks are between surgical mask and wearing no mask (3).

Healthcare workers studies aimed to understand the impact of wearing an N95 or surgical mask when executing duties related to their occupation. A survey of 250 HCWs that wore surgical or N95 masks >4 hours/day reported 58.2% ($P<0.01$), had trouble breathing on exertion. Other symptoms included excessive sweating around the mouth (67.6%), skin irritation (39%) and pain behind the ear (45.2%). The second study examined cerebral hemodynamic changes of donning an N95 mask among HCWs who reported headaches in association with mask use. Five minutes after donning the N95 mask a significant increase in mean flow volume and end-tidal CO_2 was reported. Adding a powered air-purifying respirator (PAPR) restored normal levels.

Healthy pregnant women between 13-35 weeks in gestation were evaluated for the physiological impact of N95 mask use. Two studies assessed the N95 during routine physical work (equivalent to 3 MET) and showed significantly decreased tidal volume, minute ventilation and oxygen consumption, an increase in transcutaneous partial pressure CO2, conflicting results for respiratory rate and no change in maternal heart rate, fetal heart rate or oxygen saturation across two studies. One of the studies also compared pregnant and not pregnant women and found no differences in the physiological impact of wearing an N95 mask (4).

Medical conditions in three studies included COPD (n=2), asthma (n=2) and chronic rhinitis (n=1). Information on other medical conditions was not identified. A study of N95 mask use in 97 COPD patients 7% were unable to wear the mask due to dyspnea, headache and dizziness, these tended to be individuals with more severe COPD. Those that completed the study had an increased respiratory rate, heart rate, end-tidal pCO_2 and decreased oxygen saturation compared to no mask. These levels were further impacted by light exercise (walking). A second study of mild COPD reported decreased ventilatory volumes and lower FEV_1 percentage of predicted with N95 or half face mask use compared to no mask. People with asthma had decreased ventilatory volumes and lower FEV_1 percentage of predicted with N95 or half face mask, the half face mask had a slightly lower impact. Similarly, the maximal voluntary ventilation was significantly reduced when using a surgical mask. No impact of the N95 or half face mask was significant for people with chronic rhinitis.

Overall weaknesses of the current evidence include small sample sizes, limited sample diversity, and physiologic assessments after only a short duration of mask wearing. This limits the generalizability of the findings and prevents extrapolation to situations when masks are worn for more than 4 hours. The clinical significance of the reported results were rarely discussed by the authors, thus while the results reported reached statistical significance, the clinical significance may be different.

Table 1. Evidence on the physiological effects of wearing N95 respirators, surgical masks or non-medical face masks (n=15)

STUDY	METHODS	KEY OUTCOMES
Healthy volunteers (n=8)		

Liu 2020 (3) Quasi-Experimental study China May 2020	12 healthy college males were given either a surgical mask, KN95 medical mask, a sponge mask, a gauze mask, or a disposable civilian mask which they wore while seated and reading for about 100 minutes. A questionnaire was then filled out and physiological measurements were taken.	• Self-reported thermal sensation vote (TSV) and symptoms such as dizziness, difficulty concentrating or thinking, listlessness and difficulty breathing, as well as dry skin and dry mouth were more pronounced with a KN95 mask than with a surgical or non-medical mask and were elevated compared to wearing no mask $p<0.05$. • Heart rate increased with wearing a mask ($p=0.04$), blood oxygen saturation decreased with wearing a mask ($p=0.048$) and mean skin temperature increased with wearing a mask ($p<0.01$). • The KN95 caused the largest change in these parameters followed by surgical masks > medical masks, sponge and civilian disposable masks> gauze and wearing no mask. Results in graphs. • There was no significant change in blood pressure (systolic < 4% change, $p=0.915$, diastolic <3% change, $p=0.529$). • This study is not generalizable due to small sample size and homogenous sample population.
Epstein 2020 (6) Quasi-Experimental study Israel Sep 2020	16 healthy male volunteers, participated in this multiple cross-over, self-control trial, using a standard cycle ergometry ramp protocol. Maximal exercise tests without a mask, with a surgical mask, and with an N95 respirator were conducted. Physiological parameters and time to exhaustion were compared. Heart rate (HR), oxygen saturation (SO_2), respiratory rate (RR), and	• Heart rate, respiratory rate, blood pressure, oxygen saturation, and time to exhaustion did not differ significantly among the different types of masks Compared to no mask at rest and at all stages of exercising the N95 mask was associated with a significant increase in end-tidal CO_2. The difference was more pronounced with increased load (more intense exercise). For surgical masks there was only a significant difference in the end tidal CO_2 in the last phase of the workout.

	end-tidal carbon dioxide ($EtCO_2$) and blood pressure were measured.	• This study is not generalizable due to small sample size and homogenous sample population.
Fikenzer 2020 (7) Quasi-Experimental study Germany Jul 2020	12 healthy males enrolled in the cross-over study which measured three incremental exertion tests, with either no mask, a surgical mask or an N95 mask (FFP2). The exertion tests were conducted on a semi-recumbent ergometer at a constant speed of 60–70 revolutions per minute. Workload increased until voluntary exhaustion occurred followed by a 10-min recovery period. Cardiac output (CO), stroke volume (SV), heart rate (HR), maximum oxygen consumption (VO_{2max}) and minute ventilation (VE) were monitored continuously at rest, during the exertion test and during recovery.	• Stroke volume and cardiac output and cardiac work did not differ significantly when wearing no mask a surgical mask or an N95 mask ($p>0.05$). • There was a marked effect on pulmonary parameters: Compared to no mask, minute ventilation was reduced with a surgical mask by −12.0±12.6% and with an N95 mask by −23.1±13.6%. • The VO_{2max} was significantly decreased with the N95 mask compared to both the surgical mask and no mask. The difference between the surgical mask and no mask was borderline. • This study is not generalizable due to small sample size and homogenous sample population.
Li 2005 (8) Quasi-Experimental study Hong Kong May 2005	10 healthy participants were enrolled in this cross-over trial. They performed intermittent exercise (at three low to moderate workloads) on a treadmill in a climate chamber wearing an N95 or surgical mask with and without nano-functional treatments (a treatment that repels water and has been shown to inactivate bacteria). Temperature, heart rate and blood pressure were measured.	• Differences between nano-treated and untreated N95 and surgical masks were not significant. • Average heart rate was significantly higher for those wearing an N95 mask compared to a surgical mask. • Increased intensity of exercise equated to a more pronounced difference in heart rate between mask types. • The humidity and temperature inside the nano-treated and untreated surgical masks were lower than for both N95 mask ($P=0.000$).

		• Symptoms of fatigue, dyspnea and overall discomfort were significantly worse for N95 masks. • This study is not generalizable due to small sample size and homogenous sample population.
Wong 2020 (9) Quasi-Experimental study Hong Kong Oct 2020	23 healthy volunteers of various sporting backgrounds participated in a case-crossover study where they underwent graded treadmill walking at 4km/hr for 6 minutes with and without a surgical mask on to investigate the physiological effect (heart rate and perceived exertion measured on a scale from 6 to 20) during moderate exercise.	• Surgical masks elevated heart rate when wearing the face mask during exercise compared to without (128.4 +/- 13.2 vs. 124.4 +/- 12.8 beats per minute) and participants reported a higher perceived level of exertion starting after 3 minutes of exercise (12.7 +/- 2.1 vs. 10.8 +/- 2.2). Results extracted for 6 minutes of exercise. • The author suggests that exercising with face masks at a submaximal level induces higher physiological responses. This may be due to restricted ventilation, heavier breathing, and sympathetic responses. • Due to increased cardio-respiratory burden from masked exercise the authors suggest that mask wearers be cognisant of their exertion and heart rate taking care not to exceed 150 beats/min or 70% of their age-predicted max heart rate. • This study is not generalizable due to small sample size.
Morris (2020) (10) Quasi-experimental study Denmark* 2020*	A cross-over trial with 8 male participants was conducted to evaluate the impact of a KN95 respirator when worn in 40°C and 20% humidity during light exercise of 5 MET for 45 minutes. Cognitive and fine-motor performances were assessed using tests previously demonstrated to	• Dyspnea was not significantly different at rest, but with exercise there was significantly more dyspnea in the KN95 group 51.3% (27.6) vs the no mask group 21.4% (14.5), < 0.001. • Results for no mask – KN95 mask body temperature measurements were not significantly different.

	be highly sensitive and reliable at detecting heat-related decrements in cognitive performance, including dehydration, and radiation. Dyspnea was measured using the Borg breathlessness scale.	• Other cognitive and fine motor outcomes were not significantly different for no mask vs. KN95 mask. • This study is not generalizable due to small sample size and homogenous sample population.
Dattel 2020 (2) Quasi-Experimental study USA Jul 2020	This study explored the effects of cloth face masks (composition not described) or surgical face masks. 32 instructor pilots were studied in a normobaric flight chamber wearing either a cloth mask or a surgical face mask. Measurements on CO_2, heart rate, respiration rate, and oxygen saturation were taken over a 90 minutes period.	• Instructor pilots reported comfort issues, fatigue, and restriction of movement from wearing face masks. • No differences in CO_2, heart rate, respiration rate, or oxygen level were found between the cloth mask and surgical mask after a 90 minute simulated flight at 5000ft. • This study is not generalizable due to small sample size.
Lee 2011 (11) Quasi-experimental study Singapore* 2010*	14 healthy adults participated in a study of breathing resistance caused by N95 respirators (3M 8210). Breathing resistance was measured for inspiration and expiration and total volume (l per 30s) were measured with and without an N95 respirator.	• Breathing resistance was a mean of 126% inspiratory and 122% expiratory flow resistance with the use of N95 respirators. • There was an average reduction of 37% in air exchange volume with the use of N95 respirators. • This study is not generalizable due to small sample size.
Healthcare Workers (n=2)		
Purushothaman 2020 (12) Cross-sectional study India Jul 2020	A survey was completed by 250 HCWs without comorbidities at a tertiary hospital who consistently wore either surgical masks or N95 respirators for a minimum of 4h/day. Data was collected in a self-reported questionnaire that was developed with formative research, but not pretested.	This study does not distinguish outcomes by surgical mask or N95 respirator. • 58.2% of HCWs indicated they experienced trouble breathing on exertion ($p<0.001$). No additional information on what is meant by exertion was provided. • Participants self-reported a range of discomfort, some common complaints were; excessive sweating around the mouth

		(67.6%), acne (56.0%) skin irritation (39%), and pain behind ear 45.2%.
Bharatendu 2020 (13) Quasi-Experimental study Singapore Feb-Apr 2020	154 HCWs seeking medical attention for headaches related to PPE use were studied; 25% had migraines and 80% indicated the headaches were *de novo* after using the N95 mask. Transcranial Doppler (TCD) monitoring of middle cerebral artery was performed using two validated measurements mean flow velocity (MFV), pulsatility index (PI) and end-tidal carbon-dioxide (ET-CO_2) pressure, which were recorded prior to donning the N95 respirator and five minutes after. N95 (3M® N95 respirator mask) was evaluated with and without a powered air-purifying respirator (PAPR, 3M® Versaflo® TR-300 series).	• Donning of a N95 respirator resulted in significant increase in mean flow volume, relative change 12.3% (SD 29.8, p<0.001), decrease in pulsatility index relative change 13.3% (SD 11.3, p<0.001) and end-tidal carbon dioxide levels were significantly elevated, an increase of, 3.1 mmHg (SD 1.2) in the N95 mask compared to no mask. • 24 participants used a PAPR and results indicate no difference in the mean flow volume, pulsatility index or end-tidal carbon dioxide levels within 5 minutes of donning the respirator compared to wearing no mask. Thus, powered air-purifying respirator restores N95 mask induced cerebral hemodynamic changes. • Given measurements were taken at 5 minutes, it is unknown if the changes are sustained or corrected by autoregulation.
Pregnant women (n=2)		
Tong 2015 (14) Quasi-Experimental study Singapore Sep 2011	Phase I assessed volume of O_2 uptake (VO_2) in 8 pregnant health care workers while performing simulated nursing tasks. Phase 2 compared the use of N95 masks to no masks in 20 pregnant women (27-32 weeks gestation) during two 15-minute exercise cycles on a treadmill at 3 METS (which was equivalent to the normal moderate work of a HCW recorded in phase 1).	Breathing through a N95 mask compared with no mask resulted in: • A significantly lower tidal volume (TV) at rest -0.15L (95%CI: -0/23- -0.08L) and during exercise -0.21L (-0.32- -0.10L), overall a ~23% decrease. • A significantly lowered minute ventilation (VE) by 5.55L (95%CI −7.58 % - −3.51) which is ~ 25.8% lower. • No significant change in breathing frequency with the N95 mask.

	In both Phases the women wore a tight fitting Hans Rudolph respirator mask that had an outlet that was either open to air or covered by N95 mask materials. And measurements included volumes of oxygen (VO_2) and carbon dioxide (VCO_2) tidal volume (TV), minute ventilation (VE), forced expired O_2 (FeO_2), and CO_2 concentrations.	• Significant reductions of forced expired O_2 concentration (FeO_2) -0.54% (-0.70 - -0.38) during exercise. • Significant elevations forced expired CO_2 concentration ($FeCO_2$) during exercise 0.30% (0.18, 0.42) and in the pre-exercise and post-exercise periods. • Pulmonary gas exchange: Significantly lower VO_2 by 13.8 % and VCO_2 by 17.7 % were reported. • There were no differences in the maternal or fetal heart rate, oxygen saturation or rating of perceived exertion with the N95 mask. • This study is not generalizable due to small sample size and short duration of exercise.
Roberge 2014 (4) Controlled Experiment USA Oct 2014	Controlled study of 22 pregnant (13-35 weeks) and 22 non-pregnant healthy women to determine if there is a difference in the physiological and subjective effects of wearing an N95 mask (filtering face piece respirator, FFR). Respiratory rate, chest wall skin temperature, maternal and fetal heart rate, pulse-derived oxygen saturation (SpO_2). Borg rating of perceived exertion scale 6-20. Measurements were taken with and without wearing an N95 mask during exercise and postural sedentary activities over a 1 hour period.	• Overall N95 use significantly decreased respiratory rate, a minor difference, mean 0.94 (95%CI: 0.1-2.2) breaths/min and transcutaneous partial pressure of carbon dioxide ($PtcCO_2$) increased over time during exercise for all women due to re-breathing of higher CO_2 levels generated during exercise. • There were no significant differences in measured physiological and subjective responses in pregnant women compared with non-pregnant women wearing N95 masks for 1 hour during exercise and sedentary activities. • There was no significant effect on fetal heart rate. • This study is not generalizable due to small sample size.
People with chronic conditions (n=3)		

Kyung 2020 (15) Quasi-Experimental study South Korea Mar-May 2015	97 patients with varying severity of COPD were monitored for symptoms and physiologic variables during a 10-min rest period and 6-min walking test while wearing an N95 face mask. Patients were 19-80 yrs, could walk unassisted, were not on long term oxygen therapy and did not have a history of recent hospitalization. Measurements included breathing frequency, dyspnea, heart rate, S_{pO2}, blood pressure and a symptom questionnaire that included modified Medical Research Council dyspnea scale score. Severity of air-flow obstruction in COPD was measured by using post bronchodilator FEV_1, 31 subjects had a FEV_1 < 50% at baseline.	• 7/97 subjects failed to wear the N95 mask for the entire test. A modified Medical Research Council dyspnea scale score ≥ 3 (odds ratio 167, 95% CI 8.4 to >999.9; *P* = .008) or a FEV_1 < 30% (odds ratio 163, 95% CI 7.4 to >999.9; *P* = .001) was associated with an inability to continue wearing an N95 mask. Symptoms in this group were more pronounced and included dyspnea, dizziness and headache. Among the group that completed the test: • At rest breathing frequency was increased wearing an N95 mask (20.7 breaths /min) vs. no mask (19.7). • End tidal PCO_2 (25.7 mm Hg) wearing an N95 mask vs. no mask (24.8). • S_{pO2} levels were lower with an N95 mask (96.0%) vs. no mask (96.4%). • After 6 minutes of walking, significant differences were found with heart rate (92.4 vs. 87.7), breathing frequency (25.7 vs. 23.3 breaths/min), end tidal PCO_2 (35.5 vs. 34.0 mm Hg) was higher and S_{pO2} levels were (93.0 vs. 93.8 %) lower in those with an N95 mask vs. no mask. • The authors stated that COPD patients should be warned to remove the N95 mask immediately with the onset of dyspnea, headache, or dizziness.
Harber 2010 (16) Controlled experiment USA 2010	97 individuals, 42 with asthma, 14 mild COPD, 17 chronic rhinitis and 24 healthy individuals' respiratory effects of using a dual cartridge half face mask or a N95 respirator while doing work tasks.	• Compared with an N95, tidal volume, minute ventilation and respiratory rate were slightly lower with half mask, but this may not be of clinical significance. No consistent effect was noted for volumes for COPD or asthma.

	Respiratory outcomes included tidal volume, minute ventilation, inspiratory/ expiratory time, duty cycle and flow rates.	• COPD had prolonged time to reach peak expiratory flow rate. • Those with rhinitis performed better than COPD and asthma. • Age was not a factor. • Those with asthma or mild COPD had a lower FEV_1 percentage of predicted, which was associated with ventilator volume. • This study is not generalizable due to small sample size.
Ciocan 2020 (17) Quasi-Experimental study Italy Oct 2020	10 HCWs including 3 with asthma and 3 current smokers were included in this cross-over trial. They wore a 4 layer surgical mask (AFLUID) during 4 hours of mild-moderate usual working activities and their respiratory function was monitored. A Respiratory Functional Test (RFT) was performed at three time periods and Arterial Blood Gas (ABG) samples were taken before the first and third RFT.	• Compared to no mask, Maximal Voluntary Ventilation (MVV) was reduced with a 4-layer mask (p=0.002) and remained low even during activity (p=0.041). • No significant variations in observed RFT and ABG parameters were reported although the study did not have sufficient power to detect differences. • This study is not generalizable due to small sample size.

* Location or date of study was estimated based on author affiliations and / or publication date. HCW= healthcare worker

GUIDANCE ON FACE MASK USE IN THE GENERAL POPULATION

Key guidance from Canada, the USA and WHO were identified and examined for recommendations on mask use for those with chronic medical conditions and general use in the community (Table 2).

- The Canadian Thoracic Society and Asthma Canada both indicate people with an underlying lung condition should be able to wear a non-medical face mask. However, for those that have trouble wearing a mask it is suggested to work with a healthcare provider to find a solution or avoid situations where you need a mask as much as possible to minimise your risk (18).

- The WHO's newest guidance recommends that face masks should not be worn for source control to prevent transmission from a child under 5 with COVID-19 (19). They do not specifically address if children 2-5 years old should wear a mask for protection. All guidance states children under 2 years old should not wear a mask.

Guidance from Canada (20), the USA (21) and WHO (19) state that masks should not be required for anyone who is unable to remove their mask without assistance, including children under two years old, and anyone who has trouble breathing, is unconscious, or is incapacitated due to the risk of suffocation.

- It is also suggested that people with certain disabilities or small children may be unable to wear their mask properly and thus should not wear a mask (20, 21).

Table 2. Guidance on face mask use for those with medical conditions and the general public (n=5)

STUDY	METHODS	KEY OUTCOMES
World Health Organization (19) Guidance document Switzerland Dec 2020	This is an update to WHO June 5 guidance on mask use and covers: • mask management; • SARS-CoV-2 transmission; • masking in health facilities in areas with community clusters and sporadic transmission; • mask use by the public in areas with community and cluster transmission; • alternatives to non-medical masks for the public; • exhalation valves on respirators and non-medical masks; • mask use during vigorous intensity physical activity; • Essential parameters to be considered when manufacturing non-medical masks (Annex).	• Face mask use should be part of a layered approach to public health interventions. • Masks can be for protection or source control. (Wear a medical mask if you suspect you have COVID-19). • Appropriate use, storage and cleaning guidelines are presented. • Children under 5 should not wear a mask for source control. Use of masks in older children are based on local factors and those over 12 years old should follow guidelines for adults. • Manufacturing non-medical masks: 3 layers with a hydrophilic inner layer, a hydrophobic outer layer and a hydrophobic middle layer that enhances filtration. • Exhalation valves are discouraged.
Canada.ca (20) Guidance document	Guidance on the use of non-medical masks to prevent the	• Non-medical masks protect the person wearing it and others from the spread of COVID-19.

Canada Nov 2020	spread of COVID-19 in the community. • Mask mandates • Composition of non-medical masks • Use of mask filters • Application, cleaning and storage • Children • Safety • Hearing impaired • Face shields, neck gaiters, exhalation valves	• Mandatory mask policies are put in place depending on the local spread of COVID-19. • Non-medical masks should be 3 layers, two layers of tightly woven fabric and a middle layer with filtration properties e.g. non-woven polypropylene fabric. Masks should fit snugly to the face covering the nose and mouth, but still be breathable. • Non-woven polypropylene fabric is readily available (e.g. craft fabric, interfacing or reusable shopping bags). Disposable mask filters may also be used. • Children under 2 should not wear a mask. Between 2-5 yrs mask wearing should be supervised. • Avoid stigmatization of people who cannot wear a mask due to illness or disability.
Centers for Disease Control and Prevention 2020 (21) Guidance document USA Nov 2020	Considerations for wearing masks, type not specified, to help slow the spread of COVID-19 are provided. Topics include: 1) Evidence for effectiveness of masks 2) Who should and shouldn't wear a mask 3) Difference between types of masks 4) Other types of face protection	• Face masks should not be worn by children under the age of 2 years old, anyone who has trouble breathing, and anyone who is unconscious, incapacitated, or unable to remove their mask without assistance. • Individuals with certain disabilities or children who cannot wear a mask properly should not wear one. • Most people with underlying medical conditions can and should wear a mask. Discuss with your healthcare provider if you have concerns. • Wearing a cloth mask does not raise the carbon dioxide (CO_2) level in the air you breathe.

		• Medical masks and N-95 respirators should not be used as they should be conserved for healthcare workers. • Face shields or goggles are not a substitute for masks. • The most effective cloth masks are breathable, have two-three layers, and are made of tightly woven fabrics such as cotton and cotton blends. • Those who rely on lip-reading to communicate (those that are deaf, hard of hearing, or who care for those who are hearing impaired) may be unable to wear cloth face coverings. CDC recommends a clear face covering, relying on written communication, or decreasing background noise while communicating.
Bhutani (2020) (18) Guidance document Canada July 2020	This is a guidance and position statement from the Canadian Thoracic Society on the use of face masks by the public during the SARS-CoV-2 pandemic.	• The Canadian Thoracic Society supports the recommendation from the Public Health Agency of Canada to wear a non-medical face mask in the community when it is not possible to consistently maintain a 2-meter physical distance from others. • There is no evidence that wearing a non-medical face mask will exacerbate an underlying lung condition. • Wearing a face mask alone will not prevent the spread of COVID-19 and should be complemented with other recommended public health measures such as increased hand hygiene and physical distancing. • For those experiencing challenges with wearing a mask, it is recommended they speak with their health care provider to

		develop strategies to be able to wear a face mask. If despite best efforts, wearing a mask is not possible then individuals should avoid or minimize circumstances where physical distancing is not possible.
Asthma Canada (22) Guidance document Canada 2020	Asthma Canada issued this guidance to people with asthma to address concerns related to mask use and COVID-19.	Recommendations given for people with asthma: • Masks come in different styles and material; select a mask that is most comfortable for you. • Test the mask at home to get used to how it feels. • If you cannot wear a mask without experiencing breathing issues, do not wear a mask. Instead practice 2 meter distancing and minimize time spent around people from outside your household. • Consult with your healthcare professional to go over your asthma action plan and explore other options to protect yourself.

Methods

A daily scan of the literature (published and pre-published) is conducted by the Knowledge Synthesis team in the Emerging Science Group, Public Health Agency of Canada. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square, and COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The cumulative scan results are maintained in a Refworks database and an excel list that can be searched. Details on this search strategy are available upon request. From this database and excel list, article titles and summaries will be systematically searched for the following key words: mask* OR (face AND cover*). An additional search for guidance documents and supporting evidence on persons who should not wear a mask focused on Canada and key health organizations was conducted using a snowball technique and targeting country websites. Each potentially relevant reference was analyzed to confirm its relevance and data was extracted into the review. This review contains research published up until December 2, 2020.

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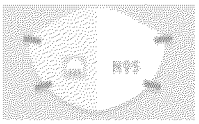
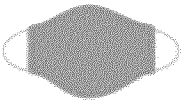
APPENDIX: TYPES OF FACE MASKS

The NCCEH blog post on masking during the COVID-19 pandemic (October 27, 2020) describes the different mask types and includes the following figure on types of masks.

	Respirator	Surgical or procedure mask	Non-medical cloth mask
			
Types	N95, 99, 100 (US, Canada), FFP2 or FFP3 (EU). Various styles including cup, flat-fold and duckbill. May also include an exhalation valve.	Typically a 3-layer laminate structure that can include a combination of non-woven air-laid paper and polypropylene.[3]	Wide variability in fabric, number of layers and design with 2-layer cotton being a common design.
Use	For use in environments where exposure to aerosols is likely. Protect against most particles (e.g., N95 block 95% of particles and provide some splash and spray protection). Medical grade N95s are tested for resistance to fluids including blood, but commercial grade are not.	For use in routine care to reduce inward and outward transfer of respiratory droplets. Filter particles > 20 µm diameter and some finer droplet nuclei.[4] Block blood and infectious materials from contact with oral, nasal and skin area. Effective against splash and sprays.	For use by the public in non-healthcare settings as source control to reduce respiratory emissions from the wearer and to reduce exposure to respiratory emissions of others.[3,5]
Approval	U.S. National Institute for Occupational Safety and Health (NIOSH) for N95 or similar and EU standards for FFP equivalents.[6] The Government of Canada lists other approved alternatives to N95s.	FDA with grading based on the level of resistance to splashing (e.g., ASTM 1 – venous pressure; ASTM 2 – arterial pressure; ASTM 3 – high velocity splash).	Not approved for use in any healthcare setting; not tested to any standard of effectiveness. **Note**: Many procedure-type masks found in retail outlets may not be assessed to any approval standards, and would also be considered non-medical masks.
Advantages	Medical grade respirators can be effective against aerosol penetration. Can be reused and disinfected with precautions.	Some protection against contact transmission, are disposable and inexpensive. Fit testing is not required.	Inexpensive and can be made from household materials. Can act as a reminder to not touch face.[6] Can be reused and laundered.[7]
Disadvantages	Filtration efficiency for aerosols is only effective if properly fit tested. Some users may experience some reduction in comfort/breathability. Expensive and may be in short supply.	Less effective against smaller particles (e.g., 0.4-1.3 µm), looser fit than N95 respirators, and therefore more penetration via leaks.[8] Not recommended for reuse or disinfection for use in healthcare environments.	Variable performance for respiratory protection and breathability depending on the material and design.[9] They do not replace other protective measures (e.g., hand hygiene and distancing).[5,10]

Emerging Evidence on COVID-19

Evergreen Rapid Review on COVID-19 Vaccine Attitudes and Uptake – Update 8

Introduction

What is the global evidence on COVID-19 vaccine uptake and the COVID-19 vaccine attitudes evidence for Canadians and specific populations?

The purpose of this evergreen rapid review is to identify and summarize literature on COVID-19 vaccination uptake and attitudes to better understand the factors associated with vaccine uptake in Canada. This report focuses on Canadian evidence on uptake and attitudes, and evidence from five eye countries related to specific populations up to July 1, 2021. Evidence on pre-defined priority populations from Australia, New Zealand, USA, and UK were included to complement areas where there was little Canadian research. Priority populations include healthcare workers, LGBTQ+, faith groups, newcomers, parents, women who are pregnant or breastfeeding, people living in rural communities, older adults, people with comorbidities, and people experiencing multiple barriers to health (e.g., homelessness, mental health and/or substance use disorder). Previous versions of this report (updates 1-7) included evidence up to June 1, 2021 on vaccine knowledge, attitudes, and behaviours and can be requested through phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca. The What's New and Key Points sections below focus on highlighting important findings from the most recently conducted studies (within the last five months).

What's New

- This update identified 40 new studies or updates to existing studies on COVID-19 vaccination uptake and attitudes including six specific to Canada. New studies are indicated throughout the tables as *new* and all tables have been moved to appendices to assist readers in navigating the document.

Vaccine Uptake

- Vaccine uptake and refusal trends continue to mirror vaccine intention trends. Across all populations, vaccine uptake was positively associated with increasing age, male gender, and prior history of receiving a flu vaccine. Those with a history of SARS-CoV-2 infection were less likely to vaccinate and Black and minority ethnic groups had the lowest uptake rates.
- To date there has been one study on vaccine uptake in Canadian healthcare workers (HCWs) completed in Dec 2020. In Montreal, 80.9% of HCWs offered a vaccine accepted and 19.1% refused. 74.1% of those that declined a vaccine reported they will accept a vaccine in the future with 53.2% wanting to delay a few months and 31.9% wanting to wait a year (1). The most common reasons for refusal were the newness of the vaccine, a preference for others to get vaccinated first, a lack of information about the vaccine, and not having enough time to make a decision (1).

- In a group of 266 liver transplant recipients in Italy, 96.6% accepted a vaccine when offered. Despite receiving adequate information, five patients (1.8%) refused vaccination due to concerns over the potential for serious adverse events. The barriers in place for the remaining four patients (1.6%) could be lifted either by providing further details regarding the vaccination or following resolution of medical and logistical issues (4).
- In a group of 85 hospitalized psychiatric patients in the UK who had the capacity to decide if they wanted a COVID-19 vaccine, 80% accepted and 20% refused. White British patients were less likely to refuse compared to Black, Asian, minority ethnic (BAME) patients (16.9% vs 30%). The reasons for refusal included concerns about the safety and side effects of the vaccine, a belief there is a low risk to their personal health from contracting COVID-19, broader distrust of healthcare services, and concerns about animal testing (5).

Vaccine Uptake Intervention Strategies

- The implementation of two text-message reminders (either on the personal or social benefits of vaccination) increased vaccine uptake rates in Israel. The aggregate effect over eight days post intervention revealed the personal benefit reminder led to a 9% relative increase compared to the social benefit reminder (23.8% vs 21.7%, P<0.0001) (2).
- Israel implemented a policy where entry to certain public places required the presentation of a "green pass" which could be acquired from either receiving a vaccine or a recent negative COVID-19 test. The implementation of this policy in February was associated with a relative increase of 22.2% in vaccine uptake after three days (2).
- In February, a community based vaccine site (Unidos en Salud UeS) was deployed to overcome barriers to COVID-19 vaccination faced by Latinx individuals in San Francisco. 56.1% reported they got vaccinated earlier because of the site and 65.3% reached out to three or more individuals to recommend the vaccine after their positive experience (3).

Adherence to Public Health Measures Post-Vaccine

- Using a Global Positioning System (GPS) in the UK, the median daily increase in average daily travel distance from a participant's registered address was 45.0m (95% CI: 25-65m, P = <0.001) between the vaccination date and 99 days after vaccination (6).
- At the beginning of the vaccination campaign (January) in Israel, those who were infected with COVID-19 were less careful about social distancing (29.7%) and mask-wearing (18.8%) compared to those who received the first dose of vaccine (12.8% and 8.2%), or those who were neither vaccinated nor infected (19.2% and 11.6%) (7).

Canada

- Two surveys conducted in June show that 84-88% of Canadians have either received a vaccine or wish to get a vaccine as soon as possible, an increase from April and May surveys (8, 9).
- In June, 89% of Canadians who had one dose reported they intend to receive a second dose, 9% have already had their second dose, 1% probably will not, and 1% were unsure (10).

- In a group of 70 parents or guardians of children aged 12-17 from Manitoba, 15% and 13% were not sure or would not vaccinate their children, respectively (11). Those who were hesitant to vaccinate their children were in households making less than $40,000/year, would not get the vaccine themselves, and didn't believe adults should get all the regular vaccines (11).
- 48% of Canadians were uncomfortable about receiving a different brand of vaccine as their second dose, whereas 46% were comfortable and 6% were unsure. Of those who received AstraZeneca as their first dose, 50% preferred to receive AZ as their second dose, 32% preferred another brand as their second dose, and 18% were unsure (10).
- Financial incentives (monetary, vouchers, complimentary items, draws for prizes, discounts) were not reported to increase the likelihood of accepting a vaccine in a study conducted in Manitoba (between 7-84% of respondents stating the incentive would not make them more likely to vaccinate). However, 70% would be concerned if only vaccine hesitant individuals received large ($50-100) incentives (11).
- Vaccine passports have high support in Quebec with 72% of residents in favour (12).

Parents

- Parental and child vaccine intentions continue to be highly correlated with each other (13-16). Among a group of American parents or caregivers surveyed in April, 61.9% intended to vaccinate their youngest child (mean age 4.7 years), 23.3% were unsure, and 14.8% did not. Having a child attend daycare more than once a week was associated with increased intentions (aPR 1.23, 95% CI: 1.05-1.45) (16).
- Similar to the general population, parents from lower-income households, who are younger, less educated, have a history of not accepting other vaccines, who are female, and ethnic minorities were more likely to reject a vaccine for their children (14, 16-19).

Other Populations of Interest

- In a UK study, those reporting Christian faith were significantly more likely to get a vaccine if vaccine passports were introduced for domestic (aOR 1.23, 95% CI: 1.08-1.41) and international (aOR 1.22 95% CI: 1.07-1.39) travel compared to atheists and agnostics (20).
- A quasi-experimental study of 709 unvaccinated registered voters in South Dakota, USA demonstrated that messaging from a religious leader had a statistically significant positive effect on intention to vaccinate, while messages from a political or medical leader did not (21).

Key Points

- There have now been 205 studies on COVID-19 vaccine uptake and attitudes conducted in Canada on the general public and in Canada, Australia, New Zealand, USA, and the UK on healthcare workers (HCWs), high-risk populations, and other populations of interest (Tables 1-7). The majority have focused on intention to vaccinate. Since vaccine rollout began in December 2020, 29 studies have evaluated vaccine uptake and 7 evaluated continued adherence to public health measures post-vaccination.

Vaccine Uptake

- Vaccine uptake and factors associated with uptake in HCWs were evaluated in 14 studies from the USA, UK, Canada, and Israel, and in two studies of adults over 70 in the UK and Poland (Table 1). The proportion of HCWs who accepted and received one dose of the vaccine ranged between 52-94% across studies. Doctors were more likely to get vaccinated compared to nurses and non-clinical HCWs.
- Vaccine uptake and factors associated with uptake were studied in the general population of the UK, USA, Israel, and New Zealand (n=6 studies) and in several specific populations: one study in people experiencing homelessness in the USA, one in disabled adults in the UK, one in stroke and transient ischaemic attack (TIA) survivors in the UK, one in older adults and high risk populations in the USA, one on dialysis patients in the USA, one in liver transplant recipients in Italy, one in patients with irritable bowel syndrome in Italy, one in a psychiatric hospital population in the UK, two in prisons in the USA and two in military units in Israel (Table 1).
- Across all populations, vaccine uptake was positively associated with increasing age and male gender. Those with a history of SARS-CoV-2 infection were less likely to vaccinate and Black, Asian, and minority ethnic groups had the lowest uptake rates.

Vaccine Intention in Canada

- Forty-nine studies on vaccine intention were from Canada: four on HCWs, 36 on the general public, three on HCWs and the general public, two on parents, one on individuals living with obesity, one on youth (aged 16-21), and two engaging expert opinion on who to vaccinate initially. The most recent studies from Mar-May report intention to vaccinate is increasing and currently varies between 66-86% in the general public and 57-82% in HCWs across the Canada. The Atlantic provinces, British Columbia, and Quebec have the highest intentions to vaccinate.

Facilitators and Barriers to Vaccine Intention

- The most common factors positively associated with intention to vaccinate in Canada and globally were male gender, older age, higher education, adequate knowledge or health literacy, trust in experts and government, history of a prior influenza vaccine, higher socioeconomic status, and heightened worry or concern about COVID-19.
- Compared to nurses and other healthcare professionals, doctors were significantly more likely to accept a COVID-19 vaccine.
- Three studies demonstrated that LGBTQ2+ were 6-25% more willing to accept a vaccine compared to non-LGBTQ2+.
- Partisanship was associated with intention to vaccinate. Those who voted liberal/democrat expressed intention to vaccinate at higher rates than other parties.
- A recommendation to get the vaccine by a healthcare provider (e.g., doctor) had a positive impact on vaccine intention.

- Intention to vaccinate varied widely by race/ethnicity, with White ethnic groups more likely to vaccinate compared to other ethnic groups such as Black, Asian, and Hispanic in studies from Canada, USA, and UK.
- Parents had lower intentions to vaccinate their children compared to themselves. Parental and child vaccine intentions were highly correlated with each other, with parents who were intending to take a vaccine being more likely to intend to vaccinate their children. Those with younger children (aged 0-4) were more hesitant compared to those with children over the age of 5.
- Religion and belief in conspiracy theories were associated with vaccine hesitancy.
- Concerns about vaccine safety and effectiveness were the two most cited reasons for vaccine refusal. Other commonly cited reasons include newness of the vaccine, and the belief that a COVID-19 vaccine is unnecessary.
- Compared to the general population, intention to vaccinate is lower in some high-risk populations such as pregnant women, people experiencing homelessness, those with substance use disorders, and vulnerable populations.
- Rural participants were slightly less likely to accept a vaccine compared to urban and suburban participants.

Overview of the Evidence

Two-hundred and five articles pertaining to COVID-19 vaccine uptake and attitudes were identified and included in this review. Of these, 99 are preprints or reports and have not completed the peer-review process. This report focuses on the global evidence on COVID-19 vaccine uptake and Canadian evidence on attitudes. To complement the Canadian literature, evidence on pre-defined priority populations from Australia, New Zealand, USA, and UK was also included. This includes healthcare workers, LGBTQ+, faith groups, newcomers, parents, women who are pregnant or breastfeeding, people living in rural communities, older adults, people with comorbidities, and people experiencing multiple barriers to health (e.g., homelessness, mental health and/or substance use disorder).

The publications reporting on COVID-19 vaccine uptake and attitudes are mainly observational studies with a few randomized controlled trials, controlled before and after studies, and quasi-experimental studies exploring factors associated with intention to vaccinate and the impact of messaging on these intentions. The outcomes in the experimental studies did not assess prevalence, but rather were designed to inform what may be most effective across a range of options. Randomized controlled trials have the added advantage of balancing the intervention groups to avoid the influence of non-comparable groups (e.g., confounding).

A formal risk of bias evaluation was not conducted. Across observational studies the reliability of the outcome is based on obtaining a representative sample of the target population that is sufficiently large to obtain a representative spectrum of results. Studies frequently did not demonstrate the representativeness of their samples to the target population in both unpublished and published studies. Longitudinal studies where a target population was sampled more than one time to monitor changes in vaccine attitudes and uptake over

time were the strongest observational study design identified. Most observational studies were cross-sectional online surveys of a target population at a single point in time. These study designs are at moderate/high risk of bias and thus, are considered medium-low quality depending on the sample size and whether the sample represents the target population as well as how well the survey tool can measure the outcome(s) of interest (e.g., was it informed by formative research, validated and pretested prior to implementation). For most of the included studies the outcomes are self-reported, which can be biased by response and social desirability biases. Other biases considered in these studies include response rate and missing data. Most studies captured in this rapid review did not report and/or account for one or more of the criteria listed above either due to conduct or reporting of the study. While there are many studies that show similar trends, the conclusions could change with additional research, larger sample size, different sampling strategies, data collection tools, and progression through the pandemic.

A key knowledge gap in this research are studies that address vaccine intentions and reasons for hesitancy in high-risk and unserved populations. The majority of studies used online surveys, and to a lesser extent telephone surveys, which may limit segments of population due to lack of access. Although the vaccine rollout has been underway for a few months, there have been minimal studies released on vaccine refusal and the knowledge and attitudes associated with actually rejecting or accepting a vaccine. This information is crucial to determine why people are accepting or refusing vaccinations to continue developing strategies to encourage vaccine uptake in those who are hesitant.

CONTENTS

COVID-19 VACCINE UPTAKE & ADHERENCE TO PUBLIC HEALTH MEASURES POST-VACCINE

Vaccine uptake and factors associated with uptake in health-care workers (HCWs) was evaluated in 14 studies from the USA, UK, Canada, and Israel (1, 22-34), two studies of adults over 70 in the UK and Poland (35, 36), two in prisons in the USA (37, 38), two in military units in Israel (39, 40), one study in people experiencing homelessness in the USA (41), one in stroke and transient ischaemic attack (TIA) survivors in the UK (42), one in disabled adults and parents in the UK (43), one study in older adults and high risk populations in the USA (44), one in patients on hemodialysis in the USA (45), one in liver transplant recipients in Italy (4), one in patients with irritable bowel syndrome in Italy (46), one in a psychiatric hospital population in the UK (5), and six studies in the general population of the UK, USA, Israel, and New Zealand (2, 15, 44, 47-49). Only studies where it is has been established or can be inferred that the entire group was offered a vaccine prior to measuring uptake were included. This includes studies from the beginning of the vaccine rollout (December 2020 onwards). Seven studies assessed adherence to public health measures post-vaccine in the UK and Israel (6, 7, 35, 50-53). High level points are listed below and detailed outcomes for each study are located in the Appendix (Table 1). These studies should be interpreted with caution as vaccine uptake and refusal were reported as secondary outcomes to other primary outcomes such as vaccine efficacy in a few studies and in other studies measurement of vaccine refusal was unclear due to reporting or the preliminary nature of the results.

Overall Trends

- Vaccine uptake was positively associated with increasing age (1, 15, 25, 26, 29, 30, 34, 38, 45, 50, 54) and male gender (1, 15, 22, 25, 26, 29, 30, 36, 45, 47).
- Those with a history of SARS-CoV-2 infection were less likely to vaccinate in four studies (25-27, 45). Other reasons for declining a vaccine included concerns over the vaccine being new, potential side effects, safety, belief there is a low risk to their personal health from contracting COVID-19, broader distrust of healthcare services, concerns about animal testing, and being experimented on (1, 4, 5, 27, 28, 30, 32, 36, 46).
- Those who did not receive the flu vaccine were less likely to get the vaccine compared to those who did in three studies in the USA (30, 32, 45).
- Ten studies evaluated vaccine uptake across different ethnic/race groups. Black and minority ethnic groups had the lowest uptake rates (5, 22, 25-27, 29, 30, 32, 34, 38, 49).
- These trends mirror the trends seen in intention to vaccinate.

Healthcare Workers

- In six studies of HCWs in hospitals across the USA, 70-94% of HCWs chose to receive the vaccine when offered (22, 27, 30-33).
- In a December survey conducted in Montreal, Canada, 80.9% of HCWs offered a vaccine accepted and 19.1% refused. 74.1% of those that declined a vaccine reported they will accept a vaccine in the future with 53.2% wanting to delay a few months and 31.9% wanting to wait a year (1).

- High rates of vaccination among HCWs in Israel were reported in two studies where all HCWs had been offered vaccine. As of Jan 21 and Jan 24, 90% (n=1500) and 79% (n=9109) of HCWs had received at least one vaccine dose (23, 24).
- Across three studies of HCWs who were offered a vaccine in hospitals in the UK, 63-89% chose to receive the vaccine (25, 26, 29).
- Across 87 care homes in the UK where all staff were offered a vaccine, 52.6% (n=1119) had received their first vaccination with a mean vaccination rate per care home of 51.4% (95% CI: 43.9-58.8%). A common reason for not receiving the vaccine was staff being off-site during vaccination sessions (36.5%). If logistical issues such as this were resolved, the mean vaccination rate per care home could have increased to 69.8% (95% CI: 63.2-76.3%) (28).
- Physicians were more likely to have accepted the vaccine compared to nurses and non-clinical HCWs (22, 27, 29, 30).

Older Adults (70+)

- In a UK study of older adults (80+) where 99.8% reported that they had been offered a vaccine, 99% had taken at least one dose, 15% had two doses, and 1% refused (35, 54).
- In a study of 1427 older adults (70+) living among the general public in Poland, 62.7% had been given the vaccine and 37.3% said they were unwilling to get vaccinated. Independent predictors of vaccine uptake were receiving an explanation by a medical professional as to why they should be vaccinated (OR 4.23, 95% CI: 2.90-5.75), living with others (OR 3.13, 95% CI: 2.03-4.26), being able to travel independently to their general practitioner (OR 1.92, 95% CI: 1.45-2.76), having chronic illnesses (OR 2.98, 95% CI: 2.05-4.01), and higher socio-economic status (OR 1.79, 95% CI: 1.33-2.15) (36).

People Experiencing Homelessness

- In a group of 90 people experiencing homelessness in Los Angeles, 17 were offered a vaccine of which 10 accepted and 7 refused. Reasons for refusal were not explored (41).

Prisons

- Across correctional facilities in Rhode Island and California, 66.5-76.4% of incarcerated individuals accepted a vaccine. Reasons for refusal were not explored (37, 38).

General Population

- A longitudinal study of the general population of the UK demonstrated vaccine refusal rates are between 1-2%. Of those who have been offered a vaccine, vaccine refusal rates were 2% in those aged 16-29, 1% in those aged 30-49, and 2% in those aged 50-69 (50, 54).
- In a North West London vaccination program where 413,919 individuals were offered a vaccine, 5.88% of people refused the vaccine and 0.7% were hesitant. Deprivation was negatively associated with declining vaccination ($r=-0.94$, $P<0.01$). For those living in the deprived areas, the highest rates of refusal were in those aged 70+ (70-74 = 17.5%; 75-80 = 19.0%; 80+ = 25.9%), the clinically extremely vulnerable (19.2%) and Black and Black British (20.0%) communities (49).
- In a longitudinal survey of adults from New Zealand, vaccine refusal rates dropped from 2% in April to 1% in May (15).

- In the UK, 5% of those identifying as other religion and 4% of Buddhists who had been offered a vaccine had declined compared to 1% reporting no religion (47).
- Two studies were conducted to measure the impact of text-message reminders on booked vaccination rates in the USA and Israel. In the USA study, an initial text reminder sent one day after an individual was notified of vaccine eligibility boosted appointment and vaccination rates by 86% and 26%, respectively (44). A second text reminder sent to those who had not scheduled an appointment eight days after the first boosted appointment and vaccination rates by 52% and 16%, respectively (44). In the Israel study, individuals received one of two text-message reminders about either the social or personal benefits to vaccination (2). The aggregate effect over eight days post intervention revealed the personal benefit reminder led to a 9% relative increase compared to the social benefit reminder (23.8% vs 21.7%, P<0.0001) (2).
- Israel implemented a Green Pass policy where entry to certain public places required the presentation of a "green pass" which could be acquired from either receiving a vaccine or a recent negative COVID-19 pass. The implementation of this policy in February was associated with a relative increase of 22.2% in vaccinate uptake after three days (2).

Military Units

- Vaccine uptake was high (84.8-89.8%) in military units across two studies in Israel (39, 55). In a group of 28 soldiers who were not intending to vaccinate, 47.4% proceeded to vaccinate after attending an on-site physician consultation to discuss their concerns (P = 0.004) (39).

Other Populations

- In the UK, 1% of those with disabilities and 1% of clinically extremely vulnerable respondents had been offered a vaccine but declined, which was slightly higher than the general population (2%) (56). 3% of parents with children aged 0-4 had been offered a vaccine and declined compared to 2% of those with children over 5 years or 1% among non-parents and those not living with dependent children (43).
- 14.2% of dialysis patients in a USA study refused a vaccine when offered. Those on dialysis for more than 5 years were more likely to refuse a vaccine (OR 1.7, 95% CI: 1.08-2.70, P=0.023) (45).
- In 377 stroke and transient ischaemic attack (TIA) survivors in the UK, 2% of respondents declined the vaccine when offered (42).
- In a group of 266 liver transplant recipients in Italy, 96.6% accepted a vaccine when offered. Despite receiving adequate information, five patients (1.8%) refused vaccination due to concerns over the potential for serious adverse events. The barriers in place for the remaining four patients (1.6%) could be lifted either by providing further details regarding the vaccination or following resolution of medical and logistical issues (4).
- In a group of 85 hospitalized psychiatric patients in the UK who had the capacity to decide if they wanted a COVID-19 vaccine, 80% accepted and 20% refused. White British patients were less likely to refuse compared to Black, Asian, minority ethnic (BAME) patients (16.9% vs 30%). The reasons for refusal included concerns about the safety and side effects of the vaccine, a belief there is a low risk to

their personal health from contracting COVID-19, broader distrust of healthcare services, and concerns about animal testing (5).

- Of 56 patients with irritable bowel syndrome in Italy, 96.4% accepted a vaccine when offered. Refusal was due to concerns over potential adverse reactions (46).

Adherence to Public Health Measures Post-Vaccine

- In a UK study of older adults (80+) who had received at least one dose within the last three weeks, 43% had met someone outside of their bubble, household, or care staff indoors, 49% met someone who they do not live with outdoors, 54% had gone shopping, and 45% had left home to participate in outdoor leisure activities (35).
- A longitudinal study in the UK demonstrated that vaccinated adults (at least one dose received) were more likely than unvaccinated adults to wash their hands when returning home (90% vs 82%), maintain social distancing when meeting up with others outside of their household/bubble (90% vs 72%), and avoiding physical contact outside their homes (86% vs 74%) (50).
- After the second-dose, 21.1% and 47.3% of respondents in the UK reported wearing a mask less and social distancing less post-vaccination and 75.7% and 48.4% did not change their behavior, respectively. Those aged 50+ were less likely to change their behaviors compared to those <50. Similar trends were seen in HCWs for social distancing, but the majority (95.7%) reported no changes in mask wearing post-vaccination (51).
- Preventative behaviors did not change in 73.2% of USA adults after receiving at least one dose of a COVID-19 vaccine. Preventative behaviors increased and decreased in 4.3% and 21.9% of the study population, respectively (53).
- At the beginning of the vaccination campaign in Israel, those who were infected with COVID-19 were less careful about social distancing (29.7%) and mask-wearing (18.8%) compared to those who received the first dose of vaccine (12.8% and 8.2%), or those who were neither vaccinated nor infected (19.2% and 11.6%) (7).
- Using a Global Positioning System (GPS) in the UK, the median daily increase in average daily travel distance from a participant's registered address was 45.0m (95% CI: 25-65m, P = <0.001) between the vaccination date and 99 days after vaccination (6).

COVID-19 VACCINE ATTITUDES IN THE GLOBAL POPULATION

The comparison of COVID-19 vaccine attitudes in the general population across different countries around the world was reported in six articles. Only studies that included Canada and reported outcomes by country were included. High level points from the most recent studies (January 2021 onwards) are listed below and detailed outcomes for all other studies are located in the Appendix (Table 2).

- As of January, countries with the highest intentions to vaccinate (63-77%) included the UK, Denmark, and the Netherlands. Intention to vaccinate in Canada was 55% (57).

- Increases in intention to vaccinate between November and January were seen in Spain (24.1%), UK (23.2%), Sweden (22.7%), Finland (20.4%), Netherlands (18.5%), Italy (15.4%), Norway (14.6%), France (14.2%), Denmark (13.3%), Germany (13.0%), Canada (11%), and Japan (0.8%) (57).
- In 11/15 countries there was a significant decrease in the proportion of individuals who reported concern about the side-effects of a vaccine. In Canada, this worry decreased from 53.3% in November to 47.9% in January (57).

COVID-19 VACCINE ATTITUDES OF THE CANADIAN GENERAL PUBLIC

The majority of research on COVID-19 vaccine attitudes has been conducted on the general public. Forty-two studies were specific to the Canadian population, of which 27 were unpublished and seven were preprints. High level points from January 2021 onwards are listed below and detailed outcomes for each study are located in the Appendix (Table 3).

Intentions to Vaccinate

- According to the most recent Canadian studies from June 2021, intention to vaccinate is between 84-88% (8, 10). The Atlantic provinces, British Columbia, and Quebec have the highest intentions to vaccinate (58-73).
- Three longitudinal studies demonstrate that intention to vaccinate continues to rise in Canada from baselines measured between September-December 2020 (10, 74, 75).
- In June, 89% of Canadians who had one dose reported they intend to receive a second dose, 9% have already had their second dose, 1% probably will not, and 1% were unsure (10).
- In a group of 70 parents or guardians of children aged 12-17 from Manitoba, 15% and 13% were not sure or would not vaccinate their children, respectively (11). Those who were hesitant to vaccinate their children were in households making less than $40,000/year, would not get the vaccine themselves, and didn't believe adults should get all the regular vaccines (11).
- 48% of Canadians were uncomfortable about receiving a different brand of vaccine as their second dose, whereas 46% were comfortable and 6% were unsure. Of those who received AstraZeneca as their first dose, 50% preferred to receive AZ as their second dose, 32% preferred another brand as their second dose, and 18% were unsure (10).
- Financial incentives (monetary, vouchers, complimentary items, draws for prizes, discounts) were not reported to increase the likelihood of accepting a vaccine in a study conducted in Manitoba (between 7-84% of respondents stating the incentive would not make them more likely to vaccinate). However, 70% would be concerned if only vaccine hesitant individuals received large ($50-100) incentives (11).
- Vaccine hesitancy dropped dramatically in Alberta from 45% in January to 25% in April to 17% in May (76).

- In Southern Ontario, 82.8% were willing to receive a vaccine and 17.2% were unwilling in a study conducted in January-February 2021 (77).
- A study in May 2021 demonstrated that most felt comfortable with the Pfizer (93%) and Moderna (89%) vaccines while less were comfortable with Johnson and Johnson (49%) and AstraZeneca (35%) vaccines. Women and those aged 55+ were more uncomfortable with the AstraZeneca (AZ) and Johnson and Johnson (J&J) vaccines compared to men and those <55. Of those who were uncomfortable with the AZ and J&J vaccines, 40% of women and 31% of men reported they would still accept these vaccine if offered (76).
- Three studies demonstrated that LGBTQ2+ were more willing to accept a vaccine compared to non-LGBTQ2+ (87.6% vs 76.4% in one study, OR=3.04, 95% CI: 1.08-8.55, p=0.04 in another, and 83.3% vs 77% in a third) (78-80).
- 71% of youth aged 12-17 intended to receive a vaccine in a survey conducted in January-February 2021 (81).
- Immigrants living in Canada for less than 10 years (80.3%) and more than 10 years (70.7%) had comparable intentions to vaccinate compared to non-immigrants (75.9%) (78). Another study showed that immigrants were slightly less likely to vaccinate (74.6%) than the general public (77%) but this varied greatly between older and younger immigrants (73.2% for 12-64 and 81.1% for those 65+) (80).
- Within visible minority groups in Canada, intention to vaccinate from lowest to highest was Black (57.0%), Latin American (58.5%), Filipino (64.2%), South East Asian (75.8%), other visible minorities (77.6%), Chinese (85.5%), and Arab (88.3%). 69.3% of those reporting an Aboriginal identity are accepting of a vaccine compared to 77.6% not reporting an Aboriginal identity (78).
- The highest intentions among visible minorities were Japanese (86.5%), Korean (85.6%), South Asian (82.5%), Chinese (79.3%), visible minority not indicated/multiple (79.1%), Southeast Asian (78.3%), West Asian (78.3%), Filipino (75.1%), Arab (68.1%), Latin American (66.0%), and Black (56.6%). Non-visible minority's intention to vaccinate was 77.6% (82).
- Intention to vaccinate among Indigenous respondents was 71.8% overall, which was significantly less than non-Indigenous respondents (77.1%). 74.2% of First Nations living off reserve were willing to vaccinate compared to 67.8% of Métis and 72.5% of Inuit. Older Indigenous people (65+) were more likely to want a vaccine compared to younger individuals (74.9% vs 71.3%) (82).
- In a survey of Indigenous residents of British Columbia, 68% stated they would like to be vaccinated as soon as possible or had been vaccinated compared to 58% of Asian and 66% of South Asian respondents (83).
- In British Columbia, intention to vaccinate was highest in East (61%) and South Asian (70%) continuing care workers. Latino and Black respondents were the most likely to refuse a vaccine (30%) and those with an Indigenous background were most likely to be unsure about their decision to vaccinate (40%). Indigenous respondents had the least amount of trust in all sources of information including healthcare providers (84).

- In Canada, those who voted Liberal or NDP in the 2019 election were more likely to indicate the intention to vaccinate compared to those who voted for other parties (58-60, 85).
- Rural participants were less likely to accept a vaccine compared to urban and suburban participants in three studies (10, 86, 87).
- Men were more likely to intend to vaccinate than women across 11 studies (58, 61, 77-79, 81, 88-92).
- The most common factors positively associated with intention to vaccinate were older age, higher education, adequate knowledge or health literacy, trust in experts and government, higher socioeconomic status, history of receiving an influenza vaccine, and heightened worry or concern about COVID-19.
- Concerns about vaccine safety and effectiveness were the two most cited reasons for vaccine refusal. Other commonly cited reasons include newness of the vaccine, and the belief that a COVID-19 vaccine is unnecessary.
- A recommendation to get the vaccine by a healthcare provider (e.g., doctor) had a positive impact on vaccine intention in five studies (74, 79, 83, 93, 94).
- Conspiracy beliefs were associated with decreased intentions to vaccinate (59, 90, 95).

Attitudes Toward Vaccine Rollout and Vaccine Passports

- Vaccine passports have high support in Quebec with 72% of residents in favour (12).
- 61% of respondents now agree that Canada should have vaccine passport, an increase from 54% in April (73).
- Two studies demonstrated high support for showing proof of vaccination when traveling by plane (79-82%), events with large crowds (69-75%), attending in-person university (71%) and lower support for showing proof of vaccination to stay in a hotel (68%), go to work (55-68%), or go to public places such as restaurants, bars, and movie theatres (55-64%) (73, 96).
- Of those who were vaccine hesitant, 7-18% of respondents across two surveys reported they could be swayed by the ability to travel, attend sporting or cultural events, or visit loved ones (11%) (96, 97).
- Of those who received an AstraZeneca vaccine, 2% fully regret getting it and 66% have serious second thoughts or doubts (76).
- 51-55% believed that Canada has done a good job procuring vaccine doses (75, 86).
- When asked about the vaccine rollout plan for British Columbia, 5% of residents rated the rollout as excellent, 30% good, 51% fair, 14% poor, and 7% very poor. Similar trends were seen for perceptions on clarity of the rollout and prioritization levels (98).
- 71% of respondents are comfortable with how the Manitoba government is determining priority groups for early vaccination (99).

- Approval of the overall vaccine rollout in Alberta was split, 48% were satisfied and 43% were dissatisfied. For the order of priority groups established by the government, 64% were satisfied and 28% were dissatisfied (100).
- In terms of vaccine distribution, 42% of Canadians believe their provincial government is doing a good job and 39% believe they are doing a bad job. Dissatisfaction was highest in AB, MB, and ON. Those in BC and QC were more approving (68).
- Two studies analyzed the perspective of experts on vaccination strategies for COVID-19. Public health experts agree that those who are the most vulnerable to severe illness and death from COVID-19 (e.g., long-term care residents, healthcare workers, those with chronic conditions, etc.) should be prioritized for vaccination (101, 102).

COVID-19 VACCINE ATTITUDES OF HEALTHCARE WORKERS

Evidence on COVID-19 vaccine attitudes of healthcare workers (HCWs) in Canada, Australia, New Zealand, UK, and the USA includes 42 studies. All studies targeted HCWs including nurses, doctors, and personal support workers. High level points from January 2021 onwards are listed below and detailed outcomes for each study are located in the Appendix (Table 4).

- The most recent studies show that intention to vaccinate in Canadian HCWs ranged between 57-82% (103-105). In the USA intention to vaccinate is between 55-93% (106-117).
- A participants' acceptance or rejection of a COVID-19 vaccine was not different between those employed within the healthcare sector compared to those not in the healthcare sector in one study from Canada (88). In the USA, two studies showed that HCWs were less likely to intend to vaccinate compared to the general population (115, 118) and two showed the opposite with HCWs having higher intentions to vaccinate compared to the general population (112, 119).
- Pregnant HCWs were 7.12 times more likely to be hesitant compared to non-pregnant HCWs (aOR 7.12, 95% CI: 4.74-10.70) (114).
- Doctors were significantly more likely to intend to vaccinate compared to nurses and other HCWs (37, 107, 110, 116, 117, 120).
- Seventeen studies demonstrated that male HCWs are more likely to intend to vaccinate than female HCWs (37, 84, 88, 105, 106, 109, 110, 114, 116, 117, 120-126).
- The proportion of those likely to get the COVID-19 vaccine was directly related to older age (37, 84, 88, 103, 105, 109, 110, 114, 116, 121, 123, 124), the likelihood of receiving an influenza vaccine (37, 84, 105, 109, 114, 126, 127) and an individuals' perceived risk of COVID-19 infection (105, 117, 123, 126).
- The main concerns about vaccination include safety, efficacy, insufficient knowledge about the vaccine, side-effects, speed of vaccination development, and believing that vaccination was not necessary (37, 84, 88, 103, 105, 106, 108-110, 112-114, 116, 119-121, 124, 126-130).
- A study of social service employees supporting individuals with intellectual disabilities in Ontario found that Indigenous, First Nations, and Metis (aOR 1.73, 95% CI: 0.67- 4.43), Latin (aOR 1.22, 95% CI:

0.21-7.24), and mixed ethnicities (aOR 1.11, 95% CI: 0.27-4.55) were more likely to refuse a vaccine compared to European ethnicity (105).

- In a Canadian study of personal support workers, 64.2% of respondents intend to vaccinate when it is available, 16.2% refuse to vaccinate, 10.7% are unsure, and 8.9% will only take the vaccine if it's mandatory. The majority (71.7%) do not believe there is enough clear education on the vaccine (131).
- In a study of 8634 non-physician HCWs in Ontario, 80.4% stated they intend to vaccinate. HCWs were more likely to intend to vaccinate if direct financial supports such as paid sick days were provided (103). Non-physician HCWs in Ontario, Canada who identified as Filipino (OR 1.07, 95% CI: 0.41-2.76, P<0.001), Caribbean (OR 3.20, 95% CI: 1.52-6.75, P<0.001), or other (OR 1.44, 95% CI: 0.93-2.22, P<0.001) ethnicity were more likely to refuse a vaccine compared to those who identified as European (103).
- In Quebec, Canada, 79.6% of nurses would definitely or probably recommend their patients vaccinate, 3.1% would not, and 17.2% were unsure. For themselves, 70.4% would definitely or probably be willing to receive the vaccine, 11.8% would refuse, and 17.8% were unsure (127).
- Two studies in the USA demonstrated that urban nurses were more willing to receive a vaccine than rural nurses when available (109, 132).
- Eleven studies evaluated intention to vaccinate in HCWs in the USA. Black HCWs were 12-84% less willing to accept the vaccine compared to White and Asian HCWs (106, 109, 112, 116, 118, 119, 121, 123, 125, 126, 133).
- Those who believed the vaccine would reduce their social isolation had higher odds of advising their patients to receive the vaccine (aOR 2.95, 95% CI: 1.32-6.59, P < 0.008) (113).
- In a UK survey of 220 general practitioners, over 50% had low confidence in counselling patients about COVID-19 vaccines (134).

COVID-19 VACCINE ATTITUDES OF HIGH-RISK POPULATIONS

It is important to develop evidence-based strategies to target high-risk populations for vaccination. Twenty-four were identified on COVID-19 vaccine attitudes in high-risk populations in Canada, Australia, UK, USA, and one global study including 16 countries. This includes older individuals, those with substance use disorders, those who are pregnant or breastfeeding, people experiencing homelessness, and vulnerable communities. High level points from January 2021 onwards are listed below and detailed outcomes for each study are located in the Appendix (Table 5).

- Pregnant women exhibited a low intention to vaccinate (41-62.1%) across three studies (19, 135, 136). Pregnant HCWs were 7.12 times more likely to be hesitant compared to non-pregnant HCWs (aOR 7.12, 95% CI: 4.74-10.70) (114). The most common reasons for hesitancy were potential side effects for their baby and the lack of safety and effectiveness data among pregnant women (19, 135, 136). Similar to the general population, women from lower-income households, aged < 25 years, history of

not accepting other vaccines, and ethnic minorities were more likely to reject a vaccine while pregnant (19, 135, 136).

- Intention to vaccinate and reasons for hesitancy were assessed in two studies in people experiencing homelessness in the USA (41, 137). One study showed that 51% would take a vaccine if offered, 32% would refuse, and 17% refused to answer (41). Common reasons for hesitancy included fear of side effects, wanting more information, concerns the vaccine makes people sick, and mistrust of the government (41, 137). Despite social exclusion and lack of access to technology, participants followed news reports about the vaccine and desired information about vaccine efficacy and safety (41).
- Intention to vaccinate was high (>79%) in six studies looking at older adults (65+) (15, 92, 138-141).
- In February, a community based vaccine site (Unidos en Salud UeS) was deployed to overcome barriers to COVID-19 vaccination faced by Latinx individuals in San Francisco. 56.1% reported they got vaccinated earlier because of the site and 65.3% reached out to 3 or more individuals to recommend the vaccine after their positive experience (3).
- In a survey of 391 Amish families from Ohio, 75.7% did not plan to vaccinate their children against COVID-19 and Swartzentruber Amish were significantly less likely to intend to vaccinate compared to other Amish affiliations (142).
- A qualitative study of vulnerable communities (e.g., homeless, mental health issues, and Gypsy, Roma, and Travellers) reveals general apprehension, skepticism, and low levels of trust pertaining to COVID-19 vaccine trials. Unique barriers were shown in each group such as a reluctance to go to the hospital, loss of confidentiality, concerns about animal products in vaccines, and belief of hidden agendas of vaccine developers and the government that should be taken into consideration when developing vaccine confidence plans (143).
- Of 87 individuals with substance use disorders in the USA, 48% were either unsure or unwilling to receive a vaccine if it were available. Reasons for hesitancy included the rush of vaccine development, potential side-effects, not believing themselves to be high risk, and worry about interactions with pre-existing conditions (144).
- Compared to former smokers and those who have never smoked, current smokers were both the most undecided (27.6 (95% CI: 26.1-29.1)) and unwilling (21.5% (95% CI: 20.2-22.9%)) to intend to vaccinate (145). In another study, willingness to receive a vaccine did not significantly differ between cannabis users and controls ($t88$ = 0.33, P = 0.74; BF_{01} = 4.3) (146). A study conducted in the USA found that the use of cigarettes, e-cigarettes, marijuana, and heavy drinking was not associated with vaccine hesitancy (147).
- Willingness to receive a COVID-19 vaccination was positively associated with the belief that the COVID-19 outbreak is going to continue for a long time, perceived severity of the disease, personal health consequences, and health consequences to others (138, 139, 148, 149).
- Similar to the general population, intention to vaccinate was positively associated with male gender (139, 150), higher education (135, 136, 139), higher income (135, 139, 150), White ethnicity (136, 139), past acceptance of flu vaccination (136), and older age (135).

- A recommendation to get the vaccine by a healthcare provider (e.g., a doctor) had a positive impact on vaccine intention in two studies on older adults (139, 141) but made little difference in pregnant women (135).

COVID-19 VACCINE ATTITUDES OF INDIVIDUALS WITH COMORBIDITIES

Twenty-three studies with evidence on COVID-19 vaccine attitudes in individuals with comorbidities in Canada, Australia, UK, and the USA were identified. There was a range of comorbidities including obesity, hypertension, chronic respiratory or autoimmune diseases, HIV, and intellectual and developmental disabilities. High level points from January 2021 are listed below and detailed outcomes for each study are located in the Appendix (Table 6).

- The majority (15/23) of studies were conducted in the USA followed by Canada (1/23), Australia (2/23), the UK (4/23), and a combination of the US/UK (1/23).
- In a study from Canada, 64.6% of those who are overweight or obese were comfortable receiving a vaccine and 35.4% were hesitant (151). Comfort levels in receiving the vaccine were positively associated with male gender, having more comorbidities, having lower depression scores, not practicing social distancing, and past acceptance of influenza vaccinations (151).
- One study demonstrated there were no significant differences in willingness to vaccinate for COVID-19 between people with hypertension compared to healthy matched controls (152). Another indicated that those who reported chronic respiratory diseases were 5.7% more willing to be vaccinated (95% CI: 0.05-0.09) compared to healthy controls (153).
- In a group of 97 cancer patients and their caregivers from the USA, intention to vaccinate increased from 71% to 82.5% after attending an educational webinar on COVID-19 vaccines specific for cancer patients and caregivers (154).
- In a study conducted at an urban dialysis center which serves a predominately Black patient population in the USA, 49% of respondents indicated they would be willing to receive a COVID-19 vaccine, 34% were unwilling, and 17% were unsure (155).
- If a vaccine was offered at a dialysis facility, vaccine hesitancy in patients on hemodialysis in the USA would decrease from 20% to 18% (156).
- Three studies analyzed intention to vaccinate in disabled adults. Two demonstrated that disabled adults had slightly less vaccine hesitancy compared adults who were not disabled in the UK (43, 140) and Australia (141). The other indicated that 62% would definitely or probably get a COVID-19 vaccine in the USA (157).
- A study of 101 Black people living with HIV in the USA demonstrated low intentions to vaccinate (32%). Low education and COVID-19 related mistrust were both associated with an increase in vaccine hesitancy (158).

- In a group of patients who received care for chronic gastrointestinal and liver conditions in the USA, they were more likely to follow their specialists' recommendation about receiving a vaccine (91%) compared to the government or their doctor (75%) or their employer (56%) (159).
- The most common reasons for hesitancy included concern about side effects, concerns about existing health conditions, lack of adequate information, mistrust in the government, and worries about long-term effects (140, 141, 155, 156, 158-163).
- Similar to the general population, intention to vaccinate was positively associated with male gender (156, 159-161, 164, 165), having more comorbidities (164, 166), higher education (148, 149, 156, 160, 165), higher income (149, 159, 165), White ethnicity (149, 156, 160), past acceptance of flu vaccination (155, 156, 159, 160, 162, 164, 165), and older age (149, 156, 157, 159-161).

COVID-19 VACCINE ATTITUDES OF OTHER POPULATIONS OF INTEREST

Sixty-one studies were identified on COVID-19 vaccine attitudes in other populations of interest in Canada, Australia, New Zealand, UK, and the USA. These populations include the LGBTQ+ community, parents, those with religious affiliations, immigrants, youth (aged 14-24), those with past SARS-CoV-2 infection, and urban and rural communities. High level points from January 2021 are listed below and detailed outcomes for each study are located in the Appendix (Table 7).

LGBTQ+

- Seven studies assessed intention to vaccinate in LGBTQ+ individuals in Canada (78-80) and the USA (167-170). Three studies demonstrated that LGBTQ2+ were 6-25% more willing to accept a vaccine compared to non-LGBTQ2+ (78, 80, 168). Two studies indicated that non-binary, pansexual, gender queer, agender, two-spirit or other were significantly more 1.6-4.38 times more likely to receive a vaccine (79, 169). Compared to gay men, participants grouped in the "Other" sexual identity (e.g., bisexual, queer, multiple identities, same-gender loving) were less likely to intend to vaccinate ($\beta = -1.102$, $P = 0.047$) (167).

Rural vs Urban Communities

- Differences in intention to vaccinate were analyzed in urban and rural residents in twelve studies. Eleven demonstrated that urban residents were marginally more likely to intend to vaccinate compared to rural residents (10, 86, 87, 109, 115, 166, 171-175), and one indicated the opposite (176).

Religious Affiliations

- Twelve studies evaluated the impact of religion on intention to vaccinate in the USA and UK, all of which associated some religions with vaccine hesitancy (126, 171, 174, 176-183). One study demonstrated that those who reported Hinduism or Judaism as their religion were more likely than atheists or agnostics to accept a vaccine (OR 1.66, 95% HPDI: 1.11-2.43) and those who reported their

religion as Muslim (OR 0.75, 95% HPDI: 0.57-0.96) or other (OR 0.72, 95% HPDI: 0.62-0.82) were less likely to intend to vaccinate (178).

- In a UK study, those reporting Christian faith were significantly more likely to get a vaccine if vaccine passports were introduced for domestic (aOR 1.23, 95% CI: 1.08-1.41) and international (aOR 1.22 95% CI: 1.07-1.39) travel compared to atheists and agnostics (20).
- A quasi-experimental study of 709 unvaccinated registered voters in South Dakota, USA demonstrated that messaging from a religious leader had statistically significant positive effect intention to vaccinate, while messages from a political or medical leader did not (21).
- Strong vaccine hesitancy was reported in a study of 102 Haredi-Orthodox Jewish adults in New York from Dec 2020-Jan 2021 with 12% of respondents willing to accept a vaccine for themselves and their family, 47% strongly hesitant, and 41% undecided. Independent predictors of vaccine hesitancy were the belief that natural infection was better than a vaccine for developing immunity, agreement that prior SARS-CoV-2 infection with antibodies precludes need to mask or practice social distancing, and loss of trust in physicians resulting from the pandemic (183).
- In a Quebec study, 28% of respondents who did not intend to receive a vaccine believe vaccination is incompatible with their religious beliefs or personal principles (90).

Parents

- Ten studies reported participants were more willing to accept a COVID-19 vaccine for themselves than for their children (16, 19, 94, 135, 151, 164, 184-187). One study showed parents were more likely to vaccinate their children compared to themselves (188). Those with younger children (aged 0-4) were more hesitant compared to those with children over the age of 5 (14, 16, 43).
- Parental and child vaccine intentions are highly correlated with each other, with parents who were intending to take a vaccine more likely to intend to vaccinate their children (11, 13-16, 151). Similar to the general population, parents from lower-income households (11, 14, 16, 19, 188), who are younger (17, 19, 188, 189), less educated (14, 16, 17, 184, 188), have a history of not accepting other vaccines (17, 19, 189), who are female (14, 16, 17, 188) and ethnic minorities (16-19, 185) were more likely to reject a vaccine for their children.
- A study of 380 parents with children aged 2-17 in Montreal revealed that parents were 61% very likely, 25% somewhat likely, 9.2% somewhat unlikely, and 4.5% very unlikely to have their child vaccinated. Visible minority parents were more likely to reject a vaccine for their children compared to non-visible minority parents (32.9% vs. 9.5%) (18).

Youth

- In a text message poll of 911 youth aged 14-24 across the United States, 80.7% reported willingness to vaccinate if proven safe and recommended. Black youth (OR = 3.31) were more likely to refuse vaccination and Asian youth (OR = 0.46) were less likely to refuse vaccination compared to White youth ($P < 0.001$) (190).
- 71% of Canadian youth aged 12-17 intended to receive a vaccine in a survey conducted in Jan-Feb 2021 (81).

Immigrants

- In a sample of 32 immigrants in the UK, 28% report they will definitely get a vaccine, 59% were unsure, and 6% would decline (191). Two UK studies demonstrate multiple barriers to vaccination for migrants such as access to technology, not having a doctor, access to vaccine information in their own language, not having vaccines at frequently used places such as walk-in clinics and charities, and clear communication that the vaccine would be provided at no cost (191, 192).
- In an Australian study, those born overseas were more likely to report intention to vaccinate compared to those born in Australia (70.7% vs 67.2%). This was more apparent for those who arrived within the last ten years (74.6%) compared to those arriving more than 10 years ago (69.1%) (141).

Past SARS-CoV-2 Infection

- Two studies from the USA demonstrate that those with a previous SARS-CoV2- infection were less likely to intend to vaccinate that those with no previous infection (115, 193).

Methods

Prior to the initiation of this rapid review, a pre-defined rapid review protocol was developed to ensure the methods were reproducible, transparent, and consistent. The protocol is available upon request. This rapid review will be kept evergreen and updates will contain key research articles published up to the latest search date.

Publications and Pre-prints

A daily scan of the literature (published and pre-published) is conducted by the Knowledge Synthesis team in the Emerging Science Group, Public Health Agency of Canada. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square, and COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The cumulative scan results are maintained in a Refworks database and an excel list that can be searched. Details on this search strategy are available upon request. From this database and excel list, article titles and summaries will be systematically searched for the following key words: ("vaccin*" OR "immuni*") AND ("accept*" OR "hesitan*" OR "preference" OR "confidence" OR "intent*" OR "willing*" OR "readiness" OR "behavio*" OR "knowledge" OR "attitude*" OR "belief*" OR "believe*" OR "perception" OR "influence*" OR "reject*" OR "refus*" OR "oppos*" OR "consent*" OR "fear" OR "motiv*" OR "anti vax*" OR "antivax*" OR "trust*" OR "mistrust*" OR "anti vaccin*" OR "pro vaccine*" OR "provax*" OR "pro vax" OR "decision*" OR "decid*" OR "uptake"). The original search was conducted on October 16, 2020. The first update was conducted on November 30, 2020, the second update on January 5, 2021, the third on February 3, 2021, the fourth on March 2, 2021, the fifth on April 2, 2021, the sixth on May 3, 2021, the seventh on June 3, 2021, and the eighth on July 2, 2021.

Grey Literature

A grey literature search was conducted to compliment the database search. The grey literature search focused on Canadian research only. Where time permits, the grey literature search will be extended to include research from Australia, New Zealand, the United States, and the United Kingdom. A detailed list of websites

searched is available in the protocol. The original grey literature search was conducted on November 5-6, 2020. The first updated grey literature search was conducted on December 9-10, 2020, the second on January 4, 2021, the third on February 1-2, 2021, the fourth on March 7, 2021, the fifth on April 13-22, 2021, the sixth on May 3-7, 2021, the seventh on June 9-11, 2021, and the eight on June 28-30, 2021.

Quality of Survey Instrument

Three criteria which determine the quality of the survey instrument were reported. These include the availability of the survey tool in the report, the use of formative research to design the survey, and evidence of pre-testing the survey. A yes or no was provided for each criteria. If the information was not reported, the answer no was selected. These criteria evaluate the degree to which the survey items evaluate the theoretical concepts the survey is focused on, are comparable to other surveys and whether the instrument was comprehensive, clear and valid when applied to the target population. There is an increased risk of bias when these features are missing (194).

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX: EVIDENCE TABLES

VACCINE UPTAKE & ADHERENCE TO PUBLIC HEALTH MEASURES POST-VACCINE

Table 1. Evidence of vaccine uptake and adherence to public health measures post-vaccination (n=37)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
VACCINE UPTAKE		
HEALTHCARE WORKERS		
CANADA		
Dzieciolowska (2021) (1) *new* Cross-sectional study Canada Dec 2020	Vaccine uptake was evaluated through an online survey in 2,761 nurses, physicians, orderlies, hospital administration working in 17 health institutions in Montreal to determine factors that are predictive on uptake. All HCWs were offered a vaccine. Question Topics: 1) Vaccine uptake 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 80.9% of those offered a vaccine accepted and 19.1% refused. • Multivariate analysis revealed that men (aOR 1.62, 95% CI: 1.16-2.26), those aged 50-59 (aOR 1.62, 95% CI: 1.07-2.44) or 60+ (aOR 3.28, 95% CI: 1.74-6.18), had occupational contact with COVID-19 patients (aOR 3.88, 95% CI: 2.29-6.58), or worked in rehabilitation centers (aOR 1.76, 95% CI: 1.17-2.66) were more likely take a vaccine when offered. • The most common concerns or reasons for refusal among those who did not accept a vaccine were the newness of the vaccine (82%), preferred that others get vaccinated first (77%), felt they lacked information about the vaccine (74%), and that they did not have enough time to make a decision (60%). • 74.1% of those that declined a vaccine reported they will accept a vaccine in the future with 53.2% wanting to delay a few months and 31.9% wanting to wait a year. • Those who never plan on accepting a vaccine were more likely to cite not trusting experts or pharmaceutical companies, preferring natural immunity, belief that the risk of vaccination outweighed risk of COVID, or that they had a past poor vaccine reaction.
USA		

Fossen (2021) (34) Cross-sectional study USA Jan-Mar 2021	This study aimed to assess vaccine uptake among 3,401 employees at a 437-bed hospital in Arlington, Virginia who were eligible to receive a COVID-19 vaccine starting in Jan 2021. Question Topics: 1) Vaccine uptake	• As of Mar 10, 2021, 71% had accepted a first dose of a COVID-19 vaccine. • Vaccine uptake was positively associated with being aged 50+ (OR 1.85, 95% CI: 1.53–2.24, P<0.01), working in a clinical department (OR 1.19, 95% CI: 1.01-1.42, P=0.02), and White race (OR 4.55, 95% CI: 3.74–5.52, P<0.01).
Jameson (2021) (31) Cohort study USA Dec 2020-Mar 2021	During a vaccination program in a medium-sized urban hospital in the Midwest region of the USA starting in Dec 2020, the BNT162b2 vaccine was offered to all 4,318 HCWs. The study aimed to determine vaccine uptake and the effectiveness of the vaccine in those who were vaccinated.	• As of Mar 24, 2021, 70% had accepted a vaccine and 30% had refused.
Oliver (2021) *preprint* (30) Cross-sectional study USA Dec 2020-Feb 2021	All staff in two large integrated healthcare systems (one private and one public) in New York City were eligible to receive a COVID-19 vaccine starting on Dec 14, 2020. An online survey of 1,933 HCWs who were offered the vaccine was conducted to assess vaccine uptake and reasons for acceptance and refusal. Question Topics: 1) Vaccine uptake Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• Of those offered the vaccine, 81% reported they had received it, 11% plan to get it but had not scheduled their appointment, and 8% chose not to receive the vaccine. • In the bivariate analysis, vaccine uptake was higher in males compared to females (88% vs 80%, p<0.001). Those who were under 40 (86%) and older than 60 (85%) had higher uptake rates compared to those 40-49 (79%) and 50-59 (74%), P<0.001. Also, non-Hispanic or undisclosed ethnicity (84%) were more likely to get a vaccine compared to Hispanic HCWs (69%), P<0.001. • In the multivariate analysis, Black HCWs were less significantly likely to get a vaccine compared to White HCWs (OR 0.38, 95% CI: 0.24-0.59, P<0.001). Compared to physicians, nurses (OR 0.37, 95% CI: 0.21-0.65, P=0.001), administrative, logistics, and management positions (OR 0.46, 95% CI: 0.36-0.78, P=0.006), and allied health

		professionals (OR 0.48, 95% CI: 0.27-0.81, P=0.007) were less likely to get the vaccine. • Those who did not receive the flu vaccine were less likely to get the vaccine compared to those who did (OR 0.28, 95% CI: 0.18-0.44, P<0.001). • Those who expressed concern about vaccine safety (OR 0.39, 95% CI: 0.28-0.55, P<0.001), concern about being experimented on (OR 0.44, 95% CI: 0.31-0.60, P<0.001), and who did not agree with statements about the vaccine's importance in protecting others (OR 0.37, 95% CI: 0.27-0.52, P<0.001) were less likely to get the vaccine.
Amin (2021) (27) Cross-sectional study USA Jan 2021	All HCWs in an emergency department at a large urban public hospital in Chicago, IL were eligible to receive the vaccine starting on Dec 17, 2020. Associations with vaccine uptake was assessed using an online survey of 240 HCWs. Question Topics: 1) Vaccine uptake Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 92% reported they received the vaccine or are scheduled to and 8% reported they will not be getting the vaccine. • Vaccine acceptance rates varied by profession with physicians having higher uptake rates compared to nurses and radiology technicians. • Of the 8% who declined vaccination, the majority identified as Black (65%) and were 51–60 years old with varying job categories. • Reasons for declining a vaccine included having previous COVID-19 infection, and concerns over the vaccine being new, and worry about side effects.
Schrading (2021) (22) Cross-sectional study USA Jan 2021	Three weeks after COVID-19 vaccination was offered to emergency department healthcare professionals (ED HCPs) across 20 high-volume urban academic medical centers, an online survey was conducted in 1321 of these individuals who were offered the vaccine. The goal was to describe differences in vaccination rates	• 86% of those who were offered the vaccine chose to receive it and 14% declined. • Among physicians and advanced practice providers, 37/674 (5.5%) declined the vaccine compared to 77/345 (22.3%) of nurses and 71/302 (23.5%) of non-clinical HCPs. Of those who declined a vaccine, the most common reasons were safety concerns (45.4%), health conditions (13.5%), and previous COVID-19 diagnosis (13.5%).

	among various types ED HCPs and reasons for declining vaccination. Question Topics: 1) Vaccine uptake Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Non-Hispanic Black HCPs had the lowest uptake rates (65.4%) followed by Hispanic or Latinx (76.7%). The highest uptake rates were in Non-Hispanic Other (88.9%), Non-Hispanic White (88.5%), and Non-Hispanic Asian (87.3%) HCPs. • Men had higher uptake rates (93.5%) compared to women (88.5%). • After vaccination, recipients stated they felt safer (86.7%) and those in their households felt safer (87.1%). Vaccinated recipients planned to use the same amount of PPE at work (89.8%) and in public (91.8%).
Pamplona (2021) (33) Cross-sectional study USA Jan 2021	Vaccine uptake and hesitancy during a vaccine program implemented between January 13-21, 2021 was recorded in 157 staff members from four Renal Research Institute clinics and one home dialysis program in New York. Question Topics: 1) Vaccine uptake 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 73.2% were vaccinated and 26.8% were unvaccinated. • 3.8% of staff reported vaccine hesitancy and did not receive a vaccine. Reasons were not reported. • The remainder of the staff who were not vaccinated included: those on a leave of absence (2.5%), pregnant or breastfeeding (5.1%), and those with past SARS-CoV-2 infection (15.3%). • Staff with a history of confirmed SARS-CoV-2 infection > 90 days ago or at some unknown time in the past were offered vaccination, but wished to receive the vaccine later.
UK		
Bell (2021) *preprint* (32) Cross-sectional and qualitative study UK	1658 healthcare workers and 261 social care workers completed an online survey and 20 participants were interviewed to gain insights into the beliefs, attitudes, and behaviours with regard to vaccination. Question topics:	• 1762 (91.9%) participants had been offered vaccination. Of those, 6.6% had declined or will decline the vaccine. • Compared to their counterparts, higher levels of declining the vaccine were seen in Black or Black Caribbean (22%), those aged 25-35 (8.4%), and Christian (6.7%) religion. • Odds of declining a vaccine were significantly increased if respondents were Black/Black British/Black mixed (aOR 5.5, 95% CI: 2.2-13.4),

Jan-Mar 2021	1) Vaccine uptake 2) Vaccine perceptions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	felt that they were under pressure from their employer to get the vaccine (aOR 1.75, 95% CI: 1.2-2.4), or were worried about side effects (aOR 1.68, 95% CI: 1.1-2.4). • Odds of accepting a vaccine were significantly increased if a flu vaccine was taken in the past two years (aOR 0.27, 95% CI: 0.1-0.47) and the combined belief that vaccines are safe, important, and effective (aOR 0.51, 95% CI: 0.3-0.8). • Reasons for declining or planning to decline a vaccine included worry about side effects (51%), concern over lack of research (50%), and concerns about effectiveness (21%). • The most common reasons for vaccinating were to protect friends/families (64%), to protect themselves (57%), and protect patients (28%). • Black or mixed Caribbean respondents were less likely to perceive the vaccine as safe, as important to protect themselves or families, believe that vaccination is required to get back to normal, believe that their friends and family do not expect them to get a vaccine, and are more concerned about side effects. • For the interview portion, all participants had been offered vaccination, 13 had been vaccinated, and 7 had declined. • Interviews revealed issues of access (lack of clarity for those not in the National Health Service to get vaccinated), perceptions of risk and severity (low perceived risk associated with not requiring a vaccine), low trust (in the vaccine, policymakers, and in pharmaceutical/health industry), vaccine effectiveness, vaccine importance to protecting other or to return to normal, pressure to vaccinate, concerns about allergies, impact on childbearing, wanting more vaccine information, and wanting assurances the vaccine was halal.

Martin (2021) *preprint* (25) Cross-sectional study UK Dec 2020-Feb 2021	Associations with vaccine uptake was assessed in 19,044 HCWs from one of the largest acute hospital trusts in the UK. All staff were eligible to receive the BNT162b2 mRNA ChAdOx1 nCoV-19 vaccines starting on Dec 12, 2020. Question Topics: 1) Vaccine uptake	• As of Feb 3, 2021 the proportion of HCWs who received one-dose of the vaccine was 64.5%. • The number of vaccinations per week peaked the week of Jan 11-17 and has been declining since. • Vaccine uptake was positively associated with increasing age (≤30 years: aOR 0.48, 95% CI: 0.44-0.53; 51-60 years: aOR 1.19, 95% CI: 1.07-1.31 compared to age 41-50) and male gender (aOR 1.24, 95% CI: 1.15-1.35). • Compared to White HCWs, vaccine uptake was lower in those of Black (aOR 0.30, 95% CI: 0.26-0.34) and South Asian ethnicity (aOR 0.67, 95%CI: 0.62-0.72). • Those with a history of SARS-CoV-2 infection were less likely to vaccinate (aOR 0.71, 95% CI: 0.60-0.85). • Those living in the most deprived areas were less likely to vaccinate (P<0.001).
Hall (2021) *preprint* (26) Cohort study UK Dec 2020-Feb 2021	The SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study is a prospective cohort study of 23,324 staff working across 36 publicly funded hospitals. Starting in Aug 2020, baseline risk factors, vaccination status, symptoms, and results from PCR and antibody testing were recorded at bi-weekly intervals. The study aimed to determine factors associated with vaccine uptake and the effectiveness of the BNT162b2 mRNA vaccine in those who were vaccinated. Question Topics: 1) Vaccine uptake	• As of Feb 5, 2021 the proportion of staff who received one and two doses of the vaccine were 89% and 8%, respectively. • Vaccine uptake was significantly lower in those with prior SARS-CoV-2 infection (aOR 0.59, 95% CI: 0.54-0.64), females (aOR 0.72, 95% CI: 0.63-0.82), under 35 years old (aOR 0.78, 95% CI: 0.64-0.96), from Black, Asian, or minority ethnic groups (aOR 0.26, 95% CI: 0.21-0.32), who lived in neighbourhoods of higher deprivation (aOR 0.75 , 95% CI: 0.65-0.87), and who worked as a porter/security/estates (aOR 0.61, 95% CI: 0.42-0.90) or midwife (aOR 0.74, 95% CI: 0.57-0.97).

Tulloch (2021) *preprint* (28) Cross-sectional study UK Jan 2021	All staff and residents in 87 care homes within the Liverpool City Council area were eligible to receive a COVID-19 vaccine starting on Dec 23, 2020. An online survey of 46 staff managers was conducted to determine associations with vaccine uptake and reasons for hesitancy. This survey was self-reported and the views of staff were compiled by one senior member of the care home. Therefore it is possible that this may not reflect the views of all staff members. Question Topics: 1) Vaccine uptake	• 52.6% (n=1119) had received their first vaccination with a mean vaccination rate per care home of 51.4% (95% CI: 43.9-58.8%). • The most common reasons for not receiving the vaccine were concerns about lack of vaccine research (37.0%), staff being off-site during vaccination sessions (36.5%), pregnancy and fertility concerns (5.6%), and concerns about allergic reactions (3.2%). • If logistical issues were resolved (e.g., staff member not on site the day vaccines were being administered), the mean vaccination rate per care home could have increased to 69.8% (95% CI: 63.2-76.3%). • Staff reported methods that would help address vaccine hesitancy included one-on-one meetings to discuss concerns (34.8% of care homes), staff meetings (15.2%), educational material (15.2%), individual discussions with general practitioners or the vaccination team (10.9%), and managers leading by example and encouragement (6.5%).
Azamgarhi (2021) (29) Cohort study UK Jan 2021	This study aimed to assess vaccine uptake and efficacy of the Pfizer BioNTech vaccine among 2260 healthcare workers at a tertiary hospital. All staff were offered their first dose of the vaccine over an 8-day period up to Jan 14, 2021. Question Topics: 1) Vaccine uptake	• 62.3% of staff received one-dose of the vaccine. Uptake increased to 72.9% after specific measures were implemented by a vaccine hesitancy working group. • Vaccine uptake was higher in men compared to women (67.3% vs 61%, P=0.004). • White (72.6%) and Asian (68.1%) HCWs were the most likely ethnic groups to vaccinate. Black/Afro-Caribbean (28.5%) and mixed-race (45%) were the least likely (P = 0.001). • By occupation, the highest vaccine uptake rates were seen in surgeons and medics (79.2%), allied health professionals (78.3%), and administration and clerical staff (73.3%). The lowest rates were in nursing (55.5%), clinical support staff (50.4%), and porters, domestic and catering staff (31.6%) (P = 0.001).

		• Vaccine uptake increased with age. 70.7% of those 55 or older received the vaccine, followed by 65.7% of those aged 35-54 and 51.9% of those aged 16-34.
ISRAEL		
Jabal (2021) (23) Cohort study Israel Dec 2020-Jan 2021	This study had two purposes: 1) to report on vaccine uptake in ~1500 HCWs located in a single medical center, and 2) to describe immunogenicity 21 days post-dose 1 BNT162b2 mRNA COVID-19 vaccine among 514 HCWs. Starting in Dec 2020, the vaccine was offered to all staff. Question Topics: 1) Vaccine uptake	• As of Jan 21, 2021 the proportion of HCWs who received one-dose of the vaccine was ~90%.
Amit (2021) (24) Cohort study Israel Dec 2020-Jan 2021	This study had two purposes: 1) to report on vaccine uptake in 9109 HCWs located in a single medical center, and 2) to evaluate reductions in SARS-CoV-2 infection and COVID-19 rates in BNT162b2 COVID-19 vaccinated HCWs. Starting in Dec 2020, the vaccine was offered to all staff. Question Topics: 1) Vaccine uptake	• As of Jan 24, 2021, the proportions of HCWs who received one and two doses of the vaccine were 79% and 66%, respectively.
PEOPLE EXPERIENCING HOMELESSNESS		
Kuhn (2021) *preprint* (41) Cross-sectional study USA	The level of vaccine uptake and hesitancy among 90 individuals experiencing homelessness in Los Angeles (18+) was evaluated using a mobile phone survey. Question Topics:	• Of the 90 participants, 17 were offered a vaccine of which 10 accepted and 7 refused. • Among the 73 who were not offered the vaccine, 51% said they would take it if offered, 32% would refuse, and 17% refused to answer. • Together, 48% refused a vaccine when offered, would refuse when offered, or refused to answer and were deemed "vaccine hesitant".

Dec 2020-Feb 2021	1) Vaccine uptake 2) Vaccine hesitancy 3) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Of those who were vaccine hesitant, the most common reasons were fear of side effects (37%), wanting to have more information (30%), and they don't get any vaccines (27%). • A multivariate analysis, those with a high COVID-19 threat perception (OR 0.25, P=0.02), and those who trusted official sources (OR 0.37, P=.08) were significantly less likely to be vaccine hesitant. Those who engaged in highly protective behavior (OR 3.63, P=0.02) and who trusted personal contacts (OR 2.70, P=0.07) were more likely to be hesitant.
PRISONS		
Chin (2021) (38) Cross-sectional study USA Dec 2020 – Mar 2021	The California Department of Corrections and Rehabilitation (CDCR) launched a vaccination program for residents of its 35 prison facilities on Dec 22, 2020. Of the 97,779 incarcerated residents, 64,633 were offered a vaccine. Question Topics: 1) Vaccine uptake	• 66.5% accepted at least one vaccine dose, and 33.5% refused. Among those who had initially declined and were subsequently reoffered vaccination (n=1,962), 45.9% accepted at least one dose. • Vaccine uptake was highest among Hispanic residents (72.6%, 99.6% CI: 72.1-73.1) and White residents (72.1%, 99.6% CI: 71.3-72.9), followed by American Indian or Alaska Native residents (67.7%, 99.6% CI: 64.4-71.0), Asian or Pacific Islander residents (67.7%, 99.6% CI: 64.8-70.6), and Black residents (54.9%, 99.6% CI: 54.3-55.5). • Those who were older and medically vulnerable were more likely to accept a vaccine compared to younger and healthier residents.
Berk (2021) *preprint* (37) Cross-sectional study USA Dec 2020 – Feb 2021	Vaccine uptake was assessed among 1,474 staff and 1,447 incarcerated individuals at the Rhode Island Department of Corrections who were offered a vaccine. The vaccine program started on Dec 22, 2020 and all first doses were administered by Feb 5 and second doses by Mar 5, 2021.	• Of the correctional staff, 68.4% accepted a vaccine and 31.6% refused. Reasons for refusal were not reported. • Of all of the incarcerated individuals, 76.4% accepted a vaccine and 23.6% refused. Reasons for refusal were not reported • In round 1 of the highest-risk incarcerated individuals (n=143), 90.9% accepted and 9.1% refused a vaccine.

	The vaccine was offered in 4 rounds: 1) highest-risk individuals (aged 65+ or 55+ with specific comorbidities), 2) smaller facilities in attempt to achieve herd immunity, 3) the largest remaining security facility: Medium Security, and 4) all individuals who had previously tested positive for COVID-19 within 90 days and individuals who had initially declined but subsequently accepted. Question Topics: 1) Vaccine uptake	• 64.5% accepted the vaccine and 34.6% refused during round 2 of the smallest facilities (n=222). • Of those in the largest security facility (n=730) during round 3, 82.9% accepted and 17.1% refused a vaccine. • In the last round of the remaining incarcerated individuals (n=352), 64.8% accepted a vaccine and 35.2% refused.
MILITARY UNITS		
Segal (2021) (55) Cross-sectional study Israel Dec 2020 – Feb 2021	Vaccination uptake rates between frontline battalions and highly essential military units (group A, n=12,642) and rear administration and support military units (group B, n=6,077) were compared. This included 70 military units comprised of 18,719 individuals of both sexes, mostly free of significant comorbidities. The vaccine program started at the end of Dec, 2020. Question Topics: 1) Vaccine uptake	• As of Feb 18, 2021, 84.8% of the entire study population had received their first dose of a COVID-19 vaccine, 3.88% had a previous SARS-CoV-2 infection, and 11.34% refused a vaccine. • Vaccine uptake was higher in Group A compared to Group B (86.4% vs 81.4%, P<0.001). Group A had a slightly lower mean age and a higher number of men (P <0.001), but similar cumulative SARS-CoV-2 cases rates (P = 0.677).
Talmy (2021) (39) Cross-sectional study Israel	This study aimed to assess real-world vaccine uptake joined with primary care communication efforts including group lectures, on-site consultations, and primary care office visits. Vaccine intentions were capture by telephone survey	• Prior to the vaccine campaign, 77.7% of soldiers intended to vaccinate, 17.6% intended to refuse, and 4.7% were unsure. • 70.3% attended a group lecture, 6.5% arrived for on-site physician consultation, and 3.7% attended primary care clinic visits.

Dec 2020 - Feb 2021	prior to the vaccine campaign. During the campaign, 511 soldiers in a military unit were offered a vaccine. The vaccination site operated during two different sessions. Those who refused vaccination following the initial session were contacted to set voluntary appointments for clinic visits to discuss their specific concerns. Question Topics: 1) Vaccine uptake 2) Vaccine intentions	• Of the 90 soldiers who stated they did not intend to receive a vaccine, 60.0% attended the group lectures, 31.1% arrived for on-site consultation, and 16.7% attended primary care visits to discuss their motives and concerns. • Between Jan 3 and Feb 18, 2021, 89.8% of soldiers received at least one dose of the vaccine. • Of the 90 soldiers who did not intend to receive a vaccine, 42.2% decided to receive a vaccine. • 47.4% of the 28 soldiers not intending to vaccinate and arriving for on-site physician consultation proceeded to vaccinate (P = 0.004).
OLDER ADULTS (70+)		
Office for National Statistics (2021) *unpublished* (35) Cross-sectional survey UK Feb 2021	Responses of 2070 adults over 80 years old were collected through an online survey to determine vaccine coverage, attitudes, and vaccinations effect on protective behaviors. Question Topics: 1) Vaccine uptake 2) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 99.8% reported that they had been offered a vaccine, 99% of which had taken at least one dose and 15% had two doses. • 41% reported common side effects including tenderness in the arms where they received an injection (26%). • 63% report that the side effects experienced would not affect their decision to get the second dose and 35% said side effects made them more likely to get a second dose. • 96% would encourage others to get vaccinated. • 86% would likely get a COVID-19 test if they developed COVID-19 symptoms. • Almost half (49%) perceived COVID-19 to be a major risk to themselves before receiving a vaccine. This decreased to 19% after receiving one dose.
Malesza (2021) *preprint* (36)	Associations with vaccine uptake were assessed in 1427 older adults (70+) living among the general public using structured interviews.	• 62.7% had been given the vaccine and 37.3% said they were unwilling to get vaccinated. • The two most significant independent predictors of vaccine uptake was receiving an explanation

Cross-sectional study Poland Jan-Feb 2021	A mass vaccination program began in the last weeks of 2020. The Minister of Health recommended that every individual aged 70+ should be encouraged to receive the COVID-19 vaccination. It is assumed that at the time of these interviews, all individuals aged 70+ were encouraged and able to receive the vaccine. Question Topics: 1) Vaccine uptake Survey tools available? No Formative research conducted? No Survey pre-tested? No	by a medical professional as to why they should be vaccinated (OR 4.23, 95% CI: 2.90-5.75) and living with others (OR 3.13, 95% CI: 2.03-4.26). Other predictors included being able to travel independently to their general practitioner (OR 1.92, 95% CI: 1.45-2.76), having chronic illnesses (OR 2.98, 95% CI: 2.05-4.01), higher socio-economic status (OR 1.79, 95% CI: 1.33-2.15), and male gender (OR 1.22, 95% CI: 0.67-1.98). • The top reasons people accepted the vaccine were self-protection (90.6%), to protect close relatives (69.3%), receiving a reminder from a doctor (67.7%), and receiving advice from a medical professional (65.0%) or from a friend (49.9%). • Reasons for not receiving the vaccine included concerns about safety (91.4%), fear of side effects (89.7%), belief that COVID-19 is not a severe disease (75.4%), did not want to be used as the subject of an experiment (69.5%), belief that vaccines are ineffective (66.7%), having medical conditions that contraindicated the vaccine (53%), having family/friends that had a bad experience from the vaccine (57.1%), disliking shots (35.3%), and believing it was inconvenient (30.8%).
GENERAL POPULATION		
Horizon Research (2021) *unpublished* (15, 195) Longitudinal study New Zealand	An online survey of adults (16+) was conducted to measure vaccine uptake. Mar-Apr, n=1,350 Apr-May, n=1387 Question Topics: 1) Vaccine uptake Survey tools available? Yes	**Apr-May** • 1% of respondents reported that they had been offered a vaccine but declined (1% drop since month prior). • Those who were unlikely to accept an offered vaccine were female, younger than the average age, had lower incomes, lower education qualifications, and had children in their households. **Mar-Apr** • 2% of respondents reported that they had been offered a vaccine but declined.

Mar-May 2021	Formative research conducted? No Survey pre-tested? No	
Office for National Statistics (2021) *unpublished* (43, 47) Longitudinal study UK Mar-May 2021	Responses from four waves of results collected from the online Opinions and Lifestyle Survey (196) were pooled to focus on demographic specific associations with vaccine hesitancy. The number of disabled, clinically extremely vulnerable, and parents was not reported. Feb-Mar: 17,201 responses pooled Mar-Apr: 16,362 responses pooled Apr-May: 15,170 responses pooled Questions Topics: 1) Vaccine uptake Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	**Apr-May** • 2% of adults who had been offered a vaccine and declined. • Refusal rates were 1% in those aged 16-29, 2% in those aged 30-49, and 1% in those 50+. • 2% of women declined a vaccine compared to 1% of men. • 5% of those identifying as other religion and 4% of Buddhists had been offered a vaccine and declined compared to 1% reporting no religion. • 63% of those who reported Muslim faith who were unlikely to be vaccinated or declined were worried about side effects. • Those in more deprived quintiles declined vaccines more frequently than those at higher deprivation quintiles (3% at the lowest quintile and 1% are the least deprived). • By occupation those in sales and customers services and elementary occupation declined vaccines at a rate of 3% compared to the average 2%. **Mar-Apr** • 3% of parents with children aged 0-4 had been offered a vaccine and declined compared to 2% of those with children over 5 years or 1% among non-parents and those not living with dependent children.
Office for National Statistics (2021) *unpublished* (48, 50, 54, 197) Longitudinal study	A weekly online survey of vaccine intentions was conducted in a nationally representative sample of UK adults. Apr 7-11: n= 6,030 April 28-May 3: n=3,830 May 19-23: n= 3,070 June 2-6: n=4,010	**June 9-13** • 2% of those aged 50 to 69 have been offered a vaccine and declined compared to 1% of those 70+ and the overall average of 3%. **May 19-23** • 18% of those aged 50-69 have received one vaccine dose and 80% (up from 25%) have received two doses. 1% have been offered a

UK Dec 2020- May 2021	June 9-13: n=3,600 *new* Question Topics: 1) Vaccine uptake Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	vaccine and declined to be vaccinated. 58% in this age group are concerned for side effects • <1% of those 70 or older have received one vaccine dose and 99% have received two doses. <1% have been offered a vaccine and declined to be vaccinated. **Apr 28-May 3** • 69% of those aged 50-69 have received one vaccine dose and 25% have received two doses. 2% have been offered a vaccine and declined to be vaccinated and 1% have not been offered a vaccine. **Apr 7-11** • 39% of those aged 30 to 49 years of age have had at least one dose and 1% have been offered a vaccine and are waiting to be vaccinated. 1% have been offered a vaccine and declined. • 19% of those aged 16 to 29 have had at least one dose and 1% have been offered a vaccine and are waiting to be vaccinated. 2% have been offered a vaccine and declined. • 98% of those the 50 to 69 years of age have received a vaccine or intend to accept a vaccine. 1% have been offered a vaccine and are waiting to be vaccinated and 1% have been offered a vaccine and declined. • 99% of those 70 years or older have either received a vaccine or are likely to accept a vaccine. 1% have been offered a vaccine and declined.
Dai (2021) *preprint* (44) Randomized control trial USA	A randomized controlled trial was conducted to measure the impact of interventions (text message reminder) in increasing the uptake in vaccine eligible populations (those aged 65+, patients with any transplant, and high-risk patients	• Receiving a basic text message significantly raised booked appointment rates within 6 days by 5.14 percentage points ($p<0.001$), and vaccination rates within 4 weeks by 2.89 percentage points ($p<0.001$) compared to the control group. This amounts to a relative increase of 85.5% and 26.3%, respectively.

Jan-Mar 2021	with qualifying pre-existing conditions) in California. RCT 1: Text message reminder including a link to schedule the appointment and either a plain text, ownership message, plain text with video, or ownership message with video one day after they receive notice of vaccine eligibility (n=132,337). RCT 2: A second text reminder was sent eight days after the initial reminder to participants that had not scheduled their first-dose appointment (n=102,675). Messages fell into 6 categories: (1) simple text (2) prosocial (3) exclusivity of early access (4) early access and prosocial (5) fresh start (6) fresh start and prosocial. Question Topics: 1) Vaccine uptake	• Receiving a text message also increased the speed of actual vaccinations with the control group taking 27 days to reach the vaccination rate of the text group at day 17. • Including a video did not significantly increase appointments or vaccinations when compared to messages without an education video likely due to low view rate (21%). • The highest impact of text messages were among those received at least one flu vaccine in the previous two years. • 12% of those who booked their appointment after the first message cancelled without rescheduling and 0.1% did not go to their appointment. • A second text reminder significantly increased scheduling the first dose appointment by 1.26% percentage points (a 52.3% increase, P <0.001) within 6 days and getting the first dose within 4 weeks by 0.68 percentage points (15.9% increase, P <0.001) compared to the control group. • All message types boosted appointment and vaccinate rates.
Senderey (2021) *preprint* (2) *new* Before and after study Israel Feb 2021	Vaccination uptake rates were compared before and after the implementation of text message reminder. Eligible unvaccinated individuals (16+) were randomly assigned to receive one of two reminders (following their receipt of the baseline reminder). There were two types of reminders, one highlighting the social benefit of vaccinating and the other the personal benefit of vaccinating.	• Vaccine uptake increased from 2.3% two days prior to intervention to 3.6% two days post intervention (P<0.001). • The personal benefit message was more effective than the social benefit message. • The aggregate effect over 8 days post intervention demonstrates that the personal benefit reminder led to a 9% relative increase compared to the social benefit reminder (23.8% vs. 21.7%, P < 0.0001). • When comparing three days before and after the implementation of the Green Pass policy, a

	Vaccines were available to all individuals aged 16+. Vaccine uptake rates were also compared before and after the implementation of the Green Pass policy where the entry to certain public places required the presentation of the "green pass" which could be acquired from receiving a vaccine or a recent negative COVID-19 test. Question Topics: 1) Vaccine uptake	relative increase of 22.2% (from 3.6% to 4.4%) was demonstrated.
Glampson (2021) *preprint* (49) Cohort study UK Dec 2020-Feb 2021	This study aimed to assess vaccine uptake and effectiveness of efficacy over a ten-week follow-up period across an integrated care system of eight Collaboration of Clinical Commissioning Groups (CCGs) leveraging a unique population-level care dataset in North West London. During the vaccine program time period, 413,919 adults (16+) were offered a vaccine. Individuals were counted as declining a vaccine if they indicated to their GP they did not want a vaccine when offered, and then did not receive a vaccine. Question Topics: 1) Vaccine uptake	• Of those offered a vaccine, 24,332 (5.88%) people declined and did not receive a vaccination. • In the vaccinated group, 2,957 individuals had initially declined but subsequently went on to receive a vaccination, indicating a hesitancy rate of 0.71%. • The Black or Black British group had the highest vaccine refusal rates (16.1%) followed by mixed ethnicity group (10.4%), other ethnic group (9.95%), and ethnicity unrecorded group (8.5%). The lowest rates of refusal was seen in the White (4.9%) and Asian and Asian British groups (3.2%). • In the Black or Black British group, those who were aged 80+ (27.9%) or were clinically extremely vulnerable (24.0%) had the highest refusal rates. • No overall difference in refusal rates was seen between men and women (5.9% vs 5.8%), younger men (aged <65) were more likely to decline than younger women (3.2% vs 2.2%), and older women (aged 65+) were more likely to decline than older men (7.9% vs 7.1%).

		• Deprivation was negatively associated with declining vaccination (r=-0.94, P <0.01). In the most deprived areas, 13.5% of individuals refused vaccination compared to 1.0% in the least deprived areas. • For those living in the deprived areas, the highest rates of refusal were in those aged 70+ (70-74 = 17.5%; 75-80 = 19.0%; 80+ = 25.9%), the clinically extremely vulnerable (19.2%) and Black and Black British (20.0%) communities.
OTHER POPULATIONS		
Office for National Statistics (2021) *unpublished* (43, 47) Longitudinal study UK Mar-May 2021	Responses from four waves of results collected from the online Opinions and Lifestyle Survey (196) were pooled to focus on demographic specific associations with vaccine hesitancy. The number of disabled, clinically extremely vulnerable, and parents was not reported. Feb-Mar: 17,201 responses pooled Mar-Apr: 16,362 responses pooled Apr-May: 15,170 responses pooled Questions Topics: 1) Vaccine uptake Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	**Apr-May** • Declining a vaccine was slightly lower among disabled respondents (1%) and clinically extremely vulnerable (CEV) (1%) compared to the average (2%). • 58% of disabled respondents had general concerns about vaccine safety and CEV respondents most were worried about fertility concerns (28%). • The largest anticipated difficulty for obtaining a vaccine was long waits and taking time off work (8%). **Mar-Apr** • 2% of those with disabilities had been offered a vaccine but declined, this was 1% higher than those without disabilities. • 3% of clinically extremely vulnerable (CEV) respondents had been offered a vaccine and declined compared to 1% of non-CEV. • 3% of parents with children aged 0-4 had been offered a vaccine and declined compared to 2% of those with children over 5 years or 1% among non-parents and those not living with dependent children.
Turner (2021) *preprint* (42) *new*	Using an online survey, the factors that influence uptake and perceptions of the COVID-19 vaccine were measured in 377	• 87% of respondents had received at least their first dose or were booked for an appointment and 8% had not been offered a vaccine yet.

Cross-sectional study UK Feb-Apr 2021	stroke and transient ischaemic attack (TIA) survivors during an early period of vaccine rollout in the UK. Question Topics: 1) Vaccine uptake 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 2% of respondents had declined the vaccine and 3% had been offered but not taken up the offer yet. • Concerns with high agreement included worry about side effects (36%), that vaccine increased stroke risk (34%), the safety of the vaccine (32%), how new the vaccine is (29%), and vaccine affecting blood thinner medication (28%). • Most respondents felt that getting the vaccine was the right thing to do (92%), they knew other people who have had the vaccine (98%), believed that it will reduce spread of COVID-19 (85%), and that the vaccine will protect them (87%). • Good understanding of how to get a vaccine appointment was demonstrated (91%). Many disagreed that that they needed to consult their doctor (61%), that they will have difficulty accessing an appointment (64%) or that they will not have time to get an appointment (74%). • Open text responses found concern over the relationship between AstraZeneca and blood clots, side effects, mistrust of the government, vaccine efficacy, uncertainty about the relationship between stroke/TIA and COVID-19, accessing vaccine appointments, and difficulties getting information specific to them.
Bowman (2021) *preprint* (45) Cross-sectional study USA Jan – Mar 2021	A dialysis program-wide vaccination program was implemented over a series of 4 visits to 12 dialysis clinics in Virginia where all 859 dialysis patients aged 18+ were offered a vaccine. Question Topics: 1) Vaccine uptake	• As of Mar 16, 79.6% of dialysis patients who were offered a vaccine accepted, and 14.2% refused. The 6.2% who did not accept or refuse a vaccine were due to either hospitalization or no-shows to treatment on the vaccine clinic day. • The likelihood of vaccine refusal decreased by 13% for every 5-year increment in age (OR 0.87, 95% CI: 0.80-0.95, P=0.002). • Women were more likely to refuse a vaccine compared to men (OR 2.40, 95% CI: 1.64-3.50, P<0.0001). • An increased likelihood of vaccine refusal was seen in those who did not receive a flu shot in

		2020 (OR 5.44, 95% CI: 3.15-9.39, P<0.0001), those on dialysis for more than 5 years (OR 1.7, 95% CI: 1.08-2.70, P=0.023), and those with a positive PCR test for COVID-19 (OR 1.56, 95% CI: 0.97-2.52, P=0.067).
Giannini (2021) (4) *new* Cross-sectional study Italy NR 2021	Acceptance and refusal rates of a COVID-19 vaccine was assessed in a group of 266 individuals who underwent liver transplantation. Question Topics: 1) Vaccine uptake	• 96.6% of patients accepted and received a COVID-19 vaccine and 3.4% did not receive a vaccine. • 5 patients refused vaccination due to concerns about severe adverse events. These patients had received adequate information about the vaccine and received the vaccinations recommended in liver transplant recipients prior to refusing. • 2 patients requested more time to decide whether or not to receive the vaccine due to concerns over potential harms. • 1 patient required further work-up for previous allergic reactions to vaccination, and 1 patient was temporarily abroad while vaccines were offered.
Gibbon (2021) (5) *new* Cross-sectional study UK NR 2021	COVID-19 vaccine uptake, and reasons for refusal was evaluated in 92 current psychiatric in-patients in a medium secure hospital in the UK. Question Topics: 1) Vaccine uptake	• 85 patients had capacity to decide if they wanted a COVID-19 vaccine. • 80% consented to accept a vaccine and 20% refused. • White British patients were less likely to refuse a vaccine compared to Black, Asian, minority ethnic (BAME) patients (16.9% vs 30%). • Of the 17 patients who refused vaccination, the reasons for refusal included: concern about the safety and side-effects of the vaccine (n=5), belief that there is a low risk to their personal health from contracting COVID-19 (n = 4), broader distrust of healthcare services (n=2), and concerns about animal testing (n=1). Five individuals were unwilling to explain their reasons for refusal.
Giannini (2021) (46) *new*	Vaccine uptake rates were assessed in 56 patients with irritable bowel	• 92.6% accepted a vaccine and 7.4% refused.

Cross-sectional study Italy NR 2021	syndrome who were followed at an irritable bowel centre. Question Topics: 1) Vaccine uptake	• The two patients who refused did so due to concerns about potential adverse reactions.
ADHERENCE TO PUBLIC HEALTH MEASURES POST-VACCINE		
United Status Census Bureaus (2021) *unpublished* (53) Longitudinal study USA May 2021	Estimates of preventative behaviours of those who have received at least one vaccine dose were collected in the biweekly online Phase 3.1 Household Pulse Survey. Week 30 May 12-24, n=192,277,515 Question Topics: 1) Vaccine uptake Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 73.2% of those that had received at least one dose of the vaccine did not change preventative behaviours post-vaccine, 21.9% decreased preventative behaviours, and 4.3% increased preventative behaviours. • Decreasing preventative behaviours was reported more among those aged 18-39 (24-25%), males (23%), White non-Hispanic (27%), those who were married (24%), had a bachelors degree or higher (30%), in household with 2 (25%) and 4 people (23%), were employed (24%), and had household incomes above $75,000 (23-37% for $200,000 and above) compared to their counterparts.
Office for National Statistics (2021) *unpublished* (50, 54, 197, 198) Longitudinal study UK	A weekly online survey of vaccine intentions was conducted in a nationally representative sample of UK adults. Apr 7-11: n= 6,030 April 28-May 3: n=3,830 June 2-6: n= 4,153 June 9-13: n=3,600 *new* Question Topics:	**June 9-13** • Social distancing with people outside their household continued to fall from 74% in May survey to 66% in June survey (88% early April). • Physical contact outside the home dropped by 1% in the latest survey to 71%. • 46% (down from 50%) of adults were meeting up indoors with people outside their households, childcare, or support bubble. **June 2-6**

Dec 2020- May 2021	1) Post-vaccine behaviors Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Social distancing with people outside their household continued to fall from 74% in May survey to 68% in June survey. • Physical contact outside the home dropped by 1% in the latest survey to 72%. • 50% of adults were meeting up indoors with people outside their households, childcare, or support bubble. • Meeting outdoors amongst adults has increased from 53% to 65% in since the last survey. **Apr 28-May 3** • 90% of vaccinated individuals (at least one dose) always or often wash their hands when returning home compared to 82% of unvaccinated. • 90% of vaccinated individuals (at least one dose) have been always/often maintaining social distancing when meeting up with people outside their household, support or childcare bubble compared to 72% of unvaccinated. • Those having received at least one dose have avoided physical contact outside their homes compared to those unvaccinated (86% vs 74%). • 25% of vaccinated adults (at least one dose) have stayed home or left only for work, exercise, essential shopping or medical needs compared to 15% of unvaccinated adults. • Fewer vaccinated adults work from home than unvaccinated (33% vs 43%).
Rahamin-Cohen (2021) *preprint* (51) Cross-sectional study Israel Mar-Apr 2021	To assess behavior changes in the vaccinated population, an online survey sent via text message was answered by 185 individuals from the general population (18+) and 23 HCWs (18+). HCW outcomes in the HCW section. Question Topics: 1) Post-vaccine behaviors	• After the second dose, 21.1% of respondents reported wearing a mask less than before receiving the vaccination and 75.7% did not change their behavior. More individuals <50 years old decreased their mask wearing (28.1%) compared to those aged 50+ (17.2%). Only 1/23 (4.3%) HCWs reported wearing a mask less post-vaccination. • When comparing social distancing behavior before and after vaccination, 48.4% reported no change and 47.3% reported a decrease in social

	Survey tools available? No Formative research conducted? No Survey pre-tested? No	distancing. This differed by age with 41.8% of the 50+ group reporting a decrease in social distancing and 53.3% reporting no change compared to 56.1% and 40.4% in the <50 group, respectively. In HCWs, 43.5% reported a decrease in social distancing and 52.2% reported no change post-vaccination.
Wright (2021) *preprint* (52) Longitudinal study UK Oct 2020 – Mar 2021	Results from an ongoing online monthly survey on 70,000 adults (18+) was used to explore changes in compliance following vaccination. Question Topics: 1) Post-vaccine behaviors Survey tools available? No Formative research conducted? No Survey pre-tested? No	• There was no evidence showing that receiving a COVID-19 vaccine reduced compliance behaviors. • Increased compliance from the beginning of the second wave of COVID-19 was shown in both vaccinated and unvaccinated individuals.
Office for National Statistics (2021) *unpublished* (35) Cross-sectional survey UK Feb 2021	Responses of 2070 adults over 80 years old were collected through an online survey to determine vaccine coverage, attitudes, and vaccinations effect on protective behaviors. Question Topics: 1) Post-vaccine behaviors Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Of those that had received at least one dose, 43% had met someone outside of their bubble, household, or care staff indoors. • Most respondents who received at least one dose ventured outside their homes to do an activity (49% met someone who they do not live with outdoors, 54% had went shopping, and 45% had left home to participate in outdoor leisure activities). Only 20% reported that they had not left home for any reason. • 25% of those received their first dose and 33% with both doses were willing to go the hospital for a medical reason.
Nguyen (2021) *preprint* (6) *new*	The rate of change in average daily travel distance from a participant's	• The median daily travel distance travelled was 8.9km (IQR: 3.50km, 24.17km) between 157 days

Cohort study UK Sep 2020-Feb 2021	registered address before and after SARS-CoV-2 vaccination was measured using Virus Watch. Virus Watch used Global Positioning System (GPS) to collect data on the movement of 228 vaccinated individuals.	prior to vaccination until the day before vaccination. • Between the day of vaccination and 100 days after vaccination, the median daily travel distance travelled was 10.30km (IQR: 4.11, 27.53km). • After removing outlier data, there was a median daily increase in movement of 45.0m (95%CI: 25m, 65m, P = <0.001) between the vaccination date and 99 days after vaccination. • After restricting the analysis to the 3rd national lockdown (Jan 4 - Apr 5, 2021), there was a median daily movement increase of 9m (95%CI: -25m, 45m, P = 0.57) in the 30 days prior to vaccination and the vaccination date, and a median daily movement increase of 10m (95%CI: -60m, 94m, p-value = 0.69) in the 30 days after vaccination.
Kaim (2021) (7) *new* Cross-sectional study Israel Jan 2021	Protective behavioral adjustments (i.e., mask wearing and social distancing) during the initial phase of the vaccination campaign was evaluated in a group of 1120 adults using an online survey. Of these individuals 64 were infected with COVID-19, 453 were vaccinated, and 603 were not vaccinated. Question Topics: 1) Post-vaccine behaviors Survey tools available? No Formative research conducted? No Survey pre-tested? No	• At the beginning of the vaccination campaign, those who were infected were less careful about social distancing (29.7%) compared to those who received the first dose of vaccine (12.8%), or those who were neither vaccinated nor infected (19.2%) (χ^2 = 19.32, P = 0.001). • Similarly, those who were infected were less careful about mask wearing (18.8%) compared to those who received the first dose of the vaccine (8.2%) and those who neither were vaccinated nor infected (11.6%) (χ^2 = 13.02, P = 0.011). • A higher level of social distancing was maintained among Non-Jewish individuals compared to Jewish individuals: those who were vaccinated (41.7% among non-Jewish vs 14.3% among Jewish; χ^2 = 22.9, P < 0.001), those who were infected (33.1% among non-Jewish vs 8.3% among Jewish; χ^2= 7.29, P = 0.026), and those who were neither vaccinated nor infected (24.3% among non-Jewish and 8.8% among Jewish; χ^2 =

		28.81, P < 0.001). Similar trends were observed for mask wearing.

GLOBAL POPULATION

Table 2. Evidence of vaccine attitudes of the global population (n=6)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
Quasi-experimental studies (n=1)		
Duch (2021) *preprint* (199) Quasi-experimental study 13 countries (Australia, Brazil, Canada, Chile, China, Colombia, France, India, Italy, Spain, Uganda, UK, USA) Nov-Dec 2020	To understand public opinions on key aspects of vaccine allocation, an online experiment of 15,536 adults (18+) across 13 countries was conducted. Participants were require to make eight binary choices about hypothetical vaccine recipients that randomly varied on five attributes including occupation, age, transmission status, risk of death from COVID-19, and income. Question Topics: 1) Vaccine perceptions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• Overall there was global consensus on which population segments should have priority for a COVID-19 vaccine. • In almost all countries and across participants of different education levels, incomes, and political ideologies, results show that the public favors prioritizing the vaccine to healthcare workers, those at high risk, those in lower income brackets, and older populations. • At least two thirds of participants in each of the countries (80% in Canada) believed that the government should assume the lead role in the distribution of COVID-19 vaccines. However, there is evidence that a large proportion of individuals would be willing to pay for a vaccine if it were available privately. This ranged from 18% of participants in France to 79% in India and Uganda. 35% of Canadians would be willing to pay for a vaccine. • There was no consensus on support for mandatory vaccination either globally or within national borders. In the global sample, 24% were strongly opposed and 38% were strongly in favor. In France 60% of participants opposed mandatory vaccination whereas in China, India, and Uganda very few people were strongly opposed.
Cross-sectional studies (n=5)		
Crespo (2021) *preprint* (57)	Change in intention to vaccinate over time was assessed using two online surveys, one in Nov 2020	• In Canada, intention to vaccinate increased from 44.2% in Nov to 55.2% in Jan.

Cross-sectional studies 15 countries: Australia, Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Singapore, South Korea, Spain, Sweden, UK Nov-Jan 2021	and the other in Jan 2021 across fifteen countries. It is unclear if and how many individuals completed both surveys. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• In the Jan survey, the countries with the highest intentions to vaccinate included the UK (77.5%), Denmark (67%), and the Netherlands (63.1%). The countries with the lowest intentions included South Korea (43.7%), France (39.2%), and Singapore (34.8%). • Increase in intention to vaccinate between Nov and Jan was seen in Spain (24.1%), UK (23.2%), Sweden (22.7%), Finland (20.4%), Netherlands (18.5%), Italy (15.4%), Norway (14.6%), France (14.2%), Denmark (13.3%), Germany (13.0%), Canada (11%), and Japan (0.8%). • Countries with a decrease in intentions between Nov and Jan included Australia (-6.6%), South Korea (-5.0%), and Singapore (-1.3%). • In 11/15 countries there was a significant decrease in the proportion of individuals who reported concern about the side-effects of a vaccine. In Canada, this concern decreased from 53.3% in Nov to 47.9% in Jan.
Clarke (2021) (200) Cross-sectional study Australia, Canada, France, Italy, Spain, UK and USA Nov-Dec 2020	An international online survey of 8209 adults from high income countries was conducted with the goal of evaluating perceptions of prioritization of global vaccine allocation on a scale 0 ('very much disagree') to 100 ('very much agree'). Question topics: 1) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• All countries favoured in order of most support: allocating based on need, by affordability, and by which country developed the vaccine. • The UK had the largest percentage of respondents who do not favor donating purchased vaccines to other countries (26%) and Italy and Spain had the lowest (15%). • Between 48% and 56% of respondents would donate their country's vaccines at some level. The highest was Canada (56%) and lowest France (48%).
World Economic Forum (2020)	An online survey of 18526 individuals globally analyzed intention to vaccinate and	• 73% stated they would get a vaccine for COVID-19 if it were available. Compared to three months earlier (Aug), this is a 4% drop.

unpublished (201) Cross-sectional study 15 countries (Australia, Brazil, Canada, China, France, Germany, India, Italy, Japan, Mexico, South Africa, South Korea, Spain, UK, and USA) Oct 2020	perceptions on the vaccine. Of these, 1000 participants were Canadian. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Intention has declined between Aug and Oct in 10/15 countries, most of all China, Australia, Spain, and Brazil. • Countries with the highest intent include India (87%), China (85%), South Korea (83%), and Brazil (81%). • France has the lowest intention to vaccinate (54%), followed by the USA (64%), and Spain (64%). • 52% indicated that they would become vaccinated within three months after vaccine becomes available to all. • 55% believe that a vaccine will not be available on the market until the third quarter of 2021. • Globally, the most common reasons for hesitancy include concerns about side-effects (34%), and concerns that clinical trials are moving too quickly (33%).
Mannan (2021) *preprint* (202) Cross-sectional study 60 countries: (Afghanistan, Algeria, Argentina, Australia, Bangladesh, Belgium, Bolivia, Botswana, Brazil, Canada, Chile, China, Columbia, Cuba, Dominican Republic, Ecuador, Egypt,	Sixty national representative online and telephone surveys were conducted capturing 26,852 responses from adults (19+) regarding vaccine acceptance and attitudes. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• 62.6% of Canadians strongly accepted a COVID-19 vaccine which was the lowest acceptance recorded among countries in North America. • 65.5% strongly agreed that it was important to get a vaccine to protect others, 57.6% agreed that pharmaceutical companies will develop a safe vaccine, and 31.7% believed that vaccines were safer if they made in America or Europe rather than other countries. • Hesitancy was demonstrated with 48.7% worried about side effects, 44.7% worried about unforeseen impacts, 43.7% had concerns over commercial profiteering, 42.6% had general mistrust of vaccine benefits, and 34.6% had a preference for natural immunity. • Vaccine acceptance for each country: **Africa** Algeria (66.3%), Egypt (43.6%), Botswana (71.2%), Kenya (61.3%), Libya (49.6%), Mali (62.4%), Mauritius (82.8%), Morocco (48.4%), Nigeria (61.5%), South Africa (79.3%)

El Salvador, England, Fiji, France, Germany, Guatemala, India. Italy, Jamaica, Japan, Kenya, Kiribati, Libya, Mali, Malaysia, Mauritius, Mexico, Morocco, Nauru, New Zealand, Nicaragua, Nigeria, Palau, Panama, Papua New Guinea, Paraguay, Peru, Poland, Russia, South Africa, Saudi Arabia, Singapore, Solomon Islands, Spain, South Korea, Sweden, Switzerland, Turkey, Tonga, Tuvalu, United States of America, Uruguay, Venezuela) Jun-Sep 2020		**Asia** Afghanistan (47.2%), Bangladesh (49.8%), China (87.4%), India (73.9%), Japan (71.4%), Malaysia (52.7%), Saudi Arabia (51.1%), Singapore (66.8%), South Korea (76.2%), Turkey (59.2%) **Oceania** Australia (89.9%), Fiji (87.2%), New Zealand (88.4%), Kiribati (89.8%), Nauru (88.3%), Palau (89.2%), Papua New Guinea (91.9%), Solomon Islands (92.6%), Tonga (92.9%), Tuvalu (90.5%) **North America** Canada (62.6%), Cuba (77.9%), Dominican Republic (79.5%), El Salvador (71.8%), Guatemala (75.0%), Jamaica (71.0%), Mexico (73.3%), Nicaragua (81.2%), Panama (87.4%), United States (74.8%) **South America** Argentina (81.3%), Brazil (86.2%), Bolivia (82.8%), Chile (79.2%), Columbia (81.8%), Ecuador (70.2%), Paraguay (67.7%), Peru (77.8%), Uruguay (75.6%), Venezuela (74.8%) **Europe** England (69.3%), Belgium (60.4%), Germany (65.2%), Italy (68.4%), France (51.9%), Poland (52.3%), Spain (72.5%), Sweden (62.7%), Switzerland (60.2%), Russia (51.3%)
Lazarus (2020) (203) Lazarus (2021) (204)	Vaccine acceptance rates and factors influencing acceptance of a COVID-19 vaccine was analyzed using an online survey of 13,426	• 71.5% of participants reported that they would be “very likely” or “somewhat likely” to take a COVID-19 vaccine

Cross-sectional study 19 countries: (Brazil, Canada, China, Ecuador, France, Germany, India, Italy, Mexico, Nigeria, Poland, Russia, Singapore, South Africa, South Korea, Sweden, UK, USA) Jun 2020	adults. The data from this survey was analyzed differently in two publications. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 48.1% reported that they would accept their employer's recommendation to take the vaccine. • China (88.6%), Brazil (85.4%), and South Africa (81.6%) had the highest acceptance rates and Nigeria (58.9%), Poland (56.3%), and Russia (54.9%) had the lowest. • The acceptance rate in Canada was 68.7%. • Individuals aged 25+ were more likely to accept the vaccine than those aged 18-24. The strongest difference was seen (OR 1.73, 95% CI: 1.48-2.02) when responses from the oldest age cohort (65+) were compared to the youngest cohort (18-24). • People with higher education, women, those who earned more income, those who reported COVID-19 illness in the family, and those who trusted their government were more likely to accept the vaccine. • Having a high/very high education may be linked to lower vaccine acceptance in Canada, Spain, and the UK.

CANADIAN GENERAL POPULATION

Table 3. Evidence of vaccine attitudes of the general public (n=42)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
Longitudinal studies (n=8)		
Leger (2021) *unpublished* (10, 69-73, 205, 206) Longitudinal study Canada & USA Nov 2020 & Jan-June 2021	An online survey of Canadian and American adults (18+) was conducted to evaluate vaccine perceptions and intentions to vaccinate. Wave 1: Nov 2020, 1516 Canadians and 1002 Americans Wave 2: Jan 2021, 1516 Canadians and 1003 Americans Wave 3: Feb 2021, 1535 Canadians and 1002 Americans	**Wave 12** • Canadians intention to be vaccinated or who have been vaccinated increased to 88% from May. • The percentage of those who did not intend to vaccinate was highest in MB and SK (18%) followed by AB (16%), among those aged 18-34 (14%, decreased from 18% at last polling), and among rural residents (16%, decreased from 22% at last polling). • Belief that vaccines are dangerous stayed at 7% since May (81% believe vaccines are safe and 12% do not know).

	Wave 4: Feb 2021, 1,532 Canadians and 1002 Americans Wave 5: Apr 2021, 1,504 Canadians and 1,002 Americans Wave 6: Apr 2021, 1,548 Canadians and 1,003 Americans Wave 7: May 2021, 1,529 Canadians, 1,003 Americans Wave 8: May 2021, 1,529 Canadians, 1,003 Americans Wave 9: May 2021, 1,624 Canadians and 1,002 Americans. Wave 10: May 2021, 1,624 Canadians and 1,002 Americans. Wave 11: June 2021, 1,539 Canadians, 1,004 Americans *new* Wave 12: June 2021, 1,542 Canadians and 1,001 Americans *new* Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	**Wave 11** • Canadians intention to be vaccinated or who have been vaccinated held steady at 86% (no change from May). • The percentage of those who did not intend to vaccinate was highest in AB (20%) followed by Atlantic Provinces (19%), among those aged 18-34 (18%), and among rural residents (22%). • 89% certainly or probably will receive a second dose, 1% probably will not, 9% already have received a second dose, and 1% were unsure. • 3% of those who reside in QC and 3% of those aged 18-24 indicated they either probably will not or certainly will not get a second dose. • 48% of Canadians were uncomfortable about receiving a different brand of vaccine as their second dose whereas 46% were comfortable and 6% were unsure. • Those in MB/SK (34%), those aged 35 to 55 (25%), and rural residents (26%) had the highest levels of not being comfortable with a different vaccine as a second dose. • 50% of those who had a first dose of Astra-Zeneca would prefer getting a second dose of Astra-Zeneca compared to 32% who would like a second dose of another brand, and 18% who did not know. • Belief that vaccines are dangerous increased 1% to 7% since May (82% believed vaccines are safe and 11% did not know). **Wave 10** • Canadians were split 50-50 on whether they were comfortable if some of their colleagues were not vaccinated. • Discomfort with unvaccinated coworkers was highest in BC (62%) and 60% of Atlantic Canada and MB/SK were comfortable. • Older (55+) Canadians were less comfortable with unvaccinated coworkers (52% uncomfortable)

		along with urban residents (53% uncomfortable) compared to rural residents (44% uncomfortable). **Wave 9** • 51% of respondents felt the vaccine campaign in their province was proceeding about the same as other provinces. QC residents felt they were doing better than other provinces whereas ON and AB felt vaccinations were slower. • Canadians had high support for showing proof of vaccination when traveling by plane (82%), attending events with large crowds (75%), attending in-person university (71%) and had lower support for going to their place of work (68%), staying in a hotel (68%), and dining in a restaurant (64%). Support for showing vaccination was consistently higher among those aged 55+. • Since earlier polling in May there was a 4% increase (to 86%) of those who had been vaccinated or intended to get a vaccine. • Provinces with the highest combined level of vaccination or intention to get a vaccine was in QC (90%), followed by AB (87%), Atlantic provinces (86%), BC (85%), and MB/SK (84%). • Belief that vaccines are safe and should be given has stayed steady at 81% but those who did not know increased 1% to 12%. • Waves 1-8 summarized in previous versions of this report.
Angus Reid (2021) *unpublished* (8, 60, 61, 66, 68, 76, 82, 83, 85) Longitudinal study Canada	Vaccine intentions and perceptions were analyzed in Canadian adults (18+) using an online survey. Wave 1: Jul 2020, n=1519 Wave 2: Sep 2020, n=1660 Wave 3: Dec 2020, n=1603 Wave 4: Jan 2021, n=1580 Wave 5: Feb 2021, n=1201 Wave 6: Mar 2021, n=1748	**Wave 10** • 84% have received at least one shot or will get vaccinated as soon as possible (an increase of 2% from May), 4% will get a vaccine but wish to wait (down from 6%), 9% will not get a vaccine (no change), and 3% were unsure (no change). • Vaccine hesitancy remains highest in AB and SK (18%). This has increased 1% in AB and decreased 6% in SK since May. • 57% of respondents would like equal emphasis on distributing first and second doses, 26% would

Jul, Sept, Dec 2020 & Jan-Feb and May-Jun 2021	Wave 7: Apr 2021, n=NR Wave 8: Apr 2021, n=1594 Wave 9: May 2011, n= 1,319 Wave 10: June 2021, n=4,948 *new* Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	prefer priority of getting all eligible first doses administered, and 16% would like the focus to be on second doses and circling back to first doses. Support for focusing on administering first doses was higher among those waiting for vaccination (39%) and among those aged 18-24 (40%). • Canadians are supportive of continuing vaccinations until everyone in Canada has been vaccinated (72%) with 18% wanting to shift focus to at risk populations globally and 10% were unsure. • Respondents felt the second dose vaccinations were progressing as well as could be expected (49%) with nearly equal split between feeling it was taking too long (27%) and that it was going at great pace (24%). 55% of QC residents felt that things were going great whereas 40% of ON residents felt things were moving too slowly. • 51% felt Canada has done a good job of securing vaccine doses and 41% felt it had been a poor job. However, 60% and 69% still had confidence that the federal and provincial government can manage vaccine distribution, respectively. **Wave 9** • 82% of respondents have either received a vaccine or wish to get a vaccine as soon as possible, up from 71% in April. • Fewer respondents report being unsure about vaccinations (3% down from 13%), wanting to wait before receiving a vaccination (6% down from 13%), or report not wanting a vaccine (9% down from 13%) compared to April responses. • 53% of respondents have received at least one dose, an increase of 36% since April. • Vaccine hesitancy is highest in SK (24%) with the level remaining stable (22% in April and 26% in January. • Vaccine hesitancy dropped dramatically in AB from 45% in January to 25% in April to 17% in May.

		• Hesitancy in BC, MB, ON, QC, and the Atlantic provinces varied between 10-12% in May. • Vaccine hesitancy was highest in males aged 35-54 (18%) followed in by females aged 18-34 (15%). • Of those that received an AstraZeneca, 2% fully regret getting it and 66% have serious second thoughts or doubts. • Canadians remain very comfortable with Pfizer and Moderna (93% and 89%, respectively) but became less confident in AstraZeneca (52% in April to 35% in May) and Janssen (54% to 49%). • Unvaccinated men are more comfortable than women to receive AstraZeneca (29% vs 36% extremely uncomfortable) however 40% women would take a vaccine they are uncomfortable with compared to 31% of men. • Wave 1-8 summarized in previous versions of this report.
Engage Manitoba (2021) *unpublished* (97, 207) Longitudinal study Canada Jan-Jun 2021	A series of online surveys in Manitoba were implemented to assess vaccine intentions within the Safely Restoring Services in Manitoba Survey. Survey 1: Jan 10-15, n=73,351 Survey 2: Feb 4-9, n= 33,687 Survey 3: Feb 25-Mar 2, n=26,909 Survey 4: Mar 18-23, n=31,776 Survey 5: Jun 4-8, n= 33,904 Question Topics: 1) Vaccine intentions 2) Vaccine perceptions	**Survey 5** • 86% have received at least one dose of a vaccine (up from 9% in survey 4). • 2% have booked their first dose appointment, 2% will get the vaccine but are in no rush (down from 13%), 4% are unsure if they will get a vaccine (down from 12%), and 5% will not get a vaccine (down from 10%). • Of those who were not sure or do not intend to be vaccinated, very few would be swayed by the ability to travel within Canada (9%), attend sporting events or cultural events (7-9%), visit facilities or events (10%), or visit loved ones (11%). **Survey 4** • 9.0% of respondents have already received a vaccination (up 4% since survey 3). • 56% intend to sign up for a vaccination as soon as they are eligible (up 1.9%).

	Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 13% report that they want a vaccine but are not in a rush (down from 16.2%). • 12% are unsure if they will get a vaccine when it's available (down from 14.2%). • 10% would refuse a vaccine (down from 10.5%). • Approval of the Manitoba governments approach to vaccinations is high in the latest survey with 33% strongly approving, 47% somewhat approving, 13% somewhat disapproving, 7% strongly disapproving.
Government of Manitoba (2021) *unpublished* (11) *new* Longitudinal study Canada May 2021	An online research panel of 600 Manitobans were surveyed to understand attitudes towards vaccination and possible incentives to increase uptake. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 87% have received a vaccine or intend to be vaccinated (74% received and 13% intend), and increase of 11% from April. • 5% will get a vaccine but were not in a rush (down from 12%), 5% were unsure if they will get a vaccine (down from 7%), and 4% will not get a vaccine (down from 5%). • From April to June there was an 18% drop in the number of people strongly approving of Manitoba's vaccine distribution (42% to 24%), 49% somewhat approve (up from 43%), 17% somewhat disapprove (up from 11%), and 10% strongly disapprove (up from 4%). • In a group of 70 parents or guardians of children aged 12-17, 15% were not sure if they will vaccinate their children, and 13% will not vaccinate their children. • Those who did not intend to vaccinate their children were in households making less than $40,000, would not get the vaccine themselves, and didn't believe adults should get all the regular vaccines. • 31% of respondents felt much more positive about COVID-19 vaccine now then when first introduced, 19% felt slightly more positive, 45% felt the same, 3% felt slightly more negative, and 2% felt much more negative.

		• 55% felt that whether they got the vaccine or not should be a choice, 42% felt that it should not be a choice, and 3% were unsure. • Those who would promote vaccination tended to be younger than 30 or over 65 and believed that adults should have all their regular vaccines. • The types of information that were the most likely to influence decision to vaccinate included information about possible side effects (42%), being able to choose the vaccine (42%), information about testing (41%), and information about how the vaccine works (36%). • The least persuasive type of information was hearing stories from celebrities who got their vaccine (90% unlikely to impact). • Women would be the most influenced by being able to choose the vaccine. • Residents of Winnipeg were more influenced than those in rural areas by getting a vaccine from a family doctor/pharmacist, speaking to their family doctor/pharmacist, having someone come to their home, and hearing stories from celebrities. • Manitobans were largely not swayed by community incentives such as being able to travel without having to isolate (50% no more likely to vaccinate), being able to visit long term care homes without restrictions (52% no more likely), entry into provinces or countries (48% no more likely), being able to attend large events (60% no more likely), attend larger gathering (54% no more likely), certain businesses/facilities to those that are vaccinated (61% no more likely). • Those aged 30 to 44 were more likely to be influenced by being able to attend larger gatherings (community, faith, or personal). • Financial incentives (monetary, vouchers, complimentary items, draws for prizes, discounts) were not reported to increase the likelihood of accepting a vaccine (between 75% and 84% stating they are not more likely by any financial incentive).

		• 70% of respondents were concerned if only hesitant individuals received large ($50-$100) incentives.
Statistics Canada (2020) & Statistics Canada (2021) *unpublished* (65, 80, 81) Longitudinal study Canada Sep 2020 – Feb 2021	An online survey conducted by Statistics Canada as part of the Canadian Community Health Survey (CCHS) assessed Canadians behaviors to safeguard their own health as well as the health of others. In the September survey, a question about vaccine intentions was added. The most recent report captures 25,321,400 responses from individuals aged 12+. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	**Jan-Feb 2021** • 82.3% of respondents were very or likely to get a COVID-19 vaccine. • Vaccine intention was highest in those over 65 years (88.1%) with a decreasing level of intention in those aged 12-17 (71.0%). • Vaccine intention was similar between males and females (82.8% vs 81.9%, respectively). **Sept-Dec 2020** • Over the sampling period 77% were willing to receive a vaccine. This represents an increase from Sept (75.5%) to Oct (74.8%), and Nov/Dec (80.3%). • Vaccine intentions were highest in Prince Edward Island (89.1%), Nova Scotia (81.5%), and British Columbia (81.4%). Vaccine intention was lowest in Prairie provinces (75.2%) • Men were more likely to vaccinate then women (77.9% vs 75.8%). • Immigrants were slightly less likely to vaccinate (74.6%) but this varied greatly between older and younger immigrants (73.2% for 12-64 and 81.1% for those 65+). • LGBTQ2+ were more likely to get a vaccine (83.3%). • The highest intentions among visible minorities were Japanese (86.5%), Korean (85.6%), South Asian (82.5%), Chinese (79.3%), visible minority not indicated/multiple (79.1%), Southeast Asian (78.3%), West Asian (78.3%), Filipino (75.1%), Arab (68.1%), Latin American (66.0%), and Black (56.6%). Non-visible minority's intention to vaccinate was 77.6%. • Older visible minorities were more likely to vaccinate than those 12-64 (77.4% vs 74.6%). • Intention to vaccinate among Indigenous respondents was 71.8% which was significantly less than Non-Indigenous respondents (77.1%). 74.2%

		of First Nations living off reserve were willing to vaccinate compared to 67.8% of Métis and 72.5% of Inuit*. • Older Indigenous people (65+) were more likely to want a vaccine compared to younger (74.9% vs 71.3%). *Use with caution. Coefficient of variation (CV) from 15.1% to 35.0%.
Impact Canada (2020) *unpublished* (74) Longitudinal study Canada Apr 2020 – Feb 2021	Vaccine confidence and hesitancy in the Canadian context was explored through the implementation of the World Health Organization (WHO) Behavioural Insights (BI) Tool on COVID-19 in eight waves of adults (18+) using the same participants where possible. Wave 1: n=2023, Wave 2: n=2,098, Wave 3: n=2,000, Wave 4: n=2,152, Wave 5: n=2,169, Wave 6: n=2,141 , Wave 7: n=2,129, Wave 8: n=2,117, Wave 9: n=2,055, Wave 10: n=2,125, Wave 11: n= 2,037 Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	**Wave 11** • Intention to get vaccinated right away has increased to 58% (up from 49% in wave 10). 24% intend to vaccinate but would like to wait, 9% would not vaccinate, and 8% were unsure. • Those who plan to wait are mostly like to want to wait 1 to 2 months (33%). • 68% have made up their mind if they will or will not get a vaccine and 25% need more information before deciding. • The two most common reasons for vaccine hesitancy included a lack of testing or research (26%) and belief that the vaccine was not safe (15%). • 47% report that getting the most effective vaccine is the most important criteria for selecting a vaccine, followed by the vaccine that is available first (15%), and fewest side effects (12%). • 56% and 22% would like more information regarding the safety and effectiveness of the vaccine, respectively. • A vaccine recommendation from a healthcare provider would likely influence 45% of respondents. **Wave 10** • Vaccine acceptance rose slightly from wave 9 (61%) to wave 10 (65%). • Intention to get vaccinated right away has increased to 49% (up from 43% in wave 9). 31%

		intend to vaccinate but would like to wait, 11% would not vaccinate, and 8% were unsure. • Of those wanting to wait for a vaccine, 42% wanted to wait several months (up from 27% in wave 9). • The top reasons for wanting to wait were to ensure safety (80%) and efficacy (64%). • Those who would decline a vaccine were asked about hypothetical incentives. 58% would like assurances that the vaccine would not be a risk for exposure to COVID-19, 56% wanted a convenient booking system, and 52% wanted a convenient location. • 56% of participants stated they would vaccinate to be able to return to work, travel, or attend large gatherings. • 63% reported that their mind was made up whether to vaccine or not and 32% would like more information before they decide.
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021) *unpublished* (12, 86, 88, 90, 91, 95) Longitudinal study Canada Apr 2020 – Jun 2021	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in Quebec. Number of participants was not clearly stated (~3300 each collection period). There were multiple collection periods, one in Apr-May 2020, Sep and Dec 2020, Apr-Jun 2021 *new*. Articles in French. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	**June** • 49% agreed that vaccinated adults should be able to gather without masks in private, 44% disagreed, and 6% were unsure. • Almost half of respondents felt that vaccinated people should be able to gather without masks in private (49%) but also agree that masks should be worn outside with people they don't live with (56%). • Vaccine passports have high support with 72% in favour (23% disagreed and 4% were unsure). • 73% of respondents disagreed that it is important to follow protective measures based on the rate of vaccination and the decrease in COVID-19 cases. **May** • 74% of respondents who have not been vaccinated yet intend to get a vaccine, a 3% drop since late April. 18% do not intend to get a vaccine

		(a 4% increase), and 8% do not know (1% decrease). • Intention to vaccinate was lowest in those aged 25-34, women, those without secondary education, who were unemployed, more deprived, were not worried about getting COVID-19, those with conspiratorial views, and those who check social media once a week or less. • Households with minors had lower intentions to vaccinate compared to single person households, and households without minors. • Immigrants were more hesitant and unsure about receiving a vaccine compared to non-immigrants. • The top three reasons among those who were not intending to vaccinate included worry about side effects, lack of confidence in vaccines in general, and the newness of the vaccine. • 28% of those who do not intend to vaccinate believe that it is incompatible with their religious beliefs or personal principles. **Earlier** • 77% of respondents who have not been vaccinated yet intend to get a vaccine, a 1% drop since early April. 14% do not intend to get a vaccine (no change), and 9% do not know (1% increase). Intention has increased 7% since December. • Intention to get a vaccine was higher among men compared to women (78% vs 76%), older respondents (79% for those 60+ vs 75% for those 18-25), and among those with university degree (85% of those with university, 78% with college). • Intention to vaccinate generally increased as communities increased in size, from living in small villages less than 10,000 (71%), towns 10,000 to 100k (73%), greater Montreal area (81%) and Montreal (79%). • 68% disagree with the statement "people vaccinated against COVID-19 should have the right

		to have private gatherings and no longer wear a mask in public" whereas 25% agreed and 7% were unsure. • In December those with low intentions to vaccinate were concerned about side effects (27%), the newness of the vaccine (24%), and not trusting vaccines in general (24%). • Those holding conspiratorial world views were less likely to accept a vaccine (51% vs. 76%). • Agreement with compulsory vaccination continues to trend downwards with 54% agreeing in December.
Saskatchewan Population Health and Evaluation Research Unit (2020) *unpublished* (208) Longitudinal study Canada May-Sep 2020	An online survey was used to evaluate intention to vaccinate in residents of Saskatchewan over time. Surveys were conducted from May-Sep. The number of individuals is not stated and it is unclear if they are the same participants over time. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• From May to Sep, intention to vaccinate dropped from 84.9% to 56.5%. • Intention to vaccinate is highest in those 65-74 years of age and lowest in those under 48 years of age.
Cross-sectional studies (n=29)		
Angus Reid (2021) *unpublished* (96) Cross-sectional study Canada	1601 Canadian adults were surveyed about their thoughts on vaccination policies (proof of and vaccine passports) online. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy	• 79% Canadians were supportive of showing proof of vaccination for international travel (excluding the US), 78% support it for commercial flights, and 76% were supportive for traveling to the USA. • Less support was shown for having proof of vaccination for attending large public events (69%), public places such as restaurants, bars, and movie theatres (55%), and at places of work (55%).

May 2021	Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• Those who were vaccine hesitant had much lower support for proof of vaccination across all presented scenarios. • 18% of those not willing to get a vaccine would be swayed to get vaccinated if proof of vaccination was required in many scenarios.
Leger (2021) *unpublished* (209) Cross-sectional study Canada Apr 2021	An online survey of 1004 participants in British Columbia was conducted to assess views on vaccines, vaccine passports, and vaccine rollout. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 16% reported they had received a vaccine. • 49% intend to tell everyone they know when they receive a vaccine, especially for respondents in urban areas (53%) compared to rural (40%). Fewer respondents would only tell immediate family and friends (42%). • 24% intend to share when they get a vaccine on social media. • Most don't feel they should be vaccinated before others (27%), or are jealous (25%), or anxious (25%) of others being vaccinated. • Vaccine passports had high support in international travellers coming to BC (77%) and BC travellers going abroad (75%). Support for passports for Canadians traveling within Canada (68%) and within BC (56%) was slightly lower. • Vaccine passports for any situation had higher support among those 55+. • 70% are happy with the order of vaccination prioritization in BC and 44% are satisfied with the rollout. • Support for health figures or leaders has decreased since Dec 2020 (Dr. Bonnie Henry: 65%, Adrian Dix: 58%, Dr. Theresa Tam: 53%, Justin Trudeau: 45%).
Statistics Canada (2021) *unpublished* (210) Cross-sectional study	Vaccine intentions and perceptions were analyzed in 1025 Canadian adults (18+) residing in the capital cities of the territories using mail invites and computer assisted telephone interview for non-responses.	• The majority of respondents had already received one dose (80%) with 16% likely to get vaccinated and few unlikely to get vaccinated (4%). • Respondents were more likely to have received a vaccine or were likely to be vaccinated if they has a post-secondary degree or higher (85% vs 68% for having received a vaccine and 13% vs 23% for likely to get vaccinated respectively).

Canada Mar-Apr 2021	Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 10% of those unlikely to be vaccinated had household income of less than $60,000 compared to 2% among those with incomes between $60,000 to more than $120,000. • Most felt vaccines were safe (95%) and effective (97%) compared to the COVID-19 vaccine which garnered lower support for safety (86%) and efficacy (88%). • 94% of respondents felt confident that Canada's process only approved safe and effective vaccines (94%). • Top sources for COVID-19 vaccination information were Public Health Agency of Canada and Health Canada (89%) and provincial, territorial or regional health authorities (85%).
Centre for Addiction and Mental Health (2021) *unpublished* (211) Cross-sectional study Canada Mar 2021	An online survey of 1000 Canadians as part of Asking Canadians web panel was conducted to measure mental health and vaccine intentions. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 66.4% of respondents who haven't received a vaccine yet definitely intend to get one, 21.8% will probably get a vaccine, and 11.8% definitely or probably will not get a vaccine.
Tang (2021) *preprint* (212) Cross-sectional study Canada Jan-Mar 2021	To assess vaccination hesitancy in population subgroups in Canada, an online survey of 14,621 panel members from the nationally representative Angus Reid Forum was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy	• Overall, 9.3% do not intend on receiving a vaccine. This was highest in AB (16.4%), MB & SK (13.8%) and lowest in QC (8.3%), the Atlantic provinces (8%), ON (7.8%), and BC (7.2%). • Vaccine hesitancy was significantly associated with those aged 40-59 years (OR 0.87, 95% CI: 0.78-0.97), being a visible minority (OR 0.56, 95% CI: 0.37-0.84), lower education, and belonging to a household of five or more people (OR 0.82, 95% CI: 0.76-0.88).

	Survey tools available? No Formative research conducted? No Survey pre-tested? No	
Syan (2021) *preprint* (77) Cross-sectional study Canada Jan – Feb 2021	Factors associated with intention to receive a COVID-19 vaccine was assessed in 1,367 adults (18+) living in Southern Ontario using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 82.8% were willing to receive a vaccine and 17.2% were unwilling. • The most common reasons for vaccine hesitancy were concern over long-term (65.5%) and immediate (60.5%) side effects, and a lack of trust in the vaccine (55.2%). • Higher intention to vaccinate was significantly associated with male gender (P=0.002) and higher education levels (P<0.001). • The perception of COVID-19 vaccine safety was significantly lower (-10.7%) than vaccines in general. Females, older adults, and those with less education reported lower perceived COVID-19 vaccine safety.
Leger (2021) *unpublished* (99) Cross-sectional study Canada Jan 2021	An online survey of 800 participants from Manitoba (18+) was conducted to investigate vaccine perceptions and intentions to vaccinate. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine rollout perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 72% reported the intention to vaccinate when a vaccine is available. • Intention to vaccinate increases with age. 82% of those aged 55+ reported they would definitely or probably intend to vaccinate compared to 65% of those aged 18-51. • Higher education and higher incomes are associated with an increased intention to vaccinate. • Vaccine safety is still a concern as 57% don't want to be in the first wave of people getting vaccinated and want to wait until safety has been established. 49% have concerns about safety but have generally pro-vaccine opinions. • >66% agree that the vaccine should be mandatory for all healthcare workers. • 71% of respondents are comfortable with how the Manitoba government is determining priority groups for early vaccination.

Leger (2021) *unpublished* (100) Cross-sectional study Canada Jan 2021	1000 residents of Alberta (18+) were surveyed online regarding their perceptions of the vaccine rollout. Question Topics: 1) Vaccine rollout perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Approval of the overall vaccine rollout in Alberta was split, 48% were satisfied and 43% were dissatisfied. • For the order of priority groups established by the government, 64% were satisfied and 28% were dissatisfied. • 44% were satisfied with the government's communication of the rollout plan and 48% were not. • More individuals were dissatisfied (56%) with the pace of the rollout compared to satisfied (35%). • 53% believe they will have the opportunity to receive a vaccine after September.
Insights West (2021) *unpublished* (67) Cross-sectional study Canada Jan 2021	Intention to vaccinate was analyzed using an online survey of 824 residents of British Columbia. Question Topics: 1) Vaccine intentions 2) Vaccine rollout perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 58% of respondents were definitely willing to be vaccinated, 22% were probably willing, 5% probably will not get vaccinated, and 7% definitely will not. • 67% of older respondents (55+) were more likely to get vaccinated compared to those in younger age groups (52% among 18-34 year olds). • 69% felt that those with underlying conditions were should have been put ahead of others on the list. • When asked about the vaccine rollout plan, 5% rated the rollout as excellent, 30% good, 51% fair, 14% poor, and 7% very poor. Similar trends were seen for perceptions on clarity of the rollout and prioritization levels.
Afifi (2021) (213) *new* Cross-sectional study Canada Nov-Dec 2020	Using survey respondents from the longitudinal Well-Being and Experiences study (2017-2020) vaccine intentions were recorded for Winnipeg adolescents aged 16-21 and their caregivers/parents using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy	• 65.4% of respondents intend to receive a vaccine, 26.1% were not sure, and 8.5% were not willing. • Parents with trade school, community college or less, with incomes of less than $49,999, experienced quite a bit COVID-19 financial strain, self-reported low knowledge of COVID-19 were associated with lower intentions to get a vaccine. • Having a self-reported health condition was associated with higher intentions to accept a vaccine. • After adjusting for sex, age and household income, children who had no experience with spanking

	Survey tools available? No Formative research conducted? No Survey pre-tested? No	(aRR 0.33, 95% CI: 0.17–0.62), no peer victimization (aRR 0.49, 95% CI: 0.25–0.96), no household substance abuse (aRR 0.41, 95% CI: 0.20–0.83), no contact with foster care/child protective office (aRR 0.34, 95% CI: 0.16–0.72), and no risk of their household running out of money (aRR 0.45 95% CI: 0.21–0.97) were more willing to get vaccinated. • Reporting no to any household challenge adverse childhood experience (ACE) was associated with willingness to vaccinate (aRR 0.45, 95% CI: 0.20–0.99). • The top concerns for being unwilling to accept a vaccine were for vaccine safety (64.5%), not knowing enough about the vaccine (60.6%), and not thinking the vaccine would be effective (23.4%).
Province of Manitoba (2020) *unpublished* (214) Cross-sectional study Canada Nov 2020	An online survey of 9872 adults in Manitoba was conducted to assess COVID-19 vaccine perceptions and intention to vaccinate. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 55% and 19% of participants reported they definitely or probably will receive the COVID-19 vaccine when available, respectively. The other participants stated they were undecided (8%), probably would not (7%) or definitely would not (12%) take the vaccine. • 61% of participants agreed with the statement "Vaccines are safe and I have no doubts about vaccinating myself or my family, as recommended by my doctor".
Independent Polling System of Society (IPSOS)/Radio Canada (2020) *unpublished* (215) Cross-sectional study	Intention to vaccinate and perceptions on the vaccine were analyzed using an online survey of 3001 adults (18+). Question Topics: 1) Vaccine intentions 2) Vaccine perceptions	• 64% of participants would probably or certainly get vaccinated, 16% definitely would not, and 21% were unsure. • Of those who would be vaccinated, 36% would get vaccinated as soon as possible, 38% would wait one or two months to see what happens, 15% would wait several months, and 11% were undecided.

Canada Nov 2020	Survey tools available? No Formative research conducted? No Survey pre-tested? No	• The majority of respondents were worried about possible side-effects and risks associated with the vaccine.
Independent Polling System of Society (2020) *unpublished* (93) Cross-sectional study Canada Nov 2020	An online survey of 1001 adults (18+) analyzed intention to vaccinate and perceptions on the vaccine. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 52% of respondents would take a COVID-19 vaccine as possible without hesitation. However, when other options, 36% would take the vaccine waiting to see if there were adverse side-effects and 28% would after waiting to see if it's effective. • 13% of participants would refuse vaccination under any circumstance. • 71% of participants say that taking a vaccine that was created and approved so quickly makes them nervous and 69% are concerned about long-term effects. • 59% of participants support mandatory COVID-19 vaccination, a drop from 61% in Sept, and 72% in July. • Some participants stated that a recommendation by a family doctor (21%), or seeing friends and family receive the vaccine (10%) would make them willing to take a vaccine. • Most agree that frontline healthcare workers (62%) and first-responders (52%) should be first in line to receive the vaccine. However, outside of these target groups, Canadians are divided on who should be a priority. • Three in ten (30%) believe that we can beat COVID-19 without a vaccine, down from 40% in Oct.
Independent Polling System of Society (2020) *unpublished* (62) Cross-sectional study	An online survey of 1000 adults analyzed intention to vaccinate and perceptions on the vaccine. Of these, 1000 participants were Canadian. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions	• 54% of Canadians would be willing to take a vaccine as soon as it is available. Atlantic Canada have the highest intentions (75%), followed by SK/MB (65%), QC (63%), BC (60%), AB (58%), and ON (57%). • 61% of participants support mandatory COVID-19 vaccination, a drop from 72% in July. • 82% indicate that they would wait for reports about the effectiveness or any side-effects of a COVID-19 vaccine before taking it.

Canada Oct 2020	3) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• The majority (88%) of participants agree that seniors and other vulnerable communities should be the first priority to receive the vaccine. • Four in ten (40%) believe that we can beat COVID-19 without a vaccine.
Toronto Public Health (2020) *unpublished* (216) Cross-sectional study Canada Oct 2020	Intention to receive a COVID-19 vaccine was evaluated using an online survey of 1201 residents of Toronto, Ontario. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 73% of participants report that when a COVID-19 vaccine is available they will "definitely" or "probably" get it. 20% will "definitely" or "probably" not receive it and 11% are undecided.
Statistic Canada (2020) *unpublished* (78) Cross-sectional study Canada Sept-Oct 2020	A telephone survey of 120,000 (18+) was conducted to assess intention to vaccinate. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Immigrants living in Canada for less than 10 years (80.3%) and more than 10 years (70.7%) had comparable intentions to vaccinate compared to non-immigrants (75.9%). • Women who were non-immigrants or who immigrated less than 10 years ago had lower intentions than men (74.7% vs 77.2% for non immigrants and 78.1% vs 82.9% for less than 10 years). • When comparing all visible minorities against Whites race, vaccine intentions were nearly identical (77.3% vs 77.0%). • Within visible minority groups intention to vaccinate from lowest to highest was Black (57.0%), Latin American (58.5%), Filipino (64.2%), South East Asian (75.8%), other visible minorities (77.6%), Chinese (85.5%), and Arab (88.3%). • 69.3% reporting an Aboriginal identity were accepting of a vaccine compared to 77.6% not reporting an Aboriginal identity.

		• 87.6% of LGBTQ2+ were willing to accept a vaccine compared to 76.4% non-LGBTQ2+. • Higher levels of education and having an underlying medical condition were associated with higher acceptance.
Ogilvie (2021) (79) Cross-sectional study Canada Aug-Sep 2020	Intention to vaccinate was assessed in 4058 adults and healthcare workers from British Columbia (25-69 years old). Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 79.8% of respondents were somewhat or very likely if available to them and was recommended for them. • 81.8% of healthcare workers report that they intend to receive a vaccine. • Non-binary, gender queer, agender, two-spirit or other were more likely to be receive a vaccine (OR 3.04, 95% CI: 1.08-8.55). • Households with two adults (OR 1.2, 95% CI: 1.00-1.43) were more likely to vaccinate but there were no significant changes in intention with number of children. • Multivariate analysis demonstrated that younger respondents (30-40 years old aOR 0.64, 95% CI: 0.49-0.83, 40-50 years old aOR 0.78, 95% CI: 0.62-0.97, 50-60 years old aOR 0.67, 95% CI: 0.55-0.82), females (aOR 0.7, 95% CI: 0.55-0.89), lower education level (aOR 0.62, 95% CI: 0.51-0.77), South Asian (aOR 0.65, 95% CI: 0.39-1.07), non-White (aOR 0.76, 95% CI: 0.61-0.95), identified as Indigenous (aOR 0.58, 95% CI 0.38-0.87), other essential non-health care workers (aOR 0.72, 95% CI: 0.6-0.87), and those who suspected they had COVID-19 (aOR 0.76, 95% CI: 0.61-0.96) had significantly lower odds of intending to receive a vaccine. • Lack of confidence in vaccines (aOR 0.66, 95% CI: 0.57-0.75) and belief in vaccine risks (aOR 0.72, 95% CI: 0.66-0.80) were associated with decreased intention to vaccinate. • Intention to vaccinate was positively associated with higher attitudinal scores towards the vaccine (aOR 1.06, 95% CI: 1.04-1.08), influenced by direct social norms (aOR 1.06, 95% CI: 1.03-1.08), indirect social family doctor/primary care physician

		opinions (aOR 1.04, 95% CI: 1.00-1.08), indirect norms from the provincial health officer (aOR 1.04, 95% CI: 1.01-1.08), and indirect family norms (aOR 1.09, 95% CI: 1.06-1.13).
Lang (2021) (87) Cross-sectional study Canada Aug 2020	An online survey of 60 adults (18+) in Alberta was conducted to assess their intention to vaccinate. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 68% of respondents would accept a vaccine if it were available, 20% would not, and 12% were unsure. • White respondents were less likely to accept a vaccine (63%) compared to other ethnicities (100%). • Those with higher education (college or university) were less likely to accept a vaccine (63%) compared to those who had attended post-secondary technical school (100%) or had a high school diploma (70%). • Intention to vaccinate was positively associated with concerns about getting COVID-19 (P <0.001) and spreading the virus (P = 0.006), and complying with public health measures such as staying home when sick (P = 0.033), masking in public (P < 0.001) and physical distancing (P = 0.005). • Respondents who received their COVID-19 health information from the Chief Medical Officer of Health media briefings (P = 0.030) and Alberta Health or Alberta Health Services websites (P = 0.040) were significantly more likely to accept a COVID-19 vaccine. • Intention to vaccinate was lower in other urban centers (29%) and rural Alberta (50%) compared to Calgary (75%) and Edmonton (80%), (*P* = 0.030).
Carleton University (2020) *unpublished* (217) Cross-sectional study	An online opinion survey regarding vaccine intentions and perceptions was conducted online in 2000 individuals. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy	• 62% will definitely get the vaccine, 24% will probably get the vaccine, 5% will not likely get the vaccine, and 9% will definitely not get the vaccine. • Resistance to a vaccine is highest in MB and SK where only 37% will definitely get vaccinated across both provinces.

Canada Jul 2020	3) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• In terms of views on mandatory vaccination, 36% strongly agree, 26% somewhat agree, 14% strongly disagree, and 7% somewhat disagree. • The most common reason (40%) for hesitancy was potential for harmful side-effects. • The 9% of respondents who expressed strong anti-vaccine views, suspicion about the influence of the pharmaceutical industry over public health care (41%) and concern about vaccine safety and the potential for harmful side-effects (29%) were the most common reasons for refusal.
Frank (2020) *unpublished* (63) Cross-sectional study Canada Jun 2020	Factors associated with willingness to vaccinate was investigated using an online survey of ~4000 adults. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 57.5% and 19% of respondents indicated they are very likely or somewhat likely to get a COVID-19 vaccine when it becomes available, respectively. • Older Canadians (65+) reported they were more likely to vaccinate (70.3%) compared to those aged 15-64 (52-58%). • Those that were born in Canada were more likely to vaccinate compared to immigrants (59.4% vs 52.0%). • Residents in the Atlantic Provinces are more likely to vaccinate (67.7%) followed by Ontario (58.8%), Prairies region (56.2%), BC (55.5%), and QC (54.3%). • Other factors associated with a higher intention to vaccinate include higher education and not having children under the age of 18. • The top two reasons for not intending to vaccinate were a lack of confidence in the safety of the vaccine (54.2%) and concerns about its risks and side-effects (51.7%).
Hetherington (2021) (218) Cross-sectional study Canada	Participants from the longitudinal cohort study All Our Families (n=1321) in Alberta were invited to participate in an online COVID-19 impact survey to understand factors associated with COVID-19 vaccine intentions among parents of 9-12 year old children.	• 60.4% of parents intended to vaccinate their children, 8.6% said they did not intend to vaccinate, and 31% were unsure. • Participants with less education were more likely to not want to vaccinate (OR 2.80, 95% CI: 1.78-4.40) or be unsure (OR 1.98, 95% CI: 1.47-2.71). A similar pattern was seen for income.

May-Jun 2020	Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• History of partial or non-vaccination was associated with intent to not vaccinate (OR 2.81, 95% CI: 1.78-4.40). There was no association between vaccination history and uncertainty regarding a COVID-19 vaccine (OR 1.29, 95% CI: 0.92-1.80). • Concerns over vaccine safety and efficacy, long-term effects, and a rushed vaccination process were reported.
Frank (2020) *unpublished* (219) Cross-sectional study Canada May-Jun 2020	An online survey of ~36,000 adults was conducted to investigate factors associated with willingness to vaccinate. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 68.2% and 15.2% of participants reported that they were very likely or somewhat likely to accept a COVID-19 vaccine, respectively. 12% were unlikely or very unlikely to vaccinate. • Those who had a high level of trust in the federal government were more likely to be willing to vaccinate compared to those with a low level of trust (77.3% vs 53.8%). • Similar trends were also seen with trust in others, and trust in federal public health authorities.
Lackner (2021) (189) Cross-sectional study Canada May-Jun 2020	The demographic, experiential, and psychological factors associated with the anticipated likelihood and speed of having children receive a COVID-19 vaccine was investigated in 455 families (857 children). Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Factors associated with a higher likelihood of having their children vaccinated include older parental age, living in the Prairies (relative to Central Canada), more complete child and parental vaccination history, positive attitudes towards vaccines in general, higher psychological avoidance of the pandemic, and a greater tendency to prioritize the risks of the disease relative to the risks of side-effects. • In some models, perceived COVID-19 risk and higher levels of state anxiety were associated with increased likelihood of having children vaccinated. • The above factors were also predictors of faster speed of intended vaccination. However, higher SES was a trend-level predictor.
Taylor (2021) (220)	An online survey of 2078 adults (18+) was used to explore the potential relationship between	• The network of anti-masks attitudes is linked to other variables such as disregard for social distancing and anti-vaccination attitudes.

Cross-sectional study Canada & USA Jun-Jul 2020	attitudes on wearing a face mask and COVID-19 vaccination. The sample consisted of 1036 participants from the USA and 1042 from Canada. Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	
Waite (2021) (92) Cross-sectional study Canada May 2020	An online survey of 1001 Canadians aged 50–64 years and 3,500 aged 65+ was conducted to evaluate intention to vaccinate against COVID-19. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Among those aged 50-64 years, 69.1% intend to vaccinate when available, 11.3% would not vaccinate, and 19.6% were unsure. • 79.5% of those 65+ intend to receive a vaccine when available, 5.6% would not vaccinate, and 14.9% were unsure. • In both age groups, those who would accept a vaccine were significantly more likely to be male and more likely to have at least one chronic condition (P< 0.05). • The preferred location to receive a vaccine in both groups was family physician office, followed by pharmacy, workplace (for those 50–64 years), and public health clinics.
Taylor (2020) (89) Cross-sectional study Canada & USA May 2020	Intentions to vaccinate and attitudes towards vaccines were measured using an online survey of 3674 adults (Canada = 1902, USA = 1772). Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes	• Significantly more Americans (25%) than Canadians (20%) responded that they would not get vaccinated if a vaccine was available, χ^2 (df = 1) = 12.41, p < 0.001. • Negative attitudes toward a COVID-19 vaccination, and vaccinations in general, were significantly correlated (p < 0.001) with the intention not to vaccinate. Mistrust of the benefit of a COVID-19 vaccine was the largest factor with respect to attitude on the decision not to get the vaccine. • Vaccination refusal was significantly associated with female gender, age, completed full or partial

	Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	college education (vs. did not complete), being unemployed, and minority status (vs. Caucasian). • Of those who indicated they would not get vaccinated (n=812), 38% would vaccinate if they were convinced the vaccine had been rigorously tested and 36% would vaccinate if they saw that enough people were vaccinated without any serious side-effects. • Compared to White ethnicity, minority status (Asian, African American/Black, Latino/Hispanic, or other) was significantly associated with vaccine refusal ($r = -0.04$, $P < 0.05$).
Carleton University (2020) *unpublished* (59) Cross-sectional study Canada May 2020	An online opinion survey regarding vaccine intentions and perceptions was conducted online in 2000 individuals. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 49% and 24% of the participants would "definitely" or "probably" get the vaccine when available, respectively. • 17% expressed uncertainty and 10% were unwilling. • 65% believe that the vaccine should be mandatory. • Age and political affiliation were significantly associated with intention to vaccinate. Older individuals were more willing to vaccinate than younger. Those who voted Liberal or NDP in the 2019 election were more likely to vaccinate compared to those who voted for other parties. • Respondents living in Atlantic Canada showed the strongest levels of intention to vaccinate compared to those in other provinces. • Those who believed one of the four health myths or conspiracy theories regarding COVID-19, were less likely to intend to vaccinate than those who did not believe the scientifically inaccurate claims about COVID-19.
Parsons Leigh (2020) (64) Cross-sectional study	COVID-19 perceptions, knowledge, attitudes, and behaviors were analyzed using an online survey of 1996 participants (18+). Question Topics:	• 75.8% (n = 1,436) of respondents reported that they would get vaccinated when a vaccine became available. • Participants responded they "strongly agree" or "agree" that they will get vaccinated in BC (72.1%),

Canada Apr-May 2020	1) Vaccine intentions 2) Vaccine knowledge Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	AB (69.9%), MB/SK (69.9%), ON (66.1%), Atlantic (63.1%), and QC (41.9%). • Participants responded they "strongly agree" or "agree" that they will not get vaccinated in AB (12.4%), QC (12.1%), ON (8.1%), Atlantic (6.6%), MB/SK (6%), and BC (4.8%). • Information about vaccines and treatments were most frequently (n = 933, 48.9%, 95% CI: 46.7-51.2%) cited as topics of misinformation, however only half (n = 937, 47.4%, 95% CI: 45.2%-49.6%) of respondents felt moderately or extremely confident that they could identify incorrect or misleading information about COVID-19.
Underschultz (2021) (221) Cross-sectional study Canada Apr 2020	COVID-19 knowledge, attitudes, and practices were analyzed using an online survey of 1593 participants (16+). The survey was primarily targeted to residents of Alberta and Ontario. Question Topics: 1) Vaccine perceptions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 93% of respondents believe that a vaccine is needed in Canada and 81% endorsed a wide-spread vaccination strategy (having everyone vaccinated). • Vaccine acceptance was significantly associated with higher knowledge scores ($p<0.001$), being worried about COVID-19 (OR 20.4; 95% CI: 8.4-49.5, $p<0.001$), optimism in controlling the pandemic (OR 8.1; 95% CI: 3.4-19.7, $p<0.001$), and feeling informed about COVID-19 (OR 3.9; 95% CI: 1.7-9.3, $p=0.0049$).
Research Co (2020) *unpublished* (58) Cross-sectional study Canada Apr 2020	Intention to vaccinate was assessed using an online survey. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• If a vaccine becomes available, 42% and 31% would "definitely" or "probably" get the vaccine, respectively. • Men were more likely to vaccinate than women (78% vs 68%). • The Atlantic (79%) and Alberta (78%) had the highest intentions to vaccinate and Saskatchewan/Manitoba (65%) had the lowest. • Intention to vaccinate was highest in those who voted liberal (79%) in the 2019 election, followed by NDP (76%), and conservative (69%).

Qualitative studies (n=1)		
Benham (2021) (222) Qualitative study Canada Aug-Sep 2020	Nine focus groups were conducted with 50 adults (18+) from Alberta to evaluate attitudes towards public health measures including vaccination. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions	• Intention to vaccinate responses were mixed. Some stated they would vaccinate right away, while others would not vaccinate as they believed COVID-19 would not impact their health or the health of their family members. • Some participants reported that they would be willing to take a vaccine but not right away. This was more prominent in the older age groups. • Participants who regularly received the annual flu vaccine were more likely to state they would take a COVID-19 vaccine when available. However, a few experienced side effects with the annual flu shot (e.g., getting sick) which would make them less likely to get a COVID-19 vaccine. • Barriers for vaccine uptake included a lack confidence that a vaccine will work, and that it may do harm.
Quasi-experimental studies (n=1)		
Poder (2021) *unpublished* (223) Quasi-experimental study Canada Oct-Nov 2020	An online survey of vaccine intentions of 1,695 Quebec adults was conducted which included an assessment of preferences through a series 12 binary choice scenarios (20,350 choice responses in total). Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• At least 7.2% always chose not to be vaccinated in any given scenario. • Depending on the scenario, 69-93% of participants would opt for the vaccine when available. • 24% of participants would make the choice to refuse the vaccine if certain conditions were not met which were determined to be in order of priority: 1) vaccine efficacy 2) possible side effects of the vaccine 3) duration of effectiveness (minimum of 9 months for acceptability) 4) the organization recommending the vaccine (Public health organizations of Québec, WHO) 5) geographic origin of vaccine (European Union or United States)

		6) waiting period to be vaccinated once the vaccine is available in Quebec (4 months maximum) 7) high priority populations (no preferences)
Expert Stakeholders		
Cross-sectional studies (n=2)		
MacDonald (2020) *preprint* (101) Cross-sectional study Canada Aug-Oct 2020	Eighteen teleconference interviews with 25 public health leaders from 10 of 13 provinces and territories were conducted to evaluate perspectives on priority groups for early vaccination. Participants were asked to rank, in order of importance, their top five priority groups for vaccination. Question Topics: 1) Vaccine strategy perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• All ten province and territories ranked long-term residents and health-care workers in their top five priority groups to receive vaccination. • Those with chronic medical conditions and seniors were also ranked in the top five priority groups by nine and eight provinces and territories, respectively. • To a lesser extent, those with Indigenous ancestry (n=4), with socioeconomic disadvantage (n=3), with infants or children (n=2), living in remote communities (n=2), and new immigrants and refugees (n=1) were ranked in the top five priority groups.
Zhao (2020) *preprint* (102) Cross-sectional study Canada Jul-Aug 2020	Among 74 expert stakeholders, an online survey was conducted to establish perspective on the relative importance of pandemic immunization strategies for different COVID-19 pandemic scenarios at the time of initial COVID-19 vaccine availability. Questions asked the respondent to rank, in order of importance, four pre-defined COVID-19 pandemic immunization strategies.	• For all pandemic scenarios, stakeholders generally ranked the strategies in the following order from most to least important: ○ Protect those who are most vulnerable to severe illness and death from COVID-19 ○ Protect healthcare capacity ○ Minimize transmission of COVID-19 • Protect critical infrastructure

	Question Topics: 1) Vaccine strategy perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	

aOR = adjusted odds ratio, CI = confidence interval, HCWs = healthcare workers, NR = not reported, RR = risk ratio

HEALTHCARE WORKERS

Table 4. Evidence of vaccine attitudes of healthcare workers (n=42)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
NORTH AMERICA		
CANADA		
Lunsky (2021) (105) Cross-sectional study Canada Jan-Feb 2021	To evaluate vaccination intent and predictors of intent, an online survey of 3371 social service employees supporting individuals with intellectual disabilities in Ontario was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 62% and 20% reported that they were very likely, or somewhat likely to accept a vaccine, and 7% and 11% somewhat unlikely or very unlikely to get the vaccine, respectively. • Compared to individuals aged 50 +, younger individuals aged 18-29 (aOR 2.74, 95% CI: 1.70–4.43) and 30-39 (aOR 1.75, 95% CI: 1.16–2.64) were more likely to refuse a vaccine when available. • Women were more likely to refuse a vaccine compared to men (aOR 1.58, 95% CI: 0.97-2.59). • Compared to European respondents, Asian (aOR 0.88, 95% CI: 0.33-2.36), African and Caribbean (aOR 0.81, 95% CI: 0.35-1.86), and unknown ethnicities (aOR 0.88, 95% CI: 0.36-2.17) were less likely to refuse a vaccine and Indigenous, First Nations, and Metis (aOR 1.73, 95% CI: 0.67- 4.43), Latin (aOR 1.22, 95% CI: 0.21-7.24), and mixed ethnicities (aOR 1.11, 95% CI: 0.27-4.55) were more likely to refuse. • Reasons to refuse a vaccine included lack of trust in the vaccine (OR 5.72, 95% CI: 3.84–8.53), fear of vaccine side effects (OR 2.30, 95% CI: 1.56–3.39),

		and belief that there was no need for the vaccine due to good health (OR 4.22, 95% CI: 2.66–6.68). • Individuals who would refuse a vaccine were less likely to believe that vaccination would protect clients (OR 0.36, 95% CI: 0.24-0.54) or family (OR 0.19, 95% CI: 0.13-0.28),be concerned about clients (OR 0.57, 95% CI: 0.34-0.97) or themselves (OR 0.51, 95% CI: 0.34-0.76) becoming ill with COVID-19, get the flu shot in a normal year (OR 0.61, 95% CI: 0.43-0.88), and get the vaccine if their co-workers did (OR 0.16, 95% CI: 0.08-0.29).
Desveaux 2021 *preprint* (103) Cross-sectional study Canada Jan 2021	Factors associated with intention to vaccinate was evaluated in 8634 non-physician HCWs (18+) in Ontario using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 80.4% of participants reported that they intend to get a COVID-19 vaccine. • Compared to their counterparts, those who were younger (<40 years old) and who had less education (less than a high school diploma) were more likely to be unwilling to intend to vaccinate (P<0.001). • HCWs who identified as Filipino (OR 1.07, 95% CI: 0.41-2.76, P<0.001), Caribbean (OR 3.20, 95% CI: 1.52-6.75, P<0.001), or Other (OR 1.44, 95% CI: 0.93-2.22, P<0.001) ethnicity were more likely to be unwilling to vaccinate compared those who identified as European. • Vaccine hesitancy was strongly associated with mistrust about how fast the vaccines were developed and vaccine safety concerns. It was also associated with various beliefs such as not requiring a vaccine due to one's own good health, low confidence that the vaccine would protect their family and patients, and that getting vaccinated was not a professional responsibility. • HCWs were more likely to intend to vaccinate if direct financial supports such as paid sick days were provided (74% vs 25%, P<0.001).
SafeCare BC (2021) *unpublished* (104)	An online survey of 1,500 continuing care workers in British Columbia was conducted to	• 57% of respondents intend to get a vaccination, 28% were not sure, and 15% did not intend to get vaccinated.

Cross-sectional study Canada Dec 2020	evaluate attitudes on COVID-19 vaccination. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Male (72% vs 56%), higher age (65+) and flu shot acceptance were predictors of intention to vaccinate. • Managers and senior leaders had the highest intentions to vaccinate (71%). Healthcare assistants were the most unsure (30%), and nurses were most likely to say no to a vaccine (20%). • Reason for hesitancy were side effects (84.6%), the newness of the vaccine (64.6%), mistrust of authorities (23.5%), belief that the vaccine will not work (16%), preferred natural remedies (10.5%), and personal or religious beliefs (8%). • Intention to vaccinate was highest in East (61%) and South Asian (70%). Latino and Black respondents were the most likely to refuse a vaccine (30%) and Indigenous respondents were most likely to be unsure about their decision to vaccinate (40%). • East/South Asian respondents were more concerned about side effects (93%) whereas White or Indigenous respondents were more concerned about newness (72% and 62%, respectively). • 33% said more support for vaccinations is needed e.g. more information to understand the development process, efficacy, and transparency of reporting adverse events. • The biggest perceived barrier to administering the vaccine was storage and handling constraints (66%). • Indigenous respondents had the least amount of trust in all sources of information including healthcare providers.
INSPQ (2020) & INSPQ (2021) *unpublished* (88, 95) Longitudinal study	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in Quebec. Number of participants was not clearly stated (~3300 each collection period). There were multiple collection periods, one in	• In May, 73% of HCWs responded with the intention to vaccinate. In Dec this decreased to 65% and increased to 71% in Dec. • Intention to vaccinate did not differ between the general public and healthcare workers and factors associated with intention to vaccinate were not differentiated between the two groups.

Canada Apr-Dec 2020	Apr-May and one in Sep and Dec. Article in French. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Those that were older (70+) were more likely to vaccinate compared to those 25-44 years old (83% vs 57%). • Men, those with a university education, and those with one or more chronic diseases are more likely to intend to vaccinate. • The most common reasons to not intend to vaccinate include fears related to taking a new vaccine, and concern regarding the effectiveness and side-effects.
Verger (2021) (127) Cross-sectional study Belgium, France & Canada Oct-Nov 2020	Intention to vaccinate and intention to recommend vaccination to patients was evaluated using an online and telephone survey in general practitioners (GPs) in France (n=1209) and French-speaking parts of Belgium (n=414) , and nurses in Quebec, Canada (n=1055). Belgium and France results can be found in the Europe section. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? Yes	• In Canada, 79.6% of nurses would definitely or probably recommend their patients vaccinate, 3.1% would not, and 17.2% were unsure. For themselves, 70.4% would definitely or probably be willing to receive the vaccine, 11.8% would refuse, and 17.8% were unsure. • 40.9% of participants reported that the safety of vaccines developed in an emergency during an epidemic cannot be guaranteed. • Opinion about the safety of vaccines developed in an emergency and distrust in the ministry of health to ensure vaccine safety were the two most important factors independently associated with vaccine hesitancy and reluctance. • Intention to vaccinate was positively associated with a history of personal vaccination against the flu.
Ogilvie (2021) (79) Cross-sectional study Canada	Intention to vaccinate was assessed in 4058 adults and healthcare workers from British Columbia (25-69 years old). Unclear how many healthcare workers in the survey. Question Topics:	• 81.8% of healthcare workers report that they intend to receive a vaccine. • Other results found in general population. • Multivariate analysis demonstrated that South Asian (aOR 0.65, 95% CI: 0.39-1.07), non-White (aOR 0.76, 95% CI: 0.61-0.95), and those who identified as Indigenous (aOR 0.58, 95% CI 0.38-

Aug-Sep 2020	1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	0.87) had significantly lower odds of intending to receive a vaccine.
The Canadian PSW Network (2020) *unpublished* (131) Cross-sectional study Canada NR 2020	Intention to vaccinate in 562 personal support workers (PSWs), nurses, and healthcare workers using an online survey. 84% of the sample were PSWs. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 64.2% of respondents intend to vaccinate when it is available, 16.2% refuse to vaccinate, 10.7% are unsure, and 8.9% will only take the vaccine if it's mandatory. • 71.7% do not believe there is enough clear education on the vaccine.
UNITED STATES & UNITED KINGDOM		
Abohelwa (2021) (224) *new* Cross-sectional study USA Mar 2021	Uptake and intention towards vaccination were gathered online from 81 residents and fellows from Lubbock campus of Texas Tech University Health Sciences Center. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 95.1% had already received the vaccine and 96.3% reported that they supported vaccination. • 3.7% did not want the vaccine. Reasons were not explored.

King (2021) *preprint* (181) Longitudinal study USA Jan-Mar 2021	As part of a monthly ongoing national COVID-19 survey, questions to measure vaccine acceptance and related factors of acceptance were collected in samples of adults (age 18-64). The number of HCWs was not reported. Jan survey: n= 791,716 Feb survey: n= 710,529 Mar survey: n= 732,308 Question Topics: 1) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• Vaccine hesitancy overall decreased from 27.5% in January to 22.1% in March. • 78.3% of healthcare workers were vaccinated with 14.1% who responded in a way that indicated that they were vaccine hesitant. • The level of hesitancy varied by healthcare profession (lowest to highest): 8.5% in pharmacists, 11.7% nurses/nurse practitioners, 12.2% in physicians, 14.1% in practitioners/technicians, 15.1% in support, 19.0% in practical/vocational nurses, and home health aids/medical assistants/paramedics/nursing assistants/psychiatric aides 20.5% to 23.1%).
Pacella-LaBarbara (2021) (117) *new* Cross-sectional study USA Jan-Feb 2021	An online survey of 475 emergency department and emergency medical service workers from Ohio, Maryland, West Virginia, and New York was conducted to determine vaccine intentions and factors associated with intention. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 79% of HCWs had received or had plans to receive the COVID-19 vaccine and 21% had no plans to receive it. • Intention to vaccinate was lower among females (OR 0.34, 95% CI: 0.34-0.91, P =0.02) and those with a history of COVID-19 infection (OR 0.55, 95% CI: 0.31-0.98, P=0.04), and higher among those with higher education (OR 3.53, 95% CI: 1.16, 10.77, P = 0.03) and high perceived COVID-19 vulnerability (OR 1.99, 95% CI: 1.37, 2.90). • All physicians were either vaccinated or intended to vaccinate (100%) compared to 27% of nurses, 21% of EMS, and 27% of other clinicians and staff.
Woolf (2021) *preprint* (114)	To assess COVID-19 vaccine hesitancy and its predictors, an online survey was conducted with 11,584 HCWs (16+). Qualitative	• 23.3% of HCWs were vaccine hesitant. • Older HCWs (aOR 0.74, 95% CI: 0.70-0.78 for each decade increase) and those with prior receipt of

Cross-sectional study and qualitative study UK Dec 2020-Mar 2021	data was collected through interviews (n=24), focus groups (n=17), and open-ended survey responses (n=58). Question Topics: 1) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	the flu vaccine (aOR 0.51, 95% CI: 0.46-0.57) were less hesitant. • Compared to White British HCWs, those from Black Caribbean (aOR 3.37, 95% CI: 2.11-5.37), Black African (aOR 2.05, 95% CI: 1.49-2.82), and White Other (aOR 1.48, 95% CI: 1.19-1.84) ethnic groups were more likely to be hesitant. • Female HCWs (aOR 1.42, 95% CI: 1.24-1.62), pregnant HCWs (aOR 7.12, 95% CI: 4.74-10.70), and those who had tested positive for SARS-CoV-2 (aOR 1.30, 95% CI: 1.14-1.47) were more likely to be hesitant. • HCWs with higher scores on a COVID-19 conspiracy beliefs scale were more likely to be hesitant (aOR 1.12, 95% CI: 1.08-1.16 for each 1 point increase on the scale). • During interviews and focus groups HCWs suggested inclusive health communication (e.g., in multiple languages) and involving HCWs with diverse backgrounds from minority communities in the vaccine rollout to improve vaccine uptake in ethnic minority communities.
Manby (2021) *preprint* (128) Qualitative study UK Dec 2020-Mar 2021	Telephone interviews were conducted with 24 healthcare workers to assess factors influencing their attitudes towards the UK's COVID-19 vaccine program. Question Topics: 1) Vaccine attitudes	• Lack of available evidence was a key driver of vaccine hesitancy. • Belief that government decisions on vaccine rollout were not supported by evidence-based science and mixed and changing government messaging negatively impacted HCWs level of trust and confidence in the vaccine program. • Although the majority reported there was sufficient evidence to show the short-term safety of COVID-19 vaccines, there were concerns raised about the impact of mutant strains on vaccine effectiveness and long-term unknown side effects, such as the impact on fertility. • Online misinformation negatively affected vaccine attitudes, especially among more junior level and Black, Asian and Minority Ethnic (BAME) HCWs,

		with reports of online conspiracy theories targeted specifically to BAME groups. • Most felt motivated to promote vaccination to their patients and many felt it was their moral obligation.
Moniz (2021) *preprint* (116) Cross-sectional study USA Feb 2021	Factors associated with intention to receive a COVID-19 vaccine was assessed in 11,387 adults (18+) at an academic healthcare centre in the Midwest USA using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 79.8% had received the vaccine, 4.8% planned to receive it as soon as possible, 8.4% were not intending to receive it soon but might in the future, and 3.2% had no intentions of ever receiving the vaccine. • Physicians (aOR 22.2, 95% CI: 9.1- 54.3), trainees (aOR 5.9, 95% CI: 3.0-11.4), and nurse practitioners/nurse midwives/physician assistants (aOR 1.9, 95% CI: 1.2-3.0) were significantly more likely to accept a vaccine compared to nurses and other clinical staff (aOR 0.8, 0.6-0.9) and all other employees (aOR 0.8, 0.6-1.0) were less likely. • Those with prior COVID-19 infection were less likely to accept a vaccine (aOR 0.4, 95% CI: 0.3-0.4). • Male HCWs were almost twice as likely to accept vaccines compared to female HCWs (aOR 1.9, 95% CI: 1.6-2.4). • Compared to non-Hispanic White respondents, non-Hispanic Asian respondents were more likely to accept a vaccine (aOR 2.3, 95% CI: 1.5-3.4) and non-Hispanic Black/Mixed/Other respondents were less likely (aOR 0.4, 95% CI: 0.4-0.5). • Mistrust of the vaccine due to how quickly it was developed and safety concerns were the two most common reasons for vaccine hesitancy.
McCabe (2021) *preprint* (166) Cross-sectional study USA	A national app distributed survey was conducted in 34,470 healthcare workers and adults from the general population to measure intent to receive a vaccine and factors associated with acceptance and refusal. Number of healthcare workers was not reported.	• 19% of healthcare workers are undecided, unlikely, or very unlikely to receive a vaccine. • Essential healthcare workers were 1.18 times more likely than non essential workers to be vaccine hesitant (aOR=1.18 95% CI: 1.06-1.32).

Dec 2020-Feb 2021	Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? Yes	
Nguyen (2021) *preprint* (118) Cross-sectional study USA & UK Jan 2021	To assess intention to vaccinate and reasons for hesitancy, an online survey was conducted in 73,650 and 1,154,988 general population adults and HCWs in the USA and UK, respectively. The number of general population versus HCWs was unclear. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• In the USA, frontline HCWs were less likely to intend to vaccinate (6% unwilling and 11% unsure) compared to the general population (2% unwilling and 7% unsure). • Compared to the USA, HCWs the UK reported greater vaccine willingness. • Compared to White ethnicity, Black (aOR 3.00, 95% CI: 2.86-3.16), Hispanic (aOR 1.59, 95% CI: 1.51-1.67), Asian (aOR 1.83, 95% CI: 1.70-1.97), and those reporting more than one race (aOR 1.43, 95% CI: 1.36-1.52) were more likely to be vaccine hesitant in the age-adjusted analysis. • Across all race and ethnicities, the most frequently stated reasons for vaccine hesitancy included concern about long-term side effects (50-57%) and adverse reactions (45-54%). Black and Hispanic individuals cited a lack of knowledge about the vaccine (45-51%) at a higher rate than White individuals (37-42%).
Kociolek (2021) (106) Cross-sectional study USA Jan 2021	An online survey was used to assess the frequency of vaccine hesitancy, reasons for hesitancy, and characteristics of those who reported hesitance in 4448 HCWs at a children's hospital in Chicago, IL. Question Topics: 1) Vaccine intentions	• Of 4277 participants, 59.8% reported they intended to vaccinate, 8.6% had already received the vaccine, 8.8% would not vaccinate, and 10.1% were unsure. • Compared to their counterparts, the proportion of those who were vaccine hesitant were female, had confirmed or suspected COVID-19 history, had high-risk medical conditions, and were not concerned about the severity of COVID-19.

	2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Black participants were more likely to be vaccine hesitant compared to non-Black (50.4% vs 15.6%) and Hispanic/Latinx more hesitant than non-Hispanic/Latinx (29.9% vs 17.1%). • Those who were in non-clinical roles were more hesitant than those in clinical roles (28.7% vs 11.9%) and hourly employees were more hesitant than salaried employees (27.6% vs 11.4%). • The most common reasons cited for vaccine hesitancy were long-term side effects (76.3%), safety (50.7%), and the mRNA method is too new (47.8%). • Among those reporting vaccine hesitancy, the most important resources for COVID-19 vaccine information were self-guided research (46.5%), primary care providers (33%), and federal and government agencies (28.8%). The most preferred communication method for vaccine information from hospital leaders was websites for self-learning (46.9%), email updates (36.7%), and Video updates from hospital leaders and vaccine experts (34.7%).
Ciardi (2021) (125) *new* Cross-sectional study USA Dec 2020-Jan 2021	428 healthcare workers were surveyed online regarding intentions, knowledge, and attitudes towards the COVID-19 vaccine. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 64% planned on getting vaccinated within 30 days with 73% planning on getting a vaccine in the next 6 months. • Respondents who were over 65 (95%), who are Asian (79%), male (79%), and those living in Manhattan (81%) were significantly more likely to accept a vaccine within 30 days. • Those that were least willing to vaccinate in the next 30 days included those aged 36–45 (57%), African Americans (40%), women (60%), and those living in the Bronx (51%). • Intention to vaccinate was highly correlated to trust in PPE and public health measures ($r = 0.222$), public heath actions (r=0.208), confidence in PPE at work (r=0.0988), and those that expect that PPE and practices will need to be continued even after vaccination (r=-0.158).

		• Higher COVID-19 infection knowledge scores and following the news closely were correlated to a positive intent to receive a vaccine (r = 0.18 and r = 0.183, respectively). • Personal experience with COVID-19 was associated with higher intent to vaccinate. • Positive general vaccine attitudes and personal risk were positively and significantly associated with COVID-19 vaccine attitudes and concern about speed of testing was negatively associated.
Enwezor (2021) *preprint* (115) Cross-sectional study USA Dec 2020 – Jan 2021	Intention to vaccinate was assessed in 20,232 adults (15,062 non-HCWs and 5,170 HCWs) using an online survey. 476 of participants had a previous COVID-19 diagnosis. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Intention to vaccinate was significantly different between HCWs (74%) and non-HCWs (77%), P=0.0014.
Dugani (2021) (113) Cross-sectional study USA Dec 2020-Jan 2021	An online survey was conducted with 128 hospitalists, comprised of 75 physicians and 53 advanced practice providers (APPs) including nurse practitioners and physician assistants in Arizona, Florida, Minnesota, and Wisconsin. This study aimed to assess potential differences between physicians and APPs in their attitudes toward COVID-19 vaccines. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes	• 93.7% of hospitalists reported receiving or planning to receive the COVID-19 vaccine (88.7% APPs and 97.3% physicians). • Hospitalists were less likely to advise 100% of patients to receive the COVID-19 vaccine (66% APPs, 74.7% physicians) compared to the influenza vaccine (83% APPs, 80% physicians). Similar trends were seen for advising patients, family, and friend. • Reported barriers for recommending the vaccine to patients included health restrictions for patients (17% APPs, 10.7% physicians) and unknown vaccine safety profile (11.3% APPs, 6.7% physicians). • Hospitalists reported that patients and coworkers receiving the vaccine would reduce their anxiety levels (83% APPs, 75.3% physicians), reduce social

	Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	isolation (60.4% APPs, 60.3% physicians), and increase emotional support (35.8% APPs, 41.1% physicians). • Those who believed the vaccine would reduce their social isolation had higher odds of advising their patients to receive the vaccine (aOR 2.95, 95% CI: 1.32-6.59, P < 0.008).
Armitage (2021) (134) Cross-sectional study UK Dec 2020 – Jan 2021	An online survey of 220 general practitioners (GPs) was conducted to assess their confidence in counselling patients about COVID-19 vaccines. Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Over 50% of general practitioners had low confidence in counselling patients about COVID-19 vaccines. • Many GPs reported no or slight confidence in counselling patients on inclusion of clinically vulnerable patients in vaccine trials (58.2%), vaccine safety in specific groups (67.3%), potential of adverse reactions not yet seen in clinical trials (74.5%), whether individuals participating in trials will be eligible to receive an approved vaccine (78.2%), and the meaning of vaccine efficacies (81.%). • 52.7% and 54.5% of GPs reported no or slight confidence in accessing credible vaccine information for themselves and directing patients towards similar information, respectively.
Berry (2021) (225) Qualitative study USA Dec-Jan 2021	Concerns raised by 193 healthcare workers and staff from skilled nursing facilities in town hall meetings were reported. Location in the USA was not reported. Question Topics: 1) Vaccine hesitancy	• Early concerns that were raised consistently included belief the vaccine was developed too quickly, short and long-term side effects, infertility and safety in pregnancy, and wanting to wait to see how well the vaccine works for others. • After early concerns were addressed, other consistent concerns involved belief that the vaccine causes COVID-19, causes Bell's palsy, requirement for a booster shot, ineffective against new variants, and previously testing positive. • Some concerns that were raised later in the discussion included uncertainty whether receiving the vaccine will change precautions (wearing a mask, social distancing etc.), fear of microchips, and safety in individuals with chronic disease. •

Grumbach (2021) (112) Cross-sectional study USA Nov 2020 – Jan 2021	An online survey of 3161 adults in the community and 1803 HCWs across 3 medical centers in the San Francisco Bay Area was conducted to assess intentions to vaccinate and reasons for acceptance and hesitancy. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• HCWs had higher intentions to vaccinate compared to the general population (83.6% vs 65.5%, P <0.001). • In HCWs, Black (aOR 0.24, 95% CI: 0.10-0.60), Latinx (aOR 0.50, 95% CI: 0.31-0.79), Asian (aOR 0.37, 95% CI: 0.27-0.51), multiracial (aOR 0.49, 95% CI: 0.29-0.82) and individuals of other races (aOR 0.28, 95% CI: 0.15-0.53) had lower intentions to vaccinate compared to White HCWs. • Reasons for intending not to vaccinate among Black, Latinx, and Asian respondents included lack of confidence in the vaccine's ability to prevent COVID-19 (aOR 2.39, 95% CI: 1.58-3.61; aOR 2.04, 95% CI: 1.58-2.64; aOR 1.85, 95% CI: 1.51-2.27, respectively), lack of trust in vaccine manufacturers (aOR 3.08, 95% CI: 2.00-4.73; aOR 1.85, 95% CI: 1.38-2.48; aOR 1.34, 95% CI: 1.04-1.72, respectively), and concerns about the rushed approval of the vaccine (aOR 2.10, 95% CI: 1.44-3.05; aOR 1.68, 95% CI: 1.34-2.10, aOR 1.81, 95% CI: 1.53-2.15, respectively).
Weng (2021) *preprint* (119) Cross-sectional study USA Nov 2020 – Jan 2021	Racial-ethnic differences in COVID-19 vaccination intentions were explored using an online survey of 3,161 adults from the general population and 1,803 HCWs in California. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• HCWs were more likely than the general public to intend to vaccinate (83.6% vs 65.5%). • In HCWs, intention to vaccinate was highest in those who were White (89%) followed by multiple races (79%), Latinx/Hispanic (78%), Asian (75%), other race (66%), and Black/African American (65%). • Latinx and Asian respondents were significantly more likely than White respondents to report a doctor's recommendation as an important reason to get vaccinated. • Compared with Whites respondents, about 15% more of the Black, Latinx, and Asian respondents identified potential for a bad reaction to the vaccine and government rushing the approval process as major reasons to not get vaccinated. They were also much more likely to report concerns about the vaccine giving them COVID-19.

Woodhead (2021) (226) *new* Qualitative study UK Oct-Jan 2021	Semi-structured online interviews were conducted with 17 HCWs and 8 senior managers to investigate how decisions are made about taking the COVID-19 vaccine and if racism and discrimination factor into the decision. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes	• Respondents fell on a continuum of those who would accept a vaccine right away (slightly more than half) to a minority who were more certain they would decline, with a third expressing hesitant views. • Respondents tended to weigh benefits and risks actively with those that are hesitant seeing benefits and risks equally and decliners focusing on risks for themselves. • Acceptors were more likely to report that they viewed getting back to normality as a positive in decision making. • Risks were characterized by worries about side effects in relation with pre-existing vulnerabilities. • Past experiences with vaccines was related to normalization views (comparing to flu vaccine) for vaccine acceptors whereas the hesitant and decliners associating it with large harmful events like the Thalidomide tragedy. • Those expressing hesitant or oppositional views cited an absence of trustworthy information which could allow of manipulation and misinformation. • All groups suspected that they would get direct and indirect messages to get vaccinated but deniers and hesitant respondents were more concerned that they may be forced to vaccinate from their institutions.
Harrison (2021) (130) *new* Qualitative study USA Dec 2020	Five focus groups completed using video-conferencing (Zoom) with 54 participants were conducted with staff from skilled nursing facilities to better understand hesitancy. Location in the USA was not reported. Question Topics: 1) Vaccine hesitancy 2) Vaccine attitudes	• Among the vaccine hesitant were four themes; (1) general concerns and personal concerns about vaccine safety and effectiveness, (2) lack of trust in the vaccine effort, (3) misinformation about the vaccine, and (4) increasing vaccine uptake. • General concerns reflected the short development and testing period, newness, long term effects, how it would impact underlying conditions, or that COVID-19 wouldn't be serious if they did get sick. • Some respondents were mistaken that the vaccine would contain live or attenuated virus.

		Misinformation rumours covered microchips, live virus, and infertility. • Lack of trust was felt both for political affiliation or historical skepticism for people of colour. • When asked about how to increase uptake respondents wanted to see easy to understand information and bringing in representation to discuss (religious groups) or be seen getting the vaccine.
Abuown (2021) (227) Cross-sectional study UK Dec 2020	Intention to vaccinate was evaluated using an online survey of 514 HCWs in London. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? Yes	• 59% were willing to take a COVID-19 vaccine, 24% were not willing, and 17% were undecided. • Doctors were more likely to accept a vaccine compare to nurses ($P < 0.001$), healthcare assistants ($P < 0.001$), pharmacists ($P < 0.001$), allied health professionals ($P < 0.01$), and administrative staff ($P < 0.01$). Hospital management staff were more likely to accept compared to nurses, healthcare assistants, and pharmacists ($P < 0.01$). • Those who accepted an influenza vaccine were less likely to reject a COVID-19 vaccine (OR 0.45, 95% CI: 0.031–0.96) and those who rejected an influenza vaccine were more likely to reject a COVID-19 vaccine (OR 8.32, 95% CI: 5.36–12.91, $P < 0.001$). • Older HCWs (61+) were significantly more likely to intend to vaccinate ($P < 0.01$). • The odds ratio of vaccine rejection was 0.51 for men (95% CI: 0.34–0.77) and 1.26 for women (95% CI: 1.12–1.42, $P < 0.001$). • Intention to vaccinate was significantly lower amongst Black HCWs compared to White ($P < 0.01$), Indian ($P < 0.001$), or other Asian backgrounds ($P < 0.01$). • Safety concerns were the most common reason for hesitancy.

Meyer (2021) (228) Cross-sectional study USA Dec 2020	An online survey to assess vaccine intentions and reasons for hesitancy in 16,292 HCWs was conducted in Pennsylvania. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 55.3% of respondents intend to get vaccinated when available, 16.3% would not accept a vaccine, and 28.4% were undecided. • Patient facing HCWs reported higher vaccine intentions than non-patient facing (57.3% vs 51.4%, P < 0.001). • Within hospital areas those working in the ER had the lowest intention to get the vaccine (51.9%), whereas those working in the ICU (63.1%) and inpatient care (60.9%) had the highest intentions. • The top reasons for hesitancy were concerns about unknown risks of the vaccine (90.3%), concerns about known side-effects (57.4%), and wanting to wait to see the impact of the vaccine on others (44.3%). • Other reasons for hesitancy include a lack of trust of the FDA process or results (21.1%), concerns of state or hospital network tracking (13.9%), concerns about the mRNA technology (11.4%), and belief they are not at high risk for severe disease (10.4%). • Splitting responses received before the vote to approve the Pfizer vaccine (92.8% of responses) and after (7.2% of responses) finds that 79% reported they would receive the vaccine compared to 53.2% intending to vaccinate before the vote.
Piltch-Loeb (2021) (229) Cross-sectional study USA Dec 2020	The effect of media channels on vaccine acceptance was evaluated using an online survey of 2,650 adults in vaccine priority groups including healthcare workers. 61.4% of the participants worked in the healthcare sector. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine perceptions	• 39.9% reported they were likely to take the vaccine in two months, 47.3% had some level of hesitancy, and 12.8% were unlikely to take the vaccine. • 61% obtained COVID-19 vaccine information from local TV and 37.8% from Facebook. • Respondents indicated that the vaccine news reported was positive (53.6%), neutral (25.3%), mostly negative (16.3%), or that they did not report seeing vaccine information (4.8%). • Overall trust in vaccine information sources was moderate to low, with 23% reporting high trust, 40.5% moderate trust, and 36.3% low trust.

	Survey tools available? No Formative research conducted? No Survey pre-tested? Yes	• In the multivariable analysis, positive predictors of intention to vaccinate included knowing someone who died of COVID-19 (RR = 1.47, 95% CI: 1.08-1.99), having some trust in vaccine information (RR = 2.01, 95% CI 1.61-2.51), having high trust in vaccine information (RR =15.6, 95% CI: 11.69-20.81), and obtaining vaccine information from national TV (RR = 1.75, 95% CI: 1.02-1.53), local TV (RR = 1.75, 95%, CI: 1.40-2.19), or national newspapers (RR =1.81, 95% CI: 1.45-2.24). • Low intention to vaccinate was associated with respondents that only used social media (RR = 0.45, 95% CI: CI 0.32-0.64) or used both social media and traditional media channels (RR = 0.81, 95% CI: CI 0.66-1.00) compared to those who only used traditional media to obtain vaccine information.
Kuter (2021) (109) Cross-sectional study USA Nov-Dec 2020	To evaluate intentions to vaccinate, an online survey was conducted at two large, academic hospitals in Philadelphia in 12,034 hospital employees. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• 63.7% reported intention to receive a COVID-19 vaccine when available, 26.3% were unsure, and 10.0% were unwilling. • Of those intending to vaccinate, 79.1% would receive the vaccine as soon as possible, 19.1% would like to wait 3–6 months after it had been administered to others, and 1.8% would after it had been administered to others for 12 months. • The two most important vaccine characteristics to respondents were safety (94.4%) and efficacy (82.8%). • If a vaccine were to include side effects such as high fever, muscle aches, chills, and headache resulting in loss of 2 days at work, only 28.3% of respondents said they would be willing to receive a vaccine. 33.2% said they were unsure. • Intention to vaccinate increased as vaccine effectiveness increased (35.8% willing to receive a vaccine with 50% effectiveness, 61.1% with 70% effectiveness, and 85.6% with 90% effectiveness). • Factors significantly associated with an intention to vaccinate were male gender (OR 2.41, 95% CI:

		2.12-2.75), older age (>65: OR 3.50, 95% CI: 2.50-4.90; 40-64: OR 1.41, 95% CI: 1.26-1.56), and higher education (post-graduate degree: OR 4.59, 95% CI: 3.83-5.50, Bachelor or Masters degree: OR 1.84, 95% CI: 1.59-2.13). • Compared to White ethnicity, intention to vaccinate was significantly lower among Blacks (OR 0.23, 95% CI: 0.19-0.27), Hispanics (OR 0.51, 95% CI: 0.39-0.67), and those reporting multiple/other races (OR 0.58, 95% CI: 0.47-0.73). • Those residing in urban areas were significantly more likely to intend to vaccinate compared to suburban (OR 0.71, 95% CI: 0.65-0.79) and rural (OR 0.41, 95% CI: 0.30-0.54) residents. • Intention to vaccinate was lower among those with poor or fair health (OR 0.73, 95% CI: 0.56-0.95) and among those who were not up-to-date on their vaccinations (OR 0.36, 95% CI: 0.18-0.71) compared to their counterparts. • The most common reasons to receive a vaccine were protection of one's family (86.7%), protecting themselves (82.9%), protecting one's community (68.8%), and getting life back to normal (59.4%). • The most frequent reasons for vaccine hesitancy or refusal were concern about side effects (89.1%), the vaccine being too new (84.0%), and lack of knowledge about the vaccine (77.9%).
Shaw (2021) (110) Cross-sectional study USA Nov-Dec 2020	Willingness to vaccinate was evaluated in 5287 HCWs from a large academic medical center in New York using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes	• 57.5% of respondents were willing to take a free vaccine, 26.4% were unsure, and 15.9% would refuse. • Men were more likely to intend to vaccinate (72.5%) compared to women (52.4%) or non-binary or non-disclosed individuals (41.0%), P<0.001. • Those that identified as Asian (73.8%) or White (58.4%) were more willing to take a vaccine compared to Other (47.6%), American Indian or Alaska Native (39.3%), or Black (30.8%) respondents, P<0.001.

	Survey pre-tested? No	• Scientists and Physicians (80.4%) and Public Safety and Spiritual Care employees (77.8%) were most likely to intend to vaccinate. Registered Nurses (41.2%), in Ancillary Services (46.4%), or as Allied Health Professionals (51.4%) were less likely, P<0.001. • Those that were older and those that were not providing direct patient care were more likely to intend to vaccinate. • White respondents agreed that a COVID-19 vaccine would be safe when approved (45.9%) more frequently than Black respondents (26.2%), P<0.001). • The most common concerns about the vaccine include safety, side-effects, efficacy, and speed of vaccine development.
Jain (2021) *preprint* (111) Cross-sectional study USA Nov-Dec 2020	Motivations, concerns, and intentions regarding COVID-19 vaccines were evaluated using an online survey in 2135 HCWs (18+) from 3 medical centers in California. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine knowledge Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 69% of HCWS would receive the vaccine if formally FDA approved, 22% were unsure, and 10% would refuse. In contrast, only 35% would receive if approved via emergency use authorization only. • 25% wanted to be among the earliest to receive a vaccine, 36% preferred vaccination after the first round, and 18% want to wait for 2+ months. • The top motivating factors for vaccination included perceived risk from COVID-19 to self (65%), and family/friends (63%). • Top vaccine concerns were side effects (28%), political involvement in the FDA's approval process (21%), distrust of pharmaceutical companies (16%), and efficacy (12%). • 19% of respondents reported being highly informed or well informed about COVID-19 vaccine candidates whereas 66% reported they were somewhat informed, and 16% were not informed at all.
O'Brien (2021) *preprint* (107)	An online survey of 2070 HCWs across the USA was conducted in Oct to determine intention to vaccinate under emergency use	• Intention to vaccinate increased from 54.2% in Oct to 76.2% in Dec. Over this time period, vaccine intention increased from 64.0% to 90.5% in

Longitudinal study USA Oct-Dec 2020	authorization. This survey was repeated in 1541 HCWs in Dec. 998 participants responded to both surveys. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	doctors, from 68.9% to 75% in paramedics, and from 46.6% to 66.9% in nurses. • For the 998 individuals who participated in both surveys, 69% were willing to vaccinate at both time points, 15% were hesitant at both time points, 13% were hesitant in Oct but were willing in Dec, and 2.9% were willing in Oct but hesitant in Dec.
Keleker (2021) (129) *new* Cross-sectional study USA Sep-Dec 2020	248 dental (DS) and 167 medical students (MS) from three dental schools and one medical school were surveyed online regarding past vaccination behaviour and current COVID-19 vaccine hesitancy. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 23% of medical students and 45% dental students reported that they were hesitant about getting the COVID-19 vaccine indicating that medical students were 2.7 times more likely to get a vaccine. • General vaccine attitudes were positive among MS with 99.4% agreeing that vaccines are important to stay healthy as a HCW and 99.4% believing there is a role for them to learn about vaccines for their patients. • MS students were significantly more likely to support mandatory vaccination for the general public (OR= 3.12, 95% CI: 2.06-4.76) and for HCWs (OR= 5.18, 95% CI: 3.15-8.76). • MS students were significantly more likely to trust information received about COVID-19 vaccines compared to DS students (OR= 3.51, 95% CI: 2.09-6.08) but were also more likely have concerns about vaccine effectiveness (OR= 2.78, 95% CI: 1.80-4.36). • MS were more unlikely than DS to say they would only get vaccinated if mandated by school or health systems (OR= 0.38, 95% CI: 0.22-0.62) as well as to report that as an adult they refused a vaccination for a reason other than illness or allergy (OR= 0.41, 95% CI: 0.23- 0.73). • In logistic analysis, being an under represented minority, believing COVID-19 vaccination should

		be mandatory for the public, believing COVID-19 vaccination is important to themselves as a HCW, trusting information about the COVID-19 vaccine was significantly associated with willingness to receive a vaccine whereas concern for adverse event and only getting a vaccine if required was associated with not being willing to accept a vaccine.
Unroe (2020) (121) Cross-sectional study USA Nov 2020	Willingness to vaccinate was evaluated in 8,243 nursing home and assisted living staff in Indiana using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 45% of respondents would be willing to take an FDA-approved vaccine as soon as it was available. • Of those who would not be willing to take the vaccine immediately, 44% would be willing to receive the vaccine at a later date. • The most common reasons for vaccine hesitancy include potential side-effects (70%), heath concerns (34%), efficacy concerns (20%), and religious reasons (12%). • Compared to their counterparts, those over the age of 60, men, and those who identify as White ethnicity were more willing to take the vaccine (P < 0.0001). • Black HCWs were 12% (95% CI: 8.6-15.7%) less willing to accept the vaccine compared to White HCWs. • Dietary, housekeeping, and administrative staff were more likely to intend to vaccinate compared to clinical care staff including nurse aids and nurses (P < 0.0001).
Shekhar (2021) (123) Cross-sectional study USA Oct-Nov 2020	Intention to vaccinate was assessed in 3479 HCWs (18+) using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No	• 36% of respondents were willing to take the vaccine as soon as it becomes available, 56% were not sure and would wait to review safety data before getting a vaccine, and 8% would refuse. • Intention to vaccinate increased with age (34% in the 18-30 group vs 47% in the >70 age group). • Male gender, higher education, higher income levels, living in the South, living in an urban area, and identifying as Liberal or Democrat were associated with higher intention to vaccinate as

	Survey pre-tested? No	soon as it becomes available compared to their counterparts. • Black (19%) and Native Americans/Alaska Native (10%) HCWs were less likely to intend to vaccinate as soon as it becomes available compared to White (37%) and Asian (44%) HCWs (p<0.001). The majority of Black (65%), Native American HCWs (80%), and all Native Hawaiian/Other Pacific Islander HCWs (100%) chose to wait to review data before receiving a vaccine. • Intention to vaccinate as soon as it become available was lower among those identifying as Hispanic or Latino (30%) compared to those who did not identify with this ethnicity (37%). • Those who believe themselves to be immune to COVID-19 (22%), who feel confident they won't get infected (27%), and those who had not taken care of COVID-19 patients (9.2%) had the highest rates of intending to refuse a vaccine. • The most prominent concerns expressed regarding vaccinating include safety/adverse effects (69%), effectiveness (69%), and rapidity of development/approval (74%). • The majority of HCWs trust their doctors and healthcare professionals recommending the vaccine (73%), but 46% do not trust information provided by the government about the vaccine and its severity and 34% do not trust regulatory authorities (e.g. CDC or FDA) overseeing the vaccine development and safety.
Caban-Martinez (2021) (133) Cross-sectional study USA	Across the USA, an online survey of 3,169 emergency medical service (EMS) workers and firefighters was conducted to evaluate intention to vaccinate. Question Topics: 1) Vaccine intentions	• 48.2% were willing to accept a vaccine when available, 27.6% were not willing, and 24.2% were unsure. • Those who were more likely to not accept a vaccine were aged 30-39 years (aOR 3.62, 95% CI: 2.00-6.55), Black race (aOR 3.60, 95% CI: 1.12-11.53]), multi-race (aOR 2.98, 95% CI: 1.61–5.51), Hispanic/Latinx ethnicity (aOR 2.39, 95% CI: 1.45-3.92), lower education (aOR 2.06, 95% CI: 1.29-

Oct 2020	Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	3.27), married or unmarried couple (aOR 1.65, 95% CI: 1.03-2.65), and of current rank firefighter/EMS (aOR 2.21, 95% CI: 1.60-3.08).
Gadoth (2021) (120) Cross-sectional study USA Sep-Oct 2020	To understand HCWs intention to vaccinate and attitudes about vaccine safety, efficacy, and acceptability in the context of the COVID-19 pandemic, an online survey of 609 HCWs was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 47.8% of participants stated they would not participate in a COVID-19 vaccine trial. • 65.5% intend to delay vaccination, of which 49.4% would prefer to wait and see how the vaccine affects others first. Compared to doctors, the adjusted proportion reporting intent to delay vaccination or refusal was 0.52, 0.54, and 0.59 among nurses, other personnel with patient contact roles, and those without patient contact, respectively. • Respondents agreed on the utility of vaccines for protecting themselves from disease (mean Likert score 4.69 95% CI: 4.64-4.73) and for protecting community health (mean Likert score 4.69 95% CI: 4.65-4.74). However, doctors held these attitudes more strongly than nurses. • Opinion was split regarding the statement that new vaccines carry more risks than older (mean Likert score 3.23 95% CI: 3.14-3.32). • Less than half the respondents (46.9%) felt a vaccine would protect them against COVID-19 and 34.8% were confident about the scientific vetting process. • Women and racial or ethnic minorities expressed more hesitant attitudes towards vaccines than their counterparts. • The major variables impacting those who planned to delay or refuse vaccination were concerns about the fast-tracked nature of vaccine development and a lack of transparency and/or publicly available information on the vaccine.
Robbins (2021) (230)	An online survey was conducted in 593 HCWs from a major tertiary	• If a vaccine became available that was freely distributed through their employer, with

Cross-sectional study UK Sep 2020	referral hospital to assess intention to vaccinate. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	appropriate safety and efficacy data, 83.4% would be likely or very likely to get a vaccine. • 58.9% would be willing to get their vaccine outside of their normal working hours (e.g., weekend) and 53.1% would be willing to travel to another location to get a vaccine. • 68.5% would be willing to get their vaccine while in their car and 76.6% would not mind waiting in a socially distanced line to get their vaccine. • 77.8% believe that HCWs should be prioritized to receive a vaccine and 82.8% believe that front-line staff directly treating patients should be prioritized over non-patient facing roles.
Manning (2021) (124) Cross-sectional study USA Aug-Sep 2020	Factors associated with intention to vaccinate were assessed using an online survey of 78 full-time nursing faculty, 105 adjunct nursing faculty, and 1029 nursing students. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• Intention to vaccinate was highest in full-time faculty (60.3%) followed by students (45.3%), and adjunct faculty (44.8%). • Men were more likely than women to intend to vaccinate (60.3% vs 44.9%, P=0.002). • Those aged 60+ had the highest intention to vaccinate (85.7%, P=0.004). • The most common reasons to intend to vaccinate included a desire to protect family, self, patients, and community, and the belief that it would be the best way to avoid getting seriously ill from COVID-19. • The most common reasons for intending not to vaccinate included the belief that the vaccine was developed too quickly to be safe, and side effects. These concerns were more commonly reported by students and adjunct clinical faculty compared to full-time faculty (P <0.05). • Mandatory vaccination as a condition of employment was supported by 52% of full-time faculty, 39% of adjunct faculty, and 35% of students.
Parente (2021) (126) *new*	Associations with vaccine acceptance were assessed online for a hypothetical vaccine with	• 37.2% of respondents were early acceptors, wanting to be vaccinated within the first month of approval.

Cross-sectional study USA Aug 2020	considerations for delay periods (1 to more than 12 months after approval) in 3,347 HCWs in Kentucky. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• 22.3% wanted to be vaccinated within 1-3 months, 11.4% within 4-6 months, 6.9% in 7-12 months, and 12.3% more than 12 months after approval. • 9.9% report that they never intend to be vaccinated. • Reasons for wanting to delay or refuse vaccination focused on the long term side effects (57.1%), the safety of the vaccine (55.0%), vaccine efficacy (37.1%), risk vs benefit of the vaccine (31.0%), cost of the vaccine (12.2%), and possible allergies (11.2%). • Asian respondents were 1.53 times more likely to report they wanted to receive a vaccine within 3 months compared to White respondents. In contrast, Black respondents were significantly less like to accept a vaccine in the same time period (OR 0.16, 95% CI: 0.10-0.25). • Early acceptance of a vaccine (within 3 months) was significantly associated with men (aOR 2.43, 95% CI: 2.00-2.95), those who got the flu shot in 2019/2020 (aOR 2.35, 95% CI: 1.75-3.18), more concern about COVID-19 (aOR 2.40, 95% CI: 2.07-2.79), and higher levels of education (aOR 1.41, 95% CI: 1.21-1.65).
Hoke (2021) (132) Cross-sectional study USA May 2020	An online survey of 350 Pennsylvania school nurses (18+) was used to evaluate intention to vaccinate and vaccine perceptions. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 84.9% of nurses were willing to vaccinate when one becomes available, 14.5% were unlikely, and 0.6% did not respond. • 63.7% supported the return to school in the absence of a vaccine. • Compared to rural nurses, urban nurses were more willing to receive a vaccine when available (OR 2.21, 95% CI: 1.41-3.46) and were more concerned about returning to school without a vaccine (OR 1.58, 95% CI: 1.05-2.38).

Sathianathan (2020) (231) Cross-sectional study USA Mar 2020	COVID-19 vaccine knowledge was compared between 4966 HCWs and 854 non-HCWs from Pennsylvania using an online survey. Question Topics: 1) Vaccine knowledge Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• When asked if a vaccine for COVID-19 would be available within 3 months, HCWs were more likely to answer correctly (false) compared to non-HCWs.

aOR = adjusted odds ratio, CI = confidence interval, HCWs = healthcare workers, PSW = personal support worker

HIGH-RISK POPULATIONS

Table 5. Evidence of vaccine attitudes of high-risk populations (n=24)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
PREGNANT OR BREASTFEEDING		
Woolf (2021) *preprint* (114) Cross-sectional study and qualitative study UK Dec 2020-Mar 2021	To assess COVID-19 vaccine hesitancy and its predictors, an online survey was conducted with 11,584 HCWs (16+). Qualitative data was collected through interviews (n=24), focus groups (n=17), and open-ended survey responses (n=58). All HCW outcomes found in HCW section. Question Topics: 1) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• Pregnant HCWs were 7.12 times more likely to be hesitant compared to non-pregnant HCWs (aOR 7.12, 95% CI: 4.74-10.70).

Skjefte (2021) (135) Cross-sectional study 16 countries: Australia, Africa, Argentina, Brazil, Chile, Colombia, India, Italy, Mexico, New Zealand, Peru, Philippines, Russia, Spain, UK, USA. Oct-Nov 2020	An online survey was used to evaluate the acceptance of COVID-19 vaccination among 5,294 pregnant women and 12,562 mothers of children younger than 18-years-old. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• For a vaccine with 90% efficacy, 52.0% of pregnant women and 73.4% of non-pregnant women indicated an intention to receive the vaccine. • 69.2% of all women intended to vaccinate their children. Acceptance levels were above 85% in India, Mexico, Brazil and Colombia and below 52% for the USA, Australia, and Russia. • Intention to vaccinate in pregnant women varied by country with acceptance levels above 80% in Mexico and India and below 45% for the USA, Australia, and Russia. • Vaccine hesitancy was associated with younger age, lower income, lower education level, not being married, and having no health insurance. • The strongest predictors of intention to vaccinate were confidence in vaccine safety and efficacy, belief in the importance of vaccines to their own country, confidence in routine childhood vaccines, worry about COVID-19, trust of public health agencies/health science, and compliance to mask guidelines. • 53.0% of respondents were confident that a nationally approved COVID-19 vaccine would be safe and 60.4% were confident the vaccine would be effective. • For pregnant women, the most common reasons to decline a vaccine were potential side effects for their baby (65.9%), concern that approval of the vaccine would be rushed for political reasons (44.9%) and the lack of safety and effectiveness data among pregnant women (48.8%). • For mothers, the most common reasons to decline a vaccine were concern that approval of the vaccine will be rushed for political reasons (39.8%), lack of safety and effectiveness data among children (32.7%), and worry about safety and side effects (28.4%). • A recommendation from a healthcare provider had a limited impact on intention. 45.9% of pregnant

		women and 54.6% of non-pregnant women would be more likely to have themselves/children vaccinated if recommended by health care providers.
Skirrow (2021) *preprint* (19) Cross-sectional and qualitative study UK Aug – Oct 2020	An online survey and semi-structured interviews were conducted in a group of 1,181 pregnant women (aged 16+) to determine views on COVID-19 vaccine acceptability for themselves when pregnant, not pregnant, and for their babies. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 81.2% of women reported that they would definitely accept or were leaning towards accepting a vaccine when not pregnant. Vaccine acceptance was significantly lower during pregnancy (62.1%, P<0.005) and for their babies (69.9%, p<0.005). • Compared to White ethnic women, ethnic minority women were twice as likely to reject a vaccine for themselves when not pregnant, pregnant and for their babies (P>0.005). • Those from lower-income households, aged < 25 years, and from some geographic regions were more likely to reject a vaccine when not pregnant, pregnant, and for their babies. • Women unvaccinated against pertussis in pregnancy were over four times more likely to reject a vaccine when not pregnant, pregnant and for their babies. • Thematic analysis revealed the most common reasons for hesitancy were vaccine safety, and a wider mistrust of vaccines in general.
Battarbee (2021) *preprint* (136) Cross-sectional study USA Jul-Oct 2020	915 pregnant women in Utah, Alabama, and New York were surveyed over the telephone or at in person visits to measure attitudes toward the COVID-19 vaccine and vaccine acceptability. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? No Formative research conducted? No	• 41% of women would accept a vaccine and this did not vary by enrolment month. • Those willing to accept a vaccine cited reasons such as wanting to protect their pregnancy (95%), to protect themselves (85%), protecting family members (79%), and protecting their community (68%). • Those that are not willing to get a vaccine during their pregnancy were unwilling do so due to concerns about safety of the vaccine during pregnancy (82%), safety for themselves (68%), vaccine efficacy (52%), and the belief that they did not need the vaccine (22%).

	Survey pre-tested? No	• Having a graduate degree increased the odds of accepting a vaccine by 2.4 times compared to those with less than a high school diploma (95% CI: 1.3-4.7). • In multivariate modelling only receiving a flu vaccine in the past year (aOR 2.1, 95% CI: 1.5-3.0) was found to increase vaccine acceptance. Conversely, only ethnicity (Hispanic and Black respondents) was associated with not accepting a vaccine (aOR 0.4, 95% CI: 0.2-0.6 each).
PEOPLE EXPERIENCING HOMELESSNESS		
Kuhn (2021) *preprint* (41) Cross-sectional study USA Dec 2020-Feb 2021	The level of vaccine uptake and hesitancy among 90 individuals experiencing homelessness in Los Angeles (18+) was evaluated using a mobile phone survey. Question Topics: 1) Vaccine uptake 2) Vaccine hesitancy 3) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Of the 90 participants, 17 were offered a vaccine of which 10 accepted and 7 refused. • Among the 73 who were not offered the vaccine, 51% said they would take it if offered, 32% would refuse, and 17% refused to answer. • Together, 48% refused a vaccine when offered, would refuse when offered, or refused to answer and were deemed "vaccine hesitant". • Of those who were vaccine hesitant, the most common reasons were fear of side effects (37%), wanting to have more information (30%), and they don't get any vaccines (27%). • A multivariate analysis, those with a high COVID-19 threat perception (OR 0.25, P=0.02), and those who trusted official sources (OR 0.37, P=.08) were significantly less likely to be vaccine hesitant. Those who engaged in highly protective behavior (OR 3.63, P=0.02) and who trusted personal contacts (OR 2.70, P=0.07) were more likely to be hesitant.
Knight (2021) *preprint* (137) Qualitative study USA	To understand the facilitators and barriers to vaccine acceptability among homeless adults (aged 20-71) a qualitative study was conducted in two samples: 1) a longitudinal cohort of 37 homeless older adults in Oakland, CA and 2) a convenience sample of 57	• Many participants indicated they were willing to receive a vaccine when available. They cited a desire to return to routine life and civic responsibility as reasons they would vaccinate. • Four themes emerged regarding vaccine hesitancy including: 1) a desire for more data about vaccine testing, safety, and approval, 2) concerns that the vaccines made people sick, 3) a desire to wait until

Jul-Oct 2020	individuals during a mobile outreach COVID-19 testing event in San Francisco, CA. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy	others had taken the vaccine before agreeing to take it themselves, and 4) mistrust of the government. Some connected this mistrust to previous experiences of racism. • Despite social exclusion and lack of access to technology, participants followed news reports about the vaccine and desired information about vaccine efficacy and safety.
OLDER ADULTS		
Horizon Research (2021) *unpublished* (15, 195, 232) Longitudinal study New Zealand Mar-May 2021	An online survey of adults (16+) was conducted to measure vaccine intentions. Mar-Apr, n=1,350 Apr-May, n=1387 May, n=1,234 *new* Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	**May** • 9% of those aged 65-74 and 14% of those aged 75+ were unlikely to get vaccinated. • The top concerns of those aged 65-74 were side effects (30%), long term effects (28%), and concern for what would happen if they had an adverse reaction (26%). Similar concerns were seen with those over 75. **Apr-May** • 81% of those aged 65-74 and 88% of those 75+ were likely to accept a vaccine.
Australia Bureau of Statistics (2021) *unpublished* (141) *new* Longitudinal study Australia	The household impacts survey is a monthly survey which collects data online and by telephone from a panel of adults (18+) on COVID-19 related topics including attitudes towards vaccines. May: n=3,371 Question Topics: 1) Vaccine intentions	• 7.6% of those aged 70+ would definitely not receive a vaccine when offered and 9.4% were unlikely to vaccinate when offered. • A recommendation from their general practitioner was the most important factor in their decision to get vaccinated in 41.1% of those aged 70+.

Apr 2020-May 2021	Survey tools available? No Formative research conducted? No Survey pre-tested? No	
Office for National Statistics (2021) *unpublished* (140) Longitudinal study UK Feb-Mar 2021	17,201 responses from four waves of results collected from the online Opinions and Lifestyle Survey (196) were pooled to focus on demographic specific associations with vaccine hesitancy. Questions Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 3% of those aged 65-69 and 5% of those aged 60-64 were vaccine hesitant. 4% of those aged 55-59 were hesitant. • Of those aged 75-79 years who were very or fairly unlikely to get a vaccine, 49% reported they were against vaccines in general, 46% cited worries about a pre-existing condition, and 31% had other reasons. • Worries among those aged 65-79 were more varied including concerns regarding side effects, long-term effects, worries about existing health conditions, not believing it to be unsafe, and wanting to see if the vaccine works. • Those aged 55-64 had additional beliefs about not being at risk or they believe they already had COVID-19.
Nikolovski (2021) (139) Cross-sectional study USA Nov 2020	A survey of 7402 older adults (65+) using a mobile health app was conducted to determine factors associated with intentions to vaccinate. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 91.3% of participants stated they were willing or somewhat willing to be vaccinated and 8.7% were unwilling or somewhat unwilling to vaccinate. • Hesitancy was highest amongst women (OR = 0.49, 95% CI: 0.45 – 0.54) and African American or Black respondents (OR = 0.24, 95% CI: 0.18 – 0.31). • Those reporting a higher income (OR = 2.60, 95% CI: 1.98 -3.42) or more education (OR = 2.31, 95% CI: 1.84 – 2.94) had higher odds for intentions to vaccinate. • Beliefs strongly associated with intention to vaccinate were protecting themselves and others (OR = 38.6, 95% CI: 32.4-46.1), safe and effective vaccine (OR = 21.6, 95% CI: 18.9-24.7), and comfortability with short term side effects (OR = 10.9, 95% CI: 9.1–13.1). • The majority of respondents wanted to talk to a healthcare provider before making a decision to vaccinate. This included both those willing to

		vaccinate (91.4% of women and 88.9% of men) and those not willing to vaccinate (68.4% of women and 62.3% of men). • Positive vaccine news was associated with an increase in intentions to vaccinate. After the results of the Pfizer phase 3 clinical trial were released, intention to vaccinate increased (OR = 1.46, 95% CI: 1.28-1.69).
Luo (2021) (150) *new* Cross-sectional study USA Oct-Nov 2020	Using the Medicare Current Beneficiary Survey, 6715 Medicare recipients (aged 65+) were asked by telephone about their COVID-19 vaccine intentions. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 61.0% (95% CI: 59.1-63.0) would be willing to get a vaccine when available and 39.0% (95% CI: 37.0-40.9) were hesitant to accept a vaccine. • 59.6% of those aged 65-74 reported they were willing to get a vaccine whereas 63.5% of those 75+ were willing. • Respondents who were aged 65-74 (aOR 0.83, 95% CI: 0.74-0.92), non-Hispanic Black (aOR 0.33, 95%, CI: 0.24-0.44), Hispanic (aOR 0.60, 95% CI: 0.47-0.77), female (aOR 0.56, 95% CI: 0.48-0.64), had an income of less than $25,000 (aOR 0.71, 95% CI: 0.62-0.81), and those who didn't think COVID-19 was more contagious (aOR 0.53, 95% CI: 0.41-0.69) or more deadly (aOR 0.51, 95% CI: 0.41-0.65) were significantly less likely to get a vaccine. • The top reasons cited for vaccine hesitancy were low trust in government (42.1%), concern for side effects (41.3%), and uncertainty about vaccine efficacy (11.3%). • Intention to receive a vaccine was significantly higher in those with internet access at home compared to those without (aOR 1.22, 95% CI: 1.01-1.49).
Callow (2021) (233) Cross-sectional study USA	To examine the impact of attitudes, subjective norms, and perceived behavioral control on attitudes towards vaccination, an online survey of 583 older adults (60+) from Delaware, Maryland, Washington DC, and Virginia was conducted.	• More favorable attitudes towards COVID-19 vaccines was seen in men ($\beta = 0.10$, $P < 0.01$), those who had previously received the flu vaccine ($\beta = 0.15$, $P < 0.001$), those who perceived the disease as more severe ($\beta = 0.11$, $P < 0.01$), and those who had a positive attitude towards vaccines in general ($\beta = 0.48$, $P < 0.001$).

Aug 2020	Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Compared to those who identified as strong Democrats, vaccine attitude scores were less favorable among moderate Democrats (β = 0.08, P < 0.05), Independents (β = 0.26, P < 0.001), moderate Republicans (β = 0.16, P < 0.001), and strong Republicans (β = 0.44, P < 0.001).
Waite (2021) (92) Cross-sectional study Canada May 2020	An online survey of 1001 Canadians aged 50–64 years and 3,500 aged 65+ was conducted to evaluate intention to vaccinate against COVID-19. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Among those aged 50-64 years, 69.1% intend to vaccinate when available, 11.3% would not vaccinate, and 19.6% were unsure. • 79.5% of those 65+ intend to receive a vaccine when available, 5.6% would not vaccinate, and 14.9% were unsure. • In both age groups, those who would accept a vaccine were significantly more likely to be male and more likely to have at least one chronic condition (P< 0.05). • The preferred location to receive a vaccine in both groups was family physician office, followed by pharmacy, workplace (for those 50–64 years), and public health clinics.
Williams (2020) (138) Cross-sectional study UK Apr 2020	Intention to vaccinate and perceptions on the vaccine were assessed in an online survey of 311 older adults (65+) and 216 patients with chronic respiratory disease (18-64 years old). Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• Of the total population (n=527), 58% and 27% would definitely or probably want to receive a vaccine once it becomes available, respectively. There were no differences between the older adult group and the chronic respiratory group (p = 0.78). • Willingness to receive a COVID-19 vaccination was positively associated with the belief that the COVID-19 outbreak is going to continue for a long time (0.09, p<0.05), and negatively associated with the belief that the media has over-exaggerated the risks of catching COVID-19 (-0.122, p<0.05). • A thematic analysis of comments in the survey revealed that 'personal health' (n = 176), 'severity of COVID-19 disease' (n = 85), and 'health consequences to others' (n = 36) were viewed as factors which facilitated vaccination whereas

		'concerns about vaccine safety' (n = 158) was considered a barrier to vaccine uptake.
SUBSTANCE USE		
Yang (2021) (147) Cross-sectional study USA Dec 2020 – Jan 2021	Vaccine intentions and hesitancy among 387 adults (18+) across the USA with a history of using tobacco products or marijuana was evaluated using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 49.1% were willing to receive a vaccine, 26.0% were not willing, and 24.9% were undecided. • The use of cigarettes, e-cigarettes, marijuana, and heavy drinking was not associated with vaccine hesitancy. • Those who were Black, lived in a suburban or rural community, who lived by themselves or with a family with five members or above, and those who were not stressed because of the COVID-19 pandemic were more likely not accept a vaccine when offered. • Compared to those who had received an influenza vaccine every year or almost every year, those who had never, only once, or in some years received an influenza vaccine were 7.0, 6.2, and 5.2 times more likely to not accept a vaccine.
Spechler (2021) *preprint* (146) Cross-sectional study USA Dec 2020-Jan 2021	A group of 45 cannabis users (reporting 10+ lifetime cannabis uses) were matched with 45 individuals who reported <10 lifetime cannabis uses to assess willingness to receive a COVID-19 vaccine using an online survey. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Willingness to receive a vaccine did not significantly differ between cannabis users and controls (t_{88} = 0.33, P = 0.74; BF_{01} = 4.3). • Among cannabis users, increased lifetime cannabis use was correlated with decreased willingness to receive a vaccine (r_{43} = -0.33, P = 0.03).
Masson (2021) (234) *new*	258 Californians with substance abuse disorder (SUD) were distributed paper surveys in substance treatment programs	• 11.2% of participants completely trust, 28.3% somewhat trust, and 28.3% slightly trust that a COVID-19 vaccine would be safe and effective.

Cross-sectional study USA Aug-Dec 2020	were surveyed regarding their trust in COVID-19 vaccines. Question Topics: 1) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	32.2% do not trust that a COVID-19 vaccine would be safe and effective. • In multivariate modelling only age (aOR 1.03, 95% CI = 1.02-1.05) and consistent mask wearing compared to less frequent mask wearing (aOR 2.48, 95% CI = 1.86-3.31) were significantly associated with vaccine trust whereas African Americans were less likely to trust vaccines compared to non-Hispanic Whites (aOR 0.41, 95 % CI = 0.23-0.70).
Jackson (2020) *preprint* (145) Cross-sectional study UK Sep-Oct 2020	As part of the COVID-19 Social Study an online survey of 29,148 current, former, and never smokers was conducted to determine general vaccine attitudes and vaccine intentions for the COVID-19 vaccine. Question Topics: 1) Vaccine attitudes 2) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Intention to vaccinate was 66% (95% CI: 64.9-67.1%) in former smokers, 65.8% (95% CI: 65.1-66.4%) in never smokers, and 50.9% (95% CI: 49.3-52.6%) in current smokers. • Current smokers were the both the most undecided (27.6%, 95% CI: 26.1-29.1%) and unwilling (21.5%, 95% CI: 20.2-22.9%) to intend to vaccinate once it was available. • Negative attitudes towards vaccines were highest among current smokers (10.6-24.0%), then former smokers (8.8-19.4%), and lowest among never smokers (5.9-17.7%). • Current smokers had the most concerns regarding unforeseen future effects, mistrust of vaccine benefit, commercial profiteering, and had a stronger preference for natural immunity.
Mellis (2021) (144) Cross-sectional study USA Sep 2020	Structured telephone and video interviews of 87 individuals who were either currently using substances, in treatment, or in recovery for substance use were conducted to determine trust and readiness for COVID-19 vaccination. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy	• 45% of respondents were immediately ready for vaccination, 8% were willing to vaccinate after a delay, 23% were uncertain, and 25% were not willing. • Respondents reported hesitancy due to the rush of the development of the vaccine, potential side-effects, not believing themselves to be high risk, and worry about interactions with pre-existing conditions. • Trusted sources for healthcare decisions included their doctor (including those that were hesitant), family, social media, television/newspapers, radio,

	Survey tools available? No Formative research conducted? No Survey pre-tested? No	official website(s), NIH/CDC, family, research data/medical journals, and the internet. • The potential of a vaccine requiring multiple doses did not change intention to vaccinate, however respondents cited potential barriers such as access to clinics and scheduling appointments.
VULNERABLE COMMUNITIES		
Marquez (2021) *preprint* (3) *new* Cross-sectional study USA Feb-May 2021	A community based vaccine site (Unidos en Salud UeS) was deployed in February to overcome barriers to COVID-19 vaccination faced by Latinx individuals in San Francisco. The community site was assessed through 997 in-person survey responses (May 2-19) for those older than 16 and city COVID-19 surveillance data. Question Topics: 1) Vaccine perceptions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 36.1% of respondents found out about the site from a friend, family member or co-worker, 21.0% by text, 17.8% seeing the site, and 11.4% by direct referral. Latinx respondents were more likely report seeing the site than having gotten a direct invite. • The top cited reason for choosing the community site was the location (28.6%), convenient scheduling (26.9%), and trusted recommendation (18.1%). • 99% of those going to the community site reported having a positive experience. • 58.4% of respondents report that they got vaccinated earlier because of the site (56.1% of Latinx and 63.2% of non-Latinx). • 90.1% of respondents felt they were more likely to recommend getting vaccine after having been vaccinated at UeS. • 65.3% of Latinx clients reached out to 3 or more people to recommend vaccination (55.9% non-Latinx).
Berenson (2021) (235) *new* Cross-sectional study USA Nov-Dec 2020	342 low income women (aged 18-45) were recruited from three reproductive clinics in Texas to anonymously fill out a paper survey in English or Spanish regarding COVID-19 vaccination intentions. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions	• 33.5% of respondents would get a vaccine as soon as possible but this increased if it was employer recommended (33.9%), if friends or family recommended it (36.7%), if it was offered for free (41.8%), or if it was recommended by their doctor (49.5%). • Accepting a doctor recommended COVID-19 vaccine was associated with those that received an annual flu shot, having had the HPV vaccine, being afraid of catching COVID-19, and their feelings

	Survey tools available? No Formative research conducted? No Survey pre-tested? No	being related to information learned from social media. • In multivariate analysis only having had an HPV vaccine and getting the flu shot every year was significantly associated with increase likelihood of accepting a vaccine if it was recommended by a doctor (aOR 2.26 95% CI: 1.07-4.79 and aOR 2.78 95% CI: 1.39-5.58 respectively). • Most respondents reported that they needed more information on vaccine safety (69.2%) and proof that it works (48.1%).
Gehlbach (2021) *preprint* (236) *new* Qualitative study USA Nov-Dec 2021	Semi-structured focus groups conducted on the video-conferencing platform Zoom with 55 Lantinx/Indigenous farm workers in California aimed to elucidate common themes related to COVID-19 attitudes and behaviours. Question Topics: 1) Vaccine perceptions 3) Vaccine attitudes	• Themes encompassed misinformation and barriers to access information (internet access, information in their preferred language, knowledge of appropriate/correct information sources for COVID-19). • Political/institutional (government and public health) mistrust factored into myths related the vaccine as a control method or an expressed desire not to be a guinea pig. • A key factor for both testing and anticipated vaccination behaviour was worry about their documentation status.
Ekezie (2020) (237) Qualitative study UK Jun-July 2020	Three focus groups and 47 semi-structured interviews were used to evaluate the perceptions of ethnic minorities and vulnerable communities towards participation in vaccine trials. The 70 included participants were South Asian, African and Afro-Caribbean, White Polish, White British, and representatives of other vulnerable groups including those with mental health issues, homeless, and Gypsy, Roma and Travellers (GRT) communities.	• General apprehension, scepticism, and low levels of trust were observed within all groups. This was influenced by lack of information and speculation concerning the possible hidden agendas of vaccine developers and the government. • Most participants reported feeling anxious and scared of getting involved or were simply not interested in participating in vaccine trials. • Although hesitant, most South Asian participants were open to participating in research but not necessarily attending hospital-based research. This group was concerned with the vaccine potentially containing animal products which are prohibited in various religions. They also strongly advocated for

		the research to not fall during Ramadan or fasting festivals. • African and Caribbean participants were the most suspicious about the speed of the vaccine development and the intentions of companies involved. There was high mistrust on what would be done with their DNA, and some belief that the vaccine was developed to eradicate Black people. • Those with mental health issues expressed worry about disclosure of mental health details and loss of confidentiality. • The homeless community was reluctant to visit hospitals except for emergencies. This group is often hard to maintain contact with, so may require more face-to-face engagement at their communal locations like food banks. • The Gypsy, Roma and Traveller participants had a very limited interest in taking vaccines and tend to have a fatalistic approach to health issues, believing "what is meant to be, will be".
Scott (2021) (142) Cross-sectional study USA Apr 2020	A survey was mailed to 391 Amish families in Ohio to determine COVID-19 vaccine intentions. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 75.7% did not intend to vaccinate their children against COVID-19. • No significant differences in intention to get a COVID-19 vaccine were seen between those with and without special needs children (14.8% vs. 7.6%, P = 0.053). • Swartzentruber Amish were significantly less likely to intend to vaccinate compared to other Amish affiliations (0.0% vs. 11.7%, P< 0.001). • The top reasons for refusal of vaccines in general included too many side effects (83.9%), they contain dangerous chemicals/preservatives (46.0%), vaccinating means not putting faith in God to protect their children (13.0%), vaccinating introduces germs (9.6%), other families don't vaccinate (7.0%), and the diseases that are vaccinated for are not a problem in their community (6.1%).

		• Citing doctors or nurses as the most influential person in the decision to vaccinate were more likely to take all recommended vaccines compared to those who took no vaccines (52.2% vs. 2.6% P < 0.001). However, families that refused all recommended vaccinations were more likely to state their bishop or minister was the most influential person in the decision to vaccinate compared to families that took all vaccines (4.4% vs 0.0%, P=0.003).
GENERAL		
Horizon Research (2021) *unpublished* (15, 195) Longitudinal study New Zealand Mar-May 2021	An online survey of adults (16+) was conducted to measure vaccine intentions. Mar-Apr, n=1,350 Apr-May, n=1387 Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 83% of those at high risk for getting very ill were intending to get vaccinated or were already vaccinated and 5% reported they definitely will not get a vaccine.

CDC = Centers for Disease Control and Prevention, NIH = National Institutes of Health

INDIVIDUALS WITH COMORBIDITIES OR DISABILITIES

Table 6. Evidence of vaccine attitudes of individuals with comorbidities (n=23)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
CANADA		

Vallis (2021) (164) Cross-sectional study Canada Jun-Oct 2020	Attitudes and concerns towards COVID-19 vaccination in individuals living with overweight and obesity were evaluated using an online survey. Two samples were used: 1) representative sample of 1089 individuals living with overweight and obesity and 2) convenience sample of 980 individuals recruited from obesity clinical services or patient organizations throughout Canada. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 64.6% of those living with obesity were comfortable receiving a vaccine and 35.4% were hesitant. • Individuals were less comfortable with their children receiving the vaccine (58.5% comfortable, 41.6% hesitant, P<0.001). • The mean score on the confidence subscale of the vaccine hesitancy scale was significantly lower than any other measure (mean = 2.26). • Fear of COVID-19 was a predictor of vaccine attitudes for all dependent measures. • Comfort levels in receiving the vaccine were positively associated with male gender, having more comorbidities, having lower depression scores, not practicing social distancing, and past acceptance of influenza vaccinations.
AUSTRALIA & NEW ZEALAND		
Horizon Research (2021) *unpublished* (15, 195, 232) Longitudinal study New Zealand Mar-May 2021	An online survey of adults (16+) was conducted to measure vaccine intentions. Mar-Apr, n=1,350 Apr-May, n=1387 May, n=1,234 *new* Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	**May** • 13% of respondents who identified as being disabled or having chronic conditions reported they were unlikely to vaccinate. • Reasons not to vaccinate included safety concerns (49%), a belief that a vaccine was not needed (21%), and a mistrust of vaccines in general (18%). **Apr-May** • 77% of those living with impairments or long-term health conditions were likely to accept a vaccine or had been vaccinated compared to 5% report they definitely will not get a vaccine. • 70% identifying themselves to be disabled were likely to accept a vaccine or had been vaccinated compared to 5% report they definitely will not get a vaccine.

Australia Bureau of Statistics (2021) *unpublished* (141) *new* Longitudinal study Australia Apr 2020-May 2021	The household impacts survey is a monthly survey which collects data online and by telephone from a panel of adults (18+) on COVID-19 related topics including attitudes towards vaccines. May: n=3,371 Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Those with disabilities or long term conditions were slightly more likely to intend to vaccinate compared to those without (68.6% for disabled vs 68.1% not disabled and 70.1% with long term health conditions vs 66.5% for those without long term health conditions). • The main factor for deciding to get a vaccine is a recommendation from their general practitioner (33.7% and 31.0% respectively for disability and chronic conditions). • Concerns for side effects dominated the reasons for not wanting to get vaccine (62.7% for those with disabilities and 62.1% with chronic conditions).
Bonner (2020) *preprint* (152) Longitudinal study Australia Apr & Jun 2020	People with self-reported hypertension (n=466) were compared to matched healthy controls (n=466) during COVID-19 lockdown to determine whether they have higher risk perceptions, anxiety, and prevention intentions. Using an online survey, vaccine intention was asked during the lockdown and again 2 months after restrictions eased. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• At baseline, 87% of the people with hypertension and 85% of the healthy matched controls stated they would get the COVID-19 vaccine. • There were no significant differences in willingness to vaccinate for COVID-19 between people with hypertension and healthy matched controls. • Despite a decrease in perceived seriousness and anxiety two months after lockdown restrictions lifted, intentions remained high (>80%) for COVID-19 vaccination at follow-up.
USA		

Ricotta (2021) *preprint* (153) Cross-sectional study USA Feb 2021	To assess vaccine acceptance in individuals with chronic respiratory or autoimmune diseases, an online survey was conducted in 1232 individuals with self-reported a chronic respiratory or autoimmune disease and 1303 healthy controls across the USA. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Compared to healthy controls, those who reported chronic respiratory diseases were 5.7% more willing to be vaccinated (95% CI: 0.05-0.09). • When asked about reasons for intending to vaccinate, those with chronic respiratory disease (OR 1.08, 95% CI: 1.03-1.13) and autoimmune diseases (OR 1.06, 95% CI: 1.01-1.11) were more likely to vaccinate to protect themselves from COVID-19 compared to controls. Those with chronic respiratory diseases were also more likely to want to safely return to work (OR 1.08, CI: 1.03-1.14). • Of those who do not intend to vaccinate, individuals with autoimmune diseases were the only group to have a significant association with a particular cause for hesitancy. These individuals were more likely to report fear of a bad vaccine reaction as the reason for hesitancy (OR 1.22, 95% CI: 1.06-1.41).
Garcia (2021) (156) Cross-sectional study USA Jan – Feb 2021	An online survey in 150 randomly selected dialysis facilities in the USA was conducted to evaluate vaccine intentions and hesitancy in 1,515 patients on hemodialysis. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 20% were reluctant to accept a vaccine even if it was considered safe for the general population. If the vaccine was offered at the dialysis facility, this hesitancy decreased to 18%. • Vaccine hesitancy was highest in patients aged 18–44 years (aOR 1.5, 95% CI, 1.0-2.3), women (aOR 1.6, 95% CI: 1.2-2.0), Black patients (aOR 1.9, 95% CI: 1.3-2.7), and patients identifying as other race or ethnicity (aOR 2.0, 95% CI: 1.1-3.7). • Vaccine hesitancy was lower in patients aged 80+ (aOR 0.4, 95% CI: 0.3-0.7), those with some college education (aOR 0.4, 95% CI: 0.2-0.6), and those who received the influenza vaccine (aOR 0.2, 95% CI: 0.1-0.3). • 53% of those who were vaccine hesitant expressed concerns about side effects.
Tsai (2021) *preprint* (160)	An international online survey was conducted to measure vaccine hesitancy among 21,943 individuals with high risk conditions such as	• 25% of respondents had received at least one vaccine with a further 7% trying to get the vaccine but unable to get one.

Cross-sectional study USA Jan-Feb 2021	with cancer, autoimmune disease, and other comorbid conditions. 74% of participants were from the USA and 4% from Canada. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 43% planned on definitely getting a vaccine, 5% probably will, 5% were unsure, 4% probably will not receive a vaccine, and 10% definitely will not accept. • Broken down by conditions, current smokers were the most hesitant (29%) followed by those with obesity (20%), type 2 diabetes (19%), hypertension (18%), and chronic lung disease (18%). • Those with past cancer treatment had a higher level hesitancy than those currently undergoing cancer treatment (13% vs 11%). • Vaccine hesitancy was associated with younger age, female gender, Black-Pacific-Island-Native American ethnicity, less education, conservative political tendencies, resistance to masks or routine influenza vaccinations, and distrust of media coverage. • Those who responded with some level of vaccine hesitancy indicated that the vaccine was too new (53%), were worried about side effects or discomfort (44%), felt the process had been implicated with politics (39%), and wanted to wait until others have taken it (33%). • 21% reported not trusting vaccines in general but were more negative towards the COVID-19 vaccine in particular (40%).
Iadarola (2021) *preprint* (157) Cross-sectional study USA Jan-Feb 2021	Intention to vaccinate was evaluated using an online survey of 825 individuals with intellectual and developmental disabilities (IDD) and their family members and care workers in New York State. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No	• 62% of respondents would definitely or probably get a COVID-19 vaccine and 13.9% had already received the vaccine. • Vaccine hesitancy was greater in those that were younger and those making decisions on behalf of a person with IDD. • Black respondents > 50 years old were more likely intend to vaccinate or already have received a vaccine compared to younger respondents (OR 3.72, 95% CI: 1.73-8.00), in addition to White respondents > 50 years old (OR 2.39, 95% CI: 1.36-4.17).

	Formative research conducted? Yes Survey pre-tested? No	• The most common reasons for vaccine hesitancy were concern about side effects (16%), belief that the vaccine was too new (15%), not wanting to be an 'experiment' for the vaccine (14%), and mistrust of the government (14%). • Hispanic and Black respondents (96% and 91%, respectively) reported concerns about being used as an 'experiment' more often than White or Asian respondents (76% and 67%, respectively). • Health professionals (92%) were the most trusted source of vaccine information followed by friends and family (74%).
McCabe (2021) *preprint* (166) Cross-sectional study USA Dec 2020-Feb 2021	A national app distributed survey was conducted in 34,470 healthcare workers and adults from the general population to measure intent to receive a vaccine and factors associated with acceptance and refusal. Number of healthcare workers was not reported. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? Yes	• Those with 3 or more pre-existing conditions were 1.19 times more likely than those without any to be vaccine hesitant (aOR 1.19, 95% CI: 1.06-1.34, P=0.0045).
Xiang (2021) (162) *new* Cross-sectional survey USA	An online survey of 401 multiple sclerosis patients across the USA (the majority in Oregon, Washington, and California) was conducted to assess vaccine intentions. Question Topics: 1) Vaccine intentions	• 70.1% were willing to get a vaccine, 7.2% would not be willing, and 22.7% were unsure. • Most respondents were motivated by wanting to protect themselves (77.6%) or their loved ones (58.7%), and to decrease chances of serious illness (53.4%). • Among those intending to decline a vaccine the top reasons included worry for potential side effects (55.2%), speed of vaccine development

Dec 2020-Jan 2021	2) Vaccine hesitancy 3) Vaccine perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	(55.2%), and wanting more safety evidence due to the rushed development (44.8%). • Undecided respondents expressed wanting population safety information (57.1%). The undecided also held beliefs that political pressure factored into vaccine trials (37.4%) and wanted people without MS to get the vaccine due to safety concerns (29.7%). • Multivariate analysis found higher intention to vaccinate among those who have talked to or plan to talk to their MS doctor about the vaccine (aOR 2.93, 95% CI: 1.32- 6.49 and 2.57, 95% CI: 1.38-4.80, respectively), prior flu vaccination (most years aOR 5.59, 95% CI: 2.44-12.77 and every year aOR 8.96, 95% CI:4.39-18.31), any amount of concern about COVID-19, any level of worry about their risk of hospitalization or death, and not socializing in public but in the home (aOR 14.07, 95% CI:1.43-138.33) or only virtual socialization (aOR 17.53, 95% CI:1.80-170.60).
Kelkar (2021) (154) Before-and-after study USA Dec 2020 – Jan 2021	This study aimed to determine if a webinar would increase knowledge about COVID-19 vaccines and impact intention to vaccinate. 264 people with cancer or their caregivers in Florida participated in the webinar and registered to take at least one online survey (pre and post webinar), of which 105 answered both surveys. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• Prior to the webinar, 71% intended to vaccinate, 5% would not receive a vaccine, and 24% were unsure. • 97/105 individuals answered the specific question about vaccine intention in both the pre- and post-webinar survey. After the webinar, 82.5% intended to vaccinate, 2.1% would not receive a vaccine, and 15.5% were unsure. • The most common reasons for hesitancy included concern about side effects vaccine (30%), a lack of information on vaccine effectiveness (14%), and a lack of trust that the vaccine is safe for cancer patients (8%).

Dalal (2021) (149) Cross-sectional study USA Dec 2020-Jan 2021	An online survey of 906 adults with an irritable bowel disease (IBD) from a Boston hospital or through IBD related social media (SM) was conducted to evaluate their intentions to be vaccinated and identify potential concerns. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Intention to get a vaccine was high among locally recruited respondents (80.9%) compared to 60.0% of those recruited from social media. • The most common reasons for hesitancy across both groups included worry about long term effects and adverse reactions, want to see how others tolerate the vaccine, worry that the vaccine did not have the regular amount of safety checks, concern that vaccine with interfere with IBD medication efficacy, and a personal history of allergic reactions. • A recommendation from their IBD healthcare provider was reported to be important in both locally acquired (92%) and social media respondents (80.6%). • From their IBD provider respondents wanted to hear about risks and benefits, receive a handout, provide information regarding safety/efficacy for those with IBD/other autoimmune disorders, and safety/efficacy with IBD medications. • Intention to vaccinate was positively associated with age (OR 2.21, 95% CI: 1.07–4.54), having a bachelors degree or more (OR 3.31, 95% CI: 1.36–8.06), being White (OR 2.13, 95% CI: 1.17–3.85), having had COVID-19 (OR 2.02, 95% CI: 1.09–3.73), or currently being on a biologic (OR 1.52 95% CI: 1.07–2.16).
Serper (2021) (159) Cross-sectional study USA Dec 2020	To assess attitudes and intentions regarding COVID-19 vaccines, an online survey was conducted with 1215 patients who receive care for chronic gastrointestinal and liver conditions (irritable bowel syndrome, cirrhosis, or liver transplant recipients) within a large healthcare system in Southeastern Pennsylvania.	• 85% completely or somewhat agreed that they would take the vaccine if available, 7% were neutral, and 8% completely or somewhat disagreed. • Reported vaccine concerns included safety (54%), effectiveness (26.7%), not being prioritized for the vaccine (39%), cost (17.4%), and inconvenience (10.3%). • Respondents were more likely to accept a COVID-19 vaccine at a medical office or pharmacy, compared to drive-through sites, places of

	Question Topics: 1) Vaccine intentions 2) Vaccine attitudes 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	employment, or community sites (e.g., church, school). • More than 75% would follow their government or doctor's recommendation about receiving the COVID-19 vaccine, 91% would follow their GI/liver specialist's recommendation, and 56% would follow their employer's recommendation. • Females (aOR 2.02, 95% CI: 1.40-2.92, P<0.001) and those with lower incomes (aOR 2.17, 95% CI: 1.26-3.74, P=0.005) were more likely to be vaccine hesitant and those aged 65+ (aOR 0.52, 95% CI: 0.30-0.92, P=0.024) and with prior receipt of annual flu vaccine (aOR 0.11, 95% CI: 0.07-0.10, p<0.0001) were less hesitant.
Ou (2021) (165) *new* Cross-sectional study USA Nov-Dec 2020	Attitudes towards a potential COVID-19 vaccine was assessed in 1308 solid organ transplant recipients (SOTRs) and 1617 non-SOTRs through an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• 50.5% of SOTRs and 60.7% of non-SOTRs intended to accept a vaccine. • 49.5% of SOTRs and 39.3% non-SOTRs did not intend to receive a vaccine. • In SOTRs, those who were unlikely or hesitant were more likely to be between 30-49 years old, women, Black, non-USA residents, had a high school diploma or less, were not married, had household income of less than $30,000, had not received a flu shot in the past year, did not plan on getting the flu vaccine in the current year, believed that transplant patients are at greater risk for illness from the vaccine, believed that the COVID-19 vaccine could lead to rejection, and did not believe vaccines to be safe for transplant patients. • 80.0% of SOTRs reported that they needed information from their doctor or an assurance of personal health/health compatibility with the vaccine (75.4%). This was 86.8% if recommended by their transplant surgeon, 71.9% if from another member of transplant team, and 64.1% if it was from their primary care doctor. • SOTRs were more likely to perceive vaccine as necessary and that vaccines work, express comfort with vaccines, not fear vaccines, trust

		pharmaceutical companies, the CDC, and vaccine in general as compared to non-SOTRs. • Fewer non-SOTRs living with an SOTR compared to those not living with an SOTR report that they intend to get vaccinated (57.6% vs 61.3%). This remained true if the vaccine was recommended by a doctor (73.9% vs 76.7%) but not if they felt that SOTRs should get a vaccine (52.2 vs 52.0%). • The announcement of Moderna efficacy slightly increased intention to vaccinate from 53.5% to 57.8% post announcement.
Rodriguez (2021) (238) *new* Cross-sectional study USA May-Dec 2020	A sample of 175 people with HIV (PWH) over the age of 18 were surveyed online to validate the Vaccine Hesitancy Scale (VHS) with a focus on understanding COVID-19 vaccine attitudes and willingness to get vaccinated. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• Lack of confidence and risks respectively explained 45.55% and 12.31% of the variance in vaccine hesitancy responses. • Mean responses find that vaccine hesitancy scores were higher among those that didn't believe the vaccine would be effective, those that wouldn't be swayed by a healthcare provider recommendation, did not think it was important they got vaccinated due to their health conditions, and that they wouldn't get vaccinated if it was required to get back to ordinary life. • Mean vaccine hesitancy scores were lower for respondents who didn't believe their health conditions would be made worse by the vaccine.
Jones (2021) (239) Cross-sectional study USA Aug – Nov 2020	An online survey of 94 adults (18+) living with HIV in Miami, Florida from underrepresented ethno-racial groups was conducted to evaluate intention to vaccinate and factors associated with hesitancy. Participants were Black non-Latinx (60%) and non-Black Latinx (40%). Question Topics:	• Compared to non-Black Latinx, Black non-Latinx participants were less likely to agree with vaccinations being important for their health (92% vs 68%, P=0.009), to believe that vaccines are effective in preventing disease (84% vs 68% P=0.029), and to believe that vaccine information is reliable and trustworthy (71% vs 36%, P=0.002). • Intention to vaccinate was positively associated with the belief that vaccines are important (OR 12.0, 95% CI: 3.22-44.8, P<0.001) and effective (OR 5.71, 95% CI: 1.78-14.59, P=0.001), agreeing that

	1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	information about vaccines is reliable and trustworthy (OR 6.76, 95% CI: 2.71-16.88, P=0.001), belief they should follow doctors orders (OR 5.28, 95% CI: 1.57-17.71, P=0.001), and believing that a vaccine is the best way to protect from disease (OR 7.07, 95% CI: 2.14-23.42, P<0.001).
Bogart (2020) (158) Cross-sectional study USA May-Jul 2020	101 Black people living with HIV were surveyed by telephone to assess associations between medical mistrust, vaccine intentions, and vaccine hesitancy. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• The most common COVID-19 vaccine beliefs were that the vaccine would be harmful (51%), they would not trust it (34%), and they would not want to get a vaccine (32%). • Multivariate analysis found that greater COVID-19 related mistrust was significantly associated with vaccine hesitancy [b (SE) = 0.85 (0.14), P < 0.000]). • Pearson correlations indicated that participants with less than a high school education showed higher levels of vaccine hesitancy (r = 0.20, P = 0.04).
Ehde (2021) (148) Cross-sectional study USA Apr-May 2020	Factors associated with intention to receive a COVID-19 vaccine was assessed in 486 adults (18+) living with multiple sclerosis using an online survey. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 66.0% of participants were willing to take a vaccine when available, 18.5% were moderately willing, and 15.5% were not willing. • Statistically significant predictors of an increased willingness to vaccinate include higher education (β =0.20, P <0.001) and perceiving oneself to be at greater risk of contracting COVID-19 (β =0.18, P =0.001). • Participants believed that healthcare providers and the National MS Society had the highest perceived trustworthiness for COVID-19 information. The perceived trustworthiness of information sources was highly associated with intention to vaccinate.
Rungkitwattana kul (2021) (155)	To evaluate intentions to vaccinate, an online survey of 90 patients at an urban dialysis center in Washington DC which serves a	• 49% of respondents indicated they would be willing to receive a COVID-19 vaccine, 34% were unwilling, and 17% were unsure.

Cross-sectional study USA Date NR	predominately African American patient population was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Intention to receive a COVID-19 vaccine was associated with having received the influenza vaccine P < 0.001. • The most common reasons for vaccine hesitancy included a lack of adequate information regarding safety and efficacy (46.8%), lack of trust in the federal government (36.4%), and a lack of trust in the vaccine manufacturers (28.9%).
UNITED KINGDOM		
Office for National Statistics (2021) & Office of National Statistics (2021) *unpublished* (43, 140) Longitudinal study UK Feb-Apr 2021	Responses from four waves of results collected from the online Opinions and Lifestyle Survey (196) were pooled to focus on demographic specific associations with vaccine hesitancy. The number of disabled or clinically extremely vulnerable were not reported. Feb-Mar: 17,201 responses pooled Mar-Apr: 16,362 responses pooled Questions Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	**Mar-Apr** • Disabled adults had slightly less vaccine hesitancy compared adults who were not disabled (5% vs 7%). Hesitancy has decreased since last reporting (8% and 9% respectively). • Clinically extremely vulnerable (CEV) respondents had significantly less hesitancy than non-CEV respondents (4% vs 7%). • Significantly more non-CEV respondents report they are likely to get a vaccine (31%) compared to less than 1% of CEV are unlikely to get vaccine. **Feb-Mar** • The most common reasons for hesitancy among disabled adults were concerns about existing health conditions (48%), followed by concerns about side effects (46%), and waiting to see if the vaccine works (43%). • The most common reasons for hesitancy among CEV adults were concerns about side effects (49%), followed by worries about long-term effects (47%), and concerns about existing health conditions (42%). • Respondents with underlying health conditions had less hesitancy that those without (6% vs 10%).
Saunders (2021)	Vaccine intentions and attitudes towards COVID-19 risks were	• 91.5% of respondents reported that they had been vaccinated (93.5% of these were first dose only).

(163) *new* Cross-sectional study UK Mar 2021	measured online in 964 individuals with chronic myeloproliferative neoplasm (MPN). Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 0.03% (29/964) were booked for their first dose, 0.05% (53/964) were not booked for a dose, of which 14 had been offered and 38 had not been offered a dose. • 0.8% (n=8) refused vaccination for reasons including side effects (n=5), quick development of the vaccine (n=4), safety (n=3), and perceived efficacy for MPNs (n=2). Open text responses included possible immune stress with consideration of past COVID-19 infection, alternative medicine didn't recommend it, and wanted to discuss with their oncology doctor. • 16.7% of those who had been vaccinated expressed concern about vaccination due to potential serious reaction (30.6%), efficacy in MPN patients (15.4%), vaccine interfere with MPN condition (14.3%) or MPN medications (10.2%). • 82.9% of the vaccinated respondents had no overall vaccine preference, 65.2% preferred Pfizer, 30.4% AstraZeneca, 2.9% Moderna, and 1.4% other. • 89.0% of respondents trusted their healthcare provider to inform them of risks and benefits. • For the 97 respondents who didn't trust their healthcare provider the main reason is that they didn't not know enough about the vaccine (34.0%), benefits (30.0%), or knowledge of MPN or vaccines in patients with MPN (12.0%), and mistrust of their primary care physician.
Bateman (2021) (240) *new* Quasi-experimental study UK	An 8 minute educational video was sent via text to a cohort of 661 rheumatology patients to measure the impact of the video on intention to vaccinate. Questions Topics: 1) Vaccine intentions	• Of the 8886 patients sent the text message with video link 2358 had viewed the video (27%) and 661 completed the evaluation. • Pre-video, 36% of patients aged 30-49, 47% of those aged 50-69, and 52% aged 70+ reported that they were aware of COVID-19 vaccines and that they were recommended for them. After video viewing this increased to 88%, 92%, and 94% for these respective age categories.

Dec 2020	Survey tools available? No Formative research conducted? No Survey pre-tested? No	• On a scale of 1 (strongly disagree) to 5 (strongly agree) respondents felt more informed (mean = 4.1), more confident about getting a vaccine (mean = 4.2), reported that they would seek vaccination (mean= 4.1), and that the video was helpful for sharing information (mean = 4.4). • Older patients (50+) were more likely to report that they learned more, felt more confident, and were more likely to get vaccinated compared to those aged 30-49.
USA & UK		
Felten (2021) (161) Cross-sectional study 56 countries Dec 2020	Vaccine intentions and hesitancy in 1258 patients with autoimmune or inflammatory rheumatic diseases (AIIRD) was evaluated using an online survey. There were 327 individuals from the UK and 114 from the USA. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• Among those with AIIRD in the UK, 39.4% would be willing to accept a vaccine, 31.3% were hesitant, and 10.5% were suspicious. • In the USA, 15.6% were willing to accept a vaccine, 9.2% were hesitant, and 5.9% were suspicious. • AIIRD patients who were suspicious of the vaccine were significantly more concerned about vaccination in general, thought it was less important to get vaccinated, were concerned about the use of a new vaccine technology, lack of hindsight regarding COVID vaccination, and potential financial links between governments and pharmaceutical companies. • Those who were hesitant or suspicious were significantly more concerned that the vaccine would induce a flare of their disease. • Men were more likely to intend to vaccinate compared to women (P<0.0001) and younger individuals were less likely than older individuals (P<0.0001).

OTHER POPULATIONS OF INTEREST

Table 7. Evidence of vaccine attitudes of other populations of interest (n=61)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
LGBTQ+		
CANADA		

Statistic Canada (2020) *unpublished* (78) Cross-sectional study Canada Sept-Oct 2020	A telephone survey of 120,000 (18+) was conducted to assess intention to vaccinate. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 87.6% of LGBTQ2+ were willing to accept a vaccine compared to 76.4% non-LGBTQ2+.
Ogilvie (2021) (79) Cross-sectional study Canada Aug-Sep 2020	Intention to vaccinate was assessed in 4058 adults and healthcare workers from British Columbia (25-69 years old). Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Non-binary, gender queer, agender, two-spirit or other were more likely to be receive a vaccine (OR 3.04, 95% CI: 1.08-8.55, P<0.04).
Statistics Canada (2020) & Statistics Canada (2021) *unpublished* (65, 80) Longitudinal study Canada	An online survey conducted by Statistics Canada as part of the Canadian Community Health Survey (CCHS) assessed Canadians behaviors to safeguard their own health as well as the health of others. In the September survey, a question about vaccine intentions was added. The most recent report captures 20,000 responses from individuals aged 12+. Question Topics:	• Over the sampling period 77% were willing to receive a vaccine. This represents an increase from Sept (75.5%) to Oct (74.8%), and Nov/Dec (80.3%). • LGBTQ2+ were more likely to get a vaccine (83.3%).

Sep-Dec 2020	1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	
USA		
Bogart (2021) (170) *new* Cross-sectional study USA Nov-Dec 2020	207 Black people drawn from the nationally representative RAND American Life Panel (ALP) and were surveyed online to assess associations between medical mistrust, vaccine intentions, and vaccine hesitancy. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Sexual or gender minorities were not statistically predictive of negative or positive intentions to get a vaccine (positive intent P = 0.56 and negative intent P = 0.41).
Teixeira da Silva (2021) (167) Cross-sectional study USA Oct-Dec 2020	Vaccines acceptance was assessed in 1350 sexual and gender minority (SGM) individuals using an online survey across the USA. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• On a 10-point scale with 10 being "highly likely and 1 being "very unlikely", intention to vaccinate was moderately high (mean score = 7, SD = 3.12). • Compared to gay men, participants grouped in the "Other" sexual identity category were less likely to intend to vaccinate (β = −1.102, P = 0.047). There were no other differences by sexual identity (bisexual, queer, multiple identities, same-gender loving). • Compared to White participants, Black (β = −0.681, P < 0.001), American Indian/Alaskan Native (β = −2.482, P < 0.001), and participants identifying with another race (β = −1.174, P < 0.001) were more willing to intend to vaccinate. Asian participants (β = 0.718, P = 0.018) were more likely to intend to vaccinate compared to White.

		• Vaccine acceptance was negatively associated with more social concerns regarding the vaccine (β = −0.10, $p < 0.001$) and medical mistrust (β = −0.06, $p < 0.05$) and positively associated with altruistic motivations (β = 0.60, $p < 0.001$).
Phillips (2021) (169) *new* Cross-sectional study USA Apr-Aug 2020	Sexual/gender minority and people living HIV (PLWH) differences in acceptance of a COVID-19 vaccine were measured through an online survey of 932 adults (over 18). Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 91.8% would consider getting a COVID-19 vaccine and 8.2% would not. • Bisexual and pansexual respondents had significantly increased odds of considering a COVID-19 vaccine (OR 1.69, 95% CI: 1.01-2.82) as compared to gay or lesbian respondents as were gender non-binary (OR 4.38, 95% CI: 1.33–14.4) compared to respondents with male gender identies or transgender (OR 2.30 95% CI: 1.08–4.88) compared to non-transgender respondents. • HIV positive individuals were significantly less likely to consider COVID-19 vaccination (OR 0.40, 95% CI: 0.23–0.67) compared to HIV negative respondents.
Melin (2021) *preprint* (168) Cross-sectional study USA Jul 2020	Factors associated with the intention to vaccinate against COVID-19 among 1016 adults (21+) living in Puerto Rico was assessed using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• In the bivariate analysis, homosexual (81.8%), bisexual (85.7%), and other (90.9%) sexual identity were all associated with increased intention to be vaccinated when compared to heterosexual (66.4%), P<0.001. • After adjustment in the multivariate regression analysis, this relationship was not significant (homosexual: aOR 0.9, P=0.72; bisexual: aOR 2.1, P=0.08; other sexual identity: aOR 3.4, P=0.25).
PARENTS		
CANADA		
Government of Manitoba (2021)	An online research panel of 600 Manitobans were surveyed to understand attitudes towards	• In a group of 70 parents or guardians of children aged 12-17, 15% were not sure if they will vaccinate their children, and 13% will not vaccinate their children.

unpublished (11) *new* Longitudinal study Canada May 2021	vaccination and possible incentives to increase uptake. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Those who did not intend to vaccinate their children were in households making less than $40,000, would not get the vaccine themselves, and didn't believe adults should get all the regular vaccines.
McKinnon (2021) *preprint* (18) Cross-sectional study Canada Jan – Apr 2021	Willingness to vaccinate children according to level of education, neighbourhood, and visible minority status was evaluated using an online survey in 380 parents with children aged 2-17 in Montreal. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Parents were 61% very likely, 25% somewhat likely, 9.2% somewhat unlikely, and 4.5% very unlikely to have their child vaccinated. • Concern over the lack of information about the vaccine's safety and possible side effects was the most common reason for hesitancy (48%). • Comparing visible minority to non-visible minority parents, 30.3% vs. 66.6% were very likely to vaccinate their children, 36.8% vs. 23.9% were somewhat likely, and 32.9% vs. 9.5% were unlikely to vaccinate, respectively.
Vallis (2021) (164) Cross-sectional study Canada Jun-Oct 2020	Attitudes and concerns towards COVID-19 vaccination in individuals living with overweight and obesity were evaluated using an online survey. Two samples were used: 1) representative sample of 1089 individuals living with overweight and obesity and 2) convenience sample of 980 individuals recruited from obesity clinical services or patient organizations.	• 64.6% of those living with obesity were comfortable receiving a vaccine and 35.4% were hesitant. • Individuals were less comfortable with their children receiving the vaccine (58.5% comfortable, 41.6% hesitant, $P<0.001$).

	Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	
Drouin (2021) *preprint* (151) Cross-sectional study Canada Aug 2020	Parental intention to have their child with asthma vaccinated against COVID-19 was assessed using an online survey in 305 parents. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 63% of parents were likely to have their child vaccinated, 19.1% were unlikely, and 17% were unsure. For themselves, 64% were likely to get vaccinated, 21% were unlikely, and 15.1% were unsure. There was a strong relationship between a parents' intention to vaccinate their children and person intention to vaccinate. • Factors significantly associated with a parents' decision to vaccinate their child included higher level of education, being employed, sex of the child (female), presence of other chronic diseases, prior influenza vaccination, parental anxiety, and consultation with a health professional.
Lackner (2021) (189) Cross-sectional study Canada May-Jun 2020	The demographic, experiential, and psychological factors associated with the anticipated likelihood and speed of having children receive a COVID-19 vaccine was investigated in 455 families (857 children). Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Factors associated with a higher likelihood of having their children vaccinated include older parental age, living in the Prairies (relative to Central Canada), more complete child and parental vaccination history, positive attitudes towards vaccines in general, higher psychological avoidance of the pandemic, and a greater tendency to prioritize the risks of the disease relative to the risks of side-effects. • In some models, perceived COVID-19 risk and higher levels of state anxiety were associated with increased likelihood of having children vaccinated. • The above factors were also predictors of faster speed of intended vaccination. However, higher SES was a trend-level predictor.
GLOBAL		

Skjefte (2021) (135) Cross-sectional study 16 countries: Australia, Africa, Argentina, Brazil, Chile, Colombia, India, Italy, Mexico, New Zealand, Peru, Philippines, Russia, Spain, UK, USA. Oct-Nov 2020	An online survey was used to evaluate the acceptance of COVID-19 vaccination among 5,294 pregnant women and 12,562 mothers of children younger than 18-years-old. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 69.2% of all women intended to vaccinate their children. Acceptance levels were above 85% in India, Mexico, Brazil and Colombia and below 52% for the USA, Australia, and Russia. • For mothers, the most common reasons to decline a vaccine were concern that approval of the vaccine will be rushed for political reasons (39.8%), lack of safety and effectiveness data among children (32.7%), and worry about safety and side effects (28.4%).
UNITED KINGDOM		
Office for National Statistics (2021) & Office of National Statistics (2021) *unpublished* (43, 140) Longitudinal study UK Feb-Apr 2021	Responses from four waves of results collected from the online Opinions and Lifestyle Survey (196) were pooled to focus on demographic specific associations with vaccine hesitancy. The number of disabled or clinically extremely vulnerable were not reported. Feb-Mar: 17,201 responses pooled Mar-Apr: 16,362 responses pooled Questions Topics: 1) Vaccine intentions 2) Vaccine hesitancy	**Mar-Apr** • Vaccine hesitancy is highest among those with children aged 0-4 (12%) compared to 8% with children over 5 (8%), and among non-parents or those not living with dependent children (6%). Vaccine hesitancy has decreased since the last survey. • In those with children aged 0-4, vaccine hesitancy was more prevalent among women than men with children aged 0-4 (16% vs 8%). This has decreased since the last survey. • Positive vaccine sentiment is lowest among 0 to 4 (88%) compared to 92% with children over 5 and 94% among non-parents or those not living with dependent children **Feb-Mar**

	Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• The top reason for hesitancy was concern about side effects which was the same for both groups of parents.
Skirrow (2021) *preprint* (19) Cross-sectional and qualitative study UK Aug – Oct 2020	An online survey and semi-structured interviews were conducted in a group of 1,181 pregnant women (aged 16+) to determine views on COVID-19 vaccine acceptability for themselves when pregnant, not pregnant, and for their babies. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 81.2% of women reported that they would definitely accept or were leaning towards accepting a vaccine when not pregnant. Vaccine acceptance was significantly lower during pregnancy (62.1%, P<0.005) and for their babies (69.9%, p<0.005). • Compared to White ethnic women, ethnic minority women were twice as likely to reject a vaccine for themselves when not pregnant, pregnant and for their babies (P>0.005). • Those from lower-income households, aged < 25 years, and from some geographic regions were more likely to reject a vaccine when not pregnant, pregnant, and for their babies. • Women unvaccinated against pertussis in pregnancy were over four times more likely to reject a vaccine when not pregnant, pregnant and for their babies. • Thematic analysis revealed the most common reasons for hesitancy were vaccine safety, and a wider mistrust of vaccines in general.
Bell (2020) (185) Cross-sectional study England Apr-May 2020	The acceptability of a future vaccine was assessed in a group of 1252 parents and guardians (aged 16+ with a child <18 months old) using an online survey. Upon completion of the online survey, participants were asked if they were interested in taking part in a follow-up telephone interview. Nineteen individuals were included. Question Topics:	• Black, Asian, Chinese, Mixed or other ethnicity were almost 3 times more likely to reject a COVID-19 vaccine for themselves and their children compared to White British, White Irish, and White other participants. • 55.8% of respondents intend to vaccinate and 34.3% were unsure but leaning towards yes. • For vaccinating their children, 48.2% were willing to accept and 40.9% were unsure but leaning towards yes.

	1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	
NEW ZEALAND		
Horizon Research (2021) *unpublished* (15, 195, 232) Longitudinal study New Zealand Mar-May 2021	An online survey of adults (16+) was conducted to measure vaccine intentions. Mar-Apr, n=1,350 Apr-May, n=1387 May, n=1,234 *new* Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	**May** • 55% of parents or caregivers of children aged 12-15 are likely to have their children vaccinated, a 1% decrease from April. • The major reasons included wanting assurances for the safety in children (59%), concern for long term effects in children (50%), and wanting to wait to see if there were side effects (28%). **Apr-May** • 56% of parents or caregivers of children aged 12-15 will allow their children to receive a vaccine. Parents who were willing to vaccinate themselves were more likely to vaccinate their children compared to those who would not vaccinate themselves (85% vs 6%). • The top concerns among those who were unsure or unlikely to vaccinate their children were a need for safety assurances (60%) and uncertainty about long-term effects (43%).
Horizon Research (2021) *unpublished* (187) Cross-sectional study New Zealand	An online survey of 1451 adults (18+) was conducted to measure vaccine acceptance for themselves and their children after vaccines were announced to available. Question Topics: 1) Vaccine intention Survey tools available? Yes	• Pasifika and Indian parents were most likely to give a vaccine to their children (72% and 68%) and Māori and Other European were least likely (40% and 41%).

Sep 2020	Formative research conducted? No Survey pre-tested? No	
Horizon Research (2021) *unpublished* (94) Cross-sectional study New Zealand Dec 2020	An online survey of 1438 adults (18+) was conducted to assess vaccine intentions, knowledge, and perceptions. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine knowledge Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 40% of parents were willing to get their children vaccinated once approved, 33% were unlikely, and 24% were unsure. The least likely to vaccinate their children were were Pasifika (39%) and Other Europeans (29%) followed by Māori (39%), NZ Europeans/Pakeha (41%), Asian (45%), and Indian (62%) parents.
USA		
Teasdale (2021) *preprint* (16) *new* Cross-sectional study USA Mar-Apr 2021	An online survey of 1,119 parents or caregivers (18+) of children under the age of 12 in New York was conducted to determine vaccine intentions for their youngest child. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 61.9% intend to vaccinate their youngest child (mean age 4.7 years), 23.3% were unsure, and 14.8% did not intend to vaccinate. • Intention to vaccinate increased when children were older and were White non-Hispanic and parents were between 30 and 44, male, and White non-Hispanic. In multivariate modelling only female parents (aPR 0.72, 95% CI: 0.61-0.85) and non-Hispanic Black parents (aPR: 0.79, 95%CI: 0.63-0.99) were associated with decreased intentions to vaccinate. • Parents were more likely to vaccinate if their child didn't have health insurance, if the child attended daycare more than once a week, had 2 children under 12, completed college or more, had a household income of $100,000, and were living in Manhattan.

		• In the adjusted model only having children attend daycare more than once a week was associated with increased intentions (aPR 1.23, 95% CI: 1.05-1.45). • 20.2% of parents had received a vaccine, 47.1% intend to get a vaccine, 20.6% were unsure, and 9.1% said they don't intend to get vaccinated (3.0% declined to answer). • Of the parents that plan on being vaccinated or had been vaccinated, 82.4% will vaccinate their child as compared to 25.4% of unsure parents and 4.5% among parents not planning on getting vaccinated.
Teasdale (2021) *preprint* (14) Cross-sectional study USA Mar 2021	To evaluate parents (18+) intentions to vaccinate their children (aged 12 or under), an online survey of 2,074 adults across the USA was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 49.4% intend to vaccinate the youngest child in their household (median child age: 4.8 years, IQR: 4.5-5.1) when a pediatric vaccine is approved, 25.6% would not accept a vaccine for their child, and 25% were unsure. Parents were more likely to vaccinate children aged 7-12 (56.5%) compared to children aged 2-6 (48%) and <2 (37.2%). • Among parents who had received a vaccine or were intending to vaccinate, 85.2% would vaccinate their children, 4.8% would not, and 10% were unsure. Only 5.7% of parents who would not get vaccinated themselves reported planning to vaccinate their child. • Reasons for vaccine hesitancy included potential safety or effectiveness concerns (78.2%), a belief that children did not need to be vaccinated (23%), medical reasons (11.2%), and religious reasons (8.5%). • Asian parents were more likely to report intentions to vaccinate their children compared to non-Hispanic Whites (aOR 1.38, 95% CI: 1.19-1.60). • Parents less likely to intend to vaccinate their children were female (aOR 0.69, 95% CI: 0.62-0.77), were less educated (aOR 0.73, 95% CI: 0.62-0.86) and had lower incomes (aOR 0.75, 95% CI: 0.64-0.88).

Czeisler (2021) *preprint* (17) Longitudinal study USA Dec 2020 – Mar 2021	An online survey was used to assess COVID-19 vaccine intentions and vaccine hesitancy among adults (18+) for themselves and their children across the USA. The survey was answered by 5,188 adults in Dec 2020 and 5,256 adults in Mar 2021. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• In March, 66.0% would definitely or most likely obtain vaccine as soon as possible, 20% would decline, and 14% were undecided. In Dec, 63.7% were willing to vaccinate, 17.5% would decline, and 18.8% were undecided. • Intentions for children and booster vaccines were similar to personal vaccine intentions. Among 2160 of individuals living with or caring for children aged 2-18 in the Mar survey, 60.4% would vaccinate those children, 21.4% would decline, and 18.1% were undecided. • Of those who would vaccinate their children, 93.5% would also vaccinate themselves. Of those who would not vaccinate their children, 56.5% would also decline the vaccine for themselves. • Vaccine hesitancy was significantly more common among adults who were younger (aOR 3.88, 95% CI: 2.02-7.46), female (aOR 1.51, 95% CI: 1.16-1.96), Black (aOR 1.60, 95% CI: 1.10-2.33), very politically conservative (aOR 3.58, 95% CI: 2.16-5.94), less educated (aOR 3.43, 95% CI: 2.11-5.59), less frequent mask usage (aOR 3.92, 95% CI: 2.52-6.10), less adherent to social gathering avoidance (aOR 2.65, 95% 1.95-3.60), had more medical mistrust (aOR 2.11, 95% CI: 1.10-4.07), or had not received influenza vaccines in 2020 (aOR 4.11, 95% CI: 3.05-5.54).
McCabe (2021) *preprint* (166) Cross-sectional study USA Dec 2020-Feb 2021	A national app distributed survey was conducted in 34,470 healthcare workers and adults from the general population to measure intent to receive a vaccine and factors associated with acceptance and refusal. Number of healthcare workers was not reported. Question Topics:	• Parents rather than non parents were more vaccine hesitant in multivariable analysis (aOR 1.24 95% CI: 1.13-1.36).

	1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? Yes	
Milan (2021) (13) Cross-sectional study USA Dec 2020	To determine how maternal post-traumatic stress disorder (PTSD) and trauma history impact a mothers' beliefs and intentions to vaccinate themselves and their children, an online survey of 240 mothers across the USA with a history of mental illness and children between 3-18 was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• PTSD diagnosis history and total potentially traumatizing events (PTEs) were significantly positively correlated with all vaccine measures. • Mother and child vaccine intentions were highly correlated with each other ($r = 0.90$, $p < 0.001$). • Among mothers with a PTSD history, 40% were vaccine hesitant compared to 23.9% of mothers without a PTSD history, X^2 ($df = 1$, $N = 238$) = 6.45, $P < 0.01$ and for their children, 38.7% of mothers with a PTSD history were hesitant compared to 25.8% without a PTSD history, X^2 ($df = 2$, $N = 238$) = 4.08, $P < 0.05$. • The most common reasons for hesitancy included concern about side effects (31%) and a need for more information and observation (24%). • Differences in vaccine hesitancy were observed between those with and without previous PTSD diagnosis. Mothers with a PTSD history were less likely to mention believe in science and more likely to say their child has specific health concerns. • Mothers indicated that the strongest influences to increase vaccine confidence would be personally reading about trials and research and recommendations from a pediatrician.
Catma (2021) (241) Cross-sectional study USA	Parental perceptions towards a COVID-19 vaccine and willingness – to-pay (WTP) for a vaccine for themselves and their children under 18 were evaluated using an online survey across the USA.	• Parents were WTP $228-291 USD for a vaccine for themselves, and $243-321 USD for their children. • Income was positively associated with adults' WTP for a vaccine for both themselves and their children.

Nov 2020	Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? Yes	• As the number of children increased in a household, the WTP for child vaccination increased. • 72% of parents believed that vaccines were important in preventing disease.
Haeder (2021) (242) Cross-sectional study USA Oct-Nov 2020	Responses from 2,404 adults were collected from an online survey aimed to investigate attitudes toward vaccine mandates. Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Households with children were less supportive for vaccination mandates for daycare and university but not for kindergarten to grade 12. • Having children in the household was predictive of favourable attitudes towards COVID-19 mandates when the attitudes about general vaccination mandates were subtracted for daycare, kindergarten to grade 12, and university.
Marques (2021) (243) *new* Cross-sectional study USA Sep-Nov 2020	99 parents and caregivers (aged 24-63) of children were approached in person in dental treatment rooms to complete a survey regarding their intention to get their children vaccinated for COVID-19. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? Yes	• 21.6% of parents say that they would allow their child to get vaccinated for COVID-19, 39.2% were unsure, and 42.3% would not allow their child to be vaccinated. • 19.6% of parents themselves say they will get vaccinated, 38.1% were not sure, and 42.3% would not get vaccinated. • 77.6% of parents reported the age of their children did not influence their decision to get a COVID-19 vaccine when available. • Intentions to vaccinate their child increased if they knew someone who had COVID-19 (OR 0.47, 95% CI: 0.24-0.93). • 40% of parents who got their child a flu vaccine every year would allow their child to be vaccinated for COVID-19. • 52.2% of parents would be influenced by a doctor recommendation for the COVID-19 vaccine compared to 42.4% who said no one would influence their decision.

Rhodes (2021) (184) Cross-sectional study USA Jul-Aug 2020	An online survey with open ended questions was used to measure vaccine hesitancy in 1381 vaccine hesitant parents (18+) with at least one child under 4 years of age across the USA. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Parents were slightly hesitant in their intentions to vaccinate their children (mean=3.55) and themselves (mean=3.58). • Those with a higher education level were more likely to accept a vaccine for both themselves and their children. • The most common source of vaccine information for parents were healthcare workers, personal research (online and traditional resources), personal beliefs and experience, and peer experts. • Open ended responses also indicate the influence non-traditional health sources such as naturopathic doctors and alternative medicine as well as sources such as forums, bloggers, personal intuition, and the experiences of friends or family.
Davis (2020) *preprint* (188) Cross-sectional study USA Jun 2020	Factors associated with 1008 parents' likelihood to vaccinate themselves and their children against COVID-19 was investigated using an online survey. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Compared to Hispanic, non-Hispanic White and Black parents; parents who identified as Other were more likely to vaccinate. • 63% of parents reported they were likely to vaccinate their children against COVID-19 and 60% were likely to get a vaccine themselves. • Factors significantly associated with likelihood to vaccinate their children and themselves include older age, male gender, being married, and higher education and income levels.
Thunstrom (2021) (186) Randomized controlled trial USA Mar 2020	3133 adults participated in an online survey regarding their intentions to vaccinate themselves and their children for COVID-19. Participants were randomized into eight information treatment groups. Each group involved specific messaging in which the probability of infection, the	• 19.5% of participants would not vaccinate themselves. • Of the 1156 participants with children, 19.7% would not vaccinate their children.

	conditional mortality rate from COVID-19, and whether the different health authorities in the US provide consistent risk information varied. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	
RELIGIOUS AFFILIATIONS		
AUSTRALIA		
Edwards (2021) (244) & Biddle (2021) *preprint* (179) Longitudinal study Australia Aug 2020 & Jan 2021	Changes in intention to vaccinate over time and reasons for this change were assessed using two online and telephone surveys. In August 3061 adults (18+) completed the survey and 3459 adults completed a similar survey in January. Both surveys were completed by 2737 individuals. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Those who had more populist views and higher levels of religiosity were less likely to intend to get the vaccine. • Those who were more religious were less likely to intend to get vaccinated (vaccine likelihood coefficient -0.022).
Smith (2021) (182) Cross-sectional study	Intention to vaccinate and reasons for hesitancy were assessed using an online survey of 1200 adults (18+).	• In bivariate analysis, less religious individuals were more likely to intend to vaccinate compared to religious people (P> 0.004). This variable was not significant in multivariate analysis.

Australia NR 2020	Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	
UNITED KINGDOM		
de Figueiredo (2021) *preprint* (20) *new* Cross-sectional study UK Apr 2021	This national online survey of 17,611 adults (18+) used Bayesian multilevel regression to estimate the impact of vaccine passports on intention to get a COVID-19 vaccine among respondents who have not yet had two vaccination doses. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• In multilevel regression controlling for baseline vaccine intention, the likelihood of getting a vaccine if vaccine passports were introduced for domestic travel was significantly increased with those reporting Christian faith (aOR 1.23, 95% CI: 1.08-1.41) compared to atheists or agnostics. • If vaccine passports were introduced for international travel, Christian faith was significantly associated with an increased intention to vaccinate (aOR 1.22 95% CI: 1.07-1.39) compared to atheists or agnostics.
Rahman (2021) *preprint* (245) Cross-sectional study UK Jan 2021	This online survey sought to improve vaccine promotion activities by gathering information regarding knowledge, attitudes, and practices regarding COVID-19 from 151 mosque attendees at two mosques. Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? Yes	• Attitudinal scores towards the vaccine were moderately positive at each mosque (62% and 69%). • Open ended questions regarding improvements to engagement and experiences with the vaccine rollout broadly encompass desires for increasing accessibility of information and vaccine sites, and hearing directly from community members. • Top sources for vaccine information included National Health Service or government websites followed by GPs.

	Survey pre-tested? No	
de Figueiredo (2020) *preprint* (178) Cross-sectional study UK Sep-Oct 2020	Using Bayesian statistical methods and an online national survey of 17,684 adults (18+), vaccine uptake was estimated and barriers to uptake were identified. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• Those who reported Hinduism or Judaism as their religion were more likely than atheists or agnostics to accept a vaccine (OR 1.66, 95% HPDI: 1.11-2.43) and those who reported their religion as Muslim (OR 0.75, 95% HPDI: 0.57-0.96) or other (OR 0.72, 95% HPDI: 0.62-0.82) were less likely to intend to vaccinate.
Chadwick (2021) (246) Cross-sectional study UK Sep-Oct 2020	This online survey of 5114 adults explored the relationship between media intake, socio-demographics, social and political attitudes, and likelihood of promoting or discouraging vaccination on social media. Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Religiosity was associated with encouraging vaccination ($\beta = -0.032$, $p < .001$).
Garry (2020) (176) Cross-sectional study UK Jul 2020	Using an online survey of 2057 adults, intention to vaccinate was evaluated. The respondents were allocated into groups with different response options (positive skew – more positive options, negative skew – more negative options, and balanced – equal positive and negative options) to study the	• Respondents that were younger, had a lower income, lived in an urban area, and were religious were less likely to vaccinate.

	impact of vaccine conspiracy theories. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	
Murphy (2021) (174) Cross-sectional study Ireland & UK Mar 2020	Using an online survey of 1041 adults (18+) in Ireland and 2025 in the UK, willingness to vaccinate against COVID-19 and reasons for vaccine hesitancy were investigated. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• In Ireland, the vaccine hesitant and resistant group were more likely to have higher levels of conspiratorial (d = 0.21) and religious (d = 0.20) beliefs.
USA		
Viskupic (2021) *preprint* (21) *new* Quasi-experimental study USA	709 unvaccinated registered voters in South Dakota were sent identical messages encouraging vaccination either from a religious, political, or medical leader to assess the impact the messenger has on interest in vaccination. A control group was provided a message unrelated to COVID-19. Question Topics:	• Mean interest in vaccination was 1.86 (95% CI: 1.61 – 2.11) in the control group. • A religious messenger generated a mean interest in vaccination of 2.32 (95% CI: 1.94-2.71, P<0.05) which was the only messenger that had a statistical difference in interest. • All messengers had statistically significant effects in respondents identifying as evangelical Christians with the strongest effect seen with a religious messenger.

Apr 2021	1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• A religious messenger also had a statistical effect among respondents younger than 65.
King (2021) *preprint* (181) Longitudinal study USA Jan-Mar 2021	As part of a monthly ongoing national COVID-19 survey, questions to measure vaccine acceptance and related factors of acceptance were collected in samples of adults (age 18-64). The number of HCWs was not reported. Jan survey: n= 791,716 Feb survey: n= 710,529 Mar survey: n= 732,308 Question Topics: 1) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• In a subset of individuals from this survey (n=143,297) by occupation categories with the highest percentage hesitant, 6.7% of individuals reported religion as a reason for vaccine hesitancy. This included construction, installation, farming/forestry/fishing, and transportation occupations.
Carmody (2021) (183) Cross-sectional study USA Dec 2020 – Jan 2021	A paper survey was used to assess vaccine attitudes and intentions in 102 Haredi-Orthodox Jewish adults (18+) in New York. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes 3) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes	• 12% of respondents would accept a vaccine for themselves and their family, 47% were strongly hesitant, and 41% were undecided. • 70% agreed that routine vaccinations were essential. • Apprehension about new vaccine technology was the most common concern about the vaccine. • There was a lack of confidence in government and health officials and only 17% agreed that mandates from the local health department would make them accept a vaccine. • Independent predictors of strong vaccine hesitancy were: 1) the belief that natural infection

	Survey pre-tested? No	was better than vaccine for developing immunity (aOR 4.28, 95% CI: 1.23–14.86, P=0.022), agreement that prior SARS-CoV-2 infection with antibodies precludes need to mask or practice social distancing (aOR 4.1, 95% CI: 1.22–13.77, P=0.022), and loss of trust in physicians resulting from the pandemic (aOR 5.01, 95% CI: 1.05–23.96, P=0.044).
Clark (2020) *preprint* (171) Cross-sectional study USA Nov-Dec 2020	An online survey of 655 adults from Oregon assessed intention to vaccinate intentions and reasons for hesitancy with an emphasis on comparing rural and urban residents. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Those reporting personal or religious concerns and those who believe COVID-19 is not serious are 9.5 and 10 times more likely to refuse a vaccine, respectively.
Graupensperger (2021) (180) Cross-sectional study USA Nov 2020	The vaccine intentions and attitudes of 647 students from a large public university in the northwest USA were evaluated using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 91.6% of students reported an intention to receive a COVID-19 vaccine. • 2.78% of students felt that a COVID-19 vaccine was incongruent with their religious beliefs.

Parente (2021) (126) *new* Cross-sectional study USA Aug 2020	Associations with vaccine acceptance were assessed online for a hypothetical vaccine with considerations for delay periods (1 to more than 12 months after approval) in 3,347 HCWs in Kentucky. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• 7.4% of respondents noted personal religious or ethical reasons as a reasons for wanting to delay or refuse vaccination.
Olagoke (2020) (177) Cross-sectional study USA Mar 2020	The relationship between religiosity and intention to vaccinate was examined using an online survey of 501 adults (18+). Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• There was a significantly negative association between intention to vaccinate and religiosity (β = − 0.15, 95% CI: − 0.23 to − 0.08, P < 0.0001) and external health locus of control (beliefs based on past experiences and having external control over them) (β = − 0.24, 95% CI: − 0.33 to − 0.15, P < 0.0001). • External health locus of control mediated 40.97% of the relationship between religiosity and intention to vaccinate as an indirect effect of β = − 0.06, 95% CI: − 0.11 to − 0.02, P = 0.006.
RURAL VS URBAN COMMUNITIES		
CANADA		
Leger (2021) *unpublished* (9, 69-71, 73, 205, 206)	An online survey of Canadian and American adults (18+) was conducted to evaluate vaccine perceptions and intentions to vaccinate. See USA section for USA.	**Wave 12** • 16% of those residing in rural areas do not intend to vaccine compared to 11% of rural and 9% of suburban residents. **Wave 11**

Longitudinal study Canada & USA Nov 2020 & Jan-June 2021	Wave 1: Nov 2020, 1516 Canadians and 1002 Americans Wave 2: Jan 2021, 1516 Canadians and 1003 Americans Wave 3: Feb 2021, 1535 Canadians and 1002 Americans Wave 4: Feb 2021, 1,532 Canadians and 1002 Americans Wave 5: Apr 2021, 1,504 Canadians and 1,002 Americans Wave 7: May 2021, 1,529 Canadians, 1,003 Americans Wave 8: May 2021, 1,529 Canadians, 1,003 Americans Wave 9: May 2021, 1,624 Canadians and 1,002 Americans Wave 10: May 2021, 1,624 Canadians and 1,002 Americans Wave 11: June 2021, 1,539 Canadians, 1,004 Americans Wave 12: June 2021, 1,542 Canadians and 1,001 Americans *new* Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 22% of rural residents do not intend to vaccinate compared to 11% of urban and 15% of suburban residents. • 26% of rural residents were not comfortable with a different vaccine as a second dose compared to 24% of urban and 20% of suburban residents. **Wave 9** • Combined levels of vaccination and intention to receive a vaccine increased from 73% to 85% in those who lived in rural communities in the latest polling. **Wave 7** • Those who lived in suburban (85%) or urban (84%) communities were more likely to intend to vaccinate compared to those who lived in rural areas (73%). **Wave 5** • Rural participants (74%) were slightly less likely to accept a vaccine compared to urban (82%) and suburban participants (81%).
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021) *unpublished* (86, 88, 91, 95)	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in Quebec. Number of participants was not clearly stated (~3300 each collection period). There were	• Intention to vaccinate generally increased as communities increased in size, from living in small villages less than 10,000 (71%), towns 10,000 to 100k (73%), greater Montreal area (81%) and Montreal (79%).

Longitudinal study Canada Apr 2020 – Apr 2021	multiple collection periods, one in Apr-May 2020, Sep and Dec 2020, and Apr 2021. Articles in French. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	
Lang (2021) (87) Cross-sectional study Canada Aug 2020	An online survey of 60 adults (18+) in Alberta was conducted to assess their intention to vaccinate. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• Intention to vaccinate was lower in other urban centers (29%) and rural Alberta (50%) compared to Calgary (75%) and Edmonton (80%), (P= 0.030).
UNITED KINGDOM		
Sethi (2021) (247) Cross-sectional study UK Sep-Oct 2020	To understand the factors in participation and perception of COVID-19 vaccination trials, 4884 adults were surveyed online. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? Yes	• 41.4% of respondents were interested in participating in vaccine trials, 27.6% were not interested, and 31.1% were unsure. • The largest percent of respondents that were not interested in participating were in villages (pop. >7500) whereas small towns (pop. 7500-24,999) were the most unsure about participating. • The odds of not participating is 0.66 times that of respondents from villages and 0.54 times for small towns. • 88% of small towns and 91% in villages aged 50-59 were not interested in participating in trials.

Garry (2020) (176) Cross-sectional study UK Jul 2020	Using an online survey of 2057 adults, intention to vaccinate was evaluated. The respondents were allocated into groups with different response options (positive skew – more positive options, negative skew – more negative options, and balanced – equal positive and negative options) to study the impact of vaccine conspiracy theories. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• Respondents that were younger, had a lower income, lived in an urban area, and were religious were less likely to vaccinate.
Murphy (2021) (174) Cross-sectional study Ireland & UK Mar 2020	Using an online survey of 1041 adults (18+) in Ireland and 2025 in the UK, willingness to vaccinate against COVID-19 and reasons for vaccine hesitancy were investigated. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Those who were vaccine hesitant were more likely to be residing in a suburb (aOR = 2.13, 95% CI: 1.01-4.49).
USA		
McCabe (2021) *preprint* (166)	A national app distributed survey was conducted in 34,470 healthcare workers and adults from the	• Respondents in less populated areas (population density 0-149) are more hesitant than those from

Cross-sectional study USA Dec 2020-Feb 2021	general population to measure intent to receive a vaccine and factors associated with acceptance and refusal. Number of healthcare workers was not reported. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? Yes	populated areas (population density over 1000) (aOR 1.31, 95% CI: 1.16-1.48).
Roess (2021) *preprint* (175) Cross-sectional study USA Dec 2020 – Jan 2021	An online survey was used to assess vaccine intentions in 1,181 parents and guardians aged 18–64 who currently have a child <18 years old at home across the USA. This study did not assess intention to vaccinate their children. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Intention to vaccinate was higher in those who lived in urban (aOR 2.04, 95%CI: 1.24–3.09) and semiurban settings (aOR 1.45, 95% CI: 0.97–2.17) compared to those in rural settings.
Enwezor (2021) *preprint* (115) Cross-sectional study USA	Intention to vaccinate was assessed in 20,232 adults (15,062 non-HCWs and 5,170 HCWs) using an online survey. 476 of participants had a previous COVID-19 diagnosis. Question Topics: 1) Vaccine intentions	• Suburban (68%) and rural (71.2%) residents were less likely than urban (81%) residents to intend to vaccinate (aRR 0.85, 95% CI: 0.83-0.88, P<0.0001).

Dec 2020 – Jan 2021	Survey tools available? No Formative research conducted? No Survey pre-tested? No	
Clark (2020) *preprint* (171) Cross-sectional study USA Nov-Dec 2020	An online survey of 655 adults from Oregon assessed intention to vaccinate intentions and reasons for hesitancy with an emphasis on comparing rural and urban residents. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Intention to vaccinate was higher in urban residents compared to rural (47% vs 41%). • Those reporting personal or religious concerns and those who believe COVID-19 is not serious are 9.5 and 10 times more likely to refuse a vaccine, respectively.
Kuter (2021) (109) Cross-sectional study USA Nov-Dec 2020	To evaluate intentions to vaccinate, an online survey was conducted at two large, academic hospitals in Philadelphia in 12,034 hospital employees. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• Those residing in urban areas were significantly more likely to intend to vaccinate compared to suburban (OR 0.71, 95% CI: 0.65-0.79) and rural (OR 0.41, 95% CI: 0.30-0.54) residents.
Haeder (2021) (242) Cross-sectional study	Responses from 2,404 adults were collected from an online survey aimed to investigate attitudes toward vaccine mandates.	• Rural residents have lower support for mandatory vaccinations for students in daycare (b = −0.418), those in kindergarten to grade 12 (b = −0.652), and for kindergarten to grade 12 teachers (b= −0.360).

USA Oct-Nov 2020	Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Rural residents were less favourable towards COVID-19 mandates when the attitudes about general vaccination mandates were subtracted for kindergarten to grade 12.
Mora (2020) *preprint* (173) Cross-sectional study USA Jul-Nov 2020	Telephone interviews of 1115 adult farm workers in California were conducted to determine intention to vaccinate and reasons for hesitancy. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Living in more rural areas such as Greenfield was significantly associated intention not to vaccinate (RR 1.19, 95% CI: 1.02-1.39).
Khubchandani (2021) (172) Cross-sectional study USA Jun 2020	Intention to vaccinate and vaccine hesitancy was assessed in 1878 adults (18+) using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• In unadjusted analyses, vaccine hesitancy was higher rural dwellers (29%) compared to their counterparts.
YOUTH		
Afifi (2021) (213) *new*	Using survey respondents from the longitudinal Well-Being and Experiences study (2017-2020) vaccine intentions were recorded	• 65.4% of respondents intend to receive a vaccine, 26.1% were not sure, and 8.5% were not willing. • Parents with trade school, community college or less, with incomes of less than $49,999,

Cross-sectional study Canada Nov-Dec 2020	for Winnipeg adolescents aged 16-21 and their caregivers/parents using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	experienced quite a bit COVID-19 financial strain, self-reported low knowledge of COVID-19 were associated with lower intentions to get a vaccine. • Having a self-reported health condition was associated with higher intentions to accept a vaccine. • After adjusting for sex, age and household income, children who had no experience with spanking (aRR 0.33, 95% CI: 0.17–0.62), no peer victimization (aRR 0.49, 95% CI: 0.25–0.96), no household substance abuse (aRR 0.41, 95% CI: 0.20–0.83), no contact with foster care/child protective office (aRR 0.34, 95% CI: 0.16–0.72), and no risk of their household running out of money (aRR 0.45 95% CI: 0.21–0.97) were more willing to get vaccinated. • Reporting no to any household challenge adverse childhood experience (ACE) was associated with willingness to vaccinate (aRR 0.45, 95% CI: 0.20–0.99). • The top concerns for being unwilling to accept a vaccine were for vaccine safety (64.5%), not knowing enough about the vaccine (60.6%), and not thinking the vaccine would be effective (23.4%).
Brandt (2021) (190) Cross-sectional study USA Oct 2020	A text message poll of 911 youth aged 14 to 24 years across the United States was conducted to evaluate barriers and facilitators for COVID-19 vaccination. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 42.7% and 33.3% reported unconditional willingness or conditional willingness to vaccinate, respectively, of which 80.7% reported willingness of vaccination if proven safe and recommended. • The most common reasons to vaccinate were protecting self (38.4%), protecting others (24.9%), vaccine importance (14.3%), and return to normalcy (11.7%). • Side effects (36.2%), efficacy (20.1%), rushed approval (18.8%), and safety (16.2%) were the most common concerns about the vaccine. • Compared to White youth, Black youth (OR = 3.31) were more likely to refuse vaccination and Asian youth (OR = 0.46) were less likely to refuse vaccination ($P < 0.001$).

		• CDC or WHO (42.3%) were the preferred sources of vaccine information, followed by healthcare providers and facilities (31.75%), the internet (17.8%), health officials (8.4%), news media (7.8%), and social media (2.5%).
IMMIGRANTS		
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021) *unpublished* (86, 88, 90, 91, 95) Longitudinal study Canada Apr 2020 – May 2021	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in Quebec. Number of participants was not clearly stated (~3300 each collection period). There were multiple collection periods, one in Apr-May 2020, Sep and Dec 2020, Apr and May 2021. Articles in French. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Immigrants were more hesitant and more unsure about receiving a vaccine compared to non-immigrants.
Australia Bureau of Statistics (2021) *unpublished* (141) *new* Longitudinal study Australia	The household impacts survey is a monthly survey which collects data online and by telephone from a panel of adults (18+) on COVID-19 related topics including attitudes towards vaccines. May: n=3,371 Question Topics: 1) Vaccine intentions	• Those born overseas were more likely to report intention to vaccinate compared to those born in Australia (70.7% vs 67.2%). This was more apparent for those who arrived within the last ten years (74.6%) compared to those arriving more than 10 years ago (69.1%). • The top factor in deciding to get the vaccine was a recommendation from their general practitioner (25.8%). • 68.1% of immigrants were concerned about possible side effects.

Apr 2020-May 2021	Survey tools available? No Formative research conducted? No Survey pre-tested? No	
Deal (2021) (248) Cross-sectional study UK Sep 2020 – Mar 2021	In depth telephone interviews were conducted with 32 recent immigrants (less than 10 years) with a precarious immigration status to define barriers and vaccine perceptions as well as generate strategies to increase uptake. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? Yes	• 28% report they definitely will get a vaccine, 31% were unsure leaning to yes, 22% were unsure, 19% were unsure leaning towards no, and 6% would definitely not vaccinate. Of the two participants who definitely would decline one indicated it was due to a lack of clinical trials and the other because of religious reasons. • Intention varied greatly between those interviewed earlier (lower intentions to accept a vaccine) and those interviewed later (higher intentions to vaccinate). • Among those who were hesitant, worries included potential side-effects and insufficient testing of the vaccine. • Three common barriers to vaccination were identified: issues of access (such as language, trust, and perceived lack of entitlement), lack of trust (poor treatment by the NHS, being charged for care, or possible immigration checks), and feeling abandoned during the pandemic causing mental and physical strain. • Undocumented migrants were particularly concerned that they were not registered at a GP office and would miss vaccine roll out. Migrants indicate that charities and walk in clinics were frequently used. • Additional challenges noted were that migrants were unaware of announcements that vaccination would not entail immigration checks. • To increase uptake migrants report increasing the ease of vaccination by rolling out the vaccine at walk in clinics and charities, providing information on side effects in their own language, clearly indicating where and how vaccines would be made

		available, and emphasizing that the vaccine would provided at no cost.
Statistics Canada (2020) & Statistics Canada (2021) *unpublished* (65, 80) Longitudinal study Canada Sep-Dec 2020	An online survey conducted by Statistics Canada as part of the Canadian Community Health Survey (CCHS) assessed Canadians behaviors to safeguard their own health as well as the health of others. In the September survey, a question about vaccine intentions was added. The most recent report captures 20,000 responses from individuals aged 12+. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Immigrants were slightly less likely to vaccinate (74.6%) but this varied greatly between older and younger immigrants (73.2% for 12-64 and 81.1% for those 65+).
Knights (2021) (192) Qualitative study UK Jun-Nov 2020	In depth semi-structured telephone interviews were conducted with 17 migrants of less than 10 years, 48 healthcare professionals, and 16 administrative staff were conducted through three phases of sampling (purposive, convenience, and snowball) to gain insights into vaccine access. Question Topics: 1) Vaccine perceptions 2) Vaccine hesitancy	• Increased digitalization of appointments and health information was felt differently by primary care professionals (PCPs) and migrants with issues of access to technology. PCPs reported that digitalization increased exclusion of marginalized groups while bringing in younger fitter patients. Conversely digitalization was also reported as an opportunity to communicate with translated targeted messages. • Migrants reported that language barriers have been increased due to lower access to friends who would translate where GPs were concerned about privacy during virtual consultations. • Migrants and PCPs felt that there was a lack of specific information for migrants regarding public health messages and the vaccine. This tied into issues of low health literacy, lack of understanding of changes in policy, mistrust in government or

		science, and gave space for misinformation and seeking information from social media about COVID-19 and vaccine. • The above issues and vaccines beliefs such as COVID-19 being a 'Western disease', fearing being a guinea pig, and reliance on home remedies also pose challenges to uptake. • Both migrants and PCPs noted that building trust between clinical practices and individuals was important which was a challenge during the pandemic. Migrants noted the tendency to seek religious or peer input into decision-making. • Migrants note the 'one size fits all' approach during the pandemic has been inflexible for dealing issues for the community around digitalization and where communication is failing.
Allen (2021) *preprint* (249) *new* Cross-sectional study USA Jul-Aug 2020	Vaccine intentions were measured In 364 Brazilian immigrants living in the USA through an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 70.9% of respondents reported that they would get a COVID-19 vaccine, 18.1% were unsure, and 11% would not get vaccinated. • Open text responses of those not planning to get the vaccine found that there was concern that the vaccine has not been tested (30.9%), may have side effects (17.6%), or would not be effective (8.8%). Other concerns were related to lack of trust with the industries in involved in its development (10.3%), the government (8.8%), and vaccines in general (8.8%). • 3.8% of those that have spent less than 4 years in the USA did not intend to vaccinate compared to 27.3% those born in the USA. More time in the country was generally associated with lower intentions and more unsure respondents. • Perception of COVID-19 pandemic also significantly impacted intention with 75.9% of those seeing it as of major significance wanting a vaccine compared to 52.6% who viewed it as a minor issue. • Those who trusted healthcare providers (73.9%) and public health agencies (76.8%) had higher

		intentions than those relying on social networks (63.6%), private networks (62.2%), or were missing trusted source response (61.9%).
PAST SARS-COV-2 INFECTION		
Enwezor (2021) *preprint* (115) Cross-sectional study USA Dec 2020 – Jan 2021	Intention to vaccinate was assessed in 20,232 adults (15,062 non-HCWs and 5,170 HCWs) using an online survey. 476 of participants had a previous COVID-19 diagnosis. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Those with no previous COVID-19 diagnosis were more likely to intend to vaccinate compared to those that had a previous COVID-19 diagnosis, (76.6% vs 60.9%, aRR 1.20, 95% CI: 1.11-1.28, P<0.0001).
Olanipekun (2021) (193) Cross-sectional study USA Apr-May 2020	119 African Americans were surveyed after COVID-19 infection recovery and discharge to assess acceptance of a safe and effective vaccine. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 54% did not intend to get vaccinated, 30% would get vaccinated, and 16% were unsure. • The top reason among those who do not intend to get vaccinated was a high level of distrust for both vaccine effectiveness and pharmaceutical industries (78.1%). Other top reasons included not trusting that the vaccine will be effective (68.8%) and fear of side effects (64.1%).

Preuves émergentes sur la COVID-19

Revue rapide et évolutive sur les attitudes à l'égard des vaccins et de l'adoption des vaccins contre la COVID-19 – Mise à jour 8

Introduction

Quelles sont les données mondiales sur les attitudes à l'égard des vaccins et l'adoption des vaccins contre la COVID-19 chez les Canadiens, ainsi que dans certaines populations?

Cette revue rapide et évolutive vise à cerner et à résumer la documentation sur l'adoption du vaccin contre la COVID-19 et les attitudes à l'égard de ce vaccin pour mieux comprendre les facteurs associés à l'adoption de ce vaccin au Canada. Elle met l'accent sur les données probantes canadiennes sur l'adoption et les attitudes, ainsi que sur les données probantes des pays partenaires du Groupe des cinq disponibles jusqu'au 1er juillet 2021. Des données probantes sur différentes populations prioritaires prédéfinies en Australie, en Nouvelle-Zélande, aux États-Unis et au Royaume-Uni ont été incluses pour compléter les domaines dans lesquels il y avait peu de recherche au Canada. Les populations prioritaires comprennent les travailleurs de la santé, les LGBTQ+, les groupes confessionnels, les nouveaux arrivants, les parents, les femmes enceintes ou qui allaitent, les personnes qui vivent dans les collectivités rurales, les adultes plus âgés, les personnes qui ont des comorbidités et celles qui se heurtent à de multiples obstacles en matière de santé. (p. ex., itinérance, troubles de santé mentale ou de toxicomanie).). Il est possible d'obtenir les versions antérieures de cette étude (mises à jour 1 à 7) qui présentent les données probantes disponibles jusqu'au 1er juin 2021 sur les connaissances, les attitudes et les comportements en matière de vaccination et de les demander en envoyant un courriel à cet effet à l'adresse phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca. Les sections Quoi de neuf et Points clés ci-dessous mettent l'accent sur les résultats importants des études les plus récentes (au cours des cinq derniers mois).

Quoi de neuf

- Cette mise à jour a cerné 40 nouvelles études ou mises à jour d'études sur l'adoption du vaccin contre la COVID-19 et les attitudes à l'égard de celui-ci, dont six spécifiques au Canada. Les nouvelles études portent la mention *nouvelle* dans chacun des tableaux et tous les tableaux ont été déplacés dans les annexes pour aider les lecteurs à naviguer dans le document.

Adoption du vaccin

- Les tendances en matière d'adoption et de refus des vaccins continuent de refléter les tendances en matière d'intention vaccinale. Dans toutes les populations, la prise en charge du vaccin était positivement associée à l'augmentation de l'âge, au sexe masculin et aux antécédents de vaccination

contre la grippe. Les personnes ayant déjà été infectées par le SRAS-CoV-2 étaient moins susceptibles de se faire vacciner, alors que les Noirs et les groupes ethniques minoritaires affichaient les taux d'adoption de la vaccination les plus élevés.

- Jusqu'à présent, une étude sur l'adoption du vaccin chez les travailleurs de la santé canadiens a été réalisée en décembre 2020. À Montréal, 80,9 % des travailleurs de la santé à qui on a proposé un vaccin l'ont accepté et 19,1 % l'ont refusé. Du nombre de personnes qui ont refusé un vaccin, 74,1 % ont déclaré qu'elles accepteraient de se faire vacciner à l'avenir, 53,2 % voulant attendre quelques mois et 31,9 % voulant attendre un an (1). Les raisons les plus courantes du refus étaient la nouveauté du vaccin, la préférence pour que les autres se fassent vacciner en premier, le manque d'information à propos du vaccin et le manque de temps pour prendre une décision (1).
- Dans un groupe de 266 transplantés hépatiques en Italie, 96,6 % ont accepté de se faire vacciner lorsqu'il leur a été proposé. Bien qu'ils aient reçu des renseignements adéquats, cinq patients (1,8 %) ont refusé de se faire vacciner en raison d'inquiétudes quant au risque d'effets indésirables graves. Les obstacles en place pour les quatre patients restants (1,6 %) ont pu être éliminés soit en fournissant des détails supplémentaires concernant la vaccination, soit après avoir réglé des problèmes médicaux et logistiques (4).
- Dans un groupe de 85 patients psychiatriques hospitalisés au Royaume-Uni qui avaient la capacité de décider s'ils voulaient recevoir le vaccin contre la COVID-19, 80 % ont accepté et 20 % ont refusé. Les patients britanniques blancs étaient moins susceptibles de refuser que les patients noirs, asiatiques ou issus de minorités ethniques (16,9 % contre 30 %). Les raisons de leur refus comprenaient des inquiétudes quant à l'innocuité et aux effets secondaires du vaccin, la conviction que le risque pour leur santé personnelle de contracter la COVID-19 est faible, une méfiance plus générale envers les services de santé et des inquiétudes quant aux tests sur les animaux (5).

Stratégies d'intervention pour l'adoption des vaccins

- La mise en œuvre de deux rappels par message texte (portant soit sur les avantages personnels, soit sur les avantages sociaux de la vaccination) a permis d'augmenter les taux d'adoption du vaccin en Israël. L'effet global sur huit jours après l'intervention a révélé que le rappel des avantages personnels a entraîné une hausse relative de 9 % par rapport au rappel des avantages sociaux (23,8 % contre 21,7 %, P<0,0001) (2).
- L'Israël a mis en place une politique selon laquelle l'entrée dans certains lieux publics nécessitait la présentation d'un « laissez-passer vert » qui pouvait être obtenu soit en recevant un vaccin, soit par un résultat négatif à un test de dépistage de la COVID-19 récent. La mise en œuvre de cette politique en février a été associée à une hausse relative de 22,2 % de l'adoption du vaccin après trois jours (2).
- En février, un site de vaccination communautaire (Unidos en Salud UeS) a été déployé pour surmonter les obstacles à la vaccination contre la COVID-19 auxquels font face les LatinsX à San Francisco. De ce nombre, 56,1 % ont déclaré s'être fait vacciner plus tôt grâce au site et 65,3 % ont contacté trois personnes ou plus pour leur recommander le vaccin après leur expérience positive (3).

Respect des mesures de santé publique après la vaccination

- À l'aide d'un système de positionnement global (GPS) au Royaume-Uni, l'augmentation médiane quotidienne de la distance de déplacement moyenne à partir de l'adresse enregistrée d'un participant était de 45,0 m (IC à 95 % : de 25 à 65 m, P = <0,001) entre la date de vaccination et 99 jours après la vaccination (6).
- Au début de la campagne de vaccination (janvier) en Israël, les personnes infectées par la COVID-19 faisaient moins attention à la distanciation sociale (29,7 %) et au port du masque (18,8 %) par rapport à celles qui avaient reçu la première dose de vaccin (12,8 % et 8,2 %), ou à celles qui n'étaient ni vaccinées ni infectées (19,2 % et 11,6 %) (7).

Canada

- Deux enquêtes effectuées en juin montrent que 84 à 88 % des Canadiens ont reçu un vaccin ou souhaitent se faire vacciner dès que possible, ce qui représente une augmentation par rapport aux résultats d'avril et de mai (8, 9).
- En juin, 89 % des Canadiens ayant reçu une dose ont déclaré avoir l'intention de recevoir une deuxième dose, 9 % ont déjà reçu leur deuxième dose, 1 % ne le feront probablement pas et 1 % étaient incertains (10).
- Dans un groupe de 70 parents ou tuteurs d'enfants âgés de 12 à 17 ans du Manitoba, 15 % et 13 % étaient incertains de se faire vacciner ou ne feraient pas vacciner leurs enfants, respectivement (11). Les personnes qui sont réticentes à faire vacciner leurs enfants faisaient partie de ménages dont le revenu était inférieur à 40 000 dollars par an, ne se feraient pas vacciner elles-mêmes et ne pensaient pas que les adultes devaient recevoir tous les vaccins habituels (11).
- 48 % des Canadiens étaient mal à l'aise à l'idée de recevoir une marque différente de vaccin pour leur deuxième dose, tandis que 46 % étaient à l'aise et 6 % étaient incertains. Parmi ceux qui ont reçu AstraZeneca comme première dose, 50 % ont préféré recevoir AstraZeneca comme deuxième dose, 32 % ont préféré une autre marque comme deuxième dose, et 18 % étaient incertains (10).
- Les incitatifs financiers (argent, bons, articles gratuits, tirages de prix, rabais) n'ont pas été signalés comme augmentant la probabilité d'accepter de se faire vacciner dans une étude menée au Manitoba (entre 7 et 84 % des répondants ont déclaré que l'incitatif ne les rendrait pas plus susceptibles de se faire vacciner). Cependant, 70 % d'entre eux seraient inquiets si seules les personnes réticentes à se faire vacciner recevaient des incitatifs importants (de 50 à100 $) (11).
- Les passeports vaccinaux bénéficient d'un soutien important au Québec, 72 % des résidents y étant favorables (12).

Parents

- Il continue d'exister une forte corrélation entre l'intention des parents de se faire vacciner et l'intention de faire vacciner leurs enfants (13 à 16). Parmi un groupe de parents ou de soignants américains interrogés en avril, 61,9 % avaient l'intention de faire vacciner leur plus jeune enfant (âge moyen : 4,7 ans), 23,3 % étaient incertains de leur choix et 14,8 % ne savaient pas et 14,8 % n'en avaient pas l'intention. Le fait que l'enfant fréquente la garderie plus d'une fois par semaine était associé à une augmentation des intentions (aPR 1,23, IC à 95 % : de 1,05 à 1,45) (16).

- Tout comme dans la population en général, les parents qui sont dans des ménages à faible revenu, qui sont plus jeunes et moins instruits, qui ont déjà refusé d'autres vaccins, qui sont des femmes ou des membres de minorités ethniques, sont ceux qui étaient plus susceptibles de refuser un vaccin pour leurs enfants (14, 16-19).

Autres populations d'intérêt

- Dans une étude britannique, les personnes déclarant être de confession chrétienne étaient significativement plus susceptibles de se faire vacciner si des passeports vaccinaux étaient instaurés pour les voyages intérieurs (RCa 1,23, IC à 95 % : de 1,08 à 1,41) et internationaux (RCa 1,22 IC à 95 % : de 1,07 à 1,39) par rapport aux athées et aux agnostiques (20).
- Une étude quasi expérimentale menée auprès de 709 électeurs inscrits non vaccinés dans le Dakota du Sud, aux États-Unis, a montré que les messages émanant d'un chef religieux avaient un effet positif statistiquement significatif sur l'intention de se faire vacciner, alors que les messages émanant d'un chef politique ou médical n'avaient aucun effet (21).

Principaux points

- L'adoption du vaccin contre la COVID-19 et les différentes attitudes à l'égard de ce vaccin ont été évaluées dans la population canadienne en général, ainsi qu'auprès des travailleurs de la santé, des populations à risque élevé et d'autres populations d'intérêt au Canada, en Australie, en Nouvelle-Zélande, aux États-Unis et au Royaume-Uni et les résultats obtenus ont été publiés dans 205 études actuellement disponibles (tableaux 1 à 7). La majorité d'entre elles ont mis l'accent sur l'intention de se faire vacciner. Depuis que le déploiement du vaccin a commencé en décembre 2020, 29 études ont évalué l'adoption du vaccin alors que sept ont examiné le respect continu des mesures de santé publique après la vaccination.

Adoption des vaccins

- L'adoption du vaccin et les facteurs associés à cette adoption chez les travailleurs de la santé ont été évalués dans le cadre de 14 études effectuées aux États-Unis, au Royaume-Uni, au Canada et en Israël, ainsi que dans deux études portant sur des adultes de plus de 70 ans menées au Royaume-Uni et en Pologne (tableau 1). La proportion de travailleurs de la santé qui ont accepté et reçu une dose du vaccin variait entre 52 et 94 % entre les études. Les médecins étaient plus susceptibles de se faire vacciner que les infirmières et les travailleurs de la santé œuvrant dans des milieux non cliniques.
- L'adoption du vaccin et les facteurs associés à l'adoption ont été étudiés dans la population générale du Royaume-Uni, des États-Unis, d'Israël et de la Nouvelle-Zélande (n=6 études) et dans plusieurs populations spécifiques : une étude sur les personnes sans domicile fixe aux États-Unis, une étude sur les adultes handicapés au Royaume-Uni, une étude sur les survivants d'un accident vasculaire cérébral (AVC) ou d'un accident ischémique transitoire (AIT) au Royaume-Uni, une étude sur les personnes âgées et les populations à haut risque aux États-Unis, une étude sur les patients dialysés aux États-Unis, une étude sur les transplantés hépatiques en Italie, une étude sur les patients atteints du syndrome du côlon irritable en Italie, une étude sur la population d'un hôpital psychiatrique au

Royaume-Uni, deux études sur les prisons aux États-Unis et deux études sur les unités militaires en Israël (tableau 1).

- Dans toutes les populations, l'adoption du vaccin a été associée positivement à un âge plus avancé et au sexe masculin. Les personnes ayant déjà été infectées par le SRAS-CoV-2 étaient moins susceptibles de se faire vacciner, alors que les Noirs, les Asiatiques et les groupes ethniques minoritaires affichaient les taux d'adoption du vaccin les plus élevés.

L'intention en ce qui concerne la vaccination au Canada

- Quarante-neuf études sur l'intention en ce qui concerne la vaccination ont été réalisées au Canada, soit quatre qui ont porté sur les travailleurs de la santé, 36 sur le grand public, trois sur les travailleurs de la santé et le grand public, deux sur des parents, une sur les personnes atteintes d'obésité, une sur les jeunes (âgés de 16 à 21 ans) et deux sur l'opinion d'experts sur les personnes qui devraient d'abord se faire vacciner. Les études les plus récentes effectuées de mars à mai, démontrent que l'intention de se faire vacciner augmente et qu'à l'heure actuelle, elle varie entre 66 et 86 % dans le grand public et entre 57 et 82 % parmi les travailleurs de la santé dans l'ensemble du Canada. Les provinces de l'Atlantique, la Colombie-Britannique et le Québec sont les provinces dans lesquelles on voit le taux le plus élevé quant à l'intention de se faire vacciner.

Facilitateurs de l'intention de se faire vacciner et obstacles à cette intention

- Les facteurs les plus souvent associés positivement à l'intention de se faire vacciner au Canada et dans le monde étaient le sexe masculin, le fait d'être plus âgé, avoir fait des études supérieures, posséder des connaissances ou des connaissances adéquates en matière de santé, faire confiance aux experts et au gouvernement, avoir déjà reçu un vaccin contre la grippe, avoir un statut socioéconomique plus élevé et être plus préoccupé par la COVID-19.
- Comparativement aux infirmières et aux autres travailleurs de la santé, les médecins étaient beaucoup plus susceptibles d'accepter un vaccin contre la COVID-19.
- Trois études ont démontré que la communauté LGBTQ2+ était de 6 à 25 % plus disposée à accepter un vaccin que la communauté non-LGBTQ2+.
- La partisanerie a été associée à l'intention de se faire vacciner. Les personnes qui ont voté pour les partis libéraux ou démocrates ont exprimé une intention plus ferme de se faire vacciner que celles qui ont voté pour les autres partis.
- Une recommandation indiquant de se faire vacciner par un fournisseur de soins de santé (p. ex., un médecin) a eu un effet positif sur l'intention de se faire vacciner.
- L'intention de se faire vacciner variait grandement selon la race ou l'origine ethnique, les Blancs étant plus susceptibles de décider de se faire vacciner que d'autres groupes ethniques comme les Noirs, les Asiatiques et les Hispaniques, selon des études menées au Canada, aux États-Unis et au Royaume-Uni.
- Les parents avaient moins l'intention de faire vacciner leurs enfants qu'eux-mêmes. Il existe une forte corrélation entre l'intention des parents de se faire vacciner et l'intention de faire vacciner leurs enfants puisque les parents qui avaient l'intention de se faire vacciner étaient plus susceptibles de

vouloir faire vacciner leurs enfants. Les personnes qui ont des enfants plus jeunes (0 à 4 ans) étaient plus réticentes envers la vaccination que celles dont les enfants ont plus de 5 ans.

- La religion et la croyance en des théories du complot étaient associées à la réticence à se faire vacciner.
- Les préoccupations en ce qui concerne l'innocuité et l'efficacité du vaccin étaient les deux raisons les plus souvent invoquées pour justifier le refus de se faire vacciner. Parmi les autres raisons fréquemment citées, mentionnons la nouveauté du vaccin et la croyance qu'un vaccin contre la COVID-19 est inutile.
- Comparativement à la population en général, l'intention de se faire vacciner est plus faible dans certaines populations à risque élevé, comme les femmes enceintes, les personnes sans abri, les personnes atteintes de troubles liés à la consommation de substances et les populations vulnérables.
- Les participants ruraux étaient légèrement moins susceptibles d'accepter un vaccin que les participants qui vivent dans les villes et les banlieues.

Vue d'ensemble des éléments de preuve

Deux cent cinq articles portant sur l'adoption du vaccin contre la COVID-19 et les attitudes associées ont été recensés et inclus dans la présente revue. De ce nombre, 99 sont des préimpressions ou des études pour lesquelles le processus d'examen par les pairs n'est pas terminé. Cette revue rapide met l'accent sur les données mondiales sur l'adoption du vaccin contre la COVID-19 et sur les données canadiennes en ce qui concerne les attitudes à l'égard de ce vaccin. Des données probantes sur les populations prioritaires prédéfinies provenant de l'Australie, de la Nouvelle-Zélande, des États-Unis et du Royaume-Uni ont également été incluses afin de compléter les données fournies par les études réalisées au Canada. Cela inclut les travailleurs de la santé, les LGBTQ+, les groupes confessionnels, les nouveaux arrivants, les parents, les femmes enceintes ou qui allaitent, les personnes qui vivent dans les collectivités rurales, les adultes plus âgés, les personnes qui ont des comorbidités et celles qui se heurtent à de multiples obstacles en matière de santé. (p. ex., itinérance, troubles de santé mentale ou de toxicomanie).

Les publications qui portent sur l'adoption du vaccin contre la COVID-19 et les attitudes associées incluent principalement des études d'observation, quelques essais cliniques randomisés, des études contrôlées avant et après, ainsi que des études quasi expérimentales ayant examiné les facteurs associés à l'intention de se faire vacciner et à l'incidence des différents messages sur cette intention. Les résultats des études expérimentales n'ont pas évalué la prévalence, mais visaient plutôt à indiquer l'option la plus efficace parmi un éventail d'options. Les essais cliniques randomisés offrent l'avantage supplémentaire d'équilibrer les groupes de traitement pour éviter l'influence associée aux groupes non comparables (p. ex., confusion).

Aucune évaluation officielle du risque de biais n'a été effectuée. La fiabilité du résultat des études d'observation est fondée sur l'obtention d'un échantillon représentatif de la population cible suffisamment grand pour obtenir un spectre de résultats représentatif. Il est fréquent que les études ne démontrent pas la représentativité de leurs échantillons par rapport à la population cible, tant dans les études non publiées que

dans les études publiées. Les études longitudinales dans lesquelles une population cible est échantillonnée plus d'une fois afin de surveiller les changements dans l'attitude à l'égard de la vaccination et de l'adoption du vaccin dans le temps ont été le modèle d'étude d'observation le plus solide ayant été relevé. Bon nombre des études d'observation étaient des enquêtes transversales effectuées en ligne, auprès d'une population cible, à un moment donné. Ces modèles d'étude présentent un risque modéré/élevé de biais et sont donc vus comme étant de qualité moyenne à faible en raison de la taille de l'échantillon et du fait qu'il représente ou non la population cible, ainsi qu'en fonction de la capacité de l'outil d'enquête à mesurer le ou les résultats d'intérêt (par exemple, l'étude était-elle fondée sur une recherche formative ayant été validée et prétestée avant sa mise en œuvre). Pour la plupart des études incluses, les résultats sont autodéclarés et peuvent donc être biaisés en raison des réponses et de la désirabilité sociale. Les autres biais pris en compte dans ces études incluent le taux de réponse et les données manquantes. La plupart des études incluses dans cette revue rapide n'ont pas déclaré un ou plusieurs des critères indiqués ci-dessus ou n'en ont pas tenu compte en raison de la réalisation de l'étude ou de la façon dont elle a été déclarée. Bien que de nombreuses études montrent des tendances semblables, les conclusions pourraient changer avec des recherches supplémentaires, un plus vaste échantillon, des stratégies d'échantillonnage et des outils de collecte de données différents, ainsi que la progression notée pendant la pandémie.

Les études portant sur l'intention de se faire vacciner et les motifs associés à la réticence dans les populations à risque élevé et non desservies constituent une lacune clé dans les connaissances associées à la présente recherche. La majorité des études ont utilisé des sondages en ligne et, dans une moindre mesure, des sondages téléphoniques, ce qui peut limiter des segments de la population en raison d'un manque d'accès. Bien que le déploiement du vaccin soit en cours depuis quelques mois, peu d'études ont été publiées sur le refus de se faire vacciner et les connaissances et attitudes associées au rejet ou à l'adoption d'un vaccin. Cette information est cruciale pour déterminer la raison pour laquelle les gens acceptent ou refusent les vaccins et ainsi pouvoir continuer à élaborer des stratégies pour encourager l'adoption du vaccin chez les personnes qui hésitent.

CONTENU

ADOPTION DU VACCIN CONTRE LA COVID-19 ET RESPECT DES MESURES DE SANTÉ PUBLIQUE APRÈS LA VACCINATION

L'adoption du vaccin et les facteurs associés ont été étudiés dans 14 études menées aux États-Unis, au Royaume-Uni et en Israël (1, 22-34) chez les travailleurs de la santé. Deux études effectuées chez des adultes de plus de 70 ans au Royaume-Uni et en Pologne (35, 36), deux études réalisées dans des prisons aux États-Unis (37, 38), deux études effectuées dans des unités militaires en Israël (39, 40), une étude sur les personnes en situation d'itinérance aux États-Unis (41), une étude sur les survivants d'un accident vasculaire cérébral (AVC) ou d'un accident ischémique transitoire (AIT) au Royaume-Uni (42), une étude sur les adultes handicapés et les parents au Royaume-Uni (43), une étude sur les personnes âgées et les populations à haut risque aux États-Unis (44), une étude sur les patients en hémodialyse aux États-Unis (45), une étude sur les transplantés hépatiques en Italie (4), une étude sur des patients atteints du syndrome du côlon irritable en Italie (46), une étude sur des patients psychiatriques hospitalisés au Royaume-Uni (5) et six études dans la population générale du Royaume-Uni, aux États-Unis, en Israël et en Nouvelle-Zélande (2, 15, 44-49) ont toutes examiné l'adoption du vaccin et les facteurs associés. Seules les études où l'on peut établir ou déduire que tout le groupe s'est vu offrir un vaccin avant de mesurer le niveau d'adoption du vaccin ont été incluses. Cela inclut les études à partir du début du déploiement du vaccin (à partir de décembre 2020). Sept études ont évalué le respect des mesures de santé publique après la vaccination au Royaume-Uni et en Israël (6, 7, 35, 50-53). Les éléments généraux sont présentés ci-dessous alors que les résultats détaillés pour chacune des études figurent dans l'annexe (Tableau 1). Ces études doivent être interprétées avec prudence, car l'adoption et le refus du vaccin ont été signalés, dans quelques études, comme des résultats secondaires à d'autres résultats primaires axés notamment sur l'efficacité du vaccin alors que dans d'autres études, la mesure dans laquelle l'adoption et le refus n'étaient pas clairs en raison de la façon de déclarer les résultats ou de la nature préliminaire de ceux-ci.

Tendances générales

- L'adoption du vaccin a été associée positivement à un âge plus avancé (1, 15, 25, 26, 29, 30, 34, 38, 45, 50, 54) et au sexe masculin (1, 15, 22, 25, 26, 29, 30, 36, 45, 47).
- Les personnes qui avaient des antécédents d'infection par le SRAS-CoV-2 étaient moins susceptibles de se faire vacciner selon quatre études (25-27, 45). Les raisons de leur refus comprenaient des inquiétudes quant à la nouveauté du vaccin, de ses effets secondaires possibles, la conviction que le risque pour leur santé personnelle de contracter la COVID-19 est faible, une méfiance plus générale envers les services de santé et des inquiétudes quant aux tests sur les animaux et le fait d'être soumis à des expériences (1, 4, 5, 27, 28, 30, 32, 36, 46).
- Trois études effectuées aux États-Unis ont indiqué que les personnes qui n'ont pas reçu le vaccin antigrippal étaient moins susceptibles de vouloir recevoir le vaccin contre la COVID-19 que celles qui l'avaient reçu (30, 32, 45).

- Dix études ont évalué l'adoption du vaccin dans différents groupes ethniques/raciaux. Les Noirs et les groupes ethniques minoritaires affichaient les taux d'adoption de la vaccination les plus faibles (5, 22, 25-27, 29, 30, 32, 34, 38, 49).
- Ces tendances correspondent aux résultats en ce qui concerne l'intention de se faire vacciner.

Travailleurs de la santé

- Dans six études réalisées dans les hôpitaux des États-Unis, de 70 à 94 % des travailleurs de la santé ont dit qu'ils se feraient vacciner lorsque le vaccin serait disponible (22, 27, 30-33).
- Dans un sondage mené en décembre à Montréal, au Canada, 80,9 % des travailleurs de la santé à qui l'on a proposé un vaccin l'ont accepté et 19,1 % l'ont refusé. Du nombre de personnes qui ont refusé un vaccin, 74,1 % ont déclaré qu'elles accepteraient de se faire vacciner à l'avenir, 53,2 % voulant attendre quelques mois et 31,9 % voulant attendre un an (1).
- Des taux élevés de vaccination chez les travailleurs de la santé en Israël ont été déclarés dans deux études dans lesquelles tous les travailleurs de la santé s'étaient vu offrir un vaccin. Au 21 janvier et au 24 janvier, 90 % (n=1500) et 79 % (n=9109) des travailleurs de la santé avaient reçu au moins une dose de vaccin (23, 24).
- Dans le cadre de trois études sur des travailleurs de la santé qui se sont vus offrir un vaccin dans des hôpitaux au Royaume-Uni, de 63 à 89 % des travailleurs ont choisi de recevoir le vaccin (25, 26, 29).
- Dans 87 maisons de santé au Royaume-Uni où tous les membres du personnel se sont vus offrir un vaccin, 52,6 % (n = 1 119) avaient reçu une première dose pour un taux de vaccination moyen par maison de 51,4 % (IC à 95 % : 43,9 à 58,8 %). Le fait que le personnel était à l'extérieur du site pendant les cliniques de vaccination (36,5 %) est l'une des raisons courantes pour lesquelles certaines personnes n'ont pas été vaccinées. Si des problèmes logistiques comme celui-ci étaient résolus, le taux moyen de vaccination par maison de santé aurait alors pu atteindre 69,8 % (IC à 95 % : de 63,2 à 76,3 %) (28).
- Les médecins étaient plus susceptibles d'avoir accepté de se faire vacciner que les infirmières et les travailleurs de la santé œuvrant dans des milieux non cliniques (22, 27, 29, 30).

Adultes plus âgés (70 ans et plus)

- Dans une étude effectuée au Royaume-Uni auprès de personnes âgées (de 80 ans et plus) dans laquelle 99,8 % ont déclaré s'être vues offrir un vaccin, 99 % ont dit avoir reçu au moins une dose et 15 % avaient reçu au moins deux doses et 1 % a refusé (35, 54).
- Dans une étude réalisée en Pologne et portant sur 1 427 adultes âgés (de 70 ans et plus), 62,7 % ont dit avoir reçu le vaccin alors que 37,3 % ont déclaré ne pas vouloir se faire vacciner. Les prédicteurs indépendants les plus importants pour l'adoption du vaccin étaient le fait d'avoir reçu une explication d'un professionnel de la santé à savoir pourquoi la personne devrait se faire vacciner (RC = 4,23, IC à 95 % : 2,90 à 5,75), de vivre avec d'autres personnes (RC = 3,13, IC à 95 % : 2,03 à 4,26), de pouvoir se rendre par ses propres moyens chez un omnipraticien (RC = 1,92, IC à 95 % : 1,45 à 2,76), d'être atteinte de maladies chroniques (RC = 2,98, IC à 95 % : 2,05 à 4,01) et d'avoir un statut socioéconomique supérieur (RC = 1,79, IC à 95 % : 1,33 à 2,15) (36).

Personnes en situation d'itinérance

- Dans un groupe de 90 personnes sans abri de Los Angeles où 17 se sont fait offrir un vaccin, 10 ont accepté de le recevoir et 7 l'ont refusé. Les motifs du refus n'ont pas été examinés (41).

Prisons

- Dans des établissements correctionnels du Rhode Island et de la Californie, 66,5 à 76,4 % des personnes incarcérées ont accepté de se faire vacciner. Les motifs du refus n'ont pas été examinés (37, 38).

Population en général

- Une étude longitudinale effectuée dans la population générale du Royaume-Uni montre que les taux de refus du vaccin se situent entre 1 et 2 %. Parmi les personnes à qui on a offert un vaccin, les taux de refus du vaccin étaient de 2 % chez les 16 à 29 ans, de 1 % chez les 30 à 49 ans et de 2 % chez les 50 à 69 ans (50, 54).
- Dans le cadre d'un programme de vaccination mis en œuvre dans le nord-ouest de Londres, où 413 919 personnes se sont vu offrir un vaccin, 5,88 % des personnes ont refusé le vaccin et 0,7 % étaient réticente. La privation était associée négativement au refus du vaccin ($r = -0,94$, $P < 0,01$). Chez les personnes qui vivaient dans les régions défavorisées, les taux de refus les plus élevés ont été observés chez les personnes de 70 ans et plus (70 à 74 ans = 17,5 %; 75 à 80 ans = 19,0 %; 80 ans et plus = 25,9 %), les personnes extrêmement vulnérables sur le plan clinique (19,2 %) et les membres des communautés noires et noires britanniques (20,0 %) (49).
- Dans un sondage longitudinal mené auprès d'adultes néo-zélandais, le taux de refus de vaccin a chuté de 2 % en avril à 1 % en mai (15).
- Au Royaume-Uni, 5 % des personnes qui s'identifiaient comme ayant une autre religion et 4 % des bouddhistes à qui on avait offert un vaccin l'avaient refusé, comparativement à 1 % des personnes qui ne déclaraient aucune religion (47).
- Deux études ont été menées pour mesurer l'incidence des rappels par messages textes sur les taux de vaccination et de rendez-vous fixés aux États-Unis et en Israël. Dans le sondage effectué aux États-Unis, un premier rappel envoyé par texto le lendemain du jour où une personne a été avisée qu'elle pouvait recevoir le vaccin a fait augmenter les taux de rendez-vous et de vaccination de 86 % et 26 %, respectivement (44). Un deuxième rappel a été envoyé par message texte à celles qui n'avaient pas pris de rendez-vous huit jours après le premier message texte a eu pour effet de faire augmenter le nombre de rendez-vous et le taux de vaccination de 52 % et de 16 % respectivement (44). Dans l'étude israélienne, les personnes ont reçu l'un des deux rappels par messages textes concernant les avantages sociaux ou personnels de la vaccination (2). L'effet global sur huit jours après l'intervention a révélé que le rappel des avantages personnels a entraîné une hausse relative de 9 % par rapport au rappel des avantages sociaux (23,8 % contre 21,7 %, $P<0,0001$) (2).
- Israël a mis en place une politique de laissez-passer vert selon laquelle l'entrée dans certains lieux publics nécessite la présentation d'un « laissez-passer » qui peut être obtenu soit en recevant un vaccin, soit en présentant un laissez-passer récent indiquant un résultat négatif au test de la COVID-

19. La mise en œuvre de cette politique en février a été associée à une augmentation relative de 22,2 % de l'adoption du vaccin après trois jours (2).

Unités militaires

- Selon deux études effectuées en Israël (39,55), le taux d'adoption du vaccin était élevé (de 84,8 à 89,8 %) dans deux unités militaires. Dans un groupe de 28 soldats qui n'avaient pas l'intention de se faire vacciner, 47,4 % se sont finalement fait vacciner après avoir consulté un médecin et abordé leurs différentes préoccupations (P = 0,004) (39).

Autres populations

- Au Royaume-Uni, 1 % des personnes handicapées et 1 % des répondants extrêmement vulnérables sur le plan clinique se sont vu offrir un vaccin, mais l'ont refusé, un pourcentage légèrement plus élevé à celui de la population en général (2 %) (56). Trois pour cent des parents qui avaient des enfants âgés de 0 à 4 ans se sont vu offrir un vaccin et l'ont refusé, comparativement à 2 % de ceux qui avaient des enfants de plus de 5 ans ou à 1 % de ceux qui ne sont pas des parents et qui ne vivent pas avec des enfants à charge (43).
- Des personnes dialysées, 14,2 % qui ont pris part à une étude aux États-Unis ont refusé un vaccin lorsqu'il leur a été proposé. Les personnes dialysées depuis plus de 5 ans étaient plus susceptibles de refuser un vaccin (RC 1,7, IC à 95 % : de 1,08 à 2,70, P=0.023) (45).
- Chez 377 survivants d'accidents vasculaires cérébraux et d'accidents ischémiques transitoires (AIT) au Royaume-Uni, 2 % des personnes interrogées ont refusé le vaccin lorsqu'il leur a été proposé (42).
- Dans un groupe de 266 transplantés hépatiques en Italie, 96,6 % ont accepté de se faire vacciner lorsque le vaccin leur a été proposé. Bien qu'ils aient reçu des renseignements adéquats, cinq patients (1,8 %) ont refusé de se faire vacciner en raison d'inquiétudes quant au risque d'effets indésirables graves. Les obstacles en place pour les quatre patients restants (1,6 %) pourraient être éliminés soit en fournissant des détails supplémentaires concernant la vaccination, soit après avoir réglé des problèmes médicaux et logistiques (4).
- Dans un groupe de 85 patients psychiatriques hospitalisés au Royaume-Uni qui avaient la capacité de décider s'ils voulaient recevoir le vaccin contre la COVID-19, 80 % ont accepté et 20 % ont refusé. Les patients britanniques blancs étaient moins susceptibles de refuser que les patients noirs, asiatiques ou issus de minorités ethniques (16,9 % contre 30 %). Les raisons de leur refus comprenaient des inquiétudes quant à l'innocuité et aux effets secondaires du vaccin, la conviction que le risque pour leur santé personnelle de contracter la COVID-19 est faible, une méfiance plus générale envers les services de santé et des inquiétudes quant aux tests sur les animaux (5)..
- Sur 56 patients atteints du syndrome du côlon irritable en Italie, 96,4 % ont accepté de se faire vacciner lorsqu'un vaccin leur a été proposé. Le refus était attribuable aux inquiétudes concernant les effets indésirables potentiels (46).

Respect des mesures de santé publique après la vaccination

- Dans une étude effectuée au Royaume-Uni chez des adultes plus âgés (80 ans et plus) parmi ceux qui avaient reçu au moins une dose au cours des trois dernières semaines, 43 % avaient rencontré quelqu'un en dehors de leur bulle, de leur ménage ou du personnel soignant à l'intérieur plutôt qu'à

l'extérieur, 49 % avaient rencontré à l'extérieur une personne avec qui elles ne vivaient pas, 54 % étaient allées magasiner et 45 % étaient sorties de la maison pour participer à des activités de loisirs en plein air (35).

- Une étude longitudinale menée au Royaume-Uni a démontré que les adultes vaccinés (ayant reçu au moins une dose) étaient plus susceptibles que les adultes non vaccinés de se laver les mains à leur retour à la maison (90 % contre 82 %), de respecter la distanciation sociale lorsqu'ils rencontrent d'autres personnes à l'extérieur de leur ménage ou de leur bulle (90 % contre 72 %) et d'éviter les contacts physiques à l'extérieur de leur domicile (86 % comparativement à 74 %) (50).
- Après la deuxième dose de vaccin, 21,1 % et 47,3 % des personnes interrogées au Royaume-Uni ont déclaré moins porter leur couvre-visage et moins respecter la distanciation sociale depuis qu'elles ont été vaccinées alors que 75,7 % et 48,4 % respectivement n'ont pas changé leur comportement. Les personnes de 50 ans et plus étaient moins susceptibles de changer de comportement que celles de moins de 50 ans. Des tendances semblables ont été observées chez les travailleurs de la santé pour ce qui est de la distanciation sociale, mais la majorité (95,7 %) d'entre eux n'ont pas indiqué de changement dans le port du couvre-visage après la vaccination (51).
- Même s'ils avaient reçu au moins une dose du vaccin contre la COVID-19, 73,2 % des adultes américains n'ont pas changé leurs comportements en ce qui concerne la prévention, alors que 4,3 % des gens ont adopté des comportements plus stricts et que 21,9 % ont modéré les changements de comportements (53).
- Au début de la campagne de vaccination en Israël, les personnes infectées par la COVID-19 faisaient moins attention à la distanciation sociale (29,7 %) et au port du masque (18,8 %) par rapport à celles qui avaient reçu la première dose de vaccin (12,8 % et 8,2 %), ou à celles qui n'étaient ni vaccinées ni infectées (19,2 % et 11,6 %) (7).
- À l'aide d'un système de positionnement global (GPS) au Royaume-Uni, l'augmentation médiane quotidienne de la distance de déplacement moyenne à partir de l'adresse enregistrée d'un participant était de 45,0 m (IC à 95 % : de 25 à 65 m, P = <0,001) entre la date de vaccination et 99 jours après la vaccination (6).

ATTITUDES DE LA POPULATION MONDIALE À L'ÉGARD DU VACCIN CONTRE LA COVID-19

La comparaison des attitudes à l'égard du vaccin contre la COVID-19 dans la population générale de différents pays du monde a été présentée dans six articles. Seules les études incluant le Canada et les résultats par pays ont été incluses. Les éléments généraux d'études les plus récentes (à partir de janvier 2021) sont présentés ci-dessous alors que les résultats détaillés pour chacune des études figurent dans l'annexe (Tableau 2).

- En janvier, le Royaume-Uni, le Danemark et les Pays-Bas comptaient parmi les pays dans lesquels la population indiquait avoir la plus forte intention de se faire vacciner (63 à 77 %). À ce moment-là, au Canada, l'intention de se faire vacciner atteignait 55 % (57).

- On a pu voir une augmentation de l'intention de se faire vacciner entre novembre et janvier en Espagne (24,1 %), au Royaume-Uni (23,2 %), en Suède (22,7 %), en Finlande (20,4 %), aux Pays-Bas (18,5 %), en Italie (15,4 %), en Norvège (14,6 %), en France (14,2 %), au Danemark (13,3 %), en Allemagne (13,0 %), au Canada (11 %) et au Japon (0,8 %) (57).
- Dans 11 des 15 pays, on a vu une diminution importante de la proportion de personnes qui se sont dites préoccupées par les effets secondaires d'un vaccin. Au Canada, cette préoccupation a diminué, passant de 53,3 % en novembre à 47,9 % en janvier (57).

ATTITUDES DE LA POPULATION CANADIENNE GÉNÉRALE À L'ÉGARD DU VACCIN CONTRE LA COVID-19

La majorité de la recherche sur les attitudes à l'égard du vaccin contre la COVID-19 a été effectuée auprès du grand public. Des quarante-deux études propres à la population canadienne, 27 sont de la littérature grise et sept sont des préimpressions. Les éléments généraux de janvier 2021 sont présentés ci-dessous et les résultats détaillés pour chacune des études figurent dans l'annexe (Tableau 3).

Intentions de se faire vacciner

- Selon les études canadiennes les plus récentes, datant de juin 2021, l'intention de se faire vacciner se situait entre 84 et 88 % (8, 10). Les provinces de l'Atlantique, la Colombie-Britannique et le Québec sont les provinces dans lesquelles l'intention de se faire vacciner atteint son niveau le plus élevé (58-73).
- Trois études longitudinales ont démontré que l'intention de se faire vacciner au Canada avait continué à augmenter à partir de niveaux de référence enregistrés entre septembre et décembre (10, 74, 75).
- En juin, 89 % des Canadiens ayant reçu une dose ont déclaré avoir l'intention de recevoir une deuxième dose, 9 % ont déjà reçu leur deuxième dose, 1 % ne le feront probablement pas et 1 % étaient incertains (10).
- Dans un groupe de 70 parents ou tuteurs d'enfants âgés de 12 à 17 ans du Manitoba, 15 % et 13 % étaient incertains de faire vacciner ou ne feraient pas vacciner leurs enfants, respectivement (11). Les personnes qui étaient réticentes à faire vacciner leurs enfants faisaient partie de ménages dont le revenu était inférieur à 40 000 dollars par an, ne se feraient pas vacciner elles-mêmes et ne pensaient pas que les adultes devaient recevoir tous les vaccins habituels (11).
- 48 % des Canadiens étaient mal à l'aise à l'idée de recevoir une marque différente de vaccin pour leur deuxième dose, tandis que 46 % étaient à l'aise et 6 % étaient incertains. Parmi ceux qui ont reçu AstraZeneca comme première dose, 50 % ont préféré recevoir AstraZeneca comme deuxième dose, 32 % ont préféré une autre marque comme deuxième dose, et 18 % étaient incertains (10).
- Les incitatifs financiers (argent, bons, articles gratuits, tirages de prix, rabais) n'ont pas été signalés comme augmentant la probabilité d'accepter de se faire vacciner dans une étude menée au Manitoba (entre 7 et 84 % des répondants ont déclaré que l'incitatif ne les rendrait pas plus susceptibles de se

faire vacciner). Cependant, 70 % d'entre eux seraient inquiets si seules les personnes réticentes à se faire vacciner recevaient des incitatifs importants (de 50 à100 $) (11).

- La réticence à se faire vacciner a chuté de façon spectaculaire en Alberta, passant de 45 % en janvier à 25 % en avril et à 17 % en mai (76).
- Une étude effectuée en janvier et en février 2021 dans le sud de l'Ontario a indiqué que 82,8 % des personnes étaient prêtes à recevoir un vaccin alors que 17,2 % n'étaient pas disposées à le faire (77).
- Une étude menée en mai 2021 a démontré que la plupart des gens se sentaient à l'aise avec les vaccins Pfizer (93 %) et Moderna (89 %), mais l'étaient moins avec les vaccins Johnson et Johnson (49 %) et AstraZeneca (35 %). Les femmes et les personnes de 55 ans et plus étaient plus mal à l'aise avec les vaccins AstraZeneca (AZ) et Johnson and Johnson (J&J) que les hommes et les personnes de moins de 55 ans. Parmi les personnes qui n'étaient pas à l'aise avec les vaccins AZ et J&J, 40 % des femmes et 31 % des hommes ont déclaré qu'ils accepteraient quand même ces vaccins s'ils leur étaient offerts (76).
- Selon trois études, les membres de la communauté LGBTQ2+ étaient plus disposés à accepter de se faire vacciner que les personnes n'appartenant pas à cette communauté (87,6 % contre 76,4 % dans une étude, RC=3,04, IC à 95 % : de 1,08 à 8,55, p=0,04 dans un autre, et 83,3 % contre 77 % dans un troisième) (78-80).
- Dans le cadre d'un sondage effectué en janvier et en février 2021, 71 % des jeunes de 12 à 17 ans ont dit avoir l'intention de se faire vacciner (81).
- Comparativement aux non-immigrants (75,9 %), les immigrants qui vivent au Canada depuis moins de 10 ans (80,3 %) et plus de 10 ans (70,7 %) ont dit avoir un intérêt comparable pour la vaccination (78). Une autre étude a montré que les immigrants étaient un peu moins susceptibles de se faire vacciner (74,6 %) que le grand public (77 %), mais cela variait grandement entre les immigrants plus âgés et les plus jeunes (73,2 % pour les 12 à 64 ans et 81,1 % pour les 65 ans et plus) (80).
- Au sein des groupes des minorités visibles au Canada, l'intention de se faire vacciner était la suivante, de la plus faible à la plus forte : les Noirs (57,0 %), les Latino-Américains (58,5 %), les Philippins (64,2 %), les Asiatiques du Sud-Est (75,8 %), les autres minorités visibles (77,6 %), les Chinois (85,5 %) et les Arabes (88,3 %). Parmi les personnes déclarant une identité autochtone, 69,3 % acceptent de se faire vacciner, contre 77,6 % des personnes n'ayant pas déclaré une telle identité (78).
- Les personnes appartenant aux minorités visibles qui avaient la plus grande intention de se faire vacciner étaient les Japonais (86,5 %), les Coréens (85,6 %), les Asiatiques du Sud (82,5 %), les Chinois (79,3 %), les minorités visibles non indiquées/multiples (79,1 %), les Asiatiques du Sud-Est (78,3 %), les Asiatiques de l'Ouest (78,3 %), les Philippins (75,1 %), les Arabes (68,1 %), les gens d'Amérique latine (66,0 %) et les Noirs (56,6 %). L'intention de se faire vacciner des membres d'une minorité non visible était de 77,6 % (82).
- Chez les répondants autochtones, 71,8 % ont dit qu'ils se feraient vacciner, ce qui est nettement inférieur au taux de réponse des répondants non autochtones (77,1 %). 74,2 % des membres des

Premières Nations qui vivent hors réserve étaient prêts à se faire vacciner, comparativement à 67,8 % des Métis et à 72,5 % des Inuits. Les Autochtones plus âgés (65 ans et plus) étaient plus susceptibles de vouloir se faire vacciner que les plus jeunes (74,9 % contre 71,3 %) (82).

- Dans un sondage effectué auprès des résidents autochtones de la Colombie-Britannique, 68 % ont déclaré qu'ils aimeraient se faire vacciner le plus tôt possible ou qu'ils l'ont déjà été, comparativement à 58 % des répondants asiatiques et 66 % des répondants sud-asiatiques (83).
- En Colombie-Britannique, l'intention de se faire vacciner était la plus forte chez les travailleurs en soins continus venus de l'Asie de l'Est (61 %) et du Sud (70 %). Les répondants latins et les Noirs étaient les plus susceptibles de refuser le vaccin (30 %) alors que ceux qui ont des antécédents autochtones sont ceux qui avaient le plus tendance à être incertains quant à la décision à savoir s'ils se feraient ou non vacciner (40 %). Les répondants autochtones étaient ceux qui avaient le moins confiance aux différentes sources d'information, y compris les fournisseurs de soins de santé (84).
- Au Canada, les personnes qui ont voté pour le Parti libéral ou le NPD aux élections de 2019 étaient plus susceptibles d'indiquer leur intention de se faire vacciner que celles qui ont voté pour d'autres partis (58-60, 85).
- Dans trois études, les participants ruraux étaient moins susceptibles d'accepter un vaccin que les participants qui vivent dans les villes et les banlieues (10, 86, 87).
- Selon onze études, les hommes étaient plus susceptibles d'avoir l'intention de se faire vacciner que les femmes (58, 61, 77-79, 81, 88-92).
- Les facteurs les plus courants associés positivement à l'intention de se faire vacciner étaient le fait d'être plus âgé, le fait d'avoir fait des études supérieures, d'avoir des connaissances ou une littéracie adéquates en matière de santé, de faire confiance aux experts et au gouvernement, d'avoir un statut socioéconomique plus élevé, d'avoir déjà reçu un vaccin contre la grippe et d'être plus préoccupé par la COVID-19.
- Les préoccupations en ce qui concerne l'innocuité et l'efficacité du vaccin étaient les deux raisons les plus souvent invoquées pour justifier le refus de se faire vacciner. Parmi les autres raisons fréquemment citées, mentionnons la nouveauté du vaccin et la croyance qu'un vaccin contre la COVID-19 est inutile.
- Une recommandation indiquant de se faire vacciner par un fournisseur de soins de santé (p. ex., un, médecin) a eu un effet positif sur l'intention de se faire vacciner dans cinq études (74, 79, 83, 93, 94).
- Les croyances associées à la conspiration et au complot étaient directement liées à l'intention de ne pas se faire vacciner (59, 90, 95).

Attitudes à l'égard du déploiement du vaccin et des passeports vaccinaux

- Les passeports vaccinaux bénéficient d'un soutien important au Québec, 72 % des résidents y étant favorables (12).

- Parmi les répondants, 61 % sont maintenant d'accord pour dire que le Canada devrait instaurer un passeport vaccinal, un chiffre en augmentation par rapport au 54 % enregistré en avril (73).
- Deux études ont démontré un appui élevé au fait de devoir présenter une preuve de vaccination lors d'un voyage en avion (79 à 82 %), d'événements où l'on retrouve une foule importante (69 à 75 %) et de la fréquentation en présentiel d'une université (71 %) alors que l'appui est plus faible en ce qui concerne le fait d'utiliser la preuve de vaccination pour pouvoir séjourner dans un hôtel (68 %), aller au bureau (55 à 68 %) ou dans des endroits publics comme des restaurants, des bars et des salles de cinéma (55 à 64 %) (73, 96).
- Parmi ceux qui étaient réticents à se faire vacciner, entre 7 et 18 % des répondants aux deux sondages ont dit que leur décision pourrait être influencée par le fait qu'un vaccin leur permettrait de pouvoir voyager, d'assister à des événements sportifs ou culturels ou de rendre visite à des êtres chers (11 %) (96, 97).
- Parmi les personnes qui ont reçu le vaccin AstraZeneca, 2 % ont dit le regretter complètement alors que 66 % ont de sérieux doutes à l'égard du vaccin (76).
- De 51 à 55 % estiment que le Canada a fait un bon travail pour obtenir des doses de vaccin (75, 86).
- Lorsqu'on leur a posé des questions sur le plan de déploiement du vaccin en Colombie-Britannique, 5 % des résidents ont jugé que le déploiement de la vaccination était excellent, 30 % ont dit qu'il était bon, 51 % ont indiqué qu'il était passable, 14 % ont dit qu'il était mauvais alors que 7 % ont mentionné qu'il était très mauvais. On a observé des tendances semblables pour ce qui est des perceptions sur la clarté des niveaux de déploiement et d'établissement des priorités (98).
- 71 % des répondants sont à l'aise avec la façon dont le gouvernement du Manitoba détermine les groupes prioritaires pour la vaccination initiale (99).
- Le taux d'approbation en ce qui concerne le déploiement global du vaccin en Alberta était divisé puisque 48 % se sont dit satisfait alors que 43 % étaient insatisfaits. En ce qui concerne l'ordre de priorité établi par le gouvernement, 64 % des répondants étaient satisfaits et 28 % étaient insatisfaits (100).
- Pour ce qui est de la distribution des vaccins, 42 % des Canadiens croient que leur gouvernement provincial fait du bon travail contrairement à 39 % qui disent l'inverse. L'insatisfaction était la plus élevée en Alberta, au Manitoba et en Ontario. Les résidents de la Colombie-Britannique et du Québec ont donné de meilleures notes à cet égard (68).
- Deux études ont analysé le point de vue des experts sur les stratégies de vaccination contre la COVID-19. Les experts de la santé publique s'accordent à dire que les personnes les plus vulnérables aux maladies graves et aux décès en raison de la COVID-19 (p. ex., les résidents des établissements de soins de longue durée, les travailleurs de la santé, les personnes souffrant de maladies chroniques) devraient avoir la priorité en ce qui concerne la vaccination (101, 102).

ATTITUDES DES TRAVAILLEURS DE LA SANTÉ À L'ÉGARD DU VACCIN CONTRE LA COVID-19

Les données probantes sur les attitudes des travailleurs de la santé à l'égard du vaccin contre la COVID-19 au Canada, en Australie, en Nouvelle-Zélande, au Royaume-Uni et aux États-Unis proviennent de 42 études. Toutes ces études ciblaient les travailleurs de la santé, y compris les infirmières, les médecins et les préposés aux services de soutien à la personne. Les éléments généraux de janvier 2021 sont présentés ci-dessous et les résultats détaillés pour chacune des études figurent dans l'annexe (Tableau 4).

- Les études les plus récentes montrent que l'intention de se faire vacciner chez les travailleurs de la santé canadiens varie de 57 à 82 % (103 à 105). Aux États-Unis, l'intention de se faire vacciner se situe entre 55 et 93 % (106-117).
- Selon une étude, aucune différence n'a été notée en ce qui concerne l'adoption ou le rejet d'un vaccin contre la COVID-19 par les participants, qu'ils travaillent ou non dans le secteur des soins de santé Canada (88). Aux États-Unis, deux études ont montré que les travailleurs de la santé étaient moins susceptibles d'avoir l'intention de se faire vacciner comparativement à la population en général (115, 118) alors que deux autres études ont montré le contraire, soit que les travailleurs de la santé avaient plus l'intention de se faire vacciner comparativement à la population en général (112, 119).
- Les travailleuses de la santé enceintes étaient 7,12 fois plus susceptibles d'hésiter que les travailleuses de la santé non enceintes (RCa 7,12, IC à 95 % : de 4,74 à 10,70) (114).
- Les médecins étaient beaucoup plus susceptibles que les infirmières et les autres travailleurs de la santé d'avoir l'intention de se faire vacciner (37, 107, 110, 116, 117, 120).
- Dix-sept études ont démontré que les travailleurs de la santé sont plus susceptibles d'avoir l'intention de se faire vacciner que les travailleuses de la santé (37, 84, 88, 105, 106, 109, 110, 114, 116, 117, 120-126).
- La proportion de personnes susceptibles de se faire vacciner contre la COVID-19 était directement liée au fait que ces personnes soient plus âgées (37, 84, 88, 103, 105, 109, 110, 114, 116, 121, 123, 124), au fait qu'elles aient déjà eu un vaccin antigrippal (37, 84, 105, 109, 114, 126, 127) et à la perception de pouvoir être infectées par la COVID-19 (105, 117, 123, 126).
- Les principales préoccupations en ce qui concerne la vaccination comprennent l'innocuité, l'efficacité, le manque de connaissances sur le vaccin, les effets secondaires, la vitesse du développement du vaccin et la croyance selon laquelle la vaccination n'était pas nécessaire (37, 84, 88, 103, 105, 106, 108-110, 112-114, 116, 119-121, 124, 126-130).
- Dans une étude sur les employés des services sociaux qui offrent du soutien aux personnes ayant une déficience intellectuelle en Ontario, les Autochtones, les Premières Nations et les Métis (RCa 1,73, IC à 95 % : de 0,67 à 4,43), les Latins (RCa 1,22, IC à 95 % : de 0,21 à 7,24) et les ethnies mixtes (RCa 1,11, IC à 95 % : de 0,27 à 4,55) étaient plus susceptibles de refuser un vaccin que les personnes d'origine européenne (105).

- Dans une étude sur les préposés aux services de soutien à la personne au Canada, 64,2 % des répondants ont dit avoir l'intention de se faire vacciner lorsque le vaccin sera disponible, 16,2 % ne veulent pas se faire vacciner, 10,7 % sont incertains et 8,9 % n'accepteront le vaccin que s'il est obligatoire. La majorité (71,7 %) de ces personnes ne croit cependant pas qu'il y ait suffisamment d'information claire à propos du vaccin (131).
- Dans une étude portant sur 8 634 travailleurs de la santé qui n'étaient pas médecins en Ontario, 80,4 % ont déclaré avoir l'intention de se faire vacciner. Les travailleurs de la santé étaient plus susceptibles d'avoir l'intention de se faire vacciner s'ils pouvaient avoir accès à un soutien financier direct, comme des congés de maladie payés (103). Les travailleurs de la santé non médecins en Ontario, au Canada, qui se sont identifiés comme étant d'origine philippine (RC 1,07, IC à 95 % : 0,41 à 2,76, P < 0,001), caraïbéenne (RC 3,20, IC à 95 % : 1,52 à 6,75, P < 0,001) ou autre (RC 1,44, IC à 95 % : 0,93 à 2,22, P < 0,001) étaient plus susceptibles de refuser un vaccin que ceux qui se sont identifiés comme étant d'origine européenne (103).
- Au Québec, 79,6 % des infirmières recommanderaient certainement ou probablement à leurs patients de se faire vacciner, 3,1 % ne le feraient pas et 17,2 % étaient incertaines. En ce qui les concerne, 70,4 % d'entre elles seraient certainement ou probablement prêtes à recevoir le vaccin, 11,8 % le refuseraient, et 17,8 % ont dit être incertaines (127).
- Deux études menées aux États-Unis ont démontré que les infirmières en milieu urbain étaient plus disposées à recevoir un vaccin que les infirmières en milieu rural lorsque celui-ci sera disponible (109, 132).
- Onze études ont évalué l'intention de se faire vacciner des travailleurs de la santé aux États-Unis. Les travailleurs noirs se sont dits de 12 à 84 % moins disposés à accepter le vaccin que les travailleurs blancs et asiatiques (106, 109, 112, 116, 118, 119, 121, 123, 125, 126, 133).
- Les personnes qui croyaient que le vaccin réduirait leur isolement social avaient plus de chances de conseiller à leurs patients de recevoir le vaccin (RCa 2,95, IC à 95 % : 1,32 à 6,59, P < 0,008) (113).
- Dans un sondage mené au Royaume-Uni auprès de 220 omnipraticiens, plus de 50 % d'entre eux n'avaient que peu confiance dans le fait de conseiller les patients au sujet des vaccins contre la COVID-19 (134).

COVID-19 ATTITUDES DES POPULATIONS À RISQUE ÉLEVÉ À L'ÉGARD DU VACCIN CONTRE LA COVID-19

Il est important de développer des stratégies fondées sur des données probantes pour cibler les populations à risque élevé afin qu'elles puissent être vaccinées. Vingt-quatre études sur les attitudes des populations à risque élevé en ce qui concerne le vaccin contre la COVID-19 ont été recensées au Canada, en Australie, au Royaume-Uni et aux États-Unis, en plus d'une étude mondiale portant sur 16 pays. Elles portaient sur des personnes âgées, des personnes ayant des troubles liés à la consommation de substances, des femmes enceintes ou qui allaitent, des personnes sans abri et des collectivités vulnérables. Les éléments généraux de

janvier 2021 sont présentés ci-dessous et les résultats détaillés pour chacune des études figurent dans l'annexe (Tableau 5).

- Trois études ont indiqué que les femmes enceintes avaient moins l'intention de se faire vacciner (41 à 62,1 %) (19, 135, 136). Les travailleuses de la santé enceintes étaient 7,12 fois plus susceptibles d'hésiter que les travailleuses de la santé non enceintes (RCa 7,12, IC à 95 % : de 4,74 à 10,70) (114). Les raisons les plus courantes pour hésiter étaient les effets secondaires potentiels pour leur bébé et le manque de données sur l'innocuité et l'efficacité chez les femmes enceintes (19, 135, 136). Tes raisons les plus courantes de leur réticence étaient les effets secondaires potentiels pour leur bébé et le manque de données sur l'innocuité et l'efficacité chez les femmes enceintes (19, 135, 136). Tout comme dans la population en général, les femmes qui sont dans des ménages à faible revenu, qui sont âgées de moins de 25 ans, qui n'ont jamais accepté d'autres vaccins, et les membres de minorités ethniques étaient plus susceptibles de refuser un vaccin pendant leur grossesse (19, 135, 136).
- L'intention de se faire vacciner et les raisons de la réticence ont été évaluées dans le cadre de deux études réalisées sur des personnes en situation d'itinérance aux États-Unis (41, 137). L'une d'elles a montré que 51 % de ces personnes accepteraient un vaccin s'il était offert, 32 % le refuseraient alors que 17 % ont refusé de répondre (41). Parmi les raisons courantes pour hésiter à se faire vacciner, mentionnons la peur des effets secondaires, le désir d'obtenir plus d'information sur le vaccin, les inquiétudes à savoir si le vaccin rend les gens malades et la méfiance à l'égard du gouvernement (41, 137). En dépit de l'exclusion sociale et du manque d'accès à la technologie, les participants ont suivi les reportages sur le vaccin et l'information souhaitée sur l'efficacité et l'innocuité du vaccin (41).
- L'intention de se faire vacciner était élevée (plus de79 %) dans six études portant sur des adultes plus âgés (65 ans et plus) (15, 92, 138-141).
- En février, un site de vaccination communautaire (Unidos en Salud UeS) a été déployé pour surmonter les obstacles à la vaccination contre la COVID-19 auxquels font face les LatinsX à San Francisco. De ce nombre, 56,1 % ont déclaré s'être fait vacciner plus tôt grâce au site et 65,3 % ont contacté trois personnes ou plus pour leur recommander le vaccin après leur expérience positive (3).
- Dans un sondage mené auprès de 391 familles amish de l'Ohio, 75,7 % ont dit ne pas avoir l'intention de faire vacciner leurs enfants contre la COVID-19 et les Amish Swartzentruber ont dit être beaucoup moins susceptibles de se faire vacciner comparativement aux autres groupes amish (142).
- Une étude qualitative portant sur les communautés vulnérables (p. ex., les sans-abri, les personnes ayant des problèmes de santé mentale, les Tziganes, les Roms et les Traveller) révèle l'appréhension et le scepticisme généraux, tout comme le faible niveau de confiance à l'égard des essais du vaccin contre la COVID-19. Des obstacles uniques ont été mentionnés pour chaque groupe, comme la réticence à se rendre à l'hôpital, la perte de confidentialité, les préoccupations au sujet des produits animaux dans les vaccins et le fait de croire que les concepteurs de vaccins et les gouvernements aient des intentions cachées. Ces éléments devraient être pris en compte au moment de développer des plans visant à donner confiance à la population à l'égard du vaccin (143).

- Dans un groupe de 87 personnes ayant des troubles liés à la consommation de drogues ou d'alcool aux États-Unis, 48 % se sont dits incertains ou peu disposés à se faire vacciner lorsque le vaccin sera disponible. Plusieurs réticences ont été indiquées, notamment la précipitation à développer les vaccins, les effets secondaires potentiels, ne pas avoir l'impression d'être à risque d'attraper le virus et l'inquiétude quant aux interactions avec des conditions préexistantes (144).
- Comparativement aux anciens fumeurs et à ceux qui n'ont jamais fumé, les fumeurs actuels étaient à la fois les plus indécis (27,6 (IC à 95 % : 26,1 à 29,1)) et réticents (21,5 % (IC à 95 % : 20,2 à 22,9 %)) à avoir l'intention de se faire vacciner (145). Dans une autre étude, la volonté de recevoir un vaccin ne différait pas de façon significative entre les consommateurs de cannabis et les témoins (t88 = 0,33, P = 0,74; BF01 = 4,3) (146). Une étude menée aux États-Unis a révélé que la consommation de cigarettes, de cigarettes électroniques, de marijuana et de boissons alcoolisées n'était pas associée à la réticence à se faire vacciner (147).
- La volonté de recevoir un vaccin contre la COVID-19 était associée positivement à la croyance que l'éclosion de la COVID-19 va se poursuivre pendant longtemps, à la gravité perçue de la maladie, aux conséquences pour la santé personnelle et aux conséquences pour la santé des autres (138, 139, 148, 149).
- Tout comme dans la population en général, l'intention de se faire vacciner était associée positivement au sexe masculin (139, 150), au niveau d'études supérieures (135, 136, 139), à un revenu plus élevé (135, 139, 150), à l'origine ethnique blanche (136, 139), à l'adoption antérieure de la vaccination contre la grippe (136) et à l'âge plus avancé (135).
- Une recommandation indiquant de se faire vacciner par un fournisseur de soins de santé (p. ex., un médecin) a eu un effet positif sur l'intention de se faire vacciner dans deux études portant sur des adultes plus âgés (139, 141), mais n'a eu que peu d'effet chez les femmes enceintes (135).

ATTITUDES DES PERSONNES ATTEINTES DE COMORBIDITÉS À L'ÉGARD DU VACCIN CONTRE LA COVID-19

Vingt-trois études avec des données probantes portant sur les attitudes à l'égard du vaccin contre la COVID-19 chez des personnes ayant des comorbidités et réalisées au Canada, en Australie, au Royaume-Uni et aux États-Unis ont été identifiées. Ces études couvraient un vaste éventail de comorbidités, y compris l'obésité, l'hypertension, les maladies respiratoires chroniques ou auto-immunes, le VIH et les déficiences intellectuelles et développementales. Les éléments généraux de janvier 2021 sont présentés ci-dessous et les résultats détaillés pour chacune des études figurent dans l'annexe (Tableau 6).

- La majorité des études (15 sur 23) ont été menées aux États-Unis, puis au Canada (1 sur 23), en Australie (2 sur 23), au Royaume-Uni (4 sur 23) ainsi que dans des études américaines et britanniques combinées (1 sur 23).
- Dans une étude réalisée au Canada, 64,6 % des personnes en surpoids ou atteintes d'obésité ont dit se sentir à l'aise de se faire vacciner alors que 35,4 % étaient réticentes (151). On a établi un lien positif entre

le degré d'adoption du vaccin et le sexe masculin, le fait d'avoir un plus grand nombre de comorbidités, des niveaux de dépression plus faibles, le fait de ne pas pratiquer la distanciation sociale et le fait d'avoir déjà reçu un vaccin contre la grippe (151).

- Une étude a montré qu'il n'y avait pas de différences significatives dans la volonté de se faire vacciner contre la COVID-19 entre les personnes souffrant d'hypertension et les témoins sains (152). Un autre a indiqué que les personnes qui ont dit être atteintes de maladies respiratoires chroniques étaient 5,7 % plus disposées à se faire vacciner (IC à 95 % : 0,05 à 0,09) que les témoins sains (153).
- Dans un groupe de 97 patients atteints de cancer et de leurs soignants des États-Unis, l'intention de se faire vacciner est passée de 71 % à 82,5 % après avoir assisté à un webinaire éducatif sur les vaccins contre la COVID-19 destinés spécifiquement aux patients atteints de cancer et à leurs soignants (154).
- Dans une étude menée dans un centre de dialyse urbain qui dessert une population de patients principalement noirs aux États-Unis, 49 % des répondants ont indiqué qu'ils seraient disposés à recevoir un vaccin contre la COVID 19, 34 % ont dit ne pas être disposés à le recevoir et 17 % étaient incertains (155).
- Si un vaccin avait été offert dans un centre de dialyse, la réticence à le recevoir chez les patients en hémodialyse aux États-Unis aurait diminué de 20 % à 18 % (156).
- Trois études ont analysé l'intention de se faire vacciner des adultes handicapés. Deux ont démontré que les adultes handicapés étaient un peu moins réticents à se faire vacciner que les adultes non handicapés (5 % contre 7 %) au Royaume-Uni (43, 140) et en Australie (141). L'autre étude, effectuée aux États-Unis, a indiqué que 62 % de ces adultes recevraient certainement ou probablement un vaccin contre la COVID-19 (157).
- Une étude menée auprès de 101 participants noirs vivant avec le VIH aux États-Unis a révélé de faibles intentions de se faire vacciner (32 %). Le faible niveau de scolarité et la méfiance à l'égard de la COVID-19 ont tous deux été associés à une augmentation de la réticence à se faire vacciner (158).
- Un groupe de patients qui ont reçu des soins pour des problèmes gastro-intestinaux et hépatiques chroniques aux États-Unis étaient plus susceptibles de suivre la recommandation de leur spécialiste au sujet de l'administration d'un vaccin (91 %) que le gouvernement ou leur médecin (75 %) ou leur employeur (56 %) (159).
- Les raisons les plus courantes pour hésiter à se faire vacciner étaient les préoccupations au sujet des effets secondaires, les préoccupations au sujet des problèmes de santé existants, le manque d'information adéquate, la méfiance à l'égard du gouvernement et les inquiétudes au sujet des effets à long terme (140, 141, 155, 156, 158-163).
- Tout comme dans la population en général, l'intention de se faire vacciner était associée positivement au sexe masculin (156, 159-161, 164, 165), à un plus grand nombre de comorbidités (164, 166), à un niveau d'études supérieures (148, 149, 156, 160, 165), à des revenus plus élevés (149, 159, 165), à l'origine ethnique blanche (149, 156, 160), au fait de s'être déjà fait vacciner contre la grippe (155, 156, 159, 160, 162, 164, 165), et d'avoir d'un âge plus avancé (149, 156, 157, 159-161).

ATTITUDES D'AUTRES POPULATIONS D'INTÉRÊT À L'ÉGARD DU VACCIN CONTRE LA COVID-19

Soixante-et-une études provenant du Canada, de l'Australie, de la Nouvelle-Zélande, du Royaume-Uni et des États-Unis ont été recensées en ce qui concerne les attitudes à l'égard de la COVID-19 dans d'autres populations d'intérêt. Ces populations comprennent la communauté LGBTQ+, les parents, ceux qui ont des affiliations religieuses, les immigrants, les jeunes (âgés de 14 à 24 ans), les personnes qui ont déjà eu une infection au SRAS-CoV-2, ainsi que les communautés urbaines et rurales. Les éléments généraux de janvier 2021 sont présentés ci-dessous et les résultats détaillés pour chacune des études figurent dans l'annexe (Tableau 7).

LGBTQ+

- Sept études ont évalué l'intention de se faire vacciner des personnes LGBTQ+ au Canada (78 à 80) et aux États-Unis (167 à 170). Trois études ont démontré que les membres de la communauté LGBTQ2+ étaient de 6 à 25 % plus disposés à accepter un vaccin que ceux de la communauté non-LGBTQ2+ (78, 80, 168). Deux études ont indiqué que les personnes non binaires, pansexuelles, allosexuelles, non-genrées, bispirituelles ou autres étaient plus susceptibles de se faire vacciner (1,6 à 4,38 %) (79, 169). Comparativement aux homosexuels, les participants regroupés dans la catégorie « Autre » identité sexuelle (p. ex., bisexuel, queer, multiples identités, amour du même genre) étaient moins susceptibles d'avoir l'intention de se faire vacciner (β = 1 102, P = 0,047) (167).

Communautés rurales et urbaines

- Douze études ont analysé les différences dans les intentions de se faire vacciner chez des résidents de la ville et de la campagne. Onze ont démontré que les résidents des villes étaient légèrement plus susceptibles d'avoir l'intention de se faire vacciner que les résidents de la campagne (10, 86, 87, 109, 115, 166, 171-175), alors qu'une a indiqué le contraire (176).

Affiliations religieuses

- Alors que douze études réalisées aux États-Unis et au Royaume-Uni ont évalué l'impact de la religion sur l'intention de se faire vacciner, toutes ces études ont associé certaines religions à la réticence à se faire vacciner (126, 171, 174, 176-183). Une étude a démontré que les personnes qui ont déclaré l'hindouisme ou le judaïsme comme religion étaient plus susceptibles que les athées ou les agnostiques d'accepter un vaccin (RC 1,66, HPDI à 95 % : 1,11 à 2,43) alors que celles qui ont déclaré que leur religion était musulmane (RC 0,75, HPDI à 95 % : 0,57 à 0,96) ou autre (RC 0,72, HPDI à 95 % : 0,62 à 0,82) étaient moins susceptibles d'avoir l'intention de se faire vacciner (178).
- Dans une étude britannique, les personnes déclarant être de confession chrétienne étaient significativement plus susceptibles de se faire vacciner si des passeports vaccinaux étaient instaurés pour les voyages intérieurs (RCa 1,23, IC à 95 % : de 1,08 à 1,41) et internationaux (RCa 1,22 IC à 95 % : de 1,07 à 1,39) par rapport aux athées et aux agnostiques (20).

- Une étude quasi expérimentale menée auprès de 709 électeurs inscrits non vaccinés dans le Dakota du Sud, aux États-Unis, a montré que les messages émanant d'un chef religieux avaient un effet positif statistiquement significatif sur l'intention de se faire vacciner, alors que les messages émanant d'un chef politique ou médical n'en avaient pas (21).
- Une étude réalisée auprès de 102 adultes juifs Haredi (ultra-orthodoxes) de New York entre décembre 2020 et janvier 2021 a révélé une forte réticence à se faire vacciner alors que 12 % des répondants étant prêts à accepter de se faire vacciner et de faire vacciner les membres de leur famille, que 47 % étaient très réticents et que 41 % étaient indécis. Les prédicteurs indépendants de la réticence à se faire vacciner étaient la croyance que l'infection naturelle était meilleure qu'un vaccin pour développer l'immunité, être d'accord avec le fait que l'infection antérieure au SRAS-CoV-2 avait créé des anticorps qui évitaient de devoir porter un couvre-visage ou de respecter la distanciation sociale, ainsi que la perte de confiance envers les médecins en raison de la pandémie (183).
- Dans une étude réalisée au Québec, 28 % des répondants qui n'avaient pas l'intention de se faire vacciner croyaient que la vaccination était incompatible avec leurs croyances religieuses ou leurs principes personnels (90).

Parents

- Dix études ont révélé que les participants étaient plus disposés à accepter un vaccin contre la COVID-19 pour eux-mêmes que pour leurs enfants (16, 19, 94, 135, 151, 164, 184-187). Une étude a montré que les parents étaient plus susceptibles de faire vacciner leurs enfants qu'eux-mêmes (188). Les personnes qui ont des enfants plus jeunes (0 à 4 ans) étaient plus réticentes envers la vaccination que celles dont les enfants ont plus de 5 ans (14, 16, 43).
- L'intention de se faire vacciner des parents et des enfants sont fortement corrélées les unes avec les autres, puisque les parents qui avaient l'intention de se faire vacciner étant plus susceptibles de vouloir faire vacciner leurs enfants (11, 13-16, 151). Tout comme dans la population en général, les parents qui sont dans des ménages à faible revenu (11, 14, 16, 19, 188), qui sont plus jeunes (17, 19, 188, 189), et moins instruits (14, 16, 17, 184, 188), qui ont déjà refusé d'autres vaccins (17, 19, 189), qui sont des femmes (14, 16, 17, 188) ou des membres de minorités ethniques (16-19, 185) sont ceux qui étaient plus susceptibles de refuser un vaccin pour leurs enfants.
- Une étude effectuée à Montréal auprès de 380 parents d'enfants de 2 à 17 ans a révélé que 61 % d'entre eux étaient très susceptibles, 25 % étaient assez susceptibles, 9,2 % étaient assez peu susceptibles et 4,5 % étaient très peu susceptibles de faire vacciner leurs enfants. Ceux qui appartenaient à une minorité visible étaient plus susceptibles de refuser de faire vacciner leurs enfants que les autres (32,9 % c. 9,5 %) (18).

Jeunes

- Dans un sondage effectué par texto auprès de 911 jeunes âgés de 14 à 24 ans aux États-Unis, 80,7 % se sont dits disposés à se faire vacciner si le vaccin était sécuritaire et qu'il était recommandé de le recevoir. Les jeunes Noirs (RC = 3,31) étaient plus susceptibles de refuser la vaccination alors que les jeunes Asiatiques (RC = 0,46) étaient moins susceptibles de refuser la vaccination que les jeunes Blancs (P < 0,001) (190).

- Dans le cadre d'un sondage effectué en janvier et en février 2021, 71 % des jeunes canadiens de 12 à 17 ans ont dit avoir l'intention de se faire vacciner (81).

Immigrants

- Dans un échantillon de 32 immigrants au Royaume-Uni, 28 % ont dit qu'ils se feront certainement vacciner, 59 % étaient incertains et 6 % refuseraient le vaccin (191). Deux études menées au Royaume-Uni font état de multiples obstacles à la vaccination des migrants, comme l'accès à la technologie, le fait de ne pas avoir de médecin, l'accès à l'information sur les vaccins dans leur propre langue, l'absence de vaccination dans des endroits où ils se rendent souvent comme les cliniques sans rendez-vous et les organismes de bienfaisance, ainsi que l'absence de communication claire selon laquelle le vaccin serait fourni gratuitement (191, 192).
- Dans une étude australienne, les personnes nées à l'étranger étaient plus susceptibles de déclarer leur intention de se faire vacciner que celles nées en Australie (70,7 % contre 67,2 %). Cela était plus évident pour les personnes arrivées au cours des dix dernières années (74,6 %) par rapport à celles qui sont arrivées il y a plus de dix ans (69,1 %) (141).

Infection antérieure au SRAS-CoV-2

- Deux études réalisées aux États-Unis ont démontré que les personnes qui avaient déjà été infectées par le SRAS-CoV-2 étaient moins susceptibles d'avoir l'intention de se faire vacciner que celles qui n'avaient pas été infectées (115, 193).

Méthodologie

Avant le début de cette revue rapide, un protocole prédéfini pour ce type de revue a été élaboré pour s'assurer que les méthodes étaient reproductibles, transparentes et uniformes. Le protocole est disponible sur demande. Cette revue rapide sera tenue à jour et les mises à jour contiendront des articles de recherche clé publiés jusqu'à la dernière date de recherche.

Publications et préimpressions

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Des détails sur cette stratégie de recherche sont disponibles sur demande. Une recherche ciblée par mot-clé dans les titres et les résumés des articles a été effectuée dans ces bases de données et dans la liste en Excel. Les termes de recherche utilisés comprenaient : (« vaccin* » OU « immuni* ») ET (« accept* » OU « hesitan* » OU « preference » OU « confidence » OU « intent* » OU « willing* » OU « readiness » OU « behavio* » OU « knowledge » OU « attitude* » OU « belief* » OU « believe* » OU « perception » OU « influence* » OU « reject* » OU « refus* » OU « oppos* » OU « consent* » OU « fear » OU

« motiv* » OU « anti vax* » OU « antivax* » OU « trust* » OU « mistrust* » OU « anti vaccin* » OU « pro vaccine* » OU « provax* » OU « pro vax » OU « decision* » OU « decid* » OU « uptake »). La recherche a été effectuée le 16 octobre 2020. La première mise à jour a été effectuée le 30 novembre 2020, la deuxième, le 5 janvier 2021, la troisième, le 3 février 2021, la quatrième, le 2 mars 2021, la cinquième, le 2 avril 2021, la sixième le 3 mai 2021, la septième le 3 juin 2021 et la huitième le 2 juillet 2021.

Littérature grise

Une recherche dans la littérature grise a été effectuée afin de compléter la recherche dans la base de données. La recherche dans la littérature grise portait uniquement sur les recherches effectuées au Canada. Lorsque le temps le permettra, la recherche dans la littérature grise sera étendue à la recherche effectuée en Australie, en Nouvelle-Zélande, aux États-Unis et au Royaume-Uni. Une liste détaillée des sites Web inclus dans la recherche est disponible dans le protocole. La recherche dans la littérature grise a été effectuée les 5 et 6 novembre 2020. La première recherche dans la littérature grise mise à jour a été effectuée les 9 et 10 décembre 2020, la deuxième, le 4 janvier 2021, la troisième, les 1er et 2 février 2021, la quatrième, le 7 mars 2021, la cinquième, entre le 13 et le 22 avril 2021, la sixième, du 3 au 7 mai 2021 et la septième, entre le 9 et le 11 juin.

Qualité de l'instrument d'enquête

Trois critères utilisés pour déterminer la qualité de l'instrument d'enquête ont été indiqués. Il s'agit notamment de la disponibilité de l'outil d'enquête utilisé dans le rapport, de l'utilisation de la recherche formative pour concevoir l'enquête et des preuves pré-test associées à l'enquête. Un oui ou un non a été fourni pour chaque critère. Si l'information n'a pas été communiquée, « non » a alors été sélectionné. Ces critères permettent d'évaluer dans quelle mesure les éléments de l'enquête évaluent les concepts théoriques sur lesquels l'enquête est axée, sont comparables à ceux d'autres enquêtes et permettent de déterminer si l'instrument était complet, clair et valable lorsqu'il était appliqué à la population cible. Il y a un risque accru de biais lorsque ces caractéristiques sont manquantes (194).

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

Préparée par : Tricia Corrin et Austyn Baumeister, LNM, Groupe des sciences émergentes, ASPC.

Connaissances mobilisées par l'Office of the Chief Science Officer phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca

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ANNEXE : TABLEAUX DES DONNÉES PROBANTES

ADOPTION DU VACCIN ET RESPECT DES MESURES DE SANTÉ PUBLIQUE APRÈS LA VACCINATION

Tableau 1. Éléments de preuve sur l'adoption du vaccin et de l'adhésion aux mesures de santé publique après la vaccination (n=37)

ÉTUDE	MÉTHODES ET OUTILS DE SONDAGE	RÉSULTATS CLÉS DE CAC
ADOPTION DE VACCINS		
TRAVAILLEURS DE LA SANTÉ		
CANADA		
Dzieciolowska (2021) (1) *nouveau* Étude transversale Canada	L'adoption du vaccin a été évaluée par un sondage en ligne menée auprès de 2 761 infirmières, médecins, aides-soignants et membres de l'administration hospitalière travaillant dans 17 établissements de santé de Montréal, afin de déterminer les facteurs prédictifs de l'adoption du	• 80,9 % des personnes à qui l'on a proposé un vaccin l'ont accepté et 19,1 % l'ont refusé. • L'analyse multivariée a révélé que les hommes (RCa 1,62, IC à 95 % : de 1,16 à 2,26), ceux âgés de 50 à 59 ans (RCa 1,62, IC à 95 % : de 1,07 à 2,44) ou 60 ans et plus (RCa 3,28, IC à 95 % : de 1,74 à 6,18), avaient des contacts professionnels avec des patients atteints de la COVID-19 (RCa 3,88, IC à 95 % : de 2,29 à 6,58), ou ont travaillé dans des centres de réadaptation (RCa 1,76, IC à

Déc. 2020	vaccin. Le vaccin a été proposé à tous les travailleurs de la santé. Sujets des questions : 1) Adoption du vaccin 2) Réticence à se faire vacciner Outils de sondage disponibles? Oui Recherches formatives menées? Non Enquête prétestée? Non	95 % : de 1,17 à 2,66) étaient plus susceptibles de se faire vacciner lorsqu'on le leur proposait. • Les préoccupations ou les raisons de refus les plus courantes chez les personnes qui n'ont pas accepté de se faire vacciner étaient la nouveauté du vaccin (82 %), le fait qu'elles préféraient que d'autres personnes soient vaccinées en premier (77 %), le fait qu'elles estimaient manquer de renseignements concernant le vaccin (74 %) et le fait qu'elles n'avaient pas assez de temps pour prendre une décision (60 %). • 74,1 % des personnes ont déclaré qu'elles accepteraient de se faire vacciner à l'avenir, 53,2 % voulant attendre quelques mois et 31,9 % voulant attendre un an. • Les personnes qui ne prévoient jamais d'accepter de se faire vacciner étaient plus susceptibles de citer le fait de ne pas faire confiance aux experts ou aux sociétés pharmaceutiques, de préférer l'immunité naturelle, de croire que le risque de la vaccination l'emporte sur le risque d'être infecté par la COVID, ou d'avoir déjà eu une mauvaise réaction à un vaccin.
États-Unis		
Fossen (2021) (34) Étude transversale États-Unis Janvier à mars 2021	Cette étude visait à évaluer l'adoption du vaccin chez 3 401 employés d'un hôpital de 437 lits à Arlington, en Virginie, qui pouvaient recevoir un vaccin contre la COVID-19 à compter de janvier 2021. Sujets des questions : 1) Adoption du vaccin	• En date du 10 mars 2021, 71 % avaient accepté la première dose d'un vaccin contre la COVID-19. • L'adoption du vaccin a été associée positivement à l'âge (50 ans et plus) (RC 1,85, IC à 95 % : 1,53 à 2,24, P < 0,01), au travail dans un service d'hospitalisation (RC 1,19, IC à 95 % : 1,01 à 1,42, P = 0,02) et à la race blanche (RC 4,55, IC à 95 % : 3,74 à 5,52, P < 0,01).
Jameson (2021) (31) Étude de cohorte	Au cours d'un programme de vaccination dans un hôpital urbain de taille moyenne dans la région du Midwest des États-Unis à partir de décembre 2020, le	• Au 24 mars 2021, 70 % avaient accepté un vaccin et 30 % l'avaient refusé.

É.-U. Décembre 2020 à mars 2021	vaccin BNT162b2 a été proposé à l'ensemble des 4 318 travailleurs de la santé. L'étude visait à déterminer l'utilisation du vaccin et l'efficacité du vaccin chez les personnes vaccinées.	
Oliver (2021) *préimpression* (30) Étude transversale ÉTATS-UNIS Décembre 2020 à février 2021	Tous les employés de deux grands systèmes de soins de santé intégrés (un privé et un public) à New York étaient admissibles à recevoir un vaccin contre la COVID-19 à compter du 14 décembre 2020. Un sondage en ligne a été réalisé auprès de 1 933 travailleurs de la santé à qui le vaccin a été offert afin d'évaluer l'adoption du vaccin, ainsi que les raisons de son acceptation et de son refus. Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Oui	• Parmi les répondants à qui le vaccin a été offert, 81 % ont dit l'avoir reçu, 11 % prévoient l'obtenir, mais n'ont pas encore pris de rendez-vous, et 8 % ont choisi de ne pas se faire vacciner. • Dans l'analyse bidirectionnelle, l'adoption du vaccin était plus élevée chez les hommes que chez les femmes (88 % comparativement à 80 %, p < 0,001). Les personnes de moins de 40 ans (86 %) et de plus de 60 ans (85 %) affichaient des taux de participation plus élevés que celles de 40 à 49 ans (79 %) et de 50 à 59 ans (74 %), P < 0,001. En outre, les personnes d'origine ethnique non hispanique ou non déclarée (84 %) étaient plus susceptibles de se faire vacciner que les travailleurs de la santé hispaniques (69 %), P < 0,001. • Dans l'analyse multivariée, les travailleurs de la santé noirs étaient moins susceptibles de se faire vacciner que les travailleurs de la santé blancs (RC = 0,38, IC à 95 % : 0,24 à 0,59, P < 0,001). Comparativement aux médecins, les infirmières (RC = 0,37, IC à 95 % : 0,21 à 0,65, P = 0,001), les personnes occupant des postes administratifs, de logistique et de gestion (RC = 0,46, IC à 95 % : 0,36 à 0,78, P = 0,006) et les professionnels paramédicaux (RC = 0,48, IC à 95 % : 0,27 à 0,81, CP = 0,007) étaient moins susceptibles de se faire vacciner. • Les personnes qui n'ont pas reçu le vaccin antigrippal étaient moins susceptibles de vouloir recevoir le vaccin contre la COVID-19 que celles qui l'avaient reçu (RC = 0,28, IC à 95 % : 0,18 à 0,44, P < 0,001).

		• Celles qui se sont dites préoccupées par l'innocuité du vaccin (RC = 0,39, IC à 95 % : 0,28 à 0,55, P < 0,001), celles qui craignent d'être des cobayes (RC = 0,44, IC à 95 % : 0,31 à 0,60, P < 0,001) et celles qui n'étaient pas d'accord avec les déclarations sur l'importance du vaccin pour protéger les autres (RC = 0,37, IC à 95 % : 0,27 à 0,52, P < 0,001) étaient moins susceptibles de se faire vacciner.
Amin (2021) (27) Étude transversale ÉTATS-UNIS Janvier 2021	À compter du 17 décembre 2020, tous les travailleurs de la santé du service d'urgence d'un grand hôpital urbain de Chicago, en Illinois, pouvaient se faire vacciner. Les liens avec l'adoption du vaccin ont été évalués dans un sondage en ligne réalisé auprès de 240 travailleurs de la santé. Sujets des questions : 2) Adoption du vaccin Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 92 % ont déclaré avoir reçu le vaccin ou prévoir se faire vacciner alors que 8 % ont déclaré qu'ils ne se feront pas vacciner. • Les taux d'acceptation du vaccin variaient selon la profession, puisque les médecins avaient des taux d'acceptation plus élevés que les infirmières et les techniciens en radiologie. • Parmi les 8 % qui ont refusé la vaccination, la majorité s'est identifiée comme étant Noirs (65 %), était âgée entre 51 et 60 ans et occupait des postes dans des catégories variées. • Parmi les raisons pour refuser le vaccin, mentionnons une infection antérieure à la COVID-19, ainsi que des préoccupations au sujet de la nouveauté du vaccin et des effets secondaires. •
Schrading (2021) (22) Étude transversale ÉTATS-UNIS Janvier 2021	Trois semaines après que le vaccin contre la COVID-19 ait été offert aux professionnels de la santé œuvrant dans les services d'urgence dans 20 centres médicaux universitaires urbains des États-Unis, un sondage en ligne a été effectué auprès de 1 321 de ces professionnels. L'objectif était de décrire les différences dans les taux de vaccination entre les divers types de professionnels de la santé œuvrant dans les services	• 86 % des personnes à qui on a offert le vaccin ont choisi de le recevoir et 14 % ont refusé. • Parmi les médecins et les fournisseurs de soins en pratique avancée, 37 sur 674 (5,5 %) ont refusé le vaccin comparativement à 77 sur 345 (22,3 %) des infirmières et à 71 sur 302 (23,5 %) des professionnels de la santé qui œuvraient dans des milieux non cliniques. Parmi ceux qui ont refusé le vaccin, les raisons les plus courantes étaient des préoccupations relatives à l'innocuité (45,4 %), des problèmes de santé (13,5 %) et un diagnostic antérieur de COVID-19 (13,5 %).

	d'urgence et les raisons pour lesquelles ils ont refusé le vaccin. Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Les professionnels de la santé noirs non hispaniques affichaient les taux d'adoption les plus faibles (65,4 %), suivis des Hispaniques ou des Latinx (76,7 %). Les taux d'adoption les plus élevés ont été observés chez les professionnels de la santé non hispaniques autres (88,9 %), blancs non hispaniques (88,5 %) et asiatiques non hispaniques (87,3 %). • Les hommes affichaient des taux d'adoption plus élevés (93,5 %) que les femmes (88,5 %). • Après la vaccination, les personnes vaccinées ont déclaré qu'elles se sentaient plus en sécurité (86,7 %) et que les membres de leur ménage se sentaient aussi plus en sécurité (87,1 %). Les personnes vaccinées prévoyaient utiliser la même quantité d'ÉPI au travail (89,8 %) et en public (91,8 %).
Pamplona (2021) (33) Étude transversale É.-U. Janvier 2021	L'adoption du vaccin et les hésitations au cours d'un programme de vaccination mis en œuvre entre le 13 et le 21 janvier 2021 ont été enregistrées auprès de 157 membres du personnel de quatre cliniques du Renal Research Institute et d'un programme de dialyse à domicile à New York. Sujets des questions : 1) Prise du vaccin 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• 73,2 % étaient vaccinés et 26,8 % n'étaient pas vaccinés. • 3,8 % du personnel a déclaré avoir hésité à se faire vacciner et n'a pas reçu de vaccin. Les raisons n'ont pas été rapportées. • Le reste du personnel qui n'a pas été vacciné comprend : les personnes en congé (2,5 %), les femmes enceintes ou qui allaitent (5,1 %) et les personnes ayant déjà été infectées par le SRAS-CoV-2 (15,3 %). • Le personnel ayant des antécédents d'infection confirmée par le SRAS-CoV-2 il y a plus de 90 jours ou à un moment inconnu dans le passé s'est vu proposer la vaccination, mais a souhaité recevoir le vaccin plus tard.
ROYAUME-UNI		

Bell (2021) *préimpression* (32) Étude transversale et qualitative ROYAUME-UNI Janvier à mars 2021	1 658 travailleurs de la santé et 261 travailleurs sociaux ont répondu à une enquête en ligne et 20 participants ont été interviewés afin de mieux comprendre les croyances, les attitudes et les comportements en matière de vaccination. Thèmes des questions : 1) Prise du vaccin 2) Perception à l'égard des vaccins Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Oui	• 1 762 (91,9 %) participants se sont vus proposer la vaccination. Parmi eux, 6,6 % ont refusé ou vont refuser le vaccin. • Par rapport à leurs homologues, des taux plus élevés de refus du vaccin ont été observés chez les Noirs ou les Noirs des Caraïbes (22 %), les personnes âgées de 25 à 35 ans (8,4 %) et les chrétiens (6,7 %). • La probabilité de refuser un vaccin était significativement plus élevée si les personnes interrogées étaient noires, britanniques ou noires mixtes (RR ajusté 5,5, IC 95 % : 2,2 % à 13,4 %), se sentaient sous pression de leur employeur pour se faire vacciner (RR ajusté 1,75, IC 95 % : 1,2 % à 2,4 %), ou s'inquiétaient des effets secondaires (RR ajusté 1,68, IC 95 % : 1,1 % à 2,4 %). • Les probabilités d'accepter un vaccin étaient significativement plus élevées si un vaccin contre la grippe avait été pris au cours des deux dernières années (RR ajusté 0,27, IC 95 % : 0,1 % à 0,47 %) et la conviction combinée que les vaccins sont sûrs, importants et efficaces (RR ajusté 0,51, IC 95 % : 0,3 % à 0,8 %). • Les raisons du refus ou de l'intention de refuser un vaccin comprennent la crainte des effets secondaires (51 %), le manque de recherche (50 %) et l'efficacité (21 %). • Les raisons les plus courantes de la vaccination sont la protection des amis et des familles (64 %), la protection personnelle (57 %) et la protection des patients (28 %). • Les répondants noirs ou métis étaient moins susceptibles de percevoir le vaccin comme sûr, comme important pour se protéger ou protéger leur famille, de croire que la vaccination est nécessaire pour revenir à la normale, de croire que leurs amis et leur famille ne s'attendent pas à ce qu'ils se fassent vacciner et de s'inquiéter davantage des effets secondaires.

		• Pour la partie entretien, tous les participants s'étaient vus proposer la vaccination, 13 avaient été vaccinés et 7 avaient refusé. • Les entretiens ont révélé des problèmes d'accès (manque de clarté pour ceux qui ne font pas partie du National Health Service pour se faire vacciner), de perception du risque et de la gravité (faible perception du risque associé au fait de ne pas avoir besoin d'un vaccin), de manque de confiance (dans le vaccin, les décideurs politiques et l'industrie pharmaceutique et de la santé), d'efficacité du vaccin, d'importance du vaccin pour protéger les autres ou pour revenir à la normale, de pression pour se faire vacciner, de préoccupations concernant les allergies, de répercussions sur la procréation, de désir de plus d'informations sur le vaccin et de désir d'avoir l'assurance que le vaccin est halal.
Martin (2021) *préimpression* (25) Étude transversale ROYAUME-UNI Décembre 2020 à février 2021	Les liens avec l'adoption du vaccin ont été évalués chez 19 044 travailleurs de la santé de l'une des plus importantes fiducies d'hôpitaux de soins actifs au Royaume-Uni. Tous les membres du personnel étaient admissibles à recevoir le vaccin ARNm BNT162b2 ChAdOx1 nCoV-19 à compter du 12 décembre 2020. Sujets des questions : 1) Adoption du vaccin	• Au 3 février 2021, la proportion des travailleurs de la santé qui avaient reçu une dose du vaccin était de 64,5 %. • Le nombre de vaccins par semaine a atteint un sommet pendant la semaine du 11 au 17 janvier et diminue depuis. • L'adoption du vaccin a été associée positivement à une augmentation de l'âge (30 ans : RCa = 0,48, IC à 95 % : 0,44 à 0,53; 51 à 60 ans : RCa = 1,19, IC à 95 % : 1,07 à 1,31 comparativement à 41 à 50 ans) et au sexe masculin (RCa = 1,24, IC à 95 % : 1,15 à 1,35). • Comparativement aux travailleurs de la santé blancs, l'adoption du vaccin était plus faible chez les Noirs (RCa = 0,30, IC à 95 % : 0,26 à 0,34) et les Asiatiques du Sud (RCa = 0,67, IC à 95 % : 0,62 à 0,72). • Les personnes qui avaient des antécédents d'infection par le SRAS-CoV-2 étaient moins susceptibles de se faire vacciner (RCa = 0,71 [IC à 95 % : 0,60 à 0,85).

		• Les personnes vivant dans les régions les plus démunies étaient moins susceptibles de se faire vacciner (p < 0,001).
Hall (2021) *préimpression* (26) Étude de cohorte ROYAUME-UNI Décembre 2020 à février 2021	L'étude SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) est une étude de cohorte prospective portant sur 23 324 membres du personnel travaillant dans 36 hôpitaux financés par le secteur public. À compter d'août 2020, les facteurs de risque de référence, l'état de la vaccination, les symptômes et les résultats des tests PCR et des tests d'anticorps ont été consignés toutes les deux semaines. L'étude visait à déterminer les facteurs associés à l'adoption du vaccin ARNm BNT162b2 et à son efficacité chez les personnes vaccinées. Sujets des questions : 1) Adoption du vaccin	• Au 5 février 2021, les proportions de membres du personnel qui avaient reçu une dose et deux doses du vaccin étaient 89 % et 8 %, respectivement. • L'adoption du vaccin a été significativement plus faible chez les personnes ayant déjà eu une infection au SRAS-CoV-2 (RCa = 0,59, IC à 95 % : 0,54 à 0,64), les femmes (RCa = 0,72, IC à 95 % : 0,63 à 0,82), les moins de 35 ans (RCa = 0,78, IC à 95 % : 0,64 à 0,96), les Noirs, les Asiatiques ou les membres des groupes ethniques minoritaires (RCa = 0,26, IC à 95 % : 0,21 à 0,32), celles qui vivent dans des quartiers plus défavorisés (RCa = 0,75, IC à 95 % : 0,65 à 0,87) et qui travaillent comme portiers/gardiens de sécurité/gardiens dans des domaines (RCa = 0,61, IC à 95 % : 0,42 à 0,90) ou sages-femmes (RCa = 0,74, IC à 95 % : 0,57 à 0,97).
Tulloch (2021) *préimpression* (28) Étude transversale ROYAUME-UNI Janvier 2021	Tous les membres du personnel et les résidents de 87 maisons de santé de la région du Conseil municipal de Liverpool pouvaient se faire vacciner contre le COVID-19 à compter du 23 décembre 2020. On a effectué un sondage en ligne auprès de 46 gestionnaires du personnel afin de déterminer les liens avec l'adoption du vaccin et les raisons qui ont fait hésiter les gens à se faire vacciner. Ce sondage était autodéclaré et les opinions des membres du personnel ont été compilées par un membre de la	• 52,6 % (n = 1 119) ont reçu leur première dose du vaccin avec un taux de vaccination moyen par maison de santé de 51,4 % (IC à 95 % : 43,9 à 58,8 %). • Les raisons les plus courantes pour ne pas s'être fait vacciner étaient les préoccupations au sujet du manque de recherche sur le vaccin (37,0 %), le fait que le personnel était à l'extérieur du site pendant les séances de vaccination (36,5 %), les préoccupations en ce qui concerne la grossesse et la fertilité (5,6 %) et les préoccupations au sujet des réactions allergiques (3,2 %). • Si les problèmes logistiques étaient résolus (p. ex., membre du personnel qui n'était pas sur place le jour où le vaccin était administré), le taux moyen de vaccination par maison de santé aurait

	direction de la maison de santé. Il est donc possible qu'il ne reflète pas le point de vue de tous les membres du personnel. Sujets des questions : 1) Adoption du vaccin	pu augmenter à 69,8 % (IC à 95 % : 63,2 à 76,3 %). • Les membres du personnel ont déclaré que les méthodes qui aideraient à réduire la réticence à l'égard de la vaccination comprenaient des réunions individuelles pour discuter des préoccupations (34,8 % des maisons de santé), des réunions destinées aux membres du personnel (15,2 %), du matériel éducatif (15,2 %), des discussions individuelles avec les omnipraticiens ou les membres de l'équipe de vaccination (10,9 %) et des gestionnaires qui prêchent par l'exemple et encouragent les membres du personnel (6,5 %).
Azamgarhi (2021) (29) Étude de cohorte ROYAUME-UNI Janvier 2021	Cette étude visait à évaluer l'adoption et l'efficacité du vaccin BioNTech de Pfizer chez 2 577 travailleurs de la santé dans un hôpital de soins tertiaires. Tous les membres du personnel ont reçu leur première dose du vaccin sur une période de 8 jours jusqu'au 14 janvier 2021. Sujets des questions : 1) Adoption du vaccin	• 60,8 % du personnel a reçu une dose du vaccin. • L'adoption du vaccin était plus élevée chez les hommes que chez les femmes (65,0 % comparativement à 58,9 %, P = 0,006). • Les travailleurs de la santé blancs (70,4 %) et asiatiques (67,1 %) étaient les groupes ethniques les plus susceptibles de se faire vacciner. Les Noirs/Afro-Caraïbéens (27 %) et les races mixtes (43 %) étaient les moins susceptibles (P = 0,001) de le faire. • Selon la profession, les plus forts taux d'adoption du vaccin ont été observés chez les chirurgiens et le personnel médical (76 %), les professionnels paramédicaux (75,4 %), ainsi que le personnel administratif et de bureau (71,5 %) Les taux les plus faibles ont été observés chez les infirmières (52,9 %), le personnel de soutien clinique (49,2 %) et les porteurs, le personnel responsable de l'entretien et celui qui s'occupe de la restauration (30,5 %) (P = 0,001). • L'adoption du vaccin a augmenté avec l'âge. 74,4 % des 55 ans et plus ont reçu le vaccin, 64,6 % des 35 à 54 ans et 50,6 % des 16 à 34 ans.
ISRAËL		

Jabal (2021) (23) Étude de cohorte Israël Décembre 2020 à janvier 2021	Cette étude avait deux objectifs : 1) faire rapport sur l'adoption du vaccin chez environ 1 500 travailleurs de la santé dans un seul centre médical, et 2) décrire l'immunogénicité 21 jours après l'administration du vaccin ARNm BNT162b21 1 contre la COVID-19 chez 514 travailleurs de la santé. À compter de décembre 2020, le vaccin a été offert à tout le personnel. Sujets des questions : 1) Adoption du vaccin	• Au 21 janvier 2021, la proportion des travailleurs de la santé qui avaient reçu une dose du vaccin était d'environ 90 %.
Amit (2021) (24) Étude de cohorte Israël Décembre 2020 à janvier 2021	Cette étude avait deux objectifs : 1) faire rapport sur l'adoption du vaccin chez les 9 109 travailleurs de la santé dans un seul centre médical, et 2) évaluer les réductions des taux d'infection par le SRAS-CoV-2 et les taux de COVID-19 chez les travailleurs de la santé ayant reçu le vaccin BNT162b2 contre la COVID-19. À compter de décembre 2020, le vaccin a été offert à tout le personnel. Sujets des questions : 1) Adoption du vaccin	• Au 24 janvier 2021, les proportions de travailleurs de la santé qui avaient reçu une dose et deux doses du vaccin étaient de 79 % et de 66 %, respectivement.
PERSONNES EN SITUATION D'ITINÉRANCE		
Kuhn (2021) *préimpression* (41) Étude transversale	Le niveau d'adoption du vaccin et d'hésitation chez 90 personnes sans abri de Los Angeles (âgées de 18 ans et plus) a été évalué à l'aide d'un sondage effectué par téléphone cellulaire.	• Parmi les 90 participants, 17 se sont vus offrir un vaccin et de ce nombre, 10 ont accepté et 7 ont refusé. • Parmi les 73 participants à qui le vaccin n'a pas été offert, 51 % ont dit qu'ils le prendraient s'il leur était offert, 32 % ont dit qu'ils ne se feraient pas vacciner et 17 % ont refusé de répondre.

ÉTATS-UNIS Décembre 2020 à février 2021	Sujets des questions : 1) Adoption du vaccin 2) Hésitation par rapport à la vaccination 3) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Dans l'ensemble, 48 % des personnes ont refusé un vaccin lorsqu'il leur était offert, ont dit qu'elles le refuseraient s'il leur était offert ou ont refusé de répondre et ont donc été jugées « hésitantes face à la vaccination ». • Parmi les participants qui hésitaient à se faire vacciner, les raisons les plus souvent mentionnées étaient la peur des effets secondaires (37 %), le désir d'avoir plus d'information (30 %) et le fait qu'ils ne veulent pas recevoir de vaccin (27 %). • Selon une analyse multivariée, les personnes qui ont une perception élevée de la menace que représente la COVID-19 (RC = 0,25, P = 0,02) et celles qui faisaient confiance à des sources officielles (RC = 0,37, P = 0,08) étaient beaucoup moins susceptibles d'hésiter à se faire vacciner. Celles qui avaient un comportement hautement protecteur (RC = 3,63, P = 0,02) et celles qui faisaient confiance à leurs contacts personnels (RC = 2,70, P = 0,07) étaient plus susceptibles d'hésiter.
PRISONS		
Chin (2021) (38) Étude transversale États-Unis Décembre 2020 à mars 2021	Le 22 décembre 2020, le California Department of Corrections and Rehabilitation (CDCR) a lancé un programme de vaccination pour les résidents de ses 35 établissements carcéraux. Des 97 779 personnes incarcérées, 64 633 ont reçu un vaccin. Sujets des questions : 1) Adoption du vaccin	• 66,5 % ont accepté au moins une dose de vaccin alors que 33,5 % l'ont refusée. Parmi ceux qui avaient refusé au départ et à qui le vaccin a de nouveau été offert (n = 1 962), 45,9 % alors ont accepté au moins une dose. • L'adoption du vaccin a été la plus élevée chez les Hispaniques (72,6 %, IC à 99,6 % : 72,1 à 73,1) et les Blancs (72,1 %, IC à 99,6 % : 71,3 à 72,9), suivis des Amérindiens ou des résidents de l'Alaska (67,7 %, IC à 99,6 % : 64,4 à 71,0), des Asiatiques ou des insulaires du Pacifique (67,7 %, IC à 99,6 % : 64,8 à 70,6), et des Noirs (54,9 %, IC à 99,6 % : 54,3 à 55,5). • Les personnes plus âgées et vulnérables sur le plan médical étaient plus susceptibles d'accepter

		un vaccin que les personnes plus jeunes et en meilleure santé.
Berk (2021) *préimpression* (37) Étude transversale États-Unis Décembre 2020 à février 2021	L'adoption du vaccin a été évaluée chez 1 474 membres du personnel et 1 447 personnes incarcérées au Rhode Island Department of Corrections à qui un vaccin a été offert. Le programme de vaccination a débuté le 22 décembre 2020. Toutes les premières doses ont été administrées au plus tard le 5 février et les deuxièmes, au plus tard le 5 mars 2021. Le vaccin a été offert en 4 phases : 1) les personnes à risque élevé (65 ans et plus ou 55 ans et plus avec des comorbidités particulières); 2) les plus petits établissements afin d'obtenir l'immunité collective; 3) le plus grand établissement à sécurité moyenne restant; 4) toutes les personnes qui avaient déjà obtenu un résultat positif au test de dépistage de COVID-19 dans les jours et les personnes qui avaient initialement refusé le vaccin, mais qui l'ont ensuite accepté. Sujets des questions : 1) Adoption du vaccin	• Parmi le personnel correctionnel, 68,4 % des gens ont accepté un vaccin et 31,6 % l'ont refusé. Les motifs du refus n'ont pas été indiqués. • Parmi toutes les personnes incarcérées, 76,4 % des gens ont accepté un vaccin et 23,6 % l'ont refusé. Les motifs du refus n'ont pas été indiqués. • Dans la première phase de vaccination, 90,9 % des personnes incarcérées à haut risque (n = 143) ont accepté le vaccin et 9,1 % l'ont refusé. • Dans la deuxième phase, soit celle qui a eu lieu dans les plus petits établissements, 64,5 % des gens ont accepté de se faire vacciner et 34,6 % l'ont refusé (n = 222). • Dans la troisième phase, parmi ceux qui se trouvaient dans le plus grand établissement (n = 730), 82,9 % ont accepté le vaccin et 17,1 % l'ont refusé. • Dans la dernière phase destinée aux personnes incarcérées restantes (n = 352), 64,8 % ont accepté le vaccin et 35,2 % l'ont refusé.
UNITÉS MILITAIRES		
Segal (2021) (55) Étude transversale	Les taux d'adoption du vaccin entre les bataillons en première ligne et les unités militaires hautement essentielles (groupe A, n = 12 642) et les unités militaires de la zone	• En date du 18 février 2021, 84,8 % de l'ensemble de la population à l'étude avait reçu la première dose d'un vaccin contre la COVID-19, 3,88 % avaient déjà eu une infection au SRAS-CoV-2 et 11,34 % avaient refusé le vaccin.

Israël Décembre 2020 à février 2021	administrative arrière et de soutien (groupe B, n = 6 077) ont été comparés. Ces 70 unités étaient composées de 18 719 personnes des deux sexes, la plupart sans comorbidités importantes. Le programme de vaccination a débuté à la fin de décembre 2020. Sujets des questions : 1) Adoption du vaccin	• L'adoption du vaccin était plus élevée dans le groupe A que dans le groupe B (86,4 % comparativement à 81,4 %, P < 0,001). L'âge moyen des membres du groupe A était légèrement inférieur et comprenait un plus grand nombre d'hommes (P < 0,001), mais les deux groupes avaient des taux cumulatifs similaires de SRAS-CoV-2 (P = 0,677).
Talmy (2021) (39) Étude transversale Israël Décembre 2020 à février 2021	Cette étude visait à évaluer l'adoption réelle du vaccin et les efforts de communication en soins primaires associés, ce qui incluait des conférences de groupe, des consultations sur place et des visites dans des bureaux de soins primaires. Les intentions en ce qui concerne la vaccination ont été recueillies par sondage téléphonique avant la campagne de vaccination. Pendant la campagne, 511 soldats d'une unité militaire se sont vu offrir un vaccin. Le site de vaccination a été accessible pendant deux périodes différentes. Les personnes qui ont refusé la vaccination après la séance initiale ont été contactées pour fixer des rendez-vous à titre volontaire pour des visites à la clinique afin de discuter de leurs préoccupations particulières. Sujets des questions : 1) Adoption du vaccin 2) Intentions en ce qui concerne la vaccination	• Avant la campagne de vaccination, 77,7 % des soldats avaient l'intention de se faire vacciner, 17,6 % avaient l'intention de refuser et 4,7 % étaient incertains. • 70,3 % ont assisté à une conférence de groupe, 6,5 % sont venus consulter un médecin sur place et 3,7 % se sont rendus dans une clinique de soins primaires. • Parmi les 90 soldats qui ont déclaré ne pas avoir l'intention de se faire vacciner, 60,0 % ont assisté aux conférences de groupe, 31,1 % sont venus pour une consultation sur place et 16,7 % ont participé à des visites de soins primaires pour discuter de leurs motifs et de leurs préoccupations. • Entre le 3 janvier et le 18 février 2021, 89,8 % des soldats ont reçu au moins une dose du vaccin. • Sur les 90 soldats qui n'avaient pas l'intention de se faire vacciner, 42,2 % ont décidé de se faire vacciner. • 47,4 % des 28 soldats qui n'ont pas l'intention de se faire vacciner et qui sont venus pour consulter un médecin ont décidé de se faire vacciner (P = 0,004).

	3)	
ADULTES PLUS ÂGÉS (70 ANS ET PLUS)		
Office for National Statistics (2021) *non publiée* (35) Enquête transversale ROYAUME-UNI Février 2021	Les réponses de 2 070 adultes de plus de 80 ans ont été recueillies au moyen d'un sondage en ligne afin de déterminer la couverture vaccinale, les attitudes et l'effet de la vaccination sur les comportements de protection. Sujets des questions : 1) Adoption du vaccin 2) Attitudes à l'égard des vaccins 3) Comportements à l'égard des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 99,8 % des personnes ont déclaré qu'on leur avait offert un vaccin, 99 % ont ajouté avoir reçu au moins une dose et 15 % ont reçu au moins deux doses (6). • 41 % ont signalé des effets secondaires courants, incluant la sensibilité du bras à l'endroit où ils ont reçu l'injection (26 %). • 63 % ont déclaré que les effets secondaires subis n'influeraient pas sur leur décision d'obtenir la deuxième dose et 35 % ont affirmé que les effets secondaires les ont rendus plus susceptibles d'obtenir une deuxième dose. • Parmi les personnes qui avaient reçu au moins une dose, 43 % avaient rencontré quelqu'un en dehors de leur bulle, de leur ménage ou du personnel soignant à l'intérieur plutôt qu'à l'extérieur. • Parmi celles qui avaient reçu au moins une dose et qui s'étaient aventurées à l'extérieur de leur maison pour faire une activité, 49 % avaient rencontré à l'extérieur quelqu'un avec qui elles ne vivaient pas, 54 % étaient allés magasiner et 45 % étaient sorties de la maison pour participer à des activités de loisirs en plein air). Seulement 20 % ont déclaré ne pas avoir quitté la maison pour quelque raison que ce soit. • 25 % des personnes qui ont reçu leur première dose et 33 % de celles qui ont reçu les deux doses étaient prêtes à aller à l'hôpital pour une raison médicale. • 96 % encourageraient d'autres personnes à se faire vacciner. • 86 % subiraient probablement un test de dépistage de la COVID-19 s'ils présentaient des symptômes de COVID-19.

		• Près de la moitié (49 %) ont perçu la COVID-19 comme un risque majeur pour elles-mêmes avant de se faire vacciner. Ce pourcentage a diminué à 19 % après avoir reçu une dose.
Malesza (2021) *préimpression* (36) Étude transversale Pologne Janvier et février 2021	Les associations avec l'adoption du vaccin ont été évaluées chez 1 477 adultes âgés (70 ans et plus) grâce à des entrevues structurées. Un programme de vaccination de masse a été lancé pendant les dernières semaines de 2020. Le ministre de la Santé a recommandé que chaque personne de 70 ans et plus soit encouragée à recevoir le vaccin contre la COVID-19. On suppose qu'au moment de ces entrevues, toutes les personnes âgées de 70 ans et plus avaient été encouragées à se faire vacciner et étaient en mesure de le faire. Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 62,7 % des personnes ont reçu le vaccin et 37,3 % ont dit ne pas vouloir se faire vacciner. • Les deux prédicteurs indépendants les plus importants pour l'adoption du vaccin étaient l'explication par un professionnel de la santé des raisons pour lesquelles elles devraient se faire vacciner (RC = 4,23, IC à 95 % : 2,90 à 5,75) et le fait de vivre avec d'autres personnes (RC = 3,13, IC à 95 % : 2,03 à 4,26). Parmi les autres prédicteurs, mentionnons la possibilité de se rendre par leurs propres moyens chez un omnipraticien (RC = 1,92, IC à 95 % : 1,45 à 2,76), le fait d'être atteintes de maladies chroniques (RC = 2,98, IC à 95 % : 2,05 à 4,01), le statut socioéconomique supérieur (RC = 1,79, IC à 95 % : 1,33 à 2,15) et le sexe masculin (RC = 1,22, IC à 95 % : 0,67 à 1,98). • Les principales raisons pour lesquelles les gens ont accepté de se faire vacciner étaient pour se protéger eux-mêmes (90,6 %), la protection des proches (69,3 %), un rappel reçu d'un médecin (67,7 %) et les conseils reçus d'un professionnel de la santé (65,0 %) ou d'un ami (49,9 %). • Parmi les raisons invoquées pour ne pas se faire vacciner, mentionnons des préoccupations au sujet de l'innocuité (91,4 %), la crainte d'effets secondaires (89,7 %), la croyance que la COVID-19 n'est pas une maladie grave (75,4 %), le fait de ne pas vouloir être utilisé comme cobaye (69,5 %), la croyance que les vaccins sont inefficaces (66,7 %), le fait d'avoir des problèmes médicaux qui rendaient les vaccins contre-indiqués (53 %), le fait d'avoir de la famille ou des amis qui avaient eu une mauvaise expérience avec le vaccin (57,1 %), le fait de ne pas aimer les

		injections (35,3 %) et le fait de croire que le vaccin était dérangeant (30,8 %).
POPULATION GÉNÉRALE		
Horizon Research (2021) *non publiée* (15, 195) Étude transversale Nouvelle-Zélande Mars à mai 2021	Un sondage en ligne a été mené auprès d'adultes (âgés de 16 ans et plus) afin de mesurer le taux d'adoption des vaccins. Mars-Avr, n=1 350 Avr-Mai, n=1 387 Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	**Avril et mai** • 1 % des répondants ont déclaré qu'on leur avait offert un vaccin, mais que ce pourcentage avait diminué (baisse de 1 % depuis le mois précédent). • Les personnes peu susceptibles d'accepter le vaccin qui leur a été offert étaient des femmes, elles étaient plus jeunes que l'âge moyen, avaient des revenus plus faibles, des qualifications moins élevées et des enfants dans leur ménage. **Mar-Apr** • 2 % des adultes à qui on avait offert un vaccin et qui l'ont refusé.
Office for National Statistics (2021) *non publiée* (43, 47) Étude longitudinale ROYAUME-UNI Mars à Mai 2021	Les réponses de quatre vagues de résultats recueillies dans le cadre du sondage en ligne sur les opinions et les modes de vie (167) ont été regroupées pour se concentrer sur les associations démographiques spécifiques à l'hésitation à se faire vacciner. Le nombre de personnes handicapées, cliniquement extrêmement vulnérables et de parents n'a pas été communiqué. Févr.-mars : 17 201 réponses regroupées Mars-avril : 16 362 réponses regroupées Avril-mai : 15 170 réponses regroupées	**Avril et mai** • 2 % des adultes à qui on avait offert un vaccin et qui l'ont refusé. • Les taux de refus du vaccin étaient de 1 % chez les 16 à 29 ans, de 2 % chez les 30 à 49 ans et de 1 % chez les 50 ans et plus. • 2 % des femmes ont refusé le vaccin comparativement à 1 % des hommes. • 5 % des personnes qui s'identifiaient comme ayant une autre religion et 4 % des bouddhistes à qui on avait offert un vaccin l'avaient refusé, comparativement à 1 % des personnes qui ne déclaraient aucune religion. • 63 % des personnes qui ont déclaré être de confession musulmane et qui étaient peu susceptibles d'être vaccinées ou qui ont refusé le vaccin étaient préoccupées par les effets secondaires.

	Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• Les personnes dans les quintiles les plus démunis ont refusé de recevoir des vaccins plus fréquemment que celles qui se trouvaient dans les quintiles de privation les plus élevés (3 % dans le quintile inférieur et 1 % dans le quintile le moins pauvre). • Par profession, 3 % des personnes qui œuvrent dans les ventes et le service à la clientèle, ainsi que les ouvriers ont refusé le vaccin comparativement à la moyenne de 2 %. **Mars-Avril** • 3 % des parents qui avaient des enfants âgés de 0 à 4 ans se sont vu offrir un vaccin et l'ont refusé, comparativement à 2 % de ceux qui avaient des enfants de plus de 5 ans ou à 1 % de ceux qui ne sont pas des parents et qui ne vivent pas avec des enfants à charge.
Office for National Statistics (2021) *non publiée* (48, 50, 54, 197) Étude longitudinale ROYAUME-UNI Décembre 2020 à mai 2021	Un sondage hebdomadaire en ligne sur les intentions de se faire vacciner a été effectué auprès d'un échantillon national représentatif d'adultes britanniques. Du 7 au 11 avril: n= 6,030 Du 28 avril au 3 mai:: n=3,830 Du 19 au 23 mai: n= 3,070 Du 2 au 6 juin n=4,010 Du 9 au 13 juin: n=3,600 *nouvelle* Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	**Du 9 au 13 juin** • 2 % des personnes âgées de 50 à 69 ans se sont fait offrir un vaccin et l'ont refusé comparativement à 1 % des personnes âgées de 70 ans et plus et à la moyenne globale de 3 %. **Du 19 au 23 mai** • 18 % des 50 à 69 ans ont reçu une dose de vaccin et 80 % (comparativement à 25 %) en ont reçu deux. 1 % des personnes à qui un vaccin a été offert l'ont refusé. 58 % des personnes de ce groupe d'âge sont préoccupées par les effets secondaires. • <1 % des personnes âgées de 70 ans et plus ont reçu une dose de vaccin et 99 % en ont reçu deux. <1 % de personnes se sont vu offrir un vaccin et ont refusé de se faire vacciner. **Du 28 avril au 3 mai** • 69 % des personnes âgées de 50 à 69 ans ont reçu une dose de vaccin et 25 % ont reçu deux doses. 2 % se sont vu proposer un vaccin et ont refusé de se faire vacciner et 1 % ne s'est pas vu proposer de vaccin.

		Du 7 au 11 avril • 39 % des adultes âgés entre 30 et 49 ans ont reçu au moins une dose et 1 % se sont vus offrir un vaccin et attendent d'être vaccinés. 1 % se sont vus offrir un vaccin et ont décliné l'offre. • 19 % des 16 à 29 ans ont reçu au moins une dose et 1 % se sont vus offrir un vaccin et attendent d'être vaccinés. 2 % se sont vus offrir un vaccin et ont décliné l'offre. • 98 % des personnes âgées de 50 à 69 ans ont reçu un vaccin ou ont l'intention d'en accepter un. 1 % se sont vues offrir un vaccin et attendent d'être vaccinées et 1 % se sont vues offrir un vaccin et l'ont refusé. • 99 % des personnes de 70 ans et plus ont reçu un vaccin ou sont susceptibles d'en accepter un. 1 % se sont vus offrir un vaccin et ont décliné l'offre.
Dai (2021) *préimpression* (44) Essai de contrôle randomisé É.-U. Janvier à mars 2021	Un essai contrôlé randomisé a été mené pour mesurer l'impact des interventions (rappel par message texte) dans l'augmentation de la vaccination dans les populations admissibles (les personnes âgées de 65 ans et plus, les patients ayant subi une transplantation, et les patients à risque élevé avec des conditions préexistantes admissibles) en Californie. ECR 1 : Rappel par message texte comprenant un lien pour prendre le rendez-vous et soit un texte simple, soit un message d'appartenance, soit un texte simple avec vidéo, soit un message d'appartenance avec vidéo, un jour après avoir reçu l'avis d'admissibilité au vaccin (n = 132 337).	• La réception d'un message texte de base a augmenté de manière significative les taux de prise de rendez-vous dans les 6 jours de 5,14 de points de pourcentage ($p < 0,001$), et les taux de vaccination dans les 4 semaines de 2,89 de points de pourcentage ($p < 0,001$) par rapport au groupe témoin. Cela représente une augmentation relative de 85,5 % et 26,3 %, respectivement. • La réception d'un message texte a également augmenté la vitesse réelle des vaccinations, le groupe témoin ayant mis 27 jours pour atteindre le taux de vaccination du groupe ayant reçu un message texte au jour 17. • L'inclusion d'une vidéo n'a pas augmenté de manière significative le nombre de rendez-vous ou de vaccinations par rapport aux messages sans vidéo éducative, probablement en raison du faible taux de visionnement (21 %). • C'est parmi les personnes ayant reçu au moins un vaccin contre la grippe au cours des deux années

	ECR 2 : Un deuxième rappel par message texte a été envoyé huit jours après le premier rappel aux participants qui n'avaient pas pris rendez-vous pour la première dose (n = 102 675). Les messages se répartissent en 6 catégories : (1) texte simple (2) prosocial (3) exclusivité de l'accès précoce (4) accès précoce et prosocial (5) nouveau départ (6) nouveau départ et prosocial. Sujets des questions : 1) Prise du vaccin	précédentes que l'impact des messages texte a été le plus fort. • 12 % des personnes qui ont pris rendez-vous après le premier message ont annulé leur rendez-vous sans le reporter et 0,1 % ne se sont pas rendues à leur rendez-vous. • Un deuxième rappel par message texte a augmenté de manière significative la prise de rendez-vous pour la première dose de 1,26 % (augmentation de 52,3 %, P < 0,001) dans les 6 jours et l'obtention de la première dose dans les 4 semaines de 0,68 % (augmentation de 15,9 %, P < 0,001) par rapport au groupe témoin. • Tous les types de messages ont permis d'augmenter les taux de rendez-vous et de vaccination.
Senderey (2021) *préimpression* (2) *nouveau* Avant et après l'étude Israël Févr. 2021	Les taux d'adoption du vaccin ont été comparés avant et après la mise en œuvre du rappel par message texte. Les personnes admissibles non vaccinées (16 ans et plus) ont été choisies au hasard pour recevoir l'un des deux rappels (après avoir reçu le rappel de base). Il y avait deux types de rappels, l'un soulignant l'avantage du vaccin sur le plan social et l'autre, l'avantage sur le plan personnel. Les vaccins étaient disponibles pour toutes les personnes âgées de plus de 16 ans. Les taux d'adoption du vaccin ont également été comparés avant et après la mise en œuvre de la politique du laissez-passer vert, selon lequel l'entrée dans certains lieux publics nécessitait la présentation du « laissez-passer	• L'adoption du vaccin est passée de 2,3 % deux jours avant l'intervention à 3,6 % deux jours après l'intervention (P<0,001). • Le message sur les avantages sur le plan personnel était plus efficace que celui sur les avantages sur le plan social. • L'effet global sur huit jours après l'intervention a révélé que le rappel des avantages sur le plan personnel a entraîné une hausse relative de 9 % par rapport au rappel des avantages sur le plan social (23,8 % contre 21,7 %, P<0,0001). • Si l'on compare trois jours avant et après la mise en œuvre de la politique du laissez-passer vert, on constate une augmentation relative de 22,2 % (de 3,6 % à 4,4 %).

	vert », qui pouvait être obtenu en recevant un vaccin ou un résultat négatif récent au test de dépistage de la COVID-19. Sujets des questions : 1) Adoption du vaccin	
Glampson (2021) *préimpression* (49) Étude de cohorte ROYAUME-UNI Décembre 2020 à février 2021	Cette étude visait à évaluer la prise vaccinale et l'efficacité de l'efficacité théorique sur une période de suivi de dix semaines dans un système de soins intégrés de huit Collaboration of Clinical Commissioning Groups (CCG) exploitant un ensemble unique de données sur les soins au niveau de la population dans le nord-ouest de Londres. Pendant la période du programme de vaccination, 413 919 adultes (16 et +) se sont vus offrir un vaccin. Les personnes ont été considérées comme refusant un vaccin si elles ont indiqué à leur médecin généraliste qu'ils ne voulaient pas du vaccin lorsqu'il leur a été proposé, puis n'ont pas été vaccinés. Sujets des questions : 1) Prise du vaccin	• Parmi les personnes à qui un vaccin a été proposé, 24 332 (5,88 %) ont refusé et n'ont pas été vaccinées. • Dans le groupe vacciné, 2 957 personnes avaient initialement refusé de se faire vacciner, mais l'ont fait par la suite, soit un taux d'hésitation de 0,71 %. • Le groupe des Noirs ou des Britanniques noirs présentait les taux de refus de vaccination les plus élevés (16,1 %), suivi du groupe ethnies mixtes (10,4 %), d'un autre groupe ethnique (9,95 %) et du groupe d'ethnie non enregistrée (8,5 %). Les taux de refus les plus faibles ont été observés dans les groupes des Blancs (4,9 %) et des Asiatiques et Britanniques asiatiques (3,2 %). • Dans le groupe des Noirs ou des Britanniques noirs, ceux qui étaient âgés de plus de 80 ans (27,9 %) ou qui étaient cliniquement extrêmement vulnérables (24,0 %) présentaient les taux de refus les plus élevés. • Aucune différence dans l'ensemble des taux de refus n'a été observée entre les hommes et les femmes (5,9 % contre 5,8 %), les hommes plus jeunes (< 65 ans) étaient plus susceptibles de refuser que les femmes plus jeunes (3,2 % contre 2,2 %), et les femmes plus âgées (65 ans et plus) étaient plus susceptibles de refuser que les hommes plus âgés (7,9 % contre 7,1 %). • La défavorisation était négativement associée au refus de la vaccination (r = -0,94, P < 0,01). Dans les zones les plus défavorisées, 13,5 % des

		individus ont refusé la vaccination, contre 1,0 % dans les zones les moins défavorisées. • Pour les personnes vivant dans les zones défavorisées, les taux de refus les plus élevés concernaient les personnes âgées de plus de 70 ans (70 à 74 = 17,5 %; 75 à 80 = 19,0 %; 80 et + = 25,9 %), les personnes cliniquement extrêmement vulnérables (19,2 %) et les communautés noires et noires britanniques (20,0 %).
AUTRES POPULATIONS		
Office for National Statistics (2021) *non publiée* (43, 47) Étude longitudinale ROYAUME-UNI Mars à mai 2021	Les réponses provenant de quatre vagues de résultats recueillis dans le cadre du sondage en ligne Opinions and Lifestyle Survey (196) ont été mises en commun pour mettre l'accent sur les associations démographiques spécifiques et la réticence à se faire vacciner. Le nombre de personnes handicapées ou extrêmement vulnérables au niveau clinique n'a pas été déclaré. Février et mars : 17 201 réponses ont été mises en commun Mars et avril : 16 362 réponses ont été mises en commun Avril et mai : 15,170 réponses ont été mises en commun Sujets des questions : 1) Prise du vaccin Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	**Avril et mai** • Comparativement à la moyenne (2 %), le taux de refus du vaccin était légèrement inférieur chez les répondants handicapés (1 %) et extrêmement vulnérables sur le plan clinique (1 %). • 58 % des répondants handicapés avaient des préoccupations générales quant à l'innocuité du vaccin, alors que les répondants extrêmement vulnérables sur le plan clinique étaient les plus préoccupés par les préoccupations en matière de fertilité (28 %). • La plus grande difficulté prévue pour l'obtention d'un vaccin était la longue attente et le fait de devoir s'absenter du travail (8 %). **Mars-avril** • 2 % des personnes handicapées se sont vu offrir un vaccin, mais l'ont refusé, soit 1 % de plus que les personnes non handicapées. • 3 % des répondants extrêmement vulnérables sur le plan clinique (VPC) se sont vu offrir un vaccin et l'ont refusé, comparativement à 1 % des répondants non VPC. • 3 % des parents qui avaient des enfants âgés de 0 à 4 ans se sont vu offrir un vaccin et l'ont refusé, comparativement à 2 % de ceux qui avaient des enfants de plus de 5 ans ou à 1 % de ceux qui ne sont pas des parents et qui ne vivent pas avec des enfants à charge.

Turner (2021) *préimpression* (42) *nouvelle* Étude transversale Royaume-Uni Fev à Avr 2021	À l'aide d'un sondage en ligne, on a évalué les facteurs qui influencent l'adoption du vaccin contre la COVID-19 et la perception à l'égard de ce vaccin chez 377 survivants d'un accident vasculaire cérébral et d'une attaque ischémique transitoire pendant une période précoce de déploiement du vaccin au Royaume-Uni. Sujets des questions : 1) Adoption du vaccin 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 87 % des répondants avaient reçu au moins une première dose ou avaient un rendez-vous alors que 8 % n'avaient pas encore reçu de vaccin. • 2 % des répondants avaient refusé le vaccin et 3 % s'étaient vus offrir le vaccin, mais ne l'avaient pas encore accepté. • Les préoccupations qui empêchaient l'atteinte d'un pourcentage élevé de personnes vaccinées comprenaient l'inquiétude au sujet des effets secondaires (36 %), le fait que le vaccin augmentait le risque d'accident vasculaire cérébral (34 %), l'innocuité du vaccin (32 %), la nouveauté du vaccin (29 %) et l'effet du vaccin sur les anticoagulants (28 %). • La plupart des répondants étaient d'avis que le vaccin était la bonne chose à faire (92 %), ont dit connaître d'autres personnes qui avaient reçu le vaccin (98 %), que le vaccin réduirait la propagation de la COVID-19 (85 %) et qu'il les protégerait (87 %). • On a pu voir une bonne compréhension de la manière d'obtenir un rendez-vous pour se faire vacciner (91 %). Bon nombre de personnes n'étaient pas d'accord pour dire qu'elles devaient consulter leur médecin (61 %), qu'elles auraient de la difficulté à obtenir un rendez-vous (64 %) ou qu'elles n'auraient pas le temps d'obtenir un rendez-vous (74 %). • Dans les réponses en texte libre, on a pu voir des préoccupations en ce qui concerne le lien entre le vaccin AstraZeneca et les caillots sanguins, les effets secondaires, la méfiance à l'égard du gouvernement, l'efficacité du vaccin, l'incertitude au sujet du lien entre les AVC/AIT et la COVID-19, l'accès aux rendez-vous pour le vaccin, et les difficultés à obtenir des renseignements spécifiquement adaptés à ces personnes.

Bowman (2021) *préimpression* (45) Étude transversale États-Unis Janvier à mars 2021	Un programme de vaccination mis en œuvre dans le cadre d'un programme de dialyse comprenant une série de quatre visites dans 12 cliniques de dialyse en Virginie a été mis en œuvre. Dans le cadre de ce programme, on a offert un vaccin à 859 patients âgés de 18 ans et plus. Sujets des questions : 1) Adoption du vaccin	• En date du 16 mars, 79,6 % des patients en dialyse à qui on avait offert un vaccin l'avaient accepté alors que 14,2 % l'avaient refusé. 6,2 % des personnes n'avaient ni accepté ni refusé le vaccin en raison d'une hospitalisation ou de l'absence de traitement le jour de la clinique de vaccination. • La probabilité de refus du vaccin a diminué de 13 % pour chaque tranche d'âge de cinq ans (RC 0,87, IC à 95 % : 0,80 à 0,95, P = 0,002). • Les femmes étaient plus susceptibles de refuser un vaccin que les hommes (RC 2,40, IC à 95 % : 1,64 à 3,50, P < 0,0001). • On a observé une probabilité accrue de refus du vaccin chez les patients qui n'ont pas reçu le vaccin antigrippal en 2020 (RC 5,44, IC à 95 % : 3,15 à 9,39, P < 0,0001), ceux qui ont été en dialyse pendant plus de 5 ans (RC 1,7, IC à 95 % : 1,08 à 2,70, P = 0,023) et ceux qui ont obtenu un résultat positif au test PCR pour la COVID-19 (RC 1,56, IC à 95 % : 0,97 à 2,52, P = 0,067).
Giannini (2021) (4) *nouveau* Étude transversale Italie NR 2021	Les taux d'adoption et de refus d'un vaccin contre la COVID-19 ont été évalués dans un groupe de 266 personnes ayant subi une transplantation hépatique. Sujets des questions : 1) Adoption du vaccin	• 96,6 % des patients ont accepté et reçu un vaccin contre la COVID-19 et 3,4 % n'ont pas reçu de vaccin. • 5 patients ont refusé de se faire vacciner en raison de crainte d'effets indésirables graves. Ces patients avaient reçu des renseignements adéquats sur le vaccin et avaient reçu les vaccins recommandés pour les transplantés hépatiques avant de refuser. • Deux patients ont demandé plus de temps pour décider de recevoir ou non le vaccin en raison de préoccupations quant aux risques potentiels. • Un patient a dû subir des examens complémentaires en raison de réactions allergiques antérieures aux vaccins, et un patient séjournait temporairement à l'étranger pendant que les vaccins étaient offerts.

Gibbon (2021) (5) *nouveau* Étude transversale R.-U. NR 2021	L'adoption du vaccin contre la COVID-19 et les raisons du refus ont été évaluées chez 92 patients hospitalisés en psychiatrie dans un hôpital de sécurité moyenne au Royaume-Uni. Sujets des questions : 1) Adoption du vaccin	• 85 patients avaient la capacité de décider s'ils voulaient recevoir le vaccin contre la COVID-19. • 80 % ont accepté de se faire vacciner et 20 % ont refusé. • Les patients britanniques blancs étaient moins susceptibles de refuser que les patients noirs, asiatiques ou issus de minorités ethniques (16,9 % contre 30 %). • Parmi les 17 patients qui ont refusé de se faire vacciner, les raisons étaient les suivantes : inquiétude quant à l'innocuité et aux effets secondaires du vaccin (n=5), conviction que le risque de contracter la COVID-19 est faible pour leur santé personnelle (n=4), méfiance générale envers les services de santé (n=2) et inquiétude quant à l'expérimentation animale (n=1). Cinq personnes n'ont pas voulu expliquer les raisons de leur refus.
Giannini (2021) (46) *nouveau* Étude transversale Italie NR 2021	Les taux d'adoption du vaccin ont été évalués chez 56 patients atteints du syndrome de l'intestin irritable et suivis dans un centre de l'intestin irritable. Sujets des questions : 1) Adoption du vaccin	• 92,6 % ont accepté de se faire vacciner et 7,4 % ont refusé. • Les deux patients qui ont refusé l'ont fait en raison de préoccupations concernant les effets indésirables potentiels.
RESPECT DES MESURES DE SANTÉ PUBLIQUE APRÈS LA VACCINATION		
United Status Census Bureaus (2021) *non publiée* (53) Étude longitudinale États-Unis	Les estimations en ce qui concerne les comportements préventifs des personnes qui ont reçu au moins une dose de vaccin ont été recueillies dans le cadre de la phase 3.1 du Household Pulse Survey effectuée toutes les deux semaines, en ligne.	• 73,2 % des personnes qui avaient reçu au moins une dose du vaccin n'ont pas modifié leurs comportements préventifs après la vaccination, 21,9 % les ont réduits et 4,3 % ont plutôt décidé de les renforcer. • La diminution des comportements préventifs a été mentionnée davantage chez les personnes âgées de 18 à 39 ans (24 à 25 %), les hommes (23 %), les Blancs non hispaniques (27 %), les personnes mariées (24 %), les titulaires d'un

Mai 2021	Semaine 30, du 12 au 24 mai, n = 192 277 515 Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	baccalauréat ou plus (30 %), dans les ménages comptant 2 (25 %) et 4 personnes (23 %), chez les personnes occupant un emploi (24 %) et ayant un revenu du ménage supérieur à 75 000 $ (entre 23 % et 37 % lorsque le revenu est de 200 000 $ et plus) comparativement à leurs homologues.
Office for National Statistics (2021) *non publiée* (50, 54, 197, 198) Étude longitudinale ROYAUME-UNI Déc 2020 à May 2021	Un sondage hebdomadaire en ligne sur les intentions de se faire vacciner a été effectué auprès d'un échantillon national représentatif d'adultes britanniques. Avril 7-11: n= 6,030 Avril 28-Mai 3: n=3,830 Juin 2-6: n= 4,153 Juin 9-13: n=3,600 *nouvelle* Sujets des questions : 1) Adoption du vaccin Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	**Du 9 au 13 juin** • La distanciation sociale avec les personnes à l'extérieur de leur ménage a continué de diminuer, passant de 74 % dans le sondage de mai à 66 % dans celui de juin (88 % au début d'avril). • Les contacts physiques à l'extérieur de la maison ont chuté de 1 % dans le dernier sondage pour s'établir à 71 %. • 46 % (en baisse par rapport à 50 %) des adultes rencontraient à l'intérieur des gens n'appartenant pas à leur ménage, à leur service de garde ou à leur bulle de soutien. **Du 2 au 6 juin** • La distanciation sociale avec les personnes à l'extérieur de leur ménage a continué de diminuer, passant de 74 % dans le sondage de mai à 68 % dans celui de juin (88 % au début d'avril). • Les contacts physiques à l'extérieur de la maison ont chuté de 1 % dans le dernier sondage pour s'établir à 72 %. • 50 % des adultes rencontraient à l'intérieur des gens n'appartenant pas à leur ménage, à leur service de garde ou à leur bulle de soutien.

		• Les rassemblements en plein air avec des adultes sont passés de 53 % à 65 % depuis le dernier sondage. **Du 28 avril au 3 mai** • 90 % des personnes vaccinées (au moins une dose) se lavent toujours ou souvent les mains en rentrant chez elles, contre 82 % des personnes non vaccinées. • 90 % des personnes vaccinées (au moins une dose) ont toujours ou souvent maintenu une distance sociale lorsqu'elles rencontrent des personnes extérieures à leur foyer, à leur entourage ou à leur bulle de garde, contre 72 % des non-vaccinés. • Les personnes ayant reçu au moins une dose ont évité les contacts physiques en dehors de leur domicile par rapport aux personnes non vaccinées (86 % contre 74 %). • 25 % des adultes vaccinés (au moins une dose) sont restés chez eux ou ne sont sortis que pour le travail, l'exercice, les achats essentiels ou les besoins médicaux, contre 15 % des adultes non vaccinés. • Les adultes vaccinés sont moins nombreux à travailler à domicile que les non-vaccinés (33 % contre 43 %).
Rahamin-Cohen (2021) *préimpression* (51) Étude transversale Israël Mars à avril 2021	Pour évaluer les changements de comportement au sein de la population vaccinée, 185 personnes de la population générale (18 et +) et 23 travailleurs sociaux (18 et +) ont répondu à une enquête en ligne envoyée par message texte. Les résultats pour les travailleurs de la santé dans la section travailleurs de la santé. Sujets des questions :	• Après la deuxième dose, 21,1 % des répondants ont déclaré porter un masque moins souvent qu'avant la vaccination et 75,7 % n'ont pas modifié leur comportement. Les personnes âgées de moins de 50 ans sont plus nombreuses à diminuer leur port du masque (28,1 %) que les personnes âgées de 50 ans et plus (17,2 %). Seulement 1 répondant sur 23 (4,3 %) des travailleurs de la santé a déclaré porter moins le masque après la vaccination. • En comparant le comportement de distanciation sociale avant et après la vaccination, 48,4 % des personnes interrogées n'ont signalé aucun

	1) Comportements post-vaccination Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	changement et 47,3 % ont signalé une diminution de la distanciation sociale. Ces résultats diffèrent selon l'âge : 41,8 % des personnes âgées de 50 ans et plus ont signalé une diminution de la distanciation sociale et 53,3 % n'ont signalé aucun changement, contre 56,1 % et 40,4 % respectivement dans le groupe des moins de 50 ans. Chez les travailleurs de la santé, 43,5 % ont signalé une diminution de la distanciation sociale et 52,2 % n'ont signalé aucun changement après la vaccination.
Wright (2021) *préimpression* (52) Étude longitudinale ROYAUME-UNI Octobre 2020 à mars 2021	Les résultats d'une enquête mensuelle en ligne portant sur 70 000 adultes (18 et +) ont été utilisés pour étudier l'évolution de l'observance après la vaccination. Sujets des questions : 1) Comportements post-vaccination Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• Aucune donnée probante n'a démontré que le fait de recevoir un vaccin contre la COVID-19 réduisait les comportements d'observance. • Une augmentation de l'observance dès le début de la deuxième vague de COVID-19 a été démontrée à la fois chez les personnes vaccinées et non vaccinées.
Office for National Statistics (2021) *non publiée* (35) Étude transversale ROYAUME-UNI	Les réponses de 2 070 adultes de plus de 80 ans ont été recueillies au moyen d'un sondage en ligne afin de déterminer la couverture vaccinale, les attitudes et l'effet de la vaccination sur les comportements de protection. Sujets des questions : 1) Comportements post-vaccination	• Parmi les personnes qui avaient reçu au moins une dose, 43 % avaient rencontré quelqu'un en dehors de leur bulle, de leur ménage ou du personnel soignant à l'intérieur plutôt qu'à l'extérieur. • Parmi celles qui avaient reçu au moins une dose et qui s'étaient aventurées à l'extérieur de leur maison pour faire une activité, 49 % avaient rencontré à l'extérieur quelqu'un avec qui elles ne vivaient pas, 54 % étaient allés magasiner et 45 % étaient sorties de la maison pour participer à des activités de loisirs en plein air). Seulement

Fev 2021	Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	20 % ont déclaré ne pas avoir quitté la maison pour quelque raison que ce soit. • 25 % des personnes qui ont reçu leur première dose et 33 % de celles qui ont reçu les deux doses étaient prêtes à aller à l'hôpital pour une raison médicale.
Nguyen (2021) *préimpression* (6) *nouveau* Étude de cohorte R.-U. Sept. 2020-févr. 2021	Le taux de changement de la distance moyenne de déplacement quotidien à partir de l'adresse enregistrée d'un participant avant et après la vaccination contre le SRAS-CoV-2 a été mesuré à l'aide de Virus Watch. Virus Watch a utilisé le système de positionnement global (GPS) pour recueillir des données sur les déplacements de 228 personnes vaccinées.	• La distance médiane parcourue quotidiennement était de 8,9 km (IQR : 3,50 km, 24,17 km) entre 157 jours avant la vaccination et la veille de la vaccination. • Entre le jour de la vaccination et 100 jours après la vaccination, la distance médiane parcourue quotidiennement était de 10,30 km (IQR : 4,11, 27,53 km). • Après suppression des données hors norme, on constate une augmentation médiane quotidienne des déplacements de 45,0 m (IC à 95 % : 25 m, 65 m, P = <0,001) entre la date de vaccination et 99 jours après la vaccination. • Après avoir restreint l'analyse au 3e confinement national (du 4 janvier au 5 avril 2021), on a constaté une augmentation médiane du mouvement quotidien de 9m (IC à 95 % : -25 m, 45 m, P = 0,57) dans les 30 jours précédant la vaccination et la date de vaccination, et une augmentation médiane des mouvements quotidiens de 10 m (IC à 95 % : -60 m, 94 m, valeur p = 0,69) dans les 30 jours suivant la vaccination.
Kaim (2021) (7) *nouveau* Étude transversale Israël	Les ajustements comportementaux de protection (c'est-à-dire le port du masque et la distanciation sociale) pendant la phase initiale de la campagne de vaccination ont été évalués dans un groupe de 1 120 adultes à l'aide d'un sondage en ligne. Parmi ces personnes, 64 étaient infectées par la COVID-19,	• Au début de la campagne de vaccination, les personnes infectées faisaient moins attention à la distanciation sociale (29,7 %) par rapport à celles qui avaient reçu la première dose de vaccin (12,8 %), ou celles qui n'étaient ni vaccinées ni infectées (19,2 %) (χ^2 = 19,32, P = 0,001). • De même, les personnes qui étaient infectées faisaient moins attention au port du masque (18,8 %) par rapport à celles qui avaient reçu la

Janv. 2021	453 étaient vaccinées et 603 n'étaient pas vaccinées. Sujets des questions : 1) Comportements après avoir reçu le vaccin Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	première dose du vaccin (8,2 %) et celles qui n'étaient ni vaccinées ni infectées (11,6 %) (χ^2 = 13,02, P = 0,011). • Un niveau plus élevé de distanciation sociale a été maintenu chez les personnes non-juives par rapport aux personnes juives : les personnes qui ont été vaccinées (41,7 % chez les non-juives contre 14,3 % chez les juives χ^2 = 22,9, P < 0,001), celles qui étaient infectées (33,1 % chez les non-juives contre 8,3 % chez les juives $\chi^{2=}$7,29, P = 0,026), et celles qui n'étaient ni vaccinées ni infectées (24,3 % chez les non-juives et 8,8 % chez les juives χ^2 = 28,81, P < 0,001). Des tendances similaires ont été observées pour le port du masque.

POPULATION MONDIALE

Tableau 2. Éléments de preuve sur les attitudes de la global population mondiale à l'égard des vaccins (n = 6)

ÉTUDE	MÉTHODES ET OUTILS D'ENQUÊTE	RÉSULTATS CLÉS POUR LES CONNAISSANCES, LES ATTITUDES ET LES COMPORTEMENTS
Études quasi expérimentales (n = 1)		
Duch (2021) *préimpression* (199) Étude quasi-expérimentale 13 pays (Australie, Brésil, Canada, Chili, Chine, Colombie, France, Inde, Italie, Espagne,	Afin de comprendre l'opinion publique sur les aspects clés de la distribution des vaccins, une expérience en ligne a été menée auprès de 15 536 adultes (âgés de 18 ans et plus) dans 13 pays. Les participants devaient faire huit choix binaires en ce qui concerne des personnes qui recevraient hypothétiquement des vaccins qui variaient aléatoirement selon cinq attributs, notamment la profession, l'âge, l'état de transmission, le risque de décès attribuable à la COVID-19 et le revenu.	• Dans l'ensemble, il y a eu consensus à propos des segments de la population qui devraient avoir la priorité pour recevoir un vaccin contre la COVID-19. • Dans presque tous les pays et parmi les participants ayant différents niveaux d'éducation et de revenus et différentes idéologies politiques, les résultats montrent que le public privilégie le fait que les travailleurs de la santé, les personnes à haut risque, les personnes à faible revenu et les populations plus âgées reçoivent le vaccin. • Au moins deux tiers des participants dans chacun des pays (80 % au Canada) croyaient que le gouvernement devrait jouer un rôle de premier plan dans la distribution des vaccins contre la

Ouganda, Royaume-Uni, États-Unis) Novembre et décembre 2020	Sujets des questions : 1) Perception des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Non	COVID-19. Cependant, il y a des preuves qu'une grande proportion de personnes seraient prêtes à payer pour un vaccin s'il était offert en privé. Ce pourcentage variait de 18 % des participants en France à environ 79 % en Inde et en Ouganda. 35 % des personnes seraient prêtes à payer pour un vaccin. • Il n'y a cependant pas eu de consensus quant au soutien à la vaccination obligatoire, que ce soit à l'échelle mondiale ou nationale. Dans l'échantillon pris à l'échelle mondiale, 24 % étaient fortement opposés et 38 % étaient fortement en faveur. En France, 60 % des participants se sont opposés à la vaccination obligatoire, alors qu'en Chine, en Inde et en Ouganda, très peu de gens s'y sont opposés fermement.
Études transversales (n=5)		
Crespo (2021) *préimpression* (57) Études transversales 15 pays : Allemagne, Australie, Canada, Danemark, Finlande, France, Italie, Japon, Pays-Bas, Norvège, Singapour, Corée du Sud, Espagne, Suède, Royaume-Uni	Les variations dans l'intention de se faire vacciner au fil du temps ont été évaluées à l'aide de deux sondages en ligne, l'un effectué en novembre 2020 et l'autre en janvier 2021 dans 15 pays. Rien n'indique le nombre de personnes qui ont répondu aux deux sondages et si des gens ont répondu aux deux. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Au Canada, l'intention de se faire vacciner a augmenté, passant de 44,2 % en novembre à 55,2 % en janvier. • Dans le sondage réalisé en janvier, les pays dans lesquels on retrouvait le plus haut niveau en ce qui concerne l'intention de se faire vacciner étaient le Royaume-Uni (77,5 %), le Danemark (67 %) et les Pays-Bas (63,1 %). Quant au niveau le plus faible, on le retrouvait en Corée du Sud (43,7 %), en France (39,2 %) et à Singapour (34,8 %). • On a pu voir une augmentation de l'intention de se faire vacciner entre novembre et janvier en Espagne (24,1 %), au Royaume-Uni (23,2 %), en Suède (22,7 %), en Finlande (20,4 %), aux Pays-Bas (18,5 %), en Italie (15,4 %), en Norvège (14,6 %), en France (14,2 %), au Danemark (13,3 %), en Allemagne (13,0 %), au Canada (11 %) et au Japon (0,8 %). • Les pays dans lesquels l'intention a diminué entre novembre et janvier étaient l'Australie (-6,6 %), la Corée du Sud (-5,0 %) et Singapour (-1,3 %).

Novembre à janvier 2021		• Dans 11 des 15 pays, on a vu une diminution importante de la proportion de personnes qui se sont dites préoccupées par les effets secondaires d'un vaccin. Au Canada, ce niveau de préoccupation a diminué, passant de 53,3 % en novembre à 47,9 % en janvier.
Clarke (2021) (200) Étude transversale Australie, Canada, France, Italie, Espagne, Royaume-Uni et États-Unis Novembre à décembre 2020	Une enquête internationale en ligne a été menée auprès de 8 209 adultes de pays à revenu élevé dans le but d'évaluer les perceptions de la priorisation de l'allocation mondiale des vaccins sur une échelle de 0 (« très en désaccord ») à 100 (« très en accord »). Thèmes des questions : 1) Perception à l'égard des vaccins Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• Tous les pays sont favorisés par ordre de soutien : allocation en fonction des besoins, de l'accessibilité financière et du pays qui a développé le vaccin. • C'est au Royaume-Uni que l'on trouve le plus grand pourcentage de personnes interrogées qui ne sont pas en faveur de faire dons de vaccins achetés à d'autres pays (26 %) et en Italie et en Espagne que l'on trouve le plus faible pourcentage (15 %). • Entre 48 % et 56 % des personnes interrogées seraient prêtes à donner les vaccins de leur pays dans une certaine mesure. Le taux le plus élevé était celui du Canada (56 %) et le plus bas celui de la France (48 %).
World Economic Forum (2020) *non publiée* (201) Étude transversale 15 pays (Australie, Brésil, Canada, Chine, France, Allemagne, Inde, Italie, Japon,	Un sondage en ligne effectué auprès de 18 526 personnes dans le monde a été utilisé pour analyser l'intention de se faire vacciner et les perceptions à l'égard du vaccin. De ceux-ci, 1 000 participants étaient canadiens. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Hésitation par rapport à la vaccination	• 73 % des personnes ont déclaré qu'elles se feraient vacciner contre la COVID-19 si le vaccin était disponible. Comparativement aux données obtenues trois mois plus tôt (août), il s'agit d'une baisse de 4 %. • L'intention de se faire vacciner a diminué entre août et octobre dans 10 des 15 pays, notamment en Chine, en Australie, en Espagne et au Brésil. • L'Inde (87 %), la Chine (85 %), la Corée du Sud (83 %) et le Brésil (81 %) sont les pays où l'on trouve le niveau d'intention le plus élevé. • La France est le pays dans lequel les gens ont le moins l'intention de se faire vacciner (54 %). Elle

Mexique, Afrique du Sud, Corée du Sud, Espagne, Royaume-Uni et États-Unis) Octobre 2020	Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	est suivie des États-Unis (64 %) et de l'Espagne (64 %). • 52 % des gens ont indiqué qu'ils se feraient vacciner dans les trois mois de la date à laquelle un vaccin sera disponible pour tout le monde. • 55 % des gens croient qu'un vaccin ne sera pas disponible sur le marché avant le troisième trimestre de 2021. • À l'échelle mondiale, les motifs d'hésitation les plus courants sont les préoccupations à propos des effets secondaires (34 %) et les préoccupations liées au fait que les essais cliniques progressent trop rapidement (33 %).
Mannan (2021) *préimpression* (202) Étude transversale 60 pays : (Afghanistan, Algérie, Argentine, Australie, Bangladesh, Belgique, Bolivie, Botswana, Brésil, Canada, Chili, Chine, Colombie, Cuba, République dominicaine, Équateur, Égypte, El Salvador, Angleterre, Fidji, France,	Soixante sondages téléphoniques et en ligne représentatifs de chacun des pays ont permis de recueillir 26 852 réponses d'adultes (âgés de 19 ans et plus) en ce qui concerne l'acceptation du vaccin et des attitudes à cet égard. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination 3) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Non	• 62,6 % des Canadiens ont fortement accepté un vaccin contre la COVID-19, soit le taux d'acceptation le plus faible parmi les pays d'Amérique du Nord. • 65,5 % étaient fortement d'accord pour dire qu'il était important d'obtenir un vaccin pour protéger les autres, 57,6 % étaient d'accord pour dire que les sociétés pharmaceutiques mettront au point un vaccin sûr, et 31,7 % étaient d'avis que les vaccins étaient plus sûrs s'ils étaient fabriqués en Amérique ou en Europe que dans d'autres pays. • La réticence a été démontrée puisque 48,7 % des répondants s'inquiétaient des effets secondaires, 44,7 % s'inquiétaient des effets imprévus, 43,7 % s'inquiétaient des profits commerciaux, 42,6 % avaient une méfiance générale à l'égard des bienfaits du vaccin et 34,6 % avaient une préférence pour l'immunité naturelle. • Acceptation du vaccin par pays : **Afrique** Algérie (66,3 %), Égypte (43,6 %), Botswana (71,2 %), Kenya (61,3 %), Libye (49,6 %), Mali (62,4 %), Maurice (82,8 %), Maroc (48,4 %), Nigéria (61,5 %), Afrique du Sud (79,3 %) **Asie** Afghanistan (47,2 %), Bangladesh (49,8 %), Chine (87,4 %), Inde (73,9 %), Japon (71,4 %), Malaisie (52,7 %), Arabie saoudite (51,1 %),

Allemagne, Guatemala, Inde. Italie, Jamaïque, Japon, Kenya, Kiribati, Libye, Mali, Malaisie, Maurice, Mexique, Maroc, Nauru, Nouvelle-Zélande, Nicaragua, Nigeria, Palau, Panama, Papouasie-Nouvelle-Guinée, Paraguay, Pérou, Pologne, Russie, Afrique du Sud, Arabie saoudite, Singapour, Espagne, Corée du Sud, Suède, Suisse, Turquie, Tonga, Tuvalu, États-Unis d'Amérique, Uruguay, Venezuela) Juin à septembre 2020		Singapour (66,8 %), Corée du Sud (76,2 %), Turquie (59,2 %) **Océanie** Australie (89,9 %), Fidji (87,2 %), Nouvelle-Zélande (88,4 %), Kiribati (89,8 %), Nauru (88,3 %), Palaos (89,2 %), Papouasie-Nouvelle-Guinée (91,9 %), Îles Salomon (92,6 %), Tonga (92,9 %), Tuvalu (90,5 %) **Amérique du Nord** Canada (62,6 %), Cuba (77,9 %), République dominicaine (79,5 %), El Salvador (71,8 %), Guatemala (75,0 %), Jamaïque (71,0 %), Mexique (73,3 %), Nicaragua (81,2 %), Panama (87,4 %), États-Unis (74,8 %) **Amérique du Sud** Argentine (81,3 %), Brésil (86,2 %), Bolivie (82,8 %), Chili (79,2 %), Colombie (81,8 %), Équateur (70,2 %), Paraguay (67,7 %), Pérou (77,8 %), Uruguay (75,6 %), Venezuela (74,8 %) **Europe** Angleterre (69,3 %), Belgique (60,4 %), Allemagne (65,2 %), Italie (68,4 %), France (51,9 %), Pologne (52,3 %), Espagne (72,5 %), Suède (62,7 %), Suisse (60,2 %), Russie (51,3 %)
Lazarus (2020) (203) Lazarus (2021) (204)	Un sondage en ligne effectué auprès de 13 426 adultes a été utilisé pour analyser les taux d'acceptation du vaccin et les facteurs qui influent sur l'acceptation de ce vaccin contre la	• 71,5 % des participants ont déclaré qu'ils seraient « très susceptibles » ou « assez susceptibles » de se faire vacciner contre la COVID-19.

Étude transversale 19 pays : (Brésil, Canada, Chine, Équateur, France, Allemagne, Inde, Italie, Mexique, Nigéria, Pologne, Russie, Singapour, Afrique du Sud, Corée du Sud, Suède, Royaume-Uni, États-Unis) Juin 2020	COVID-19. Les données de ce sondage ont été analysées différemment dans deux publications. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 48,1 % ont déclaré qu'ils accepteraient la recommandation de leur employeur de se faire vacciner. • La Chine (88,6 %), le Brésil (85,4 %) et l'Afrique du Sud (81,6 %) ont affiché les taux d'acceptation les plus élevés, tandis que le Nigéria (58,9 %), la Pologne (56,3 %) et la Russie (54,9 %) ont affiché les taux les plus faibles. • Le taux d'acceptation au Canada était de 68,7 %. • Les personnes de 25 ans et plus étaient plus susceptibles d'accepter de se faire vacciner que celles qui ont entre 18 et 24 ans. La différence la plus marquée a été observée (RC = 1,73, IC à 95 %, de 1,48 à 2,02) lorsque les réponses de la cohorte de personnes plus âgées (65 ans et plus) ont été comparées à celles de la cohorte formée de personnes plus jeunes (18 à 24 ans). • Les personnes ayant fait des études supérieures, les femmes, celles qui gagnaient plus d'argent, celles qui ont déclaré que certains membres de leur famille avaient attrapé la COVID-19 et celles qui avaient confiance en leur gouvernement étaient plus susceptibles d'accepter de se faire vacciner. • Le fait d'avoir un niveau de scolarité élevé ou très élevé peut être lié à une baisse de l'acceptation des vaccins au Canada, en Espagne et au Royaume-Uni.

POPULATION GÉNÉRALE AU CANADA

Tableau 3. Éléments de preuve sur les attitudes du grand public à l'égard des vaccins (n = 42)

ÉTUDE	MÉTHODES ET OUTILS D'ENQUÊTE	RÉSULTATS CLÉS RELATIFS AUX CONNAISSANCES, ATTITUDES ET COMPORTEMENTS
Études longitudinales (n = 8)		
Leger (2021) *non publiée*	Un sondage en ligne a été mené auprès d'adultes canadiens et américains (âgés de 18 ans et plus)	**Vague 12**

(10, 69-73, 205, 206) Étude longitudinale Canada et États-Unis Novembre 2020 et janvier 2021-juin 2021	pour évaluer les perceptions et les intentions quant à la vaccination. Vague 1 : Novembre 2020, 1 516 Canadiens et 1 002 Américains Vague 2 : Janvier 2021, 1 516 Canadiens et 1 003 Américains Vague 3 :: Février 2021, 1 535 Canadiens et 1 002 Américains Vague 4 :: Février 2021, 1 532 Canadiens et 1 002 Américains Vague 5 : Avril 2021, 1 504 Canadiens et 1 002 Américains Vague 6: Avril 2021, 1,548 Canadiens and 1,003 Américains Vague 7: Mai 2021, 1,529 Canadiens, 1,003 Américains Vague 8: Mai 2021, 1,529 Canadiens, 1,003 Américains Vague 9: Mai 2021, 1,624 Canadiens, 1,002 Américains Vague 10: Mai 2021, 1,624 Canadiens, 1,002 Américains Vague 11: Juin 2021, 1,539 Canadiens, 1,004 Américains *nouvelle* Vague 12: Juin 2021, 1,542 Canadiens, 1,001 Américains *nouvelle* Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins	• Le pourcentage des Canadiens qui ont l'intention de se faire vacciner ou qui ont été vaccinés est passé à 88 % par rapport à mai. • Le pourcentage des personnes qui n'avaient pas l'intention de se faire vacciner était le plus élevé au Manitoba et en Saskatchewan (18 %), suivis de l'Alberta (16 %), des personnes âgées de 18 à 34 ans (14 %, en baisse par rapport aux 18 % du dernier scrutin) et des résidents ruraux (16 %, en baisse par rapport aux 22 % du dernier scrutin). • La croyance que les vaccins sont dangereux est restée à 7 % depuis mai (81 % croient que les vaccins sont sûrs et 12 % ne savent pas). **Vague 11** • Le nombre de Canadiens qui ont l'intention de se faire vacciner ou qui ont été vaccinés se maintient à 86 % (aucun changement par rapport à mai). • Le pourcentage de personnes qui n'avaient pas l'intention de se faire vacciner était le plus élevé en Alberta (20 %), suivie des provinces de l'Atlantique (19 %), chez les 18 à 34 ans (18 %) et chez les résidents ruraux (22 %). • 89 % des gens ont dit qu'ils recevront certainement ou probablement une deuxième dose, 1 % ont dit qu'ils n'en recevront probablement pas, 9 % ont dit avoir déjà reçu une deuxième dose et 1 % n'étaient pas certains. • 3 % des personnes qui résident au Québec et 3 % des personnes âgées de 18 à 24 ans ont indiqué qu'elles ne recevront probablement pas ou certainement pas de deuxième dose. • 48 % des Canadiens étaient mal à l'aise à l'idée de recevoir une autre marque de vaccin comme deuxième dose, tandis que 46 % étaient à l'aise et 6 % se sont dits incertains. • Les personnes du Manitoba et de la Saskatchewan (34 %), les personnes âgées de 35 à 55 ans (25 %) et les résidents ruraux (26 %) présentaient les niveaux les plus élevés de malaise à l'égard d'un vaccin différent comme deuxième dose.

	Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 50 % de ceux qui ont reçu une première dose d'AstraZeneca préféreraient recevoir une deuxième dose d'AstraZeneca, comparativement à 32 % qui aimeraient recevoir une deuxième dose d'une autre marque, alors que 18 % ont dit ne pas savoir. • La croyance selon laquelle les vaccins sont dangereux est passée de 1 % à 7 % depuis mai (82 % croyaient que les vaccins sont sécuritaires et 11 % ont dit ne pas savoir). **Vague 10 :** • Les Canadiens étaient divisés à parts égales sur la question de savoir s'ils étaient à l'aise avec l'idée que certains de leurs collègues ne soient pas vaccinés. • L'inconfort à l'égard des collègues non vaccinés était le plus élevé en Colombie-Britannique (62 %) alors que 60 % des habitants des provinces de l'Atlantique, du Manitoba et de la Saskatchewan étaient à l'aise avec cette idée. • Les Canadiens plus âgés (55 ans et plus) étaient moins à l'aise avec l'idée des collègues non vaccinés (52 %), tout comme les résidents urbains (53 %) comparativement aux résidents ruraux (44 %). **Vague 9 :** • 51 % des répondants étaient d'avis que la campagne de vaccination dans leur province se déroulait à peu près de la même façon que dans les autres provinces. Les résidents du Québec étaient d'avis qu'ils s'en tiraient mieux que ceux des autres provinces, tandis que ceux de l'Ontario et de l'Alberta étaient d'avis que la vaccination s'effectuait plus lentement. • Les Canadiens étaient fortement favorables à l'idée de devoir présenter une preuve de vaccination lorsqu'ils prenaient l'avion (82 %), qu'ils assistaient à des événements où l'on retrouvait une foule (75 %) et s'ils fréquentaient une université en présentiel (71 %) alors qu'ils étaient moins

		favorables à l'idée de devoir présenter cette preuve lorsqu'ils devaient se rendre au travail (68 %), au moment de séjourner à l'hôtel (68 %) et de manger dans un restaurant (64 %). L'appui à la vaccination était toujours plus élevé chez les 55 ans et plus. • Depuis le sondage précédent effectué en mai, il y a eu une augmentation de 4 % (à 86 %) des personnes qui avaient été vaccinées ou avaient l'intention de se faire vacciner. • Les provinces ayant le niveau combiné de vaccination ou d'intention de se faire vacciner le plus élevé étaient le Québec (90 %), suivi de l'Alberta (87 %), des provinces de l'Atlantique (86 %), de la Colombie-Britannique (85 %) et du Manitoba et de la Saskatchewan (84 %). • La croyance selon laquelle les vaccins sont sécuritaires et devraient être administrés est demeurée stable à 81 %, mais le pourcentage des personnes incertaines est passé de 1 % à 12 %. • Les vagues 1 à 8 sont résumées dans les versions précédentes du présent rapport.
Angus Reid (2021) *non publiée* (8, 60, 61, 66, 68, 76, 82, 83, 85) Étude longitudinale Canada Juillet, septembre et décembre 2020 et janvier, février et mai-juin 2021	Un sondage en ligne a été utilisé pour analyser l'intention en ce qui concerne la vaccination et les perceptions concernant le vaccin chez des Canadiens (âgés de 18 ans et plus). Vague 1 : Juillet 2020, n = 1 519 Vague 2 : Septembre 2020, n = 1 660 Vague 3 : Décembre 2020, n = 1 603 Vague 4 :: Janvier 2021, n = 1 580 Vague 5 : Février 2021, n = 1 201 Vague 6 : Mars 2021, n = 1 748 Vague 7 : Avril 2021, n = n.d.	**Vague 10** • 84 % ont reçu au moins un vaccin ou se feront vacciner dès que possible (soit une augmentation de 2 % par rapport au mois de mai), 4 % se feront vacciner, mais souhaitent attendre (contre 6 % auparavant), 9 % ne se feront pas vacciner (aucun changement) et 3 % sont incertains (aucun changement). • La réticence à se faire vacciner reste la plus forte en Alberta et en Saskatchewan (18 %). Depuis mai, ce chiffre a augmenté de 1 % en Alberta et diminué de 6 % en Saskatchewan. • 57 % des répondants souhaitent que l'on mette autant l'accent sur la distribution des premières et des deuxièmes doses, 26 % préfèrent que l'on donne la priorité à l'administration de toutes les premières doses admissibles et 16 % souhaitent que l'on se concentre sur les deuxièmes doses et

	Vague 8: Apr 2021, n=1594 Vague 9: May 2011, n= 1,319 Vague 10: June 2021, n=4,948 *nouvelle* Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Vaccine hesitancy Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	que l'on revienne aux premières doses. Le soutien à l'idée de se concentrer sur l'administration des premières doses était plus élevé parmi les personnes en attente de vaccination (39 %) et parmi les personnes âgées de 18 à 24 ans (40 %). • Les Canadiens sont favorables à la poursuite de la vaccination jusqu'à ce que tous les Canadiens aient été vaccinés (72 %), 18 % souhaitent que l'on se concentre sur les populations à risque au niveau mondial et 10 % sont incertains. • Les personnes interrogées ont estimé que les vaccinations de la deuxième dose progressaient aussi bien qu'on pouvait s'y attendre (49 %), avec une répartition presque égale entre le sentiment que cela prenait trop de temps (27 %) et que cela allait très vite (24 %). 55 % des résidents du Québec ont estimé que les choses allaient bien alors que 40 % des résidents de l'Ontario estimaient que les choses allaient trop lentement. • 51 % des personnes interrogées estiment que le Canada a fait un bon travail pour obtenir les doses de vaccin et 41 % estiment qu'il a fait un mauvais travail. Cependant, 60 % et 69 % ont encore confiance dans la capacité des gouvernements fédéral et provinciaux à gérer la distribution des vaccins, respectivement. **Vague 9 :** • 82 % des répondants ont soit reçu un vaccin ou souhaitent le recevoir le plus tôt possible, une augmentation par rapport au chiffre de 71 % obtenu en avril. • Moins de répondants ont dit être incertains au sujet de la vaccination (en baisse de 3 % par rapport à 13 % obtenu en avril), vouloir attendre avant de recevoir un vaccin (en baisse de 6 % par rapport à 13 % obtenu en avril) ou ont dit ne pas vouloir recevoir de vaccin (en baisse de 9 % par rapport à 13 % obtenu en avril)

		• 53 % des répondants ont reçu au moins une dose du vaccin, soit une augmentation de 36 % par rapport à avril. • La réticence à se faire vacciner est la plus forte en Saskatchewan (24 %) où le niveau demeure stable (22 % en avril et 26 % en janvier). • La réticence à se faire vacciner a chuté de façon spectaculaire en Alberta, passant de 45 % en janvier à 25 % en avril et à 17 % en mai. • La réticence en Colombie-Britannique, au Manitoba, en Ontario, au Québec et dans les provinces de l'Atlantique a varié entre 10 % et 12 % en mai. • La réticence à se faire vacciner était la plus forte chez les hommes de 35 à 54 ans (18 %), puis chez les femmes de 18 à 34 ans (15 %). • Parmi les personnes qui ont reçu le vaccin AstraZeneca, 2 % ont dit le regretter complètement alors que 66 % ont de sérieux doutes à l'égard du vaccin. • Les Canadiens demeurent très à l'aise avec les vaccins Pfizer et Moderna (93 % et 89 % respectivement), mais ils ont perdu confiance en AstraZeneca (52 % en avril et 35 % en mai) et en Janssen (54 % et 49 %). • Les hommes non vaccinés sont plus à l'aise que les femmes de recevoir le vaccin AstraZeneca (29 % contre 36 % qui sont extrêmement mal à l'aise), mais 40 % des femmes accepteraient un vaccin avec lequel elles sont mal à l'aise comparativement à 31 % des hommes. • Les vagues 1 à 8 sont résumées dans les versions précédentes du présent rapport.
Engage Manitoba (2021) *non publiée* (97, 207)	Une série de sondages en ligne au Manitoba a été mise en œuvre pour évaluer les intentions de se faire vacciner dans le cadre du sondage effectué sur le Plan de	**Sondage 5** • 86 % des répondants ont reçu au moins une dose d'un vaccin (contre 9 % dans le sondage 4). • 2 % ont pris rendez-vous pour la première dose, 2 % recevront le vaccin, mais ne sont pas pressés

Étude longitudinale Canada Janvier à juin 2021	rétablissement sécuritaire des services du Manitoba. Sondage 1 10 au 15 janvier, n = 73 351 Sondage 2 4 au 9 février, n = 33 687 Sondage 3 25 février au 2 mars, n = 26 909 Sondage 4 18 au 23 mars, n = 31 776 Sondage 5: 4 au 8 juin, n= 33,904 Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	de le recevoir (contre 13 %), 4 % ne sont pas certains de se faire vacciner (contre 12 %) et 5 % ne se feront pas vacciner. • Parmi ceux qui n'étaient pas certains ou qui n'avaient pas l'intention de se faire vacciner, très peu étaient influencés par la capacité de voyager au Canada (9 %), d'assister à des événements sportifs ou culturels (7 % à 9 %), de visiter des installations ou des événements (10 %) ou de rendre visite à des êtres chers (11 %). **Sondage 4** • 9,0 % des répondants ont déjà reçu un vaccin (en hausse de 4 % depuis le troisième sondage). • 56 % ont l'intention de s'inscrire pour se faire vacciner dès qu'ils sont admissibles (hausse de 1,9 %). • 13 % ont déclaré qu'ils se feraient vacciner, mais qu'ils ne sont pas pressés (comparativement à 16,2 %). • 12 % ont dit ne pas être certains de vouloir se faire vacciner lorsqu'un vaccin sera disponible (en baisse par rapport à 14,2 %). • 10 % ont dit qu'ils refuseraient de se faire vacciner (comparativement à 10,5 %). • Le taux d'approbation de l'approche du gouvernement du Manitoba en matière de vaccination est élevé dans le dernier sondage : 33 % l'approuvent fortement, 47 % l'approuvent quelque peu, 13 % le désapprouvent quelque peu et 7 % le désapprouvent fortement.
Gouvernement du Manitoba (2021) *Non publié* (11) *nouveau*	Un groupe de recherche en ligne composé de 600 Manitobains a été interrogé pour comprendre les attitudes envers les vaccins et les mesures incitatives possibles pour augmenter le taux d'adoption.	• 87 % ont reçu un vaccin ou ont l'intention de se faire vacciner (74 % ont reçu un vaccin et 13 % ont l'intention de se faire vacciner), soit une augmentation de 11 % par rapport au mois d'avril. • 5 % se feront vacciner, mais ne sont pas pressés de le faire (par rapport à 12 %), 5 % ne sont pas

Étude longitudinale Canada Mai 2021	Sujets des questions : 1) Intentions de se faire vacciner 2) Perception des vaccins Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	certains de se faire vacciner (par rapport à 7 %) et 4 % ne se feront pas vacciner (par rapport à 5 %). • D'avril à juin, il y a eu une baisse de 18 % du nombre de personnes approuvant fortement la distribution des vaccins au Manitoba (de 42 % à 24 %), 49 % l'approuvant quelque peu (en hausse par rapport à 43 %), 17 % la désapprouvant quelque peu (en hausse par rapport à 11 %) et 10 % la désapprouvant fortement (en hausse par rapport à 4 %). • Dans un groupe de 70 parents ou tuteurs d'enfants âgés de 12 à 17 ans, 15 % sont incertains de faire vacciner leurs enfants et 13 % ne le feront pas. • Les parents qui n'avaient pas l'intention de faire vacciner leurs enfants faisaient partie de ménages dont le revenu était inférieur à 40 000 dollars, ne se feraient pas vacciner eux-mêmes et ne pensaient pas que les adultes devaient recevoir tous les vaccins habituels. • 31 % des personnes interrogées avaient un avis beaucoup plus positif sur le vaccin contre la COVID-19 maintenant qu'au moment de sa mise en place, 19 % avaient un avis légèrement plus positif, 45 % un avis identique, 3 % un avis légèrement plus négatif et 2 % un avis beaucoup plus négatif. • 55 % ont estimé que le fait de se faire vacciner ou non devrait être un choix, 42 % ont estimé que cela ne devrait pas être un choix, et 3 % étaient incertains. • Les personnes qui encouragent la vaccination ont tendance à avoir moins de 30 ans ou plus de 65 ans et pensent que les adultes devraient recevoir tous les vaccins habituels. • Les types de renseignements les plus susceptibles d'influencer la décision de se faire vacciner sont ceux sur les effets secondaires possibles (42 %), la possibilité de choisir le vaccin (42 %), l'information

		sur les tests (41 %) et l'information sur le fonctionnement du vaccin (36 %). • Le type d'information le moins convaincant était d'entendre les histoires de célébrités qui ont reçu leur vaccin (90 % d'incidence improbable). • Les femmes seraient les plus influencées par le fait de pouvoir choisir le vaccin. • Les résidents de Winnipeg ont été plus influencés que ceux des régions rurales par le fait d'obtenir un vaccin auprès d'un médecin de famille/pharmacien, de parler à leur médecin de famille/pharmacien, de faire venir quelqu'un à leur domicile et d'entendre les histoires de célébrités. • Les Manitobains n'ont pas été influencés par les incitatifs communautaires, comme la possibilité de voyager sans avoir à s'isoler (50 % pas plus susceptibles de se faire vacciner), la possibilité de visiter les maisons de soins de longue durée sans restrictions (52 % pas plus susceptibles), l'entrée dans les provinces ou les pays (48 % pas plus susceptibles), la possibilité d'assister à de grands événements (60 % pas plus susceptibles), la participation à de grands rassemblements (54 % pas plus susceptibles), l'accès à certaines entreprises ou installations pour les personnes vaccinées (61 % pas plus susceptibles). • Les personnes âgées de 30 à 44 ans étaient plus susceptibles d'être influencées par la possibilité de participer à des rassemblements plus importants (communautaires, religieux ou personnels). • Les incitatifs financiers (argent, bons, articles gratuits, tirages au sort, remises) n'ont pas été signalés comme un facteur qui augmenterait la probabilité de se faire vacciner (entre 75 % et 84 % déclarant qu'ils ne sont pas plus susceptibles de se faire vacciner par un incitatif financier). • 70 % des répondants sont préoccupés si seules les personnes réticentes reçoivent des incitatifs importants (50 à 100 dollars).

Statistics Canada (2020) & Statistics Canada (2021) *non publiée* (65, 80, 81) Étude longitudinale Canada Septembre 2020 à février 2021	Un sondage en ligne mené par Statistique Canada dans le cadre de l'Enquête sur la santé dans les collectivités canadiennes (ESCC) a évalué les comportements des Canadiens pour protéger leur propre santé et celle des autres. Une question sur les intentions de vaccination a été ajoutée au sondage de septembre. Le plus récent rapport fait état de 20 000 réponses reçues de personnes âgées de 12 ans et plus. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	**Janvier-février 2021** • 82,3 % des répondants étaient très ou probablement prêts à se faire vacciner contre la COVID-19. • L'intention de se faire vacciner était la plus élevée chez les personnes âgées de plus de 65 ans (88,1 %), avec un niveau d'intention décroissant chez les personnes âgées de 12 à 17 ans (71,0 %). • L'intention de se faire vacciner était similaire chez les hommes et les femmes (82,8 % contre 81,9 %, respectivement). **Sept à Déc. 2020** • Pendant la période d'échantillonnage, 77 % des personnes ont dit être prêtes à se faire vacciner. Cela représente une augmentation par rapport à septembre (75,5 %) à octobre (74,8 %) et à novembre-décembre (80,3 %). • L'intention de se faire vacciner était la plus élevée à l'Île-du-Prince-Édouard (89,1 %), en Nouvelle-Écosse (81,5 %) et en Colombie-Britannique (81,4 %). L'intention de se faire vacciner était la plus basse dans les Prairies (75,2 %) • Les hommes étaient plus susceptibles de se faire vacciner que les femmes (77,9 % contre 75,8 %). • Les immigrants étaient légèrement moins susceptibles de se faire vacciner (74,6 %), mais cela variait grandement entre les immigrants plus âgés et les plus jeunes (73,2 % pour les 12 à 64 ans et 81,1 % pour les 65 ans et plus). • Les membres de la communauté LGBTQ2+ étaient plus susceptibles de se faire vacciner (83,3 %). • Les personnes des minorités visibles ayant la plus forte intention de se faire vacciner étaient les Japonais (86,5 %), les Coréens (85,6 %), les Asiatiques du Sud (82,5 %), les Chinois (79,3 %), les minorités visibles non indiquées/multiples (79,1 %), les Asiatiques du Sud-Est (78,3 %), les Asiatiques de l'Ouest (78,3 %), les Philippins (75,1 %), les Arabes (68,1 %), les gens d'Amérique latine (66,0 %) et les Noirs (56,6 %). L'intention des

		non-membres d'une minorité visible de se faire vacciner était de 77,6 %. • Les minorités visibles plus âgées étaient plus susceptibles de se faire vacciner que les 12 à 64 ans (77,4 % contre 74,6 %). • Chez les répondants autochtones, 71,8 % ont dit qu'ils se feraient vacciner, ce qui est nettement inférieur au taux de réponse des répondants non autochtones (77,1 %). 74,2 % des membres des Premières Nations qui vivent hors réserve étaient prêts à se faire vacciner, comparativement à 67,8 % des Métis et à 72,5 % des Inuits*. • Les Autochtones plus âgés (65 ans et plus) étaient plus susceptibles de vouloir se faire vacciner que les plus jeunes (74,9 % contre 71,3 %). *Utiliser avec prudence. Coefficient de variation (CV) de 15,1 % à 35,0 %.
Impact Canada (2020) *non publiée* (74) Étude longitudinale Canada Avril 2020 à février 2021	La confiance et l'hésitation face au vaccin dans le contexte canadien ont été examinées par la mise en œuvre de l'Outil de l'OMS pour l'analyse des comportements face à la COVID-19 chez huit vagues d'adultes (âgés de 18 ans et plus) utilisant pour ce faire les mêmes participants, dans la mesure du possible. Vague 1 : n = 2 023, Vague 2 : n = 2 098, Vague 3 : n = 2 000, Vague 4 : n = 2 152, Vague 5 : n = 2 169, Vague 6 : n = 2 141, Vague 7 : n = 2 129, Vague 8 : n = 2 117, Vague 9 : n = 2 055, Vague 10 : n = 2 125, Vague 11: n= 2 037 Sujets des questions :	**Vague 11** • L'intention de se faire vacciner immédiatement a atteint 58 % (contre 49 % à la vague 10). 24 % ont dit avoir l'intention de se faire vacciner, mais préféraient attendre, 9 % ont dit qu'ils ne le feraient pas et 8 % se sont dits incertains. • Ceux qui prévoyaient attendre ont dit qu'ils attendraient probablement un ou deux mois avant de se faire vacciner (33 %). • 68 % des gens avaient décidé si oui ou non ils se feraient vacciner alors que 25 % avaient besoin de plus de renseignements avant de finaliser leur décision. • Les deux raisons les plus fréquentes en ce qui concerne la réticence à se faire vacciner étaient l'absence de tests ou de recherches (26 %) et la croyance que le vaccin n'était pas sécuritaire (15 %). • 47 % déclarent que le vaccin le plus efficace est le critère le plus important pour choisir un vaccin, suivi du vaccin disponible en premier (15 %) et du plus petit nombre d'effets secondaires (12 %).

	1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Non	• 56 % et 22 % ont dit qu'ils aimeraient obtenir plus d'information sur l'innocuité et l'efficacité du vaccin, respectivement. • Une recommandation d'un fournisseur de soins de santé à l'égard du vaccin influencerait probablement 45 % des répondants. **Vague 10** • L'acceptation du vaccin a légèrement augmenté entre la vague 9 (61 %) et la vague 10 (65 %). • L'intention de se faire vacciner immédiatement a atteint 49 % (contre 43 % à la vague 9). 31 % ont dit avoir l'intention de se faire vacciner, mais préféraient attendre, 11 % ont dit qu'ils ne le feraient pas et 8 % se sont dits incertains. • Parmi ceux qui voulaient attendre avant de se faire vacciner, 42 % voulaient attendre plusieurs mois (comparativement à 27 % à la vague 9). • Les principales raisons données par les gens pour attendre avant de se faire vacciner étaient qu'ils voulaient s'assurer de l'innocuité (80 %) et de l'efficacité (64 %) de ce vaccin. • On a posé des questions sur les incitatifs hypothétiques aux personnes qui ont dit qu'elles refuseraient de se faire vacciner. 58 % d'entre elles ont dit qu'elles aimeraient avoir l'assurance que le vaccin ne présente pas de risque d'exposition à la COVID-19, 56 % voulaient un système de réservation pratique et 52 % voulaient un endroit pratique où se faire vacciner. • 56 % des participants ont déclaré qu'ils se feraient vacciner pour pouvoir retourner au travail, voyager ou assister à de grands rassemblements. • 63 % ont déclaré qu'ils avaient décidé de se faire vacciner ou non et 32 % aimeraient obtenir plus d'information avant de prendre leur décision.
INSPQ (2020), INSPQ (2021), INSPQ (2021),	travailleurs de la santé au Québec. Le nombre de participants n'a pas été indiqué de façon claire (environ	**Juin** • 49 % étaient d'accord pour que les adultes vaccinés puissent se réunir sans masque en privé,

INSPQ (2021), INSPQ (2021), INSPQ (2021) *non publiée* (12, 86, 88, 90, 91, 95) Étude longitudinale Canada Avril 2020 à juin 2021	3 300 par période de collecte). Il y a eu plusieurs périodes de collecte, soit en avril-mai 2020, en septembre et en décembre 2020, et en avril-juin 2021. Ces articles sont en français. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	44 % n'étaient pas d'accord et 6 % étaient incertains. • Près de la moitié des personnes interrogées estiment que les personnes vaccinées devraient pouvoir se réunir sans masque en privé (49 %), mais sont également d'accord pour que les masques soient portés à l'extérieur avec des personnes avec lesquelles elles ne vivent pas (56 %). • Les passeports vaccinaux bénéficient d'un soutien important au Québec, 72 % des résidents y étant favorables (23 % ne sont pas d'accord et 4 % sont incertaines). • 73 % des répondants ne sont pas d'accord avec le fait qu'il est important de suivre les mesures de protection compte tenu du taux de vaccination et de la diminution des cas de COVID-19. **Mai** • 74 % des personnes interrogées qui n'ont pas encore été vaccinées ont l'intention de se faire vacciner, soit une baisse de 3 % depuis fin avril. 18 % n'ont pas l'intention de se faire vacciner (augmentation de 4 %), et 8 % ne savent pas (diminution de 1 %). • L'intention de se faire vacciner était la plus faible chez les personnes âgées de 25 à 34 ans, les femmes, les personnes n'ayant pas fait d'études secondaires, les personnes sans emploi, les personnes plus démunies, celles qui ne s'inquiétaient pas d'être infectées par la COVID-19, celles qui avaient des idées conspiratrices et celles qui consultent les médias sociaux une fois par semaine ou moins. • Les ménages avec des mineurs avaient moins l'intention de se faire vacciner que les ménages composés d'une seule personne et que les ménages sans mineurs.

		• Les immigrants étaient plus réticents et incertains à l'idée de se faire vacciner que les non-immigrants. • Les trois principales raisons invoquées par les personnes qui n'avaient pas l'intention de se faire vacciner étaient la crainte des effets secondaires, le manque de confiance dans les vaccins en général et la nouveauté du vaccin. • 28 % de personnes qui n'ont pas l'intention de se faire vacciner estiment que cela est incompatible avec leurs croyances religieuses ou leurs principes personnels. **Plus tôt** • 77 % des personnes interrogées qui ne se sont pas encore fait vacciner ont l'intention de se faire vacciner, soit une baisse de 1 % depuis début avril. 14 % n'ont pas l'intention de se faire vacciner (aucun changement), et 9 % ne savent pas (augmentation de 1 %). L'intention a gagné 7 % depuis décembre. • L'intention de se faire vacciner était plus élevée chez les hommes que chez les femmes (78 % contre 76 %), chez les répondants plus âgés (79 % pour les 60 ans et plus contre 75 % pour les 18 à 25 ans) et chez les personnes ayant un diplôme universitaire (85 % pour les universitaires, 78 % pour les collégiens). • L'intention de se faire vacciner augmente généralement à mesure que la taille des collectivités s'accroît : petits villages de moins de 10 000 habitants (71 %), villes de 10 000 à 100 000 habitants (73 %), grande région de Montréal (81 %) et Montréal (79 %). • 68 % ne sont pas d'accord avec l'affirmation « les personnes vaccinées contre la COVID-19 devraient avoir le droit de se réunir en privé et de ne plus porter de masque en public », tandis que 25 % sont d'accord et 7 % sont incertaines.

		• En décembre, les personnes ayant une faible intention de se faire vacciner étaient préoccupées par les effets secondaires (27 %), la nouveauté du vaccin (24 %) et le manque de confiance dans les vaccins en général (24 %). • Les personnes ayant une vision conspiratrice du monde étaient moins susceptibles d'accepter un vaccin (51 % contre 76 %). • Le fait d'être d'accord avec la vaccination obligatoire continue d'être à la baisse avec 54 % de personnes d'accord en décembre.
Saskatchewan Population Health and Evaluation Research Unit (2020) *non publiée* (208) Étude longitudinale Canada Mai à septembre 2020	Un sondage en ligne a été utilisé pour évaluer l'intention de se faire vacciner des résidents de la Saskatchewan au fil du temps. Les sondages ont été effectués de mai à septembre. Le nombre de personnes n'est pas précisé et on ne sait pas trop si ce sont les mêmes participants au fil du temps. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• De mai à septembre, l'intention de se faire vacciner est passée de 84,9 % à 56,5 %. • L'intention de se faire vacciner est la plus élevée chez les 65 à 74 ans et la plus faible chez les moins de 48 ans.
Études transversales (n = 29)		
Angus Reid (2021) *non publiée* (96) Étude transversale	1 601 adultes canadiens ont été interrogés en ligne sur ce qu'ils pensent des politiques relatives à la vaccination (preuves et passeports vaccinaux). Sujets des questions :	• 79 % des Canadiens sont favorables à la présentation d'une preuve de vaccination pour les voyages internationaux (à l'exception des États-Unis), 78 % pour les vols commerciaux et 76 % pour les voyages aux États-Unis. • L'idée d'avoir une preuve de vaccination pour assister à de grands événements publics (69 %), dans des endroits publics comme les restaurants,

Canada Mai 2021	1) Intentions en ce qui concerne la vaccination 2) Perception des vaccins 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	les bars et les salles de cinéma (55 %) et sur les lieux de travail (55 %) est moins soutenue. • Les personnes qui hésitaient à se faire vacciner étaient beaucoup moins favorables à la preuve de la vaccination dans tous les scénarios présentés. • 18 % des personnes qui ne sont pas disposées à se faire vacciner seraient être influencées à le faire si une preuve de vaccination était exigée dans de nombreux scénarios.
Leger (2021) *non publiée* (209) Étude transversale Canada Avril 2021	Un sondage en ligne a été mené auprès de 1 044 participants en Colombie-Britannique afin d'évaluer les points de vue sur les vaccins, les passeports vaccinaux et le déploiement des vaccins. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 16 % ont déclaré avoir reçu un vaccin. • 49 % ont l'intention de dire à tout le monde qu'ils connaissent lorsqu'ils auront reçu leur vaccin. Cela est particulièrement vrai pour les répondants des régions urbaines (53 %) comparativement aux répondants des régions rurales (40 %). Un moins grand nombre de répondants en parleraient uniquement à leur famille immédiate et à leurs amis (42 %). • 24 % ont dit avoir l'intention de publier sur les médias sociaux le fait qu'ils se sont fait vacciner. • La plupart ne croient pas qu'ils devraient être vaccinés avant les autres (27 %), ou sont jaloux (25 %) des autres personnes vaccinées ou éprouvent de l'anxiété à leur égard (25 %). • Les voyageurs internationaux qui arrivent en Colombie-Britannique (77 %) et de voyageurs de la Colombie-Britannique qui se rendent à l'étranger (75 %) ont fortement appuyé l'idée des passeports vaccinaux. Les Canadiens qui voyagent au Canada (68 %) et en Colombie-Britannique (56 %) appuyaient beaucoup moins une telle mesure. • Le passeport vaccinal dans quelque situation que ce soit a reçu un fort appui des 55 ans et plus. • 70 % des gens sont satisfaits de l'ordre de priorité de la vaccination en Colombie-Britannique et 44 % sont satisfaits du déploiement. • Le soutien aux dirigeants ou aux responsables en matière de santé a diminué depuis décembre 2020

		(Dre Bonnie Henry : 65 %, Adrian Dix : 58 %, Dre Theresa Tam : 53 %, Justin Trudeau : 45 %).
Statistics Canada (2021) *non publiée* (210) Étude transversale Canada Mars et avril 2021	Les intentions et les perceptions relatives au vaccin ont été analysées chez 1 025 adultes canadiens (âgés de 18 ans et plus) résidant dans les capitales des territoires en réponse à des invitations reçues par la poste et dans le cadre d'entrevues téléphoniques assistées par ordinateur pour les personnes qui n'ont pas répondu. Sujets des questions : 4) Intentions en ce qui concerne la vaccination 5) Perception des vaccins 6) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• La majorité des répondants avaient déjà reçu une dose (80 %), alors que 16 % étaient susceptibles de se faire vacciner et qu'un petit nombre de gens ont dit qu'ils ne se feraient pas vacciner (4 %). • Les répondants étaient plus susceptibles d'avoir reçu un vaccin ou d'être vaccinés s'ils détenaient un diplôme d'études postsecondaires ou plus élevé (85 % comparativement à 68 % pour le vaccin et 13 % comparativement à 23 % pour la probabilité de se faire vacciner, respectivement). • 10 % des personnes peu susceptibles de se faire vacciner avaient un revenu du ménage inférieur à 60 000 $, comparativement à 2 % des personnes dont le revenu se situait entre 60 000 $ et plus de 120 000 $. • La plupart des répondants étaient d'avis que les vaccins en général étaient sécuritaires (95 %) et efficaces (97 %) comparativement au vaccin contre la COVID-19, pour lequel l'innocuité (86 %) et l'efficacité (88 %) obtenaient un plus faible taux. • 94 % des répondants étaient convaincus que le processus du Canada ne permettait d'approuver que des vaccins sûrs et efficaces (94 %). • Les principales sources d'information sur la vaccination contre la COVID-19 étaient l'Agence de la santé publique du Canada et Santé Canada (89 %) et les régies de la santé au niveau provincial, territorial ou régional (85 %).
Centre for Addiction and Mental Health (2021) *non publiée* (211) Étude longitudinale	Un sondage en ligne a été mené auprès de 1 000 Canadiens dans le cadre du panel Web Qu'en pensez-vous afin de mesurer les intentions en matière de vaccination et les questions de santé mentale. Sujets des questions :	• 66,4 % des répondants qui n'ont pas encore reçu de vaccin ont dit avoir certainement l'intention de se faire vacciner, 21,8 % ont dit qu'ils se feront probablement vacciner et 11,8 % ont dit ne pas vouloir se faire vacciner.

Canada Mars 2021	1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	
Tang (2021) *préimpression* (212) Étude transversale Canada Janvier à mars 2021	Afin d'évaluer la réticence à se faire vacciner dans les sous-groupes de population au Canada, un sondage en ligne a été mené auprès de 14 621 membres du Forum Angus Reid, qui est représentatif à l'échelle nationale. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Dans l'ensemble, 9,3 % des répondants n'ont pas l'intention de se faire vacciner. Ce pourcentage était le plus élevé en Alberta (16,4 %), au Manitoba et en Saskatchewan (13,8 %) et le plus faible au Québec (8,3 %), dans les provinces de l'Atlantique (8 %), en Ontario (7,8 %) et en Colombie-Britannique (7,2 %). • La réticence à se faire vacciner était fortement associée aux personnes âgées de 40 à 59 ans (RC 0,87, IC à 95 % : 0,78 à 0,97), aux membres d'une minorité visible (RC 0,56, IC à 95 % : 0,37 à 0,84), aux personnes moins scolarisées et aux membres d'un ménage de cinq personnes ou plus (RC 0,82, IC à 95 % : 0,76 à 0,88).
Syan (2021) *préimpression* (77) Étude transversale Canada Janvier et février 2021	Un sondage en ligne a été utilisé pour évaluer les facteurs associés à l'intention de recevoir ou non un vaccin contre la COVID-19 chez 1 367 adultes (âgés de 18 ans et plus) qui vivaient dans le sud de l'Ontario. Sujets des questions : 1) Intentions en ce qui concerne la vaccination	• 82,8 % des répondants se sont dits prêts à recevoir un vaccin et 17,2 % ne voulaient pas se faire vacciner. • Les raisons les plus courantes de la réticence par rapport à la vaccination étaient les effets secondaires à long terme (65,5 %) et immédiats (60,5 %) et le manque de confiance dans le vaccin (55,2 %). • Une plus grande intention de se faire vacciner était fortement associée au sexe masculin (P = 0,002) et au fait d'avoir un plus grand niveau de scolarité (P < 0,001).

	2) Hésitation par rapport à la vaccination 3) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• La perception de l'innocuité du vaccin contre la COVID-19 était beaucoup plus faible (-10,7 %) que celle des vaccins en général. Les femmes, les adultes plus âgés et les personnes moins scolarisées ont déclaré avoir moins confiance en l'innocuité du vaccin contre la COVID-19.
Leger (2021) *non publiée* (99) Étude transversale Canada Janvier 2021	Un sondage en ligne a été mené auprès de 800 participants du Manitoba (âgés de 18 ans et plus) pour sonder les perceptions et les intentions quant à la vaccination. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Perceptions à propos du déploiement de la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 72 % des répondants ont dit avoir l'intention de se faire vacciner lorsqu'un vaccin sera disponible. • L'intention de se faire vacciner augmente avec l'âge. 82 % des 55 ans et plus ont déclaré qu'ils auraient certainement ou probablement l'intention de se faire vacciner, comparativement à 65 % des 18 à 51 ans. • Les études supérieures et un revenu supérieur étaient associés à une intention accrue de se faire vacciner. • L'innocuité du vaccin demeure une préoccupation, car 57 % des gens ne veulent pas faire partie de la première vague de personnes vaccinées et veulent attendre que l'innocuité soit établie. 49 % ont des préoccupations au sujet de l'innocuité, mais ont généralement des opinions favorables à la vaccination. • Plus de 66 % des répondants conviennent que le vaccin devrait être obligatoire pour tous les travailleurs de la santé. • 71 % des répondants sont à l'aise avec la façon dont le gouvernement du Manitoba détermine les groupes prioritaires pour la vaccination précoce.
Leger (2021) *non publiée* (100) Étude transversale	Plus de 1 000 résidents de l'Alberta (18 ans et plus) ont été sondés en ligne afin de connaître leur perception du déploiement du vaccin.	• Le taux d'approbation en ce qui concerne le déploiement global du vaccin en Alberta était divisé puisque 48 % se sont dit satisfait alors que 43 % étaient insatisfaits. • En ce qui concerne l'ordre de priorité établi par le gouvernement, 64 % des répondants étaient satisfaits et 28 % étaient insatisfaits.

Canada Janvier 2021	Sujets des questions : 1) Perceptions à propos du déploiement de la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 44 % étaient satisfaits de la communication du plan de mise en œuvre par le gouvernement alors que 48 % ne l'étaient pas. • Un plus grand nombre de personnes étaient insatisfaites (56 %) du rythme du déploiement comparativement à celles qui étaient satisfaites (35 %). • 53 % des répondants croient qu'ils auront la possibilité de recevoir un vaccin après septembre.
Insights West (2021) *non publiée* (67) Étude transversale Canada Janvier 2021	Un sondage en ligne effectué auprès de 824 résidents de la Colombie-Britannique a analysé leur intention de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perceptions à propos du déploiement de la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	• 58 % des répondants ont dit être certainement prêts à se faire vacciner, 22 % ont dit être probablement prêts, 5 % ne se feront probablement pas vacciner et 7 % ne se feront certainement pas vacciner. • 67 % des répondants âgés (âgés de 55 ans et plus) étaient plus susceptibles de se faire vacciner que ceux des groupes d'âge plus jeunes (52 % chez les 18 à 34 ans). • 69 % étaient d'avis que ceux qui avaient des problèmes sous-jacents auraient dû passer avant les autres sur la liste. • Lorsqu'on leur a posé des questions sur le plan de déploiement du vaccin, 5 % des résidents ont jugé que le déploiement de la vaccination était excellent, 30 % ont dit qu'il était bon, 51 % ont indiqué qu'il était passable, 14 % ont dit qu'il était mauvais alors que 7 % ont mentionné qu'il était très mauvais. On a observé des tendances semblables pour ce qui est des perceptions sur la clarté des niveaux de déploiement et d'établissement des priorités.
Afifi (2021) (213) *nouveau* Étude transversale Canada	Grâce aux répondants de l'étude longitudinale Well-Being and Experiences (2017-2020), les intentions de se faire vacciner ont été consignées pour les adolescents de Winnipeg âgés de 16 à 21 ans et leurs	• 65,4 % des répondants ont l'intention de se faire vacciner, 26,1 % sont incertains et 8,5 % ne sont pas disposés à le faire. • Les parents ayant fréquenté une école de métiers, un collège communautaire ou ayant une éducation inférieure, ayant un revenu inférieur à 49 999 $, ayant subi une certaine pression financière à cause de la COVID-19, ayant déclaré avoir une faible

Nov.-déc. 2020	soignants/parents à l'aide d'un sondage en ligne. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	connaissance de la COVID-19 étaient associés à de plus faibles intentions de se faire vacciner. • Le fait d'avoir un problème de santé autodéclaré était associé à des intentions plus élevées d'accepter un vaccin. • Après correction pour tenir compte du genre, de l'âge et du revenu du ménage, les enfants qui n'avaient jamais reçu de fessée (RRa 0,33, IC à 95 % : de 0,17 à 0,62), jamais connu de victimisation par les pairs (RRa 0,49, IC à 95 % : de 0,25 à 0,96), jamais connu de toxicomanie dans le ménage (RRa 0,41, IC à 95 % : de 0,20 à 0,83), n'ayant jamais eu de contact avec une famille d'accueil ou un bureau de protection de l'enfance (RRa 0,34, IC à 95 % : de 0,16 à 0,72), et n'ayant eu aucun risque que leur ménage soit à court d'argent (RRa 0,45 IC à 95 % : de 0,21 à 0,97) étaient plus disposés à se faire vacciner. • Le fait de déclarer n'avoir eu aucune expérience négative durant l'enfance au sein du foyer est associé à la volonté de se faire vacciner (RRa 0,45, IC à 95 % : de 0,20 à 0,99). • Les principaux motifs de réticence à accepter un vaccin sont l'innocuité du vaccin (64,5 %), le manque de connaissances sur le vaccin (60,6 %) et le fait de ne pas penser que le vaccin serait efficace (23,4 %).
Province of Manitoba (2020) *non publiée* (214) Étude transversale Canada Novembre 2020	Un sondage en ligne a été effectué auprès de 9 872 adultes au Manitoba pour évaluer les perceptions à l'égard du vaccin contre la COVID-19 et l'intention de se faire vacciner. Sujets des questions : 3) Intentions en ce qui concerne les vaccins 4) Perception des vaccins	• 55 % et 19 % respectivement des participants ont dit qu'ils se feraient « certainement » ou « probablement » vacciner lorsque le vaccin contre la COVID-19 sera disponible. Les autres participants ont déclaré qu'ils étaient indécis (8 %), qu'ils ne se feraient probablement pas vacciner (7 %) ou qu'ils ne se feraient certainement pas vacciner (12 %). • 61 % des participants étaient d'accord avec l'énoncé [Traduction libre] « Les vaccins sont sûrs et je n'ai aucun doute quant à la possibilité de me faire vacciner ou que ma famille se fasse vacciner, comme l'a recommandé mon médecin ».

	Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	
Independent Polling System of Society (IPSOS)/Radio Canada (2020) *non publiée* (215) Étude transversale Canada Novembre 2020	Un sondage en ligne effectué auprès de 3 001 adultes (âgés de 18 ans et plus) a analysé l'intention de se faire vacciner et les perceptions à l'égard du vaccin. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 64 % des participants se feraient probablement ou certainement vacciner, 16 % ont dit qu'ils ne se feraient certainement pas vacciner et 21 % étaient incertains. • Parmi ceux qui se feraient vacciner, 36 % le feraient le plus tôt possible, 38 % attendraient un ou deux mois pour voir ce qui se passe, 15 % attendraient plusieurs mois et 11 % se sont dits indécis. • La majorité des répondants s'inquiétaient des effets secondaires possibles et des risques associés au vaccin.
Independent Polling System of Society (2020) *non publiée* (93) Étude transversale Canada Novembre 2020	Un sondage en ligne effectué auprès de 1 001 adultes (âgés de 18 ans et plus) a analysé l'intention de se faire vacciner et les perceptions à l'égard du vaccin. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 52 % des répondants ont dit qu'ils accepteraient sans hésiter un vaccin contre la COVID-19. Cependant, lorsque d'autres options s'offrent à eux, 36 % accepteraient de se faire vacciner, mais attendraient de voir s'il a des effets secondaires indésirables alors que 28 % le prendraient, mais attendraient de voir s'il est efficace. • 13 % des participants refuseraient le vaccin, dans quelques circonstances que ce soit. • 71 % des participants disent que le fait d'accepter un vaccin qui a été créé et approuvé si rapidement les rend nerveux alors que 69 % ont dit s'inquiéter des effets à long terme. • 59 % des participants appuyaient la vaccination obligatoire contre la COVID-19, en baisse par rapport à 61 % en septembre et à 72 % en juillet. • Certains participants ont déclaré qu'une recommandation d'un médecin de famille (21 %) ou le fait de voir des amis et des membres de la

		famille recevoir le vaccin (10 %) les inciterait à se faire vacciner. • La plupart conviennent que les travailleurs de la santé de première ligne (62 %) et les premiers intervenants (52 %) devraient être les premiers à recevoir le vaccin. Cependant, en dehors de ces groupes cibles, les Canadiens sont divisés quant à savoir qui devrait être en priorité. • Trois personnes sur dix (30 %) croient que nous pouvons vaincre la COVID-19 sans vaccin, comparativement à 40 % en octobre.
Independent Polling System of Society (2020) *non publiée* (62) Étude transversale Canada Octobre 2020	Un sondage en ligne effectué auprès de 1000 adultes a analysé l'intention de se faire vacciner et les perceptions à l'égard du vaccin. De ceux-ci, 1 000 participants étaient canadiens. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 54 % des Canadiens seraient prêts à recevoir un vaccin dès qu'il sera disponible. Les provinces atlantiques sont celles où les intentions de se faire vacciner sont les plus élevées (75 %), suivies de la Saskatchewan et du Manitoba (65 %), du Québec (63 %), de la Colombie-Britannique (60 %), de l'Alberta (58 %) et de l'Ontario (57 %). • 61 % des participants appuient la vaccination obligatoire contre la COVID-19, en baisse alors que ce niveau atteignant 72 % en juillet. • 82 % indiquent qu'ils attendraient les rapports sur l'efficacité ou les effets secondaires d'un vaccin contre la COVID-19 avant de le prendre. • La majorité (88 %) des participants conviennent que les personnes âgées et d'autres collectivités vulnérables devraient avoir la priorité absolue pour recevoir le vaccin. • Quatre sur dix (40 %) croient que nous pouvons vaincre la COVID-19 sans vaccin.
Toronto Public Health (2020) *non publiée* (216) Étude transversale	L'intention de recevoir un vaccin contre la COVID-19 a été évaluée au moyen d'un sondage en ligne effectué auprès de 1 201 résidents de Toronto (Ontario). Sujets des questions : 1) Intentions en ce qui concerne les vaccins	• 73 % des participants déclarent que lorsqu'un vaccin contre la COVID-19 sera disponible, ils se feront « certainement » ou « probablement » vacciner. 20 % ont dit qu'ils ne l'accepteront « certainement » ou « probablement » pas alors que 11 % sont indécis.

Canada Octobre 2020	Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	
Statistic Canada (2020) *non publiée* (78) Étude transversale Canada Septembre et octobre 2020	Un sondage téléphonique a été effectué auprès de 120 000 participants (âgés de 18 ans et plus) pour évaluer leur intention de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• Comparativement aux non-immigrants (75,9 %), les immigrants qui vivent au Canada depuis moins de 10 ans (80,3 %) et plus de 10 ans (70,7 %) ont dit avoir un intérêt comparable pour la vaccination. • Les femmes qui n'étaient pas immigrantes ou qui ont immigré il y a moins de 10 ans avaient moins l'intention de se faire vacciner que les hommes (74,7 % contre 77,2 % pour les non-immigrants et 78,1 % contre 82,9 % pour les moins de 10 ans). • Lorsqu'on compare toutes les minorités visibles à la race blanche, les intentions en ce qui concerne la vaccination étaient presque identiques (77,3 % contre 77,0 %). • Au sein des groupes des minorités visibles, l'intention de se faire vacciner allait, de la plus faible à la plus forte, chez les Noirs (57,0 %), les Latino-Américains (58,5 %), les Philippins (64,2 %), les Asiatiques du Sud-Est (75,8 %), les autres minorités visibles (77,6 %), les Chinois (85,5 %) et les Arabes (88,3 %). • 69,3 % des personnes ayant déclaré une identité autochtone acceptaient un vaccin, comparativement à 77,6 % des personnes n'ayant pas déclaré une telle identité. • 87,6 % des membres de la communauté LGBTQ2+ étaient prêts à accepter un vaccin, comparativement à 76,4 % des personnes non membres de cette communauté. • Des niveaux de scolarité plus élevés et une condition médicale sous-jacente étaient associés à une plus grande acceptation.

Ogilvie (2021) (79) Étude transversale Canada Août et septembre 2020	On a évalué l'intention de se faire vacciner chez 4 058 adultes et travailleurs de la santé de la Colombie-Britannique (âgés de 25 à 69 ans). Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 79,8 % des répondants étaient assez ou très susceptibles de se faire vacciner si le vaccin était disponible et s'il était recommandé pour eux. • 81,8 % des travailleurs de la santé ont dit avoir l'intention de se faire vacciner. • Les personnes non binaires, allosexuelles, agentes, bispirituelles ou autres étaient plus susceptibles de recevoir un vaccin (RC = 3,04, IC à 95 % : 1,08 à 8,55). • Les ménages comptant deux adultes (RC = 1,2, IC à 95 % : 1,00 à 1,43) étaient plus susceptibles de se faire vacciner, mais il n'y a pas eu de changement important dans l'intention par rapport au nombre d'enfants. • L'analyse multivariée a démontré que les jeunes répondants (de 30 à 40 ans, RCa = 0,64, IC à 95 % : 0,49 à 0,83, de 40 à 50 ans, RCa = 0,78, IC à 95 % : 0,62 à 0,97, de 50 à 60 ans, RCa = 0,67, IC à 95 % : 0,55 à 0,82), les femmes (RCa = 0,7, IC à 95 % : 0,55 à 0,89), les personnes ayant un niveau de scolarité inférieur (RCa = 0,62, IC à 95 % : 0,51 à 0,77), les sud-asiatiques (RCa = 0,65, IC à 95 % : 0,39-1,07), les non-blancs (RCa = 0,76, IC à 95 % : 0,61-0,95), les personnes qui s'identifient comme Autochtones (RCa = 0,58, IC à 95 % : 0,38 à 0,87), les autres travailleurs essentiels n'œuvrant pas dans le domaine des soins de santé (RCa = 0,72, IC à 95 % : 0,6 à 0,87) et les personnes qui soupçonnaient avoir eu la COVID-19 (RCa = 0,76, IC à 95 % : 0,61 à 0,96) étaient beaucoup moins susceptibles de se faire vacciner. • Le manque de confiance dans les vaccins (RCa = 0,66, IC à 95 % : 0,57 à 0,75) et le fait de croire aux risques liés aux vaccins (RCa = 0,72, IC à 95 % : 0,66 à 0,0,80) ont été associés à une diminution de l'intention de se faire vacciner. • L'intention de se faire vacciner a été associée positivement à des scores attitudinaux plus élevés envers le vaccin (RCa = 1,06, IC à 95 % : 1,04 à 1,08), à l'influence des normes sociales directes

		(RCa = 1,06, IC à 95 % : 1,03 à 1,08), aux opinions indirectes des médecins de famille et des médecins de premier recours (RCa = 1,04, IC à 95 % : 1,00 à 1,08), aux normes indirectes établies par le médecin-hygiéniste de la province (RCa = 1,04, IC à 95 % : 1,01 à 1,08) et aux normes familiales indirectes (RCa = 1,09, IC à 95 % : 1,06 à 1,13).
Lang (2021) (87) Étude transversale Canada Août 2020	Une enquête en ligne a été menée auprès de 60 adultes (18 et +) de l'Alberta pour évaluer leur intention de se faire vacciner. Sujets des questions : 1) Intentions de se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• 68 % des personnes interrogées accepteraient un vaccin s'il était disponible, 20 % ne l'accepteraient pas et 12 % étaient incertaines. • Les répondants blancs étaient moins susceptibles d'accepter un vaccin (63 %) par rapport aux autres ethnies (100 %). • Les personnes ayant fait des études supérieures (collège ou université) étaient moins susceptibles d'accepter un vaccin (63 %) que celles ayant fréquenté une école technique postsecondaire (100 %) ou ayant un diplôme d'études secondaires (70 %). • L'intention de se faire vacciner était positivement associée aux craintes de contracter la COVID-19 (P < 0,001) et de propager le virus (P = 0,006), et au respect des mesures de santé publique telles que rester à la maison en cas de maladie (P = 0,033), porter le masque en public (P < 0.001) et la distanciation physique (P = 0,005). • Les répondants qui ont reçu leur information sur la COVID-19 lors des séances d'information aux médias du médecin hygiéniste en chef (P = 0,030) et sur les sites Web d'Alberta Health ou d'Alberta Health Services (P = 0,040) étaient significativement plus susceptibles d'accepter un vaccin contre la COVID-19. • L'intention de se faire vacciner était plus faible dans les autres centres urbains (29 %) et dans les régions rurales de l'Alberta (50 %) que dans les villes de Calgary (75 %) et d'Edmonton (80 %) *(P* = 0,030).

Carleton University (2020) *non publiée* (217) Étude transversale Canada Juillet 2020	Un sondage d'opinion publique sur l'intention et les perceptions concernant le vaccin a été effectué en ligne auprès de 2 000 personnes. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination 3) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 45 % ont dit qu'ils se feraient probablement vacciner, 24 % ont dit qu'ils le prendraient probablement, 5 % ont dit qu'ils ne se feraient probablement pas vacciner alors que 9 % ont dit qu'ils ne le recevront certainement pas. • La résistance au vaccin est la plus élevée au Manitoba et en Saskatchewan, où seuls 37 % des participants ont dit qu'ils se feraient assurément vacciner dans les deux provinces. • En ce qui concerne l'opinion sur la vaccination obligatoire, 36 % se sont dits tout à fait d'accord, 26 % sont plutôt d'accord, 14 % sont tout à fait en désaccord et 7 % sont plutôt en désaccord. • La raison la plus courante (40 %) de leur hésitation était la possibilité d'effets secondaires dangereux. • Parmi les 9 % de répondants qui ont exprimé de fortes opinions contre le vaccin, les soupçons quant à l'influence de l'industrie pharmaceutique sur les soins de santé publique (41 %) et les préoccupations au sujet de l'innocuité du vaccin et de la possibilité d'effets secondaires nocifs (29 %) étaient les raisons les plus fréquentes du refus.
Frank (2020) *non publiée* (63) Étude transversale Canada Juin 2020	Les facteurs associés à la volonté de se faire vacciner ont été examinés dans un sondage en ligne effectué auprès d'environ 4 000 adultes. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 57,5 % et 19 % respectivement des répondants ont indiqué qu'ils sont très susceptibles ou assez susceptibles de se faire vacciner contre la COVID-19 lorsque le vaccin il sera disponible. • Les Canadiens âgés (65 ans et plus) ont déclaré qu'ils étaient plus susceptibles de se faire vacciner (70,3 %) que les 15 à 64 ans (52 à 58 %). • Les personnes nées au Canada étaient plus susceptibles de se faire vacciner que les immigrants (59,4 % contre 52,0 %). • Les résidents des provinces de l'Atlantique sont les plus susceptibles de se faire vacciner (67,7 %), suivis de ceux de l'Ontario (58,8 %), des Prairies (56,2 %), de la Colombie-Britannique (55,5 %) et du Québec (54,3 %). • Parmi les autres facteurs associés à une plus grande intention de se faire vacciner, mentionnons

		l'éducation supérieure et le fait de ne pas avoir d'enfants de moins de 18 ans. • Les deux principales raisons de ne pas avoir l'intention de se faire vacciner étaient le manque de confiance dans l'innocuité du vaccin (54,2 %) et les préoccupations au sujet de ses risques et de ses effets secondaires (51,7 %).
Hetherington (2021) (218) Étude transversale Canada Mai et juin 2020	Les participants à l'étude de cohorte longitudinale All Our Families (n = 1 321) en Alberta ont été invités à participer à un sondage d'impact en ligne sur la COVID-19 afin de comprendre les facteurs associés aux intentions de faire vacciner contre la COVID-19 chez les parents d'enfants âgés de 9 à 12 ans. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 60,4 % des parents avaient l'intention de faire vacciner leurs enfants, 8,6 % ont dit qu'ils n'avaient pas l'intention de le faire et 31 % étaient incertains. • Les participants moins scolarisés étaient plus susceptibles de ne pas vouloir se faire vacciner (RC = 2,80, IC à 95 % : 1,78 à 4,40) ou étaient incertains (RC = 1,98, IC à 95 % : 1,47 à 2,71). On a observé une tendance semblable pour le revenu. • Des antécédents de vaccination partielle ou non-vaccination étaient associés à l'intention de ne pas se faire vacciner (RC = 2,81, IC à 95 % : 1,78 à 4,40). Il n'y avait aucun lien entre les antécédents de vaccination et l'incertitude concernant un vaccin contre la COVID-19 (RC = 1,29, IC à 95 % : 0,92 à 1,80). • On a signalé des préoccupations au sujet de l'innocuité et de l'efficacité des vaccins, des effets à long terme et d'un processus de vaccination précipité.
Frank (2020) *non publiée* (219) Étude transversale Canada	Un sondage en ligne a été effectué auprès d'environ 36 000 adultes pour étudier les facteurs associés à la volonté de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non	• 68,2 % et 15,2 % respectivement des participants ont déclaré qu'ils étaient très susceptibles ou assez susceptibles d'accepter un vaccin contre la COVID-19. 12 % étaient peu susceptibles ou très peu susceptibles de se faire vacciner. • Les personnes qui ont un niveau élevé de confiance dans le gouvernement fédéral étaient plus susceptibles d'être disposées à se faire vacciner que celles qui avaient un faible niveau de confiance (77,3 % comparativement à 53,8 %).

Mai et juin 2020	Recherches formatives effectuées? Oui Enquête prétestée? Non	• Des tendances semblables ont également été observées en ce qui concerne la confiance envers les autres et la confiance envers les autorités fédérales en matière de santé publique.
Lackner (2021) (189) Étude transversale Canada Mai et juin 2020	Les facteurs démographiques, expérientiels et psychologiques associés à la probabilité et à la rapidité prévues de recevoir un vaccin contre la COVID-19 ont été examinés dans 455 familles (857 enfants). Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• Les facteurs associés à une plus grande probabilité de faire vacciner les enfants comprennent l'âge plus avancé des parents, la vie dans les Prairies (comparativement au centre du Canada), des antécédents de vaccination plus complets pour les enfants et les parents, des attitudes positives à l'égard des vaccins en général, un plus grand évitement psychologique de la pandémie et une plus grande tendance à prioriser les risques de la maladie comparativement aux risques des effets secondaires. • Dans certains modèles, le risque perçu de COVID-19 et les niveaux plus élevés d'anxiété au pays étaient associés à une probabilité accrue de faire vacciner les enfants. • Les facteurs ci-dessus étaient également des prédicteurs de la vitesse plus rapide de la vaccination prévue. Toutefois, un statut socio-économique plus élevé était un prédicteur de tendance.
Taylor (2021) (220) Étude transversale Canada et États-Unis Juin et juillet 2020	Un sondage en ligne réalisé auprès de 2 078 adultes (âgés de 18 ans et plus) a été utilisé pour explorer le lien possible entre les attitudes à l'égard du port d'un couvre-visage et la vaccination contre la COVID-19. L'échantillon comprenait 1 036 participants des États-Unis et 1 042 du Canada. Sujets des questions : 1) Attitudes à l'égard des vaccins	• Le réseau des attitudes anti-masques est lié à d'autres variables telles que le mépris pour la distanciation sociale et les attitudes anti-vaccination.

	Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	
Waite (2021) (92) Étude transversale Canada Mai 2020	Un sondage en ligne a été effectué auprès de 1 001 Canadiens âgés de 50 à 64 ans et auprès de 3 500 Canadiens âgés de 65 ans et plus afin d'évaluer les intentions de se faire vacciner contre la COVID-19. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• Parmi les 50 à 64 ans, 69,1 % ont dit avoir l'intention de se faire vacciner lorsque les vaccins seront disponibles, 11,3 % ne se feront pas vacciner et 19,6 % étaient incertains. • 79,5 % des 65 ans et plus ont l'intention de se faire vacciner lorsque le vaccin sera disponible, 5,6 % refuseront de le faire et 14,9 % ont dit être incertains. • Dans les deux groupes d'âge, les personnes qui acceptaient de se faire vacciner étaient beaucoup plus susceptibles d'être de sexe masculin et d'avoir au moins un problème de santé chronique ($P < 0,05$). • L'endroit privilégié pour recevoir un vaccin chez ces deux groupes était le bureau du médecin de famille, suivi de la pharmacie, du lieu de travail (pour les 50 à 64 ans) et des cliniques de santé publique.
Taylor (2020) (89) Étude transversale Canada et États-Unis Mai 2020	Les intentions de se faire vacciner et les attitudes à l'égard des vaccins ont été mesurées dans un sondage en ligne réalisé auprès de 3 674 adultes (Canada = 1 902, États-Unis = 1 772). Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination 3) Attitudes à l'égard des vaccins	• Beaucoup plus d'Américains (25 %) que de Canadiens (20 %) ont répondu qu'ils ne se feraient pas vacciner même si un vaccin était disponible, χ^2 (*df* = 1) = 12,41, $p < 0,001$. • Les attitudes négatives à l'égard d'un vaccin contre la COVID-19 et de la vaccination en général étaient fortement corrélées ($p < 0,001$) avec l'intention de ne pas se faire vacciner. La méfiance à l'égard des avantages d'un vaccin contre la COVID-19 a été le facteur le plus important en ce qui concerne l'attitude quant à la décision de ne pas se faire vacciner. • Le refus de se faire vacciner a été associé de façon significative au sexe féminin, à l'âge, aux études collégiales complètes ou partielles (plutôt qu'aux études non terminées), au chômage et à

	Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	l'appartenance à une minorité (plutôt qu'à la race blanche). • Parmi ceux qui ont indiqué qu'ils ne se feraient pas vacciner (n = 812), 38 % se feraient vacciner s'ils étaient convaincus que le vaccin a été rigoureusement testé et 36 % se feraient vacciner s'ils constataient qu'un nombre suffisant de personnes ont été vaccinées sans qu'il y ait d'effets secondaires graves. • Comparativement à l'origine ethnique blanche, l'appartenance à une minorité (Asiatique, Afro-Américain/Noir, Latino/Hispanique ou autre) était fortement associée au refus de se faire vacciner (r = 0,04, p < 0,05).
Carleton University (2020) *non publiée* (59) Étude transversale Canada Mai 2020	Un sondage d'opinion publique sur l'intention et les perceptions concernant le vaccin a été effectué en ligne auprès de 2 000 personnes. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 49 % et 24 % respectivement des participants ont dit qu'ils se feraient « certainement » ou « probablement » vacciner lorsque le vaccin sera disponible. • 17 % ont exprimé de l'incertitude et 10 % ont dit qu'ils n'étaient pas disposés à le faire. • 65 % croient que le vaccin devrait être obligatoire • L'âge et l'affiliation politique étaient fortement associés à l'intention de se faire vacciner. Les personnes âgées étaient plus disposées que les plus jeunes à se faire vacciner. Ceux qui ont voté pour le Parti libéral ou le NPD aux élections de 2019 étaient plus susceptibles de se faire vacciner que ceux qui ont voté pour d'autres partis. • Les répondants qui vivent dans les provinces atlantiques affichent les niveaux les plus élevés d'intention de se faire vacciner comparativement à ceux des autres provinces. • Ceux qui croyaient à l'un des quatre mythes ou théories du complot en matière de santé concernant la COVID-19 étaient moins susceptibles d'avoir l'intention de se faire vacciner que ceux qui ne croyaient pas aux

		affirmations inexactes sur le plan scientifique au sujet de la COVID-19.
Parsons Leigh (2020) (64) Étude transversale Canada Avril et mai 2020	Un sondage en ligne a été effectué auprès de 1 996 participants (âgés de 18 ans et plus) pour analyser les connaissances, les attitudes et les comportements en ce qui concerne la COVID-19. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Connaissance des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 75,8 % (n = 1 436) des répondants ont déclaré qu'ils se feraient vacciner lorsqu'un vaccin serait disponible. • Les participants ont répondu qu'ils étaient « fortement d'accord » ou « d'accord » pour dire qu'ils se feraient vacciner en Colombie-Britannique (72,1 %), en Alberta (69,9 %), au Manitoba et en Saskatchewan (69,9 %), en Ontario (66,1 %), dans la région atlantique (63,1 %) et au Québec (41,9 %). • Les participants ont répondu qu'ils étaient « fortement d'accord » ou « d'accord » pour dire qu'ils ne se feront pas vacciner en Alberta (12,4 %), au Québec (12,1 %), en Ontario (8,1 %), dans la région de l'Atlantique (6,6 %), au Manitoba et en Saskatchewan (6 %) et en Colombie-Britannique (4,8 %). • Les renseignements sur les vaccins et les traitements étaient les plus fréquemment cités comme sujets de désinformation (n = 933, 48,9 %, IC à 95 % : 46,7 à 51,2 %), mais seulement la moitié (n = 937, 47,4 %, IC à 95 % : 45,2 à 49,6 %) des répondants se sont sentis modérément ou extrêmement sûrs de pouvoir identifier des renseignements inexacts ou trompeurs au sujet de la COVID-19.
Underschultz (2021) (221) Étude transversale Canada Avril 2020	Un sondage en ligne a été effectué auprès de 1 593 participants (âgés de 16 ans et plus) pour analyser les connaissances, les attitudes et les comportements en ce qui concerne la COVID-19. L'enquête était principalement destinée aux résidents de l'Alberta et de l'Ontario. Sujets des questions :	• 93 % des répondants estiment qu'un vaccin est nécessaire au Canada et 81 % appuient une stratégie de vaccination à grande échelle (vacciner tout le monde). • On a établi un lien important entre l'acceptation du vaccin et des résultats plus élevé en ce qui concerne les connaissances ($p < 0,001$), l'inquiétude au sujet de la COVID-19 (RC = 20,4; IC à 95 % : 8,4 à 49,5, $p < 0,001$), l'optimisme dans la lutte contre la pandémie (RC = 8,1; IC à 95 % : 3,4 à 19,7, $p < 0,001$) et le sentiment d'être informé au

	1) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	sujet de la COVID-19 (RC = 3,9; IC à 95 : 1,7 à 9,3, p = 0,0049).
Research Co (2020) *non publiée* (58) Étude transversale Canada Avril 2020	Un sondage en ligne a été utilisé pour évaluer l'intention de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Si un vaccin devenait disponible, 42 % et 31 % respectivement des répondants accepteraient « certainement » ou « probablement » de se faire vacciner. • Les hommes étaient plus susceptibles de se faire vacciner que les femmes (78 % contre 68 %). • C'est dans la région de l'Atlantique (79 %) et en Alberta (78 %) que l'intention de se faire vacciner était la plus forte alors qu'elle était la plus faible en Saskatchewan et au Manitoba (65 %). • L'intention de se faire vacciner était la plus élevée chez les personnes qui ont voté pour le Parti libéral (79 %) aux élections de 2019, suivis du NPD (76 %) et des conservateurs (69 %).
Études qualitatives (n = 1)		
Benham (2021) (222) **Étude qualitative** **Canada** **Août et septembre 2020**	Neuf groupes de discussion ont été tenus auprès de 50 adultes (âgés de 18 ans et plus) de l'Alberta afin d'évaluer les attitudes à l'égard des mesures de santé publique, y compris la vaccination. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins	• L'intention de se faire vacciner les réponses était mitigée. Certains ont déclaré qu'ils se feraient vacciner immédiatement, tandis que d'autres ne le feraient pas, car ils croyaient que la COVID-19 n'aurait pas d'incidence sur leur santé ou celle des membres de leur famille. • Certains participants ont déclaré qu'ils seraient disposés à se faire vacciner, mais pas immédiatement. Ce phénomène était plus marqué dans les groupes d'âge plus âgés. • Les participants qui recevaient régulièrement le vaccin annuel contre la grippe étaient plus susceptibles de dire qu'ils prendraient un vaccin contre la COVID-19 lorsqu'il serait disponible. Cependant, quelques-uns ont subi des effets secondaires avec le vaccin annuel contre la grippe (p. ex., maladie), ce qui les rendrait moins

		susceptibles de recevoir un vaccin contre la COVID-19. • Parmi les obstacles à l'adoption du vaccin, mentionnons le manque de confiance quant à son efficacité et à son effet nocif.
Études quasi-expérimentales (n = 1)		
Poder (2021) *non publiée* (223) Étude quasi-expérimentale Canada Octobre et novembre 2020	Un sondage en ligne portant sur les intentions de vaccination de 1 695 adultes québécois a été mené. La méthode utilisée est celle du choix expérimental discret où chaque participant a fait face à une série de 12 cartes présentant chacun deux scénarios (pour un total de 20 350 réponses) Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Non	• Au moins 7,2 % ont toujours choisi de ne pas se faire vacciner, quel que soit le scénario choisi. • Selon le scénario, 69 à 93 % des participants opteraient pour le vaccin lorsqu'il sera disponible. • 24 % des participants choisiraient de refuser le vaccin si certaines conditions n'étaient pas respectées (indiquées ici par ordre de priorité :) 1) l'efficacité du vaccin 2) les effets secondaires possibles du vaccin 3) la durée d'efficacité (minimum de 9 mois pour l'acceptabilité) 4) l'organisme recommandant le vaccin (Direction de santé publique du Québec et OMS) 5) l'origine géographique du vaccin (Union européenne ou États-Unis) 6) le délai d'attente pour être vacciné une fois le vaccin disponible au Québec (4 mois au maximum) 7) les populations très prioritaires (aucune préférence)
Intervenants experts		
Études transversales (n = 2)		
MacDonald (2020) *préimpression* (101) Étude transversale Canada	Dix-huit entrevues en téléconférence avec 25 chefs de file en santé publique de 10 des 13 provinces et territoires ont été menées afin d'évaluer les points de vue sur les groupes prioritaires pour la vaccination précoce. On a demandé aux participants de classer, par ordre d'importance,	• Les dix provinces et territoires ont classé les résidents de longue durée et les travailleurs de la santé dans leurs cinq premiers groupes prioritaires pour recevoir la vaccination. • Neuf provinces et huit territoires ont aussi classé les personnes ayant des problèmes de santé chroniques et les personnes âgées dans les cinq premiers groupes prioritaires. • Dans une moindre mesure, les personnes d'ascendance autochtone (n = 4), ayant un

Août à octobre 2020	leurs cinq principaux groupes prioritaires pour la vaccination. Sujets des questions : 1) Perceptions à propos de la stratégie de vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	désavantage socioéconomique (n = 3), ayant des nourrissons ou des enfants (n = 2), vivant dans des collectivités éloignées (n = 2) et de nouveaux immigrants et réfugiés (n = 1) ont aussi été classées dans les cinq premiers groupes prioritaires.
Zhao (2020) *préimpression* (102) Étude transversale Canada Juillet et août 2020	Un sondage en ligne a été effectué parmi 74 intervenants experts pour obtenir leur point de vue quant à l'importance relative des stratégies de vaccination contre la pandémie pour différents scénarios de pandémie de COVID-19 au moment de la disponibilité initiale du vaccin contre la COVID-19. Les répondants devaient classer, par ordre d'importance, quatre stratégies prédéfinies de vaccination contre la pandémie de COVID-19. Sujets des questions : 1) Perceptions à propos de la stratégie de vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Pour tous les scénarios de pandémie, les intervenants ont généralement classé les stratégies dans l'ordre suivant, du plus important au moins important : ○ protéger les personnes les plus vulnérables contre les maladies graves et les décès causés par la COVID-19 ○ protéger la capacité d'offrir des soins de santé ○ réduire au minimum la transmission de la COVID-19 • protéger les infrastructures essentielles

RCa = rapport de cotes ajusté, IC = intervalle de confiance, n.d. = non déclaré, RR = risque relatif

TRAVAILLEURS DE LA SANTÉ

Tableau 4. Preuve en ce qui concerne les attitudes des travailleurs de la santé à l'égard des vaccins (n = 42)

ÉTUDE	MÉTHODES ET OUTILS D'ENQUÊTE	RÉSULTATS CLÉS RELATIFS AUX CONNAISSANCES, ATTITUDES ET COMPORTEMENTS
AMÉRIQUE DU NORD		
CANADA		
Lunsky (2021) (105) Étude transversale Canada Janvier à février 2021	Pour évaluer l'intention de vaccination et les facteurs prédictifs de cette intention, une enquête en ligne a été menée auprès de 3 371 employés de services sociaux soutenant des personnes ayant une déficience intellectuelle en Ontario. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• 62 % et 20 % ont déclaré qu'il était très probable ou assez probable qu'ils acceptent un vaccin, et 7 % et 11 % qu'il était assez improbable ou très improbable qu'ils se fassent vacciner, respectivement. • Par rapport aux personnes âgées de 50 ans et plus, les jeunes personnes de 18 à 29 ans (RR ajusté 2,74, IC 95 % : 1,70 % à 4,43 %) et 30 à 39 (RR ajusté 1,75, IC 95 % : 1,16 % à 2,64 %) étaient plus susceptibles de refuser un vaccin lorsqu'il était disponible. • Les femmes étaient plus susceptibles de refuser un vaccin que les hommes (RR ajusté 1,58, IC 95 % : 0,97 % à 2,59 %). • Par rapport aux répondants européens, les Asiatiques (RR ajusté 0,88, IC 95 % : 0,33 % à 2,36 %), d'Afrique et des Caraïbes (RR ajusté 0,81, IC 95 % : 0,35 % à 1,86 %), et les ethnies non précisées (RR ajusté 0,88, IC 95 % : 0,36 % à 2,17 %) étaient moins susceptibles de refuser un vaccin et les autochtones, les Premières Nations et les Métis (RR ajusté 1,73, IC 95 % : 0,67 % à 4,43 %), les latinos (RR ajusté 1,22, IC 95 % : 0,21 à 7,24), et les gens des ethnies mixtes (RR ajusté 1,11, IC 95 % : 0,27 % à 4,55 %) étaient plus susceptibles de refuser. • Les raisons de refuser un vaccin comprennent le manque de confiance dans le vaccin (RR 5,72, IC 95 % : 3,84 à 8,53), la peur des effets secondaires du vaccin (RR 2,30, IC 95 % : 1,56 % à 3,39 %), et la conviction qu'il n'est pas nécessaire de se faire

		vacciner en raison d'une bonne santé (RR 4,22, IC 95 % : 2,66 % à 6,68 %). • Les personnes qui refuseraient un vaccin étaient moins susceptibles de croire que la vaccination protégerait les clients (RR 0,36, IC 95 % : 0,24 % à 0,54 %) ou de la famille (RR 0,19, IC 95 % : 0,13 % à 0,28 %), être préoccupé par les clients (RR 0,57, IC 95 % : 0,34 % à 0,97 %) ou eux-mêmes (OR 0,51, IC 95 % : 0,34 % à 0,76 %) tombant malade de la COVID-19, se faire vacciner contre la grippe dans une année normale (RR 0,61, IC 95 % : 0,43 % à 0,88 %), et se font vacciner si leurs collègues le font (RR 0,16, IC 95 % : 0,08 % à 0,29 %).
Desveaux 2021 *préimpression* (103) Étude transversale Canada Janvier 2021	Un sondage en ligne a été utilisé en Ontario pour évaluer les facteurs associés à l'intention de se faire vacciner chez 8 634 travailleurs de la santé (âgés de 18 ans et plus). Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 80,4 % des participants ont déclaré avoir l'intention d'obtenir un vaccin contre la COVID-19. • Comparativement à leurs homologues, les personnes plus jeunes (moins de 40 ans) et moins scolarisées (moins d'un diplôme d'études secondaires) étaient plus susceptibles de ne pas avoir l'intention de se faire vacciner ($p < 0,001$). • Les travailleurs de la santé qui se sont identifiés comme étant d'origine philippine (RC = 1,07, IC à 95 % : 0,41 à 2,76, $P < 0,001$), caraïbéenne (RC = 3,20, IC à 95 % : 1,52 à 6,75, $P < 0,001$) ou autre (RC = 1,44, IC à 95 % : 0,93 à 2,22, $P < 0,001$) étaient plus susceptibles de ne pas vouloir se faire vacciner que ceux qui se sont identifiés comme étant d'origine européenne. • La réticence à se faire vacciner était fortement associée à la méfiance quant à la rapidité de la mise au point des vaccins et aux préoccupations relatives à l'innocuité des vaccins. Elle était également associée à diverses croyances, comme le fait de ne pas avoir besoin d'un vaccin en raison de sa propre bonne santé, la faible confiance que le vaccin protégerait sa famille et ses patients, et le fait que se faire vacciner n'était pas une responsabilité professionnelle.

		• Les travailleurs de la santé étaient plus susceptibles d'avoir l'intention de se faire vacciner s'ils pouvaient avoir accès à un soutien financier direct, comme des congés de maladie payés (74 % contre 25 %, P < 0,001).
SafeCare BC (2021) *non publiée* (104) Étude transversale Canada Décembre 2020	Un sondage en ligne a été effectué auprès de 1 500 travailleurs en soins continus de la Colombie-Britannique pour évaluer les attitudes à l'égard de la vaccination contre la COVID-19. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 57 % des répondants avaient l'intention de se faire vacciner, 28 % n'étaient pas certains et 15 % n'avaient pas l'intention de se faire vacciner. • Les hommes (72 % contre 56 %), l'âge plus élevé (65 ans et plus) et l'acceptation du vaccin antigrippal étaient des prédicteurs de l'intention de se faire vacciner. • Les gestionnaires et les cadres supérieurs avaient la plus forte intention de se faire vacciner (71 %). Les aides-soignants étaient les plus incertains (30 %) alors que les infirmières étaient les plus susceptibles de dire non à un vaccin (20 %). • Les raisons de l'hésitation étaient les effets secondaires (84,6 %), la nouveauté du vaccin (64,6 %), la méfiance à l'égard des autorités (23,5 %), la croyance que le vaccin ne fonctionnera pas (16 %), les remèdes naturels préférés (10,5 %) et les croyances personnelles ou religieuses (8 %). • Les intentions de vaccination étaient les plus élevées chez les Asiatiques de l'Est (61 %) et du Sud (70 %). Les répondants latinos et les Noirs étaient les plus susceptibles de refuser le vaccin (30 %) alors que les autochtones sont ceux qui avaient le plus tendance à être incertains quant à la décision à savoir s'ils se feraient ou non vacciner (40 %). • Les répondants de l'Asie de l'Est et du Sud étaient plus préoccupés par les effets secondaires (93 %), tandis que les répondants blancs ou autochtones étaient plus préoccupés par la nouveauté (72 % et 62 %, respectivement). • 33 % ont dit qu'il faut plus de soutien pour les vaccins, p. ex., plus d'information pour comprendre le processus de développement, l'efficacité et la

		transparence de la déclaration des événements indésirables. • Le plus grand obstacle perçu à l'administration du vaccin était les contraintes associées au stockage et à la manipulation (66 %). • Les répondants autochtones étaient ceux qui avaient le moins confiance aux différentes sources d'information, y compris les fournisseurs de soins de santé.
INSPQ (2020) & INSPQ (2021) *non publiée* (88, 95) Étude longitudinale Canada Avril à décembre 2020	L'analyse de l'acceptabilité de la vaccination contre la COVID-19 a été évaluée à l'aide d'un sondage en ligne réalisé auprès d'adultes et de travailleurs de la santé au Québec. Le nombre de participants n'a pas été indiqué de façon claire (environ 3 300 par période de collecte). Il y a eu plusieurs périodes de collecte de données, une en avril et en mai, et une autre en septembre et une autre en décembre. Cet article est en français. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• En mai, 73 % des travailleurs de la santé ont répondu qu'ils avaient l'intention de se faire vacciner. En décembre, ce pourcentage est descendu à 65 % avant de remonter à 71 % en décembre. • L'intention de se faire vacciner ne différait pas entre le grand public et les travailleurs de la santé et les facteurs associés à l'intention de se faire vacciner n'étaient pas différenciés entre les deux groupes. • Les personnes plus âgées (70 ans et plus) étaient plus susceptibles de se faire vacciner que celles qui avaient entre 25 et 44 ans (83 % contre 57 %). • Les hommes, notamment ceux qui ont fait des études universitaires et ceux qui ont une ou plusieurs maladies chroniques, sont plus susceptibles d'avoir l'intention de se faire vacciner. • Les raisons les plus courantes de ne pas vouloir se faire vacciner comprennent les craintes liées à un nouveau vaccin et les préoccupations au sujet de l'efficacité et des effets secondaires.
Verger (2021) (127)	L'intention de se faire vacciner et l'intention de recommander la vaccination aux patients ont été évaluées dans un sondage effectué	• Au Canada, 79,6 % des infirmières recommanderaient certainement ou probablement à leurs patients de se faire vacciner, 3,1 % ne le feraient pas et 17,2 % étaient incertaines. En ce qui

Étude transversale Belgique, France et Canada Octobre et novembre 2020	en ligne et par téléphone auprès des omnipraticiens en France (n = 1 209) et dans les régions francophones de la Belgique (n = 414) et auprès des infirmières du Québec, au Canada (n = 1 055). Les résultats pour la Belgique et la France sont disponibles dans la section Europe. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Oui	les concerne, 70,4 % d'entre elles seraient certainement ou probablement prêtes à recevoir le vaccin, 11,8 % le refuseraient, et 17,8 % ont dit être incertaines. • 40,9 % des participants ont déclaré que l'innocuité des vaccins mis au point en urgence pendant une épidémie ne peut être garantie. • L'opinion sur l'innocuité des vaccins mis au point en urgence et la méfiance à l'égard du ministère de la Santé pour assurer l'innocuité des vaccins étaient les deux facteurs les plus importants, indépendamment, associés à l'hésitation et à la réticence à l'égard des vaccins. • L'intention de se faire vacciner a été associée positivement à des antécédents de vaccination personnelle contre la grippe.
Ogilvie (2021) (79) Étude transversale Canada Août et septembre 2020	On a évalué l'intention de se faire vacciner chez 4 058 adultes et travailleurs de la santé de la Colombie-Britannique (âgés de 25 à 69 ans). Le nombre de travailleurs de la santé qui ont pris part au sondage n'est pas indiqué clairement. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Hésitation par rapport à la vaccination	• 81,8 % des travailleurs de la santé ont dit avoir l'intention de se faire vacciner. • Autres résultats observés dans la population en général. • L'analyse multivariée a démontré que les Sud-Asiatiques (RCa = 0,65, IC à 95 % : 0,39 à 1,07), les non-blancs (RCa = 0,76, IC à 95 % : 0,61 à 0,95) et ceux qui se sont identifiés comme Autochtones (RCa = 0,58, IC à 95 % : 0,38 à 0,87) étaient beaucoup moins susceptibles d'avoir l'intention de se faire vacciner.

	Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	
The Canadian PSW Network (2020) *non publiée* (131) Étude transversale Canada s.d. 2020	Utilise un sondage en ligne pour connaître l'intention de 562 préposés aux services de soutien à la personne, infirmières et travailleurs de la santé de se faire vacciner. 84 % de l'échantillon étaient des préposés aux services de soutien à la personne. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 64,2 % des répondants ont dit avoir l'intention de se faire vacciner lorsque le vaccin sera disponible, 16,2 % ne veulent pas se faire vacciner, 10,7 % sont incertains et 8,9 % ne prendront le vaccin que s'il est obligatoire. • 71,7 % ne croient pas qu'il y ait suffisamment d'information claire à propos du vaccin.
ÉTATS-UNIS ET ROYAUME-UNI		
Abohelwa (2021) (224) *nouveau* Étude transversale É.-U. Mars 2021	Les données sur l'adoption du vaccin et l'intention de se faire vacciner ont été recueillies en ligne auprès de 81 résidents et étudiants du campus de Lubbock du Texas Tech University Health Sciences Center. Sujets des questions : 1) Intentions de se faire vacciner 2) Attitudes envers les vaccins	• 95,1 % avaient déjà reçu le vaccin et 96,3 % ont déclaré qu'ils étaient favorables à la vaccination. • 3,7 % ne voulaient pas se faire vacciner. Les raisons n'ont pas été explorées.

	Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	
King (2021) *préimpression* (181) Étude longitudinale É.-U. Janvier à mars 2021	Dans le cadre d'une enquête nationale continue mensuelle sur la COVID-19, des questions visant à mesurer l'acceptation des vaccins et les facteurs connexes d'acceptation ont été recueillies auprès d'échantillons d'adultes (âgés de 18 à 64 ans). Le nombre de travailleurs de la santé n'a pas été communiqué. Enquête de janvier : n = 791 716 Enquête de février : n = 710 529 Enquête de mars : n = 732 308 Sujets des questions : 1) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• Dans un sous-ensemble d'individus de cette enquête (n = 143 297) par catégories professionnelles présentant le plus fort pourcentage d'hésitation, 6,7 % des individus ont déclaré la religion comme raison de leur hésitation à se faire vacciner. Il s'agit notamment des professions de la construction, de l'installation, de l'agriculture, de la sylviculture et de la pêche, et des transports.
Pacella-LaBarbara (2021) (117) *nouveau* Étude transversale É.-U.	Un sondage en ligne a été mené auprès de 475 employés de services des urgences et de services médicaux d'urgence de l'Ohio, du Maryland, de la Virginie-Occidentale et de New York afin de déterminer les intentions de se faire vacciner et les facteurs associés à ces intentions.	• 79 % des travailleurs de la santé s'étaient fait vacciner ou prévoyaient se faire vacciner contre la COVID-19 et 21 % ne prévoyaient pas se faire vacciner. • L'intention de se faire vacciner était plus faible chez les femmes (OR 0,34, IC à 95 % : de 0,34 à 0,91, P =0,02) et les personnes ayant des antécédents d'infection à la COVID-19 (OR 0,55, IC à 95 % : de 0,31 à 0,98, P=0,04), et plus élevée chez

Janv.-févr. 2021	Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	les personnes ayant fait des études supérieures (OR 3,53, IC à 95 % : 1,16, 10,77, P = 0,03) et une vulnérabilité à la COVID-19 perçue élevée (OR 1,99, IC à 95 % : 1,37, 2,90). • Tous les médecins étaient soit vaccinés, soit avaient l'intention de le faire (100 %), contre 27 % des infirmières, 21 % des employés des services médicaux d'urgence et 27 % des autres cliniciens et personnels.
Woolf (2021) *préimpression* (114) Étude transversale et étude qualitative ROYAUME-UNI Décembre 2020 à mars 2021	Pour évaluer l'hésitation à se faire vacciner contre la COVID-19 et les prédicteurs à cette hésitation, une enquête en ligne a été menée auprès de 11 584 travailleurs de la santé (16 et +). Les données qualitatives ont été recueillies par le biais d'entretiens (n = 24), de groupes de discussion (n = 17) et de réponses à des enquêtes ouvertes (n = 58). Sujets des questions : 1) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• 23,3 % des travailleurs de la santé ont hésité à se faire vacciner. • Les travailleurs de la santé plus âgés (RR ajusté 0,74, IC 95 % : 0,70 % à 0,78 % pour chaque décennie d'augmentation) et ceux ayant déjà reçu le vaccin contre la grippe (RR ajusté 0,51, IC 95 % : 0,46 % à 0,57 %) étaient moins hésitants. • Par rapport aux travailleurs sanitaires britanniques blancs, ceux issus des Caraïbes noires (RR ajusté 3,37, IC 95 % : 2,11 à 5,37), Africains noirs (RR ajusté 2,05, IC 95 % : 1,49 % à 2,82 %), et Blancs autres (RR ajusté 1,48, IC 95 % : 1,19 % à 1,84 %), les groupes ethniques étaient plus susceptibles d'être hésitants. • Le personnel de la santé féminin (RR ajusté 1,42, IC 95 % : 1,24 % à 1,62 %), les travailleuses de la santé enceintes (RR ajusté 7,12, IC 95 % : 4,74 % à 10,70 %), et ceux qui avaient été testés positifs pour le SRAS-CoV-2 (RR ajusté 1,30, IC 95 % : 1,14 % à 1,47 %) étaient plus susceptibles d'être hésitants. • Les professionnels de la santé ayant obtenu des cotes plus élevées sur l'échelle des croyances conspirationnistes envers la COVID-19 étaient plus susceptibles d'être hésitants (RR ajusté 1,12, IC 95 % : 1,08 % à 1,16 % pour chaque augmentation de 1 point sur l'échelle).

		• Au cours des entrevues et des groupes de discussion, les travailleurs de la santé ont suggéré une communication inclusive en matière de santé (p. ex., en plusieurs langues) et la participation au déploiement du vaccin de travailleurs de la santé ayant des antécédents diversifiés provenant de communautés minoritaires afin d'améliorer la participation à la vaccination dans les communautés ethniques minoritaires.
Manby (2021) *préimpression* (128) Étude qualitative ROYAUME-UNI Décembre 2020 à mars 2021	Des entretiens téléphoniques ont été menés auprès de 24 travailleurs de la santé afin d'évaluer les facteurs influençant leurs attitudes envers le programme de vaccination contre la COVID-19 du Royaume-Uni. Sujets des questions : 1) Attitudes à l'égard des vaccins	• Le manque de données probantes disponibles était un facteur clé de l'hésitation à se faire vacciner. • La conviction que les décisions du gouvernement concernant le déploiement des vaccins ne sont pas étayées par des données scientifiques probantes et les messages contradictoires et changeants du gouvernement ont eu un impact négatif sur le niveau de confiance des travailleurs de la santé dans le programme de vaccination. • Bien que la majorité ait déclaré que les données probantes étaient suffisantes pour démontrer la sécurité à court terme des vaccins contre la COVID-19, des inquiétudes ont été soulevées quant aux répercussions des souches mutantes sur l'efficacité du vaccin et les effets secondaires inconnus à long terme, tels que sur la fertilité. • La désinformation en ligne a eu un impact négatif sur les attitudes à l'égard des vaccins, en particulier chez les travailleurs de la santé de niveau inférieur et les Noirs, les Asiatiques et les minorités ethniques, avec des rapports de théories de conspiration en ligne visant précisément ces groupes. • La plupart se sentaient motivés pour promouvoir la vaccination auprès de leurs patients et beaucoup estimaient que c'était leur obligation morale.

Moniz (2021) *préimpression* (116) Étude transversale États-Unis Février 2021	Les facteurs associés à l'intention de se faire vacciner contre la COVID-19 ont été évalués chez 11 387 adultes (âgés de 18 ans et plus) dans un centre de soins de santé universitaire du Midwest américain au moyen d'un sondage en ligne. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 79,8 % des répondants avaient reçu le vaccin, 4,8 % avaient l'intention de se faire vacciner le plus tôt possible, 8,4 % n'avaient pas l'intention de le recevoir bientôt, mais pourraient se faire vacciner plus tard et 3,2 % ne voulaient absolument pas se faire vacciner. • Les médecins (RCa 22,2, IC à 95 % : 9,1 à 54,3), les stagiaires (RCa 5,9, IC à 95 % : 3,0 à 11,4) et les infirmières praticiennes, infirmières sages-femmes, adjointes aux médecins (RCa 1,9, IC à 95 % : 1,2 à 3,0) étaient beaucoup plus susceptibles d'accepter un vaccin que les infirmières alors que les autres membres du personnel clinique (RCa 0,8, 0,6 à 0,9) et tous les autres employés (RCa 0,8, 0,6 à 1,0) étaient moins susceptibles de l'accepter. • Les personnes qui avaient déjà contracté la COVID-19 étaient moins susceptibles d'accepter un vaccin (RCa 0,4, IC à 95 % : 0,3 à 0,4). • Les travailleurs de la santé étaient presque deux fois plus susceptibles d'accepter des vaccins que les travailleuses de la santé (RCa 1,9, IC à 95 % : 1,6 à 2,4). • Comparativement aux répondants blancs non hispaniques, les répondants asiatiques non hispaniques étaient plus susceptibles d'accepter un vaccin (RCa 2,3, IC à 95 % : 1,5 à 3,4) et les répondants noirs, mixtes, autres non hispaniques étaient moins susceptibles (RCa 0,4, IC à 95 % : 0,4 à 0,5). • La méfiance à l'égard du vaccin en raison de la rapidité avec laquelle il a été mis au point et les préoccupations relatives à l'innocuité étaient les deux raisons les plus courantes de réticence à se faire vacciner.
McCabe (2021) *préimpression* (166)	Une enquête nationale distribuée par voie électronique a été menée auprès de 34 470 travailleurs de la santé et d'adultes de la population générale afin de mesurer l'intention	• 19 % des professionnels de la santé sont indécis, peu ou très peu enclins à se faire vacciner. • Les travailleurs de la santé essentiels étaient 1,18 fois plus susceptibles que les travailleurs non

Étude transversale É.-U. Décembre 2020 à février 2021	de recevoir un vaccin et les facteurs liés à l'acceptation et au refus. Le nombre de travailleurs de la santé n'a pas été indiqué. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Oui	essentiels d'hésiter à se faire vacciner (RR ajusté = 1,18 95 % CI : 1,06 % à 1,32 %).
Nguyen (2021) *préimpression* (118) Étude transversale É.-U. et R.-U. Janvier 2021	Pour évaluer l'intention de se faire vacciner et les raisons de l'hésitation, un sondage en ligne a été mené auprès de 73 650 et de 1 154 988 adultes et travailleurs de la santé aux États-Unis et au Royaume-Uni, respectivement. Le nombre de travailleurs de la santé dans la population générale n'était pas précisé. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	• Aux États-Unis, les travailleurs de la santé de première ligne étaient moins susceptibles d'avoir l'intention de se faire vacciner (6 % ne veulent pas et 11 % sont incertains) comparativement à la population générale (2 % ne veulent pas et 7 % ne sont pas sûrs). • Comparativement aux travailleurs de la santé des États-Unis, ceux du Royaume-Uni ont indiqué une plus grande volonté de se faire vacciner. Comparativement aux personnes de race blanche, les Noirs (RCa = 3,00, IC à 95 % : 2,86 à 3,16), les Hispaniques (RCa = 1,59, IC à 95 % : 1,51 à 1,67), les Asiatiques (RCa = 1,83, IC à 95 % : 1,70 à 1,97) et les personnes ayant déclaré plus d'une race (RCa = 1,43, IC à 95 % : 1,36 à 1,52) étaient plus susceptibles d'hésiter à se faire vacciner dans l'analyse ajustée en fonction de l'âge. • • Dans toutes les races et origines ethniques, les raisons les plus fréquemment invoquées pour justifier l'hésitation à se faire vacciner comprenaient des préoccupations au sujet des effets secondaires à long terme (50 % à 57 %) et

		des effets indésirables (45 % à 54 %). Les Noirs et les Hispaniques ont mentionné un manque de connaissances sur le vaccin (45 à 51 %) à un taux plus élevé que les Blancs (37 à 42 %).
Kociolek (2021) (106) Étude transversale ÉTATS-UNIS Janvier 2021	Un sondage en ligne a été utilisé pour évaluer la fréquence de la réticence à se faire vacciner, les raisons de la réticence et les caractéristiques des personnes qui ont dit hésiter chez 4 448 travailleurs de la santé dans un hôpital pour enfants à Chicago (Illinois). Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Sur 4 277 participants, 59,8 % ont déclaré avoir l'intention de se faire vacciner, 8,6 % avaient déjà reçu le vaccin, 8,8 % ne se feront pas vacciner et 10,1 % étaient incertains. • Comparativement à leurs homologues, la proportion de personnes qui hésitaient à se faire vacciner était des femmes, avait des antécédents confirmés ou soupçonnés de COVID-19, avait des problèmes de santé à risque élevé et ne s'inquiétait pas de la gravité de la COVID-19. • Les participants noirs étaient plus susceptibles d'hésiter à se faire vacciner que les personnes qui n'étaient pas noires (50,4 % c. 15,6 %) et les Hispaniques/Latinx étaient plus hésitants que les personnes non hispaniques/Latinx (29,9 % c. 17,1 %). • Ceux qui occupaient des postes non cliniques étaient plus hésitants que ceux qui occupaient des postes cliniques (28,7 % contre 11,9 %) et les employés horaires étaient plus hésitants que les salariés (27,6 % contre 11,4 %). • Les raisons les plus fréquemment citées pour justifier la réticence à l'égard du vaccin étaient les effets secondaires à long terme (76,3 %), l'innocuité (50,7 %) et le fait que la méthode avec ARNm est trop nouvelle (47,8 %). • Parmi ceux qui ont dit hésiter à se faire vacciner, les ressources les plus importantes pour l'information sur le vaccin contre la COVID-19 étaient la recherche autoguidée (46,5 %), les fournisseurs de soins primaires (33 %) et les organismes fédéraux et gouvernementaux (28,8 %). Les sites Web d'autoapprentissage (46,9 %), les mises à jour par courriel (36,7 %) et les mises à jour vidéo de dirigeants d'hôpitaux et

		d'experts en vaccins (34,7 %) étaient la méthode de communication préférée des dirigeants d'hôpitaux pour obtenir de l'information sur les vaccins.
Ciardi (2021) (125) *nouveau* Étude transversale É.-U. Déc. 2020-janv. 2021	428 travailleurs de la santé ont été interrogés en ligne sur leurs intentions, leurs connaissances et leurs attitudes envers le vaccin contre la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner 2) Attitudes envers les vaccins Outils de sondage disponibles? Oui Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• 64 % prévoient de se faire vacciner dans les 30 jours et 73 % dans les six prochains mois. • Les répondants qui ont plus de 65 ans (95 %), qui sont asiatiques (79 %), de sexe masculin (79 %) et ceux qui vivent à Manhattan (81 %) étaient significativement plus susceptibles d'accepter de se faire vacciner dans les 30 jours. • Les personnes les moins disposées à se faire vacciner dans les 30 prochains jours sont celles âgées de 36 à 45 ans (57 %), les Afro-Américains (40 %), les femmes (60 %) et les personnes habitant dans le Bronx (51 %). • L'intention de se faire vacciner était fortement corrélée à la confiance dans les ÉPI et les mesures de santé publique *(r* = 0,222), les mesures de santé publique (r = 0,208), la confiance dans les ÉPI au travail (r = 0,0988) et les personnes qui pensent que les ÉPI et les pratiques devront être maintenus même après la vaccination (r = 0,158). • Des notes plus élevées des connaissances sur l'infection à la COVID-19 et le fait de suivre de près les informations étaient corrélés à une intention positive de se faire vacciner (r = 0,18 et r = 0,183 respectivement) (r = 0,18 et r = 0,183, respectivement). • L'expérience personnelle avec la COVID-19 a été associée à une plus grande intention de se faire vacciner. • Les attitudes générales positives envers le vaccin et le risque personnel étaient positivement et significativement associés aux attitudes envers le vaccin contre la COVID-19, tandis que la préoccupation concernant la rapidité du test était associée négativement.

Enwezor (2021) *préimpression* (115) Étude transversale États-Unis Décembre 2020 à janvier 2021	Un sondage en ligne a évalué l'intention de se faire vacciner chez 20 232 adultes (5 170 travailleurs de la santé et 15 062 autres personnes). 476 des participants avaient déjà reçu un diagnostic de COVID-19. Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• L'intention de se faire vacciner était très différente entre les travailleurs de la santé (74 %) et ceux qui travaillaient dans d'autres domaines (77 %), P = 0,0014.
Dugani (2021) (113) Étude transversale É.-U. Décembre 2020 à janvier 2021	Une enquête en ligne a été menée auprès de 128 spécialistes en soins de courte durée, dont 75 médecins et 53 prestataires de pratiques avancées, notamment des infirmières praticiennes et infirmiers praticiens ainsi que des assistants médicaux en Arizona, en Floride, au Minnesota et au Wisconsin. Cette étude visait à évaluer les différences potentielles entre les médecins et les prestataires de pratiques avancées dans leurs attitudes envers les vaccins contre la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner 2) Attitudes à l'égard des vaccins	• 93,7 % des spécialistes en soins de courte durée ont déclaré avoir reçu ou prévu de recevoir le vaccin contre la COVID-19 (88,7 % des prestataires de pratiques avancées et 97,3 % des médecins). • Les spécialistes en soins de courte durée étaient moins susceptibles de conseiller à 100 % des patients de recevoir le vaccin contre la COVID-19 (66 % des prestataires de pratiques avancées, 74,7 % des médecins) que le vaccin contre la grippe (83 % des prestataires de pratiques avancées, 80 % des médecins). Des tendances similaires ont été observées pour le conseil aux patients, à la famille et aux amis. • Les obstacles signalés pour recommander le vaccin aux patients comprenaient des restrictions en matière de santé pour les patients (17 % des prestataires de pratiques avancées, 10,7 % des médecins) et le profil de sécurité du vaccin inconnu (11,3 % des prestataires de pratiques avancées, 6,7 % des médecins). • Les spécialistes de soins de courte durée ont déclaré que les patients et les collègues recevant le

	Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	vaccin réduiraient leur niveau d'anxiété (83 % des prestataires de pratiques avancées, 75,3 % des médecins), réduiraient l'isolement social (60,4 % des prestataires de pratiques avancées, 60,3 % des médecins) et augmenteraient le soutien émotionnel (35,8 % des prestataires de pratiques avancées, 41,1 % des médecins). • Ceux qui pensaient que le vaccin réduirait leur isolement social avaient plus de chances de conseiller à leurs patients de se faire vacciner (RR ajusté 2,95, IC 95 % : 1,32 % à 6,59 %, P < 0,008).
Armitage (2021) (134) Étude transversale ROYAUME-UNI Décembre 2020 à janvier 2021	Une enquête en ligne a été menée auprès de 220 médecins généralistes afin d'évaluer leur confiance dans le fait de conseiller leurs patients sur les vaccins contre la COVID-19. Sujets des questions : 1) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• Plus de 50 % des médecins généralistes avaient peu confiance dans le fait de conseiller leurs patients sur les vaccins contre la COVID-19. • De nombreux médecins généralistes ont déclaré n'avoir aucune ou peu de confiance pour conseiller les patients sur l'inclusion de patients cliniquement vulnérables dans les essais de vaccins (58,2 %), la sécurité des vaccins dans des groupes précis (67,3 %), le potentiel d'effets indésirables non encore observés dans les essais cliniques (74,5 %), la possibilité pour les personnes participant aux essais de recevoir un vaccin approuvé (78,2 %) et la signification de l'efficacité des vaccins (81 %). • 52,7 % et 54,5 % des médecins généralistes ont déclaré n'avoir aucune ou peu de confiance pour accéder à des informations crédibles sur les vaccins pour eux-mêmes et pour orienter les patients vers des informations similaires, respectivement.
Berry (2021) (225) Étude qualitative ÉTATS-UNIS	Les préoccupations soulevées par 193 travailleurs de la santé et membres du personnel d'établissements de soins infirmiers spécialisés lors des assemblées publiques locales ont été déclarées. La localisation aux États-Unis n'a pas été indiquée.	• Parmi les premières préoccupations qui ont été soulevées, mentionnons le fait de croire que le vaccin a été mis au point trop rapidement, les effets secondaires à court et à long terme, l'infertilité et la sécurité pendant la grossesse, et le désir d'attendre de voir comment le vaccin fonctionne pour les autres. • Une fois les premières préoccupations réglées, d'autres préoccupations qui revenaient souvent portaient sur le fait de croire que le vaccin cause la

Décembre et janvier 2021	Sujets des questions : 1) Hésitation par rapport à la vaccination	COVID-19, la paralysie de Bell, le fait qu'un vaccin de rappel soit requis, le fait qu'il est inefficace contre les nouveaux variants et un résultat positif à un test antérieur. • Parmi les préoccupations qui ont été soulevées plus tard dans la discussion, mentionnons l'incertitude à savoir si le fait de recevoir le vaccin aura un effet sur les mesures de précaution à respecter (port d'un couvre-visage, distanciation sociale, etc.), la peur des micropuces et la sécurité chez les personnes atteintes de maladies chroniques. •
Grumbach (2021) (112) Étude transversale É.-U. Novembre 2020 à janvier 2021	Une enquête en ligne a été menée auprès de 3 161 adultes de la communauté et de 1803 membres du personnel soignant de trois centres médicaux de la baie de San Francisco pour évaluer les intentions de vaccination et les raisons de l'acceptation et de l'hésitation. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• Les travailleurs de la santé avaient davantage l'intention de se faire vacciner que la population générale (83,6 % contre 65,5 %, P < 0,001). • Chez les travailleurs de la santé, les Noirs (RR ajusté 0,24, IC 95 % : 0,10 % à 0,60 %), les Latinos (RR ajusté 0,50, IC 95 % : 0,31 % à 0,79 %), les Asiatique (RR ajusté 0,37, IC 95 % : 0,27 % à 0,51 %), les communautés multiraciales (RR ajusté 0,49, IC 95 % : 0,29 % à 0,82 %) et les personnes d'autres races (RR ajusté 0,28, IC 95 % : 0,15 % à 0,53 %) avaient moins l'intention de se faire vacciner que les travailleurs de la santé blancs. • Les raisons pour lesquelles les répondants noirs, latino-américains et asiatiques avaient l'intention de ne pas se faire vacciner comprenaient le manque de confiance dans la capacité du vaccin à prévenir la COVID-19 (RR ajusté 2,39, IC 95 % : 1,58 % à 3,61 %; RR ajusté 2,04, IC 95 % : 1,58 % à 2,64 %; RR ajusté 1,85, IC 95 % : 1,51 % à 2,27 %, respectivement), le manque de confiance dans les fabricants de vaccins (RR ajusté 3,08, IC 95 % : 2,00 % à 4,73 %; RR ajusté 1,85, IC 95 % : 1,38 % à 2,48 %; RR ajusté 1,34, IC 95 % : 1,04 % à 1,72 %, respectivement), et les préoccupations concernant l'approbation précipitée du vaccin (RR ajusté 2,10, IC 95 % : 1,44 % à 3,05 %; RR ajusté 1,68, IC 95 % :

		1,34 % à 2,10 %, RR ajusté 1,81, IC 95 % : 1,53 % à 2,15 %, respectivement).
Weng (2021) *préimpression* (119) Étude transversale États-Unis Novembre 2020 à janvier 2021	Les différences raciales ethniques dans les intentions de vaccination contre la COVID-19 ont été examinées au moyen d'un sondage en ligne effectué auprès de 3 161 adultes de la population générale et de 1 803 travailleurs de la santé en Californie. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• Les travailleurs de la santé étaient plus susceptibles que le grand public d'avoir l'intention de se faire vacciner (83,6 % comparativement à 65,5 %). • Chez les travailleurs de la santé, l'intention de se faire vacciner était la plus élevée chez les Blancs (89 %), suivis des Latins ou des Hispaniques (78 %), des Asiatiques (75 %), des autres races (66 %) et des Noirs ou des Afro-Américains (65 %). • Les répondants latinx et asiatiques étaient beaucoup plus susceptibles que les répondants blancs de dire que la recommandation d'un médecin était une raison importante pour se faire vacciner. • Comparativement aux Blancs, environ 15 % de plus de Noirs, de Latins et d'Asiatiques ont indiqué que le risque d'une mauvaise réaction au vaccin et le fait que le gouvernement précipite le processus d'approbation étaient des raisons majeures de ne pas se faire vacciner. Ils étaient aussi beaucoup plus susceptibles de déclarer des préoccupations au sujet du vaccin qui leur donnait la COVID-19.
Woodhead (2021) (226) *nouveau* Étude qualitative R.-U. Oct.-janv. 2021	Des entrevues en ligne semi-structurées ont été menées auprès de 17 travailleurs de la santé et de huit cadres supérieurs afin d'étudier comment sont prises les décisions concernant l'adoption du vaccin contre la COVID-19 et si le racisme et la discrimination entrent en ligne de compte dans la décision. Sujets des questions : 1) Intentions de se faire vacciner	• Les personnes interrogées se situent dans un continuum allant de celles qui accepteraient immédiatement de se faire vacciner (un peu plus de la moitié) à une minorité qui serait plus sûre de le refuser, un tiers exprimant des opinions hésitantes. • Les personnes interrogées ont tendance à peser activement les avantages et les risques, les personnes réticentes voyant les avantages et les risques de manière égale et les personnes refusant de se faire vacciner se concentrant sur les risques pour elles-mêmes. • Les personnes acceptant de se faire vacciner étaient plus susceptibles de déclarer qu'elles

	2) Réticence à se faire vacciner 3) Attitudes envers les vaccins	considéraient le retour à la normale comme un élément positif dans la prise de décision. • Les risques étaient caractérisés par des inquiétudes concernant les effets secondaires en lien avec des vulnérabilités préexistantes. • Les expériences passées avec les vaccins étaient liées à des points de vue sur la normalisation (par rapport au vaccin contre la grippe) pour les personnes acceptant de se faire vacciner, tandis que les personnes réticentes et refusant de se faire vacciner l'associaient à de grands événements néfastes comme la tragédie de la thalidomide. • Les personnes qui ont exprimé des opinions hésitantes ou opposées ont cité l'absence de renseignements fiables qui pourraient permettre la manipulation et la désinformation. • Tous les groupes se doutaient qu'ils recevraient des messages directs et indirects les incitant à se faire vacciner, mais les personnes refusant de se faire vacciner et les personnes réticentes craignaient davantage d'être forcées à se faire vacciner par leurs institutions.
Harrison (2021) (130) *nouveau* Étude qualitative É.-U. Déc. 2020	Cinq groupes de discussion réalisés par vidéoconférence (Zoom) avec 54 participants ont été organisés avec le personnel d'établissements de soins spécialisés afin de mieux comprendre les réticences. La localisation aux États-Unis n'a pas été indiquée. Sujets des questions : 1) Réticence à se faire vacciner 2) Attitudes envers les vaccins	• Parmi les personnes qui sont réticentes à se faire vacciner, on retrouve quatre thèmes : (1) préoccupations générales et personnelles concernant l'innocuité et l'efficacité du vaccin, (2) manque de confiance dans l'effort de vaccination, (3) désinformation sur le vaccin et (4) augmentation de l'adoption du vaccin. • Les préoccupations générales portaient sur la courte période de développement et d'essai, la nouveauté, les effets à long terme, l'impact sur les conditions sous-jacentes ou le fait que la COVID-19 ne serait pas grave si elles tombaient malades. • Certains répondants ont cru à tort que le vaccin contiendrait un virus vivant ou atténué. Les rumeurs de désinformation portaient sur les micropuces, les virus vivants et l'infertilité.

		• Le manque de confiance a été ressenti à la fois pour l'affiliation politique ou le scepticisme historique pour les personnes de couleur. • Lorsqu'on leur a demandé comment augmenter le taux d'adoption, les répondants ont souhaité voir des renseignements faciles à comprendre et faire venir des représentants pour discuter (groupes religieux) ou être vus en train de recevoir le vaccin.
Abuown (2021) (227) Étude transversale ROYAUME-UNI Décembre 2020	Un sondage en ligne effectué auprès de 514 adultes à Londres a évalué l'intention de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Oui	• 59 % étaient prêts à se faire vacciner contre la COVID-19, 24 % ont dit ne pas l'être alors que 17 % étaient indécis. • Les médecins étaient plus susceptibles d'accepter un vaccin que les infirmières (P < 0,001), les auxiliaires de santé (P < 0,001), les pharmaciens (P < 0,001), les professionnels paramédicaux (P < 0,01) et le personnel administratif (P < 0,01). Les membres du personnel de gestion de l'hôpital étaient plus susceptibles d'accepter cette option que les infirmières, les aides-soignants et les pharmaciens (P < 0,01). • Ceux qui ont accepté de recevoir un vaccin antigrippal étaient moins susceptibles de refuser un vaccin contre la COVID-19 (RC 0,45, IC à 95 % : 0,031 à 0,96) et ceux qui ont refusé un vaccin contre la grippe étaient plus susceptibles de refuser le vaccin contre la COVID-19 (RC 8,32, IC à 95 % : 5,36 à 12,91, P < 0,001). • Les travailleurs de la santé plus âgés (61 ans et plus) étaient beaucoup plus susceptibles d'avoir l'intention de se faire vacciner (P < 0,01). • Le rapport de probabilité de refus du vaccin était de 0,51 pour les hommes (IC à 95 % : 0,34 à 0,77) et de 1,26 pour les femmes (IC à 95 % : 1,12 à 1,42, P < 0,001). • L'intention de se faire vacciner était beaucoup plus faible chez les travailleurs de la santé noirs que chez les Blancs (P < 0,01), les Indiens (P < 0,001) ou les autres personnes d'origine asiatique (P < 0,01).

		• Les préoccupations en matière de sécurité étaient le motif de réticence le plus courant.
Meyer (2021) (228) Étude transversale ÉTATS-UNIS Décembre 2020	Un sondage en ligne effectué en Pennsylvanie visait à évaluer les intentions de se faire vacciner et les raisons de l'hésitation chez 16 158 travailleurs de la santé. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 55 % des répondants ont l'intention de se faire vacciner lorsque le vaccin sera disponible, 16,4 % n'accepteraient pas de faire vacciner et 28,5 % étaient indécis. • Les patients qui sont en contact avec les travailleurs de la santé ont déclaré des intentions de vaccination plus élevées que ceux qui n'en ont pas (56,8 % comparativement à 51,4 %, p < 0,005). • Dans les zones dans les hôpitaux, ceux qui travaillaient à l'urgence étaient ceux qui voulaient le moins se faire vacciner (51,9 %), tandis que ceux qui travaillaient aux soins intensifs (63,1 %) et aux soins aux personnes hospitalisées (60,9 %) étaient ceux qui voulaient le plus recevoir le vaccin. • Les principales raisons qui poussaient les gens à hésiter étaient les préoccupations au sujet des risques inconnus du vaccin (90,3 %), les préoccupations au sujet des effets secondaires connus (57,4 %) et le désir d'attendre pour voir les répercussions du vaccin sur les autres (44,4 %). • Parmi les autres raisons associées à l'hésitation, mentionnons un manque de confiance à l'égard du processus ou des résultats de la FDA (21,1 %), des préoccupations au sujet du suivi par l'État ou le réseau hospitalier (13,9 %), des préoccupations au sujet de la technologie de l'ARNm (11,4 %) et la croyance qu'ils ne présentent pas un risque élevé d'être atteints d'une maladie grave (10,4 %). • La division des réponses reçues avant le vote sur l'approbation du vaccin Pfizer (92,8 % des réponses) et après (7,2 % des réponses) révèle que 79 % des répondants ont déclaré qu'ils recevraient le vaccin, comparativement à 53,2 % qui avaient dit avoir l'intention de se faire vacciner avant le vote.
Piltch-Loeb (2021) (229)	L'effet des médias sur l'acceptation des vaccins a été évalué à l'aide d'un sondage en ligne effectué	• 39,9 % ont déclaré qu'ils étaient susceptibles de se faire vacciner dans les deux mois, 47,3 % avaient

Étude transversale ÉTATS-UNIS Décembre 2020	auprès de 2 650 adultes appartenant aux groupes prioritaires pour la vaccination, y compris les travailleurs de la santé. 61,4 % des participants travaillaient dans le secteur des soins de santé. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination 3) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Oui	un certain degré d'hésitation et 12,8 % étaient peu susceptibles d'accepter le vaccin. • 61 % ont obtenu de l'information sur le vaccin contre la COVID-19 de la télévision locale et 37,8 % de Facebook. • Les répondants ont indiqué que les nouvelles sur le vaccin étaient positives (53,6 %), neutres (25,3 %), surtout négatives (16,3 %) ou qu'ils n'avaient pas vu l'information sur le vaccin (4,8 %). • Dans l'ensemble, la confiance dans les sources d'information sur les vaccins était de modérée à faible, 23 % déclarant une confiance élevée, 40,5 % une confiance modérée et 36,3 % un bas niveau de confiance. • Dans l'analyse à variables multiples, les prédicteurs positifs de l'intention de se faire vacciner comprenaient le fait de connaître une personne décédée de la COVID-19 (RR = 1,47, IC à 95 % : 1,08 à 1,99), d'avoir une certaine confiance dans l'information sur les vaccins (RR = 2,01, IC à 95 % : 1,61 à 2,51), d'avoir une grande confiance dans l'information sur les vaccins (RR = 15,6, IC à 95 % : 11,69 à 20,81), et d'obtenir des renseignements sur les vaccins par la télévision nationale (RR = 1,75, IC à 95 % : 1,02 à 1,53), la télévision locale (RR = 1,75, IC à 95 % : 1,40 à 2,19), ou des journaux nationaux (RR = 1,81, IC à 95 % : 1,45 à 2,24). • Un faible niveau quant à l'intention de se faire vacciner a été associé aux répondants qui n'utilisaient que les médias sociaux (RC = 0,45, IC à 95 % : 0,32 à 0,64) ou ont utilisé à la fois les médias sociaux et les canaux médiatiques traditionnels (RC = 0,81, IC à 95 % : 0,66 à 1,00) par rapport à ceux qui n'ont utilisé que les médias traditionnels pour obtenir des renseignements sur les vaccins.
Kuter (2021) (109)	Pour évaluer l'intention de se faire vacciner, un sondage en ligne a été mené dans deux grands hôpitaux	• 63,7 % des participants ont dit avoir l'intention de se faire vacciner contre la COVID-19 lorsque le vaccin sera disponible, 26,3 % se sont dits

Étude transversale ÉTATS-UNIS Novembre et décembre 2020	universitaires de Philadelphie auprès de 12 034 employés. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Oui	incertains et 10,0 % ont dit ne pas être disposés à se faire vacciner. • Parmi ceux qui ont l'intention de se faire vacciner, 79,1 % ont dit qu'ils recevraient le vaccin le plus tôt possible, 19,1 % aimeraient attendre de 3 à 6 mois une fois qu'il aura été administré à d'autres, et 1,8 % l'auraient fait une fois que 12 mois se seront écoulés après l'administration à d'autres personnes. • Les deux caractéristiques les plus importantes du vaccin pour les répondants étaient l'innocuité (94,4 %) et l'efficacité (82,8 %). • Si un vaccin devait comporter des effets secondaires tels qu'une forte fièvre, des douleurs musculaires, des frissons et des maux de tête entraînant une perte de deux jours de travail, seulement 28,3 % des répondants ont déclaré qu'ils seraient disposés à le recevoir. 33,2 % se sont dits incertains. • L'intention de se faire vacciner a augmenté à mesure que l'efficacité du vaccin augmentait (35,8 % se sont dits prêts à recevoir un vaccin dont l'efficacité était de 50 %, 61,1 % s'il était efficace à 70 % et 85,6 % s'il était efficace à 90 %). • Les facteurs associés de façon significative à l'intention de se faire vacciner étaient le sexe masculin (RC = 2,41, IC à 95 % : 2,12 à 2,75), l'âge plus avancé (> 65 ans : RC = 3,50, IC à 95 % : 2,50 à 4,90; 40 à 64 ans : RC = 1,41, IC à 95 % : 1,26 à 1,56) et un plus grand niveau de scolarité (diplôme d'études supérieures : RC = 4,59, IC à 95 % : 3,83 à 5,50, baccalauréat ou maîtrise : RC = 1,84, IC à 95 % : 1,59 à 2,13). • Comparativement à l'origine ethnique blanche, l'intention de se faire vacciner était considérablement plus faible chez les Noirs (RC = 0,23, IC à 95 % : 0,19 à 0,27), les Hispaniques (RC = 0,51, IC à 95 % : 0,39 à 0,67) et ceux qui ont

		déclaré des races multiples/autres (RC = 0,58, IC à 95 % : 0,47 à 0,73). • Les résidents des régions urbaines étaient beaucoup plus susceptibles d'avoir l'intention de se faire vacciner que les résidents des banlieues (RC = 0,71, IC à 95 % : 0,65 à 0,79) et des régions rurales (RC = 0,41, IC à 95 % : 0,30 à 0,54). • L'intention de se faire vacciner était plus faible chez les personnes dont la santé était mauvaise ou passable (RC = 0,73, IC à 95 %, 0,56 à 0,95) et chez celles qui n'étaient pas à jour avec leur vaccination (RC = 0,36, IC à 95 %, 0,18 à 0,71) que chez leurs homologues. • Les raisons les plus courantes pour accepter de se faire vacciner étaient la protection de la famille (86,7 %), le fait de se protéger soi-même (82,9 %), la protection de la communauté (68,8 %) et le retour à la vie normale (59,4 %). • Les raisons les plus fréquentes pour hésiter à se faire vacciner ou refuser le vaccin étaient la préoccupation au sujet des effets secondaires (89,1 %), le fait que le vaccin était trop nouveau (84,0 %) et le manque de connaissances sur le vaccin (77,9 %).
Shaw (2021) (110) Étude transversale ÉTATS-UNIS Novembre et décembre 2020	Un sondage en ligne a permis d'évaluer la volonté de se faire vacciner de 5 287 travailleurs de la santé d'un grand centre médical universitaire de New York. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non	• 57,5 % des répondants étaient prêts à accepter un vaccin offert gratuitement, 26,4 % étaient incertains et 15,9 % ont dit qu'ils le refuserait. • Les hommes étaient plus susceptibles d'avoir l'intention de se faire vacciner (72,5 %) que les femmes (52,4 %) ou les personnes non binaires ou non déclarées (41,0 %), P < 0,001. • Ceux qui se sont déclarés asiatiques (73,8 %) ou blancs (58,4 %) étaient plus enclins à se faire vacciner que les autres répondants (47,6 %), les Indiens d'Amérique ou les Autochtones de l'Alaska (39,3 %) ou les Noirs (30,8 %), P < 0,001. • Les scientifiques et les médecins (80,4 %), ainsi que les employés œuvrant en sécurité publique et dans les soins spirituels (77,8 %) étaient les plus

	Recherches formatives effectuées? Oui Enquête prétestée? Non	susceptibles d'avoir l'intention de se faire vacciner. Les infirmières autorisées (41,2 %), les membres des services auxiliaires (46,4 %) et les professionnels paramédicaux (51,4 %) étaient les moins susceptibles de se faire vacciner (P < 0,001). • Ceux qui étaient plus âgés et ceux qui ne donnaient pas de soins directs aux patients étaient plus susceptibles d'avoir l'intention de se faire vacciner. • Les répondants blancs étaient d'accord pour dire qu'un vaccin contre la COVID-19 serait sécuritaire lorsqu'il est approuvé (45,9 %) plus fréquemment que les répondants noirs (26,2 %), P < 0,001). • Les préoccupations les plus courantes au sujet du vaccin sont l'innocuité, les effets secondaires, l'efficacité et la rapidité du développement du vaccin.
Jain (2021) *préimpression* (111) Étude transversale ÉTATS-UNIS Novembre et décembre 2020	Les motivations, les préoccupations et les intentions concernant les vaccins contre la COVID-19 ont été évaluées dans un sondage en ligne mené auprès de 2 135 travailleurs de la santé (âgés de 18 ans et plus) de trois centres médicaux en Californie. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination 3) Connaissance des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 69 % des travailleurs de la santé se feraient vacciner si la FDA l'approuvait officiellement, 22 % étaient incertains et 10 % le refuseraient. En revanche, seulement 35 % se feraient vacciner si ce vaccin était approuvé pour une utilisation d'urgence seulement. • 25 % voulaient être parmi les premiers à recevoir un vaccin, 36 % préféraient se faire vacciner après le premier cycle et 18 % voulaient attendre plus de deux mois. • Les principaux facteurs qui motivaient la vaccination comprenaient le risque perçu associé à la COVID-19 pour soi-même (65 %) et pour les membres de sa famille/ses amis (63 %). • Les principales préoccupations en ce qui concerne le vaccin étaient les effets secondaires (28 %), la participation politique au processus d'approbation de la FDA (21 %), la méfiance à l'égard des sociétés pharmaceutiques (16 %) et l'efficacité (12 %). • 19 % des répondants ont déclaré être très informés ou bien informés au sujet des vaccins candidats contre la COVID-19, tandis que 66 % ont

		déclaré qu'ils étaient quelque peu informés, alors que 16 % n'étaient pas du tout informés.
O'Brien (2021) *préimpression* (107) Étude longitudinale ÉTATS-UNIS Octobre à décembre 2020	Un sondage en ligne a été réalisé en octobre auprès de 2 070 travailleurs de la santé aux États-Unis pour déterminer leur intention de se faire vacciner en vertu d'une autorisation d'utilisation d'urgence. Ce sondage a été répété chez 1 541 travailleurs de la santé en décembre. 998 participants ont répondu aux deux sondages. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• L'intention de se faire vacciner est passée de 54,2 % en octobre à 76,2 % en décembre. Pendant cette période, l'intention de se faire vacciner a augmenté de 64,0 % à 90,5 % chez les médecins, de 68,9 % à 75 % chez les ambulanciers paramédicaux et de 46,6 % à 66,9 % chez les infirmières. • En ce qui concerne les 998 personnes qui ont pris part aux deux sondages, 69 % étaient disposées à se faire vacciner les deux fois, 15 % étaient hésitantes les deux fois, 13 % étaient hésitantes en octobre, mais étaient disposées à se faire vacciner en décembre, et 2,9 % étaient disposées à se faire vacciner en octobre, mais hésitaient en décembre.
Keleker (2021) (129) *nouveau* Étude transversale É.-U. Sept.-déc. 2020	248 étudiants en médecine dentaire (DS) et 167 étudiants en médecine (MS) de trois écoles dentaires et d'une école de médecine ont été interrogés en ligne sur leur comportement vaccinal passé et leur réticence actuelle envers le vaccin contre la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner 3) Attitudes envers les vaccins	• 23 % des étudiants en médecine et 45 % des étudiants en médecine dentaire ont déclaré qu'ils étaient réticents à se faire vacciner contre la COVID-19, ce qui indique que les étudiants en médecine étaient 2,7 fois plus susceptibles de se faire vacciner. • Les attitudes générales envers les vaccins étaient positives parmi les MS, 99,4 % d'entre eux étant d'accord pour dire que les vaccins sont importants pour rester en bonne santé en tant qu'un travailleur de la santé et 99,4 % croyant qu'ils ont un rôle à jouer pour en apprendre au sujet des vaccins pour leurs patients. • Les étudiants en MS étaient significativement plus susceptibles de soutenir la vaccination obligatoire pour le grand public (OR= 3,12, IC à 95 % : de 2,06

	Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Oui Sondage prétesté? Non	à 4,76) et pour les travailleurs de la santé (OR= 5,18, IC à 95 % : de 3,15 à 8,76). • Les étudiants en MS étaient significativement plus susceptibles de faire confiance aux renseignements reçus sur les vaccins contre la COVID-19 que les étudiants en DS (OR= 3,51, IC à 95 % : de 2,09 à 6,08), mais étaient également plus susceptibles d'avoir des inquiétudes quant à l'efficacité du vaccin (OR= 2,78, IC à 95 % : de 1,80 à 4,36). • Il était plus improbable pour les MS que les DS de dire qu'ils ne se feraient vacciner que si cela était imposé par les systèmes scolaires ou de santé (OR= 0,38, IC à 95 % : de 0,22 à 0,62) ainsi que de déclarer qu'à l'âge adulte, ils ont refusé de se faire vacciner pour une raison autre qu'une maladie ou une allergie (OR= 0,41, IC à 95 % : de 0,23 à 0,73). • Dans l'analyse logistique, le fait d'appartenir à une minorité sous-représentée, de croire que la vaccination contre la COVID-19 devrait être obligatoire pour le public, de croire que la vaccination contre la COVID-19 est importante pour soi en tant que travailleur de la santé, de faire confiance aux renseignements sur le vaccin contre la COVID-19 était associé de manière significative à la volonté de recevoir un vaccin, tandis que la crainte d'avoir des effets indésirables et le fait de ne recevoir un vaccin que si nécessaire étaient associés au refus d'accepter de se faire vacciner.
Unroe (2020) (121) Étude transversale ÉTATS-UNIS Novembre 2020	Un sondage en ligne a été effectué auprès de 8 243 employés de maison de soins infirmiers et de personnes qui offrent des soins à domicile en Indiana afin d'évaluer leur volonté de se faire vacciner. Sujets des questions : 4) Intentions en ce qui concerne les vaccins	• 45 % des répondants seraient prêts à recevoir un vaccin approuvé par la FDA dès qu'il sera disponible. • Parmi ceux qui ne seraient pas prêts à recevoir le vaccin immédiatement, 44 % seraient prêts à le recevoir à une date ultérieure. • Les raisons les plus courantes de l'hésitation à se faire vacciner comprennent les effets secondaires potentiels (70 %), les préoccupations relatives à la santé (34 %), les préoccupations relatives à l'efficacité (20 %) et les motifs religieux (12 %).

	5) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Comparativement à leurs homologues, les personnes âgées de plus de 60 ans, les hommes et ceux qui se déclarent d'origine blanche étaient plus disposés à se faire vacciner (p < 0,0001). • Les travailleurs de la santé noirs étaient 12 % (IC à 95 % : 8,6 à 15,7 %) moins disposés à accepter le vaccin que les travailleurs de la santé blancs. • Le personnel responsable de l'alimentation, de l'entretien ménager et de l'administration était plus susceptible d'avoir l'intention de se faire vacciner que le personnel de soins cliniques, y compris les infirmières auxiliaires et les infirmières (p < 0,0001).
Shekhar (2021) (123) Étude transversale ÉTATS-UNIS Octobre et novembre 2020	Un sondage en ligne a évalué l'intention de se faire vacciner chez 3 479 travailleurs de la santé (âgés de 18 ans et plus). Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 36 % des répondants ont dit être prêts à se faire vacciner dès que le vaccin serait disponible, 56 % ont dit ne pas être certains et voulaient examiner les données sur l'innocuité avant de se faire vacciner, et 8 % ont dit qu'ils refuseraient le vaccin. • L'intention de se faire vacciner a augmenté avec l'âge (34 % dans le groupe des 18 à 30 ans contre 47 % dans le groupe des plus de 70 ans). • Le sexe masculin, le niveau de scolarité supérieur, les niveaux de revenu plus élevés, le fait de vivre dans le Sud, dans une région urbaine et de s'identifier comme libéral ou démocrate étaient associés à une plus grande intention de se faire vacciner dès qu'il est disponible par rapport à leurs homologues. • Les travailleurs de la santé noirs (19 %) et amérindiens/autochtones de l'Alaska (10 %) étaient moins susceptibles que les travailleurs blancs (37 %) et asiatiques (44 %) (p < 0,001) d'avoir l'intention de se faire vacciner dès que les vaccins seraient disponibles. La majorité des travailleurs de la santé noirs (65 %), amérindiens (80 %) et tous les travailleurs de la santé hawaïens/autres insulaires du Pacifique (100 %) ont choisi d'attendre d'examiner les données avant de recevoir le vaccin.

		• L'intention de se faire vacciner dès qu'un vaccin serait disponible était plus faible chez ceux qui s'identifiaient comme hispaniques ou latino-américains (30 %) que chez ceux qui ne s'identifiaient pas à cette origine ethnique (37 %). • Les travailleurs qui croient être immunisés contre la COVID-19 (22 %), qui sont sûrs de ne pas être infectés (27 %), et ceux qui n'ont pas pris soin de patients atteints du COVID-19 (9,2 %) affichaient les taux les plus élevés d'intention de refuser un vaccin. • Les principales préoccupations exprimées au sujet de la vaccination comprennent la sécurité et les effets indésirables (69 %), l'efficacité (69 %) et la rapidité du développement et de l'approbation (74 %). • La majorité des travailleurs de la santé font confiance à leurs médecins et aux professionnels de la santé qui recommandent le vaccin (73 %), mais 46 % ne font pas confiance aux renseignements fournis par le gouvernement au sujet du vaccin et de sa gravité et 34 % ne font pas confiance aux organismes de réglementation (p. ex., CDC ou FDA) pour superviser la mise au point et l'innocuité des vaccins.
Caban-Martinez (2021) (133) Étude transversale États-Unis Octobre 2020	Aux États-Unis, un sondage en ligne a été mené auprès de 3 169 travailleurs des services médicaux d'urgence et pompiers afin d'évaluer leur intention de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Non	• 48,2 % étaient disposés à se faire vacciner lorsque le vaccin sera disponible, 27,6 % étaient moyennement disposés à le recevoir et 24,2 % étaient incertains. • Les personnes les plus susceptibles de ne pas accepter le vaccin étaient âgées de 30 à 39 ans (RCa 3,62, IC à 95 % : 2,00 à 6,55), de race noire (RCa 3,60, IC à 95 % : 1,12 à 11,53), de race multiple (RCa 2,98, IC à 95 % : 1,61 à 5,51), d'origine hispanique ou latine (RCa 2,39, IC à 95 % : 1,45 à 3,92), avaient un plus faible niveau d'éducation (RCa 2,06, IC à 95 % : 1,29 à 3,27), étaient ou non mariées (RCa 1,65, IC à 95 % : 1,03 à 2,65) et cette probabilité d'accepter ou non le

	Recherches formatives effectuées? Oui Enquête prétestée? Non	vaccin variait selon le grade actuel du pompier ou du travailleur des services médicaux d'urgence (RCa 2,21, IC à 95 % : 1,60 à 3,08).
Gadoth (2021) (120) Étude transversale ÉTATS-UNIS Septembre et octobre 2020	Pour comprendre l'intention des travailleurs de la santé de se faire vacciner et les attitudes à l'égard de l'innocuité, de l'efficacité et de l'acceptabilité des vaccins dans le contexte de la pandémie de COVID-19, un sondage en ligne a été mené auprès de 609 travailleurs de la santé. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 47,8 % des participants ont déclaré qu'ils ne prendraient pas part à un essai de vaccin contre la COVID-19. • 65,5 % ont l'intention de retarder la vaccination et de ce nombre, 49,4 % préféreraient attendre et voir d'abord comment le vaccin affecte les autres. Comparativement aux médecins, le pourcentage corrigé de personnes qui ont déclaré leur intention de retarder la vaccination ou de refuser de se faire vacciner était de 0,52, de 0,54 et de 0,59 fois plus élevée chez les infirmières, les autres membres du personnel ayant des contacts avec les patients et ceux qui n'ont aucun contact avec les patients, respectivement. • Les répondants s'entendent pour dire que les vaccins sont utiles pour se protéger contre la maladie (score moyen de Likert de 4,69 IC à 95 % : 4,64 à 4,73) et pour protéger la santé de la collectivité (score moyen de Likert de 4,69 IC à 95 % : 4,65 à 4,74). Les médecins avaient toutefois une telle attitude plus souvent que les infirmières. • Les avis étaient partagés en ce qui concerne l'énoncé selon lequel les nouveaux vaccins comportent plus de risques que les vaccins plus anciens (score moyen de Likert de 3,23 IC à 95 % : 3,14 à 3,32). • Moins de la moitié des répondants (46,9 %) étaient d'avis qu'un vaccin les protégerait contre la COVID-19 et 34,8 % étaient confiants quant au processus de contrôle scientifique. • Les femmes et les minorités raciales ou ethniques ont exprimé des attitudes plus hésitantes à l'égard des vaccins que leurs homologues. • Les principales variables qui ont eu une incidence sur ceux qui prévoyaient retarder la prise du vaccin ou refuser de se faire vacciner étaient des

		préoccupations au sujet de la nature accélérée du développement du vaccin et du manque de transparence ou d'information publique à propos du vaccin.
Robbins (2021) (230) Étude transversale ROYAUME-UNI Septembre 2020	Un sondage en ligne a été mené auprès de 593 travailleurs de la santé dans un grand hôpital de référence tertiaire afin d'évaluer leur intention de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Si un vaccin était disponible et distribué gratuitement par l'entremise de leur employeur, et qu'il comportait des données appropriées sur l'innocuité et l'efficacité, 83,4 % des répondants seraient susceptibles de se faire vacciner. • 58,9 % seraient disposés à se faire vacciner en dehors de leurs heures normales de travail (p. ex., la fin de semaine) et 53,1 % seraient disposés à se rendre à un autre endroit pour se faire vacciner. • 68,5 % seraient prêts à se faire vacciner dans leur voiture et 76,6 % ne verraient pas d'inconvénient à attendre dans une file d'attente en respectant la distanciation physique pour se faire vacciner. • 77,8 % croient que les travailleurs de la santé devraient avoir la priorité pour recevoir un vaccin et 82,8 % croient que le personnel en première ligne qui traite directement les patients devrait avoir la priorité sur les gens qui n'ont aucun contact avec les patients.
Manning (2021) (124) Étude transversale ÉTATS-UNIS Août et septembre 2020	Les facteurs associés à l'intention de se faire vacciner ont été évalués dans un sondage en ligne effectué auprès de 78 membres à temps plein de la faculté des sciences infirmières, de 105 membres auxiliaires du corps professoral en soins infirmiers et de 1 029 élèves infirmiers. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins	• L'intention de se faire vacciner était la plus élevée chez les membres à temps plein de la faculté (60,3 %), suivis des étudiantes (45,3 %) et des membres auxiliaires du corps professoral. • Les hommes étaient plus susceptibles que les femmes d'avoir l'intention de se faire vacciner (60,3 % comparativement à 44,9 %, P = 0,002). • Les personnes de 60 ans et plus avaient la plus forte intention de se faire vacciner (85,7 %, P = 0,004). • Les raisons les plus courantes pour lesquelles ces personnes voulaient se faire vacciner comprenaient le désir de protéger sa famille, soi-même, les patients et la collectivité, et la conviction que ce serait la meilleure façon d'éviter

	3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Oui	de tomber gravement malade à cause de la COVID-19. • Les raisons les plus fréquentes de ne pas vouloir se faire vacciner étaient le fait de croire que le vaccin avait été mis au point trop rapidement pour être sécuritaire, et les effets secondaires. Ces préoccupations ont été plus fréquemment signalées par les étudiants et le corps professoral clinique auxiliaire que par le corps professoral à temps plein ($P < 0,05$). • La vaccination obligatoire comme condition d'emploi était soutenue par 52 % du corps professoral à temps plein, 39 % du corps professoral auxiliaire et 35 % des étudiants.
Parente (2021) (126) *nouveau* Étude transversale É.-U. Août 2020	Les associations à l'adoption des vaccins ont été évaluées en ligne pour un vaccin hypothétique en tenant compte des périodes de retard (de 1 à plus de 12 mois après l'approbation) chez 3 347 travailleurs de la santé du Kentucky. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Oui Sondage prétesté? Oui	• 37,2 % des répondants ont accepté tôt de se faire vacciner, souhaitant être vaccinés dans le premier mois de l'approbation. • 22,3 % souhaitaient être vaccinés dans les 1 à 3 mois, 11,4 % dans les 4 à 6 mois, 6,9 % dans les 7 à 12 mois et 12,3 % plus de 12 mois après l'approbation. • 9,9 % déclarent qu'ils n'ont jamais l'intention de se faire vacciner. • Les raisons invoquées pour retarder ou refuser la vaccination étaient les effets secondaires à long terme (57,1 %), l'innocuité du vaccin (55,0 %), l'efficacité du vaccin (37,1 %), les risques par rapport aux avantages du vaccin (31,0 %), le coût du vaccin (12,2 %) et les allergies possibles (11,2 %). • Les répondants asiatiques étaient 1,53 fois plus susceptibles de déclarer vouloir se faire vacciner dans les trois mois comparativement aux répondants blancs. En revanche, les répondants noirs étaient significativement moins enclins à se faire vacciner au cours de la même période (OR 0,16, IC à 95 % : de 0,10 à 0,25). • L'adoption précoce d'un vaccin (dans les 3 mois) était significativement associée aux hommes (RCa

		2,43, IC à 95 % : de 2,00 à 2,95), ceux qui ont été vaccinés contre la grippe en 2019-2020 (RCa 2,35, IC à 95 % : de 1,75 à 3,18), une plus grande inquiétude concernant la COVID-19 (RCa 2,40, IC à 95 % : de 2,07 à 2,79), et des niveaux d'éducation plus élevés (RCa 1,41, IC à 95 % : de 1,21 à 1,65).
Hoke (2021) (132) Étude transversale ÉTATS-UNIS Mai 2020	Un sondage a été effectué en ligne auprès de 350 infirmières des écoles de soins infirmiers de Pennsylvanie (âgés de 18 ans et plus) pour évaluer l'intention de se faire vacciner et les perceptions à l'égard du vaccin. Sujets des questions : 3) Intentions en ce qui concerne les vaccins 4) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 84,9 % des infirmières étaient disposées à se faire vacciner lorsqu'un vaccin sera disponible, 14,5 % ont dit qu'il était peu probable qu'elles se fassent vacciner et 0,6 % n'ont pas répondu. • 63,7 % appuyaient le retour à l'école même si les personnes n'avaient pas été vaccinées. • Comparativement aux infirmières en milieu rural, les infirmières en milieu urbain étaient plus disposées à recevoir un vaccin lorsqu'il serait disponible (RC = 2,21, IC à 95 % : 1,41 à 3,46) et étaient plus préoccupées par le retour à l'école sans avoir été vacciné (RC = 1,58, IC à 95 % : 1,05 à 2,38).
Sathianathan (2020) (231) Étude transversale ÉTATS-UNIS Mars 2020	Un sondage en ligne a été utilisé pour comparer les connaissances sur le vaccin contre la COVID-19 entre 4 966 travailleurs de la santé et 854 personnes qui travaillaient dans un secteur autre en Pennsylvanie. Sujets des questions : 1) Connaissance des vaccins Outils d'enquête disponibles? Oui	• Lorsqu'on leur a demandé si un vaccin contre la COVID-19 serait disponible dans un délai de trois mois, les travailleurs de la santé étaient plus susceptibles de répondre correctement (faux) que les personnes qui travaillent dans un autre domaine.

	Recherches formatives effectuées? Oui Enquête prétestée? Oui	

RCa = rapport des cotes ajustées, IC = intervalle de confiance

POPULATIONS À RISQUE ÉLEVÉ

Tableau 5. Preuve en ce qui concerne les attitudes des populations à risque élevé à l'égard des vaccins (n = 24)

ÉTUDE	MÉTHODES ET OUTILS D'ENQUÊTE	RÉSULTATS CLÉS RELATIFS AUX CONNAISSANCES, ATTITUDES ET COMPORTEMENTS
ENCEINTE OU QUI ALLAITENT		
Woolf (2021) *préimpression* (114) Étude transversale et étude qualitative ROYAUME-UNI Décembre 2020 à mars 2021	Pour évaluer l'hésitation à se faire vacciner contre la COVID-19 et les prédicteurs à cette hésitation, une enquête en ligne a été menée auprès de 11 584 travailleurs de la santé (16 et +). Les données qualitatives ont été recueillies par le biais d'entretiens (n = 24), de groupes de discussion (n = 17) et de réponses à des enquêtes ouvertes (n = 58). Tous les résultats concernant les travailleurs de la santé se trouvent dans la section TRAVAILLEURS DE LA SANTÉ. Sujets des questions : 1) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• Les travailleuses de la santé enceintes étaient 7,12 fois plus susceptibles d'être hésitantes que les travailleuses de la santé non enceintes (RR ajusté 7,12, IC 95 % : 4,74 % à 10,70 %).

Skjefte (2021) (135) Étude transversale 16 pays : Australie, Afrique, Argentine, Brésil, Chili, Colombie, Inde, Italie, Mexique, Nouvelle-Zélande, Pérou, Philippines, Russie, Espagne, Royaume-Uni, États-Unis. Octobre et novembre 2020	Un sondage en ligne a été utilisé pour évaluer le niveau d'acceptation de la vaccination contre la COVID-19 chez 5 294 femmes enceintes et 12 562 mères d'enfants de moins de 18 ans. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Pour un vaccin efficace à 90 %, 52,0 % des femmes enceintes et 73,4 % des femmes non enceintes ont indiqué leur intention de se faire vacciner. • 69,2 % de toutes les femmes avaient l'intention de faire vacciner leurs enfants. Les niveaux d'acceptation étaient supérieurs à 85 % en Inde, au Mexique, au Brésil et en Colombie et inférieurs à 52 % aux États-Unis, en Australie et en Russie. • L'intention de se faire vacciner des femmes enceintes variait selon le pays avec des taux d'acceptation supérieurs à 80 % au Mexique et en Inde, et inférieurs à 45 % aux États-Unis, en Australie et en Russie. • La réticence à se faire vacciner était associée à un âge plus jeune, à un revenu plus faible, à un niveau de scolarité plus faible, au fait de ne pas être marié et à l'absence d'assurance-maladie. • Les prédicteurs les plus solides de l'intention de se faire vacciner étaient la confiance dans l'innocuité et l'efficacité du vaccin, le faire de croire à l'importance des vaccins pour leur propre pays, la confiance dans les vaccins de routine donnés pendant l'enfance, l'inquiétude au sujet de la COVID-19, la confiance dans les organismes de santé publique ou la science de la santé, et la conformité aux lignes directrices sur les couvre-visage. • 53,0 % des répondants étaient convaincus qu'un vaccin contre la COVID-19 approuvé à l'échelle nationale serait sans danger alors que 60,4 % étaient convaincus qu'il serait efficace. • Chez les femmes enceintes, les raisons les plus courantes de refuser un vaccin étaient les effets secondaires potentiels pour leur bébé (65,9 %), la crainte que l'approbation du vaccin soit précipitée pour des raisons politiques (44,9 %) et le manque de données sur l'innocuité et l'efficacité chez les femmes enceintes (48,8 %).

		• Pour les mères, les raisons les plus courantes de refuser un vaccin étaient la crainte que l'approbation du vaccin soit précipitée pour des raisons politiques (39,8 %), le manque de données sur l'innocuité et l'efficacité chez les enfants (32,7 %) et les préoccupations au sujet de l'innocuité et des effets secondaires (28,4 %). • Une recommandation d'un fournisseur de soins de santé a eu une incidence limitée sur l'intention de se faire vacciner. 45,9 % des femmes enceintes et 54,6 % des femmes non enceintes seraient plus susceptibles de se faire vacciner ou de faire vacciner leurs enfants si les fournisseurs de soins de santé le recommandaient.
Skirrow (2021) *préimpression* (19) Étude de prévalence et qualitative ROYAUME-UNI Août à octobre 2020	Un sondage en ligne et des entrevues semi-structurées ont été menés auprès d'un groupe de 1 181 femmes enceintes (âgées de 16 ans et plus) afin de déterminer leurs points de vue sur l'acceptabilité du vaccin contre la COVID-19 pour elles-mêmes lorsqu'elles sont enceintes ou non enceintes, ainsi que pour leur bébé. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 81,2 % des femmes ont déclaré qu'elles accepteraient certainement un vaccin ou auraient tendance à le faire si elles n'étaient pas enceintes. L'acceptation du vaccin était beaucoup plus faible pendant la grossesse (62,1 %, P < 0,005), ainsi que pour leurs bébés (69,9 %, p < 0,005). • Comparativement aux femmes de race blanche, les femmes de minorités ethniques étaient deux fois plus susceptibles de refuser un vaccin pour elles-mêmes lorsqu'elles n'étaient pas enceintes, étaient enceintes et pour leur bébé (P > 0,005). • Les personnes de ménages à faible revenu, âgées de moins de 25 ans et provenant de certaines régions géographiques étaient plus susceptibles de refuser un vaccin lorsqu'elles n'étaient pas enceintes, enceintes et pour leurs bébés. • Les femmes non vaccinées contre la coqueluche pendant la grossesse étaient plus de quatre fois plus susceptibles de refuser un vaccin lorsqu'elles n'étaient pas enceintes, enceintes et pour leur bébé. • L'analyse thématique a révélé que les raisons les plus courantes de réticence étaient l'innocuité du vaccin et une méfiance plus grande à l'égard des vaccins en général.

Battarbee (2021) *préimpression* (136) Étude transversale ÉTATS-UNIS Juillet à octobre 2020	915 femmes enceintes de l'Utah, de l'Alabama et de l'État de New York ont été interrogées au téléphone ou lors de visites en personne afin de mesurer leurs attitudes à l'égard du vaccin contre la COVID-19 et de l'acceptabilité de ce dernier. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 41 % des femmes ont dit qu'elles accepteraient un vaccin, et cette donnée n'a pas varié en fonction du mois d'inscription à l'étude. • Les femmes disposées à accepter un vaccin ont cité des raisons comme le désir de protéger leur grossesse (95 %), de se protéger (85 %), de protéger les membres de leur famille (79 %) et de protéger leur communauté (68 %). • Celles qui ne sont pas disposées à se faire vacciner pendant leur grossesse ont dit qu'elles le refuseraient en raison de préoccupations au sujet de l'innocuité du vaccin pendant la grossesse (82 %), de l'innocuité pour elles-mêmes (68 %), de l'efficacité du vaccin (52 %) et de la croyance qu'elles n'ont pas besoin du vaccin (22 %). • Le fait d'avoir un diplôme d'études supérieures a multiplié par 2,4 la probabilité d'accepter un vaccin par rapport à celles qui n'avaient pas de diplôme d'études secondaires (IC à 95 % : 1,3 à 4,7). • Dans la modélisation multivariée, le fait de n'avoir reçu qu'un vaccin contre la grippe au cours de la dernière année (RCa = 2,1, IC à 95 % : 1,5 à 3,0) a permis d'augmenter le niveau d'acceptation du vaccin. À l'inverse, seule l'origine ethnique (répondantes hispaniques et noires) était associée au refus d'accepter un vaccin (RCa = 0,4, IC à 95 % : 0,2 à 0,6 chacun).
PERSONNES EN SITUATION D'ITINÉRANCE		
Kuhn (2021) *préimpression* (41) Étude transversale ÉTATS-UNIS	Le niveau d'adoption du vaccin et d'hésitation chez 90 personnes sans abri de Los Angeles (âgées de 18 ans et plus) a été évalué à l'aide d'un sondage effectué par téléphone cellulaire. Sujets des questions : 1) Adoption du vaccin	• Parmi les 90 participants, 17 se sont vus offrir un vaccin et de ce nombre, 10 ont accepté et 7 ont refusé. • Parmi les 73 participants à qui le vaccin n'a pas été offert, 51 % ont dit qu'ils le prendraient s'il leur était offert, 32 % ont dit qu'ils ne se feraient pas vacciner et 17 % ont refusé de répondre. • Dans l'ensemble, 48 % des personnes ont refusé un vaccin lorsqu'il leur était offert, ont dit qu'elles le refuseraient s'il leur était offert ou ont refusé de

Décembre 2020 à février 2021	2) Hésitation par rapport à la vaccination 3) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	répondre et ont donc été jugées « hésitantes face à la vaccination ». • Parmi les participants qui hésitaient à se faire vacciner, les raisons les plus souvent mentionnées étaient la peur des effets secondaires (37 %), le désir d'avoir plus d'information (30 %) et le fait qu'ils ne veulent pas recevoir de vaccin (27 %). • Selon une analyse multivariée, les personnes qui ont une perception élevée de la menace que représente la COVID-19 (RC = 0,25, P = 0,02) et celles qui faisaient confiance à des sources officielles (RC = 0,37, P = 0,08) étaient beaucoup moins susceptibles d'hésiter à se faire vacciner. Celles qui avaient un comportement hautement protecteur (RC = 3,63, P = 0,02) et celles qui faisaient confiance à leurs contacts personnels (RC = 2,70, P = 0,07) étaient plus susceptibles d'hésiter.
Knight (2021) *préimpression* (137) Étude qualitative ÉTATS-UNIS Juillet à octobre 2020	Pour comprendre les facteurs et les obstacles à l'acceptabilité du vaccin chez les adultes sans abri (âgés de 20 à 71 ans), une étude qualitative a été effectuée auprès deux échantillons de gens : 1) une cohorte longitudinale de 37 adultes âgés sans abri à Oakland, en Californie, et 2) un échantillon de proximité comprenant 57 personnes pendant une activité de dépistage mobile de la COVID-19 à San Francisco, en Californie. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination	• De nombreux participants ont indiqué qu'ils étaient disposés à recevoir un vaccin lorsqu'il serait disponible. Ils ont cité le désir de retourner à la vie de tous les jours et la responsabilité civique comme raisons pour se faire vacciner. • Quatre thèmes se sont dégagés en ce qui concerne la réticence à l'égard de la vaccination, notamment : 1) le désir d'obtenir plus de données sur les essais, l'innocuité et l'approbation du vaccin, 2) des préoccupations associées au fait que les vaccins rendaient les gens malades, 3) le désir d'attendre que d'autres aient reçu le vaccin avant d'accepter de se faire vacciner, et 4) la méfiance à l'égard du gouvernement. Certains ont fait un lien entre cette méfiance et des expériences antérieures de racisme. • En dépit de l'exclusion sociale et du manque d'accès à la technologie, les participants ont suivi les reportages sur le vaccin et l'information souhaitée sur l'efficacité et l'innocuité du vaccin.
ADULTES PLUS ÂGÉS		

Horizon Research (2021) *non publiée* (15, 195, 232) Étude longitudinale Nouvelle-Zélande Mars à mai 2021	Un sondage effectué en ligne auprès d'adultes (âgés de 16 ans et plus) visait à évaluer l'adoption du vaccin. Mars et avril, n = 1 350 Avril et mai, n = 1 387 Mai, n=1,234 *nouvelle* Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	**Mai** • 9 % des 65 à 74 ans et 14 % des 75 ans et plus étaient peu susceptibles de se faire vacciner. • Les principales préoccupations des personnes âgées de 65 à 74 ans étaient les effets secondaires (30 %), les effets à long terme (28 %) et la crainte de ce qui se produirait si elles avaient une réaction indésirable (26 %). On a observé des préoccupations semblables chez les plus de 75 ans. **Avr-mai** • 81 % des 65 à 74 ans et 88 % des personnes âgées de 75 ans et plus ont dit qu'elles se feraient probablement vacciner.
Australia Bureau of Statistics (2021) *Non publié* (141) *nouveau* Étude longitudinale Australie Avril 2020-mai 2 021	Le sondage sur les impacts sur les ménages est un sondage mensuel qui recueille des données en ligne et par téléphone auprès d'un groupe d'adultes (18 ans et plus) sur des sujets liés à la COVID-19, y compris les attitudes envers les vaccins. Mai : n=3371 Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Non	• 7.6 % des personnes âgées de plus de 70 ans ne se feraient certainement pas vacciner si on leur proposait et 9,4 % ne se feraient probablement pas vacciner si on leur proposait. • La recommandation du médecin généraliste était le facteur le plus important dans la décision de se faire vacciner chez 41,1 % des personnes âgées de 70 ans et plus.

	Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	
Office for National Statistics (2021) *non publiée* (140) Étude transversale ROYAUME-UNI Février et mars 2021	17 201 réponses provenant de quatre vagues de résultats recueillis dans le cadre du sondage en ligne Opinions and Lifestyle Survey (126) ont été mises en commun pour mettre l'accent sur les associations démographiques spécifiques et la réticence à se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 3 % des 65 à 69 ans et 5 % des 60 à 64 ans ont dit hésiter à se faire vacciner. 4 % des 55 à 59 ans aussi étaient hésitants. • Parmi les personnes âgées de 75 à 79 ans qui étaient très ou assez peu susceptibles de se faire vacciner, 49 % ont déclaré être contre les vaccins en général, 46 % ont mentionné des préoccupations au sujet d'une condition préexistante et 31 % avaient d'autres raisons. • Les inquiétudes chez les 65 à 79 ans étaient plus variées et incluaient notamment les préoccupations concernant les effets secondaires, les effets à long terme, les inquiétudes au sujet des problèmes de santé existants, le fait de ne pas croire que le vaccin est dangereux et le désir de voir si le vaccin fonctionne. • Les personnes âgées de 55 à 64 ans avaient d'autres croyances selon lesquelles elles n'étaient pas à risque ou croyaient déjà avoir eu la COVID-19.
Nikolovski (2021) (139) Étude transversale ÉTATS-UNIS Novembre 2020	Un sondage a été effectué auprès de 7 402 adultes âgés (de 65 ans et plus) à l'aide d'une application mobile sur la santé pour déterminer les facteurs associés aux intentions de se faire vacciner de cette population. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination	• 91,3 % des participants ont déclaré qu'ils étaient disposés ou plutôt disposés à se faire vacciner alors que 8,7 % n'étaient pas disposés à se faire vacciner ou étaient quelque peu réticents à le faire. • L'hésitation était la plus forte chez les femmes (RC = 0,49, IC à 95 % : 0,45 à 0,54) et les Afro-Américaines ou les Noires (RC = 0,24, IC à 95 % : 0,18 à 0,31). • Les participants qui ont déclaré un revenu plus élevé (RC = 2,60, IC à 95 % : 1,98 -3,42) ou un niveau de scolarité plus élevé (RC = 2,31, IC à 95 % : 1,84 à 2,94) étaient plus susceptibles d'avoir l'intention de se faire vacciner.

	Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	• Les croyances fortement associées à l'intention de se vacciner étaient la protection de soi et des autres (RC = 38,6, IC à 95 % : 32,4 à 46,1), un vaccin sûr et efficace (RC = 21,6, IC à 95 % : 18,9 à 24,7) et le confort avec des effets secondaires à court terme (RC = 10,9, IC à 95 % : 9,1 à 13,1). • La majorité des répondants voulaient parler à un fournisseur de soins de santé avant de prendre la décision de se faire vacciner. Cela comprend tant ceux qui sont prêts à se faire vacciner (91,4 % des femmes et 88,9 % des hommes) que ceux qui ne le sont pas (68,4 % des femmes et 62,3 % des hommes). • Les nouvelles positives concernant le vaccin étaient associées à une augmentation des intentions de se faire vacciner. Après la diffusion des résultats de l'essai clinique de phase 3 de Pfizer, l'intention de se faire vacciner a augmenté (RC = 1,46, IC à 95 % : 1,28 à 1,69).
Luo (2021) (150) *nouveau* Étude transversale É.-U. Oct.-nov. 2020	En utilisant le Medicare Current Beneficiary Survey, 6 715 bénéficiaires de Medicare (âgés de 65 ans et plus) ont été interrogés par téléphone sur leurs intentions de se faire vacciner contre la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• 61,0 % (IC à 95 % : de 59,1 à 63,0) seraient disposés à se faire vacciner lorsque les vaccins seront disponibles et 39,0 % (IC à 95 % : de 37,0 à 40,9) étaient réticents à se faire vacciner. • 59,6 % des personnes âgées de 65 à 74 ans ont déclaré être prêtes à se faire vacciner, contre 63,5 % des personnes âgées de 75 ans et plus. • Les répondants âgés de 65 à 74 ans (RCa 0,83, IC à 95 % : de 0,74 à 0,92), les Noirs non hispaniques (RCa 0,33, IC à 95 % : de 0,24 à 0,44), hispanique (RCa 0,60, IC à 95 % : de 0,47 à 0,77), les femmes (RCa 0,56, IC à 95 % : de 0,48 à 0,64), les personnes ayant un revenu inférieur à 25 000 dollars (RCa 0,71, IC à 95 % : de 0,62 à 0,81), et celles qui ne pensaient pas que la COVID-19 était plus contagieuse (RCa 0,53, IC à 95 % : de 0,41 à 0,69) ou plus mortelle (RCa 0,51, IC à 95 % : de 0,41 à 0,65) étaient significativement moins susceptibles de se faire vacciner.

		• Les principales raisons citées pour la réticence à se faire vacciner sont la faible confiance dans le gouvernement (42,1 %), la crainte des effets secondaires (41,3 %) et l'incertitude quant à l'efficacité du vaccin (11,3 %). • L'intention de se faire vacciner était significativement plus élevée chez les personnes ayant un accès à Internet à domicile que chez celles n'en ayant pas (RCa 1,22, IC à 95 % : de 1,01 à 1,49).
Callow (2021) (233) Étude transversale États-Unis Août 2020	Pour examiner l'impact des attitudes, des normes subjectives et du contrôle comportemental perçu sur les attitudes à l'égard de la vaccination, on a effectué un sondage en ligne auprès de 583 adultes (âgés de 60 ans et plus) du Delaware, du Maryland, de Washington DC et de Virginie. Sujets des questions : 1) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• On a observé des attitudes plus favorables à l'égard des vaccins contre la COVID-19 chez les hommes (β = 0,10, P < 0,01), chez les personnes qui avaient déjà reçu le vaccin contre la grippe (β = 0,15, P < 0,001), chez celles qui percevaient la maladie comme étant plus grave (β = 0,11, P < 0,01) et chez celles qui avaient une attitude positive à l'égard des vaccins en général (β = 0,48, P < 0,001). • Comparativement à ceux qui se sont identifiés comme des démocrates forts, les scores d'attitude face au vaccin étaient moins favorables chez les démocrates modérés (β = 0,08, P < 0,05), les indépendants (β = 0,26, P < 0,001), les républicains modérés (β = 0,16, P < 0,001) et les républicains forts (β = 0,44, P < 0,001).
Waite (2021) (92) Étude transversale Canada Mai 2020	Un sondage en ligne a été effectué auprès de 1 001 Canadiens âgés de 50 à 64 ans et auprès de 3 500 Canadiens âgés de 65 ans et plus afin d'évaluer les intentions de se faire vacciner contre la COVID-19. Sujets des questions :	• Parmi les 50 à 64 ans, 69,1 % ont dit avoir l'intention de se faire vacciner lorsque les vaccins seront disponibles, 11,3 % ne se feront pas vacciner et 19,6 % étaient incertains. • 79,5 % des 65 ans et plus ont l'intention de se faire vacciner lorsque le vaccin sera disponible, 5,6 % refuseront de le faire et 14,9 % ont dit être incertains. • Dans les deux groupes d'âge, les personnes qui acceptaient de se faire vacciner étaient beaucoup

	1) Intentions en ce qui concerne la vaccination 2) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	plus susceptibles d'être de sexe masculin et d'avoir au moins un problème de santé chronique (P < 0,05). • L'endroit privilégié pour recevoir un vaccin chez ces deux groupes était le bureau du médecin de famille, suivi de la pharmacie, du lieu de travail (pour les 50 à 64 ans) et des cliniques de santé publique.
Williams (2020) (138) Étude transversale ROYAUME-UNI Avril 2020	Un sondage en ligne effectué auprès de 311 adultes âgés (65 ans et plus) et de 216 patients atteints d'une maladie respiratoire chronique (âgés de 18 à 64 ans) a été utilisé pour évaluer l'intention de se faire vacciner et les perceptions à l'égard du vaccin. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Non	• Dans la population totale (n = 527), 58 % et 27 % des participants ont dit qu'ils voudraient certainement ou probablement se faire vacciner une fois que le vaccin sera disponible. Il n'y avait pas de différence entre le groupe des adultes plus âgés et le groupe des personnes ayant une maladie respiratoire chronique (p = 0,78). • La volonté de se faire vacciner contre la COVID-19 était associée positivement à la croyance que l'éclosion de la COVID-19 allait se poursuivre pendant longtemps (0,09, p < 0,05) et associée négativement à la croyance que les médias ont exagéré les risques d'attraper la COVID-19 (-0,122, p < 0,05). • Une analyse thématique des commentaires associés au sondage a révélé que la « santé personnelle » (n = 176), la « gravité de la COVID-19 » (n = 85) et les « conséquences pour la santé des autres » (n = 36) étaient vues comme des facteurs qui facilitaient la vaccination, alors que les « préoccupations au sujet de l'innocuité du vaccin » (n = 158) constituent plutôt un obstacle à l'adoption du vaccin.
CONSOMMATION DE DROGUES ET D'ALCOOL		
Yang (2021) (147) Étude transversale	L'intention de se faire vacciner et la réticence à se faire vacciner de 387 adultes (âgés de 18 ans et plus) aux États-Unis qui ont déjà utilisé des produits du tabac ou de la	• 49,1 % étaient prêts à se faire vacciner, 26,0 % ont dit ne pas l'être alors que 24,9 % étaient indécis. • La consommation de cigarettes, de cigarettes électroniques, de marijuana et de boissons

États-Unis Décembre 2020 à janvier 2021	marijuana ont été évaluées au moyen d'un sondage en ligne. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	alcoolisées n'était pas associée à la réticence à se faire vacciner. • Ceux qui étaient Noirs, qui vivaient en banlieue ou en milieu rural, qui vivaient seuls ou avec une famille de cinq membres ou plus, et ceux qui n'étaient pas stressés à cause de la pandémie de COVID-19 étaient plus susceptibles de ne pas accepter un vaccin lorsqu'il serait offert. • Comparativement à ceux qui avaient reçu un vaccin contre la grippe chaque année ou presque, ceux qui n'avaient jamais reçu de vaccin contre la grippe, une seule fois ou certaines années étaient 7,0, 6,2 et 5,2 fois plus susceptibles de ne pas accepter de vaccin.
Spechler (2021) *préimpression* (146) Étude transversale É.-U. Décembre 2020 à janvier 2021	Un groupe de 45 consommateurs de cannabis (déclarant avoir consommé plus de 10 fois du cannabis au cours de leur vie) a été apparié à 45 personnes ayant déclaré avoir consommé moins de 10 fois du cannabis au cours de leur vie afin d'évaluer la volonté de recevoir un vaccin contre la COVID-19 à l'aide d'une enquête en ligne. Sujets des questions : 1) Intentions de se faire vacciner Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• La volonté de recevoir un vaccin ne diffère pas significativement entre les consommateurs de cannabis et les témoins *(t88* = 0,33, P = 0,74; BF_{01} = 4,3). • Parmi les consommateurs de cannabis, l'augmentation de la consommation de cannabis au cours de la vie était corrélée à une volonté moindre de se faire vacciner *(r43*= -0,33, P = 0,03).
Masson (2021) (234) *nouveau*	258 Californiens souffrant de troubles liés à l'abus de substances ont reçu des sondages sur papier dans des programmes de	• 11,2 % des participants font totalement confiance, 28,3 % font plutôt confiance et 28,3 % font légèrement confiance au fait que le vaccin contre la COVID-19 serait sûr et efficace. 32,2 % ne

Étude transversale É.-U. Août-déc. 2020	traitement des toxicomanies et ont été interrogés sur leur confiance dans les vaccins contre la COVID-19. Sujets des questions : 1) Perception des vaccins Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	croient pas qu'un vaccin contre la COVID-19 soit sûr et efficace. • Dans la modélisation multivariée, seuls l'âge (RCa 1.03, IC à 95 % = de 1,02 à 1,05) et le port régulier du masque par rapport au port moins fréquent (RCa 2.48, IC à 95 % = de 1,86 à 3,31) étaient significativement associés à la confiance dans les vaccins, alors que les Afro-Américains étaient moins susceptibles de faire confiance aux vaccins que les Blancs non hispaniques (RCa 0,41, IC à 95 % = de 0,23 à 0,70).
Jackson (2020) *préimpression* (145) Étude transversale ROYAUME-UNI Sep à Oct 2020	Dans le cadre de l'étude sociale sur la COVID-19, un sondage en ligne a été mené auprès de 29 148 fumeurs actuels, anciens fumeurs et personnes n'ayant jamais fumé, afin de déterminer les attitudes générales envers le vaccin et les intentions de se faire vacciner contre la COVID-19. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• L'intention de se faire vacciner était de 66 % (IC à 95 % : de 64,9 à 67,1 %) chez les anciens fumeurs, de 65,8 % (IC à 95 % : de 65.1 à 66,4 %) chez les personnes n'ayant jamais fumé, et de 50,9 % (IC à 95 % : de 49,3 à 52,6 %) chez les fumeurs actuels. • Les fumeurs actuels étaient à la fois les plus indécis (27,6 %, IC à 95 % : de 26.1 à 29,1 %) et réticents (21,5 %, IC à 95 % : de 20,2 à 22,9 %) à avoir l'intention de se faire vacciner une fois le vaccin disponible. • Les attitudes négatives envers les vaccins étaient les plus élevées chez les fumeurs actuels (de 10,6 à 24,0 %), puis chez les anciens fumeurs (de 8,8 à 19,4 %), et les plus faibles chez les personnes n'ayant jamais fumé (de 5,9 à 17,7 %). • Les fumeurs actuels étaient les plus préoccupés par les effets futurs imprévus, avaient une méfiance envers les avantages des vaccins et la recherche de profits excessifs, et avaient une préférence plus marquée pour l'immunité naturelle.
Mellis (2021) (144)	Des entrevues téléphoniques et par vidéo structurées ont été effectuées auprès de 87 personnes qui consomment actuellement des	• 45 % des répondants ont dit qu'ils étaient immédiatement prêts à se faire vacciner, 8 % étaient prêts à se faire vacciner après un certain

Étude transversale ÉTATS-UNIS Septembre 2020	substances, suivent un traitement ou sont en cure de désintoxication pour déterminer leur confiance et leur état de préparation à la vaccination contre la COVID-19. Sujets des questions : 3) Intentions en ce qui concerne les vaccins 4) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	temps, 23 % étaient incertains et 25 % n'étaient pas prêts. • Les répondants ont déclaré hésiter en raison de la rapidité du développement du vaccin, des effets secondaires potentiels, du fait qu'ils ne croyaient pas être à risque élevé et de leurs inquiétudes au sujet des interactions avec des problèmes préexistants. • Les sources de confiance pour les décisions en matière de soins de santé incluaient le médecin (y compris ceux qui étaient hésitants), les membres de la famille, les médias sociaux, la télévision/les journaux, la radio, les sites Web officiels, les NIH/CDC, la famille, les données de recherche/revues médicales et Internet. • La possibilité qu'un vaccin nécessite des doses multiples n'a pas modifié l'intention de se faire vacciner, mais les répondants ont mentionné des obstacles potentiels comme l'accès aux cliniques et la prise de rendez-vous.
COMMUNAUTÉS VULNÉRABLES		
Marquez (2021) *préimpression* (3) *nouveau* Étude transversale É.-U. Février-mai 2021	Un site de vaccination communautaire (Unidos en Salud UeS) a été déployé en février pour surmonter les obstacles à la vaccination contre la COVID-19 auxquels sont confrontés les LatinsX à San Francisco. Le site communautaire a été évalué grâce à 997 réponses à des sondages en personne (du 2 au 19 mai) auprès des personnes âgées de plus de 16 ans et aux données de surveillance sur la COVID-19 de la ville. Sujets des questions : 1) Perception des vaccins	• 36,1 % des répondants ont découvert le site par l'intermédiaire d'un ami, d'un membre de la famille ou d'un collègue, 21 % par message texte, 17,8 % en voyant le site et 11,4 % par recommandation directe. Les répondants latinsX étaient plus susceptibles de déclarer avoir vu le site que d'avoir reçu une invitation directe. • La raison la plus souvent citée pour le choix du site communautaire est l'emplacement (28,6 %), la commodité des horaires (26,9 %) et une recommandation fiable (18,1 %). • 99 % des personnes se rendant sur le site communautaire ont déclaré avoir vécu une expérience positive. • 58,4 % des répondants déclarent s'être fait vacciner plus tôt grâce au site (56,1 % des LatinsX et 63,2 % des non-LatinsX).

	Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Oui Sondage prétesté? Non	• 90,1 % des répondants ont estimé qu'ils étaient plus susceptibles de recommander de se faire vacciner après avoir été vaccinés à l'UeS. • 65,3 % des clients latinsX ont contacté trois personnes ou plus pour recommander la vaccination (55,9 % des clients non latinsX).
Berenson (2021) (235) *nouveau* Étude transversale É.-U. Nov-Déc 2020	342 femmes à faibles revenus (âgées de 18 à 45 ans) ont été recrutées dans trois cliniques de reproduction du Texas pour répondre anonymement à un sondage papier en anglais ou en espagnol concernant les intentions de se faire vacciner contre la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner 2) Perception des vaccins Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• 33,5 % des répondants se feraient vacciner dès que possible, mais cette proportion augmente si le vaccin est recommandé par l'employeur (33,9 %), par des amis ou des membres de la famille (36,7 %), s'il est offert gratuitement (41,8 %) ou s'il est recommandé par leur médecin (49,5 %). • L'adoption d'un vaccin contre la COVID-19 recommandé par un médecin était associée au fait d'avoir reçu un vaccin annuel contre la grippe, d'avoir reçu le vaccin contre le VPH, d'avoir peur d'attraper la COVID-19 et que leurs sentiments étaient liés à des renseignements puisés dans les médias sociaux. • Dans l'analyse multivariée seule, le fait d'avoir été vacciné contre le VPH et d'avoir été vacciné contre la grippe chaque année était significativement associé à une probabilité accrue d'accepter un vaccin s'il était recommandé par un médecin (RCa 2,26 IC à 95 % : de 1,07 à 4,79 et un RCa 2,78 (IC à 95 %) : de 1,39 à 5,58 respectivement). • La plupart des répondants ont déclaré avoir besoin de plus de renseignements sur l'innocuité des vaccins (69,2 %) et de preuves de leur efficacité (48,1 %).
Gehlbach (2021) *préimpression* (236) *nouveau* Étude qualitative É.-U.	Des groupes de discussion semi-structurés menés sur la plateforme de vidéoconférence Zoom avec 55 travailleurs agricoles latinsX/autochtones en Californie visaient à éclaircir les thèmes communs liés aux attitudes et aux comportements envers la COVID-19.	• Les thèmes englobent la désinformation et les obstacles à l'accès à l'information (accès à Internet, information dans la langue de leur choix, connaissance des sources d'information appropriées/correctes concernant la COVID-19). • La méfiance politique/institutionnelle (gouvernement et santé publique) a joué dans les mythes liés au vaccin comme méthode de contrôle ou dans le désir exprimé de ne pas être un cobaye.

Nov-déc. 2021	Sujets des questions : 1) Perception des vaccins 3) Attitudes à envers les vaccins	• L'inquiétude quant à l'état de leur documentation était un facteur clé tant pour le dépistage que pour le comportement de vaccination anticipée.
Ekezie (2020) (237) Étude qualitative ROYAUME-UNI Juin et juillet 2020	Trois groupes de discussion et 47 entrevues semi-structurées ont été utilisés pour évaluer les perceptions des minorités ethniques et des communautés vulnérables à l'égard de la participation aux essais des vaccins. Parmi les 70 participants, on comptait des Sud-Asiatiques, des Africains et des Afro-Caraïbes, des Polonais blancs, des Britanniques blancs et des représentants d'autres groupes vulnérables, y compris des personnes ayant des problèmes de santé mentale, des sans-abri et des membres des communautés Tzigane, Rom et Traveller.	• L'appréhension générale, le scepticisme et le faible niveau de confiance ont été observés dans tous les groupes. Ces attitudes ont été influencées par le manque d'information et par la spéculation en ce qui concerne les intentions cachées possibles des concepteurs de vaccins et du gouvernement. • La plupart des participants ont déclaré qu'ils étaient anxieux et effrayés à l'idée de prendre part à des essais de vaccins ou qu'ils ne voulaient tout simplement pas y participer. • Bien qu'hésitants, la plupart des participants sud-asiatiques étaient ouverts à participer à des recherches, mais pas nécessairement à des recherches effectuées en milieu hospitalier. Ce groupe était préoccupé par le fait que le vaccin pourrait contenir des produits animaux interdits dans diverses religions. Ils ont également fortement recommandé que la recherche ne tombe pas pendant le ramadan ou les périodes de jeûne. • Les participants africains et caribéens étaient les plus méfiants quant à la rapidité du développement du vaccin et aux intentions des entreprises qui y prennent part. On se méfiait beaucoup de ce qu'on ferait de leur ADN, et certains croyaient que le vaccin avait été mis au point pour éradiquer les Noirs. • Les personnes ayant des problèmes de santé mentale se sont dites préoccupées par la divulgation de renseignements sur la santé mentale et la perte de confidentialité. • Les sans-abri hésitaient à se rendre dans les hôpitaux, sauf en cas d'urgence. Il est souvent difficile de maintenir le contact avec ce groupe, de

		sorte qu'il peut avoir besoin d'une plus grande participation en personne dans des lieux communautaires comme les banques alimentaires. • Les participants membres des communautés tziganes, rom et traveller avaient un intérêt très limité pour les vaccins et avaient tendance à avoir une approche fataliste des problèmes de santé, croyant « ce qui doit arriver va arriver ».
Scott (2021) (142) Étude transversale ÉTATS-UNIS Avril 2020	Un sondage a été envoyé par la poste à 391 familles amish en Ohio pour déterminer les intentions de se faire vacciner contre la COVID-19. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 75,7 % n'avaient pas l'intention de faire vacciner leurs enfants contre la COVID-19. • Aucune différence significative dans l'intention de se faire vacciner contre la COVID-19 n'a été observée entre les personnes avec et sans enfants ayant des besoins spéciaux (14,8 % c. 7,6 %, P = 0,053). • Les Swartzentruber Amish étaient beaucoup moins susceptibles d'avoir l'intention de se faire vacciner que les autres membres des Amish (0,0 % contre 11,7 %, P < 0,001). • Les principales raisons génériques pour refuser le vaccin comprenaient un trop grand nombre d'effets secondaires (83,9 %), le fait qu'ils contiennent des produits chimiques/agents de conservation dangereux (46,0 %), le fait que se faire vacciner signifie ne pas faire confiance à Dieu pour protéger leurs enfants (13,0 %), le fait que la vaccination introduit des germes (9,6 %), le fait que d'autres familles ne se feront pas vacciner (7,0 %) et que les maladies pour lesquelles ils sont vaccinés ne sont pas un problème dans leur communauté (6,1 %). • Les personnes qui citent les médecins ou les infirmières comme étant la personne la plus influente dans la décision de se faire vacciner étaient plus susceptibles de recevoir tous les vaccins recommandés que celles qui n'ont reçu aucun vaccin (52,2 % c. 2,6 % P < 0,001). Toutefois, les familles qui ont refusé tous les vaccins recommandés étaient plus susceptibles de déclarer

		que leur évêque ou leur ministre était la personne la plus influente dans la décision de se faire vacciner comparativement aux familles qui ont reçu tous les vaccins (4,4 % comparativement à 0,0 %, P = 0,003).
GENERAL		
Horizon Research (2021) *non publiée* (15, 195) Étude longitudinale Nouvelle-Zélande Mars à mai 2021	Une enquête en ligne a été menée auprès des adultes (16 ans et plus) pour mesurer le taux d'utilisation du vaccin. Mar-Avr, n=1,350 Avr-Mai, n=1,387 Sujets des questions : 1) Prise du vaccin Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• 83 % des personnes qui présentaient un risque élevé de tomber très malades avaient l'intention de se faire vacciner ou étaient déjà vaccinées, alors que 5 % ont déclaré qu'elles ne se feraient certainement pas vacciner.

CCPM = Centres pour contrôle et la prévention des maladies, NIH = Instituts nationaux de la santé

PERSONNES AYANT DES COMORBIDITÉS OU DES INCAPACITÉS

Tableau 6. Éléments de preuve des personnes atteintes de comorbidités sur les attitudes à l'égard du vaccin (n = 23)

ÉTUDE	MÉTHODES ET OUTILS D'ENQUÊTE	RÉSULTATS CLÉS RELATIFS AUX CONNAISSANCES, ATTITUDES ET COMPORTEMENTS
CANADA		
Vallis (2021) (164)	Les attitudes et les préoccupations à l'égard de la vaccination contre la COVID-19 chez les personnes en	

Étude transversale Canada Juin à octobre 2020	surpoids et atteintes d'obésité ont été évaluées par un sondage en ligne. Deux échantillons ont été utilisés : 1) un échantillon représentatif de 1 089 personnes en surpoids et atteintes d'obésité, et 2) un échantillon de proximité de 980 personnes recrutées auprès de services cliniques ou d'organisations de patients en obésité partout au Canada. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 64,6 % des personnes atteintes d'obésité se sentaient à l'aise de recevoir un vaccin alors que 35,4 % hésitaient. • Les personnes étaient moins à l'aise avec le fait que leurs enfants se fassent vacciner (58,5 % étaient à l'aise alors que 41,6 % hésitaient, P < 0,001). • Le score moyen sur la sous-échelle de la confiance dans l'échelle de l'hésitation à se faire vacciner était considérablement inférieur à toute autre mesure (moyenne = 2,26). • La peur de la COVID-19 était un prédicteur des attitudes à l'égard du vaccin pour toutes les mesures dépendantes. • On a établi un lien positif entre le degré d'acceptation du vaccin et le sexe masculin, le fait d'avoir un plus grand nombre de comorbidités, des niveaux de dépression plus faibles, le fait de ne pas pratiquer la distanciation sociale et le fait d'avoir déjà reçu un vaccin contre la grippe.
AUSTRALIE ET NOUVELLE-ZELANDE		
Horizon Research (2021) *non publiée* (15, 195, 232) Étude longitudinale Nouvelle-Zélande Mars – Mai 2021	Une enquête en ligne a été menée auprès des adultes (16 ans et plus) pour mesurer le taux d'utilisation du vaccin. Mar-Avr, n=1,350 Avr-Mai, n=1,387 Mai, n=1,234 *nouvelle* Sujets des questions : 1) Prise du vaccin Outils d'enquête disponibles? Oui	**Mai** • 13 % des personnes interrogées qui se sont identifiées comme handicapées ou souffrant de maladies chroniques ont déclaré qu'il était peu probable qu'elles se fassent vacciner. • Parmi les raisons de ne pas se faire vacciner, on trouve des préoccupations liées à l'innocuité (49 %), la conviction qu'un vaccin n'est pas nécessaire (21 %) et une méfiance envers les vaccins en général (18 %). **Avril-mai** • 77 % des personnes vivant avec des déficiences ou des problèmes de santé à long terme étaient susceptibles d'accepter un vaccin ou avaient été

	Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	vaccinées alors que 5 % des personnes ont déclaré qu'elles ne se feraient certainement pas vacciner. • 70 % des personnes qui se sont dites invalides étaient susceptibles d'accepter de se faire vacciner ou avaient été vaccinées alors que 5 % d'entre elles ont dit qu'elles ne se feraient certainement pas vacciner.
Australia Bureau of Statistics (2021) *non publiée* (141) *nouvelle* Étude longitudinale Australie Apr 2020-May 2021	L'enquête sur les répercussions sur les ménages est une enquête mensuelle qui recueille des données en ligne et par téléphone auprès d'un groupe d'adultes (18 ans et plus) sur des sujets liés à la COVID-19, y compris les attitudes à l'égard des vaccins. Mai: n=3,371 Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Les personnes handicapées ou souffrant d'un problème de santé de longue durée étaient légèrement plus susceptibles d'avoir l'intention de se faire vacciner que les autres (68,6 % pour les personnes handicapées contre 68,1 % pour les personnes non handicapées et 70,1 % pour les personnes souffrant d'un problème de santé de longue durée contre 66,5 % pour les personnes sans problème de santé de longue durée). • Le facteur principal de la décision de se faire vacciner est une recommandation de leur médecin généraliste (33,7 % et 31,0 % respectivement pour l'invalidité et les maladies chroniques). • Les inquiétudes concernant les effets secondaires ont dominé les raisons de ne pas vouloir se faire vacciner (62,7 % pour les personnes handicapées et 62,1 % pour les personnes souffrant de maladies chroniques).
Bonner (2020) *préimpression* (152) Étude longitudinale Australie	Les personnes qui ont dit souffrir d'hypertension (n = 466) ont été comparées à des témoins sains (n = 466) pendant le confinement afin de déterminer si elles ont des perceptions du risque plus élevé et souffrent d'anxiété, ainsi que pour connaître leurs intentions en matière de prévention. Un sondage en ligne a été utilisé pour évaluer	• Au départ, 87 % des personnes souffrant d'hypertension et 85 % des témoins sains ont déclaré qu'ils recevraient le vaccin contre la COVID-19. • Il n'y avait pas de différences significatives dans la volonté de se faire vacciner contre la COVID-19 entre les personnes souffrant d'hypertension et les témoins sains.

Avril et juin 2020	l'intention de se faire vacciner pendant le confinement, puis de nouveau, deux mois après l'assouplissement des restrictions. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Malgré une diminution de la gravité perçue et de l'anxiété deux mois après la levée des restrictions après le confinement, l'intention de se faire vacciner contre la COVID-19 était toujours ferme (plus de 80 %) au moment du suivi.
ÉTATS-UNIS		
Ricotta (2021) *préimpression* (153) Étude transversale ÉTATS-UNIS Février 2021	Afin d'évaluer l'acceptation du vaccin chez les personnes atteintes de maladies respiratoires chroniques ou de maladies auto-immunes, un sondage en ligne a été mené auprès de 1 232 personnes ayant une maladie respiratoire chronique ou auto-immune autodéclarée et de 1 303 témoins sains aux États-Unis. Sujets des questions : 3) Intentions en ce qui concerne les vaccins 4) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• Comparativement aux témoins en santé, les personnes qui ont dit être atteintes de maladies respiratoires chroniques étaient 5,7 % plus disposées à se faire vacciner (IC à 95 % : 0,05 à 0,09). • Lorsqu'on leur a demandé pourquoi elles avaient l'intention de se faire vacciner, les personnes atteintes de maladies respiratoires chroniques (RC = 1,08, IC à 95 % : 1,03 à 1,13) et de maladies auto-immunes (RC = 1,06, IC à 95 % : 1,01 à 1,11) étaient plus susceptibles de se faire vacciner pour se protéger contre la COVID-19 que le groupe-témoin. Les personnes atteintes de maladies respiratoires chroniques étaient également plus susceptibles de vouloir retourner au travail en toute sécurité (RC = 1,08, IC : 1,03 à 1,14). • Parmi celles qui n'ont pas l'intention de se faire vacciner, les personnes atteintes de maladies auto-immunes étaient le seul groupe à avoir une association significative avec une cause particulière d'hésitation. En fait, elles étaient plus susceptibles de dire que la crainte d'une mauvaise réaction au

		vaccin était la raison de leur hésitation (RC = 1,22, IC à 95 % : 1,06 à 1,41).
Garcia (2021) (156) Étude transversale États-Unis Janvier et février 2021	Un sondage en ligne a été mené dans 150 centres de dialyse choisis au hasard aux États-Unis afin d'évaluer les intentions en ce qui concerne la vaccination et la réticence des 1 515 patients en hémodialyse. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 20 % des patients hésitaient à accepter un vaccin même s'il était considéré sans danger pour la population en général. Si le vaccin était offert au centre de dialyse, cette hésitation diminuait à 18 %. • La réticence à se faire vacciner était la plus élevée chez les patients de 18 à 44 ans (RCa 1,5, IC à 95 %, 1,0 à 2,3), les femmes (RCa 1,6, IC à 95 %, 1,2 à 2,0), les patients noirs (RCa 1,9, IC à 95 %, 1,3 à 2,7) et les patients qui s'identifiaient comme étant d'autres races ou ethnies (RCa 2,0, IC à 95 %, 1,1 à 3,7). • La réticence à se faire vacciner était plus faible chez les patients de 80 ans et plus (RCa 0,4, IC à 95 % : 0,3 à 0,7), chez ceux qui avaient fait certaines études collégiales (RCa 0,4, IC à 95 % : 0,2 à 0,6) et chez ceux qui avaient reçu le vaccin contre la grippe (RCa 0,2, IC à 95 % : 0,1 à 0,3). • 53 % des personnes hésitant à se faire vacciner se sont dites préoccupées par les effets secondaires.
Tsai (2021) *préimpression* (160) Étude transversale É.-U. Janvier à février 2021	Une enquête internationale en ligne a été menée pour mesurer l'hésitation à se faire vacciner chez 21 943 personnes présentant des conditions à risque élevé telles que le cancer, les maladies auto-immunes et d'autres conditions de comorbidités. 74 % des participants étaient originaires des États-Unis et 4 % du Canada. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner	• 25 % des personnes interrogées avaient reçu au moins un vaccin, tandis que 7 % avaient essayé de se faire vacciner sans y parvenir. • 43 % prévoient de se faire vacciner, 5 % le feront probablement, 5 % sont incertains, 4 % ne se feront probablement pas vacciner et 10 % ne l'accepteront certainement pas. • En fonction des conditions, les fumeurs actuels étaient les plus hésitants (29 %), suivis des personnes souffrant d'obésité (20 %), de diabète de type 2 (19 %), d'hypertension (18 %) et de maladies pulmonaires chroniques (18 %). • Les personnes ayant subi un traitement anticancéreux dans le passé étaient plus hésitantes que celles qui subissent actuellement un traitement anticancéreux (13 % contre 11 %).

	Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• L'hésitation à se faire vacciner était associée à un âge plus jeune, au sexe féminin, à l'appartenance ethnique des Noirs-Pacifiques-Islandais-Amérindiens, à un faible niveau d'éducation, à des tendances politiques conservatrices, à une résistance aux masques ou aux vaccinations de routine contre la grippe et à une méfiance à l'égard de la couverture médiatique. • Ceux qui ont répondu avec un certain niveau d'hésitation ont indiqué que le vaccin était trop nouveau (53 %), qu'ils s'inquiétaient des effets secondaires ou de l'inconfort (44 %), qu'ils avaient le sentiment que le processus avait été impliqué dans la politique (39 %) et qu'ils voulaient attendre que d'autres l'aient pris (33 %). • 21 % ont déclaré ne pas faire confiance aux vaccins en général, mais étaient plus négatifs à l'égard du vaccin COVID-19 en particulier (40 %).
Iadarola (2021) *préimpression* (157) Étude transversale ÉTATS-UNIS Janvier et février 2021	L'intention de se faire vacciner a été évaluée dans un sondage en ligne effectué auprès de 825 personnes ayant des déficiences intellectuelles et développementales, ainsi que des membres de leur famille et du personnel soignant dans l'État de New York. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 62 % des répondants ont dit qu'ils se feraient certainement ou probablement vacciner contre la COVID-19 alors que 13,9 % avaient déjà reçu le vaccin. • L'hésitation à se faire vacciner était plus grande chez les personnes plus jeunes et celles qui prenaient des décisions au nom d'une personne atteinte de la maladie. • Les répondants noirs de plus de 50 ans étaient plus susceptibles d'avoir l'intention de se faire vacciner ou d'avoir déjà reçu un vaccin comparativement aux répondants plus jeunes (RC = 3,72, IC à 95 % : 1,73 à 8,00) et aux répondants blancs âgés de plus de 50 ans (RC = 2,39, IC à 95 % : 1,36 à 4,17). • Les motifs d'hésitation les plus courants étaient les préoccupations au sujet des effets secondaires (16 %), la croyance que le vaccin était trop nouveau (15 %), le désir de ne pas être un

		« cobaye » du vaccin (14 %) et la méfiance à l'égard du gouvernement (14 %). • Les répondants hispaniques et noirs (96 % et 91 % respectivement) se sont dits plus souvent préoccupés par le fait d'être utilisés comme « cobayes » que les répondants blancs ou asiatiques (76 % et 67 % respectivement). • Les professionnels de la santé (92 %) étaient la source la plus fiable d'information sur le vaccin, suivis des amis et de la famille (74 %).
McCabe (2021) *préimpression* (166) Étude transversale É.-U. Décembre 2020 à février 2021	Une enquête nationale distribuée par voie électronique a été menée auprès de 34 470 travailleurs de la santé et d'adultes de la population générale afin de mesurer l'intention de recevoir un vaccin et les facteurs liés à l'acceptation et au refus. Le nombre de travailleurs de la santé n'a pas été indiqué. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Oui	• Les personnes présentant trois pathologies préexistantes ou plus étaient 1,19 fois plus susceptibles que les autres d'hésiter à se faire vacciner (RR ajusté 1,19, IC 95 %) : 1,06 % à 1,34, P = 0,004 5).
Xiang (2021) (162) *nouveau* Enquête transversale	Un sondage en ligne a été mené auprès de 401 patients atteints de sclérose en plaques aux États-Unis (la majorité dans l'Oregon, l'État de Washington et la Californie) afin d'évaluer les intentions de se faire vacciner.	• 70,1 % étaient prêts à se faire vacciner, 7,2 % ne le seraient pas et 22,7 % étaient incertains. • La plupart des répondants étaient motivés par la volonté de se protéger (77,6 %) ou de protéger leurs proches (58,7 %), et de réduire les risques de maladie grave (53,4 %).

É.-U. Déc. 2020-janv. 2021	Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner 3) Perception des vaccins Outils de sondage disponibles? Oui Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• Parmi les personnes qui ont l'intention de refuser un vaccin, les principales raisons sont l'inquiétude quant aux effets secondaires potentiels (55,2 %), la rapidité du développement du vaccin (55,2 %) et le désir d'obtenir davantage de preuves d'innocuité en raison du développement précipité (44,8 %). • Les répondants indécis ont exprimé le désir d'obtenir des renseignements sur la sécurité de la population (57,1 %). Les indécis croyaient également que les pressions politiques influaient sur les essais de vaccins (37,4 %) et souhaitaient que les personnes non atteintes de SP reçoivent le vaccin en raison de problèmes d'innocuité (29,7 %). • L'analyse multivariée a révélé que l'intention de se faire vacciner était plus élevée chez les personnes qui avaient parlé ou prévoyaient de parler du vaccin à leur médecin spécialiste de la SP (RCa 2,93, IC à 95 % : de 1,32 à 6,49 et 2,57, IC à 95 % : de 1,38 à 4,80, respectivement), une vaccination antérieure contre la grippe (la plupart des années RCa 5,59, IC à 95 % : de 2,44 à 12,77 et chaque année RCa 8,96, IC à 95 % : de 4,39 à 18,31), tout niveau d'inquiétude concernant la COVID-19, tout niveau d'inquiétude concernant leur risque d'hospitalisation ou de décès, et le fait de ne pas pouvoir socialiser en public, mais à la maison (RCa 14,07, IC à 95 % : de 1,43 à 138,33) ou de n'avoir que des relations sociales virtuelles (RCa 17,53, IC à 95 % : de 1,80 à 170,60).
Kelkar (2021) (154) Étude avant/après États-Unis	Cette étude visait à déterminer si un webinaire améliorerait les connaissances sur les vaccins contre la COVID-19 et aurait une incidence sur l'intention de se faire vacciner. 264 personnes atteintes de cancer ou leurs soignants en Floride ont participé au webinaire, puis se sont inscrits pour répondre à au moins un sondage en ligne	• Avant le webinaire, 71 % des personnes avaient l'intention de se faire vacciner, 5 % ont précisé qu'elles ne se feraient pas vacciner et 24 % étaient incertaines. • 97 personnes sur 105 ont répondu à la question précise portant sur l'intention en ce qui concerne la vaccination dans les sondages avant et après le webinaire. Après le webinaire, 82,5 % des personnes avaient l'intention de se faire vacciner,

Décembre 2020 à janvier 2021	(avant et après le webinaire). De ce nombre, 105 ont répondu aux deux sondages. Sujets des questions : 4) Intentions en ce qui concerne la vaccination 5) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	2,1 % ont précisé qu'elles ne se feraient pas vacciner et 15,5 % étaient incertaines. • Les raisons les plus courantes pour hésiter à se faire vacciner étaient les préoccupations au sujet des effets secondaires du vaccin (30 %), le manque d'information sur l'efficacité du vaccin (14 %) et le manque de confiance quant à l'innocuité du vaccin pour les patients atteints de cancer (8 %).
Dalal (2021) (149) Étude transversale ÉTATS-UNIS Décembre 2020 à janvier 2021	Un sondage en ligne a été effectué auprès de 906 adultes atteints d'une maladie du côlon irritable dans un hôpital de Boston ou dans les médias sociaux associés au côlon irritable avant d'évaluer leurs intentions de se faire vacciner et de cerner les préoccupations possibles. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• L'intention de se faire vacciner était élevée chez les répondants recrutés localement (80,9 %) comparativement à 60,0 % de ceux recrutés sur les médias sociaux. • Les motifs de réticence les plus courants dans les deux groupes comprenaient les inquiétudes au sujet des effets à long terme et des effets indésirables, le désir de voir comment les autres tolèrent le vaccin, l'inquiétude que le vaccin n'ait pas fait l'objet de vérifications d'innocuité régulières, l'inquiétude associée au fait que le vaccin nuise à l'efficacité des médicaments contre le côlon irritable et des antécédents personnels de réactions allergiques. • Une recommandation d'un de leurs fournisseurs de soins de santé en lien avec le côlon irritable a été jugée être un élément important, tant chez les répondants acquis localement (92 %) que dans les médias sociaux (80,6 %). • De leur fournisseur de soins, les répondants voulaient notamment en savoir plus sur les risques et les avantages, recevoir des documents écrits, obtenir de l'information sur l'innocuité et

		l'efficacité des médicaments contre le côlon irritable et d'autres maladies auto-immunes. • On a établi un lien positif entre l'intention de se faire vacciner et l'âge (RC = 2,21, IC à 95 % : 1,07 à 4,54), le fait d'être titulaire d'un baccalauréat ou d'un autre diplôme d'études supérieures (RC = 3,31, IC à 95 % : 1,36 à 8,06), d'être blanc (RC = 2,13, IC à 95 % : 1,17 à 3,85), d'avoir eu la COVID-19 (RC = 2,02, IC à 95 % : 1,09 à 3,73) ou de prendre actuellement un produit biochimique (RC = 1,52 IC à 95 % : 1,07 à 2,16).
Serper (2021) (159) Étude transversale É.-U. Décembre 2020	Pour évaluer les attitudes et les intentions concernant les vaccins contre la COVID-19, une enquête en ligne a été menée auprès de 1 215 patients soignés pour des affections gastro-intestinales et hépatiques chroniques (syndrome du côlon irritable, cirrhose ou transplantation hépatique) au sein d'un grand système de santé du sud-est de la Pennsylvanie. Sujets des questions : 1) Intentions de se faire vacciner 2) Attitudes à l'égard des vaccins 3) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• 85 % étaient tout à fait ou plutôt d'accord avec le fait qu'ils se feraient vacciner si le vaccin était disponible, 7 % étaient neutres et 8 % étaient tout à fait ou plutôt en désaccord. • Les préoccupations signalées à l'égard des vaccins comprenaient la sécurité (54 %), l'efficacité (26,7 %), le fait de ne pas être prioritaire pour le vaccin (39 %), le coût (17,4 %) et les inconvénients (10,3 %). • Les personnes interrogées étaient plus susceptibles d'accepter un vaccin contre la COVID-19 dans un cabinet médical ou une pharmacie, par rapport aux sites avec service au volant, aux lieux de travail ou aux sites communautaires (par exemple, église, école). • Plus de 75 % suivraient la recommandation de leur gouvernement ou de leur médecin concernant le vaccin contre la COVID-19, 91 % suivraient la recommandation de leur gastro-entérologue ou de leur spécialiste du foie et 56 % suivraient la recommandation de leur employeur. • Femmes (RR ajusté 2,02, IC 95 % : 1,40 % à 2,92 %, P < 0,001) et ceux dont les revenus sont plus faibles (RR ajusté 2,17, IC 95 % : 1,26 % à 3,74 %, P = 0,005) étaient plus susceptibles d'hésiter à se faire vacciner et les personnes âgées de 65 ans et plus (RR ajusté 0,52, IC 95 % : 0,30 % à 0,92 %, P =

		0,024) et avec la réception préalable d'un vaccin annuel contre la grippe (RR ajusté 0,11, IC 95 % : 0,07 % à 0,10 %, p < 0,000 1) étaient moins hésitants.
Ou (2021) (165) *nouveau* Étude transversale É.-U. Nov.-déc. 2020	Les attitudes envers un éventuel vaccin contre la COVID-19 ont été évaluées chez 1 308 transplantés d'organes solides (TOS) et 1 617 non-transplantés d'organes solides par l'intermédiaire d'un sondage en ligne. Sujets des questions : 1) Intentions de se faire vacciner 2) Attitudes envers les vaccins Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Oui Sondage prétesté? Oui	• 50,5 % des TOS et 60,7 % des non-TOS avaient l'intention de se faire vacciner. • 49,5 % des TOS et 39,3 % des non-TOS n'avaient pas l'intention de se faire vacciner. • Chez les TOS, les personnes peu enclines ou réticentes étaient plus susceptibles d'être âgées de 30 à 49 ans, d'être des femmes, d'être de race noire, de ne pas résider aux États-Unis, d'avoir un diplôme d'études secondaires ou moins, de ne pas être mariées, d'avoir un revenu familial inférieur à 30 000 dollars, de ne pas avoir été vaccinées contre la grippe au cours de l'année écoulée, de ne pas prévoir de se faire vacciner contre la grippe cette année, de penser que les patients transplantés courent un plus grand risque de contracter une maladie à cause du vaccin, de penser que le vaccin contre la COVID-19 pourrait entraîner un rejet et de ne pas croire que les vaccins sont sûrs pour les patients transplantés. • 80,0 % des TOS ont déclaré avoir besoin d'information de la part de leur médecin ou d'une assurance que leur santé personnelle soit compatible avec le vaccin (75,4 %). Ils étaient 86,8 % à être recommandés par leur chirurgien transplanteur, 71,9 % par un autre membre de l'équipe de transplantation et 64,1 % par leur médecin traitant. • Les TOS étaient plus susceptibles de percevoir le vaccin comme nécessaire et que les vaccins fonctionnent, d'exprimer leur niveau de confort envers les vaccins, de ne pas craindre les vaccins, de faire confiance aux entreprises pharmaceutiques, aux CDC et aux vaccins en général, par rapport aux non-TOS.

		• Les non-TOS qui vivent avec un TOS sont moins nombreux que ceux qui ne vivent pas avec un TOS à déclarer avoir l'intention de se faire vacciner (57,6 % contre 61,3 %). Cela restait vrai si le vaccin était recommandé par un médecin (73,9 % contre 76,7 %), mais pas s'ils estimaient que les TOS devaient se faire vacciner (52,2 % contre 52,0 %). • L'annonce de l'efficacité de Moderna a légèrement augmenté l'intention de se faire vacciner, de 53,5 % à 57,8 % après l'annonce.
Rodriguez (2021) (238) *nouveau* Étude transversale É.-U. Mai-déc. 2020	Un échantillon de 175 personnes séropositives âgées de plus de 18 ans a été interrogé en ligne afin de valider l'échelle de réticence à se faire vacciner (ERV), dans le but de comprendre les attitudes envers le vaccin contre la COVID-19 et la volonté de se faire vacciner. Sujets des questions : 1) Intentions de se faire vacciner 2) Attitudes envers les vaccins 3) Réticence à se faire vacciner Outils de sondage disponibles? Oui Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• Le manque de confiance et les risques expliquent respectivement 45,55 % et 12,31 % de la variance des réponses quant à la réticence à se faire vacciner. • Les réponses moyennes révèlent que les niveaux de réticence à se faire vacciner sont plus élevés chez les personnes qui ne croient pas à l'efficacité du vaccin, chez celles qui ne se laisseraient pas influencer par la recommandation d'un professionnel de la santé, chez celles qui ne pensent pas qu'il soit important de se faire vacciner en raison de leur état de santé et qui ne se feraient pas vacciner si cela était nécessaire pour reprendre une vie normale. • Les niveaux moyens de réticence à se faire vacciner étaient plus faibles chez les personnes qui ne pensaient pas que leur état de santé serait aggravé par le vaccin.
Jones (2021) (239) Étude transversale États-Unis	Un sondage en ligne effectué auprès de 94 adultes (âgés de 18 ans et plus) vivant avec le VIH à Miami, en Floride, appartenant à des groupes ethnoraciaux sous-représentés afin d'évaluer l'intention de se faire vacciner et les facteurs associés à la réticence. Les participants étaient des Noirs non	• Comparativement aux Latinx non noirs, les participants noirs non latins étaient moins susceptibles de dire que les vaccins sont importants pour leur santé (92 % comparativement à 68 %, P = 0,009), de croire que les vaccins sont efficaces pour prévenir les maladies (84 % comparativement à 68 % P = 0,029) et de croire que l'information sur le vaccin est fiable et

Août à novembre 2020	latinx (60 %) et des Latinx non noirs (40 %). Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination 3) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Non	digne de foi (71 % comparativement à 36 %, P = 0,002). • L'intention de se faire vacciner a été associée positivement à la croyance selon laquelle les vaccins sont importants (RC 12,0, IC à 95 % : 3,22 à 44,8, P < 0,001) et efficaces (RC 5,71, IC à 95 % : 1,78 à 14,59, P = 0,001), au fait de reconnaître que l'information sur les vaccins est fiable et digne de confiance (RC 6,76, IC à 95 % : 2,71 à 16,88, P = 0,001), au fait de croire qu'ils devraient se conformer aux ordonnances du médecin (RC 5,28, IC à 95 % : 1,57 à 17,71, P = 0,001) et de croire qu'un vaccin est le meilleur moyen de se protéger contre la maladie (RC 7,07, IC à 95 % : 2,14 à 23,42, P < 0,001).
Bogart (2020) (158) Étude transversale ÉTATS-UNIS Mai à juillet 2020	101 personnes noires vivant avec le VIH ont été interrogées par téléphone afin d'évaluer les liens entre la méfiance médicale, les intentions quant à la vaccination et l'hésitation face à la vaccination. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Les croyances les plus courantes au sujet du vaccin contre la COVID-19 étaient que le vaccin serait nocif (51 %), qu'ils n'y feraient pas confiance (34 %) et qu'ils ne voudraient pas se faire vacciner (32 %). • L'analyse multivariée a révélé qu'une plus grande méfiance liée à la COVID-19 était fortement associée à l'hésitation à se faire vacciner [b (SE) = 0,85 (0,14), P < 0,000]). • Les corrélations de Pearson indiquaient que les participants n'ayant pas terminé leurs études secondaires présentaient des niveaux plus élevés d'hésitation à se faire vacciner (r = 0,20, P = 0,04).
Ehde (2021) (148)	Un sondage en ligne a été utilisé pour évaluer les facteurs associés à l'intention de recevoir ou non un vaccin contre la COVID-19 chez	• 66,0 % des participants étaient disposés à se faire vacciner lorsque le vaccin sera disponible, 18,5 % étaient moyennement disposés à le recevoir et 15,5 % n'en voulaient pas.

Étude transversale ÉTATS-UNIS Avril et mai 2020	486 adultes (âgés de 18 ans et plus) atteints de sclérose en plaques. Sujets des questions : 4) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• Les prédicteurs statistiquement significatifs d'une volonté accrue de se faire vacciner comprennent l'enseignement supérieur (β = 0,20, P < 0,001) et la perception d'être plus à risque de contracter la COVID-19 (β = 0,18, P = 0,001). • Les participants étaient d'avis que les fournisseurs de soins de santé et la société de la sclérose en plaques avaient la plus grande fiabilité perçue pour l'information sur la COVID-19. La fiabilité perçue des sources d'information était fortement associée à l'intention de se faire vacciner.
Rungkitwattanakul (2021) (155) Étude transversale ÉTATS-UNIS Date n.d.	Pour évaluer les intentions en matière de vaccination, on a effectué un sondage en ligne auprès de 90 patients dans un centre de dialyse urbain de Washington DC. qui dessert une population de patients principalement afro-américains. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 49 % des répondants ont indiqué qu'ils seraient disposés à recevoir un vaccin contre la COVID 19, 34 % n'étaient pas disposés à le recevoir et 17 % étaient incertains. • L'intention de se faire vacciner contre la COVID-19 était associée au fait d'avoir déjà reçu le antigrippal P < 0,001. • Les raisons les plus courantes de l'hésitation à se faire vacciner étaient le manque d'information adéquate sur l'innocuité et l'efficacité (46,8 %), le manque de confiance envers le gouvernement fédéral (36,4 %) et le manque de confiance envers les fabricants de vaccins (28,9 %).
ROYAUME-UNI		
Office for National Statistics (2021) & Office of National Statistics (2021)	Les réponses provenant de quatre vagues de résultats recueillis dans le cadre du sondage en ligne Opinions and Lifestyle Survey (167) ont été mises en commun pour mettre l'accent sur les associations	**Mars avril** • Les adultes handicapés avaient un peu moins d'hésitation à se faire vacciner que les adultes non handicapés (5 % contre 7 %). L'hésitation a diminué depuis le dernier rapport (8 % et 9 % respectivement).

non publiée (43, 140) Étude longitudinale Royaume-Uni Fev-Avr 2021	démographiques spécifiques et la réticence à se faire vacciner. Le nombre de personnes handicapées, de personnes extrêmement vulnérables sur le plan clinique et de parents n'a pas été déclaré. Fév.-Mar: 17 201 réponses ont été mises en commun Mar-Avr: 16 362 réponses ont été mises en commun Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• Les répondants cliniquement extrêmement vulnérables (RCE) ont eu beaucoup moins d'hésitation que les répondants non RCE (4 % contre 7 %). • Les répondants non RCE sont nettement plus nombreux à déclarer qu'il est probable qu'ils se fassent vacciner (31 %), alors que moins de 1 % des RCV ne le feront probablement pas. **Fév. à mars** • Les adultes handicapés étaient un peu moins réticents à se faire vacciner que les adultes non handicapés (8 % comparativement à 9 %). • Les motifs d'hésitation les plus courants chez les adultes handicapés étaient les préoccupations au sujet des problèmes de santé existants (48 %), suivies des préoccupations au sujet des effets secondaires (46 %) et de l'attente de voir si le vaccin fonctionne (43 %). • Les répondants extrêmement vulnérables sur le plan clinique avaient beaucoup moins d'hésitation que les autres répondants (4 % contre 9 %). • Les motifs d'hésitation les plus courants chez ces adultes extrêmement vulnérables étaient les préoccupations au sujet des effets secondaires (49 %), suivies des inquiétudes au sujet des effets à long terme (47 %) et des préoccupations au sujet des problèmes de santé existants (42 %). • Les répondants qui avaient des problèmes de santé sous-jacents étaient moins hésitants que ceux qui n'en avaient pas (6 % comparativement à 10 %). • Les préoccupations au sujet des effets à long terme (42 %), suivies des préoccupations au sujet des effets secondaires (37 %) et des effets sur les problèmes de santé existants (34 %) sont les raisons les plus courantes d'hésitation chez les personnes ayant des problèmes de santé sous-jacents.

Saunders (2021) (163) *nouvelle* Étude transversale Royaume-Uni Mars 2021	Les intentions de se faire vacciner et les attitudes à l'égard des risques associés à la COVID-19 ont été mesurées en ligne chez 964 personnes atteintes d'une néoplasie myéloprolifératives chronique (NMP). Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 91,5 % des répondants ont déclaré avoir été vaccinés (93,5 % d'entre eux ont reçu la première dose seulement). • 0,03 % (29 sur 964) avaient réservé leur rendez-vous pour la première dose, 0,05 % (53 sur 964) n'avaient pas pris de rendez-vous pour une dose et de ces personnes, 14 s'étaient vues offrir une dose de vaccin alors qu'aucune dose n'avait été offerte aux 38 autres. • 0,8 % (n = 8) ont refusé la vaccination pour des raisons comme les effets secondaires (n = 5), la mise au point rapide du vaccin (n = 4), l'innocuité (n = 3) et l'efficacité perçue en raison de la NMP (n = 2). Les réponses en texte libre mentionnaient un stress immunitaire possible en tenant compte de l'infection antérieure à la COVID-19, le fait que les dispensateurs de médecines douces ne l'aient pas recommandé et d'autres voulaient en discuter avec leur oncologue. • 16,7 % des personnes vaccinées ont exprimé des préoccupations au sujet de la vaccination en raison d'une réaction grave possible (30,6 %), de l'efficacité chez les patients atteints de NMP (15,4 %), de l'interférence du vaccin avec leur NMP (14,3 %) ou avec les médicaments qu'elles prennent pour leur NMP (10,2 %). • 82,9 % des répondants vaccinés n'avaient aucune préférence générale pour le vaccin, 65,2 % préféraient Pfizer, 30,4 % AstraZeneca, 2,9 % Moderna et 1,4 % un autre vaccin. • 89,0 % des répondants faisaient confiance à leur fournisseur de soins de santé pour les informer des risques et des avantages. • Pour les 97 répondants qui ont dit ne pas faire confiance à leur fournisseur de soins de santé, la principale raison est qu'ils ne connaissaient pas suffisamment le vaccin (34,0 %), les avantages (30,0 %) ou la connaissance de la NMP ou des

		vaccins chez les patients atteints de NMP (12,0 %) et la méfiance à l'égard de leur médecin principal.
Bateman (2021) (240) *nouveau* Étude quasi expérimentale R.-U. Déc. 2020	Une vidéo éducative de huit minutes a été envoyée par message texte à une cohorte de 661 patients en rhumatologie afin de mesurer l'incidence de la vidéo sur l'intention de se faire vacciner. Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• Sur les 8 886 patients ayant reçu le message texte avec le lien vidéo, 2 358 ont visionné la vidéo (27 %) et 661 ont répondu à l'évaluation. • Avant la vidéo, 36 % des patients âgés de 30 à 49 ans, 47 % de ceux âgés de 50 à 69 ans et 52 % de ceux âgés de 70 ans et plus ont déclaré qu'ils connaissaient les vaccins contre la COVID-19 et qu'ils leur étaient recommandés. Après le visionnement de la vidéo, ce pourcentage est passé à 88 %, à 92 % et à 94 % pour ces catégories d'âge respectives. • Sur une échelle de 1 (pas du tout d'accord) à 5 (tout à fait d'accord), les personnes interrogées se sont senties mieux informées (moyenne = 4,1), plus confiantes pour se faire vacciner (moyenne = 4,2), ont déclaré qu'elles se feraient vacciner (moyenne = 4,1) et que la vidéo était utile pour transmettre l'information (moyenne = 4,4). • Les patients plus âgés (50+) étaient plus susceptibles de déclarer qu'ils avaient appris davantage, qu'ils se sentaient plus confiants et qu'ils étaient plus enclins à se faire vacciner que ceux âgés de 30 à 49 ans.
ETATS-UNIS ET ROYAUME-UNI		
Felten (2021) (161) Étude transversale 56 pays Décembre 2020	L'intention de se faire vacciner et la réticence à se faire vacciner ont été évaluées chez 1 258 patients atteints d'une maladie auto-immune ou d'une maladie rhumatismale inflammatoire à l'aide d'un sondage en ligne auquel ont répondu 327 personnes au Royaume-Uni et 114 personnes aux États-Unis. Sujets des questions :	• Parmi les personnes atteintes d'une maladie auto-immune ou d'une maladie rhumatismale inflammatoire au Royaume-Uni, 39,4 % étaient prêtes à accepter de se faire vacciner, 31,3 % hésitaient et 10,5 % étaient méfiantes. • Aux États-Unis, 15,6 % d'entre elles étaient prêts à accepter un vaccin, 9,2 % étaient hésitantes et 5,9 % étaient méfiantes. • Les patients atteints d'une maladie auto-immune ou d'une maladie rhumatismale inflammatoire qui se méfiaient du vaccin étaient beaucoup plus préoccupées par la vaccination en général, pensaient qu'il était moins important de se faire

	1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Non	vacciner, s'inquiétaient de l'utilisation d'une nouvelle technologie dans le vaccin, du manque de recul concernant la vaccination contre la COVID, et les liens financiers potentiels entre les gouvernements et les sociétés pharmaceutiques. • Les personnes hésitantes ou suspectes craignaient beaucoup plus que le vaccin ne provoque une flambée de leur maladie. • Les hommes étaient plus susceptibles d'avoir l'intention de se faire vacciner que les femmes (P < 0,0001) et les personnes plus jeunes étaient moins susceptibles de le faire que les personnes plus âgées (P < 0,0001).

AUTRES POPULATIONS D'INTÉRÊT

Tableau 7. Éléments de preuve sur les attitudes d'autres populations d'intérêt à l'égard des vaccins (n = 61)

ÉTUDE	MÉTHODES ET OUTILS D'ENQUÊTE	RÉSULTATS CLÉS RELATIFS AUX CONNAISSANCES, ATTITUDES ET COMPORTEMENTS
LGBTQ+		
CANADA		
Statistic Canada (2020) *non publiée* (78) Étude transversale Canada Septembre et octobre 2020	Un sondage téléphonique a été effectué auprès de 120 000 participants (âgés de 18 ans et plus) pour évaluer leur intention de se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 87,6 % des membres de la communauté LGBTQ2+ étaient prêts à accepter un vaccin, comparativement à 76,4 % des personnes non membres de cette communauté.

Ogilvie (2021) (79) Étude transversale Canada Août et septembre 2020	On a évalué l'intention de se faire vacciner chez 4 058 adultes et travailleurs de la santé de la Colombie-Britannique (âgés de 25 à 69 ans). Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• Les personnes non binaires, allosexuelles, agentes, bispirituelles ou autres étaient plus susceptibles de recevoir un vaccin (RC = 3,04, IC à 95 % : 1,08 à 8,55, P < 0,04).
Statistics Canada (2020) & Statistics Canada (2021) *non publiée* (65, 80) Étude longitudinale Canada Septembre à décembre 2020	Un sondage en ligne mené par Statistique Canada dans le cadre de l'Enquête sur la santé dans les collectivités canadiennes (ESCC) a évalué les comportements des Canadiens pour protéger leur propre santé et celle des autres. Une question sur les intentions de vaccination a été ajoutée au sondage de septembre. Le plus récent rapport fait état de 20 000 réponses reçues de personnes âgées de 12 ans et plus. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• Pendant la période d'échantillonnage, 77 % des personnes ont dit être prêtes à se faire vacciner. Cela représente une augmentation par rapport à septembre (75,5 %) à octobre (74,8 %) et à novembre-décembre (80,3 %). • Les membres de la communauté LGBTQ2+ étaient plus susceptibles de se faire vacciner (83,3 %).

ÉTATS-UNIS		
Bogart (2021) (170) *nouveau* Étude transversale É.-U. Nov.-déc. 2020	207 personnes de race noire ont été sélectionnées dans le groupe RAND American Life Panel (ALP) représentatif au niveau national et ont été interrogées en ligne afin d'évaluer les associations entre la méfiance envers la médecine, les intentions de se faire vacciner et la réticence à se faire vacciner. Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• Les minorités sexuelles ou de genre ne permettaient pas de prédire statistiquement une intention négative ou positive de se faire vacciner (intention positive P = 0,56 et intention négative P = 0,41).
Teixeira da Silva (2021) (167) Étude transversale ÉTATS-UNIS Octobre à décembre 2020	Un sondage en ligne effectué aux États-Unis a évalué l'acceptation des vaccins chez 1 350 personnes appartenant à des minorités sexuelles et de genre. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Sur une échelle de 10 points, 10 signifiant « très probable » et 1 « très improbable », l'intention de se faire vacciner était moyennement élevée (score moyen = 7, écart-type = 3,12). • Comparativement aux homosexuels, les participants regroupés dans la catégorie « Autre » identité sexuelle étaient moins susceptibles d'avoir l'intention de se faire vacciner (β = 1,102, P = 0,047). Il n'y avait pas d'autres différences selon l'identité sexuelle (bisexuelle, queer, identités multiples, amour du même sexe). • Comparativement aux participants blancs, les Noirs (β = 0,681, P < 0,001), les Amérindiens/Autochtones de l'Alaska (β = 2,482, P < 0,001) et les participants s'identifiant à une autre race (β = 1,174, P < 0,001) étaient plus disposés à vouloir se faire vacciner. Les participants asiatiques (β = 0,718, P = 0,018)

		étaient plus susceptibles d'avoir l'intention de se faire vacciner que les Blancs. • L'acceptation du vaccin a été associée négativement à davantage de préoccupations sociales concernant le vaccin (β = 0,10, p < 0,001) et de méfiance médicale (β = 0,06, p < 0,05) et associée positivement à des motivations altruistes (β = 0,60, p < 0,001).
Phillips (2021) (169) *nouveau* Étude transversale É.-U. Avril-août 2020	Les différences entre les minorités sexuelles/de genre et les personnes vivant avec le VIH dans l'adoption d'un vaccin contre la COVID-19 ont été mesurées par un sondage en ligne auprès de 932 adultes (plus de 18 ans). Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• 91.8 % envisageraient de se faire vacciner contre la COVID-19 et 8,2 % ne le feraient pas. • Les répondants bisexuels et pansexuels avaient une probabilité significativement plus élevée d'envisager un vaccin contre la COVID-19 (OR 1,69, IC à 95 % : de 1,01 à 2,82) par rapport aux répondants gais ou lesbiennes qui étaient de genre non-binaire (OR 4,38, IC à 95 % : de 1,33 à 14,4) par rapport aux répondants ayant une identité sexuelle masculine ou transgenre (OR 2,30 IC à 95 % : de 1,08 à 4,88) par rapport aux répondants non transgenres. • Les personnes séropositives étaient significativement moins susceptibles d'envisager de se faire vacciner contre la COVID-19 (OR 0,40, IC à 95 % : de 0,23 à 0,67) par rapport aux répondants séronégatifs.
Melin (2021) *préimpression* (168) Étude transversale ÉTATS-UNIS Juillet 2020	Un sondage en ligne a été utilisé pour évaluer les facteurs associés à l'intention de se faire vacciner contre la COVID-19 chez 1 016 adultes (âgés de 21 ans et plus) vivant à Porto Rico. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination	• Dans l'analyse bidirectionnelle, les identités sexuelles homosexuelle (81,8 %), bisexuelle (85,7 %) et autre (90,9 %) étaient toutes associées à une intention accrue de se faire vacciner comparativement à l'identité sexuelle hétérosexuelle (66,4 %), P < 0,001. • Après ajustement dans l'analyse de régression multivariée, cette relation n'était pas significative (homosexuel : RCa = 0,9, P = 0,72; bisexuel : RCa = 2,1, P = 0,08; autre identité sexuelle : RCa = 3,4, P = 0,25).

	Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	
PARENTS		
CANADA		
Gouvernement du Manitoba (2021) *Non publié* (11) *nouvelle* Étude longitudinale Canada Mai 2021	Un groupe de recherche en ligne composé de 600 Manitobains a été interrogé pour comprendre les attitudes envers le vaccin et les mesures incitatives possibles pour augmenter le taux de participation. Sujets des questions : 1) Intentions de se faire vacciner 2) Perception des vaccins Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• Dans un groupe de 70 parents ou tuteurs d'enfants âgés de 12 à 17 ans, 15 % sont incertains de faire vacciner leurs enfants et 13 % ne le feront pas. • Les parents qui n'avaient pas l'intention de faire vacciner leurs enfants faisaient partie de ménages dont le revenu était inférieur à 40 000 dollars, ne se feraient pas vacciner eux-mêmes et ne pensaient pas que les adultes devaient recevoir tous les vaccins habituels.
McKinnon (2021) *préimpression* (18) Étude transversale Canada Janvier à avril 2021	La volonté de faire vacciner les enfants selon leur niveau de scolarité, leur quartier et leur appartenance à une minorité visible a été évaluée lors d'un sondage en ligne effectué auprès de 380 parents ayant des enfants âgés de 2 à 17 ans à Montréal. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination	• 61 % des parents ont dit qu'il était très probable qu'ils fassent vacciner leur enfant, 25 % ont dit que c'était assez probable, 9,2 % ont dit qu'il était peu probable qu'ils le fassent alors que 4,5 % ont dit qu'il était très peu probable qu'ils fassent vacciner leur enfant. • Les préoccupations au sujet du manque d'information sur l'innocuité du vaccin et les effets secondaires possibles étaient la raison la plus courante de la réticence (48 %). • Si l'on compare les parents membres d'une minorité visible aux parents non membres d'une minorité visible, 30,3 % comparativement à 66,6 % d'entre eux étaient très susceptibles de

	Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	faire vacciner leurs enfants, 36,8 % comparativement à 23,9 % étaient plutôt susceptibles de le faire et 32,9 % comparativement à 9,5 %, respectivement, n'étaient pas susceptibles de faire vacciner leurs enfants.
Vallis (2021) (164) Étude transversale Canada Juin à octobre 2020	Les attitudes et les préoccupations à l'égard de la vaccination contre la COVID-19 chez les personnes en surpoids et atteintes d'obésité ont été évaluées par un sondage en ligne. Deux échantillons ont été utilisés : 1) un échantillon représentatif de 1 089 personnes en surpoids et atteintes d'obésité, et 2) un échantillon de proximité de 980 personnes recrutées auprès de services cliniques ou d'organisations de patients en obésité. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 64,6 % des personnes atteintes d'obésité se sentaient à l'aise de recevoir un vaccin alors que 35,4 % hésitaient. • Les personnes étaient moins à l'aise avec le fait que leurs enfants se fassent vacciner (58,5 % étaient à l'aise alors que 41,6 % hésitaient, $P < 0,001$).
Drouin (2021) *préimpression* (151) Étude transversale	L'intention des parents de faire vacciner leur enfant souffrant d'asthme contre la COVID-19 a été évaluée au moyen d'un sondage en ligne auprès de 305 parents. Sujets des questions :	• 63 % des parents étaient susceptibles de faire vacciner leur enfant, 19,1 % ont dit qu'il était peu probables qu'ils le fassent et 17 % étaient incertains. Pour eux-mêmes, 64 % des parents ont dit qu'ils se feraient probablement vacciner, 21 % ont dit que cela était peu probable et 15,1 % étaient incertains. Il y avait un lien étroit entre l'intention des parents de faire vacciner leurs

Canada Août 2020	1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	enfants et l'intention de la personne de se faire vacciner. • Les facteurs associés de façon importante à la décision d'un parent de faire vacciner son enfant comprenaient un niveau de scolarité plus élevé, un emploi, le sexe de l'enfant (femme), la présence d'autres maladies chroniques, la vaccination antérieure contre la grippe, l'anxiété parentale et la consultation d'un professionnel de la santé.
Lackner (2021) (189) Étude transversale Canada Mai et juin 2020	Les facteurs démographiques, expérientiels et psychologiques associés à la probabilité et à la rapidité prévues de recevoir un vaccin contre la COVID-19 ont été examinés dans 455 familles (857 enfants). Sujets des questions : 2) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• Les facteurs associés à une plus grande probabilité de faire vacciner les enfants comprennent l'âge plus avancé des parents, la vie dans les Prairies (comparativement au centre du Canada), des antécédents de vaccination plus complets pour les enfants et les parents, des attitudes positives à l'égard des vaccins en général, un plus grand évitement psychologique de la pandémie et une plus grande tendance à prioriser les risques de la maladie comparativement aux risques des effets secondaires. • Dans certains modèles, le risque perçu de COVID-19 et les niveaux plus élevés d'anxiété au pays étaient associés à une probabilité accrue de faire vacciner les enfants. • Les facteurs ci-dessus étaient également des prédicteurs de la vitesse plus rapide de la vaccination prévue. Toutefois, un statut socio-économique plus élevé était un prédicteur de tendance.
À L'ÉCHELLE MONDIALE		
Skjefte (2021) (135) Étude transversale 16 pays : Australie,	Un sondage en ligne a été utilisé pour évaluer le niveau d'acceptation de la vaccination contre la COVID-19 chez 5 294 femmes enceintes et 12 562 mères d'enfants de moins de 18 ans. Sujets des questions :	• 69,2 % de toutes les femmes avaient l'intention de faire vacciner leurs enfants. Les niveaux d'acceptation étaient supérieurs à 85 % en Inde, au Mexique, au Brésil et en Colombie et inférieurs à 52 % aux États-Unis, en Australie et en Russie. • Pour les mères, les raisons les plus courantes de refuser un vaccin étaient la crainte que l'approbation du vaccin soit précipitée pour des

Afrique, Argentine, Brésil, Chili, Colombie, Inde, Italie, Mexique, Nouvelle-Zélande, Pérou, Philippines, Russie, Espagne, Royaume-Uni, États-Unis. Octobre et novembre 2020	1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	raisons politiques (39,8 %), le manque de données sur l'innocuité et l'efficacité chez les enfants (32,7 %) et les préoccupations au sujet de l'innocuité et des effets secondaires (28,4 %).
UNITED KINGDOM		
Office for National Statistics (2021) & Office of National Statistics (2021) *non publiée* (43, 140) Étude transversale ROYAUME-UNI Février à avril 2021	Les réponses provenant de quatre vagues de résultats recueillis dans le cadre du sondage en ligne Opinions and Lifestyle Survey (130) ont été mises en commun pour mettre l'accent sur les associations démographiques spécifiques et la réticence à se faire vacciner. Le nombre de personnes handicapées ou extrêmement vulnérables au niveau clinique n'a pas été déclaré. Février et mars : 17 201 réponses ont été mises en commun Mars et avril : 16 362 réponses ont été mises en commun Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination	**Mars et avril** • L'hésitation à se faire vacciner est la plus forte chez les parents ayant des enfants de 0 à 4 ans (12 %) comparativement à 8 % chez les parents dont les enfants sont âgés de plus de 5 ans (8 %) et à 6 % chez les personnes qui ne vivent pas avec des enfants à charge. L'hésitation par rapport à la vaccination a diminué depuis le dernier sondage. • Chez les personnes ayant des enfants âgés de 0 à 4 ans, la réticence à se faire vacciner était plus prévalente chez les femmes que chez les hommes (16 % comparativement à 8 %). Ce nombre a cependant diminué depuis le dernier sondage. • Le sentiment positif à l'égard de la vaccination est le plus fort chez les parents qui ont des enfants de 0 à 4 ans (88 %) comparativement à 92 % chez ceux dont les enfants ont de plus de 5 ans et à 94 % chez les personnes qui ne vivent pas avec des enfants à charge. **Février et mars** • La principale raison pour hésiter portait sur les effets secondaires et cette préoccupation était la même pour les deux groupes de parents.

	Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	
Skirrow (2021) *préimpression* (19) Étude de prévalence et qualitative ROYAUME-UNI Août à octobre 2020	Un sondage en ligne et des entrevues semi-structurées ont été menés auprès d'un groupe de 1 181 femmes enceintes (âgées de 16 ans et plus) afin de déterminer leurs points de vue sur l'acceptabilité du vaccin contre la COVID-19 pour elles-mêmes lorsqu'elles sont enceintes ou non enceintes, ainsi que pour leur bébé. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• 81,2 % des femmes ont déclaré qu'elles accepteraient certainement un vaccin ou auraient tendance à le faire si elles n'étaient pas enceintes. L'acceptation du vaccin était beaucoup plus faible pendant la grossesse (62,1 %, P < 0,005), ainsi que pour leurs bébés (69,9 %, p < 0,005). • Comparativement aux femmes de race blanche, les femmes de minorités ethniques étaient deux fois plus susceptibles de refuser un vaccin pour elles-mêmes lorsqu'elles n'étaient pas enceintes, étaient enceintes et pour leur bébé (P > 0,005). • Les personnes de ménages à faible revenu, âgées de moins de 25 ans et provenant de certaines régions géographiques étaient plus susceptibles de refuser un vaccin lorsqu'elles n'étaient pas enceintes, enceintes et pour leurs bébés. • Les femmes non vaccinées contre la coqueluche pendant la grossesse étaient plus de quatre fois plus susceptibles de refuser un vaccin lorsqu'elles n'étaient pas enceintes, enceintes et pour leur bébé. • L'analyse thématique a révélé que les raisons les plus courantes de réticence étaient l'innocuité du vaccin et une méfiance plus grande à l'égard des vaccins en général.
Bell (2020) (185) Étude transversale Angleterre	Un sondage en ligne a été utilisé pour évaluer l'acceptabilité d'un futur vaccin auprès d'un groupe de 1 252 parents et tuteurs (âgés de 16 ans et plus et ayant un enfant de moins de 18 mois). À la fin du sondage en ligne, on a demandé aux participants s'ils	• Les Noirs, les Asiatiques, les Chinois, les personnes d'ethnicité mixte ou les autres groupes ethniques étaient presque trois fois plus susceptibles de refuser le vaccin contre la COVID-19 pour eux-mêmes et leurs enfants que les Britanniques blancs, les Irlandais blancs et les autres participants blancs.

Avril et mai 2020	voulaient participer à une entrevue téléphonique de suivi. Dix-neuf personnes ont pris part à l'entrevue. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	• 55,8 % des répondants ont l'intention de se faire vacciner et 34,3 % étaient incertains, mais tendaient vers le oui. • En ce qui concerne leurs enfants, 48,2 % étaient prêts à accepter que leurs enfants se fassent vacciner alors que 40,9 % étaient incertains, mais tendaient vers le oui.
NOUVELLE-ZÉLANDE		
Horizon Research (2021) *non publiée* (15, 195, 232) Étude longitudinale Nouvelle-Zélande Mar-Mai 2021	Une enquête en ligne a été menée auprès des adultes (16 ans et plus) pour mesurer le taux d'utilisation du vaccin. Mar-Avr, n=1,350 Avr-Mai, n=1387 Mai, n=1,234 *nouvelle* Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	**Mai** • 55 % des parents ou des personnes qui s'occupent d'enfants âgés de 12 à 15 ans sont susceptibles de faire vacciner leurs enfants, soit une baisse de 1 % par rapport à avril. • Les principales raisons sont les suivantes : désir d'obtenir des garanties quant à l'innocuité du produit chez les enfants (59 %), inquiétude quant aux effets à long terme chez les enfants (50 %) et désir d'attendre pour voir s'il y a des effets secondaires (28 %). **Avril-mai** • 56 % des parents ou des personnes qui s'occupent d'enfants âgés de 12 à 15 ans autoriseront leurs enfants à recevoir un vaccin. Les parents qui étaient disposés à se faire vacciner eux-mêmes étaient plus susceptibles de faire vacciner leurs enfants que ceux qui ne le feraient pas (85 % contre 6 %). • Les principales préoccupations des personnes incertaines ou peu susceptibles de faire vacciner

		leurs enfants sont le besoin d'avoir des garanties d'innocuité (60 %) et l'incertitude quant aux effets à long terme (43 %).
Horizon Research (2021) *non publiée* (187) Étude transversale Nouvelle-Zélande Septembre 2020	Un sondage en ligne a été réalisé auprès de 1 451 adultes (âgés de 18 ans et plus) pour mesurer le niveau d'acceptation des vaccins pour eux-mêmes et leurs enfants après l'annonce de la disponibilité des vaccins. Sujets des questions : 2) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	• Les parents pasifika et indiens étaient les plus susceptibles de faire vacciner leurs enfants (72 % et 68 %) alors que les Māori et autres Européens étaient les moins susceptibles (40 % et 41 %).
Horizon Research (2021) *non publiée* (94) Étude transversale Nouvelle-Zélande Décembre 2020	Un sondage effectué en ligne auprès de 1 438 adultes (âgés de 18 ans et plus) visait à évaluer les intentions, les connaissances et les perceptions relatives au vaccin. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins 3) Connaissance des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non	• 40 % des parents étaient prêts à faire vacciner leurs enfants après l'approbation du vaccin, 33 % ont dit que c'était peu probable qu'ils les fassent vacciner et 24 % ont dit être incertains. Les parents les moins susceptibles de faire vacciner leurs enfants étaient les Pasifika (39 %) et les autres Européens (29 %), suivis des Māori (39 %), des Européens/Pakeha de Nouvelle-Zélande (41 %), des Asiatiques (45 %) et des Indiens (62 %).

	Enquête prétestée? Non	
ÉTATS-UNIS		
Teasdale (2021) *préimpression* (16) *nouveau* Étude transversale É.-U. Mars-avril 2021	Un sondage en ligne a été mené auprès de 1 119 parents ou personnes qui s'occupent (18 ans et plus) d'enfants de moins de 12 ans à New York afin de déterminer les intentions de faire vacciner leur plus jeune enfant. Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• 61,9 % avaient l'intention de vacciner leur plus jeune enfant (âge moyen de 4,7 ans), 23,3 % étaient incertains et 14,8 % n'avaient pas l'intention de le faire. • L'intention de faire vacciner augmentait lorsque les enfants étaient plus âgés et de race blanche non hispanique et que les parents étaient âgés de 30 à 44 ans, de sexe masculin et de race blanche non hispanique. Dans la modélisation multivariée, seuls les parents de sexe féminin (aPR 0,72, IC à 95 % : de 0,61 à 0,85) et les parents noirs non hispaniques (aPR : 0,79, IC à 95 % : de 0,63 à 0,99) étaient associés à une diminution des intentions de se faire vacciner. • Les parents étaient plus susceptibles de vacciner leur enfant s'ils n'avaient pas d'assurance maladie, si leur enfant fréquentait une garderie plus d'une fois par semaine, s'ils avaient deux enfants de moins de 12 ans, s'ils avaient terminé des études universitaires ou plus, si le revenu du ménage était de 100 000 dollars et s'ils vivaient à Manhattan. • Dans le modèle ajusté, seul le fait que les enfants fréquentent la garderie plus d'une fois par semaine était associé à une augmentation des intentions (aPR 1,23, IC à 95 % : de 1,05 à 1,45). • 20,2 % des parents avaient reçu un vaccin, 47,1 % avaient l'intention de se faire vacciner, 20,6 % étaient incertains et 9,1 % ont déclaré ne pas avoir l'intention de se faire vacciner (3,0 % ont refusé de répondre). • Parmi les parents qui prévoient de se faire vacciner ou qui ont été vaccinés, 82,4 % feront vacciner leur enfant, contre 25,4 % des parents incertains et 4,5 % des parents qui ne prévoient pas de se faire vacciner.

Teasdale (2021) *préimpression* (14) Étude transversale États-Unis Mars 2021	Afin d'évaluer les intentions des parents (âgés de 18 ans et plus) de faire vacciner leurs enfants (âgés de 12 ans ou moins), un sondage en ligne a été mené auprès de 2 074 adultes aux États-Unis. Sujets des questions : 2) Intentions en ce qui concerne la vaccination 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• 49,4 % ont dit avoir l'intention de faire vacciner le plus jeune enfant de leur ménage (âge médian de l'enfant : 4,8 ans, EI : 4,5 à 5,1) lorsqu'un vaccin pédiatrique sera approuvé, 25,6 % ont dit qu'ils n'accepteraient pas de faire vacciner leur enfant, et 25 % étaient incertains. Les parents étaient plus susceptibles de faire vacciner les enfants âgés de 7 à 12 ans (56,5 %) que ceux qui avaient entre 2 et 6 ans (48 %) et 2 ans et moins (37,2 %). • Parmi les parents qui avaient reçu un vaccin ou qui avaient l'intention de se faire vacciner, 85,2 % ont dit qu'ils feraient vacciner leurs enfants, 4,8 % ne le feraient pas et 10 % ont dit être incertains. Seulement 5,7 % des parents qui ne se sont pas fait vacciner ont déclaré qu'ils prévoyaient faire vacciner leur enfant. • Parmi les raisons associées à la réticence à se faire vacciner, mentionnons des préoccupations possibles quant à l'innocuité ou à l'efficacité (78,2 %), la croyance que les enfants n'avaient pas besoin d'être vaccinés (23 %), des raisons médicales (11,2 %) et des raisons religieuses (8,5 %). • Les parents asiatiques étaient plus susceptibles de dire qu'ils voulaient faire vacciner leurs enfants que les Blancs non hispaniques (RCa 1,38, IC à 95 % : 1,19 à 1,60). • Les parents sont moins susceptibles d'avoir l'intention de faire vacciner leurs enfants s'ils sont de sexe féminin (RCa 0,69, IC à 95 % : 0,62 à 0,77), étaient moins instruits (RCa 0,73, IC à 95 % : 0,62 à 0,86) et avaient des revenus plus faibles (RCa 0,75, IC à 95 % : 0,64 à 0,88).
Czeisler (2021) *préimpression* (17) Étude longitudinale	Un sondage en ligne a été utilisé pour évaluer l'intention de se faire vacciner contre la COVID-19 et la réticence à se faire vacciner chez des adultes (18 ans et plus) américains, tant pour eux-mêmes	• En mars, 66,0 % des gens ont dit qu'ils se feraient certainement ou fort probablement vacciner le plus rapidement possible, 20 % ont dit qu'ils refuseraient le vaccin et 14 % étaient indécis. En décembre, 63,7 % ont dit qu'ils se feraient

États-Unis Décembre 2020 à mars 2021	que pour leurs enfants. En décembre 2020, 5 188 adultes ont répondu au sondage alors que 5 256 adultes y ont répondu en mars 2021. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	vacciner, 17,5 % ont dit qu'ils refuseraient le vaccin et 18,8 % étaient indécis. • Les intentions en ce qui concerne la vaccination pour les enfants et les vaccins de rappel étaient semblables aux intentions en ce qui concerne les vaccins personnels. Dans le cadre du sondage réalisé en mars, chez les 2 160 personnes qui vivaient avec des enfants de 2 à 18 ans ou qui s'occupaient, 60,4 % des personnes ont dit qu'elles feraient vacciner ces enfants, 21,4 % ont refusé le vaccin et 18,1 % étaient indécis. • Parmi ceux qui feraient vacciner leurs enfants, 93,5 % ont dit qu'eux aussi se feraient vacciner. Parmi ceux qui ne feraient pas vacciner leurs enfants, 56,5 % ont dit qu'ils refuseraient également de se faire vacciner. • La réticence à se faire vacciner était beaucoup plus fréquente chez les adultes plus jeunes (RCa 3,88, IC à 95 % : 2,02 à 7,46), les femmes (RCa 1,51, IC à 95 % : 1,16 à 1,96), les Noirs (RCa 1,60, IC à 95 % : 1,10 à 2,33), les personnes très conservatrices sur le plan politique (RCa 3,58, IC à 95 % : 2,16 à 5,94), moins instruites (RCa 3,43, IC à 95 % : 2,11 à 5,59), celles qui portaient moins souvent le couvre-visage (RCa 3,92, IC à 95 % : 2,52 à 6,10), celles qui se conformaient moins à la demande visant à éviter les rassemblements (RCa 2,65, IC à 95 % : 1,95 à 3,60), étaient plus méfiantes envers les médecins (RCa 2,11, IC à 95 % : 1,10 à 4,07) ou n'avait pas reçu de vaccin contre la grippe en 2020 (RCa 4,11, IC à 95 % : 3,05 à 5,54).
McCabe (2021) *préimpression* (166) Étude transversale	Une enquête nationale distribuée par voie électronique a été menée auprès de 34 470 travailleurs de la santé et d'adultes de la population générale afin de mesurer l'intention de recevoir un vaccin et les facteurs liés à l'acceptation et au refus. Le	• Dans l'analyse multivariable, les parents hésitaient davantage à se faire vacciner que les non-parents (RR ajusté 1,24, IC 95 %) : 1,13 % à 1,36 %).

É.-U. Décembre 2020 à février 2021	nombre de travailleurs de la santé n'a pas été indiqué. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Oui	
Milan (2021) (13) Étude transversale États-Unis Décembre 2020	Pour déterminer l'incidence du trouble de stress post-traumatique (TSPT) et des antécédents de traumatisme sur les croyances et les intentions des mères de se faire vacciner et de faire vacciner leurs enfants, un sondage en ligne a été mené auprès de 240 mères aux États-Unis ayant des antécédents de maladie mentale et des enfants âgés de 3 à 18 ans. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	• Un historique du diagnostic de TSPT et des événements potentiellement traumatisants sont en corrélation significative et positive avec toutes les mesures du vaccin. • Il existe une forte corrélation entre l'intention de la mère et de l'enfant de se faire vacciner ($r = 0,90$, $p < 0,001$). • Parmi les mères ayant des antécédents de TSPT, 40 % hésitaient à se faire vacciner comparativement à 23,9 % des mères sans de tels antécédents, X^2 ($df = 1$, $N = 238$) = 6,45, $P < 0,01$ et pour leurs enfants, 38,7 % des mères ayant des antécédents de TSPT hésitaient comparativement à 25,8 % sans de tels antécédents, X^2 ($df = 2$, $N = 238$) = 4,08, $P < 0,05$. • Les motifs de réticence les plus courants incluaient les préoccupations à propos des effets secondaires (31 %) et le besoin d'avoir plus d'information et d'observations (24 %). • On a observé des différences dans la réticence à se faire vacciner entre les personnes ayant déjà reçu un diagnostic de TSPT et celles qui n'en avaient pas reçu. Les mères qui avaient des antécédents de TSPT étaient moins susceptibles de dire qu'elles

		croyaient en la science et plus susceptibles de dire que leur enfant avait des problèmes de santé particuliers. • Les mères ont indiqué que les facteurs les plus importants pour augmenter la confiance dans le vaccin seraient la lecture, par elles-mêmes, d'essais et de recherches et les recommandations d'un pédiatre.
Catma (2021) (241) Étude transversale États-Unis Novembre 2020	Les perceptions des parents à l'égard d'un vaccin contre la COVID-19 et leur volonté de payer pour un vaccin pour eux-mêmes et leurs enfants de moins de 18 ans ont été évaluées dans un sondage en ligne effectué aux États-Unis. Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Oui	• Les parents étaient d'accord pour payer entre 228 $ et 291 $ US pour un vaccin pour eux-mêmes et entre 243 $ et 321 $ US pour leurs enfants. • Le revenu était associé positivement à la volonté de payer des adultes pour un vaccin, tant pour eux-mêmes que pour leurs enfants. • À mesure que le nombre d'enfants augmentait dans un ménage, la volonté de payer pour le vaccin des enfants augmentait. • 72 % des parents croyaient que les vaccins étaient importants pour prévenir la maladie.
Haeder (2021) (242) Étude transversale É.-U. Octobre à novembre 2020	Les réponses de 2 404 adultes ont été recueillies dans le cadre d'une enquête en ligne visant à étudier les attitudes à l'égard des vaccins obligatoires. Sujets des questions : 1) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non	• Les ménages avec enfants étaient moins favorables à l'obligation de vaccination dans les crèches et à l'université, mais pas dans les écoles maternelles et primaires. • Le fait d'avoir des enfants dans le foyer permet de prédire les attitudes favorables à l'égard des mandats contre la COVID-19 lorsque les attitudes à l'égard des mandats de vaccination généraux sont soustraites pour la garderie, la maternelle à la 12e année et l'université.

	Enquête prétestée? Non	
Marques (2021) (243) *nouveau* Étude transversale É.-U. Sept.-nov. 2020	99 parents et personnes s'occupant d'enfants (âgés de 24 à 63 ans) ont été approchés en personne dans des salles de soins dentaires pour répondre à un sondage concernant leur intention de faire vacciner leurs enfants contre la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Oui	• 21,6 % des parents disent qu'ils autoriseraient leur enfant à être vacciné contre la COVID-19, 39,2 % sont incertains et 42,3 % n'autoriseraient pas leur enfant à être vacciné. • 19,6 % des parents disent eux-mêmes qu'ils se feront vacciner, 38,1 % sont incertains et 42,3 % ne se feront pas vacciner. • 77, 6 % des parents ont déclaré que l'âge de leurs enfants n'avait pas influencé leur décision de se faire vacciner contre la COVID-19 lorsqu'il était disponible. • L'intention de faire vacciner son enfant augmentait si l'on connaissait une personne atteinte de COVID-19 (OR 0,47, IC à 95 % : de 0,24 à 0,93). • 40 % des parents qui font vacciner leur enfant contre la grippe chaque année autoriseraient leur enfant à être vacciné contre la COVID-19. • 52,2 % des parents seraient influencés par la recommandation d'un médecin pour se faire vacciner contre la COVID-19, contre 42,4 % qui ont déclaré que personne n'influencerait leur décision.
Rhodes (2021) (184) Étude transversale ÉTATS-UNIS Juillet et août 2020	Un sondage en ligne comportant des questions ouvertes a été utilisé pour mesurer l'hésitation à l'égard de la vaccination chez 1 381 parents hésitants à l'égard de la vaccination (âgés de 18 ans et plus) qui ont au moins un enfant de moins de 4 ans aux États-Unis. Sujets des questions : 2) Intentions en ce qui concerne les vaccins 3) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non	• Les parents se sont dits légèrement hésitants en ce qui concerne leur intention de faire vacciner leurs enfants (moyenne = 3,55) et eux-mêmes (moyenne = 3,58). • Les personnes ayant un niveau de scolarité supérieur étaient plus susceptibles d'accepter un vaccin pour elles-mêmes et leurs enfants. • Les sources les plus courantes d'information sur les vaccins pour les parents étaient les travailleurs de la santé, la recherche personnelle (ressources en ligne et traditionnelles), les croyances et l'expérience personnelles, et les collègues experts. • Les réponses ouvertes indiquent également l'influence de sources de santé non traditionnelles comme les docteurs en naturopathie et en médecine alternative, ainsi que de sources comme

	Recherches formatives effectuées? Non Enquête prétestée? Non	les forums, les blogueurs, l'intuition personnelle et les expériences d'amis ou de membres de la famille.
Davis (2020) *préimpression* (188) Étude transversale ÉTATS-UNIS Juin 2020	Les facteurs associés à la probabilité que 1 008 parents se fassent vacciner et fassent vacciner leurs enfants contre la COVID-19 ont été examinés dans un sondage en ligne. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Comparativement aux parents hispaniques, blancs non hispaniques et noirs, les parents qui se sont identifiés comme Autres étaient plus susceptibles de se faire vacciner. • 63 % des parents ont déclaré qu'ils étaient susceptibles de faire vacciner leurs enfants contre la COVID-19 et 60 % ont dit qu'il était probable qu'eux aussi se fassent vacciner. • Les facteurs fortement associés à la probabilité de faire vacciner leurs enfants et de se faire vacciner comprennent l'âge, le sexe masculin, le fait d'être marié, ainsi que le niveau de scolarité et de revenu plus élevés.
Thunstrom (2021) (186) Essai clinique randomisé ÉTATS-UNIS Mars 2020	Un sondage en ligne effectué auprès de 3 133 adultes sur leurs intentions de se faire vacciner et de faire vacciner leurs enfants contre la COVID-19. Les participants ont été répartis aléatoirement en huit groupes de traitement de l'information. Chaque groupe a vu des messages précis dans lesquels la probabilité d'infection, le taux de mortalité conditionnelle de la COVID-19 et la question de savoir si les différentes autorités sanitaires des États-Unis fournissaient des renseignements cohérents sur les risques variaient. Sujets des questions :	• 19,5 % des participants ont dit qu'ils ne se feraient pas vacciner. • Sur les 1 156 participants ayant des enfants, 19,7 % ne feraient pas vacciner leurs enfants.

	1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	
AFFILIATIONS RELIGIEUSES		
AUSTRALIE		
Edwards (2021) (244) & Biddle (2021) *préimpression* (179) Étude longitudinale Australie Août 2020 et janvier 2021	Les changements dans l'intention de se faire vacciner au fil du temps et les raisons de ce changement ont été évalués dans deux sondages en ligne et téléphoniques. En août, 3 061 adultes (âgés de 18 ans et plus) ont répondu au sondage, puis 3 459 adultes ont répondu à un sondage semblable en janvier. Les deux sondages ont été remplis par 2 377 personnes. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Ceux qui avaient des visions plus populistes et des niveaux de religiosité plus élevés étaient moins susceptibles d'avoir l'intention de se faire vacciner. • Les personnes les plus religieuses étaient moins susceptibles d'avoir l'intention de se faire vacciner (coefficient de vraisemblance du vaccin -0,022). •
Smith (2021) (182) Étude transversale	L'intention de se faire vacciner et les raisons pour hésiter à accepter la vaccination ont été évaluées au moyen d'un sondage en ligne	• Dans l'analyse bivariée, les personnes moins religieuses étaient plus susceptibles d'avoir l'intention de se faire vacciner que les personnes religieuses (P > 0,004). Cette variable n'était pas significative dans l'analyse multivariée.

Australie s.d. 2020	effectué auprès de 1 200 adultes (âgés de 18 ans et plus). Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	
ROYAUME-UNI		
de Figueiredo (2021) *préimpression* (20) *nouveau* Étude transversale R.-U. Avril 2021	Ce sondage national en ligne mené auprès de 17 611 adultes (18 ans et plus) a utilisé une régression bayésienne à plusieurs niveaux pour estimer l'incidence des passeports vaccinaux sur l'intention de se faire vacciner contre la COVID-19 parmi les répondants qui n'ont pas encore reçu deux doses de vaccin. Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Oui Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• Dans une régression à plusieurs niveaux contrôlant l'intention initiale de se faire vacciner, la probabilité de se faire vacciner en cas d'introduction de passeports vaccinaux pour les voyages nationaux était significativement plus élevée chez les personnes déclarant être de confession chrétienne (RCa 1,23, IC à 95 % : de 1,08 à 1,41) par rapport aux athées ou aux agnostiques. • Si des passeports vaccinaux étaient mis en place pour les voyages internationaux, la foi chrétienne était significativement associée à une intention accrue de se faire vacciner (RCa 1,22 IC à 95 % : de 1,07 à 1,39) par rapport aux athées ou aux agnostiques.
Rahman (2021) *préimpression* (245)	Cette enquête en ligne visait à améliorer les activités de promotion du vaccin en recueillant des informations sur les	• Les scores d'attitude à l'égard du vaccin étaient modérément positifs dans chaque mosquée (62 % et 69 %).

Étude transversale ROYAUME-UNI Janvier 2021	connaissances, les attitudes et les pratiques concernant la COVID-19 auprès de 151 participants à deux mosquées. Sujets des questions : 1) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• Les questions ouvertes concernant les améliorations à apporter à la participation et aux expériences relatives à la mise en place du vaccin englobent largement le souhait d'accroître l'accessibilité de l'information et des sites de vaccination, et d'entendre directement les membres de la communauté. • Les principales sources d'information sur les vaccins étaient les sites web du National Health Service ou du gouvernement, suivis par les médecins généralistes.
de Figueiredo (2020) *préimpression* (178) Étude transversale ROYAUME-UNI Septembre et octobre 2020	À l'aide des méthodes statistiques bayésiennes et d'un sondage national en ligne effectué auprès de 17 684 adultes (âgés de 18 ans et plus), on a estimé l'adoption du vaccin et déterminé les obstacles à cette adoption. Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	• Ceux qui ont déclaré l'hindouisme ou le judaïsme comme religion étaient plus susceptibles que les athées ou les agnostiques d'accepter un vaccin (RC = 1,66, HPDI à 95 % : 1,11 à 2,43) et ceux qui ont déclaré que leur religion était musulmane (RC = 0,75, HPDI à 95 % : 0,57 à 0,96) ou autre (RC = 0,72, HPDI à 95 % : 0,62 à 0,82), étaient moins susceptibles d'avoir l'intention de se faire vacciner.
Chadwick (2021) (246) Étude transversale ROYAUME-UNI	Cette enquête en ligne menée auprès de 5 114 adultes a exploré la relation entre la consommation de médias, les données sociodémographiques, les attitudes sociales et politiques, et la probabilité de promouvoir ou de	• La religiosité était associée à l'encouragement de la vaccination ($\beta = -0{,}032$, $p < 0{,}001$).

Septembre à octobre 2020	décourager la vaccination sur les médias sociaux. Sujets des questions : 1) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	
Garry (2020) (176) Étude transversale ROYAUME-UNI Juillet 2020	L'intention de se faire vacciner a été évaluée à l'aide d'un sondage en ligne effectué auprès de 2 057 adultes. Les répondants ont été répartis en groupes ayant des options de réponse différentes (asymétrie positive – plus d'options positives, asymétrie négative – plus d'options négatives et équilibrées – autant d'options positives que négatives) pour étudier l'impact des théories de conspiration sur le vaccin. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	• Les répondants plus jeunes, qui avaient un revenu plus faible, qui vivaient dans une région urbaine et qui étaient religieux étaient moins susceptibles de se faire vacciner.
Murphy (2021) (174)	Un sondage en ligne effectué auprès de 1 041 adultes (âgés de 18 ans et plus) en Irlande et de	• En Irlande, le groupe des personnes qui hésitaient à se faire vacciner et résistaient au vaccin était plus susceptible d'avoir des niveaux plus élevés de

Étude transversale Irlande et Royaume-Uni Mars 2020	2 025 adultes au Royaume-Uni a évalué la volonté de se faire vacciner contre la COVID-19 et les raisons de l'hésitation à se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	croyances conspirationnistes (d = 0,21) et religieuses (d = 0,20).
ÉTATS-UNIS		
Viskupic (2021) *préimpression* (21) *nouveau* Étude quasi expérimentale É.-U. Avril 2021	709 électeurs inscrits non vaccinés du Dakota du Sud ont reçu des messages identiques encourageant la vaccination, émanant d'un leader religieux, politique ou médical, afin d'évaluer l'incidence du messager sur l'intérêt envers la vaccination. Un groupe témoin a reçu un message sans rapport avec la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Oui Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• L'intérêt moyen envers la vaccination était de 1,86 (IC à 95 % : de 1,61 à 2,11) dans le groupe témoin. • Un messager religieux a suscité un intérêt moyen envers la vaccination de 2,32 (IC à 95 % : de 1,94 à 2,71, P<0,05) qui était le seul messager présentant une différence statistique d'intérêt. • Tous les messagers ont eu des effets statistiquement significatifs sur les répondants s'identifiant comme chrétiens évangéliques, l'effet le plus fort étant observé avec un messager religieux. • Un messager religieux a également eu un effet statistique chez les répondants de moins de 65 ans.

King (2021) *préimpression* (181) Étude longitudinale É.-U. Janvier à mars 2021	Dans le cadre d'une enquête nationale continue mensuelle sur la COVID-19, des questions visant à mesurer l'acceptation des vaccins et les facteurs connexes d'acceptation ont été recueillies auprès d'échantillons d'adultes (âgés de 18 à 64 ans). Le nombre de travailleurs de la santé n'a pas été communiqué. Enquête de janvier : n = 791 716 Enquête de février : n = 710 529 Enquête de mars : n = 732 308 Sujets des questions : 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• Dans un sous-ensemble d'individus de cette enquête (n = 143 297) par catégories professionnelles présentant le plus fort pourcentage d'hésitation, 6,7 % des individus ont déclaré la religion comme raison de leur hésitation à se faire vacciner. Il s'agit notamment des professions de la construction, de l'installation, de l'agriculture, de la sylviculture et de la pêche, et des transports.
Carmody (2021) (183) Étude transversale États-Unis Décembre 2020 à janvier 2021	Un sondage sur papier a été utilisé pour évaluer les attitudes et les intentions à l'égard de la vaccination chez 102 adultes juifs Haredi (ultra-orthodoxes) (âgés de 18 ans et plus) de New York. Sujets des questions : 1) Intentions en ce qui concerne la vaccination 2) Attitudes à l'égard des vaccins 3) Hésitation par rapport à la vaccination	• 12 % des répondants ont dit qu'ils accepteraient un vaccin pour eux-mêmes et les membres de leur famille, 47 % hésitaient fortement et 41 % étaient indécis. • 70 % ont convenu que les vaccins de routine étaient essentiels. • L'appréhension en ce qui concerne la nouvelle technologie associée aux vaccins était la préoccupation la plus courante en ce qui concerne la vaccination. • Il y avait également un manque de confiance dans le gouvernement et les responsables de la santé, et seulement 17 % des gens ont dit les mandats

	Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	adoptés par le ministère de la Santé local les obligeraient à accepter un vaccin. • Les prédicteurs indépendants d'une forte hésitation à se faire vacciner étaient les suivants : 1) la croyance que l'infection naturelle était meilleure que le vaccin pour développer l'immunité (RCa 4,28, IC à 95 % : 1,23 à 14,86, P = 0,022), l'idée selon laquelle l'infection antérieure au SRAS-CoV-2 qui a laissé des anticorps n'oblige pas à porter un couvre-visage ou un masque ou à respecter la distanciation sociale (RCa 4,1, IC à 95 % : 1,22 à 13,77, P = 0,022) et la perte de confiance envers les médecins à la suite de la pandémie (RCa 5,01, IC à 95 % : 1,05 à 23,96, P = 0,044).
Clark (2020) *préimpression* (171) Étude transversale ÉTATS-UNIS Novembre et décembre 2020	Un sondage en ligne mené auprès de 655 adultes de l'Oregon a évalué leur intention de se faire vacciner et les raisons de leur hésitation en mettant l'accent sur la comparaison des résidents ruraux et urbains. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Les personnes qui signalent des préoccupations personnelles ou religieuses et celles qui croient que la COVID-19 n'est pas grave sont 9,5 et 10 fois plus susceptibles de refuser un vaccin, respectivement.
Graupensperger (2021) (180) Étude transversale	Les intentions et les attitudes à l'égard du vaccin de 647 étudiants d'une grande université publique du nord-ouest des États-Unis ont	• 91,6 % des étudiants ont déclaré avoir l'intention de se faire vacciner contre la COVID-19. • 2,78 % des élèves étaient d'avis qu'un vaccin contre la COVID-19 était incompatible avec leurs croyances religieuses.

ÉTATS-UNIS Novembre 2020	été évaluées au moyen d'un sondage en ligne. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	
Parente (2021) (126) *nouveau* Étude transversale É.-U. Août 2020	Les associations avec l'adoption des vaccins ont été évaluées en ligne pour un vaccin hypothétique en tenant compte des périodes de retard (de 1 à plus de 12 mois après l'approbation) chez 3 347 travailleurs de la santé du Kentucky. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Oui Sondage prétesté? Oui	• 7,4 % des répondants ont mentionné des raisons personnelles religieuses ou éthiques comme raisons de vouloir retarder ou refuser de se faire vacciner.
Olagoke (2020) (177)	La relation entre la religion et l'intention de se faire vacciner a été examinée dans un sondage en	• Il y avait un lien très négatif entre l'intention de se faire vacciner et la religion (β = -0,15, IC à 95 % : -0,23 à -0,08, p < 0,0001) et le locus de contrôle

Étude transversale ÉTATS-UNIS Mars 2020	ligne réalisé auprès de 501 adultes (âgés de 18 ans et plus). Sujets des questions : 1) Intentions en ce qui concerne les vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	sanitaire externe (croyances basées sur les expériences passées et sur le fait d'exercer un contrôle externe sur celles-ci) (β = -0,24, IC à 95 % -0,33 à 0,15, P < 0,0001). -0,33 à 0,15, P < 0,0001). • Le locus de contrôle sanitaire externe est à l'origine de 40,97 % du lien entre la religiosité et l'intention de se faire vacciner comme effet indirect de β = -0,06, IC à 95 % : -0,11 à -0,02, P = 0,006.
COMMUNAUTÉS RURALES ET URBAINES		
CANADA		
Leger (2021) *non publiée* (9, 69-71, 73, 205, 206) Étude longitudinale Canada et États-Unis Novembre 2020 et janvier à juin 2021	Un sondage en ligne a été mené auprès d'adultes canadiens et américains (âgés de 18 ans et plus) pour évaluer les perceptions et les intentions quant à la vaccination. Voir la section sur les États-Unis pour les résultats américains. Vague 1 : Novembre 2020, 1 516 Canadiens et 1 002 Américains Vague 2 : Janvier 2021, 1 516 Canadiens et 1 003 Américains Vague 3 : Février 2021, 1 535 Canadiens et 1 002 Américains Vague 4 : Février 2021, 1 532 Canadiens et 1 002 Américains Vague 5 : Avril 2021, 1 504 Canadiens et 1 002 Américains Vague 7: Mai 2021, 1 529 Canadiens et 1 003 Américains	**Vague 12** • 16 % des personnes vivant dans des zones rurales n'ont pas l'intention de se faire vacciner, contre 11 % des personnes vivant dans les villes et 9 % des personnes vivant dans les banlieues. **Vague 11** • 22 % des personnes vivant dans des zones rurales n'ont pas l'intention de se faire vacciner, contre 11 % des personnes vivant dans les villes et 15 % des personnes vivant dans les banlieues. • 26 % des personnes vivant dans des zones rurales n'étaient pas à l'aise avec un vaccin différent comme deuxième dose, contre 24 % des personnes vivant dans les villes et 20 % des personnes vivant dans les banlieues. **Vague 9** • Les niveaux combinés de vaccination et d'intention de se faire vacciner sont passés de 73 % à 85 % chez les personnes vivant dans des zones rurales lors du dernier sondage. **Vague 7** • Les personnes qui vivaient dans des banlieues (85 %) ou dans les villes (84 %) étaient plus

	Vague 8: Mai 2021, 1,529 Canadiens et 1,003 Américains Vague 9: Mai 2021, 1,624 Canadiens et 1,002 Américains Vague 10: Mai 2021, 1,624 Canadiens et 1,002 Américains Vague 11: Juin 2021, 1,539 Canadiens, 1,004 Américains Vague 12: Juin 2021, 1,542 Canadiens and 1,001 Américains *nouvelle* Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	susceptibles d'avoir l'intention de se faire vacciner que celles qui vivaient dans des zones rurales (73 %). **Vague 5** • Les participants vivant dans des zones rurales (74 %) étaient légèrement moins susceptibles de se faire vacciner que les participants vivant dans les villes (82 %) et les banlieues (81 %).
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021) *non publiée* (86, 88, 91, 95) Étude longitudinale Canada Avril 2020 à avril 2021	L'analyse de l'acceptabilité de la vaccination contre la COVID-19 a été évaluée à l'aide d'un sondage en ligne réalisé auprès d'adultes et de travailleurs de la santé au Québec. Le nombre de participants n'a pas été indiqué de façon claire (environ 3 300 par période de collecte). Il y a eu plusieurs périodes de collecte, soit en avril-mai 2020, en septembre et en décembre 2020, et en avril 2021 *nouvelle*. Ces articles sont en français. Sujets des questions :	L'intention était la plus faible dans les villages de moins de 10 000 habitants (76 %) comparativement à ceux de Montréal (79 %), dans les villages de 10 à 100 000 habitants (80 %) et dans les zones entourant la grande région de Montréal (81 %).

	1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	
Lang (2021) (87) Étude transversale Canada Août 2020	Une enquête en ligne a été menée auprès de 60 adultes (18 et +) de l'Alberta pour évaluer leur intention de se faire vacciner. Sujets des questions : 1) Intentions de se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	• L'intention de se faire vacciner était plus faible dans les autres centres urbains (29 %) et dans les zones rurales de l'Alberta (50 %) que dans les villes de Calgary (75 %) et d'Edmonton (80 %), (P = 0,030).
ROYAUME-UNI		
Sethi (2021) (247) Étude transversale ROYAUME-UNI Septembre à octobre 2020	Pour comprendre les facteurs de participation et de perception des essais de vaccination contre la COVID-19, 4 884 adultes ont été interrogés en ligne. Sujets des questions : 1) Intentions de se faire vacciner 2) Perception à l'égard des vaccins Outils d'enquête disponibles? Oui	• 41,4 % des répondants étaient intéressés par la participation à des essais de vaccins, 27,6 % n'étaient pas intéressés et 31,1 % étaient incertains. • Le plus grand pourcentage de répondants qui ne souhaitaient pas participer se trouvait dans les villages (pop. > 7 500) alors que les petites villes (pop. 7 500 à 24 999) étaient les plus incertains quant à leur participation. • La probabilité de ne pas participer est 0,66 fois celle des répondants des villages et 0,54 fois celle des petites villes. • 88 % des répondants des petites villes et 91 % des répondants des villages âgés de 50 à 59 ans

	Des recherches formatives ont-elles été menées? Non Enquête prétestée? Oui	n'étaient pas intéressés par la participation à des essais.
Garry (2020) (176) Étude transversale ROYAUME-UNI Juillet 2020	L'intention de se faire vacciner a été évaluée à l'aide d'un sondage en ligne effectué auprès de 2 057 adultes. Les répondants ont été répartis en groupes ayant des options de réponse différentes (asymétrie positive – plus d'options positives, asymétrie négative – plus d'options négatives et équilibrées – autant d'options positives que négatives) pour étudier l'impact des théories de conspiration sur le vaccin. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Perception des vaccins Outils d'enquête disponibles? Oui Recherches formatives effectuées? Non Enquête prétestée? Non	• Les répondants plus jeunes, qui avaient un revenu plus faible, qui vivaient dans une région urbaine et qui étaient religieux étaient moins susceptibles de se faire vacciner.
Murphy (2021) (174) Étude transversale Irlande et Royaume-Uni Mars 2020	Un sondage en ligne effectué auprès de 1 041 adultes (âgés de 18 ans et plus) en Irlande et de 2 025 adultes au Royaume-Uni a évalué la volonté de se faire vacciner contre la COVID-19 et les raisons de l'hésitation à se faire vacciner. Sujets des questions : 1) Intentions en ce qui concerne les vaccins	• Les personnes qui hésitaient à se faire vacciner étaient plus susceptibles de résider en banlieue (RCa = 2,13, IC à 95 % : 1,01 à 4,49).

	2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Non	
ÉTATS-UNIS		
McCabe (2021) *préimpression* (166) Étude transversale É.-U. Décembre 2020 à février 2021	Une enquête nationale distribuée par voie électronique a été menée auprès de 34 470 travailleurs de la santé et d'adultes de la population générale afin de mesurer l'intention de recevoir un vaccin et les facteurs liés à l'acceptation et au refus. Le nombre de travailleurs de la santé n'a pas été indiqué. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Oui Des recherches formatives ont-elles été menées? Non Enquête prétestée? Oui	• Les répondants des zones moins peuplées (densité de population 0 à 149) sont plus hésitants que ceux des zones peuplées (densité de population supérieure à 1000) (RR ajusté 1,31, IC 95 % : 1,16 % à 1,48 %).
Roess (2021) *préimpression* (175) Étude transversale États-Unis	Un sondage en ligne a été effectué aux États-Unis pour évaluer l'intention de se faire vacciner chez 1 181 parents et tuteurs âgés de 18 à 64 ans qui ont actuellement un enfant de moins de 18 ans à la maison aux États-Unis. Cette étude n'a pas évalué l'intention de faire vacciner leurs enfants.	• L'intention de se faire vacciner était plus élevée chez les personnes qui vivaient en milieux urbains (RCa 2,04, IC à 95 % : 1,24 à 3,09) et semi-urbains (RCa 1,45, IC à 95 % : 0,97 à 2,17) par rapport à celles qui vivaient dans des milieux ruraux.

Décembre 2020 à janvier 2021	Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	
Enwezor (2021) *préimpression* (115) Étude transversale États-Unis Décembre 2020 à janvier 2021	Un sondage en ligne a évalué l'intention de se faire vacciner chez 20 232 adultes (5 170 travailleurs de la santé et 15 062 autres personnes). 476 des participants avaient déjà reçu un diagnostic de COVID-19. Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Les résidents des banlieues (68 %) et des zones rurales (71,2 %) étaient moins susceptibles que ceux des zones urbaines (81 %) d'avoir l'intention de se faire vacciner (RRa 0,85, IC à 95 % : 0,83 à 0,88, P < 0,0001).
Clark (2020) *préimpression* (171) Étude transversale ÉTATS-UNIS Novembre et décembre 2020	Un sondage en ligne mené auprès de 655 adultes de l'Oregon a évalué leur intention de se faire vacciner et les raisons de leur hésitation en mettant l'accent sur la comparaison des résidents ruraux et urbains. Sujets des questions : 1) Intentions en ce qui concerne les vaccins	• L'intention de se faire vacciner était plus élevée chez les résidents urbains que chez ceux qui vivent dans les régions rurales (47 % contre 41 %). • Les personnes qui signalent des préoccupations personnelles ou religieuses et celles qui croient que la COVID-19 n'est pas grave sont 9,5 et 10 fois plus susceptibles de refuser un vaccin, respectivement.

	2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	
Kuter (2021) (109) Étude transversale ÉTATS-UNIS Novembre et décembre 2020	Pour évaluer l'intention de se faire vacciner, un sondage en ligne a été mené dans deux grands hôpitaux universitaires de Philadelphie auprès de 12 034 employés. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Oui Enquête prétestée? Oui	• Les résidents des régions urbaines étaient beaucoup plus susceptibles d'avoir l'intention de se faire vacciner que les résidents des banlieues (RC = 0,71, IC à 95 % : 0,65 à 0,79) et des régions rurales (RC = 0,41, IC à 95 % : 0,30 à 0,54).
Haeder (2021) (242) Étude transversale É.-U. Octobre à novembre 2020	Les réponses de 2 404 adultes ont été recueillies dans le cadre d'une enquête en ligne visant à étudier les attitudes à l'égard des vaccins obligatoires. Sujets des questions : 1) Attitudes à l'égard des vaccins Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non	• Les habitants des zones rurales sont moins favorables à la vaccination obligatoire des élèves en garderie (b = -0,418), des élèves de la maternelle à la 12^{e} année (b = -0,652) et des enseignants de la maternelle à la 12^{e} année (b = -0,360). • Les habitants des zones rurales étaient moins favorables aux mandats contre la COVID-19 lorsque les attitudes à l'égard des mandats de vaccination générale étaient soustraites de la maternelle à la 12^{e} année.

	Enquête prétestée? Non	
Mora (2020) *préimpression* (173) Étude transversale ÉTATS-UNIS De juillet à novembre 2020	Des entrevues téléphoniques ont été effectuées auprès de 1 115 travailleurs agricoles adultes en Californie afin de déterminer leur intention de se faire vacciner et les raisons de leur hésitation. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Le fait de vivre dans des régions plus rurales comme Greenfield était fortement associé à l'intention de ne pas se faire vacciner (RR = 1,19, IC à 95 % : 1,02 à 1,39).
Khubchandani (2021) (172) Étude transversale ÉTATS-UNIS Juin 2020	Un sondage en ligne a évalué l'intention de se faire vacciner et l'hésitation par rapport à la vaccination chez 1 878 adultes. Sujets des questions : 1) Intentions en ce qui concerne les vaccins 2) Hésitation par rapport à la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Dans les analyses non ajustées, la réticence à se faire vacciner était plus élevée chez les habitants des régions rurales (29 %) que chez leurs homologues.
JEUNESSE		

Afifi (2021) (213) *nouveau* Étude transversale Canada Nov.-déc. 2020	Grâce aux répondants de l'étude longitudinale Well-Being and Experiences (2017-2020), les intentions de se faire vacciner ont été consignées pour les adolescents de Winnipeg âgés de 16 à 21 ans et leurs soignants/parents à l'aide d'un sondage en ligne. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• 65,4 % des répondants ont l'intention de se faire vacciner, 26,1 % sont incertains et 8,5 % ne sont pas disposés à le faire. • Les parents ayant fréquenté une école de métiers, un collège communautaire ou ayant une éducation inférieure, ayant un revenu inférieur à 49 999 $, ayant subi une certaine pression financière à cause de la COVID-19, ayant déclaré avoir une faible connaissance de la COVID-19 étaient associés à de plus faibles intentions de se faire vacciner. • Le fait d'avoir un problème de santé autodéclaré était associé à des intentions plus élevées d'accepter un vaccin. • Après correction pour tenir compte du genre, de l'âge et du revenu du ménage, les enfants qui n'avaient jamais reçu de fessée (RRa 0,33, IC à 95 % : de 0,17 à 0,62), jamais connu de victimisation par les pairs (RRa 0,49, IC à 95 % : de 0,25 à 0,96), jamais connu de toxicomanie dans le ménage (RRa 0,41, IC à 95 % : de 0,20 à 0,83), n'ayant jamais eu de contact avec une famille d'accueil ou un bureau de protection de l'enfance (RRa 0,34, IC à 95 % : de 0,16 à 0,72), et n'ayant eu aucun risque que leur ménage soit à court d'argent (RRa 0,45 IC à 95 % : de 0,21 à 0,97) étaient plus disposés à se faire vacciner. • Le fait de déclarer n'avoir eu aucune expérience négative durant l'enfance au sein du foyer est associé à la volonté de se faire vacciner (RRa 0,45, IC à 95 % : de 0,20 à 0,99). • Les principaux motifs de réticence à accepter un vaccin sont l'innocuité du vaccin (64,5 %), le manque de connaissances sur le vaccin (60,6 %) et le fait de ne pas penser que le vaccin serait efficace (23,4 %).
Brandt (2021) (190) Étude transversale	Un sondage par message texte a été réalisé auprès de 911 jeunes âgés de 14 à 24 ans à travers les États-Unis afin d'évaluer les	• 42 7 % et 33,3 % ont déclaré une volonté inconditionnelle ou une volonté conditionnelle de se faire vacciner, respectivement, dont 80,7 % ont déclaré être prêts à se faire vacciner s'il est prouvé que la vaccination est sûre et recommandée.

É.-U. Octobre 2020	obstacles et les facilitants à la vaccination contre la COVID-19. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• Les raisons les plus courantes de se faire vacciner sont la protection de soi (38,4 %), la protection des autres (24,9 %), l'importance du vaccin (14,3 %) et le retour à la normale (11,7 %). • Les effets secondaires (36,2 %), l'efficacité (20,1 %), l'approbation précipitée (18,8 %) et la sécurité (16,2 %) étaient les préoccupations les plus courantes concernant le vaccin. • Par rapport aux jeunes blancs, les jeunes noirs (RR = 3,31) étaient plus susceptibles de refuser la vaccination et les jeunes asiatiques (RR = 0,46) étaient moins susceptibles de refuser la vaccination (P < 0,001). • Les CDC ou l'OMS (42,3 %) étaient les sources préférées d'information sur les vaccins, suivis des prestataires et établissements de santé (31,75 %), d'Internet (17,8 %), des responsables de la santé (8,4 %), des médias d'information (7,8 %) et des médias sociaux (2,5 %).
IMMIGRANTS		
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021) *non publiée* (86, 88, 90, 91, 95) Étude longitudinale Canada Avril 2020 à mai 2021	L'analyse de l'acceptabilité du vaccin contre la COVID-19 a été évaluée à l'aide d'un sondage en ligne auprès d'adultes et de travailleurs de la santé au Québec. Le nombre de participants n'a pas été clairement indiqué (~3 300 par période de collecte). Il y a eu plusieurs périodes de collecte, une en avril-mai 2020, une en septembre et en décembre 2020, une en avril et en mai 2021 *nouvelle*. Articles en français. Sujets des questions : 1) Intentions de se faire vacciner 2) Hésitation à se faire vacciner	• Les immigrants étaient plus hésitants et plus incertains à l'idée de se faire vacciner que les non-immigrants.

	Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Non Enquête prétestée? Non	
Australia Bureau of Statistics (2021) *Non publié* (141) *nouveau* Étude longitudinale Australie Avril 2020-mai 2021	Le sondage sur les impacts sur les ménages est un sondage mensuel qui recueille des données en ligne et par téléphone auprès d'un groupe d'adultes (18 ans et plus) sur des sujets liés à la COVID-19, y compris les attitudes envers les vaccins. Mai : n=3 371 Sujets des questions : 1) Intentions de se faire vacciner Outils de sondage disponibles? Non Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• Les personnes nées à l'étranger étaient plus susceptibles de déclarer leur intention de se faire vacciner que celles nées en Australie (70,7 % contre 67,2 %). Cela est plus évident pour celles qui sont arrivées au cours des dix dernières années (74,6 %) que pour celles qui sont arrivées il y a plus de dix ans (69,1 %). • Le facteur le plus important dans la décision de se faire vacciner était une recommandation de leur médecin généraliste (25,8 %). • 68,1 % des immigrants étaient préoccupés par les effets secondaires possibles.
Deal (2021) (248) Étude transversale ROYAUME-UNI Septembre 2020 à mars 2021	Des entretiens téléphoniques approfondis ont été menés avec 32 immigrants récents (moins de 10 ans) ayant un statut d'immigration précaire afin de définir les barrières et les perceptions à l'égard de la vaccination ainsi que de générer des stratégies pour augmenter la participation.	• 28 % déclarent qu'ils se feront certainement vacciner, 31 % sont incertains et penchent vers l'affirmative, 22 % sont incertains, 19 % sont incertains et penchent vers la négative, et 6 % ne se feront certainement pas vacciner. Parmi les deux participants qui refuseraient définitivement, l'un a indiqué que c'était en raison du manque d'essais cliniques et l'autre pour des raisons religieuses. • L'intention variait fortement entre les personnes interrogées plus tôt (intentions plus faibles

	Sujets des questions : 3) Intentions de se faire vacciner 4) Perception à l'égard des vaccins 5) Hésitation à se faire vacciner Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Oui	d'accepter un vaccin) et celles interrogées plus tard (intentions plus élevées de se faire vacciner). • Parmi les hésitants, les inquiétudes portent sur les effets secondaires potentiels et l'insuffisance des tests du vaccin. • Trois barrières communes à la vaccination ont été déterminées : les problèmes d'accès (tels que la langue, la confiance et la perception d'un manque de droit), le manque de confiance (mauvais traitement de la part du Service national de santé, être facturé pour des soins, ou d'éventuels contrôles d'immigration), et le sentiment d'être abandonné pendant la pandémie causant une tension mentale et physique. • Les sans-papiers étaient particulièrement préoccupés par le fait qu'ils n'étaient pas enregistrés dans un cabinet de médecin généraliste et qu'ils manqueraient le déploiement des vaccins. Les migrants indiquent que les organisations caritatives et les cliniques sans rendez-vous sont fréquemment utilisées. • D'autres difficultés ont été relevées : les migrants n'étaient pas au courant des annonces selon lesquelles la vaccination n'entraînerait pas de contrôles d'immigration. • Pour augmenter l'adoption du vaccin, les migrants ont indiqué qu'il était plus facile de se faire vacciner en déployant le vaccin dans les cliniques sans rendez-vous et les organisations caritatives, en fournissant des informations sur les effets secondaires dans leur propre langue, en indiquant clairement où et comment les vaccins seraient disponibles et en soulignant que le vaccin serait fourni gratuitement.
Statistics Canada (2020) & Statistics Canada (2021)	Un sondage en ligne mené par Statistique Canada dans le cadre de l'Enquête sur la santé dans les collectivités canadiennes (ESCC) a évalué les comportements des	• Les immigrants étaient légèrement moins susceptibles de se faire vacciner (74,6 %), mais cela variait grandement entre les immigrants plus âgés et les plus jeunes (73,2 % pour les 12 à 64 ans et 81,1 % pour les 65 ans et plus).

non publiée (65, 80) Étude longitudinale Canada Septembre à décembre 2020	Canadiens pour protéger leur propre santé et celle des autres. Une question sur les intentions de vaccination a été ajoutée au sondage de septembre. Le plus récent rapport fait état de 20 000 réponses reçues de personnes âgées de 12 ans et plus. Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Oui Recherches formatives effectuées? Oui Enquête prétestée? Oui	•
Knights (2021) (192) Étude qualitative ROYAUME-UNI Juin à novembre 2020	Des entretiens téléphoniques semi-structurés approfondis ont été menés auprès de 17 migrants de moins de 10 ans, 48 professionnels de la santé et 16 membres du personnel administratif à travers trois phases d'échantillonnage (intentionnel, de convenance et sondage cumulatif) afin d'obtenir des informations sur l'accès aux vaccins. Sujets des questions : 1) Perception à l'égard des vaccins 2) Hésitation à se faire vacciner	• La numérisation accrue des rendez-vous et des informations sur la santé a été ressentie différemment par les professionnels des soins primaires et les migrants ayant des problèmes d'accès à la technologie. Les professionnels des soins primaires ont indiqué que la numérisation a augmenté l'exclusion des groupes marginalisés tout en amenant des patients plus jeunes et plus en forme. Inversement, la numérisation a également été signalée comme une opportunité de communiquer avec des messages ciblés traduits. • Les migrants ont signalé que les barrières linguistiques se sont accrues en raison d'un accès plus faible à des amis qui traduiraient, alors que les médecins généralistes s'inquiétaient de la confidentialité lors des consultations virtuelles. • Les migrants et les professionnels des soins primaires ont estimé qu'il y avait un manque d'informations sur les messages relatifs à la santé publique et le vaccin ciblant les migrants. Cette situation est liée à des problèmes de faibles

		connaissances en matière de santé, de manque de compréhension des changements de politique, de méfiance à l'égard du gouvernement ou de la science, et a donné lieu à une désinformation et à la recherche d'informations sur les médias sociaux à propos de la COVID-19 et du vaccin. • Les problèmes susmentionnés et les croyances liées aux vaccins, comme le fait que la COVID-19 soit une « maladie occidentale », la peur d'être un cobaye et la dépendance aux remèdes maison, constituent également des obstacles à l'adoption du vaccin. • Les migrants et les professionnels des soins primaires ont noté qu'il était important d'établir la confiance entre les pratiques cliniques et les individus, ce qui a été un défi pendant la pandémie. Lesmigrants ont noté la tendance à rechercher les conseils de la religion ou des pairs dans la prise de décision. • Les migrants notent que l'approche « même pour tous » adoptée pendant la pandémie s'est avérée inflexible pour traiter les problèmes de la communauté liés à la numérisation et aux défaillances de la communication.
Allen (2021) *préimpression* (249) *nouveau* Étude transversale É.-U. Juillet-août 2020	Les intentions de se faire vacciner ont été mesurées chez 364 immigrants brésiliens vivant aux États-Unis par l'intermédiaire d'un sondage en ligne. Sujets des questions : 1) Intentions de se faire vacciner 2) Réticence à se faire vacciner Outils de sondage disponibles? Non	• 70,9 % des personnes interrogées ont déclaré qu'elles se feraient vacciner contre la COVID-19, 18,1 % étaient incertaines et 11 % ne se feraient pas vacciner. • Les réponses ouvertes des personnes ne prévoyant pas de se faire vacciner ont révélé qu'elles craignaient que le vaccin n'ait pas été testé (30,9 %), qu'il puisse entraîner des effets secondaires (17,6 %) ou qu'il ne soit pas efficace (8,8 %). Les autres préoccupations étaient liées au manque de confiance envers les industries impliquées dans son développement (10,3 %), le gouvernement (8,8 %) et les vaccins en général (8,8 %).

	Des recherches formatives ont-elles été menées? Non Sondage prétesté? Non	• 3,8 % des personnes qui ont passé moins de quatre ans aux États-Unis n'avaient pas l'intention de se faire vacciner, contre 27,3 % de celles qui sont nées aux États-Unis. Plus de temps passé au pays était généralement associé à des intentions plus faibles et à des répondants plus incertains. • La perception de la pandémie de COVID-19 a également eu une incidence significative sur l'intention de se faire vacciner : 75,9 % des personnes qui la considèrent comme un problème majeur souhaitent un vaccin, contre 52,6 % qui la considèrent comme un problème mineur. • Les personnes qui faisaient confiance aux professionnels de la santé (73,9 %) et aux agences de santé publique (76,8 %) avaient des intentions plus élevées que celles qui se fiaient aux réseaux sociaux (63,6 %), aux réseaux privés (62,2 %) ou qui n'avaient pas de réponse de source fiable (61,9 %).
INFECTION PASSÉE AU SARS-COV-2		
Enwezor (2021) *préimpression* (115) Étude transversale États-Unis Décembre 2020 à janvier 2021	Un sondage en ligne a évalué l'intention de se faire vacciner chez 20 232 adultes (5 170 travailleurs de la santé et 15 062 autres personnes). 476 des participants avaient déjà reçu un diagnostic de COVID-19. Sujets des questions : 1) Intentions en ce qui concerne la vaccination Outils d'enquête disponibles? Non Recherches formatives effectuées? Non Enquête prétestée? Non	• Les personnes qui n'avaient pas reçu de diagnostic antérieur de COVID-19 étaient plus susceptibles d'avoir l'intention de se faire vacciner que celles qui avaient reçu un diagnostic antérieur de COVID-19 (76,6 % comparativement à 60,9 %, RRa 1,20, IC à 95 % : 1,11 à 1,28, P < 0,0001).
Olanipekun (2021) (193)	119 Afro-Américains ont été interrogés après la guérison et la sortie de l'infection à la COVID-19	• 54 % n'avaient pas l'intention de se faire vacciner, 30 % le feraient et 16 % étaient incertains.

Étude transversale É.-U. Avril à mai 2020	pour évaluer l'acceptation d'un vaccin sûr et efficace. Sujets des questions : 1) Intentions de se faire vacciner Outils d'enquête disponibles? Non Des recherches formatives ont-elles été menées? Oui Enquête prétestée? Non	• La principale raison invoquée par ceux qui n'ont pas l'intention de se faire vacciner est une grande méfiance à l'égard de l'efficacité des vaccins et des industries pharmaceutiques (78,1 %). Les autres principales raisons sont le manque de confiance dans l'efficacité du vaccin (68,8 %) et la peur des effets secondaires (64,1 %).

Emerging Evidence on COVID-19

Evergreen Rapid Review on COVID-19 Vaccine Attitudes and Uptake in Canada – Update 9

Introduction

What is the evidence on COVID-19 vaccine attitudes and uptake in Canada?

The purpose of this evergreen rapid review is to identify and summarize literature on COVID-19 vaccination uptake and attitudes to better understand the factors associated with vaccine uptake in Canada. This report focuses on Canadian evidence on uptake and attitudes up to August 1, 2021. All studies included in this review were conducted in Canada or were multinational studies with Canadian specific data. Previous versions of this report (updates 1-8) included evidence up to July 1, 2021 on vaccine uptake and attitudes in Canada, global evidence on vaccine uptake, and vaccine attitudes in pre-defined priority populations from Australia, New Zealand, USA, and UK to complement areas where there was little Canadian research. These can be requested at phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca. The What's New section below focuses on highlighting important findings from the most recently conducted studies (within the last four months).

What's New

- This update identified 9 new studies or updates to existing studies on COVID-19 vaccination uptake and attitudes in Canada. New studies are indicated throughout the tables as *new* and all tables are located in the appendices to assist readers in navigating the document.

Intentions to Vaccinate

- Two surveys conducted in July indicate that 86-91% of Canadians have either received a vaccine or wish to get a vaccine as soon as possible, an increase from May and June surveys (1, 2).
- A longitudinal study in Quebec demonstrated that 87% of parents intend to vaccinate their children, up 1% from June (1).
- Non-permanent residents in Canada were less likely to vaccinate (11%) compared to non-immigrants (5%), and immigrants living in Canada for more than 10 years (4%) (3). Another study in Saskatchewan indicated those who were born outside of Canada and living in Canada less than 20 years were more vaccine hesitant compared to those born in Canada (RRR 3.14, 95% CI: 1.56-6.34) (4).
- A study conducted in May-June 2021 exploring the relationship between ethnicity/race and intention to vaccinate in Canada found higher levels of vaccine hesitancy among Black (33%) and non-Black visible minorities (25%) compared to Whites (19%). Black Canadians aged 25-34 had the highest levels of vaccine hesitancy (54%). Drivers of vaccine hesitancy among Black Canadians were the ability to take paid time off, concern that vaccines cause autism, and vaccine safety concerns (5).

- Vaccine hesitancy was higher amongst Black and non-Black Canadians born in Canada compared to those born outside of Canada in study conducted in June 2021 (5).
- Those having Indigenous status in Saskatchewan were more vaccine hesitant compared to non-Indigenous status (RRR 1.65, 95% CI: 1.01-2.70) (4).

Incentives to Vaccinate

- A survey across Canada revealed that 50% of respondents supported vaccine incentives such as lotteries, 36% opposed incentives, and 14% were unsure. Support for incentives was highest in Quebec and among those aged 18-34, and lowest among those aged 55+ and rural residents (6).

Vaccine Attitudes

- 66% of Canadians wanted full vaccination (two doses) as a requirement to allow people to cross the USA-Canada border (6). Another survey indicated that 69% wanted to wait until at least 75% of Canadians were fully vaccinated before opening the Canada-USA border (7).
- Support for mandatory vaccination was 53% for the general population and 81% for healthcare workers. The highest support was demonstrated among those aged 55+ (6).

Vaccine Behaviors

- 76% of those who were unwilling or unsure about vaccination were planning on resuming everything they did before with no hesitation compared to 34% of those after their first dose and 27% of those after two doses (8).
- 53% of respondents agreed that people vaccinated against COVID-19 should be able to gather and no longer wear masks in public, 41% disagreed, and 6% did not know (9).

Key Points

- There have now been 62 studies on COVID-19 vaccine uptake and attitudes conducted in Canada (Tables 1-9). The majority of studies have been conducted on the general population and focused on intention to vaccinate. There is a severe lack of studies on high-risk and underserved populations in Canada such as Indigenous, youth, those with substance abuse disorders, LGBTQ+, and the homeless. Since vaccine rollout began in December 2020, only one study has evaluated vaccine uptake in HCWs.

Vaccine Uptake

- The one study on vaccine uptake and factors associated with uptake in HCWs from Montreal was conducted in December 2020 (Table 1). Of the HCWs offered a vaccine, 80.9% accepted and 19.1% refused. The most common reasons for refusal were the newness of the vaccine, a preference for others to get vaccinated first, lack of information, and not having enough time to make a decision.
- Increasing age and male gender were positively associated with vaccine uptake. These trends are similar to those reported in the global literature and mirror the trends seen in intention to vaccinate.

Vaccine Intentions

- The most recent studies from July 2021 report intention to vaccinate is increasing and currently varies between 86-91% in the general public. Intention to vaccinate in HCWs varied between 80-82% but this

was from studies conducted in January 2021. Alberta and Saskatchewan currently have the highest percentage of the population who do not intend to vaccinate.

Facilitators and Barriers to Vaccine Intention

- The most common factors positively associated with intention to vaccinate were male gender, older age, higher education, adequate knowledge or health literacy, trust in experts and government, history of a prior influenza vaccine, higher socioeconomic status, and heightened worry or concern about COVID-19.
- Three studies demonstrated that LGBTQ2+ were 6-11% more willing to accept a vaccine compared to non-LGBTQ2+.
- Partisanship was associated with intention to vaccinate. Those who voted liberal/democrat expressed intention to vaccinate at higher rates than those who voted for other parties.
- A recommendation to get the vaccine by a healthcare provider (e.g., doctor) had a positive impact on vaccine intention.
- Intention to vaccinate varied widely by race/ethnicity, with White ethnic groups more likely to vaccinate compared to other ethnic groups such as Black and Hispanic.
- Parents had lower intentions to vaccinate their children compared to themselves. Parental and child vaccine intentions were highly correlated with each other, with parents who were intending to take a vaccine being more likely to intend to vaccinate their children.
- Religion and belief in conspiracy theories were associated with vaccine hesitancy.
- Concerns about vaccine safety and effectiveness were the two most cited reasons for vaccine hesitancy. Other commonly cited reasons include newness of the vaccine, and the belief that a COVID-19 vaccine is unnecessary.
- Rural participants were slightly less likely to accept a vaccine compared to urban and suburban participants.
- Immigrants were slightly less likely to accept a vaccine compared to non-immigrants.
- Facilitators and barriers in Canada are similar to those reported in the global literature.

Overview of the Evidence

Sixty-two studies pertaining to COVID-19 vaccine uptake and attitudes were identified and included in this review. Of these, nine are preprints and 32 are reports which have not completed the peer-review process. This report focuses on evidence on COVID-19 vaccine uptake and attitudes in Canada.

The publications reporting on COVID-19 vaccine uptake and attitudes are mainly observational studies with a few quasi-experimental studies exploring factors associated with intention to vaccinate and the impact of messaging on these intentions. The outcomes in the experimental studies did not assess prevalence, but rather were designed to inform what may be most effective across a range of options.

A formal risk of bias evaluation was not conducted. Across observational studies the reliability of the outcome is based on obtaining a representative sample of the target population that is sufficiently large to obtain a representative spectrum of results. Studies frequently did not demonstrate the representativeness of their samples to the target population in both unpublished and published studies. Longitudinal studies where a target population was sampled more than one time to monitor changes in vaccine attitudes and uptake over time were the strongest observational study design identified. Most observational studies were cross-sectional online surveys of a target population at a single point in time. These study designs are at moderate/high risk of bias and thus, are considered medium-low quality depending on the sample size and whether the sample represents the target population as well as how well the survey tool can measure the outcome(s) of interest (e.g., was it informed by formative research, validated and pretested prior to implementation). For most of the included studies the outcomes are self-reported, which can be biased by response and social desirability biases. Other biases considered in these studies include response rate and missing data. Most studies captured in this rapid review did not report and/or account for one or more of the criteria listed above either due to conduct or reporting of the study. While there are many studies that show similar trends, the conclusions could change with additional research, larger sample size, different sampling strategies, data collection tools, and progression through the pandemic.

A key knowledge gap in this research are studies that address vaccine intentions and reasons for hesitancy and refusal rates in high-risk and unserved populations. The majority of studies used online surveys, and to a lesser extent telephone surveys, which may limit segments of population due to lack of access. Although the vaccine rollout has been underway for over half a year, there have been minimal studies released on vaccine refusal and the knowledge and attitudes associated with actually rejecting or accepting a vaccine. This information is crucial to determine why people are accepting or refusing vaccinations to continue developing strategies to encourage vaccine uptake in those who are hesitant.

CONTENTS

COVID-19 VACCINE UPTAKE

Vaccine uptake and factors associated with uptake in health-care workers (HCWs) was evaluated in one study (10). Only studies where it is has been established or can be inferred that the entire group was offered a vaccine prior to measuring uptake were included. This includes studies from the beginning of the vaccine rollout (December 2020 onwards). High level points are listed below and detailed outcomes for each study are located in the Appendix (Table 1).

- In a December survey conducted in Montreal, Canada, 80.9% of HCWs offered a vaccine accepted and 19.1% refused. 74.1% of those that declined a vaccine reported they will accept a vaccine in the future with 53.2% wanting to delay a few months and 31.9% wanting to wait a year (10). The most common reasons for refusal were the newness of the vaccine (82%), preference that others get vaccinated first (77%), felt they lacked information about the vaccine (74%), and that they did not have enough time to make a decision (60%) (10).
- Vaccine uptake was positively associated with increasing age and male gender (10).
- These trends are similar to those reported in the global literature (11) and mirror the trends seen in intention to vaccinate.

COVID-19 VACCINE ATTITUDES OF THE GENERAL PUBLIC

The majority of research on COVID-19 vaccine attitudes has been conducted on the general public. Forty-five studies were specific to the Canadian population, of which 29 were unpublished and three were preprints. High level points from January 2021 onwards are listed below and detailed outcomes for each study are located in the Appendix (Table 2).

Intentions to Vaccinate

- According to the most recent Canadian studies from June-July 2021, intention to vaccinate is between 84-91% (1, 8, 12, 13). Alberta and Saskatchewan populations currently have the lowest intentions to vaccinate (3, 8, 12-14).
- Three longitudinal studies demonstrate that intention to vaccinate continues to rise in Canada from baselines measured between September-December 2020 (8, 12, 15).
- In June, 89% of Canadians who had one dose reported they intend to receive a second dose, 9% have already had their second dose, 1% probably will not, and 1% were unsure (12).

- Vaccine hesitancy dropped dramatically in Alberta from 45% in January to 25% in April to 17% in May (16).
- 71% of youth aged 12-17 intended to receive a vaccine in a survey conducted in January-February 2021 (17).
- There has been one study conducted in 2021 (May-June) exploring the relationship between ethnicity/race and intention to vaccinate (5). 21% of Canadians were vaccine hesitant with higher levels among Black (33%) and non-Black visible minorities (25%) compared to Whites (19%). Black Canadians aged 25-34 had the highest levels of vaccine hesitancy (54%). Drivers of vaccine hesitancy among Black Canadians were the ability to take paid time off, concern that vaccines cause autism, and vaccine safety concerns (5).
- Five studies conducted in 2020 demonstrated that compared to White ethnicity, visible minorities are less likely to accept a vaccine (18-22).
- Intention to vaccinate among Indigenous respondents ranged between 68-71% in two studies conducted in March 2021 (23, 24). In one of the studies, 74.2% of First Nations living off reserve were willing to vaccinate compared to 67.8% of Métis and 72.5% of Inuit (23). Older Indigenous people (65+) were more likely to want a vaccine compared to younger individuals (74.9% vs 71.3%) (23).
- Those having Indigenous status in Saskatchewan were more vaccine hesitant compared to non-Indigenous status (RRR 1.65, 95% CI: 1.01-2.70) (4).
- In Canada, those who voted Liberal or NDP in the 2019 election were more likely to indicate the intention to vaccinate compared to those who voted for other parties (25-28).
- Rural participants were less likely to accept a vaccine compared to urban and suburban participants in three studies (12, 29, 30).
- Men were more likely to intend to vaccinate than women across 12 studies (17, 18, 20, 22, 25, 31-37).
- The most common factors positively associated with intention to vaccinate were older age, higher education, adequate knowledge or health literacy, trust in experts and government, higher socioeconomic status, history of receiving an influenza vaccine, and heightened worry or concern about COVID-19.
- Concerns about vaccine safety and effectiveness were the two most cited reasons for vaccine refusal. Other commonly cited reasons include newness of the vaccine, and the belief that a COVID-19 vaccine is unnecessary.
- A recommendation to get the vaccine by a healthcare provider (e.g., doctor) had a positive impact on vaccine intention in five studies (15, 22, 24, 38, 39).
- Conspiracy beliefs were associated with decreased intentions to vaccinate (26, 33, 40, 41).

Vaccine Preferences

- 48% of Canadians were uncomfortable about receiving a different brand of vaccine as their second dose, whereas 46% were comfortable and 6% were unsure. Of those who received AstraZeneca as

their first dose, 50% preferred to receive AZ as their second dose, 32% preferred another brand as their second dose, and 18% were unsure (12).

- A study in May 2021 demonstrated that most felt comfortable with the Pfizer (93%) and Moderna (89%) vaccines while less were comfortable with Johnson and Johnson (49%) and AstraZeneca (35%) vaccines. Women and those aged 55+ were more uncomfortable with the AstraZeneca (AZ) and Johnson and Johnson (J&J) vaccines compared to men and those <55. Of those who were uncomfortable with the AZ and J&J vaccines, 40% of women and 31% of men reported they would still accept these vaccines if offered (16).

Incentives to Vaccinate

- Financial incentives (monetary, vouchers, complimentary items, draws for prizes, discounts) were not reported to increase the likelihood of accepting a vaccine in a study conducted in Manitoba (between 7-84% of respondents stating the incentive would not make them more likely to vaccinate). However, 70% would be concerned if only vaccine hesitant individuals received large ($50-100) incentives (42).
- A second survey conducted across Canada demonstrated that 50% of respondents supported vaccine incentives such as lotteries, 36% opposed incentives, and 14% were unsure. Support for incentives was highest in Quebec and among those aged 18-34 and lowest among those aged 55+ and rural residents (6).

Vaccine Attitudes

- Vaccine passports have high support in Quebec with 72-73% of residents in favor (9, 43).
- 61% of respondents now agree that Canada should have vaccine passport, an increase from 54% in April (44).
- Four studies demonstrated high support for showing proof of vaccination when traveling by plane (71-82%), events with large crowds (67-75%), attending in-person university (71%) and lower support for showing proof of vaccination to stay in a hotel (68%), go to work (55-68%), or go to public places such as restaurants, bars, and movie theatres (35-64%) (6, 8, 9, 45).
- Of those who were vaccine hesitant, 7-18% of respondents across two surveys reported they could be swayed by the ability to travel, attend sporting or cultural events, or visit loved ones (11%) (45, 46).
- Of those who received an AstraZeneca vaccine, 2% fully regret getting it and 66% have serious second thoughts or doubts (16).
- 66% of Canadians wanted full vaccination (two doses) as a requirement to allow people to cross the USA-Canada border (6). Another survey indicated that 69% wanted to wait until at least 75% of Canadians were fully vaccinated before opening the Canada-USA border (7).
- Support for mandatory vaccination was 53% for the general population and 81% for healthcare workers. The highest support was demonstrated among those aged 55+ (6).
- 51-55% believed that Canada has done a good job procuring vaccine doses (13, 29).
- 71% of respondents were comfortable with how the Manitoba government was determining priority groups for early vaccination in January 2021 (47).

- Approval of the overall vaccine rollout in Alberta was split, 48% were satisfied and 43% were dissatisfied in study conducted in January 2021. For the order of priority groups established by the government, 64% were satisfied and 28% were dissatisfied (48).
- There is currently no evidence on attitudes or interest in a booster or third dose of the vaccine.

Post-Vaccine Behaviors

- 76% of those who were unwilling or unsure about vaccination were planning on resuming everything they did before with no hesitation compared to 34% of those with their first dose or 27% with both doses (8).
- 53% of respondents agreed that people vaccinated against COVID-19 should be able to gather and no longer wear masks in public, 41% disagree, and 6% did not know (9).

COVID-19 VACCINE ATTITUDES OF HEALTHCARE WORKERS

Evidence on COVID-19 vaccine attitudes of healthcare workers (HCWs) was identified in seven studies. All studies targeted HCWs including nurses, doctors, and personal support workers. The most recent studies were conducted in January 2021. High level points are listed below and detailed outcomes for each study are located in the Appendix (Table 3).

- The two most recent studies conducted in January 2021 showed that intention to vaccinate in HCWs ranged between 80-82% (49, 50).
- A participants' acceptance or rejection of a COVID-19 vaccine was not different between those employed within the healthcare sector compared to those not in the healthcare sector in one study (32).
- Three studies demonstrated that male HCWs are more likely to intend to vaccinate than female HCWs (19, 32, 50).
- The proportion of those likely to get the COVID-19 vaccine was directly related to older age (19, 32, 49, 50), the likelihood of receiving an influenza vaccine (19, 50, 51), higher education (49), and an individuals' perceived risk of COVID-19 infection (50).
- The main concerns about vaccination include safety, efficacy, insufficient knowledge about the vaccine, side-effects, speed of vaccination development, and believing that vaccination was not necessary (19, 32, 49-51).
- A study of social service employees supporting individuals with intellectual disabilities in Ontario found that Indigenous, First Nations, and Metis (aOR 1.73, 95% CI: 0.67- 4.43), Latin (aOR 1.22, 95% CI: 0.21-7.24), and mixed ethnicities (aOR 1.11, 95% CI: 0.27-4.55) were more likely to refuse a vaccine compared to European ethnicity (50).
- In a study of 8634 non-physician HCWs in Ontario, 80.4% stated they intend to vaccinate. HCWs were more likely to intend to vaccinate if direct financial supports such as paid sick days were provided (49). Those who identified as Filipino (OR 1.07, 95% CI: 0.41-2.76, P<0.001), Caribbean (OR 3.20, 95% CI: 1.52-6.75, P<0.001), or other (OR 1.44, 95% CI: 0.93-2.22, P<0.001) ethnicity were more likely to refuse a vaccine compared to those who identified as European (49).

- In a 2020 study of personal support workers, 64.2% of respondents intend to vaccinate when it is available, 16.2% refuse to vaccinate, 10.7% are unsure, and 8.9% will only take the vaccine if it's mandatory. The majority (71.7%) do not believe there is enough clear education on the vaccine (52).

COVID-19 VACCINE ATTITUDES OF HIGH-RISK POPULATIONS

It is important to develop evidence-based strategies to target high-risk populations for vaccination. This includes older individuals, those with substance use disorders, those who are pregnant or breastfeeding, people experiencing homelessness, and vulnerable communities. One study was identified on COVID-19 vaccine attitudes in older adults conducted in May 2020. High level points are listed below and detailed outcomes for the study are located in the Appendix (Table 4).

- There is a severe lack of evidence on high risk populations in Canada. Previous versions of this report included studies on high risk populations from the other Five Eye countries (Australia, New Zealand, UK, USA) to complement the lack of Canadian studies (11).
- Intention to vaccinate was high (79.5%) in one study conducted in May 2020 looking at older adults (65+) (35).
- Willingness to receive a COVID-19 vaccination was positively associated with male gender and having at least one chronic condition ($P<0.05$) (35).

COVID-19 VACCINE ATTITUDES OF LGBTQ+ INDIVIDUALS

Four studies were identified on COVID-19 vaccine attitudes in LGBTQ+ individuals. All four studies were conducted between August-December 2020, prior to vaccine rollout. High level points are listed below and detailed outcomes for the studies are located in the Appendix (Table 5).

- Four studies demonstrated that LGBTQ2+ were more willing to accept a vaccine compared to non-LGBTQ2+ (20, 22, 37, 53).
- LGBTQ2+ individuals were 6-11% more willing to accept a vaccine compared to non-LGBTQ2+ (20, 53). The third study from British Columbia indicated that non-binary, pansexual, gender queer, agender, two-spirit or other were significantly more likely (OR 3.04, 95% CI: 1.08-8.55, $P<0.04$) to receive a vaccine compared to heterosexual women (22).

COVID-19 VACCINE ATTITUDES OF PARENTS

Vaccine attitudes in parents were explored in seven studies. Three of the studies were conducted in the first half of 2021 and the remaining three in 2020. High level points are listed below and detailed outcomes for the studies are located in the Appendix (Table 6).

- Two studies reported parents were more willing to accept a COVID-19 vaccine for themselves than for their children (54, 55).

- A longitudinal study in Quebec revealed that 87% of parents intend to vaccinate their children, up 1% from June (1).
- In a survey conducted in May 2021 of 70 parents or guardians of children aged 12-17, 15% were not sure if they would vaccinate their children, and 13% would not vaccinate their children (42).
- A study of 380 parents with children aged 2-17 in Montreal revealed that parents were 61% very likely, 25% somewhat likely, 9.2% somewhat unlikely, and 4.5% very unlikely to have their child vaccinated. Visible minority parents were more likely to reject a vaccine for their children compared to non-visible minority parents (32.9% vs. 9.5%) (56).
- Parental and child vaccine intentions are highly correlated with each other, with parents who were intending to take a vaccine more likely to intend to vaccinate their children (42, 54). Similar to the general population, parents from lower-income households (42, 57), who are younger (58), less educated (57), and have a history of not accepting other vaccines (57, 58) were less likely to intend to vaccinate their children.

COVID-19 VACCINE ATTITUDES OF IMMIGRANTS

Evidence on COVID-19 vaccine attitudes of immigrants was identified in six studies. Two were conducted in 2020 and four in 2021. High level points from 2021 studies are listed below and detailed outcomes are located in the Appendix (Table 7).

- Vaccine hesitancy was higher amongst Black and non-Black Canadians born in Canada compared to those born outside of Canada (5).
- Non-permanent residents were more unlikely to vaccinate (11%) compared to non-immigrants (5%), immigrants living in Canada for more than 10 years (4%), and among immigrants living in Canada for less than 10 years (3%) (3).
- A study conducted in Saskatchewan revealed those who were born outside of Canada and living in Canada less than 20 years were more vaccine hesitant compared to those born in Canada (RRR 3.14, 95% CI: 1.56-6.34) (4).

COVID-19 VACCINE ATTITUDES OF INDIVIDUALS WITH COMORBIDITIES

One study with evidence on COVID-19 vaccine attitudes in individuals with comorbidities in Canada was identified. High level points from this study with evidence from October 2020 are listed below and detailed outcomes for this study are located in the Appendix (Table 8).

- There is a severe lack of evidence on individuals with comorbidities in Canada. There was a range of comorbidities found in literature from the other Five Eye countries (Australia, New Zealand, UK, USA) including obesity, hypertension, chronic respiratory or autoimmune diseases, HIV, and intellectual and developmental disabilities. Previous versions of this report can be accessed for more information on these populations to complement the lack of Canadian studies (11).

- In October 2020, 64.6% of those who are overweight or obese were comfortable receiving a vaccine and 35.4% were hesitant (55). Comfort levels in receiving the vaccine were positively associated with male gender, having more comorbidities, having lower depression scores, not practicing physical distancing, and past acceptance of influenza vaccinations (55).

COVID-19 VACCINE ATTITUDES IN CANADA COMPARED TO THE GLOBAL POPULATION

The comparison of COVID-19 vaccine attitudes in the general population across different countries around the world was reported in six articles. Only studies that included Canada and reported outcomes by country were included. The most recent studies were conducted in January 2021. High level points from the most recent studies are listed below and detailed outcomes for all other studies are located in the Appendix (Table 9).

- As of January, countries with the highest intentions to vaccinate (63-77%) included the UK, Denmark, and the Netherlands. Intention to vaccinate in Canada was 55% (59).
- Increases in intention to vaccinate between November and January were seen in Spain (24.1%), UK (23.2%), Sweden (22.7%), Finland (20.4%), Netherlands (18.5%), Italy (15.4%), Norway (14.6%), France (14.2%), Denmark (13.3%), Germany (13.0%), Canada (11%), and Japan (0.8%) (59).
- In 11/15 countries there was a significant decrease in the proportion of individuals who reported concern about the side-effects of a vaccine. In Canada, this worry decreased from 53.3% in November to 47.9% in January (59).

Methods

Prior to the initiation of this rapid review, a pre-defined rapid review protocol was developed to ensure the methods were reproducible, transparent, and consistent. The protocol is available upon request. This rapid review will be kept evergreen and updates will contain key research articles published up to the latest search date.

Publications and Pre-prints

A daily scan of the literature (published and pre-published) is conducted by the Knowledge Synthesis team in the Emerging Science Group, Public Health Agency of Canada. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square, and COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The cumulative scan results are maintained in a Refworks database and an excel list that can be searched. Details on this search strategy are available upon request. From this database and excel list, article titles and summaries will be systematically searched for the following key words: ("vaccin*" OR "immuni*") AND ("accept*" OR "hesitan*" OR "preference" OR "confidence" OR "intent*" OR "willing*" OR "readiness" OR "behavio*" OR "knowledge" OR "attitude*" OR

"belief*" OR "believe*" OR "perception" OR "influence*" OR "reject*" OR "refus*" OR "oppos*" OR "consent*" OR "fear" OR "motiv*" OR "anti vax*" OR "antivax*" OR "trust*" OR "mistrust*" OR "anti vaccin*" OR "pro vaccine*" OR "provax*" OR "pro vax" OR "decision*" OR "decid*" OR "uptake"). The original search was conducted on October 16, 2020. The first update was conducted on November 30, 2020, the second update on January 5, 2021, the third on February 3, 2021, the fourth on March 2, 2021, the fifth on April 2, 2021, the sixth on May 3, 2021, the seventh on June 3, 2021, the eighth on July 2, 2021, and the ninth on August 4, 2021.

Grey Literature

A grey literature search was conducted to compliment the database search. In prior versions the grey literature search was extended to include research from Australia, New Zealand, the United States, and the United Kingdom. The grey literature search is now exclusively focused on Canadian research. A detailed list of websites searched is available in the protocol. The original grey literature search was conducted on November 5-6, 2020. The first updated grey literature search was conducted on December 9-10, 2020, the second on January 4, 2021, the third on February 1-2, 2021, the fourth on March 7, 2021, the fifth on April 13-22, 2021, the sixth on May 3-7, 2021, the seventh on June 9-11, 2021, the eighth on July 28-30, 2021, and the ninth on July 27-30, 2021.

Quality of Survey Instrument

Three criteria which determine the quality of the survey instrument were reported. These include the availability of the survey tool in the report, the use of formative research to design the survey, and evidence of pre-testing the survey. A yes or no was provided for each criteria. If the information was not reported, the answer no was selected. These criteria evaluate the degree to which the survey items evaluate the theoretical concepts the survey is focused on, are comparable to other surveys and whether the instrument was comprehensive, clear and valid when applied to the target population. There is an increased risk of bias when these features are missing (60).

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX: EVIDENCE TABLES

VACCINE UPTAKE

Table 1. Evidence of vaccine uptake (n=1)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
VACCINE UPTAKE		
HEALTHCARE WORKERS		
Dzieciolowska (2021) (10) Cross-sectional study Canada Dec 2020	Vaccine uptake was evaluated through an online survey in 2,761 nurses, physicians, orderlies, hospital administration working in 17 health institutions in Montreal to determine factors that are predictive on uptake. All HCWs were offered a vaccine. Question Topics: 1) Vaccine uptake 2) Vaccine hesitancy	• 80.9% of those offered a vaccine accepted and 19.1% refused. • Multivariate analysis revealed that men (aOR 1.62, 95% CI: 1.16-2.26), those aged 50-59 (aOR 1.62, 95% CI: 1.07-2.44) or 60+ (aOR 3.28, 95% CI: 1.74-6.18), had occupational contact with COVID-19 patients (aOR 3.88, 95% CI: 2.29-6.58), or worked in rehabilitation centers (aOR 1.76, 95% CI: 1.17-2.66) were more likely take a vaccine when offered. • The most common concerns or reasons for refusal among those who did not accept a vaccine were the newness of the vaccine (82%), preferred that others get vaccinated first (77%),

	Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	felt they lacked information about the vaccine (74%), and that they did not have enough time to make a decision (60%). • 74.1% of those that declined a vaccine reported they will accept a vaccine in the future with 53.2% wanting to delay a few months and 31.9% wanting to wait a year. • Those who never plan on accepting a vaccine were more likely to cite not trusting experts or pharmaceutical companies, preferring natural immunity, belief that the risk of vaccination outweighed risk of COVID, or that they had a past poor vaccine reaction.

CANADIAN GENERAL POPULATION

Table 2. Evidence of vaccine attitudes of the general public (n=45)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
Longitudinal studies (n=9)		
Leger (2021) *unpublished* (6, 12, 44, 61-67) Longitudinal study Canada & USA Nov 2020 & Jan-Jul 2021	An online survey of Canadian and American adults (18+) was conducted to evaluate vaccine perceptions and intentions to vaccinate. Wave 1: Nov 2020, 1516 Canadians and 1002 Americans Wave 2: Jan 2021, 1516 Canadians and 1003 Americans Wave 3: Feb 2021, 1535 Canadians and 1002 Americans Wave 4: Feb 2021, 1,532 Canadians and 1002 Americans Wave 5: Apr 2021, 1,504 Canadians and 1,002 Americans Wave 6: Apr 2021, 1,548 Canadians and 1,003 Americans Wave 7: May 2021, 1,529 Canadians, 1,003 Americans	**Wave 14** • In a July 2021 survey, 66% of Canadians want full vaccination (two doses) as a requirement to allow people to cross the USA-Canada border. • 50% of respondents supported vaccine incentives such as lotteries, 36% opposed incentives, and 14% did not know. • Support for incentives was highest in QC and among those aged 18-34 and lowest among those aged 55+ and rural residents. • Most (66%) Canadians believed that those who are medically able to be vaccinated have a responsibly to be vaccinated and should have greater freedoms than those who do not get vaccinated, whereas 26% believe that it would be unfair to place restrictions on the unvaccinated even if medically able to get vaccinated. • 53% think COVID-19 vaccines should be mandatory with the highest support among those aged 55+ and lowest in AB and those aged 18-34.

	Wave 8: May 2021, 1,529 Canadians, 1,003 Americans Wave 9: May 2021, 1,624 Canadians and 1,002 Americans. Wave 10: May 2021, 1,624 Canadians and 1,002 Americans. Wave 11: June 2021, 1,539 Canadians, 1,004 Americans Wave 12: June 2021, 1,542 Canadians and 1,001 Americans Wave 13: July 2021, 1,518 Canadians, 1,003 Americans *new* Wave 14: July 2021, 1,529 Canadians, 1,001 Americans *new* Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Most respondents feel comfortable going to outdoor gatherings (73%), eating on patios (72%), going to outdoor shows or sporting events (65%), going to work (56%), indoor gatherings with family/friends (55%), and eating in a dining room of a restaurant (51%) with the possibility of unvaccinated persons present. • Fewer respondents were comfortable going to in person class (48%), going to spas (47%), going to the cinema (45%), indoors shows or sports (41%), using public transit (40%), the gym (38%), fly on an airplane (37%), or go to a bar/nightclub (32%) with unvaccinated persons. • 81% respondents support mandatory vaccination for healthcare professionals or hospital employees with highest support among QC residents and those aged 55+. • 71% want vaccine passports for air travel. • 35% would like a vaccine passport required for patio/terrace dining. • In general, 58% of support vaccine passports for essential and non-essential activities, 30% disagreed, and 13% did not know. **Wave 13** • 76% were either very or somewhat confident that vaccination will protect against variants including Delta with 9% not confident at all and 13% not very confident. • Confidence in the vaccine as protection against variants is highest among those aged 55+ and suburban residents. • The groups with lowest confidence in vaccines as protection against variants are those residing in AB, aged 35 to 64, and living in rural areas. **Wave 12** • Canadians intention to be vaccinated or who have been vaccinated increased to 88% from May. • The percentage of those who did not intend to vaccinate was highest in MB and SK (18%)

		followed by AB (16%), among those aged 18-34 (14%, decreased from 18% at last polling), and among rural residents (16%, decreased from 22% at last polling). • Belief that vaccines are dangerous stayed at 7% since May (81% believe vaccines are safe and 12% do not know). **Wave 11** • Canadians intention to be vaccinated or who have been vaccinated held steady at 86% (no change from May). • The percentage of those who did not intend to vaccinate was highest in AB (20%) followed by Atlantic Provinces (19%), among those aged 18-34 (18%), and among rural residents (22%). • 89% certainly or probably will receive a second dose, 1% probably will not, 9% already have received a second dose, and 1% were unsure. • 3% of those who reside in QC and 3% of those aged 18-24 indicated they either probably will not or certainly will not get a second dose. • 48% of Canadians were uncomfortable about receiving a different brand of vaccine as their second dose whereas 46% were comfortable and 6% were unsure. • Those in MB/SK (34%), those aged 35 to 55 (25%), and rural residents (26%) had the highest levels of not being comfortable with a different vaccine as a second dose. • 50% of those who had a first dose of Astra-Zeneca would prefer getting a second dose of Astra-Zeneca compared to 32% who would like a second dose of another brand, and 18% who did not know. • Belief that vaccines are dangerous increased 1% to 7% since May (82% believed vaccines are safe and 11% did not know). **Wave 10**

		• Canadians were split 50-50 on whether they were comfortable if some of their colleagues were not vaccinated. • Discomfort with unvaccinated coworkers was highest in BC (62%) and 60% of Atlantic Canada and MB/SK were comfortable. • Older (55+) Canadians were less comfortable with unvaccinated coworkers (52% uncomfortable) along with urban residents (53% uncomfortable) compared to rural residents (44% uncomfortable). **Wave 9** • 51% of respondents felt the vaccine campaign in their province was proceeding about the same as other provinces. QC residents felt they were doing better than other provinces whereas ON and AB felt vaccinations were slower. • Canadians had high support for showing proof of vaccination when traveling by plane (82%), attending events with large crowds (75%), attending in-person university (71%) and had lower support for going to their place of work (68%), staying in a hotel (68%), and dining in a restaurant (64%). Support for showing vaccination was consistently higher among those aged 55+. • Since earlier polling in May there was a 4% increase (to 86%) of those who had been vaccinated or intended to get a vaccine. • Provinces with the highest combined level of vaccination or intention to get a vaccine was in QC (90%), followed by AB (87%), Atlantic provinces (86%), BC (85%), and MB/SK (84%). • Belief that vaccines are safe and should be given has stayed steady at 81% but those who did not know increased 1% to 12%. • Waves 1-8 summarized in previous versions of this report.
Angus Reid (2021)	Vaccine intentions and perceptions were analyzed in Canadian adults (18+) using an online survey.	**Wave 12** • In a July 2021 survey, 69% of Canadians wanted to wait until at least 75% of Canadians were fully

unpublished (7, 8, 13, 16, 23, 24, 27, 28, 31, 68, 69) Longitudinal study Canada Jul, Sept, Dec 2020 & Jan-Feb and May-Jul 2021	Wave 1: Jul 2020, n=1519 Wave 2: Sep 2020, n=1660 Wave 3: Dec 2020, n=1603 Wave 4: Jan 2021, n=1580 Wave 5: Feb 2021, n=1201 Wave 6: Mar 2021, n=1748 Wave 7: Apr 2021, n=NR Wave 8: Apr 2021, n=1594 Wave 9: May 2011, n= 1,319 Wave 10: June 2021, n=4,948 Wave 11: July 2021, n= 2,040 *new* Wave 12: July 2021, n= 2,040 *new* Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	vaccinated before opening the Canada-USA border, 38% would be okay with 50% of Canadians being vaccinated, and 22% say right away. • 53% of respondents reported they were not concerned about becoming sick but 9% reported they would feel less worried if 70% of eligible Canadians were vaccinated. • 54% felt the timing was right to remove the requirement for 2 weeks of isolation for returning double vaccinated Canadians, 25% felt it was too soon, and 21% felt it took too long. **Wave 11** • 86% of respondents reported they would get vaccinated right away or have had at least one dose, up 2% from June. • 8% would not get vaccinated down 1% since June. • Levels of those who are uncertain or would like to eventually get vaccinated but want to wait remained steady from last polling at 3%. • AB continued to lead the way in the levels of unwillingness to vaccinate at 22%, an increase of 5% since May. The next highest provinces are SK and MB both at 15% unwilling. • 52.9% of the 315 respondents who received a different brand to their first dose felt total comfortable with receiving different brands, 26.5% were fairly comfortable, 18.9% were a little uncomfortable, and 3.8% are very uncomfortable. • 23% reported they were very likely to spend time with someone who is unvaccinated, 31% were pretty likely, 30% were unlikely, and 16% very unlikely. Those aged 18-24 were more likely to report being very likely to spend time with the unvaccinated. • 49% of respondents felt comfortable asking about others vaccination status, 22% felt it was not okay, and 29% felt it depended on who it was. Those who were unwilling or unsure about vaccination, those who voted Conservative in the past, and

		those who were younger were less comfortable with asking about vaccination status. • 76% of those who were unwilling or unsure about vaccination were planning on resuming everything they did before with no hesitation compared to 34% of those their first dose or 27% with both doses. • Vaccine passport requirements had generally high support for activities like boarding a plane (75%), international travel (75%), travel to the US (73%), attending events (67%), at work (61%), and public places like restaurants (59%). **Wave 10** • 84% have received at least one shot or will get vaccinated as soon as possible (an increase of 2% from May), 4% will get a vaccine but wish to wait (down from 6%), 9% will not get a vaccine (no change), and 3% were unsure (no change). • Vaccine hesitancy remains highest in AB and SK (18%). This has increased 1% in AB and decreased 6% in SK since May. • 57% of respondents would like equal emphasis on distributing first and second doses, 26% would prefer priority of getting all eligible first doses administered, and 16% would like the focus to be on second doses and circling back to first doses. Support for focusing on administering first doses was higher among those waiting for vaccination (39%) and among those aged 18-24 (40%). • Canadians are supportive of continuing vaccinations until everyone in Canada has been vaccinated (72%) with 18% wanting to shift focus to at risk populations globally and 10% were unsure. • Respondents felt the second dose vaccinations were progressing as well as could be expected (49%) with nearly equal split between feeling it was taking too long (27%) and that it was going at great pace (24%). 55% of QC residents felt that

		things were going great whereas 40% of ON residents felt things were moving too slowly. • 51% felt Canada has done a good job of securing vaccine doses and 41% felt it had been a poor job. However, 60% and 69% still had confidence that the federal and provincial government can manage vaccine distribution, respectively. **Wave 9** • 82% of respondents have either received a vaccine or wish to get a vaccine as soon as possible, up from 71% in April. • Fewer respondents report being unsure about vaccinations (3% down from 13%), wanting to wait before receiving a vaccination (6% down from 13%), or report not wanting a vaccine (9% down from 13%) compared to April responses. • 53% of respondents have received at least one dose, an increase of 36% since April. • Vaccine hesitancy is highest in SK (24%) with the level remaining stable (22% in April and 26% in January. • Vaccine hesitancy dropped dramatically in AB from 45% in January to 25% in April to 17% in May. • Hesitancy in BC, MB, ON, QC, and the Atlantic provinces varied between 10-12% in May. • Vaccine hesitancy was highest in males aged 35-54 (18%) followed in by females aged 18-34 (15%). • Of those that received an AstraZeneca, 2% fully regret getting it and 66% have serious second thoughts or doubts. • Canadians remain very comfortable with Pfizer and Moderna (93% and 89%, respectively) but became less confident in AstraZeneca (52% in April to 35% in May) and Janssen (54% to 49%). • Unvaccinated men are more comfortable than women to receive AstraZeneca (29% vs 36% extremely uncomfortable) however 40% women

		would take a vaccine they are uncomfortable with compared to 31% of men. • Wave 1-8 summarized in previous versions of this report.
Engage Manitoba (2021) *unpublished* (46, 70) Longitudinal study Canada Jan-Jun 2021	A series of online surveys in Manitoba were implemented to assess vaccine intentions within the Safely Restoring Services in Manitoba Survey. Survey 1: Jan 10-15, n=73,351 Survey 2: Feb 4-9, n= 33,687 Survey 3: Feb 25-Mar 2, n=26,909 Survey 4: Mar 18-23, n=31,776 Survey 5: Jun 4-8, n= 33,904 Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	**Survey 5** • 86% have received at least one dose of a vaccine (up from 9% in survey 4). • 2% have booked their first dose appointment, 2% will get the vaccine but are in no rush (down from 13%), 4% are unsure if they will get a vaccine (down from 12%), and 5% will not get a vaccine (down from 10%). • Of those who were not sure or do not intend to be vaccinated, very few would be swayed by the ability to travel within Canada (9%), attend sporting events or cultural events (7-9%), visit facilities or events (10%), or visit loved ones (11%). **Survey 4** • 9.0% of respondents have already received a vaccination (up 4% since survey 3). • 56% intend to sign up for a vaccination as soon as they are eligible (up 1.9%). • 13% report that they want a vaccine but are not in a rush (down from 16.2%). • 12% are unsure if they will get a vaccine when it's available (down from 14.2%). • 10% would refuse a vaccine (down from 10.5%). • Approval of the Manitoba governments approach to vaccinations is high in the latest survey with 33% strongly approving, 47% somewhat approving, 13% somewhat disapproving, 7% strongly disapproving.
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021),	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in	**July** • In a July 2021 survey, 91% of respondents have either had one or both doses of vaccines, 2% intend to vaccinate, and 7% have no intention.

INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021) *unpublished* (1, 9, 29, 32-34, 40, 43, 71) Longitudinal study Canada Apr 2020 – Jun 2021	Quebec. Number of participants was not clearly stated (~3300 each collection period). There were multiple collection periods, one in Apr-May 2020, Sep and Dec 2020, Apr-Jul 2021 *new*. Articles in French. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Of the unvaccinated, 18% intend to vaccinate, 69% have no intention, and 13% were unsure. • Among the unvaccinated, those who had no intention to vaccinate were more likely to be women (70%), aged 25-34 (73%) and 35-44 (70%), those with secondary or less (72%), workers in a healthcare environment (87%), full time workers (76%), households with minors (78%), non-immigrants (72%), others as compared to French (70%), those in the highest deprivation quintile (72%), rural villages (72%), those not worried about getting COVID-19 (76%), those who do not always follow preventative measures (72%), have conspiratorial world views (74%), and never check social media on COVID-19 (74%) or check several times a day (73%). • The top reasons to not vaccinate were concern about side effects (21%) followed by fear of its newness (17%) and lack of confidence in vaccines in general (17%). • Agreement over whether the COVID-19 vaccine is danger free was not clear cut with 63% agreeing that it is danger free and 26% disagreeing. • 7% reported that vaccination is incompatible with their religious beliefs but was slightly higher among those aged 18-24 (10%), 25-34 (12%), 35-44 (10%), and those with no intention to vaccinate (38%). • 56% are concerned about vaccine effectiveness against variants whereas 39% are not, and 5% are not sure with little difference among those with different vaccine intentions. • 53% of respondents agreed that people vaccinated against COVID-19 should be able to gather and no longer wear masks in public, 41% disagree, and 6% did not know. • 75% were in support of vaccine passports for access to events and places. • 71% (1% increase from June) disagreed that given vaccination rates and cases it's less important to

		follow preventative measure whereas 27% agreed, and 3% did not know. • Outcomes on parental intention to vaccinate is located in Table 6. **June** • 49% agreed that vaccinated adults should be able to gather without masks in private, 44% disagreed, and 6% were unsure. • Almost half of respondents felt that vaccinated people should be able to gather without masks in private (49%) but also agree that masks should be worn outside with people they don't live with (56%). • Vaccine passports have high support with 72% in favour (23% disagreed and 4% were unsure). • 73% of respondents disagreed that it is important to follow protective measures based on the rate of vaccination and the decrease in COVID-19 cases. **May** • 74% of respondents who have not been vaccinated yet intend to get a vaccine, a 3% drop since late April. 18% do not intend to get a vaccine (a 4% increase), and 8% do not know (1% decrease). • Intention to vaccinate was lowest in those aged 25-34, women, those without secondary education, who were unemployed, more deprived, were not worried about getting COVID-19, those with conspiratorial views, and those who check social media once a week or less. • Households with minors had lower intentions to vaccinate compared to single person households, and households without minors. • Immigrants were more hesitant and unsure about receiving a vaccine compared to non-immigrants. • The top three reasons among those who were not intending to vaccinate included worry about side effects, lack of confidence in vaccines in general, and the newness of the vaccine.

		• 28% of those who do not intend to vaccinate believe that it is incompatible with their religious beliefs or personal principles. **Earlier** • 77% of respondents who have not been vaccinated yet intend to get a vaccine, a 1% drop since early April. 14% do not intend to get a vaccine (no change), and 9% do not know (1% increase). Intention has increased 7% since December. • Intention to get a vaccine was higher among men compared to women (78% vs 76%), older respondents (79% for those 60+ vs 75% for those 18-25), and among those with university degree (85% of those with university, 78% with college). • Intention to vaccinate generally increased as communities increased in size, from living in small villages less than 10,000 (71%), towns 10,000 to 100k (73%), greater Montreal area (81%) and Montreal (79%). • 68% disagree with the statement "people vaccinated against COVID-19 should have the right to have private gatherings and no longer wear a mask in public" whereas 25% agreed and 7% were unsure. • In December those with low intentions to vaccinate were concerned about side effects (27%), the newness of the vaccine (24%), and not trusting vaccines in general (24%). • Those holding conspiratorial world views were less likely to accept a vaccine (51% vs. 76%). • Agreement with compulsory vaccination continues to trend downwards with 54% agreeing in December.
Government of Manitoba (2021) *unpublished* (42)	An online research panel of 600 Manitobans were surveyed to understand attitudes towards vaccination and possible incentives to increase uptake.	• 87% have received a vaccine or intend to be vaccinated (74% received and 13% intend), and increase of 11% from April. • 5% will get a vaccine but were not in a rush (down from 12%), 5% were unsure if they will get a

Longitudinal study Canada May 2021	Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	vaccine (down from 7%), and 4% will not get a vaccine (down from 5%). • From April to June there was an 18% drop in the number of people strongly approving of Manitoba's vaccine distribution (42% to 24%), 49% somewhat approve (up from 43%), 17% somewhat disapprove (up from 11%), and 10% strongly disapprove (up from 4%). • 31% of respondents felt much more positive about COVID-19 vaccine now then when first introduced, 19% felt slightly more positive, 45% felt the same, 3% felt slightly more negative, and 2% felt much more negative. • 55% felt that whether they got the vaccine or not should be a choice, 42% felt that it should not be a choice, and 3% were unsure. • Those who would promote vaccination tended to be younger than 30 or over 65 and believed that adults should have all their regular vaccines. • The types of information that were the most likely to influence decision to vaccinate included information about possible side effects (42%), being able to choose the vaccine (42%), information about testing (41%), and information about how the vaccine works (36%). • The least persuasive type of information was hearing stories from celebrities who got their vaccine (90% unlikely to impact). • Women would be the most influenced by being able to choose the vaccine. • Residents of Winnipeg were more influenced than those in rural areas by getting a vaccine from a family doctor/pharmacist, speaking to their family doctor/pharmacist, having someone come to their home, and hearing stories from celebrities. • Manitobans were largely not swayed by community incentives such as being able to travel without having to isolate (50% no more likely to vaccinate), being able to visit long term care homes without restrictions (52% no more likely),

		entry into provinces or countries (48% no more likely), being able to attend large events (60% no more likely), attend larger gathering (54% no more likely), certain businesses/facilities to those that are vaccinated (61% no more likely). • Those aged 30 to 44 were more likely to be influenced by being able to attend larger gatherings (community, faith, or personal). • Financial incentives (monetary, vouchers, complimentary items, draws for prizes, discounts) were not reported to increase the likelihood of accepting a vaccine (between 75% and 84% stating they are not more likely by any financial incentive). • 70% of respondents were concerned if only hesitant individuals received large ($50-$100) incentives. • Outcomes on intention to vaccinate in parents can be located in Table 6.
Statistics Canada (2020) & Statistics Canada (2021) *unpublished* (17, 53, 72) Longitudinal study Canada Sep 2020 – Feb 2021	An online survey conducted by Statistics Canada as part of the Canadian Community Health Survey (CCHS) assessed Canadians behaviors to safeguard their own health as well as the health of others. In the September survey, a question about vaccine intentions was added. The most recent report captures 25,321,400 responses from individuals aged 12+. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	**Jan-Feb 2021** • 82.3% of respondents were very or likely to get a COVID-19 vaccine. • Vaccine intention was highest in those over 65 years (88.1%) with a decreasing level of intention in those aged 12-17 (71.0%). • Vaccine intention was similar between males and females (82.8% vs 81.9%, respectively). **Sept-Dec 2020** • Over the sampling period 77% were willing to receive a vaccine. This represents an increase from Sept (75.5%) to Oct (74.8%), and Nov/Dec (80.3%). • Vaccine intentions were highest in Prince Edward Island (89.1%), Nova Scotia (81.5%), and British Columbia (81.4%). Vaccine intention was lowest in Prairie provinces (75.2%) • Men were more likely to vaccinate then women (77.9% vs 75.8%). • The highest intentions among visible minorities were Japanese (86.5%), Korean (85.6%), South Asian (82.5%), Chinese (79.3%), visible minority not indicated/multiple (79.1%), Southeast Asian

		(78.3%), West Asian (78.3%), Filipino (75.1%), Arab (68.1%), Latin American (66.0%), and Black (56.6%). Non-visible minority's intention to vaccinate was 77.6%. • Older visible minorities were more likely to vaccinate than those 12-64 (77.4% vs 74.6%). • Intention to vaccinate among Indigenous respondents was 71.8% which was significantly less than Non-Indigenous respondents (77.1%). 74.2% of First Nations living off reserve were willing to vaccinate compared to 67.8% of Métis and 72.5% of Inuit*. • Older Indigenous people (65+) were more likely to want a vaccine compared to younger (74.9% vs 71.3%). • Outcomes on intention to vaccinate in LGBTQ+ and immigrants can be located in Tables 5&7. *Use with caution. Coefficient of variation (CV) from 15.1% to 35.0%.
Impact Canada (2020) *unpublished* (15) Longitudinal study Canada Apr 2020 – Feb 2021	Vaccine confidence and hesitancy in the Canadian context was explored through the implementation of the World Health Organization (WHO) Behavioural Insights (BI) Tool on COVID-19 in eight waves of adults (18+) using the same participants where possible. Wave 1: n=2023, Wave 2: n=2,098, Wave 3: n=2,000, Wave 4: n=2,152, Wave 5: n=2,169, Wave 6: n=2,141 , Wave 7: n=2,129, Wave 8: n=2,117, Wave 9: n=2,055, Wave 10: n=2,125, Wave 11: n= 2,037 Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy	**Wave 11** • Intention to get vaccinated right away has increased to 58% (up from 49% in wave 10). 24% intend to vaccinate but would like to wait, 9% would not vaccinate, and 8% were unsure. • Those who plan to wait are mostly like to want to wait 1 to 2 months (33%). • 68% have made up their mind if they will or will not get a vaccine and 25% need more information before deciding. • The two most common reasons for vaccine hesitancy included a lack of testing or research (26%) and belief that the vaccine was not safe (15%). • 47% report that getting the most effective vaccine is the most important criteria for selecting a vaccine, followed by the vaccine that is available first (15%), and fewest side effects (12%).

	Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• 56% and 22% would like more information regarding the safety and effectiveness of the vaccine, respectively. • A vaccine recommendation from a healthcare provider would likely influence 45% of respondents. **Wave 10** • Vaccine acceptance rose slightly from wave 9 (61%) to wave 10 (65%). • Intention to get vaccinated right away has increased to 49% (up from 43% in wave 9). 31% intend to vaccinate but would like to wait, 11% would not vaccinate, and 8% were unsure. • Of those wanting to wait for a vaccine, 42% wanted to wait several months (up from 27% in wave 9). • The top reasons for wanting to wait were to ensure safety (80%) and efficacy (64%). • Those who would decline a vaccine were asked about hypothetical incentives. 58% would like assurances that the vaccine would not be a risk for exposure to COVID-19, 56% wanted a convenient booking system, and 52% wanted a convenient location. • 56% of participants stated they would vaccinate to be able to return to work, travel, or attend large gatherings. • 63% reported that their mind was made up whether to vaccine or not and 32% would like more information before they decide.
Dubé (2021) (41) *new* Longitudinal study Canada	During the first and second wave of the pandemic vaccine attitudes and intentions, and preventative behaviours were assessed in a weekly web panel of 3300 Quebec residents. This is a formal analysis of the INSPQ study with some additional information.	• In 2020, the intention to vaccinate started at 74% in April and grew to 76% until May, dropped to 66% in September before rebounding to 73% in December. • In multivariate analysis intention to vaccinate was higher in men (aOR 1.80, 95% CI: 1.56-2.06), those with college (aOR 1.37, 95% CI: 1.17-1.60) or university (aOR 2.01, 95% CI: 1.66-2.43), having or

Apr 2020-Dec 2020	Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	living with someone chronic medical conditions (aOR 1.39, 95% CI: 1.18-1.63), and those that are afraid (aOR 1.58, 95% CI: 1.32-1.89) or moderately afraid (aOR 1.51,95% CI: 1.26-1.82) of COVID-19. • Increasing age was associated with higher intentions to vaccine (age 18-24: aOR 1.86, 95% CI: 1.46-2.36, age 45-59: aOR 1.29, 95% CI: 1.08-1.53, age 60-69: aOR 2.14, 95% CI: 1.73-2.65, age 70+: aOR 3.44, 95% CI: 2.57-4.58) compared to those aged 25-44. • Those who were less deprived were more likely to intend to vaccinate compared to those in the most deprived quintile (Q1: aOR 1.53, 95% CI: 1.20-1.94, Q2: aOR 1.34, 95% CI: 1.06-1.68, Q3: aOR 1.25, 95% CI: 1.00-1.58). • Those without conspiratorial world views were more likely to vaccinate (aOR 2.68, 95% CI: 2.28-3.14) compared to those who hold conspiratorial world views.
Saskatchewan Population Health and Evaluation Research Unit (2020) *unpublished* (73) Longitudinal study Canada May-Sep 2020	An online survey was used to evaluate intention to vaccinate in residents of Saskatchewan over time. Surveys were conducted from May-Sep. The number of individuals is not stated and it is unclear if they are the same participants over time. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• From May to Sep, intention to vaccinate dropped from 84.9% to 56.5%. • Intention to vaccinate is highest in those 65-74 years of age and lowest in those under 48 years of age.
Cross-sectional studies (n=31)		
Independent Polling System of Society (IPSOS) (2021)	An online survey of 1000 Canadians (18+) analyzed perceptions about COVID-19 vaccination in the face of emerging variants.	• 62% of respondents felt that vaccination would help avoid a fourth wave in Canada however 69% were still worried about a potential fourth wave.

unpublished (74) *new* Cross-sectional study Canada Jul 2021	Question Topics: 1) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Belief that vaccination would prevent a fourth wave was highest in BC (66%) followed by SK/MB (64%), ON (63%), QC (62%), ATL (61%), and AB (59%).
Innovative Research Group (2021) *new* *unpublished* (5) Cross-sectional study Canada May-Jun 2021	An online poll of 2,838 adults with a specific over sampling of Black Canadians (n=502) was conducted to evaluate COVID-19 vaccine intentions and hesitancy. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 21% of Canadians were vaccine hesitant with higher levels among Black Canadians (33%) and non-Black visible minorities (25%) compared to White Canadians (19%). • Vaccine intentions were highest among non-Black visible minorities (32%) followed by Black Canadians (22%), and White Canadians (16%). • 60% of respondents overall have been vaccinated (65% of White Canadians, 45% Black Canadians, and 43% non-Black visible minorities). • Of those who have not received a vaccine, 48% of White Canadians would get vaccinated compared to 40% of Black and 56% of non-Black Canadians. • 54% of 25-34 old Black Canadians were vaccine hesitant. • Vaccine hesitancy was higher amongst Black Canadians and Non-Black Canadians born in Canada than those born outside of Canada. • The top reasons for hesitancy were a lack of trust/not enough testing (29%) followed by side effects/safety concerns (26%) which mirrored the top concerns of Black Canadians (21% and 23% respectively). The most dissimilar responses were seen for don't want it/my choice (7% among Black Canadians and 2% among White) and mixed messages/rumours (10% among Black Canadians and 1% among White). • Factor analysis finds trust in healthcare providers and vaccine makers, having a university education, being older than 55, confidence in how to get

		vaccinated, being able to take paid time off to get vaccinated, being in Atlantic Canada, feeling at high risk for COVID-19, and being male drive vaccine confidence for Black Canadians. • Drivers of not getting vaccinated among Black Canadians are the ability to take paid time off if they get COVID-19, concern that vaccines cause autism, and vaccine safety concerns. • 78% of Black Canadians and non-Black minorities were confident they knew how to get a vaccine but only 39% of Black and 38% non-Black minorities agree that they can take paid time off to get a vaccine. • 20% of Black and 17% non-Black minorities either strongly or somewhat agree that vaccines may cause autism compared to 9% of White Canadians.
Angus Reid (2021) *unpublished* (45) Cross-sectional study Canada May 2021	1601 Canadian adults were surveyed about their thoughts on vaccination policies (proof of and vaccine passports) online. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 79% Canadians were supportive of showing proof of vaccination for international travel (excluding the US), 78% support it for commercial flights, and 76% were supportive for traveling to the USA. • Less support was shown for having proof of vaccination for attending large public events (69%), public places such as restaurants, bars, and movie theatres (55%), and at places of work (55%). • Those who were vaccine hesitant had much lower support for proof of vaccination across all presented scenarios. • 18% of those not willing to get a vaccine would be swayed to get vaccinated if proof of vaccination was required in many scenarios.
Muhajarine (2021) *preprint* (4) *new* Cross-sectional study Canada	9,252 responses collected from 7,265 Saskatchewan adults (18+) were enrolled from landlines and online to complete an online survey regarding vaccine acceptance and hesitancy. Question Topics: 1) Vaccine intentions	• 76.1% of respondents had either been vaccinated or were willing to get vaccinated, 13.3% were vaccine hesitant, and 10.6% had refused a vaccine. • In multivariate analysis vaccine hesitancy was associated with women (RRR 2.16, 95% CI: 1.57-2.99), those with less education (no formal /completed high school RRR 2.45, 95% CI: 1.65-3.62), born outside of Canada and lived in Canada less than 20 years (RRR 3.14, 95% CI: 1.56-6.34),

Apr-May 2021	2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	having Indigenous status (RRR 1.65, 95% CI: 1.01-2.70), those with unsecure financial situations (RRR 2.2, 95% CI: 1.67-2.91), and those slightly/hardly concerned about COVID-19 (RRR 2.46, 95% CI: 1.6-3.78) compared to their counterparts. Similar trends were seen with vaccine refusal.
Leger (2021) *unpublished* (75) Cross-sectional study Canada Apr 2021	An online survey of 1004 participants in British Columbia was conducted to assess views on vaccines, vaccine passports, and vaccine rollout. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 16% reported they had received a vaccine. • 49% intend to tell everyone they know when they receive a vaccine, especially for respondents in urban areas (53%) compared to rural (40%). Fewer respondents would only tell immediate family and friends (42%). • 24% intend to share when they get a vaccine on social media. • Most don't feel they should be vaccinated before others (27%), or are jealous (25%), or anxious (25%) of others being vaccinated. • Vaccine passports had high support in international travellers coming to BC (77%) and BC travellers going abroad (75%). Support for passports for Canadians traveling within Canada (68%) and within BC (56%) was slightly lower. • Vaccine passports for any situation had higher support among those 55+. • 70% are happy with the order of vaccination prioritization in BC and 44% are satisfied with the rollout. • Support for health figures or leaders has decreased since Dec 2020 (Dr. Bonnie Henry: 65%, Adrian Dix: 58%, Dr. Theresa Tam: 53%, Justin Trudeau: 45%).
Statistics Canada (2021) *unpublished* (3, 76) Cross-sectional study	Vaccine intentions and perceptions were analyzed in the second round COVID-19 Vaccination Coverage Survey (CVCS) involving Canadian adults (18+) in the provinces using mail invites and computer assisted telephone interviews for non-responses.	**Round 2** • Vaccine coverage from highest to lowest (at least one dose) was: SK (54%), QC (47%), BC (46%), AB (46%), ON (45%), NL (43%), MB (42%), NB (40%), NS (36%), and PE (33%). • The highest levels of those unlikely to vaccinate were in MB (8%), SK (7%), BC and AB (6%), ON, QC, NB, NS, PE, NL (5%).

Canada Mar-May 2021	<u>Round 1:</u> n= 1,025 capital cites of the territories <u>Round 2:</u> n= 10,678 in 10 provinces *new* Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Intention to vaccinate was lowest among those aged 18-49 (7% unlikely to vaccinate) followed by 5% among those 50-49, and 3% among those 60+. • Men, those with less education, and those with smaller household incomes were less likely to intend to vaccinate. • The most common reasons for not getting a vaccine yet was not being in an age priority category (47%), not being able to get an appointment yet (13%), and not wanting to be vaccinated at this time (8%). • Among those not wanting to be vaccinated, the top reasons were lacking trust in the safety in the vaccine (45%) or effectiveness (30%), and not believing they are at high risk for COVID-19 (26%). • The top trusted sources for vaccine information were PHAC (84%), health scientists and researchers (70%), and provincial, territorial, regional health authorities (68%). • Outcomes for immigrants found in Table 7. **Round 1** • The majority of respondents had already received one dose (80%) with 16% likely to get vaccinated and few unlikely to get vaccinated (4%). • Respondents were more likely to have received a vaccine or were likely to be vaccinated if they has a post-secondary degree or higher (85% vs 68% for having received a vaccine and 13% vs 23% for likely to get vaccinated respectively). • 10% of those unlikely to be vaccinated had household income of less than $60,000 compared to 2% among those with incomes between $60,000 to more than $120,000. • Most felt vaccines were safe (95%) and effective (97%) compared to the COVID-19 vaccine which garnered lower support for safety (86%) and efficacy (88%). • 94% of respondents felt confident that Canada's process only approved safe and effective vaccines (94%).

		• Top sources for COVID-19 vaccination information were Public Health Agency of Canada and Health Canada (89%) and provincial, territorial or regional health authorities (85%).
Centre for Addiction and Mental Health (2021) *unpublished* (77) Cross-sectional study Canada Mar 2021	An online survey of 1000 Canadians as part of Asking Canadians web panel was conducted to measure mental health and vaccine intentions. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 66.4% of respondents who haven't received a vaccine yet definitely intend to get one, 21.8% will probably get a vaccine, and 11.8% definitely or probably will not get a vaccine.
Tang (2021) *preprint* (14) Cross-sectional study Canada Jan-Mar 2021	To assess vaccination hesitancy in population subgroups in Canada, an online survey of 14,621 panel members from the nationally representative Angus Reid Forum was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Overall, 9.3% do not intend on receiving a vaccine. This was highest in AB (16.4%), MB & SK (13.8%) and lowest in QC (8.3%), the Atlantic provinces (8%), ON (7.8%), and BC (7.2%). • Vaccine hesitancy was significantly associated with those aged 40-59 years (OR 0.87, 95% CI: 0.78-0.97), being a visible minority (OR 0.56, 95% CI: 0.37-0.84), lower education, and belonging to a household of five or more people (OR 0.82, 95% CI: 0.76-0.88).
Syan (2021) *preprint* (36) Cross-sectional study	Factors associated with intention to receive a COVID-19 vaccine was assessed in 1,367 adults (18+) living in Southern Ontario using an online survey.	• 82.8% were willing to receive a vaccine and 17.2% were unwilling. • The most common reasons for vaccine hesitancy were concern over long-term (65.5%) and immediate (60.5%) side effects, and a lack of trust in the vaccine (55.2%).

Canada Jan – Feb 2021	Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Higher intention to vaccinate was significantly associated with male gender (P=0.002) and higher education levels (P<0.001). • The perception of COVID-19 vaccine safety was significantly lower (-10.7%) than vaccines in general. Females, older adults, and those with less education reported lower perceived COVID-19 vaccine safety.
Leger (2021) *unpublished* (47) Cross-sectional study Canada Jan 2021	An online survey of 800 participants from Manitoba (18+) was conducted to investigate vaccine perceptions and intentions to vaccinate. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine rollout perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 72% reported the intention to vaccinate when a vaccine is available. • Intention to vaccinate increases with age. 82% of those aged 55+ reported they would definitely or probably intend to vaccinate compared to 65% of those aged 18-51. • Higher education and higher incomes are associated with an increased intention to vaccinate. • Vaccine safety is still a concern as 57% don't want to be in the first wave of people getting vaccinated and want to wait until safety has been established. 49% have concerns about safety but have generally pro-vaccine opinions. • >66% agree that the vaccine should be mandatory for all healthcare workers. • 71% of respondents are comfortable with how the Manitoba government is determining priority groups for early vaccination.
Leger (2021) *unpublished* (48) Cross-sectional study Canada Jan 2021	1000 residents of Alberta (18+) were surveyed online regarding their perceptions of the vaccine rollout. Question Topics: 1) Vaccine rollout perceptions Survey tools available? No Formative research conducted? No	• Approval of the overall vaccine rollout in Alberta was split, 48% were satisfied and 43% were dissatisfied. • For the order of priority groups established by the government, 64% were satisfied and 28% were dissatisfied. • 44% were satisfied with the government's communication of the rollout plan and 48% were not. • More individuals were dissatisfied (56%) with the pace of the rollout compared to satisfied (35%).

	Survey pre-tested? No	• 53% believe they will have the opportunity to receive a vaccine after September.
Insights West (2021) *unpublished* (78) Cross-sectional study Canada Jan 2021	Intention to vaccinate was analyzed using an online survey of 824 residents of British Columbia. Question Topics: 1) Vaccine intentions 2) Vaccine rollout perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 58% of respondents were definitely willing to be vaccinated, 22% were probably willing, 5% probably will not get vaccinated, and 7% definitely will not. • 67% of older respondents (55+) were more likely to get vaccinated compared to those in younger age groups (52% among 18-34 year olds). • 69% felt that those with underlying conditions were should have been put ahead of others on the list. • When asked about the vaccine rollout plan, 5% rated the rollout as excellent, 30% good, 51% fair, 14% poor, and 7% very poor. Similar trends were seen for perceptions on clarity of the rollout and prioritization levels.
Afifi (2021) (79) Cross-sectional study Canada Nov-Dec 2020	Using survey respondents from the longitudinal Well-Being and Experiences study (2017-2020) vaccine intentions were recorded for Winnipeg adolescents aged 16-21 and their caregivers/parents using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 65.4% of respondents intend to receive a vaccine, 26.1% were not sure, and 8.5% were not willing. • Parents with trade school, community college or less, with incomes of less than $49,999, experienced quite a bit COVID-19 financial strain, self-reported low knowledge of COVID-19 were associated with lower intentions to get a vaccine. • Having a self-reported health condition was associated with higher intentions to accept a vaccine. • After adjusting for sex, age and household income, children who had no experience with spanking (aRR 0.33, 95% CI: 0.17–0.62), no peer victimization (aRR 0.49, 95% CI: 0.25–0.96), no household substance abuse (aRR 0.41, 95% CI: 0.20–0.83), no contact with foster care/child protective office (aRR 0.34, 95% CI: 0.16–0.72), and no risk of their household running out of money (aRR 0.45 95% CI: 0.21–0.97) were more willing to get vaccinated. • Reporting no to any household challenge adverse childhood experience (ACE) was associated with willingness to vaccinate (aRR 0.45, 95% CI: 0.20–0.99).

		• The top concerns for being unwilling to accept a vaccine were for vaccine safety (64.5%), not knowing enough about the vaccine (60.6%), and not thinking the vaccine would be effective (23.4%).
Province of Manitoba (2020) *unpublished* (80) Cross-sectional study Canada Nov 2020	An online survey of 9872 adults in Manitoba was conducted to assess COVID-19 vaccine perceptions and intention to vaccinate. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 55% and 19% of participants reported they definitely or probably will receive the COVID-19 vaccine when available, respectively. The other participants stated they were undecided (8%), probably would not (7%) or definitely would not (12%) take the vaccine. • 61% of participants agreed with the statement "Vaccines are safe and I have no doubts about vaccinating myself or my family, as recommended by my doctor".
Independent Polling System of Society (IPSOS)/Radio Canada (2020) *unpublished* (81) Cross-sectional study Canada Nov 2020	Intention to vaccinate and perceptions on the vaccine were analyzed using an online survey of 3001 adults (18+). Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 64% of participants would probably or certainly get vaccinated, 16% definitely would not, and 21% were unsure. • Of those who would be vaccinated, 36% would get vaccinated as soon as possible, 38% would wait one or two months to see what happens, 15% would wait several months, and 11% were undecided. • The majority of respondents were worried about possible side-effects and risks associated with the vaccine.
Independent Polling System of Society (2020) *unpublished* (38)	An online survey of 1001 adults (18+) analyzed intention to vaccinate and perceptions on the vaccine. Question Topics: 1) Vaccine intentions	• 52% of respondents would take a COVID-19 vaccine as possible without hesitation. However, when other options, 36% would take the vaccine waiting to see if there were adverse side-effects and 28% would after waiting to see if it's effective. • 13% of participants would refuse vaccination under any circumstance.

Cross-sectional study Canada Nov 2020	2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 71% of participants say that taking a vaccine that was created and approved so quickly makes them nervous and 69% are concerned about long-term effects. • 59% of participants support mandatory COVID-19 vaccination, a drop from 61% in Sept, and 72% in July. • Some participants stated that a recommendation by a family doctor (21%), or seeing friends and family receive the vaccine (10%) would make them willing to take a vaccine. • Most agree that frontline healthcare workers (62%) and first-responders (52%) should be first in line to receive the vaccine. However, outside of these target groups, Canadians are divided on who should be a priority. • Three in ten (30%) believe that we can beat COVID-19 without a vaccine, down from 40% in Oct.
Racey (2021) (37) *new* Cross-sectional study Canada Aug-Nov 2020	5,076 public school teachers in British Columbia participated in an online survey regarding the likelihood of accepting a vaccine. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 89.7% of respondents were either likely or very likely to accept a COVID-19 vaccine, 4.6% were neutral, and 5.7% were either unlikely or very unlikely to accept a vaccine. • Indigenous status was not significantly associated with increased or decreased intentions. • Intention to vaccinate was positively associated with having a science/engineering educational background (aOR 1.36, 95% CI: 1.04-1.79), male gender (aOR 1.41, 95% CI: 1.07-1.88), viewing public health, school boards/teachers union, and healthcare providers as a reliable source of information (aOR 1.43, 95% CI: 1.12-1.83, aOR 1.51, 95% CI: 1.22-1.87, and aOR 1.51, 95% CI: 1.22-1.87 respectively), viewing healthcare providers as reliable sources of information (aOR 1.51, 95% CI: 1.22-1.87), higher vaccine knowledge (aOR 1.58 95% CI: 1.38-1.80), and viewing COVID-19 as a serious illness (aOR 5.79, 95% CI: 4.09-8.19). . • Intention to vaccinate was negatively associated with prior delay or refusal of vaccination (aOR 0.19,

		95% CI: 0.15-0.24), lack of confidence in vaccines and (aOR 0.5, 95% CI: 0.44-0.58) and perceived risk of vaccination (aOR 0.36, 95% CI: 0.31-0.42). • LGBTQ+ outcomes located in Table 5.
Independent Polling System of Society (2020) *unpublished* (82) Cross-sectional study Canada Oct 2020	An online survey of 1000 adults analyzed intention to vaccinate and perceptions on the vaccine. Of these, 1000 participants were Canadian. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 54% of Canadians would be willing to take a vaccine as soon as it is available. Atlantic Canada have the highest intentions (75%), followed by SK/MB (65%), QC (63%), BC (60%), AB (58%), and ON (57%). • 61% of participants support mandatory COVID-19 vaccination, a drop from 72% in July. • 82% indicate that they would wait for reports about the effectiveness or any side-effects of a COVID-19 vaccine before taking it. • The majority (88%) of participants agree that seniors and other vulnerable communities should be the first priority to receive the vaccine. • Four in ten (40%) believe that we can beat COVID-19 without a vaccine.
Toronto Public Health (2020) *unpublished* (83) Cross-sectional study Canada Oct 2020	Intention to receive a COVID-19 vaccine was evaluated using an online survey of 1201 residents of Toronto, Ontario. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 73% of participants report that when a COVID-19 vaccine is available they will "definitely" or "probably" get it. 20% will "definitely" or "probably" not receive it and 11% are undecided.
Statistic Canada (2020) *unpublished* (20) Cross-sectional study	A telephone survey of 120,000 (18+) was conducted to assess intention to vaccinate. Question Topics: 1) Vaccine intentions	• When comparing all visible minorities against Whites race, vaccine intentions were nearly identical (77.3% vs 77.0%). • Within visible minority groups intention to vaccinate from lowest to highest was Black (57.0%), Latin American (58.5%), Filipino (64.2%),

Canada Sept-Oct 2020	Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	South East Asian (75.8%), other visible minorities (77.6%), Chinese (85.5%), and Arab (88.3%). • 69.3% reporting an Aboriginal identity were accepting of a vaccine compared to 77.6% not reporting an Aboriginal identity. • Higher levels of education and having an underlying medical condition were associated with higher acceptance. • Outcomes on intention to vaccinate in LGBTQ+ and immigrants can be found in Tables 5&7.
Ogilvie (2021) (22) Cross-sectional study Canada Aug-Sep 2020	Intention to vaccinate was assessed in 4058 adults and healthcare workers from British Columbia (25-69 years old). Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 79.8% of respondents were somewhat or very likely if available to them and was recommended for them. • Households with two adults (OR 1.2, 95% CI: 1.00-1.43) were more likely to vaccinate but there were no significant changes in intention with number of children. • Multivariate analysis demonstrated that younger respondents (30-40 years old aOR 0.64, 95% CI: 0.49-0.83, 40-50 years old aOR 0.78, 95% CI: 0.62-0.97, 50-60 years old aOR 0.67, 95% CI: 0.55-0.82), females (aOR 0.7, 95% CI: 0.55-0.89), lower education level (aOR 0.62, 95% CI: 0.51-0.77), South Asian (aOR 0.65, 95% CI: 0.39-1.07), non-White (aOR 0.76, 95% CI: 0.61-0.95), identified as Indigenous (aOR 0.58, 95% CI 0.38-0.87), other essential non-health care workers (aOR 0.72, 95% CI: 0.6-0.87), and those who suspected they had COVID-19 (aOR 0.76, 95% CI: 0.61-0.96) had significantly lower odds of intending to receive a vaccine. • Lack of confidence in vaccines (aOR 0.66, 95% CI: 0.57-0.75) and belief in vaccine risks (aOR 0.72, 95% CI: 0.66-0.80) were associated with decreased intention to vaccinate. • Intention to vaccinate was positively associated with higher attitudinal scores towards the vaccine (aOR 1.06, 95% CI: 1.04-1.08), influenced by direct social norms (aOR 1.06, 95% CI: 1.03-1.08), indirect

		social family doctor/primary care physician opinions (aOR 1.04, 95% CI: 1.00-1.08), indirect norms from the provincial health officer (aOR 1.04, 95% CI: 1.01-1.08), and indirect family norms (aOR 1.09, 95% CI: 1.06-1.13). • Outcomes on intention to vaccinate in HCWs and LGBTQ+ can be found in Tables 2 & 5.
Lang (2021) (30) Cross-sectional study Canada Aug 2020	An online survey of 60 adults (18+) in Alberta was conducted to assess their intention to vaccinate. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? No Survey pre-tested? No	• 68% of respondents would accept a vaccine if it were available, 20% would not, and 12% were unsure. • White respondents were less likely to accept a vaccine (63%) compared to other ethnicities (100%). • Those with higher education (college or university) were less likely to accept a vaccine (63%) compared to those who had attended post-secondary technical school (100%) or had a high school diploma (70%). • Intention to vaccinate was positively associated with concerns about getting COVID-19 (P <0.001) and spreading the virus (P = 0.006), and complying with public health measures such as staying home when sick (P = 0.033), masking in public (P < 0.001) and physical distancing (P = 0.005). • Respondents who received their COVID-19 health information from the Chief Medical Officer of Health media briefings (P = 0.030) and Alberta Health or Alberta Health Services websites (P = 0.040) were significantly more likely to accept a COVID-19 vaccine. • Intention to vaccinate was lower in other urban centers (29%) and rural Alberta (50%) compared to Calgary (75%) and Edmonton (80%), (*P* = 0.030).
Carleton University (2020) *unpublished* (84)	An online opinion survey regarding vaccine intentions and perceptions was conducted online in 2000 individuals.	• 62% will definitely get the vaccine, 24% will probably get the vaccine, 5% will not likely get the vaccine, and 9% will definitely not get the vaccine.

Cross-sectional study Canada Jul 2020	Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Resistance to a vaccine is highest in MB and SK where only 37% will definitely get vaccinated across both provinces. • In terms of views on mandatory vaccination, 36% strongly agree, 26% somewhat agree, 14% strongly disagree, and 7% somewhat disagree. • The most common reason (40%) for hesitancy was potential for harmful side-effects. • The 9% of respondents who expressed strong anti-vaccine views, suspicion about the influence of the pharmaceutical industry over public health care (41%) and concern about vaccine safety and the potential for harmful side-effects (29%) were the most common reasons for refusal.
Frank (2020) *unpublished* (85) Cross-sectional study Canada Jun 2020	Factors associated with willingness to vaccinate was investigated using an online survey of ~4000 adults. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 57.5% and 19% of respondents indicated they are very likely or somewhat likely to get a COVID-19 vaccine when it becomes available, respectively. • Older Canadians (65+) reported they were more likely to vaccinate (70.3%) compared to those aged 15-64 (52-58%). • Those that were born in Canada were more likely to vaccinate compared to immigrants (59.4% vs 52.0%). • Residents in the Atlantic Provinces are more likely to vaccinate (67.7%) followed by Ontario (58.8%), Prairies region (56.2%), BC (55.5%), and QC (54.3%). • Other factors associated with a higher intention to vaccinate include higher education and not having children under the age of 18. • The top two reasons for not intending to vaccinate were a lack of confidence in the safety of the vaccine (54.2%) and concerns about its risks and side-effects (51.7%).
Frank (2020) *unpublished* (86)	An online survey of ~36,000 adults was conducted to investigate factors associated with willingness to vaccinate.	• 68.2% and 15.2% of participants reported that they were very likely or somewhat likely to accept a COVID-19 vaccine, respectively. 12% were unlikely or very unlikely to vaccinate.

Cross-sectional study Canada May-Jun 2020	Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Those who had a high level of trust in the federal government were more likely to be willing to vaccinate compared to those with a low level of trust (77.3% vs 53.8%). • Similar trends were also seen with trust in others, and trust in federal public health authorities.
Taylor (2021) (87) Cross-sectional study Canada & USA Jun-Jul 2020	An online survey of 2078 adults (18+) was used to explore the potential relationship between attitudes on wearing a face mask and COVID-19 vaccination. The sample consisted of 1036 participants from the USA and 1042 from Canada. Question Topics: 1) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• The network of anti-masks attitudes is linked to other variables such as disregard for social distancing and anti-vaccination attitudes.
Waite (2021) (35) Cross-sectional study Canada May 2020	An online survey of 1001 Canadians aged 50–64 years and 3,500 aged 65+ was conducted to evaluate intention to vaccinate against COVID-19. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Among those aged 50-64 years, 69.1% intend to vaccinate when available, 11.3% would not vaccinate, and 19.6% were unsure. • 79.5% of those 65+ intend to receive a vaccine when available, 5.6% would not vaccinate, and 14.9% were unsure. • In both age groups, those who would accept a vaccine were significantly more likely to be male and more likely to have at least one chronic condition (P< 0.05). • The preferred location to receive a vaccine in both groups was family physician office, followed by pharmacy, workplace (for those 50–64 years), and public health clinics.
Taylor (2020) (18)	Intentions to vaccinate and attitudes towards vaccines were	• Significantly more Americans (25%) than Canadians (20%) responded that they would not

Cross-sectional study Canada & USA May 2020	measured using an online survey of 3674 adults (Canada = 1902, USA = 1772). Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	get vaccinated if a vaccine was available, χ^2 (*df* = 1) = 12.41, $p < 0.001$. • Negative attitudes toward a COVID-19 vaccination, and vaccinations in general, were significantly correlated ($p < 0.001$) with the intention not to vaccinate. Mistrust of the benefit of a COVID-19 vaccine was the largest factor with respect to attitude on the decision not to get the vaccine. • Vaccination refusal was significantly associated with female gender, age, completed full or partial college education (vs. did not complete), being unemployed, and minority status (vs. Caucasian). • Of those who indicated they would not get vaccinated (n=812), 38% would vaccinate if they were convinced the vaccine had been rigorously tested and 36% would vaccinate if they saw that enough people were vaccinated without any serious side-effects. • Compared to White ethnicity, minority status (Asian, African American/Black, Latino/Hispanic, or other) was significantly associated with vaccine refusal (r = −0.04, P < 0.05).
Carleton University (2020) *unpublished* (26) Cross-sectional study Canada May 2020	An online opinion survey regarding vaccine intentions and perceptions was conducted online in 2000 individuals. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 49% and 24% of the participants would "definitely" or "probably" get the vaccine when available, respectively. • 17% expressed uncertainty and 10% were unwilling. • 65% believe that the vaccine should be mandatory. • Age and political affiliation were significantly associated with intention to vaccinate. Older individuals were more willing to vaccinate than younger. Those who voted Liberal or NDP in the 2019 election were more likely to vaccinate compared to those who voted for other parties. • Respondents living in Atlantic Canada showed the strongest levels of intention to vaccinate compared to those in other provinces.

		• Those who believed one of the four health myths or conspiracy theories regarding COVID-19, were less likely to intend to vaccinate than those who did not believe the scientifically inaccurate claims about COVID-19.
Parsons Leigh (2020) (88) Cross-sectional study Canada Apr-May 2020	COVID-19 perceptions, knowledge, attitudes, and behaviors were analyzed using an online survey of 1996 participants (18+). Question Topics: 1) Vaccine intentions 2) Vaccine knowledge Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 75.8% (n = 1,436) of respondents reported that they would get vaccinated when a vaccine became available. • Participants responded they "strongly agree" or "agree" that they will get vaccinated in BC (72.1%), AB (69.9%), MB/SK (69.9%), ON (66.1%), Atlantic (63.1%), and QC (41.9%). • Participants responded they "strongly agree" or "agree" that they will not get vaccinated in AB (12.4%), QC (12.1%), ON (8.1%), Atlantic (6.6%), MB/SK (6%), and BC (4.8%). • Information about vaccines and treatments were most frequently (n = 933, 48.9%, 95% CI: 46.7-51.2%) cited as topics of misinformation, however only half (n = 937, 47.4%, 95% CI: 45.2%-49.6%) of respondents felt moderately or extremely confident that they could identify incorrect or misleading information about COVID-19.
Underschultz (2021) (89) Cross-sectional study Canada Apr 2020	COVID-19 knowledge, attitudes, and practices were analyzed using an online survey of 1593 participants (16+). The survey was primarily targeted to residents of Alberta and Ontario. Question Topics: 1) Vaccine perceptions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 93% of respondents believe that a vaccine is needed in Canada and 81% endorsed a wide-spread vaccination strategy (having everyone vaccinated). • Vaccine acceptance was significantly associated with higher knowledge scores ($p<0.001$), being worried about COVID-19 (OR 20.4; 95% CI: 8.4-49.5, $p<0.001$), optimism in controlling the pandemic (OR 8.1; 95% CI: 3.4-19.7, $p<0.001$), and feeling informed about COVID-19 (OR 3.9; 95% CI: 1.7-9.3, $p=0.0049$).

Research Co (2020) *unpublished* (25) Cross-sectional study Canada Apr 2020	Intention to vaccinate was assessed using an online survey. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• If a vaccine becomes available, 42% and 31% would "definitely" or "probably" get the vaccine, respectively. • Men were more likely to vaccinate than women (78% vs 68%). • The Atlantic (79%) and Alberta (78%) had the highest intentions to vaccinate and Saskatchewan/Manitoba (65%) had the lowest. • Intention to vaccinate was highest in those who voted liberal (79%) in the 2019 election, followed by NDP (76%), and conservative (69%).
Qualitative studies (n=1)		
Benham (2021) (90) Qualitative study Canada Aug-Sep 2020	Nine focus groups were conducted with 50 adults (18+) from Alberta to evaluate attitudes towards public health measures including vaccination. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions	• Intention to vaccinate responses were mixed. Some stated they would vaccinate right away, while others would not vaccinate as they believed COVID-19 would not impact their health or the health of their family members. • Some participants reported that they would be willing to take a vaccine but not right away. This was more prominent in the older age groups. • Participants who regularly received the annual flu vaccine were more likely to state they would take a COVID-19 vaccine when available. However, a few experienced side effects with the annual flu shot (e.g., getting sick) which would make them less likely to get a COVID-19 vaccine. • Barriers for vaccine uptake included a lack confidence that a vaccine will work, and that it may do harm.
Quasi-experimental studies (n=1)		
Poder (2021) *unpublished* (91) Quasi-experimental study	An online survey of vaccine intentions of 1,695 Quebec adults was conducted which included an assessment of preferences through a series 12 binary choice scenarios (20,350 choice responses in total).	• At least 7.2% always chose not to be vaccinated in any given scenario. • Depending on the scenario, 69-93% of participants would opt for the vaccine when available. • 24% of participants would make the choice to refuse the vaccine if certain conditions were not

Canada Oct-Nov 2020	Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	met which were determined to be in order of priority: 1) vaccine efficacy 2) possible side effects of the vaccine 3) duration of effectiveness (minimum of 9 months for acceptability) 4) the organization recommending the vaccine (Public health organizations of Québec, WHO) 5) geographic origin of vaccine (European Union or United States) 6) waiting period to be vaccinated once the vaccine is available in Quebec (4 months maximum) 7) high priority populations (no preferences)
Expert Stakeholders		
Cross-sectional studies (n=2)		
MacDonald (2020) (92) Cross-sectional study Canada Aug-Oct 2020	Eighteen teleconference interviews with 25 public health leaders from 10 of 13 provinces and territories were conducted to evaluate perspectives on priority groups for early vaccination. Participants were asked to rank, in order of importance, their top five priority groups for vaccination. Question Topics: 1) Vaccine strategy perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• All ten province and territories ranked long-term residents and health-care workers in their top five priority groups to receive vaccination. • Those with chronic medical conditions and seniors were also ranked in the top five priority groups by nine and eight provinces and territories, respectively. • To a lesser extent, those with Indigenous ancestry (n=4), with socioeconomic disadvantage (n=3), with infants or children (n=2), living in remote communities (n=2), and new immigrants and refugees (n=1) were ranked in the top five priority groups.
Zhao (2020) *preprint* (93)	Among 74 expert stakeholders, an online survey was conducted to establish perspective on the relative importance of pandemic	• For all pandemic scenarios, stakeholders generally ranked the strategies in the following order from most to least important:

Cross-sectional study Canada Jul-Aug 2020	immunization strategies for different COVID-19 pandemic scenarios at the time of initial COVID-19 vaccine availability. Questions asked the respondent to rank, in order of importance, four pre-defined COVID-19 pandemic immunization strategies. Question Topics: 1) Vaccine strategy perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	○ Protect those who are most vulnerable to severe illness and death from COVID-19 ○ Protect healthcare capacity ○ Minimize transmission of COVID-19 • Protect critical infrastructure

aOR = adjusted odds ratio, CI = confidence interval, HCWs = healthcare workers, NR = not reported, RR = risk ratio

HEALTHCARE WORKERS

Table 3. Evidence of vaccine attitudes of healthcare workers (n=7)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
Lunsky (2021) (50) Cross-sectional study Canada Jan-Feb 2021	To evaluate vaccination intent and predictors of intent, an online survey of 3371 social service employees supporting individuals with intellectual disabilities in Ontario was conducted. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes	• 62% and 20% reported that they were very likely, or somewhat likely to accept a vaccine, and 7% and 11% somewhat unlikely or very unlikely to get the vaccine, respectively. • Compared to individuals aged 50 +, younger individuals aged 18-29 (aOR 2.74, 95% CI: 1.70–4.43) and 30-39 (aOR 1.75, 95% CI: 1.16–2.64) were more likely to refuse a vaccine when available. • Women were more likely to refuse a vaccine compared to men (aOR 1.58, 95% CI: 0.97-2.59). • Compared to European respondents, Asian (aOR 0.88, 95% CI: 0.33-2.36), African and Caribbean (aOR 0.81, 95% CI: 0.35-1.86), and unknown ethnicities (aOR 0.88, 95% CI: 0.36-2.17) were less

	Survey pre-tested? No	likely to refuse a vaccine and Indigenous, First Nations, and Metis (aOR 1.73, 95% CI: 0.67- 4.43), Latin (aOR 1.22, 95% CI: 0.21-7.24), and mixed ethnicities (aOR 1.11, 95% CI: 0.27-4.55) were more likely to refuse. • Reasons to refuse a vaccine included lack of trust in the vaccine (OR 5.72, 95% CI: 3.84–8.53), fear of vaccine side effects (OR 2.30, 95% CI: 1.56–3.39), and belief that there was no need for the vaccine due to good health (OR 4.22, 95% CI: 2.66–6.68). • Individuals who would refuse a vaccine were less likely to believe that vaccination would protect clients (OR 0.36, 95% CI: 0.24-0.54) or family (OR 0.19, 95% CI: 0.13-0.28),be concerned about clients (OR 0.57, 95% CI: 0.34-0.97) or themselves (OR 0.51, 95% CI: 0.34-0.76) becoming ill with COVID-19, get the flu shot in a normal year (OR 0.61, 95% CI: 0.43-0.88), and get the vaccine if their co-workers did (OR 0.16, 95% CI: 0.08-0.29).
Desveaux 2021 *preprint* (49) Cross-sectional study Canada Jan 2021	Factors associated with intention to vaccinate was evaluated in 8634 non-physician HCWs (18+) in Ontario using an online survey. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 80.4% of participants reported that they intend to get a COVID-19 vaccine. • Compared to their counterparts, those who were younger (<40 years old) and who had less education (less than a high school diploma) were more likely to be unwilling to intend to vaccinate (P<0.001). • HCWs who identified as Filipino (OR 1.07, 95% CI: 0.41-2.76, P<0.001), Caribbean (OR 3.20, 95% CI: 1.52-6.75, P<0.001), or Other (OR 1.44, 95% CI: 0.93-2.22, P<0.001) ethnicity were more likely to be unwilling to vaccinate compared those who identified as European. • Vaccine hesitancy was strongly associated with mistrust about how fast the vaccines were developed and vaccine safety concerns. It was also associated with various beliefs such as not requiring a vaccine due to one's own good health, low confidence that the vaccine would protect

		their family and patients, and that getting vaccinated was not a professional responsibility. • HCWs were more likely to intend to vaccinate if direct financial supports such as paid sick days were provided (74% vs 25%, P<0.001).
SafeCare BC (2021) *unpublished* (19) Cross-sectional study Canada Dec 2020	An online survey of 1,500 continuing care workers in British Columbia was conducted to evaluate attitudes on COVID-19 vaccination. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 57% of respondents intend to get a vaccination, 28% were not sure, and 15% did not intend to get vaccinated. • Male (72% vs 56%), higher age (65+) and flu shot acceptance were predictors of intention to vaccinate. • Managers and senior leaders had the highest intentions to vaccinate (71%). Healthcare assistants were the most unsure (30%), and nurses were most likely to say no to a vaccine (20%). • Reason for hesitancy were side effects (84.6%), the newness of the vaccine (64.6%), mistrust of authorities (23.5%), belief that the vaccine will not work (16%), preferred natural remedies (10.5%), and personal or religious beliefs (8%). • Intention to vaccinate was highest in East (61%) and South Asian (70%). Latino and Black respondents were the most likely to refuse a vaccine (30%) and Indigenous respondents were most likely to be unsure about their decision to vaccinate (40%). • East/South Asian respondents were more concerned about side effects (93%) whereas White or Indigenous respondents were more concerned about newness (72% and 62%, respectively). • 33% said more support for vaccinations is needed e.g. more information to understand the development process, efficacy, and transparency of reporting adverse events. • The biggest perceived barrier to administering the vaccine was storage and handling constraints (66%). • Indigenous respondents had the least amount of trust in all sources of information including healthcare providers.

INSPQ (2020) & INSPQ (2021) *unpublished* (32, 40) Longitudinal study Canada Apr-Dec 2020	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in Quebec. Number of participants was not clearly stated (~3300 each collection period). There were multiple collection periods, one in Apr-May and one in Sep and Dec. Article in French. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• In May, 73% of HCWs responded with the intention to vaccinate. In Dec this decreased to 65% and increased to 71% in Dec. • Intention to vaccinate did not differ between the general public and healthcare workers and factors associated with intention to vaccinate were not differentiated between the two groups. • Those that were older (70+) were more likely to vaccinate compared to those 25-44 years old (83% vs 57%). • Men, those with a university education, and those with one or more chronic diseases are more likely to intend to vaccinate. • The most common reasons to not intend to vaccinate include fears related to taking a new vaccine, and concern regarding the effectiveness and side-effects.
Verger (2021) (51) Cross-sectional study Belgium, France & Canada Oct-Nov 2020	Intention to vaccinate and intention to recommend vaccination to patients was evaluated using an online and telephone survey in general practitioners (GPs) in France (n=1209) and French-speaking parts of Belgium (n=414) , and nurses in Quebec, Canada (n=1055). Belgium and France results can be found in the Europe section. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? Yes Formative research conducted? No Survey pre-tested? Yes	• In Canada, 79.6% of nurses would definitely or probably recommend their patients vaccinate, 3.1% would not, and 17.2% were unsure. For themselves, 70.4% would definitely or probably be willing to receive the vaccine, 11.8% would refuse, and 17.8% were unsure. • 40.9% of participants reported that the safety of vaccines developed in an emergency during an epidemic cannot be guaranteed. • Opinion about the safety of vaccines developed in an emergency and distrust in the ministry of health to ensure vaccine safety were the two most important factors independently associated with vaccine hesitancy and reluctance. • Intention to vaccinate was positively associated with a history of personal vaccination against the flu.

Ogilvie (2021) (22) Cross-sectional study Canada Aug-Sep 2020	Intention to vaccinate was assessed in 4058 adults and healthcare workers from British Columbia (25-69 years old). Unclear how many healthcare workers in the survey. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 81.8% of healthcare workers report that they intend to receive a vaccine. • Other results found in general population. • Multivariate analysis demonstrated that South Asian (aOR 0.65, 95% CI: 0.39-1.07), non-White (aOR 0.76, 95% CI: 0.61-0.95), and those who identified as Indigenous (aOR 0.58, 95% CI 0.38-0.87) had significantly lower odds of intending to receive a vaccine.
The Canadian PSW Network (2020) *unpublished* (52) Cross-sectional study Canada NR 2020	Intention to vaccinate in 562 personal support workers (PSWs), nurses, and healthcare workers using an online survey. 84% of the sample were PSWs. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 64.2% of respondents intend to vaccinate when it is available, 16.2% refuse to vaccinate, 10.7% are unsure, and 8.9% will only take the vaccine if it's mandatory. • 71.7% do not believe there is enough clear education on the vaccine.

aOR = adjusted odds ratio, CI = confidence interval, HCWs = healthcare workers, PSW = personal support worker

HIGH-RISK POPULATIONS

Table 4. Evidence of vaccine attitudes of high-risk populations (n=1)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
OLDER ADULTS		

Waite (2021) (35) Cross-sectional study Canada May 2020	An online survey of 1001 Canadians aged 50–64 years and 3,500 aged 65+ was conducted to evaluate intention to vaccinate against COVID-19. Question Topics: 1) Vaccine intentions 2) Vaccine attitudes Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Among those aged 50-64 years, 69.1% intend to vaccinate when available, 11.3% would not vaccinate, and 19.6% were unsure. • 79.5% of those 65+ intend to receive a vaccine when available, 5.6% would not vaccinate, and 14.9% were unsure. • In both age groups, those who would accept a vaccine were significantly more likely to be male and more likely to have at least one chronic condition (P< 0.05). • The preferred location to receive a vaccine in both groups was family physician office, followed by pharmacy, workplace (for those 50–64 years), and public health clinics.

LGBTQ+

Table 5. Evidence of vaccine attitudes of LGBTQ+ (n=4)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
LGBTQ+		
Racey (2021) (37) *new* Cross-sectional study Canada Aug-Nov 2020	5,076 public school teachers in British Columbia participated in an online survey regarding the likelihood of accepting a vaccine. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Those identifying as female gender or non-Binary/genderqueer/S2/other were less likely to intend to vaccinate compared to those who identified as male. • 22.6% of non-Binary/genderqueer/S2/other (n=31) do not intended to vaccinate and 77.4% do. • General population outcomes found in Table 1.
Statistic Canada (2020) *unpublished* (20)	A telephone survey of 120,000 (18+) was conducted to assess intention to vaccinate. Question Topics: 1) Vaccine intentions	• 87.6% of LGBTQ2+ were willing to accept a vaccine compared to 76.4% non-LGBTQ2+.

Cross-sectional study Canada Sept-Oct 2020	Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	
Ogilvie (2021) (22) Cross-sectional study Canada Aug-Sep 2020	Intention to vaccinate was assessed in 4058 adults and healthcare workers from British Columbia (25-69 years old). Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Non-binary, gender queer, agender, two-spirit or other were more likely to be receive a vaccine compared to heterosexual woemn (OR 3.04, 95% CI: 1.08-8.55, P<0.04).
Statistics Canada (2020) & Statistics Canada (2021) *unpublished* (53, 72) Longitudinal study Canada Sep-Dec 2020	An online survey conducted by Statistics Canada as part of the Canadian Community Health Survey (CCHS) assessed Canadians behaviors to safeguard their own health as well as the health of others. In the September survey, a question about vaccine intentions was added. The most recent report captures 20,000 responses from individuals aged 12+. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes	• Over the sampling period 77% were willing to receive a vaccine. This represents an increase from Sept (75.5%) to Oct (74.8%), and Nov/Dec (80.3%). • LGBTQ2+ were more likely to get a vaccine (83.3%).

	Survey pre-tested? Yes	

PARENTS

Table 6. Evidence of vaccine attitudes of parents (n=7)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
PARENTS		
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021) *unpublished* (1, 9, 29, 32-34, 40, 43, 71) Longitudinal study Canada Apr 2020 – Jun 2021	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in Quebec. Number of participants was not clearly stated (~3300 each collection period). There were multiple collection periods, one in Apr-May 2020, Sep and Dec 2020, Apr-Jul 2021 *new*. Articles in French. Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? No Survey pre-tested? No	**July** • 87% of parents intend to vaccinate their children (up 1% from June), 11% have no intention (up from 8%), and 3% were unsure (down from 6%). • General population outcomes found in Table 1.
Government of Manitoba (2021) *unpublished* (42) Longitudinal study Canada	An online research panel of 600 Manitobans were surveyed to understand attitudes towards vaccination and possible incentives to increase uptake. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions	• In a group of 70 parents or guardians of children aged 12-17, 15% were not sure if they will vaccinate their children, and 13% will not vaccinate their children. • Those who did not intend to vaccinate their children were in households making less than $40,000, would not get the vaccine themselves, and didn't believe adults should get all the regular vaccines.

May 2021	Survey tools available? No Formative research conducted? No Survey pre-tested? No	
McKinnon (2021) *preprint* (56) Cross-sectional study Canada Jan – Apr 2021	Willingness to vaccinate children according to level of education, neighbourhood, and visible minority status was evaluated using an online survey in 380 parents with children aged 2-17 in Montreal. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Parents were 61% very likely, 25% somewhat likely, 9.2% somewhat unlikely, and 4.5% very unlikely to have their child vaccinated. • Concern over the lack of information about the vaccine's safety and possible side effects was the most common reason for hesitancy (48%). • Comparing visible minority to non-visible minority parents, 30.3% vs. 66.6% were very likely to vaccinate their children, 36.8% vs. 23.9% were somewhat likely, and 32.9% vs. 9.5% were unlikely to vaccinate, respectively.
Vallis (2021) (55) Cross-sectional study Canada Jun-Oct 2020	Attitudes and concerns towards COVID-19 vaccination in individuals living with overweight and obesity were evaluated using an online survey. Two samples were used: 1) representative sample of 1089 individuals living with overweight and obesity and 2) convenience sample of 980 individuals recruited from obesity clinical services or patient organizations. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No	• 64.6% of those living with obesity were comfortable receiving a vaccine and 35.4% were hesitant. • Individuals were less comfortable with their children receiving the vaccine (58.5% comfortable, 41.6% hesitant, P<0.001).

	Formative research conducted? Yes Survey pre-tested? No	
Drouin (2021) *preprint* (54) Cross-sectional study Canada Aug 2020	Parental intention to have their child with asthma vaccinated against COVID-19 was assessed using an online survey in 305 parents. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• 63% of parents were likely to have their child vaccinated, 19.1% were unlikely, and 17% were unsure. For themselves, 64% were likely to get vaccinated, 21% were unlikely, and 15.1% were unsure. There was a strong relationship between a parents' intention to vaccinate their children and person intention to vaccinate. • Factors significantly associated with a parents' decision to vaccinate their child included higher level of education, being employed, sex of the child (female), presence of other chronic diseases, prior influenza vaccination, parental anxiety, and consultation with a health professional.
Lackner (2021) (58) Cross-sectional study Canada May-Jun 2020	The demographic, experiential, and psychological factors associated with the anticipated likelihood and speed of having children receive a COVID-19 vaccine was investigated in 455 families (857 children). Question Topics: 1) Vaccine intentions Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• Factors associated with a higher likelihood of having their children vaccinated include older parental age, living in the Prairies (relative to Central Canada), more complete child and parental vaccination history, positive attitudes towards vaccines in general, higher psychological avoidance of the pandemic, and a greater tendency to prioritize the risks of the disease relative to the risks of side-effects. • In some models, perceived COVID-19 risk and higher levels of state anxiety were associated with increased likelihood of having children vaccinated. • The above factors were also predictors of faster speed of intended vaccination. However, higher SES was a trend-level predictor.
Hetherington (2021) (57) Cross-sectional study Canada	Participants from the longitudinal cohort study All Our Families (n=1321) in Alberta were invited to participate in an online COVID-19 impact survey to understand factors associated with COVID-19	• 60.4% of parents intended to vaccinate their children, 8.6% said they did not intend to vaccinate, and 31% were unsure. • Participants with less education were more likely to not want to vaccinate (OR 2.80, 95% CI: 1.78-4.40) or be unsure (OR 1.98, 95% CI: 1.47-2.71). A similar pattern was seen for income.

May-Jun 2020	vaccine intentions among parents of 9-12 year old children. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• History of partial or non-vaccination was associated with intent to not vaccinate (OR 2.81, 95% CI: 1.78-4.40). There was no association between vaccination history and uncertainty regarding a COVID-19 vaccine (OR 1.29, 95% CI: 0.92-1.80). • Concerns over vaccine safety and efficacy, long-term effects, and a rushed vaccination process were reported.

IMMIGRANTS

Table 7. Evidence of vaccine attitudes of immigrants (n=6)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
Innovative Research Group (2021) *new* *unpublished* (5) Cross-sectional study Canada May-Jun 2021	An online poll of 2,838 adults with a specific over sampling of Black Canadians (n=502) was conducted to evaluate COVID-19 vaccine intentions and hesitancy. Question Topics: 1) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• Vaccine hesitancy was higher amongst Black Canadians and Non-Black Canadians born in Canada than those born outside of Canada. • General population outcomes located in Table 1.
INSPQ (2020), INSPQ (2021), INSPQ (2021), INSPQ (2021), INSPQ (2021) *unpublished* (29, 32-34, 40)	Analysis of the acceptability of vaccination against COVID-19 was evaluated using an online survey of adults and healthcare workers in Quebec. Number of participants was not clearly stated (~3300 each collection period). There were multiple collection periods, one in Apr-May 2020, Sep and Dec 2020,	• Immigrants were more hesitant and more unsure about receiving a vaccine compared to non-immigrants.

Longitudinal study Canada Apr 2020 – May 2021	Apr and May 2021. Articles in French. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	
Statistics Canada (2021) *unpublished* (3, 76) Cross-sectional study Canada Mar-May 2021	Vaccine intentions and perceptions were analyzed in the second round COVID-19 Vaccination Coverage Survey (CVCS) involving Canadian adults (18+) in the provinces using mail invites and computer assisted telephone interviews for non-responses. Round 1: n= 1,025 capital cites of the territories Round 2: n= 10,678 in 10 provinces *new* Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	**Round 2** • 11%* of non-permanent residents were unlikely to vaccinate compared to 5% of non-immigrants, 4% among immigrants in Canada for more than 10 years, and 3% among immigrants living in Canada for less than 10 years. • General population outcomes located in Table 1
Muhajarine (2021) *preprint* (4) *new*	9,252 responses collected from 7,265 Saskatchewan adults (18+) were enrolled from landlines and online to complete an online survey	• Those who were born outside of Canada and living in Canada less than 20 years were more vaccine hesitant compared to those born in Canada (RRR 3.14, 95% CI: 1.56-6.34).

Cross-sectional study Canada Apr-May 2021	regarding vaccine acceptance and hesitancy. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? No Survey pre-tested? No	• General population outcomes found in Table 1.
Statistics Canada (2020) & Statistics Canada (2021) *unpublished* (53, 72) Longitudinal study Canada Sep-Dec 2020	An online survey conducted by Statistics Canada as part of the Canadian Community Health Survey (CCHS) assessed Canadians behaviors to safeguard their own health as well as the health of others. In the September survey, a question about vaccine intentions was added. The most recent report captures 20,000 responses from individuals aged 12+. Question Topics: 1) Vaccine intentions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• Immigrants were slightly less likely to vaccinate (74.6%) but this varied greatly between older and younger immigrants (73.2% for 12-64 and 81.1% for those 65+).
Statistic Canada (2020) *unpublished* (20) Cross-sectional study	A telephone survey of 120,000 (18+) was conducted to assess intention to vaccinate. Question Topics: 1) Vaccine intentions	• Immigrants living in Canada for less than 10 years (80.3%) and more than 10 years (70.7%) had comparable intentions to vaccinate compared to non-immigrants (75.9%). • Women who were non-immigrants or who immigrated less than 10 years ago had lower intentions than men (74.7% vs 77.2% for non immigrants and 78.1% vs 82.9% for less than 10 years).

Canada Sept-Oct 2020	Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	

INDIVIDUALS WITH COMORBIDITIES OR DISABILITIES

Table 8. Evidence of vaccine attitudes of individuals with comorbidities (n=1)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
CANADA		
Vallis (2021) (55) Cross-sectional study Canada Jun-Oct 2020	Attitudes and concerns towards COVID-19 vaccination in individuals living with overweight and obesity were evaluated using an online survey. Two samples were used: 1) representative sample of 1089 individuals living with overweight and obesity and 2) convenience sample of 980 individuals recruited from obesity clinical services or patient organizations throughout Canada. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy Survey tools available? No Formative research conducted? Yes Survey pre-tested? No	• 64.6% of those living with obesity were comfortable receiving a vaccine and 35.4% were hesitant. • Individuals were less comfortable with their children receiving the vaccine (58.5% comfortable, 41.6% hesitant, P<0.001). • The mean score on the confidence subscale of the vaccine hesitancy scale was significantly lower than any other measure (mean = 2.26). • Fear of COVID-19 was a predictor of vaccine attitudes for all dependent measures. • Comfort levels in receiving the vaccine were positively associated with male gender, having more comorbidities, having lower depression scores, not practicing social distancing, and past acceptance of influenza vaccinations.

CANADA COMPARED TO GLOBAL POPULATION

Table 9. Evidence of vaccine attitudes of the global population (n=6)

STUDY	METHODS & SURVEY TOOLS	KEY KAB OUTCOMES
Quasi-experimental studies (n=1)		

Duch (2021) *preprint* (94) Quasi-experimental study 13 countries (Australia, Brazil, Canada, Chile, China, Colombia, France, India, Italy, Spain, Uganda, UK, USA) Nov-Dec 2020	To understand public opinions on key aspects of vaccine allocation, an online experiment of 15,536 adults (18+) across 13 countries was conducted. Participants were require to make eight binary choices about hypothetical vaccine recipients that randomly varied on five attributes including occupation, age, transmission status, risk of death from COVID-19, and income. Question Topics: 1) Vaccine perceptions Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• Overall there was global consensus on which population segments should have priority for a COVID-19 vaccine. • In almost all countries and across participants of different education levels, incomes, and political ideologies, results show that the public favors prioritizing the vaccine to healthcare workers, those at high risk, those in lower income brackets, and older populations. • At least two thirds of participants in each of the countries (80% in Canada) believed that the government should assume the lead role in the distribution of COVID-19 vaccines. However, there is evidence that a large proportion of individuals would be willing to pay for a vaccine if it were available privately. This ranged from 18% of participants in France to 79% in India and Uganda. 35% of Canadians would be willing to pay for a vaccine. • There was no consensus on support for mandatory vaccination either globally or within national borders. In the global sample, 24% were strongly opposed and 38% were strongly in favor. In France 60% of participants opposed mandatory vaccination whereas in China, India, and Uganda very few people were strongly opposed.
Cross-sectional studies (n=5)		
Crespo (2021) *preprint* (59) Cross-sectional studies 15 countries: Australia, Canada, Denmark, Finland, France, Germany, Italy,	Change in intention to vaccinate over time was assessed using two online surveys, one in Nov 2020 and the other in Jan 2021 across fifteen countries. It is unclear if and how many individuals completed both surveys. Question Topics: 1) Vaccine intentions	• In Canada, intention to vaccinate increased from 44.2% in Nov to 55.2% in Jan. • In the Jan survey, the countries with the highest intentions to vaccinate included the UK (77.5%), Denmark (67%), and the Netherlands (63.1%). The countries with the lowest intentions included South Korea (43.7%), France (39.2%), and Singapore (34.8%). • Increase in intention to vaccinate between Nov and Jan was seen in Spain (24.1%), UK (23.2%), Sweden (22.7%), Finland (20.4%), Netherlands (18.5%), Italy (15.4%), Norway (14.6%), France

Japan, Netherlands, Norway, Singapore, South Korea, Spain, Sweden, UK Nov-Jan 2021	Survey tools available? No Formative research conducted? No Survey pre-tested? No	(14.2%), Denmark (13.3%), Germany (13.0%), Canada (11%), and Japan (0.8%). • Countries with a decrease in intentions between Nov and Jan included Australia (-6.6%), South Korea (-5.0%), and Singapore (-1.3%). • In 11/15 countries there was a significant decrease in the proportion of individuals who reported concern about the side-effects of a vaccine. In Canada, this concern decreased from 53.3% in Nov to 47.9% in Jan.
Clarke (2021) (95) Cross-sectional study Australia, Canada, France, Italy, Spain, UK and USA Nov-Dec 2020	An international online survey of 8209 adults from high income countries was conducted with the goal of evaluating perceptions of prioritization of global vaccine allocation on a scale 0 ('very much disagree') to 100 ('very much agree'). Question topics: 1) Vaccine perceptions Survey tools available? No Formative research conducted? No Survey pre-tested? No	• All countries favoured in order of most support: allocating based on need, by affordability, and by which country developed the vaccine. • The UK had the largest percentage of respondents who do not favor donating purchased vaccines to other countries (26%) and Italy and Spain had the lowest (15%). • Between 48% and 56% of respondents would donate their country's vaccines at some level. The highest was Canada (56%) and lowest France (48%).
World Economic Forum (2020) *unpublished* (96) Cross-sectional study 15 countries (Australia, Brazil, Canada, China, France, Germany, India,	An online survey of 18526 individuals globally analyzed intention to vaccinate and perceptions on the vaccine. Of these, 1000 participants were Canadian. Question Topics: 1) Vaccine intentions 2) Vaccine perceptions 3) Vaccine hesitancy	• 73% stated they would get a vaccine for COVID-19 if it were available. Compared to three months earlier (Aug), this is a 4% drop. • Intention has declined between Aug and Oct in 10/15 countries, most of all China, Australia, Spain, and Brazil. • Countries with the highest intent include India (87%), China (85%), South Korea (83%), and Brazil (81%). • France has the lowest intention to vaccinate (54%), followed by the USA (64%), and Spain (64%).

Italy, Japan, Mexico, South Africa, South Korea, Spain, UK, and USA) Oct 2020	Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? Yes	• 52% indicated that they would become vaccinated within three months after vaccine becomes available to all. • 55% believe that a vaccine will not be available on the market until the third quarter of 2021. • Globally, the most common reasons for hesitancy include concerns about side-effects (34%), and concerns that clinical trials are moving too quickly (33%).
Mannan (2021) *preprint* (97) Cross-sectional study 60 countries: (Afghanistan, Algeria, Argentina, Australia, Bangladesh, Belgium, Bolivia, Botswana, Brazil, Canada, Chile, China, Columbia, Cuba, Dominican Republic, Ecuador, Egypt, El Salvador, England, Fiji, France, Germany, Guatemala, India. Italy, Jamaica, Japan, Kenya, Kiribati, Libya, Mali, Malaysia,	Sixty national representative online and telephone surveys were conducted capturing 26,852 responses from adults (19+) regarding vaccine acceptance and attitudes. Question Topics: 1) Vaccine intentions 2) Vaccine hesitancy 3) Vaccine attitudes Survey tools available? Yes Formative research conducted? Yes Survey pre-tested? No	• 62.6% of Canadians strongly accepted a COVID-19 vaccine which was the lowest acceptance recorded among countries in North America. • 65.5% strongly agreed that it was important to get a vaccine to protect others, 57.6% agreed that pharmaceutical companies will develop a safe vaccine, and 31.7% believed that vaccines were safer if they made in America or Europe rather than other countries. • Hesitancy was demonstrated with 48.7% worried about side effects, 44.7% worried about unforeseen impacts, 43.7% had concerns over commercial profiteering, 42.6% had general mistrust of vaccine benefits, and 34.6% had a preference for natural immunity. • Vaccine acceptance for each country: **Africa** Algeria (66.3%), Egypt (43.6%), Botswana (71.2%), Kenya (61.3%), Libya (49.6%), Mali (62.4%), Mauritius (82.8%), Morocco (48.4%), Nigeria (61.5%), South Africa (79.3%) **Asia** Afghanistan (47.2%), Bangladesh (49.8%), China (87.4%), India (73.9%), Japan (71.4%), Malaysia (52.7%), Saudi Arabia (51.1%), Singapore (66.8%), South Korea (76.2%), Turkey (59.2%) **Oceania** Australia (89.9%), Fiji (87.2%), New Zealand (88.4%), Kiribati (89.8%), Nauru (88.3%), Palau (89.2%), Papua New Guinea (91.9%), Solomon Islands (92.6%), Tonga (92.9%), Tuvalu (90.5%)

Mauritius, Mexico, Morocco, Nauru, New Zealand, Nicaragua, Nigeria, Palau, Panama, Papua New Guinea, Paraguay, Peru, Poland, Russia, South Africa, Saudi Arabia, Singapore, Solomon Islands, Spain, South Korea, Sweden, Switzerland, Turkey, Tonga, Tuvalu, United States of America, Uruguay, Venezuela) Jun-Sep 2020		**North America** Canada (62.6%), Cuba (77.9%), Dominican Republic (79.5%), El Salvador (71.8%), Guatemala (75.0%), Jamaica (71.0%), Mexico (73.3%), Nicaragua (81.2%), Panama (87.4%), United States (74.8%) **South America** Argentina (81.3%), Brazil (86.2%), Bolivia (82.8%), Chile (79.2%), Columbia (81.8%), Ecuador (70.2%), Paraguay (67.7%), Peru (77.8%), Uruguay (75.6%), Venezuela (74.8%) **Europe** England (69.3%), Belgium (60.4%), Germany (65.2%), Italy (68.4%), France (51.9%), Poland (52.3%), Spain (72.5%), Sweden (62.7%), Switzerland (60.2%), Russia (51.3%)
Lazarus (2020) (98) Lazarus (2021) (99) Cross-sectional study 19 countries: (Brazil, Canada, China, Ecuador, France, Germany, India, Italy, Mexico,	Vaccine acceptance rates and factors influencing acceptance of a COVID-19 vaccine was analyzed using an online survey of 13,426 adults. The data from this survey was analyzed differently in two publications. Question Topics: 1) Vaccine intentions Survey tools available? Yes	• 71.5% of participants reported that they would be "very likely" or "somewhat likely" to take a COVID-19 vaccine • 48.1% reported that they would accept their employer's recommendation to take the vaccine. • China (88.6%), Brazil (85.4%), and South Africa (81.6%) had the highest acceptance rates and Nigeria (58.9%), Poland (56.3%), and Russia (54.9%) had the lowest. • The acceptance rate in Canada was 68.7%. • Individuals aged 25+ were more likely to accept the vaccine than those aged 18-24. The strongest difference was seen (OR 1.73, 95% CI: 1.48-2.02)

Nigeria, Poland, Russia, Singapore, South Africa, South Korea, Sweden, UK, USA) Jun 2020	Formative research conducted? Yes Survey pre-tested? Yes	when responses from the oldest age cohort (65+) were compared to the youngest cohort (18-24). • People with higher education, women, those who earned more income, those who reported COVID-19 illness in the family, and those who trusted their government were more likely to accept the vaccine. • Having a high/very high education may be linked to lower vaccine acceptance in Canada, Spain, and the UK.

Emerging Evidence on COVID-19

Rapid Review on Protective Immunity

Introduction

Do antibodies to SARS-CoV-2 confer immunity against reinfection with SARS-CoV-2, is there long-term protective immunity (greater than 6 months post-infection) and does past infection with the original wild-type SARS-CoV-2 protect against the current variants of concern?

Understanding the extent and limits of protective immunity has important implications for the COVID-19 pandemic. Immunity arising from coronaviruses in general varies tremendously, from a few months for the seasonal coronaviruses associated with the common cold, to 2-3 years for the emerging coronaviruses such as SARS-CoV-1 and MERS (1). For SARS-CoV-2, it is known that most people develop immune responses after infection, however, for how long and to what extent this protects people from reinfection is not yet clear.

Reinfection with SARS-CoV-2 appears to be uncommon but there are challenges to studying this. RT-PCR testing is excellent for identifying the presence of virus in making the initial diagnosis, but it will also be positive in the presence of non-infectious virus particles (RNA fragments) so, on its own, it cannot confirm reinfection. To address this, several definitions of reinfection have been proposed both in the literature and by public health organizations (e.g., ECDC, PAHO). For the purposes of this review, confirmed reinfection is at least one documented negative RT-PCR test between episodes and genomic sequence data from both episodes to distinguish two different genetic clades or viral lineages (2). Suspected cases of reinfection are defined in this review as those with clinically or lab confirmed initial infection with a positive RT-PCR test >90 days from first episode or episodes occurring less than 90 days apart but with epidemiological evidence of re-exposure to SARS-CoV-2 (2, 3). There are also challenges in assessing long-term immunity from COVID-19. This arises from the fact that not all people who have positive antibodies for SARS-CoV-2 are immune and not everyone who has been diagnosed with COVID-19 develops antibodies after infection. Some people who are diagnosed with COVID-19 do not have detectable antibody levels but still recover, even when they have severe disease. This is likely influenced by strong cell-mediated immune responses, specifically from CD4+ and CD8+ T-cells that may contribute to long-term immunity against reinfection. Evidence suggests neutralizing antibodies and immune cell activity specific to SARS-CoV-2 are good indicators of protective immunity. A number of techniques and tests have been developed to measure immune responses. The variation and interplay of antibodies, B and T cell response to infection, and the variety of detection techniques available not only complicate the assessment of long-term immunity, it also complicates the question of whether immunity to the original wild-type SARS-CoV-2 protects against the current variants of concern.

This rapid review summarizes the evidence from the most recent studies on reinfection, persistence of antibodies and other immune markers for more than 6 months following initial SARS-CoV-2 infection and preliminary evidence on immunity against variants of concern published before February 11, 2021. Animal models of disease were not included.

Key Points

- Forty-nine studies were identified including fifteen recent cohort studies on risk of reinfection, twenty-one studies on the kinetics and durability of antibodies and other immunity markers at >6 months from initial SARS-CoV-2 infection, ten studies on antibody response or immunity and the new variants of concern and three relevant systematic reviews.
- Overall we found that the risk of reinfection was low, most people had markers of immunity at 6 months and in preliminary studies the B.1.351 variant was not as readily neutralized by convalescent sera.

Risk of reinfection:

- The best evidence to date on protective immunity comes from reinfection data reported in fifteen recently published cohort studies with both prospective and retrospective designs. More preliminary evidence from twenty-one case reports/series on risk of confirmed reinfection in 30 cases are reported in Appendix 1.
- The included studies report that previous infection resulting in antibodies seems to be associated with protection from reinfection for up to seven months.
- Cohorts that used only confirmed cases of reinfection in their risk estimates reported higher levels of protection (96-99%) (4-6) than those that included suspected cases of reinfection (83-94%) (7-11). This trend was echoed by the adjusted risk of reinfection estimates. In a cohort of confirmed reinfections from Qatar, the risk of reinfection was 0.01% (95%CI: 0.01-0.02%, n=133266). In cohorts of suspected reinfections from the UK and Mexico, the risk of reinfection was 0.7% (95%CI: 0.6-0.8, n=36,509) (12) and 0.26% (n=100,432) (13), respectively.
- The median time between initial infection and reinfection in the case reports (Appendix 1) was 81 days (range 13-250), in the confirmed reinfection cohorts it was 52-65 days (range 15-212) (5, 6), and in the suspected reinfection cohorts is was 56-172 days (range 40-227) (8, 13). The latter may have data points that are misclassified and instead represent re-positive results or recurrence, both of which have been reported in the literature.
- Based on both confirmed and suspected reinfection cohorts, individuals with evidence of previous infection had much lower attack rates of infection at follow-up up to 9 months compared to those who were seronegative or RT-PCR negative at baseline (0%-3.4% vs. 1.29%-28.7%) (4, 7, 9-11, 14-17). Several studies indicate that those who did not seroconvert may not have the same degree of protection from reinfection as those with high titers of antibodies (4, 14, 18). However, after reinfection the majority of cases showed an IgG response (14).
- Higher and prolonged IgG response was correlated with a lower risk of reinfection. Older age, duration of symptoms, and number of symptoms were correlated with higher IgG responses after primary infection (18).

Immune response markers >6 months post infection:

- Twenty-two recently published studies with follow-up of > 30 observations beyond 6 months post infection (up to 9 months) provide evidence to support immunity based on circulating antibody levels, B-cells and T-cells against SARS-CoV-2 (Table 2). The relationship between these correlates of immunity and protection against SARS-CoV-2 infection or reinfection by either wild type SARS-CoV-2 or emerging variants of concern are not fully understood.
- Eight studies report cellular immune response linked to memory B cells (i.e., immune cells that produce virus targeting antibodies) and T cells (i.e., immune cells that guide cell mediated adaptive immune responses) following a natural infection likely confer some long-term immunity to subsequent reinfections (1, 19, 20).
    - Memory B-cell and T-cell activity were elevated and expanded beyond 6 months post infection, which may be better measures of protective immunity compared to circulating antibodies that wane overtime after recovering from SARS-CoV-2 infection (21-24).
    - In 80% of individuals that had mild to moderate COVID-19, a high frequency of total memory B cells specific to the Receptor Binding Domain (RBD) of SARS-CoV-2 virus were identified (25).
    - CD8+ T cell activity was variable, and not directly comparable primarily due to differences in peptide sequences used in cell simulation. One study reported SARS-CoV-2 CD8+ T-cells to be detectable in 50% of cases between 6-8 months, while another study reported CD8+ T-cells memory responses to be significantly increased between 6-9 months post infection (21, 25). Whereas memory CD4+ T-cell activity continued to be detected in 92% of individuals between 6-8 months (25).
    - A single study reports a correlation between IgG and IgM seropositivity and CD8+ T-cell activity among those that had severe COVID-19 (23).
- Long-term trends in antibodies were described in twenty studies:
    - Eleven studies report the majority (>86%) of individuals remained positive for circulating SARS-CoV-2 specific neutralizing antibodies (NAb), S protein and/or RBD IgG antibodies ≥6 months from infection (18, 19, 24-27, 27, 28, 28-30).
    - NAb levels were higher and S protein IgG levels were lower than among severe COVID-19 cases when compared to those who experienced mild to moderate COVID-19 (18, 19, 24-27, 27, 28, 28-30).
    - Only 25-50% of participants remained positive for N protein antibodies (class variable or not specified) beyond 6 months (17, 17, 27, 29-31), which was comparatively less time than other virus targeting antibodies. (17, 27, 29, 30)

Immunity and new variants of concern:

- Preliminary experiments (n=10) on neutralization of the variants of concern have shown *in vitro* evidence that B.1.1.7 can be neutralized while B.1.351 is less likely to be neutralized by antibodies from wild-type SARS-CoV-2.

Reviews:

- Relevant rapid and systematic reviews include COVID-19 research up to June–September, 2020, on correlates of immunity from studies early in the pandemic. These are included as resources for research on time points earlier than 6 months.

Overview of the Evidence

Reinfection studies included prospective cohorts, some of which were large, multi-center studies that were at low risk of bias and have high generalizability. Multivariable analyses to account for potential confounding were not always conducted and this may bias the results. Retrospective cohorts of medical record data or routinely collected surveillance data on COVID-19 were also captured. Some of these studies appeared to have good generalizability as they represented large or national databases. Others were more focused on healthcare workers at a single center or specific patient groups. However, retrospective cohorts are at higher risk of bias due to the retrospective nature of the study, missing data, and confounding. The case reports/series included in the appendix are at high risk of bias due to selection bias and lack of a comparator group. However, they offer additional data on the case attributes and timing of reinfection.

The long-term immunity studies mainly included longitudinal evidence from observational studies, particularly of, prospective cohort, case series and cross-sectional design, which are at moderate to high risk of selection biases and confounding. For example, most studies reported clinical infection severity among study participants, but many do not appear to have considered differences in baseline immune status influenced by co-morbid conditions (e.g., cancer, heart conditions, kidney disease, diabetes, etc.) within study samples. Immune responses ≥ 6 months after a SARS-CoV-2 infection were highly variable across studies. Differences in study participant demographics, baseline immune status, clinical severity of infections, investigated immune outcomes, follow-up time and measurement methods likely contributed to observed heterogeneity. Variability may also come from the application of different antibody and immune cell detection methods with different test sensitivity and specificity parameters. All of these factors make it difficult to compare results across studies and introduce detection bias (29).

Preliminary evidence from *in vitro* studies using convalescent or vaccinated sera have examined the neutralization of variants of concern, mainly B.1.1.7 and B.1.351. These studies give us an early indication of potentially how well the circulating antibodies will recognise the variants, but they do not tell us how cross-reactive immune memory may be affected and their generalizability is limited. Additional research and monitoring of the convalescent and vaccinated populations will add further insight in the near future.

Knowledge gaps:

- Lack of high quality studies on the duration and efficacy of protection by neutralizing antibodies.
- Lack of understanding of how the immunological measures (e.g., neutralizing antibody titers) correlate to protection. Clinical effectiveness data is also needed to provide a definitive assessment of vaccine mediated protection.
- The role of specific antibodies, B cells and T cells in the elimination of infection have not been definitively identified in humans.
- Additional evidence is needed on variants of concern and the role of cross-reactive immune memory on reinfection from these variants.

CONTENTS

RISK OF REINFECTION

The European CDC has created a flowchart for assessing reinfection (2) and further definitions to differentiate confirmed reinfection from relapse/reactivation and recurrence have been proposed (3). The definitions used in this review are based on these published guidelines.

Confirmed reinfection requires: Confirmed initial infection by RT-PCR AND confirmed second infection by RT-PCR AND negative RT-PCR result(s) collected between first and second infection AND genomic sequence data from both episodes to distinguish two different viral isolates

Suspected reinfection requires: Positive RT-PCR test >90 days from first episode (either clinically or lab confirmed) OR <90 days between episodes but epidemiological evidence of re-exposure to SARS-CoV-2.

The best evidence to date on protective immunity comes from the few recently published cohort studies on risk of reinfection. Small case reports/series detailing suspected reinfections have been excluded, however, cases of confirmed reinfection have been summarized in Appendix 1. Studies of prolonged and recurrent infections are also excluded but have previously been summarized in an Infectious Period rapid review, available through the emerging science secretariat.

Results of reinfection cohort studies (n=15):

- Previous infection resulting in antibodies seems to be associated with protection from reinfection for up to seven months, however there has been a small proportion of people that have become reinfected. Reasons for reinfection or lack of protective immunity are not well understood.
- Only three studies calculated risk of reinfection estimates from confirmed reinfection cases. These studies reported a high estimate of protection against reinfection in cohorts from the UK (>96%) and Qatar (>99%) (4-6).
- Prospective cohorts of suspected reinfections from the UK and France suggest past SARS-CoV-2 infection provides protective immunity for up to 6 months in 83-90% of individuals (7-9). Retrospective cohorts from the USA and UK indicated 90-94% of previously infected individuals had protection for up to 6 months (10, 11).
- Risk of reinfection was low across studies based on large general population retrospective cohorts. In Qatar, the adjusted risk for confirmed reinfection was 0.01% (95%CI: 0.01-0.02%, n=133266) (5). Risk estimates were slightly higher in cohorts that included suspected reinfection: In the UK the risk was 0.7% (95%CI: 0.6-0.8, n=36,509) (12) and in Mexico the risk was 0.26% (n=100,432) (13).
- Time to reinfection was a median of 52-65 days (range 15-212) in the confirmed reinfection cohorts (5, 6) vs. 56-172 (range 40-227) in the suspected reinfection cohorts (8, 13). The latter may have data points that are misclassified and instead represent re-positive results or recurrence, both of which has been reported in the literature.
- Individuals with evidence of previous infection had much lower attack rates of infection at follow-up times of up to 9 months compared to those who were seronegative or PCR negative at baseline (0%-3.4% vs. 1.29%-28.7%) (4, 7, 9-11, 14-17). Several studies indicate that those who did not seroconvert may not have the same degree of protection from reinfection as those with high titers of antibodies (4, 14, 18). However, after reinfection the majority of cases showed IgG responses (14).
    - Healthcare workers with positive SARS-CoV-2 anti-spike IgG responses had lower rates of PCR-positive tests after 31 weeks of follow-up compared to healthcare workers with no IgG responses at the start of the study (0.13 vs. 1.09 per 10,000 days at risk) (7).
- Higher and prolonged IgG response was correlated with a lower risk of reinfection. Older age, duration of symptoms, and number of symptoms are correlated with higher IgG responses after primary infection (18).
- A surveillance study conducted in the UK, reporting a rate of suspected reinfection of 0.7%, found that reinfection was more positively correlated with the overall regional increase in cases rather than the regional increase in the B.1.1.7 percentage, indicating that the immunity built up from initial infection likely also provides protection against the B.1.1.7 variant (12).
- The symptomology reported during reinfection has been highly variable:

- One study found that patients with serious primary disease were more likely to develop severe symptoms during reinfection (13). However, as no mass screening was in effect, second-time asymptomatic cases of SARS-COV-2 infection are not likely to be identified. Many reports of reinfection may be biased toward identification of more severe cases.
- Another study found that 88.5% of cases had more symptoms upon reinfection than initial infection, however overall severity of symptoms was not reported (14).
- Two studies reported that reinfection was less severe than primary infections (5, 6).

Table 1: Cohort studies evaluating the risk of reinfection with SARS-CoV-2 (N=15)

STUDY	METHOD	KEY OUTCOMES
Confirmed reinfection (n=3)		
Jeffery-Smith (2021) (4) Outbreak investigation and longitudinal study UK Apr-Oct 2020	Two long-term care homes that had experienced an outbreak in the first wave of COVID-19 experienced a second outbreak. Outbreak investigations and SARS-CoV-2 serology were conducted to assess the role of prior antibodies in the protection against SARS-CoV-2 reinfection.	Nasal swabs -1.1% (1/88) of individuals that had confirmed previous SARS-CoV-2 exposure (either seropositive or PCR positive) from the first outbreaks (5 months earlier) became PCR-positive during the second outbreaks compared with 24.7% (18/73) of those with seronegative status after the first outbreaks. -Prior exposure had a protective effectiveness of 96.2% (95% CI: 72.7%–99.5%) against infections during the second outbreaks for an estimated risk ratio of 0.038 (95% CI: 0.005–0.273; p < 0.0001). -Whole genome sequencing found that the second COVID-19 outbreaks were caused by SARS-CoV-2 strains that were genetically different from their respective first outbreaks.
Abu-Raddad (2021) (6) *Preprint* Retrospective cohort study Qatar Apr-Dec 2020	SARS-CoV-2 antibody-positive persons with a PCR-positive swab ≥14 days after the first-positive antibody test were followed for a median of 17 weeks (range: 0-45) for evidence of reinfection (n=43,044). Seronegative individuals (n=149,923) were also followed for incidence of infection. Viral	Nasopharyngeal and oropharyngeal swabs -314 seropositive individuals had a PCR-positive swab ≥14 days after the first-positive antibody test. - 32/314 suspected cases had good evidence for reinfection (Ct ≤30 for reinfection swab), 97 cases with some evidence (Ct >30 for reinfection swab), while evidence was weak for the remaining 185 cases. -For cases with good evidence for reinfection (32/314, 10.2%), the median time between the first-positive antibody test and the reinfection swab was 52 days (range: 15-212 days). Reinfections were less severe than primary infections. -Genome sequencing demonstrated that 5/16 cases, for which paired specimens were available, were confirmed reinfection for a confirmation rate of 31.6%.

	genome sequencing was conducted for paired viral specimens (n=16) to confirm reinfection.	-The reinfection risk among antibody-confirmed cases was 0.10% (95% CI: 0.08-0.11%) and the reinfection incidence rate was 0.66 per 10,000 person-weeks (95% CI: 0.56-0.78). -The infection risk for seronegative individuals was estimated at 2.15% (95% CI: 2.08-2.22%), with an infection incidence of 13.69 per 10,0000 person weeks (95% CI: 13.22-14.14) -A decreasing trend in the incidence rate of reinfection with each additional month of follow-up demonstrated that protective immunity did not wane over the seven months. -Efficacy of natural infection against reinfection was estimated to be 95.2% (95% CI: 94.1-96.0%).
Abu-Raddad (2020) (5) *Preprint* Retrospective cohort study Qatar Feb-Aug 2020	All SARS-CoV-2 laboratory-confirmed cases with at least one RT-PCR positive swab that was ≥45 days after a first-positive swab were individually investigated for evidence of reinfection (n= 133,266 cases). Viral genome sequencing of the paired first-positive and reinfection viral specimens was conducted to confirm reinfection in a small subset of cases (n=12).	Nasopharyngeal and oropharyngeal swabs -243 persons (0.18%) had a subsequent positive swab ≥45 days after the first-positive swab. Of these, 54 cases (22.2%) had strong or good evidence for reinfection (PCR positivity was associated with contextual evidence supporting the status of reinfection). -Median time between first and reinfection swab was 64.5 days (45-129, range). -Only one person was hospitalized at time of reinfection, this case only had mild infection. -Only four cases of reinfection were confirmed by viral genome sequencing. -Risk of reinfection was estimated at 0.01% (95% CI: 0.01-0.02%) and incidence rate of reinfection was estimated at 0.36 (95% CI: 0.28-0.47) per 10,000 person-weeks. -The authors conclude that reinfection is a rare phenomenon and immunity against reinfection likely lasts at least a few months after first infection.
Suspected reinfection (n=12)		
Lumley (2020) (7) Prospective cohort study UK Apr-Nov 2020	Followed asymptomatic and symptomatic staff (n=12,541) at Oxford University Hospitals for up to 31 weeks to estimate the relative incidence of PCR-positive test results and new symptomatic infection according to antibody status.	Nasal and oropharyngeal swab -Health care workers with positive SARS-CoV-2 anti spike IgG assays at baseline have lowers rates of PCR-positive tests at follow up than workers with negative baselines results (0.13 vs 1.09 per 10,000 days at risk). -The incidence of positive PCR tests was inversely associated with anti-spike antibody titers, suggesting previous infection resulting in antibodies to SARS-CoV-2 is associated with protection from reinfection for at least 6 months. -Of the three seropositive health care workers that had subsequent PCR-positive tests for SARS-CoV-2 infection, only one had previously tested positive for SARS-CoV-2, 190 days

		prior. This case was asymptomatic upon possible reinfection, with negative RT-PCR tests 2 and 4 days later and no subsequent rise in antibody titers -Reinfection results could be consistent with a re-exposure to SARS-CoV-2 that did not lead to symptoms but could also plausibly have been a false positive. Caution should be used when interpreting the results of this study.
Hall (2021) (8) *Preprint* Prospective cohort study UK Jun-Nov 2020	Asymptomatic and symptomatic staff (n=20,787) working at hospital sites participating in the SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) Study were followed for 5 months to estimate the relative incidence of PCR-positive test results according to baseline antibody and/or PCR results.	Swab type not specified -6,614 (32%) participants had evidence of prior infection and were assigned to the positive cohort, 14,173 (68%) participants that had no evidence of prior infection were assigned to the negative cohort. -On follow-up, 409 new infections in the negative cohort and 44 reinfections were identified. Of these, 22% of new infections and 66% of reinfections were asymptomatic. -The incidence density was 3.3 and 17.0 for new RT-PCR positive infections per 100000 days follow-up. -The cumulative incidence for probable, possible, and all reinfections was 0.3, 2.3 and 6.7 per 1,000 participants, respectively, whereas all new infections were 22.4 per 1000 participants. -Previous infection was found to have a significant protective effect. Considering only probable reinfections, the participants in the positive cohort had a very low odds of reinfection (adjusted OR: 0.01, 95% CI 0.00-0.03). The adjusted OR considering both probable and possible reinfections was 0.17 (95% CI 0.13-0.24). -The median interval between the historic PCR positive date or date of primary infection and the reinfection PCR positive date was 162 days (95-223) or 172 days (90-227), respectively.
Dimeglio (2021) (9) *LTE* Prospective cohort study France Jun-Dec 2020	Healthcare workers (n=8758) were screened for serum SARS-CoV-2 anti-spike antibodies and neutralizing antibody titers after the first wave of epidemic (June/July). Serology was investigated over time and new infections were identified during follow-up in Nov/Dec.	Swab type not reported -The median follow-up was 167 days (IQR:156-172). -Among the seropositive group, 1.8% (5/276) were positive at follow-up compared to 12.1% (1028/8482) of the seronegative group ($p<0.01$). -The five individuals who tested seropositive at baseline and then experienced infection during follow-up included two with low/undetectable neutralizing antibody titers after the first infection, and three with above-median titers. -The data indicate that previous infection provided protective immunity for at least 167 days.
Clarke (2021) (17)	Longitudinally screened patients	Nasopharyngeal swab

Preprint Prospective cohort study UK Feb 2020-Jan 2021	receiving in-centre haemodialysis (n=356) for SARS-CoV-2 seropositivity (anti-NP or anti-RBD antibodies) and RT-PCR positivity. Recorded positive PCR test results at >60 days following a positive serological test at baseline, to prevent capture of persistent viral detection rather than reinfection.	-Patients with initial seropositive results were significantly less likely to test positive by PCR at follow up compared to patients that were initially seronegative: 3.4% (5/129) vs. 13.2% (30/227), p<0.005. -Immune responses to natural SARS-CoV-2 infection in haemodialysis patients lasted for up to 6 months, even in patients who had mild or asymptomatic infection.
Dobaño (2021) (18) *Preprint* Prospective cohort study Spain Mar-Nov 2020	Evaluates the seroprevalence and levels of antibodies 149-270 days after the onset of symptoms in a cohort of 173 primary health care workers with confirmed infection (via RT-PCR) at the first peak of the pandemic (March-April 2020). Three venous blood collection time points between September and November 2020 were used in assessing immunity and possible reinfection among these healthcare workers as part of a 1.5 year long cohort study.	-The percentage of seropositivity at follow-up combining RBD and S antigens was 60.69% for IgM, 76.30% for IgA, and 90.17% for IgG. -2.3% reinfections (4/173). Two symptomatic cases were seronegative prior to reinfection, one asymptomatic case was seropositive, and one had unknown serostatus. Reinfections occurred between 3-8 months post initial infection. -Having been admitted to hospital, presenting with fever, anosmia and/or hypogeusia, and previous allergies were associated with higher levels of antibodies during follow-up (5-9 months later). -Older age, duration of symptoms, and number of symptoms correlated with higher IgGs.
Graham (2021) (12) *Preprint*	General population longitudinal data that was prospectively collected using the	Swab type not reported -304 individuals reported two positive tests separated by more than 90 days, 249 of which had a symptom free period between

Longitudinal surveillance study UK Sept-Dec 2020	COVID Symptom Study app was combined with surveillance data from the Covid-19 UK Genetics Consortium to study rate of reinfection, as well as other COVID-19 disease characteristics. Reinfection was defined as two RT-PCR positive tests separated by more than 90 days with an asymptomatic period for more than seven days between PCR tests. Assessed risk of reinfection for the new variant B.1.1.7 by calculating the correlations between number of possible reinfections and the proportion of new variant cases over time.	the two tests, for a rate of reinfection estimate of 0.7% (95%CI: 0.6-0.8) (249/36,509). -Reinfection rate did not vary across regions or time. -Reinfection was more positively correlated with the overall regional increase in cases rather than the region increase in the B.1.1.7 percentage, indicating that the immunity built up from the initial infection may also provide protection against the B.1.1.7. variant.
Ali (2020) (14) *Preprint* Retrospective Cohort Iraq May-Oct 2020	To investigate the impact of the immunoglobulin (IgG) level on reinfection in recovered COVID-19 patients (n=829 patients admitted between May and Oct to a single center), IgG levels against SARS-CoV-2 were measured just following recovery (a negative RT-PCR result defined as a Ct-value >36.7) and patients were	Pharyngeal swabs -Of the 87 patients that tested negative for IgG following initial recovery, 25 (28.7%) were considered reinfected, confirmed by positive RT-PCR result. This was higher than in the group of 742 patients that tested positive for IgG following initial recovery (1/742, 0.13%). This suggests that patients with low IgG levels following initial infection may be more susceptible to reinfection. -The occurrence of reinfection in the group ranged from 26 to 138 days after recovery from the initial infection. -88.5% of cases had more symptoms upon reinfection than initial infection, however overall severity of symptoms was not reported. -95% of cases were positive for IgG following reinfection. -Result are preliminary and methods were poorly described in this study. It is unclear if patients were enrolled and prospectively followed or whether reinfection status is based on

	presumably followed to assess reinfection.	medical records. Caution should be used when interpreting the results of this study.
Harvey (2020) (10) Retrospective cohort study USA Jan-Aug 2020	Analysis of a national sample from a de-identified dataset based on commercial laboratory tests and medical claims and records (n= 3 257 478). Patients were identified at baseline as either SARS-CoV-2 antibody-positive or antibody-negative then assessed in 30 day intervals (up to >90) for nucleic acid amplification test (NAAT) positivity.	Swab type not specified -Seronegative patients (n=2,876,773) were followed for a median of 47 days (IQR: 8-88) and seropositive patients (n=378,606) were followed for a median of 54 days (IQR: 17-92). - 18.4% of patients converted from seropositive at baseline to seronegative during follow-up of 90 or more days after first antibody test. -Patients who were seropositive and had a NATT test during follow-up (n=41587) were at a decreased risk of SARS-CoV-2. NAAT positive: 2.7% from 31 to 60 days, 1.1% from 61 to 90 days, and 0.3% at more than 90 days. Whereas approximately 3% of individuals who were seronegative had a NAAT positive test during each follow-up period. -This corresponds to a ratio of positive NAAT results among patients who had a positive antibody test at index vs those with a negative antibody test at index: 0.67 (95% CI: 0.6-0.74) at 31 to 60 days; to 0.29 (95% CI: 0.24-0.35) at 60 to 90 days; and to 0.10 (95% CI: 0.05-0.19) at more than 90 days.
Breathnach (2021) (11) *LTE* Retrospective cohort study UK Feb-Dec 2020	Analyzed laboratory data to compare risk of having a positive SARS-CoV-2 PCR assay in the second wave of the pandemic between patients who had evidence of COVID-19 (PCR positivity or seropositivity) in the first wave of infections (n=10,727) vs. patients who had a previous negative PCR or antibody test (n=55,274). Cases where the second positive result occurred ≤ 90 days from the first wave were excluded.	Swab type not reported -Only eight patients with evidence of past COVID-19 had a positive PCR result during the second wave (0.07%, 8/10,727). PCR positivity was higher during the second wave for patients with no evidence of COVID-19 in the first wave (1.29%, 713/55,274). -This implies a protective effect and relative risk of 0.06 (95% CI: 0.03-0.12) for those with evidence of infection in the first wave.
Hanrath (2020) (16)	Analysis of healthcare worker testing data	Nasopharyngeal and oropharyngeal swabs

Preprint Retrospective cohort study UK Mar-Nov 2020	during an initial (Mar 10-July 6, 2020) and following second wave (July 7-Nov 20, 2020) of the pandemic, to address the question of whether previous SARS-CoV-2 infection was associated with protection. The primary endpoint for analysis was symptomatic SARS-CoV-2 infection confirmed by RT-PCR during the second wave. Asymptomatic PCR screening was also conducted on a pilot basis.	-1038 HCWs with evidence of previous infection (positive PCR and/or Ab) and 10,137 without (negative Ab, without positive PCR) were identified during the first wave. -During the second wave, 2243 healthcare workers underwent PCR testing for symptoms. 128 of which had previous confirmed infection and 2115 did not. -No reinfections were identified in those with previous infection (test positivity 0%) during second wave follow-up median 173 (IQR: 162–229) days, while test positivity for those without previous infection was 13.7% (290/2115, 95% CI: 12.3–15.2). -Considering the population as a whole, test positivity was 0/1038 (0% [95% CI: 0–0.4) for those with previous infection, compared to 290/10,137 (2.9% [95% CI: 2.6–3.2) for those without (P<0.0001). -Similar results were found in the asymptomatic pilot test: no positive results in the group with previous infection 0/106 (0%, 95% CI: 0–3.5), compared to 22/375 (5.9%, 95% CI: 3.9–8.7, P = 0.011) positive PCR results in the group without previous infection.
Murillo-Zamora (2020) (13) *Preprint* Retrospective cohort Mexico Mar-Jul 2020	RT-PCR was performed on samples from 100,432 patients. Reinfection was defined by the reappearance of COVID-19 symptoms at 28+ days from the first positive COVID-19 test. Clinical and epidemiological data of interest were obtained from medical files and death certificates. Linear regression models were used to evaluate factors associated with the risk of severe symptomatic SARS-CoV-2 reinfection.	Nasopharyngeal or deep nasal swabs -258 laboratory-confirmed cases of 'reinfection' were identified (0.26%). -Time between first and second time episodes was 56 days (IQR: 40-81). No significant differences were observed between patients with non-severe and severe primary disease. -When severe and non-severe second-time infections were compared, patients with more serious primary disease were more likely to develop severe symptoms (39.5% vs. 5.5%, p <0.001), as well as those aged 50 years old or above (52.6% vs. 12.3%, p < 0.001). -In multiple analyses, factors associated with more severe symptomatic reinfection were increasing age, personal history of obesity, asthma, type 2 diabetes mellitus and chronic kidney disease. -Subjects with previous severe COVID-19 had a 20% increased risk of also presenting severe symptoms during secondary disease.
Xu (2020) (15)	COVID-19 patients (n=185) who had	Pharyngeal and anal swabs

Retrospective cohort study China Jan-Apr, 2020	undergone antibody testing were followed up every two weeks to assess immune responses (IgG and IgM) and reinfection over time. The mean follow-up time was 45.7 days.	-No reinfection or evidence of transmission occurred in any patient after discharge. -Of the 35 IgM positive cases, 12 cases turned IgM negative during the follow up. -There were 154 (82.4%) patients with positive IgG results and 33 (17.6%) patients with negative IgG results at 53 days from disease onset. Compared with the IgG negative group, the IgG positive group patients were older, had a longer hospital stay, higher proportion of antibiotic use, higher proportion of severe cases, and higher proportion of CT abnormalities.

LTE= letter to editor, RBD= receptor binding protein

LONG-TERM (>6 MONTHS) IMMUNE RESPONSE MARKERS

This section summarizes twenty-one studies that report immune responses measured ≥ 6 months (up to 9 months) following SARS-CoV-2 infection in studies with >30 observations. Twenty studies reported on circulating antibody levels and eight studies reported on long-term immune responses linked to B-cells and/or T-cells. The majority of included studies (n=19) were prospective cohorts or case series that followed the serology of RT-PCR confirmed COVID-19 cases over time, while the remaining studies were cross-sectional (n=3).

Overall, there was a lot of variability across studies due to differences in study participants, COVID-19 infection severity, frequency and duration of follow-up, investigated immune outcomes and measurement methods, which limit the synthesis of results across studies. Furthermore, the association between detectable immune response markers and protection against re-infection from both the wild-type and emerging VOC is largely unknown.

Key outcomes from B-cell and T-cell immune responses at ≥6 months post infection (n=8):

- Memory B cells (i.e., immune cells that produce virus targeting antibodies) and memory T cells (i.e., immune cells that guide cell mediated adaptive immune responses) following a natural infection likely confer some long-term immunity to reinfection (1, 19, 20). The viral antigen targets, activity, and counts of these memory cells were most frequently measured by flow cytometry cell analysis techniques and various assays. The variability of molecular biology techniques and the viral antigen markers used across studies limit the comparability of study results (17, 21-23, 23-25, 30, 32).
- B-cells are immune cells responsible for the production of antibodies targeting SARS-CoV-2 antigens (1, 19, 20). B-cells can be broadly classified into antibody secreting cells (plasma cells) and memory cells (20). Activated plasma cells produce and secrete circulating antibodies targeting SARS-CoV-2 antigens, while the latter do not actively secrete antibodies but retain the memory to protect against subsequent infections and establish long-term immunity (20).

- Four studies measure and report on B-cell activity alongside circulating antibodies beyond 6 months of infection (23-25, 30). Flow cytometry was the most frequently applied method for detecting B-cell specificity and activity.
    - Memory B-cells specific for S and N proteins, and RBD, viral antigens, were detected in participants at post-infection follow-up beyond 6 months and findings were that the cell counts remained stable or increased in abundance and B-cell clones expanded and matured (23-25, 30).
    - 80% (n=29/36) of mild to moderate COVID-19 cases had high frequencies of total memory B-cells specific to RBD antibodies (IgG+, IgM+, or IgA+) (25) beyond 180 days post infection.
    - In a cohort of previously hospitalized COVID-19 cases B-cell percentages were reported to be highest among IgG and IgM antibody negative participants (range 16.1 ± 6.4 to 16.7 ± 5.5) compared to IgG and IgM positive individuals (range 7.2 ± 3.1 to 7.5 ± 3.8) (23).
    - A single study notes the reduction of S protein antibody secreting B-cells and an increase in memory B-cells targeting SARS-CoV-2 viral antigens, in both severe and mild COVID-19 cases (30). This study also reported SARS-CoV-2 RBD B-cells were minimally cross-reactive with other human coronavirus antigens (30).
- T-cells are immune cells classified by surface receptors CD4+ or CD8+. The primary role of T-cells can be separated into the production of antibodies via B-cell activation (CD4+ T-cells) or the destruction of infected cells presenting certain antigens (CD8+ T-cells) (20, 33). Most of the included studies measured T-cell activity based on simulation by SARS-CoV-2 peptide sequences. The variability and/or the lack of detail on peptide sequences used in simulation studies limit the comparability of study results.
- Six studies report on T-cell outcomes in previously infected cases beyond 6 months post infection (17, 21-23, 25, 32). These studies isolated peripheral blood mononuclear cells from serum samples and analyzed T-cell activity by flow cytometry and/or the simulation of isolated cells with pools of SARS-CoV-2 peptide sequences (i.e., amino acids that make up viral proteins).
    - T-cell responses were highly variable. Generally, the breadth and magnitude of memory T-cell responses increased as time from symptom onset increased and circulating IgG and IgM antibodies waned (21-24).
    - CD8+ T-cells were found to be less robust than CD4+ T-cell responses beyond 6 months from infection in some studies (21, 25, 32). CD8+ T-cell activity was detected in 50% of mild to moderate cases at 6-8 months post infection, while memory CD4+ T-cell activity continued to be detected in 92% of individuals in the same sample (25). Another study found memory CD8+ T-cells to have increased between 6-9 months post infection (21).
    - One study found CD8+ T-cell activity to be correlated with IgG and IgM seropositivity throughout the course of COVID-19 infection in a sample of severe COVID-19 infections (23).

Key outcomes from circulating antibodies immune responses at ≥6 months post infection (n=20):

- Humoral immunity, also called antibody mediated immunity, generally refer to circulating antibodies that are directed at viral antigens (1, 19, 20). Among included studies, circulating antibodies in serum samples were measured by antibody affinity assays, pseudovirus neutralization assays, flow cytometry, and other molecular biology based techniques. The range of reported antibody outcomes included total antibodies, neutralizing antibodies (NAb), antibody class (i.e., IgG, IgM, IgA) which were frequently further described by subclass (i.e., IgG1, IgG3) and/or binding affinity to SARS-CoV-2 viral antigens. Many studies often specified the viral antigen targets of the measured Ig antibodies, which include viral structural proteins: spike (S) protein, S1 or S2 subunit of the S protein, nucleocapsid (N), envelope (E), membrane (M) proteins, receptor binding domain (RBD) proteins, and accessory proteins (i.e., open reading frame (ORF) proteins).
- Studies found SARS-CoV-2 specific antibodies to be detectable in the majority of previously infected individuals beyond 6 months from infection, but seroprevalence of different antibody types was variable. Longitudinal trends in antibody ≥ 6 months post infection across include studies are outlined below, by viral antigen specificity and clinical severity.
- Neutralizing antibodies (NAb) target the SARS-CoV-2 S protein and/or the RBD to neutralize the binding of the virus to ACE2 receptors of potential host cells (27, 28, 34, 35). NAb were detected in ~ 91% of mild cases at 6 months post infection (25, 29); levels remained elevated among individuals with severe COVID-19, in comparison to individuals with less severe disease (24, 26).
- S protein IgG levels were consistently high and detectable across studies, and stable or elevated in 86%-99% of those with less severe infections (18, 19, 25, 27, 27, 28, 28-30). The long-term maintenance of S protein IgG in serum beyond 6 months of infection appears to be reduced among those with severe infection (26, 36).
- RBD IgG antibodies and S protein IgG antibodies were detected in 88-90% of mild to moderate COVID-19 cases, as well as among hemodialysis patients (17, 18, 25). A study quantifying the decrease in antibody levels between baseline and 6 months post infection in mild to moderate cases reported the following reductions, 15% RBD IgA, 33% RBD IgG, and 53% RBD IgM (24).
- Multiple studies confirm the correlation between RBD Ig antibodies (all Ig classes), and the neutralization activity targeting SARS-CoV-2 (27, 28). This association was consistent among those with mild to moderate and severe infections.
- Generally, N protein antibodies (class variable or not specified) appeared to reduce and wane relatively more rapidly than NAb, S protein, RBD antibodies (17, 27, 29, 30). Less than 25-50% of participants remained positive for N protein antibodies (class variable or not specified) beyond 6 months after infection, and reductions do not appear to be linked to infection severity (17, 17, 27, 29-

31). The half life of N protein IgG antibodies was estimated to range from 59-68 days (95% CI 55-90 days), much shorter than the estimated half lives of other antibodies (25, 26).

  - A single study reports the persistence of high N protein Ig levels at approximately 5 months post infection to may be associated with long term effects of COVID-19, such as fatigue, anosmia and ageusia (22).

- One study compared circulating antibodies between infected children and adults (37). Children had lower levels of antibodies against S and N proteins (Ig class of measured antibodies could not be identified) and the proportion of global antibodies against accessory proteins were greater and more stable among children than adults (37).

Table 2: Immune responses more than 6 months after SARS-CoV-2 infection (n=21)

STUDY	METHOD	KEY OUTCOMES
Circulating Antibody, B-cell and T-cell Immune Responses		
Dan (2021) (25) Cross-sectional USA Mar – Nov 2020	Assessed protective immune responses, based on memory CD4+ T-cell, CD8+ T-cell, B-cells, and antibody levels, among RT-PCR confirmed COVID-19 convalescent cases (n=188); 93% of participants were not hospitalized. Some serum samples (n=43/188) were collected between 6 to 8 months after infection. ELISA, pseudovirus neutralizing antibody assays, flow cytometry were applied to detect antibodies and immune cell frequencies and activities. SARS-CoV-2 memory CD8+ T-cells were measured using a series of peptide pools covering the entirety of the SARS-CoV-2 open reading frames (ORFs), most common were S protein, M protein, N protein and ORF3a.	Immune outcomes at 6-8 months post infection identified in the study: Antibody dynamics - S protein IgA was detectable in the majority of participants. - S protein IgG, RBD IgG titers demonstrated modest declines but were relatively stable. - The proportion of participants positive for S protein IgG decreased from 98% (54/55) to 90% (36/40), from one month to 6-8 months post infection. - 88% (35/40) of participants were positive for RBD IgG. - 90% (36/40) of participants were positive for NAb. SARS-CoV-2 specific memory B-cell activity - Memory B-cells specific for the S protein, N protein, RBD, viral antigens were detected in almost all participants, and were more abundant at post-infection follow-up. - 80% (n=29/36) had higher frequencies of total (IgG+, IgM+, or IgA+) RBD memory B cells (25) were present at beyond 180 days post infection. SARS-CoV-2 specific memory T-cell activity - 70% (40/57) of participants had CD8+ T-cells at 1 months post infection, while 50% (18/36) of

		participants were positive for these cells at more than 6 months post infection. - 93% (53/57) of participants had memory CD4+ T-cells at 1 month post infection, while 92% of (33/36) of participants were positive for these cells at more than 6 months post infection. In summary, while there was heterogeneity of immune responses associated with circulating SARS-CoV-2 antibody levels, cellular immunity through stable memory B-cell and T-cells was established beyond 6 months post infection.
Shen (2021) (23) Case series China Jul- Aug 2020	Serum samples were collected at multiple time points post admission to rehab (i.e., 0, 2 and 4 weeks) from a group of previously infected participants (n=110) whose hospital discharge from acute SARS-CoV-2 was a minimum of 6 months prior. Infections were confirmed by RT-PCR. Serum IgM and IgG antibodies, IL6, CD3+, CD8+, CD4+ T-cells , NK cell and B cell levels were measured by assay and flow cytometry. Notable differences in the percentage of serum CD3+ , CD8+ and CD4+ T-cells , NK cells and B cells (no additional details provided), by IgM and IgG antibody positivity were confirmed by correlation analysis.	- Overall, 29.1% (32/110) participants were positive for IgM and IgG antibodies, 34.5% (38/110) were only IgG positive, 36.4% (n=40) were negative for both IgM and IgG antibodies. - No significant differences in demographics, clinical presentation or co-morbid conditions could be identified between the antibody positive and negative groups. T-cell dynamics, 6+ months post hospitalization, by antibody positivity: - CD8+ T-cell decreased slightly over the sampling period. - CD8+ T-cell percentage was greatest (range from 48.6 ± 7.3 to 43.7 ± 9.7) among IgG and IgM antibody positive participants at all follow-up time points. - CD8+ T-cell percentage was lowest (range from 25.5 ± 9.3 to 25.9 ± 10.1) among IgG and IgM antibody negative participants. - NK-cells increased slightly over the sampling period. - Increase in NK cells percentage was highest among IgG and IgM antibody negative participants at all follow-up points (range 25.7 ± 6.3 to 27.1 ± 8.3), and lowest among IgG and IgM positive participants (range 13.7 ± 7.4 to 15.0 ± 9.6). B-cell dynamics, 6+ months post hospitalization, based on antibody positivity:

		- B-cell levels remained stable among antibody positive and antibody negative participants, but significantly increased among IgM negative and IgG positive participants during follow-up time points. - B-cell percentages were highest among IgG and IgM antibody negative participants (range 16.1 ± 6.4 to 16.7 ± 5.5) compared to IgG and IgM positive individuals (range 7.2 ± 3.1 to 7.5 ± 3.8). - The authors conclude loss of IgM antibodies in serum led to gradual improvements in cellular immunity linked to NK and B-cells. The authors suggest serum lymphocyte percentages (CD3+, CD8+ and CD4+ T-cells , NK cells and B lymphocytes) to be correlated with changes in serum IgM and IgG antibody levels, but not related to inflammatory cytokines or the severity of infection (i.e. Hs-CRP or IL6), among previously hospitalized and recovered patients.

Gaebler (2020) (24)
 	
Case series
 	
USA
Apr-Oct 2020
	Serum samples from seroconverted SARS-CoV-2 cases (n=87) were collected at 1.3 and 6.2 months (range 165-223 days) post infection. Infection and seroconversions were confirmed by RT-PCR, and 10% of the sample was hospitalized for infection. RBD IgG, IgM, IgA antibody, NAb levels were measured by ELISA and pseudovirus neutralization assay. B-cell levels and activity was measured by flow cytometry.	RBD antibody levels were significantly reduced at 6 months post infection. Overall, antibody reductions were inversely proportional and directly correlated with initial antibody levels (i.e., individuals with the highest antibody levels during early infection experienced the greatest decrease).
		- Antibody dynamics at 6 months post infection identified in the study:
		  - RBD IgM reduced by 53%
		  - RBD IgG reduced by 33%
		  - RBD IgA reduced by 15%
		  - NAb activity demonstrated a 5 fold reduction
		The number of RBD-specific memory B-cells in the majority of individuals remained unchanged. However, these cells did display maturation, varied clonal expansion and turnover between 1.3 to 6.2 months post infection.
		The authors conclude the observed changed among memory B-cells to be suggestive of long-term immunity, as well as the ability to mount

		rapid and effective immune responses to reinfection.
Sokal (2020) (30) Case series France Mar 2020	Serum samples from infected individuals (n=39) were collected at three time points, in the first month following symptom onset, at 3 months and 6 months post symptom onset. Approximately 53% (n=21) of the sample experienced severe infection. N protein, S protein, RBD IgG antibody levels were measured by ELISA. Virus antigen specific memory B-cell responses were measured by ELISA B-cell receptor sequencing and flow cytometry.	Immune outcomes up to 6 months post symptom onset identified in the study: Antibody dynamics: - N protein IgG antibodies underwent a rapid decrease in both mild and severe cases. This reduction was more pronounced among mild cases, and N protein IgG titers were undetectable in 50% on the mildly symptomatic participants by 6 months. - S protein IgG antibodies were stable overtime, only 9% of mild cases had undetectable antibody levels at 6 months follow up. The antibody levels were significantly higher at 3-6 months post infection follow-up among participants with severe infections. B-cell activity: - S protein and RBD specific B-cell clones, as well as cross-reactive B-cell clones from previous beta-corona virus exposures underwent somatic maturation and significant expansion. - S protein antibody secreting cells were marginally detectable at 6 months, at which time point S protein B-cells mostly resided in the CD21+CD27+CD38-CD71int/- resting memory B-cell compartment in both severe and mild. - Active B-cells remained detectable up to 6 months post infection. These B-cell clones are assumed to contribute to long-term immunity in convalescent patients.
Bilich (2020) (22) *Preprint* Case series Germany *Spring 2020	Convalescents with mild to moderate infection (n=51) were longitudinally followed up at approximately 1 month (median 40 days; range 35-56 days) and 5 months (median 159 days; range 141-183 days) post positive RT-PCR results. T-cell activity was measured by IFN-g ELISPOT assays and single epitope	Antibody dynamics at approximately 5 months post RT-PCR results identified in the study: - A greater than two fold decrease in S protein IgG and IgA antibodies was noted among 31-44% of participants, between the two follow-up time points. - A less than 2 fold reduction in N protein antibody levels were noted in 13% of participants up to second follow-up.

	mapping. IgG and IgA antibody levels were measured by immunoassay.	- High N protein antibody titers, at 5 months post infection, were associated with higher prevalence of post-infection symptoms, such as fatigue, anosmia and ageusia. T-cell immune responses at 5 months post infection: - The percentage of participants with detectable T-cells specific to viral antigens increased from 93% to 100% by the second follow up time point. A sub-group of T-cells targeting specific viral ORF derived epitopes (HLA-DR epitopes; HLA class 1 epitopes), associated with long-term post infection immunity against SARS-CoV-2, persisted among participants up to at 6 months post infection.
Clarke (2021) (17) *Preprint* Prospective cohort UK Feb 2020 - Jan 2021	Hemodialysis patients with end stage kidney disease were screened for SARS-CoV-2 antibodies and the results in this paper are for antibodies at time 0 (n=356) and 6 months (n=301). Infection was confirmed by PCR. N protein and RBD IgG antibodies were measured by CIMA and ELISA assay. T-cell activity was measured by ELISPOT assay in participants who had seroreverted at 6 months (n=11). Clinical severity of infection among participants followed-up at 6 months was not provided.	190 were negative for N protein antibodies and 129 were positive for N protein antibodies at time 0. At 6 months samples were available for 111/129 N protein antibody positive group to examine long-term immunity: - N protein IgG antibodies could not be detected in 36% (n=40) of the initially positive participants. - RBD IgG antibodies were more persistent than N protein IgG antibodies, 87% (n=97) of the initially seropositive sample remained positive for RBD IgG antibodies (including 70% (n=28) of individuals who were negative for N protein IgG). - 64% (n=71) of participants continued to be seropositive for N protein antibodies, but levels were significantly lower in comparison to initial screening point ($p<0.0001$). - 10% (n=12) of the initially seropositive participants were seronegative for RBD and N protein antibodies, but 80% of these individuals demonstrated SARS-CoV-2 antigen specific T-cell activity.
T-cell Immune Responses		
Breton 2020 (32)	Paired serum samples were collected from SARS-CoV-2 positive participants (n=41),	Compared to uninfected participants, significant shifts in circulating CD4+ and CD8+ T-cell

Prospective cohort USA Mar-Oct 2020	who had mainly mild disease, up to 6 month post infection. Infections were confirmed by RT-PCR. Serum samples from infected participants were compared to uninfected individuals (n=20). T-cell phenotypes and SARS-CoV-2 antigen specificity were measured by flow cytometry, ELISPOT and other assays.	compartments which persisted for 6 months after SARS-CoV-2 infection, was noted. SARS-CoV-2 T-cell activity up to 6 months after infection: - Both CD8+ and CD4+ T-cell proportions returned to near physiologic levels by 6.1 months - Antigen specific CD4+ T-cells that expressed memory markers as well as IL-2, IFN-g, TNF-a, CD154 and polyfunctional cytokine responses were markedly increased in convalescent sera, compared to uninfected participants; the relative frequency of the cells had decreased (22-32%) at 6.1 month follow-up. - CD8+ T-cells that produced Mip-1b, CD107a, IL-2, INF-g and TNF-a persisted at 6.1 month follow up, although at lower levels than previously measures. - 95-97% of previously infected participant serum provided evidence of antigen specific CD4+ and CD8+ T-cells activity at both 1.3 and 6.1 months post infection. When compared to CD4+ T-cell activity at 6.1 months, CD8+ T-cell responses were far more variable and generally less robust.
Li (2020) (21) *Preprint* Cross-sectional China Apr-Sep 2020	Convalescent COVID-19 individuals (n=31) and unexposed controls (n=11) were included in the study; exposure status confirmed by RT-PCR. The median period between disease onset and serum collection was 169 days (range: 83 to 274 days). Analysis examined differences between T-cell responses in first 6 months and 6-9 months post infection. 56.6% (17/31) of the infected cases were hospitalized, 19% (6/31) were asymptomatic. T-cell activity was measured by flow	- A proportion of T-cells weakly responded to viral proteins in uninfected individuals, but with a much lower magnitude than that observed among previously infected individuals. - At the time of final follow-up, 45% of previously infected individuals remained IgG positive, and 29% remained IgG and IgM positive. CD4+ T-cell responses were observed to be more robust among individuals who had become negative for IgG antibodies. - Loss of memory CD4+ and CD8+ T-cell responses were observed in 16.13% and 25.81% of previously infected individuals. Loss of memory CD4 T-cells was more frequent in asymptomatic individuals. - CD4+ and CD8+ T-cell responses were highly variable. Generally, the breadth and magnitude

	cytometry, and viral S protein, N protein, M protein sequences was used for cell simulation.	of the cell responses increased as time from symptom onset increased. T-cell dynamics, in the first 6 months post symptom onset, in comparison to 6-9 months post symptom onset: - Over the first 6 months post disease onset reductions in the magnitude of cytokine producing CD4+ T-cells against S protein, N protein, and M protein were noted. Then CD4+ T-cells then increased during the 6-9 months post infection period. - No change was observed in cytokine producing CD8+ T-cell. - There was a significant increase in the number of reactive memory CD8+ T-cell pools (i.e. the breath and magnitude of responses) between 6-9 months post symptom.
Circulating Antibody Immune Responses		
Levi (2021) (38) *Preprint* Prospective cohort Italy Apr- Aug 2020	Measured changes in serum antibody levels over a 5 month period in a sample of healthcare workers from multiple health care facilities (n=4534). S protein (S1 and S2) specific IgG levels were measured by assays (IgG ≥ 12 AU/mL set as a threshold). Of the HCWs with IgG levels above threshold, 14% (n=91/613) were asymptomatic. Factors associated with antibody dynamics were identified through logistic regression analysis.	- IgG levels were found to be higher among HCWs that had symptomatic COVID-19, when compared to asymptomatic and paucisymptomatic HCWs. - The symptoms reported to be associated with sustained and increased IgG levels at 5 months included fever, cough, muscle pain, asthenia, tachycardia and anosmia/dysgeusia. - Regression analysis only found those presenting with anosmia/dysgeusia (OR 2.75, 95% CI 1.753 – 4.301) to be significantly associated with IgG maintenance. Note: Study results may be biased as increases in HCW antibody levels were noted in regions most impacted by SARS-CoV-2, and reduced in regions least impacted (i.e., antibody levels could be increasing because of re-infections).
Dobaño (2021) (18) *Preprint* Prospective cohort Spain	Evaluated antibody levels and seropositivity in a sample of primary health care workers (n=173), 149-270 days after symptom onset; serum samples were collected at three time points. Infections were confirmed by PCR.	Antibody dynamics approximately 5-9 months after symptom onset, identified in the study: - 92.49% of participants were positive for at least one immunoglobulin isotype, indicative of highly stable and persistent immunity. - 60% of participants were positive for RBD and S protein IgM, 76.30% for RBD and S protein

Mar-Dec 2020	The majority of the sample was mild to moderate cases, and 14% were hospitalized. Levels of S protein and RBD IgM, IgA and IgG antibodies were measured by assay (not specified). Factors associated with higher levels of antibodies were identified by stepwise multivariable regression analyses.	IgA, and 90.17% for RBD and S protein IgG antibodies. - Factors associated with higher levels of antibodies at follow-up were hospital admission, fever, anosmia and/or hypogeusia, and previous allergies.
Wagner (2020) (28) *Preprint* Prospective cohort Austria Apr – Oct 2020	A large seroprevelance study (n=1655) identified individuals with positive S protein IgG and/or IgA antibodies (n=168). Only 42% of participants reported experiencing symptoms compatible with infection in the 3 months prior to recruitment. Serum samples of seropositive individuals were collected at 3 and 6 months post initial test results (n=1292/1655). S1 subunit of S protein, N protein, RBD antibodies, and NAb antibodies were detected through serological assays.	Antibody dynamics at 6 months post initial seropositive test results, identified in the study: - S1 IgG levels, which suggest exposure rather than protective immunity persisted in 90% of (9/10) the seropositive cases. - N protein IgG was no longer detectable in 55.5% of the sample. - RBD IgM had decreased at 3 months (from initial seropositive results) in 53.3% of the sample, but remained stable from 3 to 6 months. - 50% of the initially RBD IgM as well as N protein IgG seropositive at baseline were seronegative at 6 months. - S1 protein IgA was decreased at 6 months compared to baseline. - RBD total antibodies correlated best with NAb (a surrogate marker for protection from the virus) and both were maintained at 6 months. - RBD antibody levels were found to be independent of infection attributed symptoms and severity. - The authors concluded RBD antibody specific assays can reliably detect SARS-CoV-2 specific antibodies for at least six months following infection.
Zhou (2020) (36) Prospective cohort	S protein IgM and IgG antibody levels were tested in convalescent serum samples of convalescent COVID-19 participants (n=165). All participants had been	Antibody dynamics up to 7 months post initial hospitalization event, identified in the study: - S protein IgM decreased after peaking around 22-28 days of; 79% of individuals were

China Spring 2020*	hospitalized and infections confirmed by RT-PCR. ELISA was used to measure antibody levels in serum samples. All samples were collected between day 1 through 7 months from symptom onset, 28 serum samples informed the 7 month post infection data point.	negative for these antibodies at 7 months post infection. - S protein IgG levels increased from day 1 to 28 with peak levels being maintained up to 4 months post symptom onset, but dropped sharply at 7 months.
Vanshylla (2021) (39) *Preprint* Prospective cohort Germany Apr- Dec 2020	Antibody levels in a sample of recovered individuals (n=131/963), detected in serum samples collected up to 10 months post symptom onset or confirmatory diagnosis; 41.8% of the convalescent COVID-19 individuals had been hospitalized and infection confirmed by RT-PCR. NAb and S protein IgG levels were measured by multiple assays, and inform linear regression mixed effects modeling estimates antibody half-lives.	Antibody dynamics 4-10 months post symptom onset or confirmatory diagnosis, identified in the study: - S protein IgG levels decreased between 1-4 months post infection, then were constant for the remaining months of follow-up. - 73% of individuals were positive for S1 IgG at 9-10 months post infection, a 13% reduction from 1 month post infection. - Half-life of S protein IgG estimated to be 8.7 months. NAb levels and activity were found to decrease rapidly over the initial two months post infection, but neutralizing functions of purified IgG antibodies, including against the S protein, were maintained up to seven months post infection. These results suggest a more stable and long-term memory IgG B cell repertoire and stable levels of IgG in the majority of individuals recovered from infection.
Whitcombe (2020) (27) *Preprint* Case series New Zealand Spring 2020*	Serum samples from RT-PCR confirmed convalescent COVID-19 individuals who had mild/moderate disease (n=112) was collected, 80/189 serum samples from 50 participants had multiple samples and informed the 4-8 months post-infection onset time points. Samples were assayed to identify IgG, IgM and IgA antibodies and	Antibody dynamics 4-8 months post infection onset compared to baseline levels, identified: - 99% (79/80) of participants had anti-RBD IgG and 96% (77/80) had anti-S protein IgG. - RBD 64% (51/80), S protein IgG1 antibodies 59% (47/80) and IgG3 S protein antibodies 60% (48/80) persisted. - <30% of participants remained positive for N protein antibodies, which waned quickly.

	subclasses (IgG1, 2, 3 and 4) specific to N protein, S protein, and RBD, as well as neutralizing antibodies (NAbs) by an in-house Triplex assay.	- 90% (72/80) NAbs were detectable. Across the study these were relatively stable and correlated with RBD IgA (Pearson's r ≥ 0.87). Using paired serum samples (n=50 participants) the rate of decay for Nabs to halve was estimated to be 146 days (95% CI: 100-199), which is considerably shorter than the exponential decay (625 days) or growth-decay (425 days) models predicted.
Han (2021) (40) *Preprint* Prospective Cohort China Dec 2019 – Mar 2020	Acute and convalescent plasma of RT-PCR confirmed severe COVID-19 individuals was tested for RBD, S protein and N protein IgG (n-=104). Follow up was approximately 6-7 months (median 195 days; range 188-201 day) post infection. Serum samples from 31 healthy controls with no follow-up also included. Ab levels measured by ELISA and micro neutralization assay. Correlations between convalescent antibody levels and virus neutralization activity estimated by ANOVA.	Antibody dynamics approximately 6-7 months after symptom onset: - All measured viral antigen specific antibodies were significantly higher among infected cases at both acute and convalescent time points, when compared to healthy controls. - Viral antigen specific antibodies were not significantly different based on participant age or gender. - RBD and N protein IgG levels were significantly lower from the acute to convalescent time points ($p<0.000$); no significant reductions in S protein IgG levels. - Median reductions between acute and convalescent serum estimated at 15.90% (IQR, 7.83 to 30.91%) for S protein IgG, 51.63% (IQR, 31.25 to 66.30%) N protein IgG, and 58.98% (IQR, 48.15 to 68.25%) RBD IgG, - Significant ($p<0.0001$) and strong correlations between virus neutralization activity and NAb levels with RBD IgG levels; significant ($p<0.0001$) and moderate correlations between RBD and N protein IgG levels were noted in convalescent sera.
Choe (2021) (29) Cross-sectional South Korea Feb – Oct 2020	Serum samples from RT-PCR confirmed COVID-19 individuals (n=58), 7 asymptomatic and 51 mildly symptomatic participants were collected 8 months post infection. Antibody levels were investigated using multiple immunoassays.	Antibody dynamics 8 months post infection: - 91.4% of participants remained positive for N protein Ig antibodies - 25.9% of participants positive for N protein IgG - 86% participants positive for S protein IgG antibodies, and 69% participants positive for S1 protein IgG antibodies - 53.4% of participant sera demonstrated positive NAb activity

		The detection of antibodies was confirmed to vary by applied immunoassay methods.
Zhang (2020) (31) Case series China Jan – July 2020	Serum samples from convalescent COVID-19 participants were (n=54/112) collected between 158-194 days post symptom onset, and compared to antibody levels during the acute infection phase. Infections among all participants were confirmed by RT-PCR, 77.7% were mild cases and 22.3% were severe. N protein and RBD IgG and IgM antibody levels were measured by ELISA.	Antibody dynamics approximately 5-6 months post symptom onset : - All participants were positive for N protein antibodies (Ig class not specified), antibody levels had decreased when compared to their acute infection titers. Both mild (median 46.31% (IQR 5.37%–68.96%) and severe (median 46.02% (IQR 11.01%–65.75%) infection groups experienced similar reductions in N protein antibody titres.
Kwada (2020) (41) *Preprint* Case series Japan Apr – Nov 2020	Serum samples from seropositive HCWs from a hospital outbreak, 42/45 were RT-PCR confirmed and severity not reported, were followed-up on a monthly basis up to seven months post diagnosis (n=45). Total Ig N protein and S protein antibody levels were measured up to 7 months post infection (n=45).	Antibody dynamics approximately 7 months post infection diagnosis: - 33% (n=15) N protein Ig levels significantly increased and was maintained, 33% (n=16) these antibodies initially increased and declined, 31% (n=14) antibodies increased modestly and persisted. - Individuals with high and maintained Ig N protein antibodies also had higher levels of S protein antibody at 7 months post diagnosis. Levels of N protein antibodies showed no apparent correlation with either COVID-19 contact or symptoms. - Authors suggest N protein pan Ig levels may not be related to disease recovery.
Dehgani-Mobaraki (2020) (42) *Preprint* Prospective cohort Italy Mar – Nov 2020	Serum samples were collected from RT-PCR confirmed COVID-19 participants (n=30/114) 1 month to 8 months after diagnosis up to 5 time points. Blood samples collected at multiple time points were assayed to measure antibody. Target viral antigens are not specified. Individuals with mild (n=17) and moderate to severe	IgG antibody persistency was demonstrated in 76.7 % of the subjects (n=23/30) at 8 months post diagnosis. Generally, IgG antibody levels were more elevated from baseline levels among moderate to severe cases, when compared to mild cases. Antibody dynamics up to 8 months post infection identified in the study: In mild cases at 1 vs. 8 months post diagnosis:

	infection (n=13) were equally represented in the study sample.	- IgM levels significantly (p-value <0.001) decreased from 0.50 (0.46-0.52) to 0.21 (0.18-0.35). - IgG levels increased from 1.84 (0.68-3.54) to 3.13 (1.05-3.66). In moderate-severe cases at 1 vs. 8 months post diagnosis: - IgM levels significantly reduced from 0.64 (0.64-1.07) to 0.54 (0.25-0.81). - IgG levels 2.37 (1.14-20.7) remained persistent 1.89 (0.83-8.53).
Pradenas (2020) (26) Prospective Cohort Spain Apr – Oct 2020	Serum samples were collected at time of diagnosis, 3 and 6 month from 210 COVID-19 RT-PCR confirmed cases (106 mild, 104 hospitalized). Only 28/210 participants contribute to the longitudinal data. RBD, S protein S2, N protein IgG antibody, as well as NAb levels, were measured by ELISA and pseudovirus assay.	Antibody dynamics, up to 6 months post symptom onset/diagnosis identified in the study: - Beyond 30 days since infection onset, the half-life for RBD IgG 86 days, S protein S2 IgG 108 days, N protein IgG 59 days were estimated. - NAb antibody levels in participants that had a mild or asymptomatic infection developed a 10 fold lower maximal neutralization titer than severe cases, but remained steady with insignificant decay up to 6 months. - Compared to the mild or asymptomatic, hospitalized participants had higher NAb titers though to end of follow-up. These antibody levels underwent an initial rapid decline that slowed and stabilized after 80 days. - The authors, based on assumed NAb activity threshold of 1:250 to prevent reinfection, suggest hospitalized participants have a higher capacity for long-term neutralization and preventing infection.
Hachim (2021) (37) *Preprint* Prospective cohort Hong Kong Apr – Nov 2020	Serum samples from infected children (n=122) and adults (n=36) were compared to samples from never infected participants (n=33); infections were confirmed by RT-PCR. 36% of the samples and 25% of adult samples were from asymptomatic COVID-19. Children serum samples ranged from 0-206 days post symptom onset (mean+/-	- The model of specific antibodies in pediatric samples (n=58/122) up to 6 months indicates antibodies to both structural proteins (S1, S2, S2', M, E and N) and non-structural proteins (NSP1, ORF3a, ORF3b and ORF7a ORF6, ORF8 and ORF10) are stable or increased. - Antibodies specific to accessory protein ORF7b antibody were significantly reduced.

	stdev: 39±47 days) and the adult samples ranged from 24-123 days post symptom onset (mean±stdev: 54±20 days). Long-term follow-up included 58/122 up to 206 days post symptom onset and only 16/122 had data points between 4 to 6 months post symptom onset and informed a linear mixed effect model. Serum samples underwent LIPS and ELISA assay targeting S protein, S1, S2 subunits, N protein, E protein, M protein, as well as antibodies specific to non-structural and accessory proteins, NSP1 and ORF proteins were measured.	

ELISA = enzyme linked immunoassay, E protein = envelope, Ig= Immunoglobulin antibodies, LTE= letter, LIPS = luciferase immunoprecipiation system assay, M protein = membrane, NAb = neutralizing antibodies, N protein = nucleocapsid, ORF = open reading frame, S = spike protein, RBD= receptor binding domain

VARIANTS OF CONCERN AND IMMUNITY

Variants of SARS-CoV-2 have acquired mutations, which occurs frequently and often does not change the characteristics of the virus. However, at times mutations are acquired that change the epidemiology and/or virulence of the virus (e.g. changes in transmission, severity or mortality or disease, immune evasion or affects diagnostic testing). Recently several variants of concern have been identified, as of February 2021 those include: B.1.1.7 (43), B.1.351 (44) and P.1 or P.2 (45):

- B.1.1.7 aka VOC 202012/01 aka 201/501Y.V1 aka Kent variant first reported in the UK has been reported to have increased transmissibility and maybe severity. Reported in many countries.
- B.1.351 aka 501Y.V2 aka 20H7501Y.V2 first reported in South Africa has been reported to cause higher transmission, viral loads and immune escape. The combination of E484K, K417N and N501Y mutations results in higher binding affinity. This variant has been reported in many countries, but has not spread to the same extent as B.1.1.7 as of February 2021.

- P.1 aka B.1.1.28.1 and P.2 aka B.1.1.28.2 (and maybe B.1.1.33) aka 20J/501Y.V3 have been primarily circulated in Brazil. The key mutations are similar to B.1.351: K417T, E484K, N501Y. This variant has been reported in several counties including Canada and its epidemiology is currently unclear. No relevant studies were identified on this variant.

Studies on immunity against variants of concern were included in this section of the review, due to the preliminary nature of this research, no restrictions on study design or number of observations were placed on included studies. Ten preliminary *in vitro* experiments that looked at whether neutralizing antibodies from convalescent COVID-19 individuals or individuals who received one or two doses of a COVID-19 vaccine were effective against B.1.1.7 or B.1.351 were identified.

- Across studies, B.1.1.7 was reported to be neutralized with similar or slightly reduced efficacy compared to wild-type SARS-CoV-2 by both convalescent and vaccinated sera, with stronger neutralization following the second dose of vaccine (46-48). Weaker neutralizing of B.1.1.7 response was seen for those who one had one dose of vaccine compared to two doses (49).
- For B.1.351, studies note this variant evaded neutralization in a high proportion of samples from both convalescent and vaccinated sera (50-52). A single study also shows that vaccination of convalescent individuals resulted in an increase in neutralizing antibodies, however neutralization of B.1.351 was still lower than the wild-type SARS-CoV-2 (53). Thus, there is some evidence from neutralization experiments that immunity from wild-type SARS-CoV-2 may not be effective against B.1.351. The impact of B.1.351 immune evasion has yet to be established.

Table 3: Data on convalescent or vaccine immunity against variants of concern (N=10)

STUDY	METHOD	KEY OUTCOMES
B.1.351		
Wibmer (2020) (52) *In vitro* experiment NA Jan 2021*	Neutralization and binding of non-neutralizing antibodies against B.1.351 were evaluated using convalescent serum (n=44) from both severe (n=14) and mild/moderate (n=30) cases. The study also explores the evasion of B.1.351 from specific antibodies in neutralization assays.	- Convalescent plasma was used to evaluate neutralizing activity of B.1.351. - Individuals reporting more severe SARS-CoV-2 had higher neutralizing antibody titres s average ID50 titre 4212 (n=14) vs. average ID50 titre 488 (n=30) mild/moderate cases against wild-type SARS-CoV-2. - The same samples assessed against B.1.351 showed no detectable neutralization activity in 48% (21/44), with only three samples (7%) retaining titres of ID50 >400. - They also show against B.1.351 non-neutralizing antibodies were able to bind to the RBD with a small proportion, 32% (14/44), experiencing a 5-fold reduction. - The mutation E484K has been shown to reduce neutralization sensitivity. This has implications

		for rates of reinfections and vaccine effectiveness.
Stamatatos (2021) (53) preprint *In vitro* experiment USA* Jan 2021*	We collected blood and isolated serum and PBMC from persons with previously confirmed SARS-CoV-2 infection (n=10) who later received a single dose of either the Pfizer/BioNTech or Moderna mRNA vaccine.	- Before immunization 9/10 convalescent serum neutralized wild-type and 5/10 for B.1.351. - After immunization there was a 50-fold increase in binding signal, but binding was significantly lower from B.1.351. - Neutralizing potency of several specific antibodies were also evaluated with varying results across antibodies. B.1.351 virus was more resistant to neutralizing antibodies.
Cele (2021) (54) Preprint *In vitro* experiment South Africa* Jan 2021*	Using 6 convalescent plasma samples collected in the first wave (up to August). A focus forming microneutralization assay was used to quantify neutralization.	- Using convalescent plasma from the first wave of COVID-19 the decrease in neutralization ranged from 6-200 fold.
B.1.351 and B.1.1.7 or combinations of their mutations		
Collier (2021) (51) preprint *In vitro* experiment UK* Jan 2021*	Neutralising antibody responses following a single immunization of BNT162b2 vaccine was evaluated. Serum and peripheral blood mononuclear cells samples were collected 3 weeks post vaccination from 24 participants median age 82. Pseudoviruses expressing the wild-type Spike protein, the 8 mutations found in the B.1.1.7 Spike protein or with the addition of E484K mutation were used for these experiments.	- Antibody response was heterogeneous with almost 100-fold variation in IgG titres to S and Spike RBD across the 24 vaccinated participants. - Pseudovirus bearing S protein with the full set of mutations present in the B.1.1.7 variant (i.e., H69/V70, 144, N501Y, A570D, P681H, T716I, S982A, D1118H) did result in small reduction in neutralisation by sera from vaccinated participants. - Adding in the E484K mutation (found in B.1.351 variant) resulted in a significant loss of neutralising activity compared with wild type and B.1.1.7; mean fold change for the E484K B.1.1.7 Spike was 9.6 compared to 2.4 for B.1.1.7 alone ($p<0.05$)
Wang (2021) (50)	Antibody and memory B cell responses in a cohort of 20 volunteers who received either the Moderna (mRNA-1273) or Pfizer-	- 8 weeks after the second vaccine injection volunteers showed high levels of IgM, and IgG anti-SARS-CoV-2 spike protein (S) and receptor binding domain (RBD) binding titers.

In vitro experiment USA* Jan 2021*	BioNTech (BNT162b2) vaccines is investigated. Vaccine sera neutralizing activity against variants with E484K or N501Y or the K417N:E484K:N501Y mutations were investigated. As well as the individual neutralizing activity against 17 of the most potent antibodies.	- The plasma neutralizing activity, and the relative numbers of RBD-specific memory B cells in vaccinated individuals were equivalent to individuals who recovered from natural infection. - The activity against SARS-CoV-2 variants encoding E484K or N501Y or the K417N:E484K:N501Y combination was reduced by a small but significant margin. - Neutralization by 14 of 17 of the most potent antibodies tested was either reduced or abolished by the variants.
Wang (2021) (55) Preprint *In vitro* experiment USA* Feb 2021*	20 convalescent sera from more than one month post SARS-CoV-2 infection were collected in Spring 2020. 10 had severe COVID-19, 10 were not severe. 12 vaccinated sera (Moderna, 2 doses with sera collected at day 42.) 10 vaccinated sera (Pfizer, 2 doses with sera collected on day 28) Pseudoviruses were developed to represent the wild type SARS-CoV-2, B.1.1.7 and B.1.351	- Compared to the wild type neutralization was lower. - No substantial loss in convalescent sera, Moderna and Pfizer against B.1.1.7. - 9.4 fold lower in convalescent sera, 12.4 fold lower for Moderna and 10.5 fold lower for Pfizer against B.1.351. - Loss of potency was 16/20 for B.1.351 and activity was maintained for B.1.1.7 pseudoviruses.
B.1.1.7		
Muik (2021) (47) *In vitro* experiment UK* Jan 2021*	Using sera immune sera from 40 people 23-73 years old 7-21 days post 2nd dose of vaccine BNT162b2, the authors evaluated whether the B.1.1.7 spike interferes with antibody binding using neutralization assays. Based studies of antibody correlates of disease protection for influenza virus vaccines, a 20% reduced titer does not indicate a biologically significant change in neutralization activity.	- The immune sera had slightly reduced but overall largely preserved neutralizing titers against the B.1.1.7 lineage pseudovirus. These data indicate that the B.1.1.7 lineage will not escape BNT162b2-mediated protection.
Edara (2021) (48) Preprint	Blood samples collected from 20 COVID-19 cases (8-24 days post symptom onset), convalescent COVID-19 individuals (30-90 days	- Neutralization titers correlated between the EHC-83E and B.1.1.7 variants across acutely infected COVID-19 patients (R2 =0.7971; p<0.0001), convalescent COVID-19 individuals

In vitro experiment USA* Jan 2021*	PSO) and 14 vaccinated (2 doses of mRNA-1273 vaccine) were tested for neutralizing antibody response against a panel of SARS-CoV-2 variants including D614G and B.1.1.7.	(R2= 0.8092; p<0.0001), and mRNA1273 vaccinated individuals (R2= 0.7639; p= 0.0027). - The neutralizing antibodies from COVID-19 cases and vaccinated individuals were effective against B.1.1.7.
Shen (2021) (49) Preprint *In vitro* experiment USA* Jan 2021*	Sera (n=40) of those vaccinated mRNA-1273, Moderna collected at day 29 post first dose and 28 days post second dose. Sera (n=28) from Novavax trial were collected at random times >2 weeks post second dose. Convalescent sera (n=15) were from an observational study that collected samples between 1-8 weeks post resolution of symptoms or 2-10 post last positive test and were preselected to represent high, medium and low neutralization titres. Pseudotyped viruses were developed for several SARS-CoV-2 isolates including B.1.1.7 and evaluated using neutralization assays.	- The B.1.1.7 variant was neutralized by all vaccine sera, although with modestly diminished susceptibility compared to the D614G variant. - The same was seen for convalescent sera, however the decrease was less than for vaccine sera. - Sera with weaker neutralizing activity exhibited a reduction in activity against B.1.1.7. Most of the weak neutralizing activity against B.1.1.7 was post first dose of vaccine and the decreased activity against B.1.1.7 was less after the second dose of vaccine. - B.1.1.7 exhibited partial and modest escape from specific antibodies; COVA1-18, COVA2-15, S309 and B38; and DH1042 and H4, respectively.
Rees-Spear (2021) (46) preprint *In vitro* experiment UK* Jan 2021*	Neutralization of a series of mutated spike pseudotypes including B.1.1.7 were evaluated with a panel of antibodies and 36 convalescent COVID-19 serum samples.	- Most convalescent samples neutralized B.1.1.7, however potency was reduced in 3/36 samples by 5-10 fold. - Serum samples form those who had severe COVID-19 showed more resilience compared to those with mild COVID-19, 56% of whom showed a 3-fold drop in potency against at least one mutant. - Neutralization activity of some spike-specific monoclonal antibodies was dramatically reduced by B.1.1.7 and other Spike mutations.

*Date or locations is based on publication date or author affiliations.

REVIEW LITERATURE

The systematic review identified offer summaries of what was known in June and September 2020. As such the studies included in these review include early research on relevant immune outcomes <6 months from initial COVID-19.

Table 4: Systematic reviews and rapid reviews relevant to immunity (n=3)

STUDY	METHOD	KEY OUTCOMES
Poland (2020) (1) Review NA Oct 2020*	This review discusses what was known about human humoral and cellular immune responses to SARS-CoV-2 as of the search date Sept 24, 2020.	- The article reviews humoral and cellular immunity and presents some data on kinetics and durability of antibody response and correlation with T-cell response. Many inconsistencies were noted in the initial research. - Knowledge gaps include high-quality studies on duration of protection by neutralizing antibodies and a good understanding of how the immunological measures being used correlate to protection.
Post (2020) (19) Systematic review NA Jun 2020	A systematic review on antibody response to SARS-CoV-2 with a search date of June 26, 2020. 150 papers were included. Inclusion criteria included follow-up of greater than 28 days and measured antibody titres. High variability across includes studies and study designs was reported by the author. See appendix 2 for a figure on antibody kinetics over time.	- Inconsistency in antibody correlates were seen across the literature. - IgM (seroconversion 4-14d, peak 2-5 weeks and declining to undetectable levels around 6 weeks) was consistently detected before IgG. - IgG (seroconversion 12-15 d, peak 3-7 weeks, plateaued until at least 8 weeks with longest follow-up of 12 weeks still detecting antibodies). - IgA infrequently studied showed seroconversion between 4-11 days, with outliers reporting 24 days. - Neutralizing antibodies detected 7-15 days after symptom onset, peaking 14-22 days and then declining over 6 weeks. AT 39 days one study had 79% of participants with low neutralizing antibody titres, 3% with high titres. Mild cases had lower neutralizing antibodies. - Animal studies show promising initial results for protective immunity; however studies were small and short in duration. There are studies that have demonstrated correlations with disease severity. An inverse relationship with viral load has been inconsistently reported and no association with re-detection was reported. Studies cannot speak to lasting immunity.
Shrotri (2021) (33) Systematic Review NA Jun 2020	A systematic review that critically evaluates and synthesises published and pre-print literature from Jan 2020-Jun 26 2020 on T-cell mediated	- Symptomatic adult cases consistently show a reduction in peripheral T cell counts in the acute infection phase, which positively correlates with increased disease severity, duration of RNA positivity, and non-survival. The observed relative reductions in CD4+ and CD8+ T cell were variable. - Asymptomatic and paediatric cases display preserved T-cell counts.

	immunity post SARS-CoV-2 infection. 61 publications included in the review.	- Severe or critical COVID-19 cases developed more robust, virus-specific T-cell responses. Elevated levels of pro-inflammatory cytokines, interleukin-6 (IL-6), to lesser degree, interleukin-10 (IL-10), and tumour necrosis factor alpha (TNF-α) were identified in severe cases. - Longitudinal follow-up (14-44 days post infection) suggested recovery of T-cell subset counts alongside clinical recovery and viral clearance. - T-cell memory and effector function in early convalescents (up to approximately 3 months post onset) was demonstrated against viral antigens S, M and N proteins. T cell response breath and magnitude were generally enhanced among individuals recovering from sever infections. Cytokine producing activity of CD 8+ T cells specific to M and N proteins displayed wider functionality than those targeting S proteins among individuals with mild disease. CD3+ T cells were reduced in severe infections. - Cross-reactive T-cells among unexposed or individuals previously exposed to other coronaviruses (e.g., pre-pandemic seasonal corona virus strains, SARS-CoV-1) were often identified and appear long-term; in some cases maintained up to 17 years post infection. Cross-reactive T-cells targeting viral S protein and N proteins were the identified cross-reactive immune cells. The impact of cross-reactivity on SARS-CoV-2 infections remains largely unclear, but assumed to be low due to variability in coronavirus epitopes.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Three separate searches were conducted to identify citations relevant to reinfection, immunity and variants and immunity. Search terms used included:
REINFECTION TERMS (reinfect* or re-infect* or recurren* or re-positive).
IMMUNITY TERMS (antibod* or CD+ or CD4 or CD8) across studies with the Immunology tag

VARIANT TERMs (B1.1.7 or 501Y.V1 or 202012/01 or B.1.351 or 501Y.V2 or P1 or P2 or B.1.1.28 or B.1.1.33 or 501Y.V3) AND (neutralization antibodies)
This review contains research published up to Feb 11, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

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APPENDIX 1:

Reinfections, case reports/series (n=21)

- Thirty cases of confirmed reinfection were identified. The median time between initial infection and infection was 81 days (range 13-250).
- Confirmed cases of reinfection have been reported in China (56-59), South Korea (60), Brazil (61, 62), the United States (63-65), Belgium (66, 67), Spain (68), France (69, 70) the United Kingdom (71), the Netherlands (72), Ecuador (73), India (74, 75), and Iran (76).

- Onward transmission via reinfection cases was suspected in two reports (67, 68). In many studies, contact tracing/follow-up was not conducted. Infectivity and onward transmission during reinfection has not been sufficiently studied and remains a substantial knowledge gap.
- Symptomology among primary and re-infections has been heterogeneous in the literature. Seventeen cases experienced both asymptomatic/mild primary infections and reinfections (56, 57, 60, 62, 66, 67, 69, 74, 75). Three cases reported severe symptoms during primary infection and mild symptoms during reinfection (56, 65). Ten cases experienced mild/moderate symptoms during primary infection and more severe symptoms during reinfection (61, 63, 64, 68, 70-73, 76).
- A confirmed case of reinfection due to the Variant of Concern-202012/01 of lineage B.1.1.7 was reported in the United States (65). Immunological findings suggest that poorly developed or waned antibodies formed after the primary infection in March were not protective against reinfection with the new mutated variant acquired in July (65). Cases of reinfection with the E484K spike mutation in Brazil (61) and South African SARS-CoV-2 variant 501Y.V2 in France (70) have also been reported.
- Immunology findings indicate that the waning of humoral immunity may have predisposed patients to reinfection with a different strain of SARS-CoV-2. Those who do not seroconvert may not have the same degree of protection from reinfection as those with high titers of antibodies. The greater magnitude of antibody responses or T cell responses generated during severe COVID-19 may confer more robust and/or long-lasting protection. Alternatively, subsequent infections may be more severe due to acquisition of a more pathogenic strain (i.e. with viral escape mutations), or even a greater inoculum of infection as the second exposure (i.e. from household exposure) (63). Additional research is needed to understand the role of immunity in protection against SARS-CoV-2 post initial acute infection and how common reinfection is.

Appendix Table: Case reports of genetically confirmed reinfection with SARS-CoV-2 (N=21)

Reference	Method	Key Outcomes
Case series/reports of confirmed reinfection (n=21)		
Zhang (2020) (56) Case series China Jan-Apr 2020	Describes six cases of confirmed reinfection. Analysis supported by viral whole genome sequencing, phylogenomic analysis, serology, and epidemiological data.	Swab type not reported -Time between episodes ranged from 19 to 57 days. -There were five adults (33-84 years) and one 2-year-old child. Two were critical COVID-19 patients (P1, P6), and the other four had moderate primary infections (P2-P5). Three cases (P1-P3) developed symptoms again during the second episode, with P1 and P2 showing pulmonary inflammatory lesions, while the other cases were asymptomatic. - There was no difference in the infection duration and the viral loads between the first and second episodes.

		- P2 and P4 had low anti-RBD IgM/IgG (≤1:40) responses to the primary infection. In the other three patients (P1, P3 and P6), titers reached 1:80-1:320 for RBD-IgM and IgG. During the secondary infection, cases P1 and P2 displayed secondary immune responses with an increase in serum antibody titers. -All six paired-genomes were attributed to different lineages or descending lineages with 3-11 distinct SNPs between first and second episodes. Five of these six pairs were D614G mutants.
To, Hung, Chan, (2020); To, Hung, Ip, (2020); Chan (2020) (57-59) Case report China Mar-Aug 2020	These case reports describe a confirmed case of reinfection in a 33 year old male in Hong Kong with a travel history to Spain. Analysis supported by viral whole genome sequencing, phylogenomic analysis, serology, and epidemiological data.	Respiratory samples -Immunocompetent case tested re-positive for SARS-CoV-2 viral RNA 142 days after the first symptomatic episode. -First episode: mild symptoms, Ct 30.5 -Second episode: Asymptomatic, Ct 26-32 -Serum samples collected on days 10, 43, and 148 (day 3 of reinfection) did not detect antibodies against SARS-CoV-2. A strong IgG antibody response to N protein developed by day 5 of reinfection, suggesting that antibody against SARS-CoV-2 developed on reinfection. IgM was not detected. Reinfection coincided with a stronger interleukin-21 memory type response on day 148 than on days 10 and 43. -First and second viral genomes belonged to different clades/lineages, differing by 24 nucleotides. First genome clustered with viruses from Hong Kong, while second genome clustered with viruses from Spain. Epidemiological data, including a recent trip from Spain.
Lee (2020) (60) Case series South Korea Mar-May 2020	Describes six patients who recovered from COVID-19 and retested positive by RT-PCR after discharge. One confirmed case is reported in a 21 year old woman. Analysis supported by viral whole genome sequencing, phylogenomic analysis, and serology.	Nasopharyngeal, oropharyngeal, and sputum swabs -Time between episodes was 26 days. -First episode: mild, Ct ~22.5, seronegative -Second episode: mild, Ct ~31, seropositive, antibody levels increased 10 days after onset of the patient's reinfection episode, then decreased but remained positive within the following 3 weeks. - Phylogenetic analysis revealed that the virus strain from the second episode clustered in clade "V" with the strain from the first episode clustered in clade "G".
Vasques Nonaka (2021) (61)	Describes the first case of reinfection with the E484K spike mutation in Brazil in a 45 year old	Nasopharyngeal swab -Time between episodes was 147 days.

Case report Brazil May-Oct 2020	female. Analysis supported by whole genome sequencing and phylogenomic analysis.	-First episode: mild, Cts of N, E and RdRp targets were 25, 26, and 27, antibody testing not done -Second episode: moderate, Cts of N, E and RdRp targets were 21, 12 and 17, IgG test was performed 4 weeks after symptom onset and was positive. -The viral variant from the first episode was identified as B.1.1.33 lineage while the variant from the second episode was B.1.1.248 harboring the E484K mutation, located in a key residue of the receptor binding domain.
Fintelman-Rodrigues (2021) (62) *Preprint* Case series Brazil Mar-May 2020	Describes four patients who recovered from COVID-19 and retested positive. Two cases, a 57 year old woman and a 34 year old man were confirmed reinfection. Analysis supported by viral whole genome sequencing, phylogenomic analysis, and serology.	Nasopharyngeal swab Case 1 -Time between episodes was ~62 days. -First episode: mild symptoms, Ct 36 (~10^3 copies/ml), upregulation of markers of innate immune response (IL-6, IL-8 and TNF-α, IL-10, CXCL-10, IFN-y) but IgG anti-SARS-CoV-2 IgM, IgA or IgG antibodies were not detected. -Second episode: moderate symptoms, Ct 22 (~10^7 copies/ml), anti-SARS-CoV-2 immunoglobulins were detected along with low to non-neutralizing activity one week after onset. - Genome sequencing showed that the first and second episodes were associated with the emerging clades 19A and 20B, respectively. Case 2 -Time between episodes was ~53 days. -First episode: mild symptoms, Ct 36 (~10^3 copies/ml), upregulation of markers of innate immune response (IL-6, IL-8 and TNF-α, IL-10, CXCL-10, IFN-y) but IgG anti-SARS-CoV-2 IgM, IgA or IgG antibodies were not detected. -Second episode: moderate symptoms, Ct 17 (~109 copies/ml), anti-SARS-CoV-2 immunoglobulins not detected one week after onset, but were detectable 40 days after onset. - Genome sequencing of both episodes were associated with clade 20B, but they clustered apart on the phylogeny with significant statistical support with differing genetic markers between strains.
Larson (2020) (63) Case report	Describes a confirmed case of reinfection in a 42 year old healthy male military healthcare provider in Virginia. Analysis supported by viral	Respiratory swabs -Time between episodes was 51 days. -First episode: mild symptoms, no antibody test done.

United States Mar-Jun 2020	whole genome sequencing, phylogenomic analysis, and epidemiological data.	-Second episode: severe symptoms, IgG reactive on day 8 post symptom onset. -Viral culture was attempted but was unsuccessful. -Comparison of the sequence obtained from the initial and second episode identified several potential variations, including one high confidence variation. - The phylogenetic analysis placed the virus causing the second episode in lineage B.1.26, and the genome encoded the D614G variation in the spike protein. -Authors hypothesize that the second infection was more severe, potentially due to immune enhancement, acquisition of a more pathogenic strain, or perhaps a greater inoculum of infection as the second exposure was from within the household.
Tillett (2020) (64) *Preprint* Case report United States Apr-Jun 2020	Describes a confirmed case of reinfection in a 25 year old case in Nevada. Analysis supported by whole genome sequencing, phylogenomic analysis, and epidemiological data.	Nasopharyngeal swabs -Time between episodes was 48 days. -First episode: mild symptoms, Ct 35.2, no antibody test done. -Second episode: severe symptoms, requiring hospitalization and oxygen therapy, Ct 35.3, IgG/IgM reactive 7 days post symptom onset. - First and second viral genomes belonged to the same clade but differed by seven nucleotides. -The case may have been re-exposed to the virus by an infected parent.
Goldman (2020) (65) *Preprint* Case report United States Mar-Jul 2020	Describes a confirmed case of reinfection in a resident of a skilled nursing facility, aged between 60-69, with a history of severe emphysema and hypertension. Analysis supported by whole genome sequencing, phylogenomic analysis, and serology.	Nasopharyngeal swabs Time between episodes was 118 days. -First episode: severe symptoms, Ct 22.8, no antibody test done. -Second episode: mild symptoms, Ct 43.3, IgG antibodies against receptor binding domain (RBD), spike, and nucleocapsid were detected and showed a decreasing trend from day 14 to 42 after reinfection symptoms onset. -Immunological findings suggest that poorly developed or waned antibodies against the D614 virus formed after primary infection in March were not protective against reinfection with the D614G spike variant acquired in July. -Comparison of strain sequences from March and July revealed 10 high confidence intra-host single nucleotide variants of which 5 type the March sequence to clade 19B, and 5 type the July sequence to 20A.

Van Elslande (2020) (66) *LTE* Case report Belgium Mar-Jun 2020	Describes a confirmed case of reinfection in a 51 year old woman who took a daily dose of inhaled corticosteroids for asthma. Analysis supported by whole genome sequencing.	Nasopharyngeal swabs -Time between episodes was 93 days. -First episode: moderate symptoms, Ct 25.6, no antibody test done. -Second episode: mild symptoms, Ct 32.6, positive for anti-SARS-CoV-2 nucleocapsid antibodies one week post symptom onset. -First and second viral genomes belonged to different clades and differed by 11 nucleotides. Full length genome sequencing revealed the initial infection was caused by a lineage B.1.1 SARS-CoV-2 virus, while the relapsing infection was caused by a lineage A.
Selhorst (2020) (67) *Preprint* Case report Belgium Mar-Sep 2020	A case of reinfection was observed in a Belgian nosocomial outbreak involving 3 patients and 2 health care workers. Whole genome sequencing was performed on swabs of all individuals including the reinfection case's first episode. IgA, IgM, IgG, and neutralizing antibody responses were quantified in serum of all individuals, and viral infectiousness was measured in the swabs of the reinfection case.	Nasopharyngeal swabs -Case was positive for the first time in March 2020. The case worked at a facility were a nosocomial outbreak occurred and tested positive again in September 2020, 185 days after initial infection. -First episode: Mild symptoms, Ct 13, high IgG and neutralizing antibody levels after 3 months, IgA and IgM not detected at 3 months post diagnosis. -Second episode: Mild symptoms, Ct 19-25, replicating virus as indicated by RT-qPCR for negative strand RNA, yet culture was unsuccessful. Rapid rise in neutralizing antibodies within 14 days of symptom onset, with high IgG titers and low IgA and IgM titers. -Both initial and reinfections were mild. -Analysis of the sequences revealed a total of 18 nucleotide differences, with the strains belonging to different clades. This strain that cause reinfection matched that of three patients involved in the outbreak. -It was unclear whether the reinfection case played a role in transmission, however she provides the only link between some of the patients.
Lago (2020) (68) *Preprint* Case report Spain	Describes a confirmed case of reinfection in a 53-year old woman with asthma. Analysis supported by host genetics, viral whole genome sequencing, phylogenomic viral analysis, and epidemiological data obtained from interviews with the involved subjects.	Nasopharyngeal swabs -Time between episodes was 140 days. -First episode: mild, Ct 30, no antibody test done. -Second episode: severe, Ct 22-33, no antibodies detected on admission but titer of 7.04 detected 17 days after admission. -Case had contact with a confirmed COVID-19 case 12 days prior to second episode. Genomic analysis showed that the strain between the case and her

Apr-Aug 2020		close contact were identical. Further, reinfection was supported by phylogenetic analysis which revealed that the strain involved in the second episode was circulating in Madrid during the same time frame, but not during the range corresponding to the first episode. -The husband and daughter of the case tested positive for SARS-CoV-2 11 and 7 days, respectively, after the onset of the cases' second episode. The daughter's husband and four children also developed infection. Epidemiological and genomic data demonstrates that onward transmission occurred from the case to her husband and daughter during her second episode.
Zucman (2021) (70) Case report France Sep 2020-Jan 2021	Describes a case of reinfection caused by the South African variant 501Y.V2 in a 58 year old immunocompetent male. Analysis support by epidemiological data and whole genome sequencing.	Nasopharyngeal swab -Time between episodes was 129 days. -First episode: mild, no antibody testing done -Second episode: severe, IgG positive seven days after onset. -Genome sequencing identified D80A, E484K and N501Y mutations in the spike region, characterizing the 501Y.V2 lineage B.1.351 variant. -While the strain from the first episode was not available for sequencing, the occurrence of the primary infection one month before emergence of the 501Y.V2 strain in South Africa and three months before its first description in France rules out persistent viral shedding.
Colson (2020) (69) *LTE* Case report France Apr-Aug 2020	Describes a confirmed case of reinfection in a 70 year old immunocompetent man. Analysis supported by viral whole genome sequencing, phylogenomic viral analysis, and serology.	Nasopharyngeal swabs -Time between episodes was 105 days. -First episode: mild, Ct 27, IgG negative 2 weeks after onset but positive 4 weeks after onset (indicating seroconversion). -Second episode: asymptomatic, Ct 18, -Genomic analysis showed that the first and second viral strains differed by 34 nucleotides. The strain from the first episode was most closely related to strains from Nextrain clase 20A, circulating in the geographic area at that time during the first outbreak. The virus strain from the second episode was most closely related to the Marseille 4 lineage that emerged in the cases geographical area during the second outbreak.
Harrington (2021) (71)	Described a confirmed case of reinfection with caused by the 'new	Nose and throat swabs -Time between episodes was 250 days.

LTE Case report UK Apr-Dec 2020	variant' VOC-202012/01 of lineage B.1.1.7 in a 78 year old man with diabetes mellitus, diabetic nephropathy on haemodialysis, chronic obstructive pulmonary disease (COPD), mixed central and obstructive sleep apnoea, ischaemic heart disease. Analysis supported by viral whole genome sequencing, phylogenomic analysis, and serology.	-First episode: mild, Ct 26, SARS-CoV-2 IgM and IgG antibodies targeting viral nucleocapsid 'N' antigen were detectable on six occasions from two months after initial infection to 8 months after infection with no evidence of antibody waning. -Second episode: severe, Ct 28, no serology reported -Whole genome sequencing and phylogenetics showed that the virus strain in the first episode belonged to lineage B.2 while the virus strain in the second episode belonged to lineage B.1.1.7 and accumulated 18 amino-acid replacements across the genome.
Mulder (2020) (72) *LTE* Case report Netherlands Timeline not specified	Describes a confirmed case of reinfection in a 89 year old woman, suffering from cancer (Waldenström's macroglobulinemia), treated with B-cell-depleting therapy. Analysis supported by whole genome sequencing.	Nasopharyngeal swabs -Time between episodes was 54 days. -First episode: moderate symptoms, Ct 26.2, no antibody test done. -Second episode: severe symptoms resulting in death, Ct 25.2, WANTAI SARS-CoV-2 Ab and IgM ELISA were both negative. -The two strains differed at ten nucleotide positions and the sequences did not cluster in the phylogenetic tree.
Prado-Vivar (2020) (73) Case report Ecuador May-Jul 2020	Describes a confirmed case of reinfection in a 46 year old man. Analysis supported by viral whole genome sequencing and serology.	Oropharyngeal swabs -Time between episodes was 63 days. -First episode: mild symptoms, Ct 36.85, IgG negative & IgM positive six days after symptom onset. -Second episode: moderate symptoms, Ct 30.82, IgG and IgM positive 30 days post symptom onset. -First and second viral genomes belonged to different clades. For the first infection, the genome was assigned to the B1.p9 GISAID clade while the variant associated with the second episode was assigned to the A.1.1 GISAID clade.
Gupta (2020) (74) *LTE* Case report India May-Sep 2020	Describes confirmed cases of reinfection in two healthy healthcare workers (25 year old man and 28 year old woman) detected during routine surveillance. Analysis supported by whole genome sequencing.	Nasopharyngeal/oropharyngeal swabs Case 1 -Time between episodes was 108 days. -First episode: asymptomatic, Ct 36, no antibody test done. Second episode: asymptomatic, Ct 16.6, no antibody test done. -First and second viral genomes revealed 9 unique variant differences. Case 2 -Time between episodes was 111 days.

		-First episode: asymptomatic, Ct 28.16, no antibody test done. -Second episode: asymptomatic, Ct 16.92, no antibody test done. -First and second viral genomes revealed 10 unique variant differences. The genetic variation 22882T>G(S:N440K) was found within the receptor binding domain of the second episode viral genome. -The authors suggest that asymptomatic reinfection may be a potentially underreported entity.
Shastri (2020) (75) *Preprint* Case series India May-Jul 2020	Describes confirmed cases of reinfection in four frontline healthcare workers (27 year old male, 31 year old male, 27 year old male, 24 year old female). Analysis supported by whole genome sequencing, phylogenomic analysis, and serology.	Nasopharyngeal and oropharyngeal swabs -Time between episodes was 60, 59, 13, and 48 days. -First episode: two mild cases and two asymptomatic cases -Second episode: All cases were mild -Three cases were negative for anti-nucleocapsid antibodies after the second infection. -The authors hypothesize that those who do not seroconvert may not have the same degree of protection from reinfection as those with high titres of antibodies. -Comparative genomic and protein-based annotation analyses revealed differences in the presence and absence of specific mutations in the virus sequences from the first and second episode in all four paired samples.
Salehi-Vaziri 2021 (76) Preprint Case series Iran Mar-Apr 2020	Describes three confirmed COVID-19 cases that presented with possible re-infection some months after initial symptom resolution. Epidemiological data and whole genome sequencing supported the possibility of reinfection in two of the cases (32 year old male and a 42 year old male).	Nasopharyngeal and oropharyngeal swabs Case 1 -Time between episodes was 63 days. -First episode: mild, IgM positive -Second episode: moderate, IgG titration was assessed as 4.89 AU/ml which significantly increased after two months. - Genome sequencing revealed a D614G mutation of S gene from the second isolated sample. Case 2 -Time between episodes was 111 days. -First episode: mild, antibody testing not done -Second episode moderate, IgG titration was 17.5 IU/ml which decreased to 6.5 IU/ml after almost two weeks. - Genome sequencing revealed a D614G mutation of S gene from the second isolated sample.

LTE= letter to the editor

APPENDIX 2:

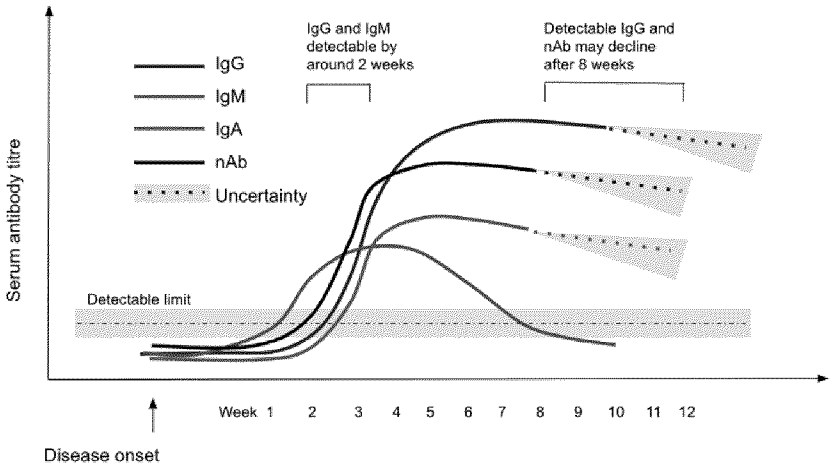

Figure 3 Post (2020) (19)

Nouveaux éléments de preuve sur la COVID-19

Revue rapide sur l'immunité protectrice, mise à jour 1

Introduction

Les anticorps contre le SRAS-CoV-2 confèrent-ils une immunité contre la réinfection par le SRAS-CoV-2? Offrent-ils une immunité protectrice à long terme (plus de six mois après l'infection) et l'infection antérieure par la souche sauvage originale du SRAS-CoV-2 protège-t-elle contre les variants préoccupants actuels?

Comprendre l'étendue et les limites de l'immunité protectrice aura d'importantes répercussions sur la pandémie de COVID-19 puisque l'immunité généralement associée aux coronavirus varie énormément et va de quelques mois pour les coronavirus saisonniers associés au rhume commun à deux ou à trois ans pour les coronavirus émergents comme le SRAS-CoV-1 et le SRMO (1). Dans le cas du SRAS-CoV-2, on sait que la plupart des gens développent une réponse immunitaire après l'infection ou après avoir été pleinement vaccinés, mais on ne sait pas encore pendant combien de temps et dans quelle mesure elle les protège contre la réinfection.

La réinfection au SRAS-CoV-2 semble peu fréquente, mais il n'est pas facile d'étudier cette question. Même si le test RT-PCR convient parfaitement pour déterminer la présence du virus dans le diagnostic initial, il continue de donner un résultat positif en présence de particules de virus non infectieux (fragments d'ARN), ce qui indique qu'il ne peut donc à lui seul être utilisé pour confirmer la réinfection. Plusieurs définitions de la réinfection ont été proposées tant dans la littérature disponible que par des organismes de santé publique (p. ex., CDC, CIRC) pour tenter de régler ce problème. Aux fins de la présente revue rapide, un cas confirmé de réinfection est défini comme une infection subséquente chez une personne qui a obtenu au moins un résultat négatif au test RT-PCR documenté entre les épisodes et pour lequel les données de séquence génomique des deux épisodes sont disponibles afin de permettre de distinguer deux clades génétiques ou lignées virales différentes (2). Parallèlement à cela, un cas présumé ou soupçonné de réinfection est défini comme tout cas dont l'infection initiale a été confirmée en clinique ou en laboratoire par un résultat positif à un test RT-PCR effectué plus de 90 jours après le premier épisode ou après un épisode qui se produit moins de 90 jours après le premier épisode, mais avec des preuves épidémiologiques de réexposition au SRAS-CoV-2 (2, 3).

Alors que le nombre de personnes partiellement et pleinement vaccinées commence à augmenter dans le monde, la recherche sur les infections ayant percé, soit les infections qui se produisent après la vaccination contre la COVID-19, commence à émerger. On voit une certaine hétérogénéité dans les études quant à la façon de définir les termes « pleinement vacciné » et « infection ayant percé ». La présente revue porte donc sur des articles rédigés à propos d'infections ayant percé. Ces infections, qui sont apparues plus de 14 jours après la fin de la première série de vaccins contre la COVID-19, sont déterminées par la découverte de l'ARN du SRAS-CoV-2 ou d'un antigène détecté sur un spécimen respiratoire recueilli conformément à la définition de cas établie par le CDC au titre de Breakthrough Infection Post-Vaccination ou Infections ayant percé (ou infections sporadiques) en français (4).

Il est également difficile d'évaluer l'immunité à long terme face à la COVID-19. Cela s'explique par le fait que les réponses immunitaires varient, que seules certaines personnes développent des anticorps spécifiques aux antigènes SARS-CoV-2 offrant une immunité protectrice suffisante et que seules certaines des personnes qui ont reçu un diagnostic de COVID-19 conservent des taux d'anticorps détectables après l'infection. Il ne faut

pas non plus oublier qu'une faible proportion des personnes infectées par le SRAS-CoV-2 ne semblent pas avoir de taux détectables d'anticorps neutralisants, mais se rétablissent tout de même, un état de fait qui n'est pas encore bien compris (5). Les données probantes indiquent que tant l'activité des anticorps neutralisants que celle des cellules immunitaires propres au SRAS-CoV-2 sont de bons indicateurs de l'immunité protectrice. Les variations dans les anticorps et l'interaction de ceux-ci, les réponses des lymphocytes B et T à l'infection, ainsi que la variété des techniques de détection compliquent l'évaluation de l'immunité à long terme.

Il ne faut pas oublier que les variants du SARS-CoV-2 ont acquis des mutations, ce qui est inévitable en raison des passages successifs du virus dans le corps de millions de personnes. La plupart des petites mutations ne modifient pas les caractéristiques du virus. Cependant, avec le temps, certaines mutations vont provoquer des changements dans la transmissibilité ou la gravité de la maladie, ou dans la létalité qui lui est associée, en plus de pouvoir modifier la précision des tests de diagnostic et d'entraîner une évasion immunitaire (6). En avril 2021, trois variants préoccupants (VP) ont été identifiés, soit B.1.1.7 (7), B.1.351 (8) et P.1 (9). De nombreux variants d'intérêt sont actuellement étudiés et surveillés afin de déterminer s'ils sont ou non préoccupants (6).

Des études *in vitro* sur la neutralisation des VP ont montré que la neutralisation des variants B.1.351 et P.1 était inférieure à celle des variants originaux, mais les résultats des expériences d'immunité cellulaire et des expériences effectuées sur des modèles animaux ont permis de conclure que l'activité immunitaire était toujours stimulée. Il n'est donc pas évident de savoir dans quelle mesure ces VP pourront entraîner un échappement immunitaire à la suite de l'infection naturelle ou de la vaccination (10-16). Les données sur la réinfection et les infections sporadiques après avoir reçu le vaccin porteront sur la mesure dans laquelle différents VP peuvent échapper à l'immunité naturelle ou générée par vaccin.

Cette revue rapide résume donc les données probantes tirées des études récentes sur la réinfection, les infections ayant percé, la persistance des anticorps et d'autres marqueurs immunitaires détectés pendant plus de six mois après l'infection initiale par le SRAS-CoV-2 ou la vaccination, y compris, le cas échéant, la preuve sur l'immunité contre les VP publiée avant le 9 avril 2021. En raison de l'abondance des données sur les humains, les modèles animaux et les études *in vitro* n'ont pas été inclus.

Points clés

- Soixante-douze études ont été recensées, dont trente sur le risque de réinfection, sept sur l'infection ayant percé, trente-six sur la cinétique et la durabilité des anticorps et d'autres marqueurs immunitaires plus de six mois après l'infection initiale par le SRAS-CoV-2 ou la vaccination et quatre revues rapides ou systématiques.
- Dans l'ensemble, nous avons constaté que le risque de réinfection était faible, que le risque d'infection sporadique par les variants originaux ou par le VP B.1.1.7 était plus élevé même après la vaccination, mais qu'il était malgré tout assez faible. Six mois après l'infection, la majorité des personnes étudiées avaient encore des marqueurs détectables de l'immunité, mais une faible proportion de cas n'avait pas établi de taux d'anticorps détectables ou les taux d'anticorps avaient baissé en moins de six mois.

Risque de réinfection :

- Les meilleures données probantes à ce jour sur l'immunité protectrice naturelle proviennent des données sur la réinfection figurant dans une étude clinique et dans 29 études de cohorte prospectives et rétrospectives.
- Les études incluses indiquent que la présence d'anticorps découlant d'une infection antérieure est associée à une protection contre la réinfection pouvant atteindre huit mois (Tableau 1).
- Les cohortes qui n'ont utilisé que des cas confirmés de réinfection dans leurs estimations du risque ont déclaré des niveaux de protection plus élevés (96 à 99 %) (17 à 20) que celles qui incluaient des cas soupçonnés de réinfection (83 à 96 %) (21 à 28).
    - Les analyses ajustées du risque de réinfection dans certaines grandes cohortes comprenaient : des études effectuées au Qatar 0,01 % (IC à 95 % : 0,01 à 0,02 %, n = 1 366) (18), au Royaume-Uni 0,7 % (IC à 95 % : 0,6 à 0,8, n = 36 509) (29) et au Mexique 0,26 % (n = 100 432) (30), respectivement.
    - De petites études de cohorte ont cependant indiqué une protection complète pendant 5 à 10 mois (31 à 33).
    - Selon les cohortes avec réinfection confirmée et soupçonnée, les personnes qui avaient reçu un diagnostic clinique ou de laboratoire d'infection antérieure ont affiché pendant un maximum de dix mois des taux d'attaque de l'infection beaucoup plus faibles lors du suivi que celles qui avaient obtenu un taux séronégatif ou un résultat négatif au test RT-PCR au départ (0 % à 3,4 % c. 1,29 % à 28,7 %) (17, 21, 23 à 26, 31 à 38).
- La protection contre la réinfection était la même pour les variants originaux et pour le B.1.1.7 (29). Aucune protection contre la réinfection par le VP B.1.351 n'a été signalée dans un essai effectué en Afrique du Sud (39).
- Le temps médian entre l'infection initiale et la réinfection dans les cohortes avec réinfection confirmée variait entre 52 et 201 jours (plage de 15 à 297) (18, 19, 22) et, dans les cohortes avec réinfection soupçonnée, entre 56 et 241 jours (plage de 40 à 345 jours) (22, 23, 27, 28, 30, 40 à 42). Ces dernières données peuvent inclure des points de données mal classés représentant plutôt des résultats positifs ou récurrents ayant tous deux été recensés dans la littérature.
- Les personnes réinfectées (environ 50 %) étaient plus susceptibles d'être asymptomatiques que les personnes qui en étaient à leur première infection (19,2 %) (22, 27).
- Plusieurs études indiquent que les personnes qui n'ont pas eu de séroconversion n'ont peut-être pas le même degré de protection contre la réinfection que celles qui ont des titres d'anticorps élevés (17, 34, 43). Toutefois, après la réinfection, la majorité des cas ont montré une réponse par anticorps IgG (34).
- Une réponse par anticorps IgG plus élevée et prolongée a donc été corrélée avec un risque plus faible de réinfection. Un plus grand âge (p = 0,001), la durée des symptômes (p = 0,002) et le nombre de

symptômes (p < 0,001) ont été corrélés avec des réponses par anticorps IgG plus élevées après l'infection primaire (43).

- Des données contradictoires sur l'âge comme facteur de risque de réinfection ont été rapportées dans toutes les études, certaines indiquant des groupes plus âgés (plus de 65 ans) et d'autres, des groupes plus jeunes (10 à 29 ans) (30, 41, 42, 44).
- Des maladies chroniques sous-jacentes ont été associées à la réinfection (30).

Infection sporadique après une vaccination complète :

- Des essais contrôlés randomisés et des études d'observation en situation réelle ont démontré que l'infection sporadique associée au virus de type sauvage et au variant B.1.1.7 était moins virulente après l'administration de deux doses de vaccin (tableau 2).
- Dans des études en situation réelle, lorsque les vaccins Pfizer-BioNTech, Moderna ou Oxford-AstraZeneca étaient utilisés, cela a réduit l'incidence de l'infection par le SRAS-CoV-2 de plus de 90 % alors que l'immunité naturelle après l'infection entraînait une réduction de l'incidence de 85 % (45-47).
- Les essais cliniques et les investigations en situation réelle portant sur les vaccins Pfizer-BioNTech et Oxford-AstraZeneca ont démontré une protection efficace et similaire (p > 0,05) contre le variant B.1.1.7 par rapport au variant original (45, 48).

Marqueurs de réponse immunitaire plus de six mois après l'infection :

- Trente-sept études comprenant un suivi avec plus de 30 observations effectué plus de six mois après l'infection (jusqu'à douze mois) fournissent des preuves basées sur les taux d'anticorps circulants et les taux de lymphocytes B et T contre le SRAS-CoV-2 (tableau 3). La relation spécifique entre ces corrélations d'immunité et de protection contre l'infection par le SRAS-CoV-2 ou la réinfection n'est cependant pas bien comprise.
- Onze études font état d'une réponse immunitaire cellulaire liée aux lymphocytes B mémoires (soit les cellules immunitaires qui produisent les virus qui ciblent les anticorps) et aux lymphocytes T mémoires (c.-à-d. les cellules immunitaires qui guident les réponses immunitaires adaptatives des cellules) après une infection naturelle qui confère probablement une certaine immunité à long terme contre les réinfections ultérieures.
    - Le fait que le niveau d'activité des lymphocytes B et T mémoires était élevé et qu'il se soit poursuivi pendant plus six mois après l'infection pourrait constituer une meilleure mesure de l'immunité protectrice que les anticorps circulants dont le niveau diminue avec le temps, une fois la personne rétablie après l'infection par le SRAS-CoV-2 (49 à 52).
    - De façon générale, la portée et l'ampleur des réactions des lymphocytes T se sont maintenues (et augmentaient parfois) au-delà de six mois après l'infection ou l'apparition des symptômes (49 à 54). Une étude signale que les lymphocytes T de 95 % des cas bénins sont demeurés sensibles à au moins un bassin de peptides du SARS-CoV-2, et a quantifié une médiane de

200 cellules par million de cellules mononuclées de sang périphérique (PBMC) (ou 1 cellule sur 5 000) pour être spécifique au SRAS-CoV-2 après un suivi de 6 mois (55).

- Elle a permis de voir chez 80 % des personnes qui avaient eu une forme bénigne à modérée de l'infection par la COVID-19 une fréquence élevée de lymphocytes B mémoires totaux spécifiques contre le domaine de liaison au récepteur (RBD) du virus SRAS-CoV-2 (56).
- Dans certaines études, on a constaté que les lymphocytes T CD8+ étaient moins robustes que les réponses des lymphocytes T CD4+ obtenues plus de six mois après l'infection (49, 54, 56, 57), mais les répercussions de ces résultats sur les réponses à long terme des lymphocytes T n'ont pas encore été établies.

- La cinétique des anticorps à long terme a été décrite dans 33 études menées de 6 à 12 mois après l'apparition des symptômes.
  - Les études font régulièrement état du fait que la majorité (entre 70 et 99 %) des personnes ont continué à obtenir des résultats positifs pour les anticorps neutralisants spécifiques au SRAS-CoV-2, les anticorps IgG contre la protéine S ou les anticorps IgG anti-RBD six mois après l'infection (32, 43, 52, 56, 58, 59, 59, 59, 60, 60 à 65).
  - Une étude a mentionné des résultats semblables obtenus six mois après la vaccination complète chez les personnes ayant reçu le vaccin Moderna (64).
  - Les taux d'anticorps neutralisants étaient plus élevés et les taux d'IgG contre la protéine S étaient plus faibles chez les personnes qui avaient eu une forme grave de la COVID-19 que chez celles dont l'infection avait été bénigne ou modérée (43, 52, 56, 58 à 60, 60 à 63).
  - Les taux d'IgG spécifiques contre la protéine N étaient très variables (25 % à 98 %) dans les échantillons de l'étude inclus obtenus plus de six mois après l'infection (37, 59, 61, 62, 66).
  - Les enfants présentaient des niveaux plus faibles d'anticorps IgG contre les protéines S et N et dans une étude, la proportion globale d'anticorps contre les protéines accessoires était plus élevée et plus stable chez les enfants que chez les adultes (67).

Revues :

- Les revues rapides et systématiques pertinentes comprennent la recherche sur la COVID-19 effectuée entre juin et décembre 2020 sur les corrélations avec l'immunité figurant dans des études menées au début de la pandémie (tableau 4). Elles sont incluses comme ressources pour la recherche effectuée à chacun des temps de mesure, soit avant les six derniers mois.

Vue d'ensemble des éléments de preuve

Les études sur la réinfection comprenaient des cohortes prospectives, dont certaines grandes études multicentriques, qui présentent un faible risque de biais et une capacité de généralisation élevée. Des analyses à variables multiples conçues pour tenir compte de la confusion possible n'ont pas toujours été effectuées, ce qui peut donc fausser les résultats. Des cohortes rétrospectives comprenant des données tirées des dossiers médicaux ou des données de surveillance recueillies de façon régulière sur le COVID-19 ont également été incluses. Certaines de ces études semblaient avoir une bonne capacité de généralisation, car elles utilisaient de grandes bases de données nationales. D'autres se concentraient davantage sur les travailleurs de la santé dans un seul centre hospitalier ou sur des groupes de patients spécifiques. Les cohortes rétrospectives présentent toutefois un risque plus élevé de biais en raison de la nature rétrospective de l'étude, des données manquantes et des facteurs de confusion possible.

Les études sur les infections ayant percé ou sporadiques comprenaient des essais contrôlés randomisés, des études de cohorte prospectives et des études cas-témoins. Les essais contrôlés en double aveugle avec placebo constituent l'étalon-or pour mesurer les répercussions d'une intervention, mais ils ne fournissent pas nécessairement d'estimation précise de l'efficacité de la vaccination dans le monde réel, et ne sont pas non plus aussi susceptibles de se produire pendant un scénario actuel de pandémie. Bien que les études d'observation fournissent une évaluation réelle à propos d'une intervention, elles peuvent également présenter un plus grand nombre de biais. Cela inclut notamment la nature rétrospective des études cas-témoins et la dépendance aux symptômes autodéclarés dans de nombreuses études de cohorte.

Les études sur l'immunité à long terme comprenaient surtout des données longitudinales tirées d'études d'observation, notamment de cohortes prospectives, de séries de cas et d'études transversales, qui présentent un risque modéré à élevé de biais de sélection et de confusion. Ainsi, la plupart des études ont fait état de la gravité de l'infection clinique chez les participants ayant pris part à l'étude, mais bon nombre d'entre elles ne semblent pas avoir tenu compte des différences dans l'état immunitaire de référence dans leurs échantillons, état qui peut être influencé par différentes comorbidités (p. ex., cancer, problèmes cardiaques, maladie rénale, diabète, etc.). Tout comme la réponse immunitaire à l'infection initiale varie grandement, les réponses immunitaires obtenues six mois après une infection au SRAS-CoV-2 sont également très variables. Les différences dans les données démographiques des participants à l'étude, l'état immunitaire de référence, la gravité clinique des infections, les résultats immunitaires étudiés, le temps de suivi et les méthodes de mesure ont probablement contribué à une partie de l'hétérogénéité que nous avons observée. La variabilité peut également découler du recours à différentes méthodes de détection des anticorps et des cellules immunitaires utilisant divers paramètres de sensibilité et de spécificité des tests. Tous ces facteurs font en sorte qu'il est difficile de comparer les résultats entre les études (61).

Lacunes dans les connaissances :

- Il n'y a pas d'études de grande qualité sur la durée, l'efficacité potentielle et l'efficacité réelle de la protection fournie par les anticorps neutralisants.

- Il est difficile de comprendre la corrélation entre les mesures immunologiques (p. ex., les titres d'anticorps neutralisants) et la protection. Des données sur l'efficacité clinique seront aussi requises pour fournir une évaluation définitive de la protection assurée par le vaccin.
- Le rôle des anticorps spécifiques et des lymphocytes B et T dans l'élimination de l'infection n'a pas été déterminé de façon définitive chez les humains.
- La majorité des éléments de preuve sur l'immunité protectrice contre les variants préoccupants actuels sont associés au variant B.1.1.7. Il faudra des preuves supplémentaires à propos des autres variants préoccupants en plus des expériences préliminaires *in vitro* et des modèles animaux.

TABLE DES MATIÈRES

RISQUE DE RÉINFECTION

Le Centre européen de prévention et de contrôle des maladies a créé un organigramme pour évaluer la réinfection (2) et d'autres définitions visant à établir une distinction entre la réinfection confirmée et la rechute/réactivation et la récidive ont également été proposées (3) ou sont en cours d'élaboration. Les définitions utilisées dans cette revue sont donc fondées sur ces lignes directrices publiées.

Une réinfection confirmée exige : une infection initiale confirmée par test RT-PCR ET une deuxième infection confirmée par test RT-PCR ET un ou des résultats négatifs au test RT-PCR effectué entre la première et la deuxième infection ET des données de séquence génomique provenant des deux épisodes qui permettront de distinguer deux isolats viraux différents.

Une réinfection présumée exige : un résultat positif au test RT-PCR obtenu plus de 90 jours après le premier épisode (confirmé cliniquement ou en laboratoire) OU un résultat positif au test RT-PCR obtenu moins de 90 jours entre les épisodes, avec une preuve épidémiologique de réexposition au SRAS-CoV-2.

Les meilleures données probantes à ce jour sur l'immunité protectrice proviennent de quelques études de cohorte sur le risque de réinfection ayant récemment été publiées. Bien que les rapports/séries de cas de petite envergure présentant les détails des réinfections présumées aient été exclus, les cas de réinfection confirmée jusqu'au 11 février 2021 ont été résumés dans une version antérieure de cette revue rapide disponible par l'entremise du Secrétariat des sciences émergentes de l'ASPC.

Résultats des études sur la réinfection (n = 30) :

- Les anticorps créés après une infection antérieure semblent être associés à une protection contre la réinfection pouvant durer jusqu'à huit mois, mais une faible proportion de personnes ont cependant été réinfectées. Les raisons de la réinfection ou de l'absence d'immunité protectrice ne sont pas bien comprises.
- Seules trois études ont calculé les estimations du risque de réinfection à partir des cas confirmés de réinfection. Elles ont fait état d'une estimation élevée de protection contre la réinfection dans les cohortes du Royaume-Uni (> 96 %) et du Qatar (> 99 %) (17 à 19). En outre, dans une cohorte comprenant 6 771 personnes infectées pendant la première vague en France (de janvier à mai 2020), seulement 31 réinfections confirmées (0,47 %) ont eu lieu pendant la période de suivi (juin 2020 à janvier 2021) (20).
- D'importantes cohortes prospectives avec réinfections présumées (n < 1 000) provenant du Royaume-Uni et de la France ont montré que l'infection antérieure par le SRAS-CoV-2 offrait une immunité protectrice pendant un maximum de sept mois chez 83 à 96 % des personnes (21 à 23, 26). Quant aux cohortes rétrospectives provenant des États-Unis, du Royaume-Uni et de l'Autriche, elles ont permis de voir que 90 à 94 % des personnes précédemment infectées avaient bénéficié d'une protection pouvant aller jusqu'à six ou huit mois (24, 25, 27, 28). Il existe de multiples petites études de cohorte portant sur des personnes déjà infectées (n < 150) qui n'ont déclaré aucun cas de réinfection pendant la période de 5 à 10 mois utilisée à des fins de suivi (protection complète) (31 à 33).
- Une vaste étude de surveillance menée au Danemark a révélé que la protection contre la réinfection dans la population était supérieure à 80 % chez les personnes âgées de moins de 65 ans lors du suivi de 7 mois, mais qu'elle était beaucoup plus faible (47 %) chez les personnes âgées de 65 ans et plus (68). Une étude menée en Israël a révélé que le plus grand nombre de réinfections s'était produit chez des personnes âgées de 10 à 29 ans (environ 50 %) (41). Le risque de réinfection parmi les différents groupes d'âge est probablement lié à un certain nombre de facteurs, y compris la tendance épidémiologique/comportementale en vigueur dans la région à ce moment-là (p. ex., les populations plus jeunes semblaient être plus touchées pendant la deuxième vague de COVID-19), ainsi que la possibilité d'une baisse de l'immunité chez les adultes plus âgés.
- Le risque de réinfection était faible dans toutes les études fondées sur de vastes cohortes rétrospectives composées de la population en général. Au Qatar, le risque ajusté de réinfection confirmée était de 0,01 % (IC à 95 % : 0,01 à 0,02 %, n = 133 266) (18). Les estimations du risque étaient légèrement plus élevées dans les cohortes qui incluaient la réinfection présumée. Ainsi, au Royaume-Uni, il était de 0,7 % (IC à 95 % : 0,6 à 0,8, n = 36 509) (29) alors qu'au Mexique, le risque était de 0,26 % (n = 100 432) (30).
- Le temps de réinfection était une médiane de 52 à 65 jours (intervalle de 15 à 212 jours) dans les cohortes avec réinfection confirmée (18, 19) comparativement à 56 à 241 (intervalle de 40 à 345 jours) dans les cohortes avec réinfection présumée (22, 27, 30, 40 à 42). Ces dernières données peuvent

inclure des points de données mal classés représentant plutôt des résultats positifs ou récurrents ayant tous deux été recensés dans la littérature.

- Les personnes qui ont eu un diagnostic clinique ou en laboratoire d'infection antérieure ont affiché pendant un maximum de neuf mois des taux d'attaque de l'infection beaucoup plus faibles lors du suivi que celles qui avaient obtenu un taux séronégatif ou un résultat négatif au test PCR au départ (0 % à 3,4 % c. 1,29 % à 41,2 %) (17, 21, 23 à 26, 34 à 38). Plusieurs études indiquent que les personnes qui n'ont pas eu de séroconversion n'ont peut-être pas le même degré de protection contre la réinfection que celles qui ont des titres d'anticorps élevés (17, 34, 43). Toutefois, après la réinfection, la majorité des cas ont montré une réponse par anticorps IgG (34).
    - Les travailleurs de la santé qui avaient des réponses IgG positives contre le SRAS-CoV-2 présentaient des taux plus faibles de résultats positifs au test PCR après 31 semaines de suivi comparativement aux travailleurs de la santé qui n'avaient aucune réponse IgG au début de l'étude (0,13 c. 1,09 par 10 000 jours-risque) (21). Une tendance semblable a été observée dans une cohorte provenant de la population générale en Suisse (0,3 c. 4,8 par 10 000 jours à risque) (38).
- Une réponse par anticorps IgG plus élevée et prolongée a donc été corrélée avec un risque plus faible de réinfection. Un plus grand âge ($p = 0,001$), la durée des symptômes ($p = 0,002$) et le nombre de symptômes ($p < 0,001$) ont été corrélés avec des réponses par anticorps IgG plus élevées après l'infection primaire (43).
- Deux études ont indiqué que l'immunité obtenue après l'infection initiale protégeait contre la réinfection par le variant B.1.1.7 (22, 29). Le volet avec placebo d'un essai contrôlé randomisé portant sur le vaccin Novavax n'a vu aucune différence dans l'infection ou la réinfection entre les sujets séronégatifs et séropositifs, même si la majorité des cas (92,7 %) étaient causés par le variant B.1.351, ce qui indique que l'infection antérieure ne protégeait pas contre la réinfection par le variant B.1.351 (39). Deux autres études ont relevé un pic de réinfection en décembre 2020 et en janvier 2021, ce qui pourrait être lié à l'émergence des variants préoccupants (25, 41)
- La symptomatologie déclarée pendant la réinfection a été très variable :
    - Une étude a révélé que le plus grand âge et les comorbidités étaient associés à une réinfection plus sévère (30). Cette étude a également indiqué que les patients ayant eu une atteinte initiale grave étaient plus susceptibles de développer des symptômes graves pendant la réinfection. Toutefois, comme aucun dépistage de masse n'était en vigueur, les cas asymptomatiques à la suite de la réinfection par le SRAS-COV-2 ne seront probablement pas identifiés. De nombreux rapports de réinfection peuvent être biaisés vers l'identification de cas plus graves.
    - Les sujets qui avaient déjà eu une forme grave de la COVID-19 présentaient un risque de 20 % supérieur d'avoir des symptômes graves lors d'une réinfection.

- Une étude a révélé qu'un plus grand nombre de cas étaient symptomatiques pendant le deuxième épisode (84 %) que pendant le premier (53 %) (42). Une autre étude a révélé que 88,5 % des cas présentaient plus de symptômes lors de la réinfection que lors de l'infection initiale, mais la gravité globale des symptômes n'a pas été indiquée (34).
- Des admissions aux soins intensifs et des décès après des réinfections ont été signalés en France (4 sur 46, 8,7 %) (20). Cette étude a aussi révélé que la majorité des réinfections présentaient soit un état clinique similaire dans les deux épisodes (22 sur 46, 47,8 %) ou une forme plus légère lors du deuxième épisode (14 sur 46, 30,4 %).
- Deux études n'ont révélé aucune différence statistiquement significative dans la gravité des symptômes, l'hospitalisation ou les caractéristiques de laboratoire entre les deux épisodes ($p > 0,05$) (40, 69).
- Deux études ont indiqué que la réinfection était moins grave que les infections primaires (18, 19).

Tableau 1 : Études évaluant le risque de réinfection avec le SRAS-CoV-2 (n = 30)

ÉTUDE	MÉTHODE	PRINCIPAUX RÉSULTATS
Réinfection confirmée (n=4)		
Abu-Raddad (2021) (19) *Prépublication* Étude de cohorte rétrospective Qatar Avril à décembre 2020	Les personnes positives à l'anticorps du SRAS-CoV-2 qui ont eu un écouvillonnage positif 14 jours ou plus après le premier résultat positif au test de détection des anticorps ont été suivies pendant une période médiane de 17 semaines (intervalle de 0 à 45) pour pouvoir obtenir des preuves de réinfection (n = 43 044). On a également suivi des personnes séronégatives (n = 149 923) pour déterminer l'incidence de l'infection. Le séquençage du génome	Écouvillonnage de sécrétions rhinopharyngées et oropharyngées – 314 personnes séropositives ont eu un résultat d'écouvillon positif 14 jours ou plus après le premier résultat positif au test de détection des anticorps. – 32 cas présumés sur 314 présentaient de bonnes preuves de réinfection (Ct ≤ 30 avec écouvillonnage positif pour la réinfection), 97 cas comprenaient quelques preuves (Ct > 30 avec écouvillonnage positif pour la réinfection), tandis que les preuves étaient faibles pour les 185 cas restants. – Dans les cas où l'on trouvait de bonnes preuves de réinfection (32 sur 314, 10,2 %), le temps médian entre le premier résultat positif au test de détection des anticorps et l'écouvillonnage positif pour la réinfection était de 52 jours (intervalle de 15 à 212 jours). Les réinfections étaient moins graves que les infections primaires. – Le séquençage du génome a démontré que 5 cas sur 16 pour lesquels des spécimens jumelés étaient disponibles ont été jugés être des réinfections confirmées, soit un taux confirmé de 31,6 %. – Le risque de réinfection parmi les cas confirmés par des anticorps était de 0,10 % (IC à 95 % : 0,08 à 0,11 %)

	viral a été effectué pour des spécimens viraux jumelés (n = 16) afin de confirmer la réinfection.	alors que le taux d'incidence de la réinfection était de 0,66 par 10 000 semaines-personnes (IC à 95 % : 0,56 à 0,78). – Le risque d'infection pour les personnes séronégatives a été estimé à 2,15 % (IC à 95 % : 2,08 à 2,22 %), avec une incidence d'infection de 13,69 pour 10 000 semaines-personnes (IC à 95 % : 13,22 à 14,14). – Une tendance à la baisse du taux d'incidence de réinfection pendant chacun des mois de suivi supplémentaires a démontré que l'immunité protectrice n'avait pas diminué en sept mois. – L'efficacité de l'infection naturelle contre la réinfection a été estimée à 95,2 % (IC à 95 % : 94,1 à 96,0 %). -
Abu-Raddad (2020) (18) *Prépublication* Étude de cohorte rétrospective Qatar Février à août 2020	Tous les cas d'infection au SRAS-CoV-2 confirmés en laboratoire et ayant obtenu au moins un écouvillonnage positif lors du test RT-PCR 45 jours ou plus après un premier écouvillonnage positif ont fait l'objet d'une enquête individuelle pour trouver des preuves de réinfection (n = 133 266 cas). Le séquençage du génome viral des spécimens viraux appariés, soit le premier résultat positif et le résultat de réinfection, a été effectué pour confirmer la réinfection dans un petit sous-ensemble de cas (n = 12).	Écouvillonnage de sécrétions rhinopharyngées et oropharyngées – 243 personnes (0,18 %) ont obtenu un résultat positif à l'écouvillonnage effectué 45 jours ou plus après le premier écouvillonnage positif. De ce nombre, 54 cas (22,2 %) présentaient des preuves solides ou valables de réinfection (la positivité du résultat du test PCR était associée à des preuves contextuelles appuyant l'état de réinfection). – Le temps médian entre le premier écouvillonnage et celui effectué pour vérifier la réinfection était de 64,5 jours (entre 45 et 129 jours). – Une seule personne a été hospitalisée lors de la réinfection, alors qu'il n'avait été atteint que d'une forme bénigne de l'infection. – Seuls quatre cas de réinfection ont été confirmés par séquençage du génome viral. – Le risque de réinfection a été estimé à 0,01 % (IC à 95 % : 0,01 à 0,02 %) et le taux d'incidence de réinfection a été estimé à 0,36 (IC à 95 % : 0,28 à 0,47) par 10 000 semaines-personnes. Les auteurs concluent que la réinfection est un phénomène rare et que l'immunité contre la réinfection dure probablement au moins quelques mois après la première infection.
Brouqui (2021) (20) *nouvelle*	Les cas confirmés de COVID-19 pendant les	Sécrétions rhinopharyngées prélevées par écouvillonnage

Cohorte rétrospective. France Janvier 2020 à janvier 2021	deux vagues (janvier à mai 2020 et juin 2020 à janvier 2021) ont été analysés à des fins de preuve de réinfection. La réinfection a été définie comme le fait d'avoir obtenu deux résultats positifs pour le SRAS-CoV-2 au test qRT-PCR effectué sur des échantillons recueillis à plus de 90 jours d'intervalle après rétablissement clinique, ainsi qu'avoir obtenu au moins un résultat négatif au test qPCR après le premier résultat positif. Le génotypage du virus a également été effectué.	- Pendant la première vague, 6 771 sur 90 602 personés testées ont obtenu un résultat positif au test qRT-PCR. Conformément à la définition, 46 cas ont été jugés être des réinfections. De ce nombre, 31 ont reçu un diagnostic de réinfection confirmée fondé sur des preuves génomiques (0,47 %). - Parmi les réinfections, 22 sur 46 (47,8 %) présentaient un état clinique similaire lors des deux épisodes, 14 sur 46 (30,4 %) ont eu une forme plus légère de la maladie lors du deuxième épisode et 10 sur 46 (21,7 %) ont vu leur situation s'aggraver passant d'une maladie asymptomatique à une forme légère ou modérée ou grave ou critique. Quatre cas ont été admis aux soins intensifs ou sont décédés lors du deuxième épisode.
Jeffery-Smith (2021) (17) Enquête sur des poussées et étude longitudinale Royaume-Uni Avril à octobre 2020	Deux foyers de soins de longue durée dans lesquels une éclosion s'était produite pendant la première vague de COVID-19 ont connu une deuxième éclosion. Des enquêtes sur des poussées et la sérologie du SRAS-CoV-2 ont été effectuées pour évaluer le rôle des anticorps antérieurs dans la protection contre la réinfection au SRAS-CoV-2.	Écouvillonnage du nez -1,1 % (1 sur 88) des personnes qui avaient eu une exposition antérieure confirmée au SRAS-CoV-2 (séropositivité ou résultat positif au test PCR) lors de la première éclosion (5 mois plus tôt) ont obtenu un résultat positif lors de la deuxième éclosion, comparativement à 24,7 % (18 sur 73) des personnes qui avaient un statut séronégatif après la première éclosion. – L'efficacité protectrice de l'exposition antérieure était de 96,2 % (IC à 95 % : 72,7 % à 99,5 %) contre l'infection pendant la deuxième éclosion, pour un rapport de risque estimé de 0,038 (IC à 95 % : 0,005 à 0,273; p < 0,0001). - – Le séquençage du génome entier a révélé que la deuxième éclosion de COVID-19 avait été causée par des souches de SRAS-CoV-2 génétiquement différentes des souches trouvées pendant les premières éclosions dans chacun des foyers.

Réinfection soupçonnée (n=26)		
Hall (2021) (22) *nouveaux résultats* Cohorte prospective Royaume-Uni Juin 2020 à janvier 2021	Les membres du personnel asymptomatiques et symptomatiques (n = 25 661) qui travaillent dans les hôpitaux participant à l'étude SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) ont été suivis pendant sept mois afin d'estimer l'incidence relative des résultats positifs au test PCR selon les résultats initiaux du PCR ou les résultats initiaux obtenus pour les anticorps. Une réinfection possible a été définie comme toute personne qui a obtenu deux résultats positifs lors de tests PCR effectués sur des échantillons recueillis après un intervalle de 90 jours ou un participant positif aux anticorps dont le résultat du nouveau test PCR était positif au moins quatre semaines après le premier résultat positif aux anticorps. Un cas probable exige en outre des données sérologiques	Écouvillonnage de sécrétions nasales et oropharyngées - 8 278 (32 %) participants avaient des preuves d'infection antérieure et ont donc été ajoutés à la cohorte positive alors que 17 383 (68 %) participants qui n'avaient aucune preuve d'infection antérieure ont plutôt été affectés à la cohorte négative. - 13 401 participants (52,2 %) de la cohorte ont été vaccinés pendant la période de suivi (entre décembre 2020 et le 11 janvier 2021). Ce chiffre comprenait 9 468 personnes faisant partie de la cohorte négative et 3 933 de la cohorte positive. - Lors du suivi, on a détecté 1 704 nouvelles infections dans la cohorte négative et 155 réinfections. De ce nombre, 19,7 % des nouvelles infections et 49,7 % des réinfections étaient asymptomatiques. - La densité d'incidence était de 7,6 par 100 000 dans la cohorte positive et de 57,3 par 100 000 dans la cohorte négative. - Les participants de la cohorte positive présentaient un risque de nouvelle infection 99,8 % inférieur à celui des participants de la cohorte négative, RTI ajusté (RTIa) de 0,002 (IC à 95 % de 0,00 à 0,01). - Lorsqu'on limite les infections uniquement aux personnes ayant eu des symptômes de COVID-19, les participants de la cohorte positive présentaient une incidence de nouvelle infection inférieure de 93 % à celle des participants de la cohorte négative, RTIa 0,074 (IC à 95 %, 0,06 à 0,10). - En utilisant la définition la plus sensible de la réinfection, soit celle qui inclut également les cas possibles ou probables, les participants de la cohorte positive avaient une incidence de nouvelle infection inférieure de 84 % à celle des participants de la cohorte négative, RTIa 0,159 (IC à 95 %, 0,13 à 0,19).

	quantitatives ou des données génomiques virales au soutien obtenues à partir des échantillons disponibles. L'effet du variant B.1.1.7 a été inclus dans l'analyse en créant une variable binaire indiquant à quel moment le PCR de la négativation de la détection du gène S (SGTF) représentait 50 % ou plus des résultats positifs pour chacune des régions.	- L'infection asymptomatique (RTIa 0,48 IC à 95 %, 0,37 à 0,63) est celle qui a fourni la moins bonne protection. - Les auteurs n'ont trouvé aucune preuve que la prévalence accrue du variant B.1.1.7 a eu un effet négatif sur les taux de réinfection pendant le suivi. Les modèles suggéraient cependant que l'effet protecteur de l'infection précédente augmentait lorsque le variant était dominant (RTI de 0,18, IC à 95 %, 0,15 à 0,23) comparativement au RTI de 0,13 (0,10 à 0,17). - L'intervalle médian entre la date historique du résultat positif au test PCR ou la date de l'infection primaire et la date du résultat positif au test PCR pour la réinfection était de 201 jours (entre 95 et 297) ou de 241 jours (entre 90 et 345), respectivement.
Lumley (2021) (45) *Prépublication* *nouvelle* Cohorte prospective Royaume-Uni Septembre 2020 à février 2021	Des travailleurs de la santé ont été suivis afin d'étudier et de comparer la protection contre l'infection par le SRAS-CoV-2 que conférait la vaccination (résultats présentés dans le tableau 2) et l'infection antérieure (déterminée à l'aide de la teneur en anticorps anti-spicule). Le suivi a débuté de plus de 60 jours après le premier test positif de détection des anticorps obtenu soit avec un test PCR positif ou après la réception du premier vaccin. Pour évaluer	Écouvillonnage de sécrétions nasales et oropharyngées - Comparativement à 1 travailleur de la santé séropositif (0,08 %) sur 1 273, 294 travailleurs de la santé séronégatifs sur 10 513 (2,7 %) ont eu une infection symptomatique pendant la période de suivi. L'incidence était donc 98 % inférieure chez les travailleurs de la santé séropositifs (RTI ajusté : 0,02 (IC à 95 % : < 0,01 à 0,18; p < 0,001). - Les taux de résultats positifs au test PCR, sans égard aux symptômes, étaient les plus élevés chez les travailleurs de la santé séronégatifs non vaccinés (635 cas), avec une incidence inférieure de 85 % chez les travailleurs de la santé séropositifs non vaccinés (12 cas, RTIa = 0,15 (IC à 95 % : 0,08 à 0,26, p < 0,001). - Rien n'indique que la SGTF ait modifié l'étendue de la protection contre une infection ayant donné un résultat positif au test PCR chez les travailleurs de la santé séropositifs (RTIa c. non-SGTF, 0,43 (IC à 95 %, 0,12 à 1,52; p = 0,19). Rien n'indique non plus que le

	l'incidence du variant B.1.1.7 sur le risque d'infection ou de réinfection, les auteurs ont analysé les résultats positifs du test PCR avec et sans négativation de la détection du gène S (SGTF) alors que le séquençage du génome a été utilisé pour les résultats confirmés comme étant associés au variant B.1.1.7.	variant B.1.1.7 a modifié l'étendue de la protection détectée par tout résultat positif au test PCR chez les personnes séropositives (RTIa c. non-B.1.1.7 = 0,40 (IC à 95 %, 0,10 à 1,64; p = 0,20). - Les travailleurs de la santé séronégatifs avaient la charge virale la plus élevée (valeur Ct médiane : 18,3) alors que les travailleurs séropositifs non vaccinés avaient la charge virale la plus faible (valeur Ct médiane : 27,2).
Lumley (2020) (21) Étude de cohorte prospective Royaume-Uni Avril à novembre 2020	Suivi du personnel asymptomatique et symptomatique (n = 12 541) dans les hôpitaux de l'Université d'Oxford pendant un maximum de 31 semaines pour estimer l'incidence relative des résultats positifs au test PCR et des nouvelles infections symptomatiques à l'aide de l'état des anticorps.	Écouvillonnage de sécrétions nasales et oropharyngées – Les travailleurs de la santé qui ont obtenu des résultats positifs lors des épreuves biologiques effectuées sur les anticorps IgG anti spicule pour le SRAS-CoV-2 ont obtenu moins de résultats positifs au test PCR effectué lors du suivi que ceux dont les résultats de départ étaient négatifs (0,13 par rapport à 1,09 par 10 000 jours-risque). – L'incidence des résultats positifs aux tests PCR a été inversement associée aux titres d'anticorps anti spicule, ce qui suggère que l'infection antérieure qui a entraîné la création d'anticorps au SRAS-CoV-2 est associée à une protection contre la réinfection durant au moins six mois. -Des trois travailleurs de la santé séropositifs qui ont ensuite obtenu des résultats positifs au test PCR pour l'infection par le SRAS-CoV-2, un seul avait déjà obtenu un résultat positif pour le SRAS-CoV-2 190 jours auparavant. Asymptomatique lors d'une possible réinfection, ce cas a obtenu des résultats négatifs aux tests RT-PCR effectués deux et quatre jours plus tard et aucune augmentation subséquente n'a été remarquée lors du titrage des anticorps. - – Les résultats indiquant une réinfection peuvent être compatibles avec une réexposition au SRAS-CoV-2 n'ayant pas entraîné de symptômes, mais ils peuvent être des faux positifs. Il faut donc faire

		preuve de prudence au moment d'interpréter les résultats de cette étude.
Clarke (2021) (37) Étude de cohorte prospective Royaume-Uni Février 2020 à janvier 2021	Patients recevant de l'hémodialyse dans un centre (n = 356) qui ont été soumis à une sélection longitudinale pour la séropositivité au SRAS-CoV-2 (anticorps anti-NP ou anti-RBD) et un résultat positif au test RT-PCR. Les résultats positifs au test PCR obtenus plus de 60 jours après un test sérologique initial ont été enregistrés pour éviter de détecter une infection virale persistante plutôt qu'une réinfection.	Sécrétions rhinopharyngées prélevées par écouvillonnage – Les patients qui avaient obtenu des résultats séropositifs initiaux étaient beaucoup moins susceptibles d'obtenir un résultat positif au test PCR effectué au moment du suivi que ceux qui avaient obtenu au départ un résultat sérologique, soit 3,4 % (5 sur 129) comparativement à 13,2 % (30 sur 227), p < 0,005. - – Les réactions immunitaires à l'infection naturelle par le SRAS-CoV-2 chez les patients atteints d'hémodialyse ont duré jusqu'à six mois, même chez ceux qui ont eu une forme bénigne ou asymptomatique de l'infection.
Krutikov (2021) (26) *Prépublication* *nouvelle* Cohorte prospective Royaume-Uni Juin 2020 à février 2021	Les résidents (n = 682) et les membres du personnel (n =1 429) de 100 établissements de soins de longue durée ont subi chaque semaine et chaque mois des tests RT-PCR afin de détecter le SRAS-CoV-2. Toute personne qui obtenait un résultat positif n'a pas eu à repasser le test dans les 90 jours suivants. L'on a demandé aux participants s'ils acceptaient qu'on prélève trois échantillons	Sécrétions rhinopharyngées prélevées par écouvillonnage - Des anticorps de référence ont été détectés chez 226 résidents (33 %) et 408 membres du personnel (29 %). - Chez les résidents, un total de 93 personnes négatives aux anticorps ont obtenu un résultat positif au test PCR de suivi (0,054 par mois à risque) comparativement à 4 personnes positives aux anticorps (0,007 par mois à risque). - Au sein du personnel, un total de 111 personnes négatives aux anticorps ont obtenu un résultat positif au test PCR de suivi (0,042 par mois à risque) comparativement à 10 personnes positives aux anticorps (0,009 par mois à risque). - Dans l'analyse de régression de Cox, les rapports de risque ajustés relatifs pour un test PCR positif à

	de sang à trois temps de mesure à des intervalles de six à huit semaines en juin (prélèvement de référence), en août et en octobre 2020 afin d'obtenir les titres d'anticorps. Tous les résultats positifs aux tests PCR effectués après octobre 2020 ont été jugés indiquer une infection ou une réinfection.	l'infection étaient de 0,15 (0,05 à 0,44) pour les résidents séropositifs par rapport aux résidents séronégatifs et de 0,39 (0,19 à 0,82) pour le personnel séropositif par rapport au personnel séronégatif. - La majorité des réinfections étaient symptomatiques (11 sur 14), mais personne n'a été admis à l'hôpital ou n'est décédé à cause de l'infection. - La valeur Ct médiane des cas de réinfection était de 36 (plage de 30,1 à 37,0).
Dimeglio (2021) (23) *Lettre à la rédaction* Étude de cohorte prospective France Juin à décembre 2020	Après la première vague de l'épidémie (juin/juillet), les travailleurs de la santé (n = 8 758) ont fait l'objet de titres pour les anticorps neutralisants et les anticorps anti spicule du SRAS-CoV-2. Cette sérologie a ensuite été étudiée et de nouvelles infections ont été déterminées lors du suivi en novembre/décembre.	Type d'écouvillon non indiqué – Le suivi médian était de 167 jours (EI : 156 à 172). – Lors du suivi, 1,8 % (5 participants sur 276) du groupe séropositif a été déclaré positif comparativement à 12,1 % (1 028 sur 8 482) du groupe séronégatif ($p < 0,01$). – Parmi les cinq personnes séropositives initialement, puis infectées pendant la période de suivi, les titres d'anticorps neutralisants étaient faibles ou indétectables après la première infection pour deux d'entre elles alors que les titres des trois autres étaient supérieurs à la médiane. - Les données indiquent que l'infection précédente a fourni une immunité protectrice pendant au moins 167 jours.
Barbaro (2021) (33) *Prépublication* *nouvelle* Cohorte prospective Italie Avril à octobre 2020	Les travailleurs de la santé (n = 344) ont subi des tests de détection de l'ARN du SARS-CoV-2 combinés à la détection des anticorps IgM et IgG, une fois par semaine pendant quatre semaines consécutives.	Sécrétions rhinopharyngées prélevées par écouvillonnage - Un total de 14 travailleurs sur 344 (4,07 %) ont eu des résultats positifs pour le SRAS-CoV-2 avec le test RT-PCR. Le résultat du test de détection des anticorps IgG ou IgM était positif chez 12 des 14 (85,7 %) et négatif chez 15 des 330 (4,55 %) sujets positifs pour le SRAS-CoV-2.

	Les participants qui ont obtenu des résultats positifs à la sérologie du SRAS-CoV-2 ont fait l'objet d'un suivi pendant cinq mois avec tests RT-PCR et sérologies.	- 25 sujets ont été suivis pendant cinq mois, mais aucune réinfection n'a été détectée.
Dehgani-Mobaraki (2021) (31) *Prépublication* Cohorte prospective Italie Mars à novembre 2020	Les personnes qui ont reçu un résultat positif au test RT-PCR pour le SRAS-CoV-2 pendant le mois de mars 2020 (n = 30) ont fait l'objet d'un suivi pendant 10 mois afin d'obtenir des preuves de la présence et de la persistance des anticorps spécifiques au SRAS-CoV-2.	Écouvillons respiratoires - Aucun cas de réinfection n'a été signalé dans cette cohorte. - Remarque : cette étude ne décrit pas la méthode utilisée pour détecter les réinfections potentielles (aucune description des tests RT-PCR effectués lors du suivi).
Dobaño (2021) (43) *Preprint* Prospective cohort Spain Mar-Nov 2020	Évalue la séroprévalence et les niveaux d'anticorps de 149 à 270 jours après l'apparition des symptômes dans une cohorte de 173 agents de soins de santé primaires atteints d'une infection confirmée (par test RT-PCR) pendant le premier pic de la pandémie (mars et avril 2020). Trois points temporels de prélèvement de sang veineux entre septembre et novembre 2020 ont été utilisés pour évaluer	Écouvillons respiratoires - Lors du suivi, le pourcentage obtenu de séropositivité combinant les antigènes RBD et S était de 60,69 % pour l'IgM, de 76,30 % pour l'IgA et de 90,17 % pour l'IgG. - Il y a eu 2,3 % de réinfections (4 travailleurs sur 173). Deux cas symptomatiques étaient séronégatifs avant la réinfection alors qu'un cas asymptomatique était séropositif et que l'état sérologique d'un autre était inconnu. Les réinfections se sont produites entre trois et huit mois après l'infection initiale. - Le fait d'avoir été admis à l'hôpital, de faire de la fièvre, de l'anosmie ou de l'hypogueusie et avoir eu des allergies antérieures a été associé à des niveaux plus élevés d'anticorps pendant le suivi (cinq à neuf mois plus tard). - Une corrélation a été effectuée entre des IG plus élevés et l'âge avancé, la durée des symptômes et le nombre de symptômes.

	l'immunité et la réinfection possible chez ces travailleurs de la santé dans le cadre d'une étude de cohorte ayant duré un an et demi.	
Garcia-Abellan (2021) (32) *Prépublication* *nouvelle* Cohorte prospective Mars à décembre 2020 Espagne	Des échantillons de sang et des échantillons provenant d'écouvillons nasopharyngiens ont été utilisés pour mesurer l'ARN du SRAS-CoV-2 et les anticorps IgG contre la protéine S et contre la protéine N pendant le séjour à l'hôpital, puis 1, 2 et 6 mois après le congé. Le séquençage du génome du SRAS-CoV-2 a aussi été effectué. La réinfection présumée du SRAS-CoV-2 a été définie en fonction des critères établis par le CDC. Des preuves plus solides de réinfection exigeraient des preuves génomiques provenant de deux lignées distinctes.	Sécrétions rhinopharyngées prélevées par écouvillonnage - Parmi 146 patients inclus dans l'analyse, 11,8 % (valeur Ct médiane = 38) et 3 % (valeur Ct médiane = 36) ont obtenu un résultat positif au test RT-PCR pour le SRAS-CoV-2 après 2 mois et 6 mois, respectivement, mais aucune réinfection n'a été démontrée.
Shinde (2021) (39) *nouvelle* Essai clinique randomisé	Essai de phase 2b du NVX-CoV2373, un vaccin à nanoparticules. Au total, 4 877 participants randomisés ont pris part à l'étude et ont reçu au moins une fois une dose du vaccin. De ce	Écouvillonnage du nez - Parmi les cas associés aux critères d'évaluation principale pour lesquels le séquençage du génome entier était disponible, le variant B.1.351 a été trouvé dans 38 (92,7 %) cas sur 41. - En ce qui concerne les participants qui ont reçu le placebo, l'incidence de COVID-19 symptomatique

Afrique du Sud Août à novembre 2020	nombre, 2 199 ont reçu le vaccin NVX-CoV2373 et 2 188, un placebo. La sérologie au niveau de référence a été déterminée et des tests RT-PCR de suivi ont également été effectués. Le séquençage du génome du virus entier a été effectué sur des échantillons provenant du nez des participants.	était semblable pendant les deux premiers mois du suivi chez les participants séronégatifs et séropositifs de référence avec des taux de 5,3 % (IC à 95 %, 4,3 à 6,6) et de 5,2 % (IC à 95 %, 3,6 à 7,2) respectivement, ce qui indique que l'infection antérieure ne protégeait pas contre la réinfection par le variant B.1.351.
Graham (2021) (29) *Prépublication* Étude de surveillance longitudinale Royaume-Uni Mars à décembre 2020	Les données longitudinales sur la population en général recueillies prospectivement grâce à l'application COVID Symptom Study ont été combinées à des données de surveillance provenant du Covid-19 UK Genetics Consortium pour étudier le taux de réinfection et d'autres caractéristiques de la COVID-19. La réinfection a été définie comme deux résultats positifs aux tests RT-PCR effectués à plus de 90 jours d'intervalle avec une période asymptomatique de plus de sept jours entre les tests PCR. L'évaluation du risque de réinfection pour le nouveau variant B.1.1.7 a été obtenue en	Type d'écouvillon non indiqué – 304 personnes ont obtenu deux résultats positifs aux tests effectués à un intervalle supérieur à 90 jours, dont 249 ont eu une période sans symptôme entre les deux tests, pour un taux de réinfection estimé à 0,7 % (IC à 95 % : 0,6 à 0,8) (249 personnes sur 36 509). – Le taux de réinfection n'a pas varié selon les régions ou avec le temps. La réinfection était corrélée de façon plus positive avec l'augmentation régionale globale des cas plutôt qu'avec l'augmentation régionale du pourcentage du variant B.1.1.7, ce qui indique que l'immunité cumulée après l'infection initiale pourrait aussi offrir une protection contre le variant B.1.1.7.

	calculant les corrélations entre le nombre de réinfections possibles et la proportion de nouveaux cas de variants au fil du temps.	
Hansen (2021) (68) *nouvelle* Étude de surveillance et cohorte rétrospective Danemark Février à décembre 2020	Analyse des données tirées de la base de données danoise sur la microbiologie (MiBa) pour toutes les personnes ayant subi un test PCR pour le SRAS-CoV-2. Les taux d'infection pendant la deuxième vague ont été comparés chez les personnes ayant obtenu un résultat positif ou négatif au test pendant la première vague. L'analyse principale a exclu les personnes qui avaient obtenu un premier résultat positif entre les deux flambées et celles qui sont décédées avant la deuxième. Une analyse alternative dans le cadre de laquelle chaque personne ayant obtenu un résultat au test PCR a fait l'objet d'un suivi de la date de son premier test jusqu'au 31 décembre 2020, ou 90 jours après tout	Prélèvements de gorge - Pendant la première vague, 533 381 personnes ont été testées, dont 11 727 (2,2 %) ont obtenu un résultat positif au test PCR. Pendant la deuxième, 3,48 millions de personnes ont été testées, dont 150 159 (4,32 %) ont obtenu un résultat positif. - Le taux quotidien d'infection pendant la deuxième vague chez les personnes qui avaient déjà obtenu un résultat positif au test était de 5,35 par 100 000. - Le taux quotidien d'infection au cours de la deuxième vague chez les personnes n'ayant pas obtenu de résultat positif au test était de 27,06 par 100 000. - Le ratio de risque d'infection ajusté était de 0,195 (IC à 95 %, 0,155 à 0,246) chez celles qui avaient déjà obtenu un résultat positif comparativement à celles qui n'en avaient pas obtenu. - La protection contre la réinfection a été estimée à 80,5 % (IC à 95 %, 75,4 à 84,5). - L'analyse de l'autre cohorte a donné des estimations semblables, soit RR ajusté de 0,212 (0,179 à 0,251), protection estimée à 78,8 % (74,9 à 82,1). - La protection était plus faible chez les 65 ans et plus, avec un niveau observé de 47,1 % (IC à 95 %, 24,7 à 62,8). - On a également pu voir une différence de protection selon le sexe. - Le suivi a permis de voir que la protection n'avait cependant pas diminué avec le temps puisqu'elle atteignait 69,3 % (74,4-83,3) de 3 à 6 mois après le début du suivi contre 77,7 % (70,9-82,9) à 7 mois.

	résultat positif à un nouveau test.	
Leidi (2021) (38) *Prépublication* *nouvelle* Cohorte rétrospective appariée Suisse Avril 2020 à janvier 2021	Entre avril et juin 2020, un échantillon aléatoire formé de personnes représentatives (n = 8 344) ont pris part à un essai sérologique pour le SARS-CoV-2. Les participants ont été répartis en deux groupes, selon leur taux d'anticorps de référence. Les participants séropositifs ont été jumelés à deux cas-témoins de contrôle séronégatifs. Tous les participants séropositifs lors du test de dépistage du SRAS-CoV-2 effectué pendant le suivi ont fait l'objet d'une exploration clinique axée sur la réinfection. La probabilité de réinfection était fondée sur le jugement clinique, la symptomatologie et l'évolution de la valeur ou du temps en fonction du seuil établi pour le cycle de tests RT-PCR.	Écouvillonnage oropharyngé ou nasopharyngien - Des 8 344 personnes incluses dans la sérologie effectuée entre avril et juin 2020, 498 avaient des anticorps IgG anti-sous-unité S1 de la protéine S pour le SARS-CoV-2 et on avait suffisamment de données à leur égard pour les inclure dans l'étude. - Ces cas ont été appariés à 996 cas-témoins séronégatifs. - Parmi toutes les personnes séropositives incluses dans l'étude, cinq cas étaient probablement des réinfections (1 %, 5 sur 498), ce qui correspond à une incidence de 0,3 (IC à 95 %, 0,1 à 0,7) par 1 000 semaines-personnes. - Le taux d'infections confirmées par le SRAS-CoV-2 était beaucoup plus élevé chez les personnes séronégatives (15,5 %, 154 sur 996), ce qui correspond à un taux d'incidence de 4,8 (IC à 95 %, 4,6 à 6,2) par 1 000 semaines-personnes (p < 0,001). - Les sujets séropositifs étaient 94 % moins susceptibles d'avoir une infection par le SRAS-CoV-2 ayant été confirmée par virologie comparativement aux sujets n'ayant pas d'anticorps contre le SARS-CoV-2 détectables au départ (rapport de danger = 0,06, IC à 95 %, 0,02 à 0,14, p < 0,001).
Breathnach (2021) (25) *Lettre à la rédaction* Étude de cohorte rétrospective	On a analysé des données de laboratoire afin de comparer le risque d'obtenir un résultat positif au test PCR pour le SRAS-CoV-2	Type d'écouvillon non indiqué – Seuls huit patients ayant des preuves d'un COVID-19 antérieur ont obtenu un résultat positif au test PCR pendant la deuxième vague (0,07 %, 8 sur 10 727). La positivité au test PCR était plus élevée pendant la deuxième vague chez les patients qui n'avaient eu

Royaume-Uni Février à décembre 2020	pendant la deuxième vague de la pandémie chez des patients qui avaient eu des preuves de COVID-19 (positivité ou séropositivité au test PCR) pendant la première vague (n = 10 727) comparativement à d'autres qui avaient déjà obtenu un résultat négatif au test PCR ou un résultat négatif au test de détection des anticorps (n = 55 274). Les cas dans lesquels le deuxième résultat positif s'est produit 90 jours ou moins après la première vague ont été exclus.	aucune preuve de COVID-19 durant la première vague (1,29 %, 713 sur 55 274). - – Cela sous-entend un effet protecteur et un risque relatif de 0,06 (IC à 95 % : 0,03 à 0,12) pour les personnes ayant présenté des preuves d'infection durant la première vague.
Hanrath (2020) (36) *Lettre à la rédaction* Étude de cohorte rétrospective Royaume-Uni De mars à novembre 2020	Analyse des données d'analyse pour les travailleurs de la santé pendant la première vague (du 10 mars au 6 juillet 2020) et après la deuxième vague (du 7 juillet au 20 novembre 2020) de la pandémie afin de déterminer si l'infection au SRAS-CoV-2 antérieure pouvait être associée à une protection. Le principal indicateur de résultat de l'analyse était une infection symptomatique	Écouvillonnage de sécrétions rhinopharyngées et oropharyngées -1 038 travailleurs de la santé présentant des signes d'infection antérieure (résultat positif au test PCR ou Ab) et 10 137 sans aucun signe (Ab négatif, sans résultat positif au test PCR) ont été sélectionnés pendant la première vague. – Au cours de la deuxième vague, 2 433 travailleurs de la santé ont subi des tests PCR afin de déceler des symptômes. 128 d'entre eux avaient déjà été infectés alors que 2 115 ne l'avaient pas été. – Aucune réinfection n'a été décelée chez les personnes qui avaient déjà été infectées (positivité de 0 % au test) au cours de la deuxième vague, médiane de 173 jours de suivi (EI : 162 à 229) tandis que le niveau de tests positifs chez les personnes qui n'avaient pas été infectées auparavant était de 13,7 % (290 sur 2 115, IC à 95 % : 12,3 à 15,2). – Si l'on tient compte de l'ensemble de la population, la positivité au test était de 0 sur 1 038 (0 % [IC à 95 % : 0 à

	au SRAS-CoV-2 confirmée par un test RT-PCR pendant la deuxième vague. Le dépistage asymptomatique par PCR a également été effectué dans le cadre d'un projet pilote.	0,4) pour celles qui ont eu la COVID-19 comparativement à 290 sur 10 137 (2,9 % [IC à 95 % : 2,6 à 3,2) pour celles qui ne l'ont pas eu (P < 0,0001)). - – Des résultats semblables ont été observés dans le test pilote chez les asymptomatiques puisqu'il n'y a eu aucun résultat positif dans le groupe ayant déjà eu une infection (0 sur 106) (0 %, IC à 95 % : 0 à 3,5), comparativement à 22 sur 375 (5,9 %, IC à 95 % : 3,9 à 8,7, P = 0,011) ayant obtenu des résultats positifs dans le groupe de personnes n'ayant pas eu le virus.
Sheehan (2021) (27) *nouvelle* Cohorte rétrospective. États-Unis Mars 2020 à février 2021	Les patients qui ont passé un test PCR de détection de la COVID-19 ont été inclus. La réinfection a été définie comme se produisant 90 jours après l'infection initiale.	Type d'écouvillon non précisé - 612 611 tests ont été effectués auprès de 386 336 personnes, dont 9,9 % ont donné un résultat positif. - Après au moins 90 jours, 1 278 (14,4 %) des patients positifs ont passé un nouveau test et 62 réinfections ont alors été notées. - Sur ces 62 réinfections, 31 étaient symptomatiques (50 %). - L'intervalle de réinfection moyen était de 138,9 ± 46,3 jours (plage : 90,2 à 294,9 jours). - Parmi les personnes ayant obtenu des résultats négatifs aux tests initiaux, 27,9 % (39 487 sur 141 480) ont passé un nouveau test et 5 449 d'entre elles (13,8 %) ont obtenu un résultat positif. - La protection contre la réinfection associée à l'infection antérieure était de 81,8 % (IC à 95 % 76,6, 85,8). - La protection globale contre l'infection symptomatique était de 84,5 % (IC à 95 % 77,9, 89,1) alors qu'elle était supérieure à 90 % entre 6 et 8 mois après l'infection. - Le risque de réinfection a été le plus élevé juste après 90 jours (ce qui peut représenter une excrétion virale prolongée), puis a diminué (voir la figure 3 dans les articles).
Harvey (2020) (24)	Analyse d'un échantillon national obtenu à partir	Type d'écouvillon non précisé

Étude de cohorte rétrospective États-Unis Janvier à août 2020	d'un ensemble de données dépersonnalisé fondé sur des analyses de laboratoire commerciales, des réclamations et des dossiers médicaux (n = 3 257 478). Au départ, les patients ont été déterminés comme étant positifs aux anticorps du SRAS-CoV-2, soit négatifs aux anticorps. Ils ont ensuite été évalués à des intervalles de 30 jours (jusqu'à plus de 90 jours) pour déterminer la positivité du test d'amplification des acides nucléiques (TAAN).	– On a suivi des patients séronégatifs (n = 2 876 773) pendant une période médiane de 47 jours (EI : 8 à 88) alors que les patients séropositifs (n = 378 606) ont été suivis pendant une période médiane de 54 jours (EI : 17 à 92). - 18,4 % des patients sont passés d'un état initialement séropositif à séronégatif pendant le suivi de 90 jours ou plus après le premier test de détection des anticorps. – Les patients séropositifs qui ont subi un test TAAN pendant le suivi (n = 41 587) présentaient un risque réduit d'avoir le SRAS-CoV-2. Résultats positifs pour le TAAN : 2,7 % de 31 à 60 jours, 1,1 % de 61 à 90 jours et 0,3 % pour plus de 90 jours. En revanche, environ 3 % des personnes séronégatives ont obtenu un résultat positif au test TAAN effectué pendant chacune des périodes de suivi. - – Cela correspond à un ratio de résultats positifs au TAAN pour les patients qui ont obtenu un résultat positif au test d'anticorps à l'indice comparativement à ceux qui ont obtenu un résultat négatif au test d'anticorps à l'indice, soit 0,67 (IC à 95 % : 0,6 à 0,74) entre 31 et 60 jours; 0,29 (IC à 95 % : 0,24 à 0,35) entre 60 et 90 jours et 0,10 (IC à 95 % : 0,05 à 0,19) après plus de 90 jours.
Pilz (2021) (28) *nouvelle* Cohorte rétrospective. Autriche Février à novembre 2020	Comparaison des probabilités de réinfection par le SRAS CoV 2 de 19 survivants qui ont eu la COVID pendant la première vague (de février au 30 avril 2020) par rapport aux probabilités d'infection du reste de la population générale à l'aide du suivi des infections confirmées par PCR dans les deux groupes pendant la deuxième vague (du	Type d'écouvillon non précisé - 40 réinfections possibles ont été découvertes dans le groupe des survivants (0,27 %) par rapport à 253 581 nouvelles infections dans la population en général (2,85 %), ce qui correspond à un rapport des cotes de 0,09 (IC à 95 %, 0,07 à 0,13) pour les infections dans le groupe des survivants par rapport à la population en général. - - L'intervalle moyen entre la première infection et la réapparition provisoire était de 212 jours (écart-type ± 25 jours). - 8 patients ont été hospitalisés lors de la première infection et 5 lors de la réinfection.

	1er septembre au 30 novembre 2020).	
Salehi (2021) (40) *Prépublication* *nouvelle* Cohorte rétrospective. Iran Mars 2021*	On a évalué les résultats des tests RT-PCR utilisés pour détecter le SRAS-CoV-2 pendant les six premiers mois de la pandémie. Les patients qui avaient obtenu deux résultats positifs à trois mois d'intervalle, avec un résultat négatif au test PCR entre les deux tests, ont été inclus.	Type d'écouvillon non précisé - Au total, 32 567 tests ont été effectués. 37 cas ont été inclus dans l'étude. - Il n'y avait aucune différence statistiquement significative dans la gravité des symptômes, l'hospitalisation ou les caractéristiques de laboratoire entre les deux épisodes (p > 0,05). - L'intervalle moyen qui s'est écoulé entre les deux épisodes était de 117 ± 61,42 jours.
Sadr (2021) (69) *Prépublication* *nouvelle* Cohorte rétrospective. Iran Mai à septembre 2020	Des tests RT-PCR et des évaluations des symptômes ont été effectués pendant une période de suivi de 6 mois chez des patients ayant obtenu un résultat positif de COVID-19 confirmé par test PCR. Le diagnostic de réinfection était basé sur les résultats des tests RT-PCR, les symptômes types et le long laps de temps (supérieur à 90 jours) entre les deux résultats positifs au test RT-PCR.	Sécrétions rhinopharyngées prélevées par écouvillonnage - Une réinfection associée à des symptômes légers a été détectée chez 3 des 82 patients (3,7 %). - Tous les patients se sont rétablis sans complication et aucun n'a nécessité de réadmission ou d'autre traitement médical. - Les problèmes médicaux sous-jacents, les antécédents récents d'utilisation de médicaments immunosuppresseurs, la gravité de la maladie, la durée de l'admission et le besoin d'être admis aux soins intensifs pendant le premier épisode de l'infection n'étaient pas significativement différents entre les patients qui avaient un résultat positif au test RT-PCR lors du suivi et ceux qui n'en avaient pas eu (p > 0,05).
Ali (2020) (34) *Prépublication* Cohorte rétrospective	Étudie l'impact du niveau d'immunoglobuline (IgG) sur la réinfection chez les sujets rétablis	Écouvillons pharyngés – Sur les 87 patients qui se sont révélés négatifs à l'IgG après leur rétablissement initial, 25 (28,7 %) ont été jugés avoir été réinfectés, ce qui a été confirmé par un résultat positif au test RT-PCR. Ce taux était plus élevé que dans le groupe de 742 patients dont le test de

Irak Mai à octobre 2020	Les niveaux d'IgG par rapport au SRAS-CoV-2 ont été mesurés juste après le rétablissement (un résultat négatif au test RT-PCR étant défini une valeur Ct > 36,7) chez des patients rétablis qui ont attrapé la COVID-19 (n = 829 patients admis entre mai et octobre dans un seul centre) et ont probablement été suivis pour en évaluer la réinfection.	dépistage de l'IgG était positif après le rétablissement initial (1 patient sur 742, soit 0,13 %). Cela suggère que les patients qui présentaient de faibles taux d'IgG après une infection initiale pourraient être plus sujets à une réinfection. – La réinfection dans le groupe s'est produite entre 26 et 138 jours après guérison de l'infection initiale. – 88,5 % des cas présentaient plus de symptômes lors de la réinfection que lors de l'infection initiale, mais la gravité globale des symptômes n'a pas été indiquée. – 95 % des cas étaient positifs pour l'IgG après la réinfection. - – Les résultats de cette étude sont préliminaires et les méthodes utilisées ont été mal décrites. L'on ne sait pas si les patients ont été inscrits et suivis prospectivement ou si l'état de réinfection est fondé sur leurs dossiers médicaux. Il faut donc faire preuve de prudence au moment d'interpréter les résultats de cette étude.
Perez (2021) (41) *Prépublication* *nouvelle* Cohorte rétrospective. Israël Mars 2020 à janvier 2021	Utilisation des données de la base de données informatisée centrale de Maccabi Healthcare Services pour sélectionner des patients ayant obtenu deux résultats positifs au test PCR à au moins 100 jours d'intervalle.	Type d'écouvillon non précisé - Au total, parmi les 149 735 personnes dont les données figuraient dans le MHS et qui avaient obtenu un résultat positif au test PCR, 154 avaient obtenu deux résultats positifs à au moins 100 jours d'intervalle et ont donc été incluses dans cette étude, ce qui représente une proportion de 0,1 % de réinfection. - Soixante-treize personnes (47,4 %) présentaient des symptômes au moment où les deux résultats positifs aux tests PCR ont été obtenus. - Le nombre de réinfections a atteint un sommet en janvier 2021. - 30 personnes ont alors été réinfectées plus de 200 jours après leur premier résultat positif au test PCR. - Le plus grand nombre de réinfections a eu lieu chez les personnes âgées de 10 à 19 ans (environ 46, 30 %), suivies des 20 à 29 ans (environ 30, 19 %) (voir la figure 1 dans l'article).

Mukherjee (2021) (42) *nouvelle* Cohorte rétrospective. Inde De janvier à octobre 2020	La base de données d'essais en laboratoire pour la COVID-19 disponible auprès du Indian Council of Medical Research (ICMR) a été utilisée pour déterminer les participants admissibles à l'étude. Les personnes ayant été réinfectées par le SRAS-CoV-2 ont été jointes par téléphone et ont répondu à des questions sur les symptômes ressentis pendant les différents épisodes. La réinfection a été définie comme toute personne ayant obtenu un résultat positif au test de dépistage du SRAS-CoV-2 à deux occasions distinctes, soit par des tests moléculaires ou un test d'antigène rapide, à un intervalle d'au moins 102 jours, avec un test moléculaire négatif entre les deux.	Type d'écouvillon non précisé - Des 9 533 637 personnes testées avant le 30 juin, 693 297 avaient obtenu un résultat positif (7,3 %). 1 300 (1,4 %) personnes ont subi un autre test moléculaire dans l'intervalle provisoire de 102 jours. Cinquante-huit des 1 300 tests (4,5 %) ont donné un résultat positif à deux reprises à un intervalle de 102 jours, ainsi qu'un résultat négatif provisoire. Trente-huit patients susceptibles d'avoir été réinfectés (38 sur 58, 65,5 %) ont pu être rejoints dans le cadre du sondage téléphonique. - La plupart des réinfections présumées sont apparues chez les hommes (29, 76,3 %) appartenant au groupe d'âge des 20 à 40 ans (30, 78,9 %). Douze d'entre eux (31,6 %) étaient des travailleurs de la santé. - L'intervalle médian (EI) entre les deux épisodes avec résultat positif au test de détection du SRAS-CoV-2 était de 119 jours (108,75 à 144,25) et variait entre 102 et 160 jours. - Pendant le deuxième épisode, on a vu un plus grand nombre de cas symptomatiques (32, 84,2 %) que lors du premier (20, 52,6 %). Des 18 participants asymptomatiques lors du premier épisode, 12 ont signalé des symptômes lors du deuxième épisode et la moitié d'entre eux a indiqué avoir eu des symptômes plus graves alors que l'autre moitié a plutôt déclaré des symptômes plus légers ou sans différence. La durée des symptômes ne différait pas entre les deux épisodes. - Parmi les 13 participants pour lesquels la valeur Ct appariée pour l'un ou l'autre des gènes de confirmation (RdRp/ORF) pour les deux épisodes était disponible, neuf (69 %) avaient une valeur inférieure lors du deuxième épisode.
Murillo-Zamora (2020) (30)	Le test RT-PCR a été réalisé sur des	Écouvillonnage du nez ou écouvillonnage nasal profond – On a déterminé 258 cas de « réinfection » confirmés en laboratoire (0,26 %).

Prépublication Cohorte rétrospective. Mexique Mars à juillet 2020	échantillons provenant de 100 432 patients. La réinfection a été définie comme la réapparition des symptômes de la COVID-19 plus de 28 jours après le premier test positif pour la COVID-19. Des données cliniques et épidémiologiques d'intérêt ont été récupérées des dossiers médicaux et des certificats de décès. Des modèles de régression linéaire ont été utilisés pour évaluer les facteurs associés au risque de réinfection symptomatique et à une forme grave du SRAS-CoV-2.	– L'intervalle entre le premier et le deuxième épisode était de 56 jours (EI : 40 à 81). Aucune différence significative n'a été observée entre les patients atteints d'une atteinte initiale grave ou non. – Lorsqu'on a comparé les réinfections graves ou non, les patients atteints d'une atteinte initiale plus grave étaient plus susceptibles d'avoir des symptômes graves (39,5 % c. 5,5 %, p < 0,001), tout comme ceux qui étaient âgés de 50 ans et plus (52,6 % c. 12,3 %, p < 0,001). – Dans de multiples analyses, les facteurs associés à une réinfection symptomatique plus grave étaient l'âge, les antécédents personnels d'obésité, l'asthme, le diabète sucré de type 2 et les maladies rénales chroniques. - Les sujets qui avaient déjà eu une forme grave de la COVID-19 présentaient un risque de 20 % supérieur d'avoir des symptômes graves lors d'une réinfection.
Xu (2020) (35) Étude de cohorte rétrospective Chine Janvier à avril 2020	Les patients qui ont eu la COVID-19 (n = 185) et qui avaient subi des tests de détection des anticorps ont été suivis toutes les deux semaines afin d'évaluer leurs réactions immunitaires (IgG et IgM) et la réinfection au fil du temps. La durée moyenne du suivi était de 45,7 jours.	Écouvillons pharyngés et anaux – Aucune réinfection ni aucun signe de transmission ne se sont produits chez les patients ayant eu leur congé. – Sur les 35 cas ayant obtenu des résultats positifs pour IgM, 12 ont été négatifs pendant le suivi. - – 154 patients (82,4 %) ont obtenu des résultats d'IgG positifs alors que 33 patients (17,6 %) ont obtenu des résultats négatifs 53 jours après le début de la maladie. Comparativement au groupe ayant eu des résultats négatifs pour l'IgG, les patients du groupe positif étaient plus âgés, avaient séjourné plus longtemps à l'hôpital, avaient pris une plus grande proportion d'antibiotiques, représentaient une proportion plus élevée de cas graves et

		présentaient un plus grand nombre d'anomalies lors du Ct.

RBD= protéine de liaison de récepteur

INFECTIONS SPORADIQUES

Bien que les vaccins contre la COVID-19 soient extrêmement efficaces pour prévenir les maladies graves, on s'attend à ce que certains cas sporadiques se produisent après la vaccination et à ce que le degré dans lequel la vaccination prévient l'infection soit encore à l'étude. Il est important de faire le suivi des infections sporadiques, en particulier celles qui causent des maladies graves, des hospitalisations et des décès, pour comprendre l'immunité protectrice que fournit la vaccination.

La présente étude a donc utilisé la définition de cas établie par les CDC pour les infections sporadiques (4) : Personne dont l'ARN ou l'antigène du SRAS-CoV-2 a été détecté dans un échantillon respiratoire prélevé 14 jours ou plus après la fin de la première série de vaccins contre la COVID-19. Les études qui ne comprenaient que des estimations des infections symptomatiques à la suite de la vaccination, plutôt que le nombre total global d'infections sporadiques (c.-à-d. asymptomatiques ou symptomatiques), ont donc été exclues.

- Deux essais cliniques randomisés sur l'efficacité du vaccin ont démontré que l'infection sporadique de type sauvage et celle associée au variant B.1.1.7 après deux doses de vaccin étaient faibles.
    - Oxford-AstraZeneca a démontré une efficacité de 61,7 % (IC à 95 % : 36,7 à 76,9) par rapport au variant B.1.1.7 et de 77,3 % (IC à 95 % : 65,4 à 85,0) pour les autres lignées (48).
    - Des estimations d'efficacité plus élevées pour Oxford-AstraZeneca ont également été signalées (90 %) (46).
- Cinq études d'observation de l'efficacité réelle des vaccins démontrent également que l'infection sporadique de type sauvage et celle associée au variant B.1.1.7 étaient plus faibles à court terme après deux doses de vaccin.
    - On a pu voir, chez les personnes qui ont reçu les vaccins Pfizer, Moderna ou Oxford-AstraZeneca, une réduction de plus de 90 % de l'incidence de l'infection par le SRAS-CoV-2, ce qui signifie que les infections sporadiques sont rares (45 à 47).
    - La protection était encore plus élevée pour les travailleurs de la santé vaccinés chez qui on avait détecté des preuves d'infection par le SRAS-CoV-2 avant la vaccination (efficacité de 96 % pendant une période de suivi de 39 222 jours-personnes) (45).
    - Comparativement à l'immunité naturelle après l'infection (réduction de 85 %) vue chez les travailleurs de la santé, la vaccination a permis de réduire de 90 % l'incidence de résultats positifs aux tests PCR plus de 14 jours après la deuxième dose de vaccin (2 cas, RTIa = 0,10 (IC à 95 % : 0,02 à 0,38; p < 0,001) (45).
    - Deux études ont fait état de niveaux élevés de protection (supérieurs à 90 %) contre l'infection tant chez les personnes plus jeunes que chez les personnes âgées ayant reçu le vaccin Pfizer (46, 70).

- Les données préliminaires indiquent que l'efficacité du vaccin est semblable tant pour les variants de type sauvage que pour le B.1.1.7 (45). Dans une étude sur les infections sporadiques associées aux variants en Israël, on n'a dénombré aucun cas d'infection causé par le variant B.1.351 14 jours après l'administration de la deuxième dose du vaccin Pfizer (71). Il faut faire preuve de prudence en ce qui concerne cette conclusion puisque le variant B.1.351 ne représentait que 1 % des variants en circulation lorsque cette étude a été effectuée et que seulement 8 des infections qui sont produites sur 79 avaient eu lieu dans le groupe de personnes vaccinées dans les 14 jours suivant l'administration de la deuxième dose du vaccin.

TABLEAU 2 : *NOUVELLES* Études évaluant les infections sporadiques ayant percé après la vaccination (N = 7)

ÉTUDE	MÉTHODOLOGIE	PRINCIPAUX RÉSULTATS
Essais (n = 2)		
Emary (2021) (48) Essai clinique randomisé Royaume-Uni Octobre 2020 à janvier 2021	Des volontaires (âgés de 18 ans et plus) qui se sont inscrits aux phases 2 et 3 des études sur l'efficacité du vaccin au Royaume-Uni ont reçu aléatoirement (1:1) le médicament ChAdOx1 nCoV-19 ou un vaccin conjugué contre le méningocoque de sérogroupe C (MenACWY) et fourni des écouvillons des voies respiratoires supérieures chaque semaine, échantillons qui ont également été examinés afin de voir si les volontaires développaient des symptômes de COVID-19. Des volontaires qui ont reçu deux doses standards (groupe	- Entre le 1er octobre 2020 et le 14 janvier 2021, 520 participants sur 8 534 ont contracté une infection par le SRAS-CoV-2, soit 173 personnes vaccinées et 347 cas-témoins. L'estimation de l'efficacité globale pour tous les cas (n = 520) était de 50,9 % (IC à 95 %, 41,0 à 59,0). - Il y a eu 75 cas associés au variant B.1.1.7, dont 21 dans le groupe des personnes vaccinées et 54 dans le groupe témoin, pour une efficacité du vaccin de 61,7 % (IC à 95 %, 36,7 à 76,9). - Il y a eu 144 cas associés à d'autres variants, dont 27 dans le groupe des personnes vaccinées et 117 dans le groupe témoin, pour une efficacité du vaccin de 77,3 % (IC à 95 %, 65,4 à 85,0). - Parmi les cas pour lesquels il n'y a pas eu de résultats de séquence (n = 301), l'infection par le SRAS-CoV-2 a été signalée chez 125 personnes vaccinées et 176 témoins.

	SD/SD) ou une faible dose suivie d'une dose standard (groupe LD/SD) ont également été inclus dans l'analyse. L'analyse d'efficacité incluait notamment la forme symptomatique de la COVID-19 qui a été détectée chez les participants séronégatifs dont l'écouvillon évalué par la technique d'amplification des acides nucléiques (TAAN) a donné un résultat positif plus de 14 jours après avoir reçu une deuxième dose de vaccin.	
Miron (2021) (72) Nouvelle analyse des essais cliniques randomisés Israël Juillet à décembre 2020	On a analysé l'efficacité à l'aide des données tirées de deux essais cliniques de phase 3 portant sur les vaccins à ARNm BNT162b2 et ARNm 1273. Les valeurs cumulatives de l'infection ont été extraites par jour après la vaccination. L'essai sur le BNT162b2 comprenait 21 720 participants (âgés de 16 à 91 ans) ayant reçu une deuxième dose le 21e jour, tandis que l'essai sur le vaccin ARNm 1273 comprenait	- Dans le cas du BNT162b2, l'incidence cumulative de COVID-19 a augmenté en moyenne de 0,01 % par semaine entre les jours 21 et 111 pour atteindre 0,29 %, comparativement aux témoins chez qui l'incidence a atteint 2,22 % le jour 111. L'efficacité du BNT162b2 les jours 7, 14 et 21 était de 12 %, de 80 % et de 94 % respectivement, avec une efficacité moyenne de 94 % jusqu'au jour 111. - Dans le cas du vaccin avec ARNm 1273, l'incidence cumulative de COVID-19 a augmenté en moyenne de 0,01 % par semaine entre les jours 21 et 111 pour atteindre 0,19 %, comparativement aux témoins chez qui l'incidence a atteint 2,84 % le jour 111. L'efficacité du vaccin avec ARNm 1273 les jours 7, 14 et 21 était de 33 %, de 62 % et de 90 % respectivement, avec une efficacité moyenne de 95 % jusqu'au jour 111.

	15 181 participants (âgés de 18 à 95 ans) ayant reçu une deuxième dose le 28e jour. Les participants ont été jumelés à des participants témoins ayant reçu le placebo. L'efficacité du vaccin a été évaluée chaque jour (jour 0 à 111), avec une moyenne mobile de 7 jours. L'efficacité a été comparée à celle du vaccin ChAdOx sans ARNm.	- L'efficacité du ChAdOx à dose unique a atteint 90 % au jour 80, alors qu'avec la double dose, elle a atteint 90 % au jour 110.
Études d'observation (n = 5)		
Lumley (2021) (45) *Prépublication* Étude de cohorte prospective Royaume-Uni Septembre 2020 à février 2021	Des travailleurs de la santé (n = 13 109) ont été suivis afin d'étudier et de comparer la protection contre l'infection par le SRAS-CoV-2 conférée par deux doses de vaccin (soit le vaccin Pfizer-BioNTech ou le vaccin Oxford-AstraZeneca) lorsque les symptômes apparaissaient au moins 14 jours après l'admission de la deuxième dose. La protection contre une infection antérieure a également été examinée (résultats dans le tableau 1). Le personnel est demeuré exposé au	- Au total, 940 travailleurs de la santé séronégatifs ont été suivis après l'administration d'une deuxième dose du vaccin Pfizer-BioNTech ou du vaccin Oxford-AstraZeneca (suivi de 39 222 jours-personnes). - La vaccination a réduit de 90 % l'incidence de toute réponse positive lors du test PCR effectué plus de 14 jours après l'administration de la deuxième dose du vaccin (2 cas, RTIa = 0,10 (IC à 95 % : 0,02 à 0,38; p < 0,001), comparativement à une réduction de 85 % obtenue grâce à l'immunité naturelle après l'infection. L'incidence était également inférieure de 96 % chez les travailleurs de la santé séropositifs ayant déjà été vaccinés (1 cas, RTIa = 0,04 (IC à 95 % : 0,01 à 0,27; p = 0,001). - L'effet des estimations des variants préoccupants n'a été calculé qu'après la première dose de vaccin. Rien n'indique cependant que la SGTF ou le variant B.1.1.7 a modifié l'étendue de la protection contre toute infection donnant un résultat positif lors du test PCR chez les travailleurs de la santé déjà

	risque d'infection jusqu'à la fin de l'étude, ou jusqu'à ce que le résultat du test PCR soit positif. Pour évaluer l'incidence du variant B.1.1.7 sur le risque d'infection ou de réinfection, les auteurs ont analysé les résultats positifs du test PCR avec et sans négativation de la détection du gène S (SGTF) alors que le séquençage du génome a été utilisé pour les résultats confirmés comme étant associés au variant B.1.1.7. La protection a été calculée comme 100*(1-RTI).	séronégatifs après l'administration d'une première dose de vaccin (p > 0,05).
Aran (2021) (46) *Prépublication* Analyse des données de surveillance Israël Décembre 2020 à février 2021	Les cas quotidiens de SRAS-CoV-2 positifs et le nombre d'hospitalisations en raison des formes graves ou critiques de la maladie ont été téléchargés de la base de données publique sur la COVID-19 du ministère israélien de la Santé. Le nombre de cas positifs chez les personnes ayant reçu le vaccin BNT162b2 est stratifié par âge, soit 60 ans et plus et moins de 60 ans selon le	- 2 918 008 personnes ont reçu leur deuxième dose du vaccin BNT162b2. Parmi toutes les personnes vaccinées, 52 014 ont obtenu un résultat positif au test de dépistage du SRAS-CoV-2. - À compter du jour 14 après l'administration de la deuxième dose, on a vu une réduction de 96 % du nombre de cas chez les personnes de 60 ans et plus alors que cette réduction a atteint 94 % chez les personnes de moins de 60 ans. - Même si on ne tient compte que des personnes pour qui il s'est écoulé plus de 20 jours après l'administration de la deuxième dose pour calculer le nombre prévu de cas, l'efficacité vaccinale pour les personnes de 60 ans et plus atteint toujours 91 % pour les cas positifs.

	nombre de jours qui s'est écoulé depuis la vaccination : entre le jour 0 et le jour 13 après l'administration de la première dose (groupe 1), entre le jour 14 et le jour 20 après l'administration de la première dose (groupe 2), entre le jour 0 et le jour 6 après l'administration de la deuxième dose (groupe 3), entre le jour 7 et le jour 13 après l'administration de la deuxième dose (groupe 4) et à compter du jour 14 (groupe 5). L'efficacité des vaccins a été analysée.	
Haas (2021) (70) Analyse des données de surveillance Israël Janvier à mars 2021	Les données de surveillance de la santé publique à l'échelle nationale ont été utilisées pour surveiller la couverture vaccinale et l'incidence de la COVID-19, ainsi que pour estimer l'efficacité du vaccin BNT162b2. La prévalence du variant B.1.1.7 du SARS-CoV-2 a été déterminée à l'aide de la négativation de la détection du gène S (SGTF) dans certains spécimens.	- Jusqu'au 6 mars 2021, 51,5 % (n = 3 335 261) des personnes âgées de 16 ans et plus en Israël ont reçu deux doses du vaccin BNT162b2. - Parmi toutes les infections par le SRAS-CoV-2 détectées chez les personnes âgées de plus de 15 ans, 102 012 (72,9 %) n'avaient pas été vaccinées et 4 543 (3,2 %) avaient reçu deux doses et l'infection était apparue plus de 7 jours après la deuxième dose. - Les estimations de l'efficacité du vaccin calculées plus de 7 jours après l'administration de la deuxième dose étaient les suivantes : 94,1 % (IC à 95 %, 93,4 à 94,7) contre l'infection par le SRAS-CoV-2, efficacité qui a ensuite augmenté jusqu'à atteindre 96,2 % (IC à 95 %, 95,9 à 96,5) plus de 14 jours après

		administration de la deuxième dose du vaccin BNT162b2. - Dans tous les groupes d'âge, à mesure que la couverture vaccinale augmentait, l'incidence du SRAS-CoV-2 diminuait considérablement chez les personnes vaccinées. Des baisses plus marquées et plus soutenues ont été observées dans les groupes de personnes plus âgées ayant une couverture vaccinale plus élevée.
Kustin (2021) (71) *Prépublication* Étude cas/témoin Israël Janvier 2020 à mars 2021	Examen de la répartition des variants du SRAS-CoV-2 parmi les infections détectées chez les personnes vaccinées et parmi les infections correspondantes chez les personnes non vaccinées. Les auteurs ont effectué l'analyse en utilisant les infections sporadiques qui sont définies comme les personnes qui ont obtenu un résultat positif lors d'un test PCR effectué au moins une semaine après avoir reçu la deuxième dose du vaccin (dénommée comme étant pleinement efficace ou PE). Ils indiquent également le nombre de cas d'infection détectée plus de 14 jours après l'administration de la deuxième dose. Ils ont effectué le séquençage PCR et du génome viral	- Le variant B.1.1.7 était la souche de virus prédominante en Israël pendant toute la période d'échantillonnage et avec le temps, il a pris de plus en plus de place. La souche B.1.351 représentait, quant à elle, moins de 1 % de l'échantillon total. - Il n'y avait aucune différence statistiquement significative dans les taux d'infection par le B.1.1.7 dans les cas « entièrement vaccinés » par rapport aux témoins non vaccinés (RC : 6:4, p = 0,38). - On trouvait cependant une proportion beaucoup plus élevée de B.1.351 dans les cas « entièrement vaccinés » par rapport aux témoins non vaccinés (RC : 8:1, p = 0,02). - 79 (49 %) des personnes « entièrement vaccinées » ont obtenu des résultats positifs les jours 7 à 13 qui ont suivi l'administration de la deuxième dose alors que 76 (51 %) en obtenaient encore, plus de 14 jours après la deuxième dose. - Sur les huit cas « entièrement vaccinés » chez qui on a détecté la souche de B.1.351, tous ont été infectés entre 7 et 13 jours après l'administration de la deuxième dose. Aucun cas associé à la souche B.1.351 n'a été vu 14 jours après réception de la deuxième dose.

	sur 149 paires de personnes « entièrement vaccinées » et sur 147 paires de personnes « partiellement vaccinées » (une seule dose)	
Thompson 2021 (47) Étude de cohorte prospective États-Unis Décembre 2020 à mars 2021	Des cohortes prospectives formées de membres du personnel œuvrant dans les soins de santé, de premiers intervenants et d'autres travailleurs essentiels et de première ligne dans huit emplacements aux États-Unis ont été incluses. Une surveillance active des symptômes associés à la COVID-19 a été effectuée par l'envoi chaque semaine de messages textes et de courriels, ainsi que par des déclarations directes reçues des participants et l'accès à leurs dossiers médicaux. Les participants ont effectué eux-mêmes chaque semaine un écouvillonnage avec cornet nasal moyen, et ce, qu'ils aient ou non des symptômes associés à la COVID-19, en plus d'effectuer un prélèvement nasal	- Au total, l'étude a analysé les échantillons provenant de 3 950 participants pour évaluer l'efficacité du vaccin. - Trois infections confirmées par PCR se sont produites pendant les 78 902 jours-personnes avec vaccination complète (14 jours après l'administration de la deuxième dose; taux d'incidence = 0,04 par 1 000 jours-personnes). - La vaccination complète avec deux doses de vaccins ARNm a permis d'obtenir une protection efficace à 90 % (IC à 95 % = 68 % à 97 %) contre l'infection par le SRAS-CoV-2 confirmée par test RT-PCR.

	supplémentaire et de fournir un échantillon de salive dès l'apparition des symptômes associés à la COVID-19. L'efficacité du vaccin a été analysée chez des participants ayant reçu une immunisation complète avec deux doses des vaccins avec ARNm (BNT162b2 de Pfizer-BioNTech et ARNm 1273 de Moderna) contre la COVID-19.	

MARQUEURS DE RÉPONSE IMMUNITAIRE À LONG TERME (PLUS DE SIX MOIS)

Cette section résume trente-six études qui font état des réponses immunitaires mesurées longitudinalement pendant six mois ou plus (jusqu'à neuf mois) après l'infection par le SRAS-CoV-2. Les études incluses se limitaient à celles qui ont déclaré plus de 30 observations obtenues plus de 6 mois après l'infection par le SRAS-CoV-2. Vingt-cinq études ont examiné les niveaux d'anticorps sériques circulants ou la séropositivité après l'infection, trois études ont porté exclusivement sur les marqueurs ou les niveaux d'activité des lymphocytes T, alors que huit études ont fait état de multiples marqueurs immunitaires pour les cellulaires et les anticorps (c.-à-d. lymphocytes B, lymphocytes T ou anticorps) dans le même échantillon. La majorité des études incluses étaient des cohortes prospectives ou des séries de cas qui suivaient la sérologie des cas dans lesquels des tests RT-PCR ont confirmé la COVID-19 au fil du temps.

Dans l'ensemble, on a vu beaucoup de variabilité entre les études en raison des différences entre les participants à l'étude, de la gravité de l'infection par la COVID-19, de la fréquence et de la durée du suivi, des résultats immunitaires étudiés et des méthodes de mesure, ce qui limite la synthèse des résultats entre les études. En outre, le lien entre les marqueurs immunitaires à long terme mesurés et la protection contre la réinfection face aux variants préoccupants et à la souche sauvage est en grande partie inconnu.

Principaux résultats pour les réponses immunitaires des lymphocytes B et T obtenues six mois après l'infection (n = 11) :

- les lymphocytes B mémoires (soit les cellules immunitaires qui produisent les virus qui ciblent les anticorps) et les lymphocytes T mémoires (c.-à-d. les cellules immunitaires qui guident les réponses immunitaires adaptatives des cellules) après une infection naturelle confèrent probablement une certaine immunité à long terme à toute réinfection (1, 63, 73). Les cibles, l'activité et le nombre des antigènes viraux de ces cellules mémoires ont été le plus souvent mesurés au moyen de techniques d'analyse des cellules de cytométrie de flux et de diverses épreuves biologiques. La variabilité des techniques de biologie moléculaire et les marqueurs d'antigènes viraux utilisés dans les études limitent cependant la comparabilité des résultats.
- Les lymphocytes B sont les cellules immunitaires responsables de la production d'anticorps ciblant les antigènes du SRAS-CoV-2 (1, 63, 73). Elles peuvent être réparties globalement en cellules sécrétrices d'anticorps (cellules plasmatiques) et en cellules mémoires (73). Les cellules plasmatiques activées produisent et sécrètent des anticorps circulants qui ciblent les antigènes du SRAS-CoV-2 tant que ces derniers ne sécrètent pas activement d'anticorps, mais conservent ces éléments en mémoire pour se protéger contre les infections subséquentes et créer une immunité à long terme (73).
- Quatre études mesurent et indiquent l'activité des lymphocytes B et des anticorps circulants plus de six mois après l'infection (51, 52, 56, 62). La cytométrie de flux est la méthode la plus fréquemment utilisée pour détecter la spécificité et l'activité des lymphocytes B.
    - Les lymphocytes B mémoires spécifiques à la protéine S et à la protéine N, ainsi que les antigènes viraux RBD, ont été détectés chez les participants lors du suivi effectué plus de six mois après l'infection, ce qui indique que le nombre de cellules est demeuré stable ou a grandement augmenté et que les clones des lymphocytes B mémoires se sont étendus et ont évolué (51, 52, 56, 62).
    - 80 % (n = 29 personnes sur 36) des cas bénins à modérés de COVID-19 présentaient des fréquences élevées de lymphocytes B mémoires totaux spécifiques aux anticorps RBD (IgG+, IgM+ ou IgA+) (56) plus de 180 jours après l'infection.
    - Dans une cohorte où l'on trouve des cas de COVID-19 ayant déjà été hospitalisés, les pourcentages de lymphocytes B étaient les plus élevés chez les participants négatifs aux anticorps IgG et IgM (intervalle de 16,1 ± 6,4 à 16,7 ± 5,5) comparativement aux participants positifs à ces anticorps (intervalle de 7,2 ± 3,1 à 7,5 ± 3,8) (51)
    - Une seule étude mentionne la réduction des anticorps contre la protéine S qui sécrètent les lymphocytes B et une augmentation des lymphocytes B mémoires qui ciblent les antigènes viraux SRAS-CoV-2, dans les formes graves et bénignes de COVID-19 (62). Cette étude a également révélé que les lymphocytes B du RBD du SRAS-CoV-2 présentaient une réaction croisée minimale avec d'autres antigènes du coronavirus humain (62).

- Les lymphocytes T sont des cellules immunitaires classées en fonction des récepteurs de surface CD4+ ou CD8+. Le rôle principal des lymphocytes T peut être divisé selon qu'ils produisent des anticorps par activation des lymphocytes B (lymphocytes T CD4+) ou détruisent les cellules infectées présentant certains antigènes (lymphocytes T CD8+) (73, 74). Les lymphocytes T sécrètent également des cytokines pour coordonner les réponses immunitaires dans les cellules immunitaires (73, 74). Les études incluses ont isolé des cellules mononuclées de sang périphérique à partir d'échantillons sériques, avant de mesurer le nombre de lymphocytes T, les phénotypes ou l'activité après simulation avec divers bassins de séquences peptidiques du SARS-CoV-2 (c.-à-d. les acides aminés qui constituent les protéines virales) (49-51, 53 à 57). La variabilité ou le manque de détails sur les séquences de peptides utilisées dans les études de simulation limitent la comparabilité des résultats.
- Neuf études font état des résultats associés à la présence des lymphocytes T dans des cas infectés plus de six mois après l'infection (37, 49-51, 53 à 57).
    - L'ampleur des réponses des lymphocytes T mémoires s'est maintenue (et a même augmenté dans certains échantillons) plus de six mois après l'infection ou l'apparition des symptômes (37, 49 à 51, 53 à 55, 57). Une étude mentionne que les lymphocytes T présents dans 95 % de l'échantillon à l'étude provenant de cas légèrement symptomatiques sont demeurés sensibles à au moins un bassin de peptides du SARS-CoV-2, et quantifie donc un total médian de 200 cellules par million de cellules mononuclées de sang périphérique (ou 1 cellule sur 5 000) spécifiques au SRAS-CoV-2 lors du suivi effectué après six mois (55).
    - Dans certaines études, on a constaté que les lymphocytes T CD8+ étaient moins robustes que les réponses des lymphocytes T CD4+ obtenues plus de six mois après l'infection (49, 54, 56, 57). L'activité des lymphocytes T CD8+ a été détectée dans 50 % des cas bénins à modérés de six à huit mois après l'infection, tandis que l'activité des lymphocytes T mémoires CD4+ a continué d'être détectée chez 92 % des personnes du même échantillon (56).
    - Une étude a révélé une corrélation entre l'activité des lymphocytes T CD8+ et la séropositivité à l'IgG et de l'IgM pendant toute la durée de l'infection par COVID-19 dans un échantillon de personnes atteintes d'une forme grave de COVID-19 (51). Une autre étude a, quant à elle, signalé une forte corrélation entre la protéine S, les anticorps IgG contre le RBD et les lymphocytes T CD4+ spécifiques à la protéine N et à la protéine S du SARS-CoV-2 (54).
    - L'IL-2 était la cytokine dominante libérée par les lymphocytes T CD4+ six mois ou plus après l'infection (55, 57).

Principaux résultats tirés des réponses immunitaires aux anticorps circulants six mois ou plus après l'infection (n = 33) :

- l'immunité humorale, aussi appelée immunité à médiation humorale ou immunité médiée par les anticorps, désigne généralement les anticorps circulants qui sont envoyés vers les antigènes viraux (1, 63, 73). Parmi les études incluses, les anticorps circulants qui se trouvaient dans les échantillons de sérum ont été mesurés par des épreuves biologiques visant à établir l'affinité envers les anticorps, des essais de neutralisation des pseudovirus, la cytométrie de flux et d'autres techniques fondées sur la biologie moléculaire. Les résultats déclarés en ce qui concerne les anticorps comprenaient les anticorps totaux, les anticorps neutralisants, la catégorie d'anticorps (c.-à-d. IgG, IgM, IgA) qui étaient fréquemment décrits plus en détail par les sous-catégories (c.-à-d. IgG1, IgG3) ou l'affinité de liaison avec les antigènes viraux du SRAS-CoV-2. De nombreuses études ont souvent précisé les antigènes viraux cibles des anticorps Ig ayant été mesurés, ce qui inclut les protéines structurales virales comme la protéine de spicule (S), les sous-unités S1 ou S2 de la protéine S, les protéines de nucléocapsides (N), l'enveloppe (E), les protéines de la membrane (M), le domaine de liaison au récepteur (RBD) des protéines et les protéines accessoires. (c.-à-d. les protéines de cadre de lecture ouvert (ORF)).
- Des études ont révélé que des anticorps spécifiques au SRAS-CoV-2 étaient détectables chez la majorité des personnes infectées plus de six mois après l'infection, mais la séroprévalence des différents types d'anticorps était variable. Les tendances longitudinales des anticorps évaluées plus de six mois après l'infection sont décrites ci-dessous, selon la spécificité de l'antigène viral et la gravité clinique.
- Les anticorps neutralisants ciblent la protéine S ou le RBD du SRAS-CoV-2 pour neutraliser la liaison du virus avec les récepteurs ACE2 des cellules hôtes potentielles (59, 60, 75, 76). Les anticorps neutralisants ont été détectés dans 53,4 % à 100 % des cas examinés de 6 à 8 mois après l'infection (53, 56, 59, 61, 77 à 79). Les taux sont restés élevés chez les personnes ayant eu une forme grave de la COVID-19, comparativement aux personnes ayant eu une forme moins grave (52, 53, 58, 78, 79).
    - Une nouvelle étude a révélé que, comparativement aux cas ayant eu la forme légère de la maladie, la probabilité de persistance des anticorps neutralisants six mois après l'infection était 30 fois plus élevée (RC 30,3 (IC à 95 %, 10,0 à 107,9)) chez les personnes ayant eu la forme grave et 5 fois plus élevée (RC 5,2 (IC à 95 %, 1,8 à 16,7)) chez celles qui ont eu la forme modérée (53).
    - Un petit essai de phase 1 a révélé que l'immunité obtenue après la vaccination avec Moderna après 6 mois et, comme dans le cas de l'infection, les résultats indiquaient que les anticorps anti-RBD et les anticorps neutralisants étaient détectables 6 mois plus tard chez tous les participants (64).

- Les taux d'IgG de la protéine S étaient constamment élevés et détectables dans toutes les études, alors qu'ils étaient stables ou élevés chez 86 % à 99 % des personnes atteintes de formes moins graves (43, 56, 59, 60, 60, 28, 28 à 30). La présence à long terme de l'IgG contre la protéine S dans le sérum après six mois d'infection semble cependant être plus faible chez les personnes ayant eu une forme grave de l'infection (50, 81 à 83).
- Les anticorps IgG contre le RBD et les anticorps IgG contre la protéine S ont été détectés dans 76 à 90 % des formes bénignes à modérées de COVID-19, ainsi que chez les patients en hémodialyse (37, 43, 56, 84).
    - Une étude a révélé que les taux d'anticorps IgG contre RBD diminuent et se stabilisent environ 9 mois après l'infection (89 % des échantillons étaient positifs 6 ou 7 mois après l'infection et 81 % l'étaient encore 11 ou 12 mois après l'infection), même si les titres obtenus étaient 70 % inférieurs aux valeurs obtenues 1 mois après l'infection (84).
    - De multiples études confirment la corrélation entre les anticorps Ig RBD (toutes les classes d'Ig) et l'activité de neutralisation ciblant le SRAS-CoV-2 (59, 60). Cette association était cohérente avec les données obtenues pour les personnes ayant été atteintes des formes bénignes à graves de la COVID-19.
- Les anticorps à base de protéine N (variable de classe ou variable non précisée) ont diminué plus rapidement que les anticorps neutralisants, la protéine S et les anticorps RBD (32, 37, 59, 61, 62, 83)
    - Lademi-vie des anticorps IgG contre la protéine N a été estimée entre 59 et 76,4 jours (IC à 95 % : 55 à 90 jours) dans l'ensemble des études, soit une durée bien plus courte que la demi-vie relative estimée des autres anticorps (56, 58, 59, 80).
    - Une seule étude signale que la persistance des taux élevés d'Ig contre la protéine N environ cinq mois après l'infection pourrait être associée à des effets à long terme de la COVID-19, comme la fatigue, l'anosmie et l'agueusie (50).
- Une étude a comparé les anticorps circulants chez des enfants et chez des adultes ayant été infectés (67) et a permis de voir que les enfants présentaient des niveaux plus faibles d'anticorps contre les protéines S et N (la classe Ig des anticorps mesurés n'a pu être identifiée) et que la proportion d'anticorps globaux contre les protéines accessoires était plus grande et plus stable chez les enfants que chez les adultes (67).

Tableau 3 : Réactions immunitaires observées plus de six mois après l'infection par le SRAS-CoV-2 (n = 36)

ÉTUDE	MÉTHODOLOGIE	PRINCIPAUX RÉSULTATS
Anticorps circulants, réponses immunitaires des lymphocytes B et T		
Chia 2021 (53) *nouvelle* Cohorte prospective Singapour Janvier 2020 à janvier 2021	Les participants qui ont pris part à cet échantillon longitudinal (n = 164) ont été recrutés entre le 30 janvier 2020 et le 14 août 2020 à partir de cas ayant obtenu un résultat positif au test PCR de détection du SRAS-CoV-2 et a recueilli des échantillons de sang entre 30 et 60 jours, puis 90 jours et 180 jours après l'apparition des symptômes. Différents types de COVID-19, allant de la forme légère à la forme grave, ont été inclus. Un test ELISA de neutralisation du virus de substitution a été utilisé pour mesurer les anticorps IgG alors que le test IFN-γ-ELISpot avec six bassins de peptides du SARS-CoV-2 a été effectué sur les lymphocytes T provenant des cellules mononuclées de sang périphérique pour en déterminer la réactivité.	128/164 cases had a day 180 sample. Neutralization was considered significant at 30%. Five distinct groups were identified (predicted longevity of NAb in days): - 12% did not develop NAb - 27% had variable antibodies that waned by 6 months (median 96 days) - 28% had slow waning antibodies that were positive at 6 months (median 201 days) - 32% had minimal NAb decay at 6 months (median 580 days) - 2% had a delayed response where NAb levels peaked >90 days In a multivariable model disease severity was an independent predictor of persistent antibodies at 180 days: - Moderate disease OR= 5.2 (95%CI 1.8-16.7) - Severe disease OR= 30.3 (10.0 -107.9) Levels of RBD IgG antibody avidity correlated with NAb levels. Cytokine Levels: - 180 days post-symptom onset, higher levels of pro-inflammatory cytokines (IFN-γ, IL-12p70, and IL-17A), pro-inflammatory chemokine (IP-10), and growth factors (human growth factor) were observed in the persistent group compared with all other groups. T-cell activity (23 samples from each group): - All patients in each group had substantial specific T-cells at 180 days with no difference between groups.

		T-cell response was multi-specific and reacted to N protein, M protein, and S protein.
Peluso (2021) (54) *Prépublication* *nouvelle* Étude transversale États-Unis Avril 2020 et 2021	Les taux de lymphocytes T, d'anticorps neutralisants et d'anticorps spécifiques au SRAS-CoV-2 ont été mesurés chez des personnes présentant différents niveaux de gravité de l'infection tout comme les déclarations mentionnant des séquelles associées à la COVID longue (n = 70). Des échantillons de sérum ont été prélevés longitudinalement de 1 (médiane de 53 jours) à 8 mois après l'apparition des symptômes. Les lymphocytes T CD4+ et CD8+ ont été simulés dans des bassins peptiques contenant des protéines S et N, avant que l'activité cellulaire ne soit mesurée par les dosages biologiques AIM et ICS. On a également mesuré les taux d'anticorps IgG spécifiques contre la protéine S, la protéine N et le RBD (test Luminex) et l'activité des anticorps neutralisants (test avec pseudovirus). Des analyses de corrélation de Spearman et de régression linéaire ont été utilisées pour déterminer les corrélations entre les marqueurs immunitaires mesurés.	Résultats immunitaires obtenus de 6 à 8 mois après l'infection identifiés dans l'étude : - Une médiane de 23,1 % (EI 10,3, 36,6) pour les lymphocytes T d'IFNγ+ CD8+ (protéine N et protéine S) et 61,5 % (EI 44,4, 76,0) des lymphocytes T d'IFNγ CD4+ (protéine N et protéine S) ont produit du TNFα à chacun des points temporels échantillonnés (P < 0,001). - Les réponses des lymphocytes T CD 4+ et CD 8+ sont demeurées stables chez les participants, indépendamment de la gravité de la maladie. - L'ampleur des réponses précoces des lymphocytes T CD4+, des taux plus élevés de protéine N, de protéine S et d'anticorps IgG contre le RBD dépendait de la gravité initiale de l'infection. - Les niveaux d'anticorps contre la protéine S et le RBD sont fortement corrélés avec les lymphocytes T CD4+ spécifiques aux protéines N et S. - Il y a eu une corrélation entre la réponse des anticorps neutralisants et celles des lymphocytes T CD4+. - On a signalé que des réponses plus élevées à long terme des lymphocytes T CD8+ étaient liées à des comorbidités préexistantes de maladie pulmonaire. Les chercheurs n'ont pas été en mesure de déterminer des différences importantes dans les réponses des lymphocytes T ou des anticorps du SRAS-CoV-2 au fil du temps en fonction des séquelles laissées par l'infection aiguë.

Dan (2021) (56) Étude transversale États-Unis Mars à novembre 2020	Une évaluation des réponses immunitaires de protection, fondée sur les lymphocytes T mémoires CD4+ et CD8+, les lymphocytes B mémoires et les niveaux d'anticorps, a été effectuée parmi des personnes rétablies, dont la COVID-19 a été confirmée par test RT-PCR (n = 188). À noter que 93 % des participants n'ont pas été hospitalisés. Certains échantillons de sérum (n = 43 sur 188) ont été prélevés entre six et huit mois après l'infection. On a utilisé le test ELISA, des épreuves de neutralisation des anticorps par pseudovirus et la cytométrie en flux pour détecter les anticorps et les fréquences et activités des cellules immunitaires. Les lymphocytes T mémoires CD8+ du SRAS-CoV-2 ont été mesurés à l'aide d'une série d'ensembles de peptides couvrant l'ensemble des protéines de cadre de lecture ouvert (ORF) du SRAS-CoV-2, les plus courants étant la protéine S, la protéine M, la protéine N et l'ORF3a.	Résultats immunitaires obtenus de 6 à 8 mois après l'infection identifiés dans l'étude : Dynamique des anticorps - Les IgA contre la protéine S étaient détectables chez la majorité des participants. - Les titres d'IgG et d'IgG contre la protéine S et d'IgG contre le RBD ont affiché des baisses modestes, mais étaient relativement stables. - La proportion de participants positifs à l'IgG contre la protéine S, est passée de 98 % (54 sur 55) à 90 % (36 sur 40), d'un mois à six ou huit mois après l'infection. - 88 % (35 sur 40) des participants étaient positifs pour l'IgG contre le RBD. - 90 % (36 sur 40) des participants étaient positifs pour les anticorps neutralisants. Activité des lymphocytes B mémoires spécifiques du SRAS-CoV-2 - Les lymphocytes B mémoires spécifiques à la protéine S, à la protéine N, au RBD et aux antigènes viraux ont été détectées chez presque tous les participants, et étaient plus abondants lors du suivi post-infection. - 80 % (n = 29 participants sur 36) présentaient des fréquences plus élevées de lymphocytes B mémoire totaux (IgG+, IgM+ ou IgA+) plus de 180 jours après l'infection. Activité des lymphocytes T mémoires spécifiques au SRAS-CoV-2 - 70 % (40 sur 57) des participants avaient des lymphocytes T CD8+ un mois après l'infection, tandis que 50 % (18 sur 36) des participants ont obtenu des résultats positifs pour ces lymphocytes plus de six mois après l'infection. - 93 % (53 sur 57) des participants avaient des lymphocytes T mémoires CD4+ un mois après l'infection, tandis que 92 % (33 sur 36) des participants ont obtenu des résultats positifs pour ces lymphocytes plus de six mois après l'infection. En résumé, malgré l'hétérogénéité des réponses immunitaires associées au niveau d'anticorps

		circulants pour le SRAS-CoV-2, l'immunité cellulaire a pu être établie plus de six mois après l'infection grâce aux lymphocytes B et T mémoires.
Shen (2021) (51) Série de cas Chine Juillet et août 2020	Des échantillons de sérum ont été prélevés à de multiples moments après l'admission en centre de rétablissement (c.-à-d. 0, 2 et 4 semaines) d'un groupe de participants ayant déjà été infectés (n = 110) et dont le congé de l'hôpital après une forme aiguë du SRAS-CoV-2 avait eu lieu au moins six mois auparavant. Les infections ont été confirmées par des tests RT-PCR. Les niveaux des anticorps sériques IgM et IgG, d'IL6, de CD3+, des lymphocytes T CD8+, CD4+, des cellules NK et des lymphocytes B ont été mesurés par des essais et une cytométrie en flux. Des différences notables dans le pourcentage de lymphocyte T sériques CD3+, CD8+ et CD4+, de cellules NK et de lymphocytes B (aucun détail supplémentaire fourni), par la positivité des anticorps IgM et IgG, ont été confirmées par l'analyse de corrélation.	- Dans l'ensemble, 29,1 % (32 sur 110) des participants étaient positifs pour les anticorps IgM et IgG, 34,5 % (38 sur 110) étaient seulement positifs pour l'IgG et 36,4 % (n = 40) étaient négatifs pour les anticorps IgM et IgG. - Il n'a pas été possible de cerner de différences significatives entre les groupes ayant obtenu des résultats positifs et négatifs en ce qui concerne la démographie, la présentation clinique ou les comorbidités. Dynamique des lymphocytes T, six mois et plus après l'hospitalisation, selon la positivité des anticorps : les lymphocytes T CD8+ ont légèrement diminué pendant la période d'échantillonnage. - Le pourcentage de lymphocytes T CD8+ était le plus élevé (de 48,6 ± 7,3 à 43,7 ± 9,7) chez les participants positifs aux anticorps IgG et IgM à tous les moments pendant le suivi. - Le pourcentage de lymphocytes T CD8+ était le plus faible (de 25,5 ± 9,3 à 25,9 ± 10,1) chez les participants négatifs aux anticorps IgG et IgM. - Les cellules NK ont légèrement augmenté au cours de la période d'échantillonnage. - L'augmentation du pourcentage de cellules NK était la plus élevée chez les participants négatifs aux anticorps IgG et IgM à tous les moments pendant le suivi (intervalle de 25,7 ± 6,3 à 27,1 ± 8,3), et la plus faible chez les participants positifs aux anticorps IgG et IgM (de 13,7 ± 7,4 à 15,0 ± 9,6). Dynamique des lymphocytes B, six mois et plus après l'hospitalisation, selon la positivité des anticorps : les concentrations de lymphocytes B sont demeurées stables chez les participants positifs aux anticorps et chez ceux qui étaient négatifs, mais ont augmenté de façon significative chez les participants positifs aux IgM et aux IgG au moment des différents suivis.

		- Les pourcentages de lymphocytes B étaient les plus élevés chez les participants négatifs aux anticorps IgG et IgM (intervalle de 16,1 ± 6,4 à 16,7 ± 5,5) comparativement aux participants positifs à ces anticorps (intervalle de 7,2 ± 3,1 à 7,5 ± 3,8). - Les auteurs concluent que la perte d'anticorps IgM dans le sérum a entraîné une amélioration graduelle de l'immunité cellulaire liée aux cellules NK et aux lymphocytes B. Ils suggèrent que les pourcentages de lymphocytes sériques (CD3+, CD8+ et CD4+, de lymphocytes T, de cellules NK et de lymphocytes B) sont corrélés avec les changements des niveaux des anticorps sériques IgM et IgG, mais non liés aux cytokines inflammatoires ou à la gravité de l'infection (c.-à-d. Hs-CRP ou IL6), chez les patients qui ont été hospitalisés, puis se sont rétablis.

Gaebler (2020) (52)
 	
Série de cas
 	
États-Unis
Avril à octobre 2020
	Des échantillons de sérum ont été prélevés 1,3 et 6,2 mois (de 165 à 223 jours) après l'infection chez des personnes séropositives au SRAS-CoV-2 (n = 87). L'infection et les séroconversions ont été confirmées par test RT-PCR, et 10 % des personnes appartenant à l'échantillon ont été hospitalisées en raison de l'infection. Les concentrations d'anticorps IgG, IgM, IgA RBD et d'anticorps neutralisants ont été mesurées au moyen du test ELISA et d'une épreuve de neutralisation du pseudovirus. Les niveaux et l'activité des lymphocytes B ont été mesurés par cytométrie en flux.	Les niveaux d'anticorps RBD avaient grandement diminué six mois après l'infection. Dans l'ensemble, la diminution du niveau d'anticorps était inversement proportionnelle aux niveaux initiaux d'anticorps (c.-à-d. les personnes dont les niveaux d'anticorps étaient les plus élevés au début de l'infection et qui ont connu la plus forte diminution) et directement corrélée avec ceux-ci.
		- Dynamique des anticorps six mois après l'infection identifiée dans l'étude :
		  - Réduction de 53 % de l'IgM contre le RBD
		  - Réduction de 33 % de l'IgG contre le RBD
		  - Réduction de 15 % de l'IgA contre le RBD
		  - L'activité des anticorps neutralisants était cinq fois moindre.
		Le nombre de lymphocytes B mémoires spécifiques au RBD est demeuré inchangé pour la majorité des personnes. Toutefois, ces cellules présentaient une maturation, une expansion clonale variée et un renouvellement entre 1,3 et 6,2 mois après l'infection.
		Les auteurs concluent que les changements observés dans les lymphocytes B mémoires sont

		révélateurs d'une immunité à long terme, ainsi que de la capacité de créer des réponses immunitaires rapides et efficaces à la réinfection.
Sokal (2020) (62) Série de cas France Mars à octobre 2020	Des échantillons de sérum ont été prélevés chez des personnes infectées (n = 39) à trois moments, soit le premier mois, puis trois mois et six mois après l'apparition des symptômes. Environ 53 % (n = 21) des patients dans l'échantillon ont été atteints d'une forme grave de l'infection. Le test ELISA a été utilisé pour mesurer les concentrations d'anticorps contre les protéines N et S et les concentrations d'IgG contre le RBD. Les réponses des lymphocytes B mémoires spécifiques aux antigènes viraux ont été mesurées par des tests ELISA avec séquençage et cytométrie en flux des récepteurs des lymphocytes B.	Résultats immunitaires obtenus à 6 mois après l'apparition des symptômes identifiés dans l'étude : Dynamique des anticorps - Les anticorps IgG contre la protéine N ont rapidement diminué chez les personnes ayant eu des formes bénignes et graves de l'infection. Cette réduction était plus prononcée dans les cas bénins, et après six mois, les IgG contre la protéine N dans les titres étaient indétectables chez 50 % des participants légèrement symptomatiques. - Les anticorps IgG contre la protéine S étaient stables au fil du temps puisque seulement 9 % des personnes ayant eu une forme bénigne présentaient des niveaux d'anticorps indétectables au suivi de six mois. Les niveaux d'anticorps étaient beaucoup plus élevés chez les participants atteints d'une forme grave de l'infection dans les trois à six mois suivants. Activité des lymphocytes B : - les clones des lymphocytes B spécifiques à la protéine S et au RBD, ainsi que les clones de lymphocytes B à réaction croisée issus d'expositions antérieures au virus bêta-corona ont subi une maturation somatique et une expansion importante. - Tant pour les formes graves que bénignes de l'infection, les cellules sécrétrices d'anticorps contre la protéine S étaient marginalement détectables à six mois, alors que les lymphocytes B de la protéine S résidaient principalement dans le compartiment des lymphocytes B mémoire CD21+CD27+CD38-CD71$^{int/-}$ au repos pour les formes graves et bénignes. - Les lymphocytes B actifs sont demeurés détectables jusqu'à six mois après l'infection.

		On présume que ces clones de lymphocytes B contribuent à l'immunité à long terme chez les patients en convalescence.
Bilich (2020) (50) *Prépublication* Série de cas Allemagne *Printemps 2020	Les convalescents atteints d'une forme bénigne à modérée (n = 51) de l'infection ont fait l'objet d'un suivi longitudinal environ un mois (médiane 40 jours; intervalle de 35 à 56 jours) et cinq mois (médiane 159 jours; intervalle de 141 à 183 jours) après avoir obtenu un résultat positif au test RT-PCR. L'activité des lymphocytes T a été mesurée par les essais IFN-g ELISPOT et la cartographie de l'épitope unique. Les niveaux d'anticorps IgG et IgA ont, quant à eux, été mesurés au moyen d'un essai immunologique.	La dynamique des anticorps effectuée environ cinq mois après les résultats du test RT-PCR mentionnés dans l'étude a permis d'obtenir les résultats suivants : - on a observé une diminution du double des anticorps IgG et IgA contre la protéine S chez un pourcentage de participants variant entre 31 et 44 % entre les deux dates du suivi. - Jusqu'au deuxième suivi, une réduction inférieure à deux fois les niveaux d'anticorps dans la protéine N a été notée chez 13 % des participants. - Des titres d'anticorps protéiques à teneur élevée en protéine N, effectués cinq mois après l'infection, ont été associés à une prévalence plus élevée de symptômes post-infection, comme la fatigue, l'anosmie et l'agueusie. Réactions immunitaires des lymphocytes T 5 mois après l'infection : - le pourcentage de participants ayant des lymphocytes T détectables propres aux antigènes viraux a augmenté de 93 % à 100 % lors du deuxième suivi. Un sous-groupe de lymphocytes T ciblant des épitopes viraux spécifiques dérivés des ORF (épitopes HLA-RD; épitopes HLA classe 1), associés à l'immunité post-infection à long terme contre le SRAS-CoV-2, a persisté chez certains participants jusqu'à six mois après l'infection.
Clarke (2021) (37) Cohorte prospective Royaume-Uni Février 2020 à janvier 2021	Les patients en hémodialyse atteints d'une maladie rénale en phase terminale ont fait l'objet d'un dépistage afin de détecter la présence des anticorps du SRAS-CoV-2, et les résultats présentés dans le présent article portent sur les anticorps au temps 0 (n = 356), puis six mois plus	De tous les participants, 190 ont obtenu un résultat négatif pour les anticorps à base de protéine N alors que 129 autres ont obtenu un résultat positif à la date 0. Après six mois, des échantillons prélevés dans le groupe ayant obtenu un résultat positif aux anticorps de la protéine N (111 sur 129), ont été utilisés pour examiner l'immunité à long terme :

	tard (n = 301). Les infections ont été confirmées par des tests PCR. Les anticorps des protéines N et IgG RBD ont été mesurés à l'aide des tests CIMA et ELISA. L'activité des lymphocytes T a été mesurée par un test ELISPOT effectué chez des participants ayant eu une sérologie à six mois (n = 11). La gravité clinique de l'infection chez les participants ayant fait l'objet d'un suivi à six mois n'a pas été indiquée.	- les anticorps IgG à base de protéine N n'ont pu être détectés chez 36 % (n = 40) des participants ayant obtenu initialement un résultat positif. - Les anticorps IgG contre le RBD étaient plus persistants que les anticorps IgG contre la protéine N puisque 87 % (n = 97) des personnes faisant partie de l'échantillon séropositif initial ont continué à obtenir un résultat positif pour les anticorps IgG contre le RBD (y compris 70 % (n = 28) des personnes ayant obtenu un résultat négatif pour l'IgG contre la protéine N). - 64 % (n = 71) des participants ont continué d'être séropositifs pour les anticorps à base de protéine N, mais les concentrations étaient considérablement plus faibles comparativement au point de dépistage initial (p < 0,0001). 10 % (n = 12) des participants séropositifs initiaux étaient séronégatifs pour les anticorps RBD et de la protéine N, mais 80 % de ces personnes ont démontré une activité des lymphocytes T spécifiques de l'antigène du SRAS-CoV-2.
Réponses immunitaires des lymphocytes T		
Zuo (2021) (55) *nouvelle* Étude transversale Royaume-Uni Mars 2020	Des échantillons de sérum ont été prélevés chez des cas confirmés par RT-PCR (n = 100) six mois après l'infection. Aucune personne faisant partie de l'échantillon de l'étude n'a été hospitalisée pendant la phase aiguë de l'infection. Les lymphocytes T ont été simulés avec des bassins de protéine S de protéine N et de protéine M du SARS-CoV-2. L'ampleur et les phénotypes des lymphocytes T ont été	Réponses des lymphocytes T 6 mois après l'infection : - 95 % des lymphocytes T (n = 90 sur 95) de l'échantillon ont répondu à au moins un des peptides testés, avec un total médian de 200 cellules par million de cellules mononuclées de sang périphérique (ou 1 sur 5 000 cellules) spécifiques au SRAS-CoV-2. - Les réponses des lymphocytes T aux bassins peptidiques testés sont corrélées avec les taux maximaux d'anticorps. - 18 % des lymphocytes T de l'échantillon n'étaient pas sensibles à la protéine S alors que 8 % de l'échantillon n'a pas réagi aux peptides protéiques N et M.

	mesurés à l'aide du test ELISPOT et de la cytométrie de flux.	- L'IL-2 était la cytokine dominante libérée par les lymphocytes T CD4+. - Les réponses médianes des lymphocytes T à toutes les concentrations de peptides testées étaient environ 50 % plus élevées chez les participants qui avaient eu une infection symptomatique; 42 % plus élevées pour la protéine S et 55 % plus élevées pour les protéines N et M. - Aucune différence n'a été observée dans le rapport CD4:CD8 pour les infections symptomatiques. Les chercheurs ont donc conclu que la gravité de l'infection primaire établissait un « point fixe » pour l'immunité cellulaire pouvant encore persister six mois après l'infection.
Breton (2020) (57) Cohorte prospective États-Unis Mars à octobre 202	Des échantillons de sérum jumelés ont été prélevés jusqu'à six mois après l'infection chez des participants atteints d'une forme peu grave de l'infection ayant obtenu un résultat positif au SRAS-CoV-2 (n = 41). Les infections ont été confirmées par des tests RT-PCR. Les échantillons de sérum des participants infectés ont été comparés à ceux des individus non infectés (n = 20). Les phénotypes des lymphocytes T et la spécificité de l'antigène du SRAS-CoV-2 ont été mesurés par cytométrie en flux, avec le test ELISPOT et d'autres tests.	Comparativement aux participants non infectés, on a observé des changements importants dans les compartiments des lymphocytes T CD4+ et CD8+ circulants qui ont persisté six mois après l'infection par le SRAS-CoV-2. Activité des lymphocytes T du SRAS-CoV-2 jusqu'à six mois après l'infection : - à 6,1 mois, les proportions de lymphocytes T CD8+ et CD4+ étaient presque revenues aux niveaux physiologiques. - Les lymphocytes T CD4+ spécifiques à l'antigène qui exprimaient des marqueurs mémoire, ainsi que les réponses pour IL-2, IFN-g, TNF-a, CD154 et pour la cytokine polyfonctionnelle ont été nettement plus élevées dans le sérum des convalescents, comparativement aux participants non infectés, alors que la fréquence relative des cellules avait, quant à elle, diminué (22 à 32 %) lors du suivi de 6,1 mois. - Les lymphocytes T CD8+ qui ont produit des réponses pour Mip-1b, CD107a, IL-2, INF-g et TNF-a étaient encore détectables au suivi de 6,1 mois, bien qu'à des niveaux inférieurs aux mesures précédentes.

		- 95 à 97 % des sérums de participants ayant déjà été infectés ont fourni des preuves d'activité des lymphocytes T spécifiques aux antigènes CD4+ et CD8+ 1,3 et 6,1 mois après l'infection. Comparativement à l'activité des lymphocytes T CD4+ à 6,1 mois, les réponses des lymphocytes T CD8+ étaient beaucoup plus variables et généralement moins robustes.
Li (2020) (49) *Prépublication* Étude transversale Chine Avril à septembre 2020	L'étude a porté sur des personnes ayant eu la COVID-19 (n=31) et sur des témoins non exposés (n = 11) (l'état d'exposition ayant été confirmé par un test RT-PCR). La période médiane entre l'apparition de la maladie et le prélèvement sérique était de 169 jours (intervalle de 83 à 274 jours). L'analyse a examiné les différences entre les réponses des lymphocytes T pendant les six premiers mois, puis pendant les six à neuf mois qui ont suivi l'infection. 56,6 % (17 sur 31) des cas infectés ont été hospitalisés alors que 19 % (6 sur 31) étaient asymptomatiques. L'activité des lymphocytes T a été mesurée par cytométrie en flux alors que les séquences de protéines virales S, N et M ont été utilisées pour la simulation cellulaire.	- Une proportion des lymphocytes T ont réagi faiblement aux protéines virales chez les personnes non infectées, mais à un niveau beaucoup plus faible que la réaction observée chez les personnes ayant déjà été infectées. - Lors du dernier suivi, 45 % des personnes précédemment infectées étaient encore séropositives à l'IgG et 29 %, à l'IgG et à l'IgM. On a aussi remarqué que les réponses des lymphocytes T CD4+ étaient plus fortes chez les personnes ayant eu un résultat négatif pour les anticorps IgG. - Une perte dans le nombre de réponses des lymphocytes T mémoires CD4+ et CD8+ a été observée chez 16,13 % et 25,81 % des personnes précédemment infectées. La perte de lymphocyte T mémoires CD4 s'est révélée plus fréquente chez les personnes asymptomatiques. - Les réponses des lymphocytes T CD4+ et CD8+ étaient très variables. De façon générale, la portée et l'ampleur des réactions cellulaires augmentaient avec le temps suivant l'apparition des symptômes. Dynamique des lymphocytes T, au cours des six premiers mois suivant l'apparition des symptômes, comparativement à la période de six à neuf mois suivant l'apparition des symptômes : - au cours des 6 premiers mois après l'apparition de la maladie, on a noté une réduction de l'ampleur des lymphocytes T CD4+

		productrices de cytokines par rapport aux protéines S, N et M. Elle a ensuite augmenté pendant la période de six à neuf mois suivant l'infection. - Aucun changement n'a été observé chez les lymphocytes T CD8+ produisant de la cytokine. - Il y a eu une augmentation marquée du nombre de bains de lymphocyte T mémoire CD8+ réactifs (c.-à-d. la portée et l'ampleur des réponses) entre 6 et neuf mois après les symptômes.
Réponses immunitaires associées aux anticorps circulants		
Doria-Rose (2021) (64) Lettre à la rédaction *nouvelle* Essai clinique randomisé États-Unis Août 2020 à mars 2021	L'immunité du vaccin a été évaluée chez 33 participants adultes en bonne santé dans le cadre d'un essai en cours de phase 1 portant sur des anticorps et effectué 180 jours après avoir reçu la deuxième dose du vaccin ARNm-1273 de Moderna.	Six mois après l'administration, l'activité des anticorps était élevée chez tous les participants (données indiquées dans le graphique) et était semblable dans tous les groupes d'âge. Une activité a pu être détectée par un test de pseudo-neutralisation chez presque tous les participants alors chez tous les participants, le test avec colorant mNeonGreen a généré une activité de neutralisation par réduction des foyers de virus vivants. - Les résultats de neutralisation étaient plus faibles chez les participants âgés de plus de 55 ans (P < 0,02).
Li (2021) (84) *Prépublication* *nouvelle* Cohorte prospective Chine Février 2020 à janvier 2021	Dans le cadre d'une transfusion de plasma de convalescent, 869 donneurs ont été recrutés et échantillonnés pendant une période allant jusqu'à 12 mois. Tous avaient obtenu un diagnostic confirmé de COVID-19. L'ensemble de détection des anticorps IgG portant le marquage CE a été utilisé	Taux de positivité des anticorps IgG contre le RBD après le diagnostic (seuil du titre < 1:80) : - 89,4 % après 6 ou 7 mois - 81,4 % après 11 ou 12 mois - 5,4 % des donneurs de plasma de convalescent n'ont jamais eu de titres détectables. Après 9 mois, les titres d'anticorps IgG contre le RBD ont commencé à se stabiliser à un TMG d'environ 200. Le titre d'anticorps IgG contre le

	pour tester le titre de l'IgG spécifique au RBD.	RBD après 12 mois était 70 % plus bas que la valeur obtenue le premier mois après le diagnostic.
den Hertog (2021) (85) *nouvelle* Cohorte basée sur la population Pays-Bas Avril à octobre 2020	Au cours des sept mois qui ont suivi l'infection, 353 personnes séroconverties qui ont pris part à une étude de sérosurveillance pour des personnes de tout âge ont été examinées afin de déceler la désintégration des anticorps. L'avidité des anticorps IgG contre la sous-unité S1 de la protéine S du SARS-CoV-2 a été étudiée comme marqueur de l'immunité cellulaire sous-jacente. Dosage biologique : test immunitaire avec billes fluorescentes effectué à l'interne, capable de mesurer les taux d'IgG, d'IgM et d'IgA.	Nombre d'anticorps présents pendant le premier mois suivant la séroconversion de l'IgG et nombre d'anticorps présents après 6 mois : - IgG 99 % contre 92 % (IC à 95 %, 89 à 95) - IgM 64 % contre 33 % (28 à 39) - IgA 62 % contre 37 % (31 à 43) - On a estimé que la diminution des taux d'IgG avait doublé en 158 jours (IC à 95 %, 136 à 189) et que l'indice d'avidité des anticorps IgG contre la sous-unité S1 de la protéine S du SARS-CoV-2 avait augmenté de plus du double pendant ces 7 mois. Après 6 mois, les personnes dont les anticorps IgG avaient fait l'objet d'une séroréversion étaient plus susceptibles d'avoir été asymptomatiques ou d'avoir été atteints de la forme bénigne alors que celles qui avaient eu une forme symptomatique de COVID-19 étaient plus susceptibles d'être positifs à l'IgM ou à l'IgA et d'afficher une plus forte augmentation de l'indice d'avidité des anticorps IgG contre la sous-unité S1 de la protéine S du SARS-CoV-2 pendant les 7 mois (p = 0,02).
L'Huillier (2021) (65) *nouvelle* Cohorte prospective Suisse Mars à octobre 2020	Les travailleurs de la santé dont le SRAS-CoV-2 a été confirmé entre le 17 mars et le 15 avril 2020 ont été recrutés dans un seul hôpital. Des prélèvements sanguins de suivi ont été effectués dans 196 cas sur 200 au mois 1, au mois 3 et au mois 6 après le diagnostic. Les anticorps dirigés contre le SARS-CoV-2 ont été mesurés à l'aide du test	Nombre d'anticorps présents pendant le premier mois suivant la séroconversion de l'IgG et nombre d'anticorps présents après 6 mois : - Tous les participants avaient des anticorps anti-RBD au mois 6. Le taux géométrique médian a augmenté entre le mois 1 et le mois 6 pour atteindre 123,3 U/ml (IC à 95 % : 103,4 à 147,0; p < 0,001) et seulement 4,6 % des participants ont vu leurs valeurs d'anticorps anti-RBD diminuer. - Au mois 6, 98 % (192 sur 196) des participants avaient des anticorps contre la protéine N. La moyenne géométrique a diminué entre le

	immunologique Elecsys pour la détermination qualitative dirigé contre le RBD et du test immunologique Elecsys pour la détermination semi-quantitative anti-N (des tests qui mesurent tous deux les taux d'immunoglobuline totale). Un test de neutralisation du virus substitut offert sur le marché et un test de neutralisation par réduction des plages ont été utilisés pour à des fins de neutralisation.	mois 3 et le mois 6 pour atteindre (34,0, IC à 95 % : 28,0 à 41,3). - Les titres des anticorps inhibiteurs de la région de liaison ACE2 sur le RBD (Ig totale) ont diminué au fil du temps dans l'ensemble de la cohorte. Au mois 6 : - 7,7 % (15 sur 196) avaient des titres d'anticorps inhibiteurs au moins deux fois plus élevés qu'au mois 1 - 58,2 % (114 sur 196) avaient des titres deux fois moindres - 34,2 % (67 sur 196) des titres sont demeurés stables (variation de 0,5 à 2 fois) Les résultats du PRNT indiquent une activité de neutralisation dans 92,9 % de PRNT90 et dans 99,5 % de PRNT50.
Garcia-Abellan (2021) (32) *Prépublication* *nouvelle* Cohorte prospective Espagne Mars à décembre 2020	146 cas confirmés de SRAS-CoV-2 ont été recrutés pour un échantillonnage en série effectué 1, 2 et 6 mois après le congé de l'hôpital. Les anticorps IgG de la protéine N et de la sous-unité S1 de la protéine S ont été mesurés avec les tests Anti-SARS-CoV-2 NCP ELISA (IgG) et Anti-IgG/A/M SARS-CoV-2 ELISA, Euroimmun, Lubeck, Allemagne.	On a suivi 134 cas pendant 6 mois. 7,8 % de ces cas ont signalé des symptômes persistants associés à la COVID-19 et 3 % (4 sur 134) ont obtenu un résultat positif au test RT-PCR (valeur Ct médiane = 36). Aucune réinfection n'a eu lieu, comme cela a été confirmé par le séquençage. - La séroréversion s'est produite chez 29 patients. 27 (27,6 %) patients avaient des anticorps IgG contre la protéine N alors que 6 (6 %) avaient des anticorps IgG contre la protéine S au mois 6. Les données présentées dans les graphiques indiquent que les anticorps IgG contre le RBD étaient stables jusqu'au mois 6, mais que les anticorps IgG contre la protéine N avaient diminué par rapport à la valeur obtenue 30 jours après l'infection.
Dispinseri (2021) (78) *Prépublication* *nouvelle*	150 cas ont été inscrits à l'étude de cohorte clinique-biologique (COVID-BioB) avec	46 cas ont pris part à des visites supplémentaires effectuées six mois ou plus (médiane de 204 jours, plage de 145 à 250) après l'infection.

Cohorte prospective Italie Février à novembre 2020	points d'échantillonnage fixés 1 (n = 87), 3 (n = 77) et 6 (n = 46) mois après la date de congé. 12 autres cas non hospitalisés ont été suivis jusqu'à un maximum de 5 visites. Un test d'immunoprécipitation en phase liquide révélé par la luciférase (LIPS) a été utilisé pour mesurer les anticorps. Le test de neutralisation du SARS-CoV-2 basé sur un vecteur lentiviral a été utilisé pour examiner la neutralisation de la protéine S comme bon marqueur substitut pour les anticorps neutralisants.	- Les titres d'anticorps neutralisants diminuaient l'ID50 dans 1/660 (plage de 1/< 40 à 10 900) et aucun cas n'était négatif. - Les anticorps neutralisants et les anticorps IgG de la protéine S ont persisté chez la grande majorité des patients rétablis, peu importe la gravité de la maladie, l'âge et les comorbidités pendant un maximum de huit mois après l'apparition des symptômes (données dans les graphiques). Dans les cas où la personne a été hospitalisée, il y avait une corrélation entre les anticorps neutralisants et la forme grave de la maladie.
Van Elslande (2021) (80) *Lettre à la rédaction* *nouvelle* Cohorte prospective Belgique Printemps 2021*	Des échantillons de sérum ont été prélevés chez des travailleurs de la santé dont le diagnostic avait été confirmé par la méthode RT-PCR (n = 118) entre 1 et 3 mois (28 à 103 jours) et entre 7 et 10 mois (209 à 315 jours) après le diagnostic. La majorité des cas échantillonnés présentaient des symptômes légers, et six personnes ont dû être hospitalisées en raison d'une infection aiguë.	Résultats immunitaires de 7 à 10 mois après le diagnostic : - La positivité des anticorps IgG contre la protéine S a été observée dans 92,4 % de l'échantillon alors que la positivité des anticorps IgG contre la protéine N a été observée dans 17,8 %. - - La demi-vie moyenne a été estimée à 76,4 jours (IC à 95 %, 68,3 à 86,7) pour les anticorps IgG contre la protéine N, et à 198,8 jours (IC à 95 %, 143,6 à 323) pour les anticorps IgG contre la protéine S. - On estime que 50 % des patients sont devenus séronégatifs pour les anticorps contre la

	Les anticorps IgG spécifiques contre la protéine S et la protéine N du SRAS-CoV-2 ont été mesurés à l'aide de tests IgG II Quant. La demi-vie des anticorps a été estimée par régression linéaire.	protéine N 201,2 jours (IC à 95 %, 179,9 à 228,3) après le diagnostic alors que 50 % des patients sont également devenus séronégatifs pour les anticorps contre la protéine S 803,2 jours (IC à 95 %, 580,2 à 1305,0) après le diagnostic.
De Giorgi (2021) (86) *Prépublication* *nouvelle* Cohorte prospective États-Unis Avril à novembre 2020	105 donneurs de plasma convalescent pour la COVID-19 sur 202 ont fourni des échantillons répétés (tous les 28 jours ou plus) pendant un maximum de 9 mois après leur diagnostic. 91 % d'entre eux avaient eu une forme légère de la COVID-19. Les échantillons de plasma ont été utilisés pour effectuer des tests sur le SARS-CoV-2. Les anticorps totaux et les anticorps IgG ont également été analysés. Un essai de neutralisation par réduction de la fluorescence a été utilisé pour déterminer les titres de neutralisation.	Lors de l'évaluation initiale, 97,5 %, 74,3 % et 73,8 % des échantillons présentaient une activité totale, une activité associée aux anticorps IgG et une activité neutralisante. - 93 % des 105 donneurs présentaient des taux détectables d'anticorps IgG 9 mois après le rétablissement. - Les taux des anticorps IgG ont diminué lors du suivi chez 30,7 % des donneurs, mais la séroconversion était rare (3,8 %). - 63 % des donneurs avaient des anticorps neutralisants détectables jusqu'à 9 mois après le rétablissement. - 25 % des donneurs avaient eu une séroréversion pendant le suivi, alors que 12 % n'avaient pas d'anticorps neutralisants détectables. - Chez ceux qui avaient des titres de départ élevés, 82,9 % ont maintenu des titres détectables au fil du temps comparativement à ceux qui avaient des titres de départ faibles puisque seuls 39,6 % de ceux-ci sont restés détectables au fil du temps. Aucune réinfection ne s'est produite dans cette cohorte.
Noh (2021) (77) *nouvelle* Cohorte prospective	Des échantillons de sérum ont été prélevés chez des cas dont le diagnostic de COVID-19 a été confirmé par test RT-PCR (n = 97) présentant	Résultats immunitaires obtenus 6 mois après le diagnostic indiqués dans l'étude : - Deux mois après le diagnostic, les taux d'IgG sont passés de 91,7 % à 66 %. De même, le titre géométrique médian de l'IgG obtenu

Corée Juin 2020 à janvier 2021	différentes gravités d'infection (cas asymptomatiques (n = 14), symptomatiques/non symptomatiques (n = 42) et pulmonaires (n = 41) 8 semaines, 9 à 20 semaines et 22 à 27 semaines après le diagnostic. Le nombre médian de jours entre le diagnostic et le prélèvement final de l'échantillon de sérum était de 184 (plage de 182 à 185) jours. Des tests sur les anticorps IgG contre la protéine N et des tests de neutralisation par réduction des plages (PRNT) ont été utilisés pour mesurer les titres d'anticorps neutralisants. Les titres géométriques médians ont été calculés afin de comparer les titres IgG obtenus lors des différentes étapes de collecte.	après 6 mois était 46,2 % inférieur à celui obtenu après 2 mois. - Quant à la séropositivité, elle avait, elle aussi, diminué de 100 % par rapport au niveau obtenu après 2 mois jusqu'à atteindre 86,9 %. Quant au titre géométrique médian pour les anticorps neutralisants, il avait également diminué de 68,3 %, comparativement aux niveaux obtenus après 2 mois - Les anticorps neutralisants étaient cependant plus hauts dans les cas où l'on trouvait une excrétion virale durant plus de 21 jours. Les taux d'anticorps IgG et d'anticorps neutralisants étaient plus élevés six mois après le diagnostic dans les cas pulmonaires, comparativement aux cas moins graves.
Ortega (2021) (87) *Prépublication* *nouvelle* Cohorte prospective Espagne Mars à octobre 2020	Des échantillons de sérum ont été prélevés et la cinétique des anticorps a été mesurée chez des travailleurs de la santé séropositifs et symptomatiques (n = 76) 1, 3 et 6 mois après l'apparition des symptômes. Les taux d'anticorps IgG, IgM et IgA spécifiques à la protéine S du SRAS-CoV-2 (sous-unités S1, S2), à la RBD, à la protéine N et à	Séropositivité des anticorps 6 mois après l'apparition des symptômes : - La plupart des taux d'anticorps testés sont demeurés stables au fil du temps. 71 % des participants sont demeurés positifs pour les anticorps IgG contre la protéine S alors que 69 % le sont restés pour l'IgA. - Les taux d'anticorps IgM et IgG contre la protéine N ont diminué pendant la période de suivi. Plus de cinq mois après l'apparition des symptômes, on a pu voir que la séropositivité des anticorps IgM contre la protéine N était

	l'extrémité C terminale de la protéine N, ainsi que les antigènes HCoV ont été mesurés au moyen d'un test Luminex. La capacité des anticorps neutralisants par rapport au RBD-ACE-2 a été mesurée par cyrtométrie de flux.	à 34 % alors que celle des anticorps IgG était à 26 % contre cette même protéine N. - La capacité des anticorps neutralisants a augmenté pendant environ 3 mois après l'apparition des symptômes et est demeurée stable pendant 5,3 mois supplémentaires après l'apparition des symptômes. - Six mois après l'apparition des symptômes, les taux d'IgG et d'IgA pour tous les antigènes testés ont montré une corrélation modérée à forte avec la capacité des anticorps neutralisants (r_s = 0,24 à 0,76, p < 0,05). Les auteurs mentionnent que les taux d'IgG et d'IgA pour le HCoV étaient beaucoup plus élevés chez les individus séropositifs asymptomatiques que chez les individus séropositifs symptomatiques et ont donc conclu que la réactivité croisée aux antigènes HCoV endémiques pouvait avoir des effets protecteurs contre la gravité du virus SRAS-CoV-2.
Sakhi (2021) (83) *nouvelle* Cohorte prospective France Mars à octobre 2020	Des échantillons de sérum ont été prélevés chez des patients en hémodialyse et une sérologie des anticorps IgG contre la protéine N du SRAS-CoV-2 (n = 73) a été effectuée environ 51 jours après le diagnostic. 81 % (n = 60 sur 74) des échantillons de sérum de cet échantillon ont été prélevés six mois après le diagnostic. Les taux sériques de la protéine S du SRAS-CoV-2 et des anticorps IgG spécifiques contre la protéine N ont été mesurées.	Résultats immunitaires obtenus 6 mois après le diagnostic indiqués dans l'étude : - 25 % (n = 15 sur 60) de l'échantillon présentaient des taux indétectables des anticorps IgG contre la protéine N du SRAS-CoV-2 (c.-à-d. font l'objet d'une séroréversion). De ces cas, 21 % (n = 3/14) étaient également négatifs pour les anticorps contre la protéine S. - 97 % (n = 43 sur 45) des cas qui étaient séropositifs pour les anticorps IgG contre la protéine N du SRAS-CoV-2 sont également demeurés positifs pour les anticorps contre la protéine S. Un lien a ensuite été établi entre une infection aiguë non grave et une désintégration plus rapide

		des anticorps IgG contre la protéine S du SRAS-CoV-2.
Rockstroh (2021) (79) *nouvelle* Cohorte prospective Allemagne Mars 2020 à janvier 2021	Des échantillons de sérum ont été prélevés chez des cas dont le diagnostic avait été confirmé par RT-PCR (n = 57) moins de 2 mois après l'apparition des symptômes (médiane de 1 mois) et ont fait l'objet d'un suivi pendant 6 à 9 mois après l'apparition des symptômes (médiane de 7,9 EI de 6,6 à 8 mois). Ces cas comprenaient des personnes non hospitalisées (n = 38), des personnes hospitalisées qui avaient des symptômes graves (n = 15) et des personnes qui ont dû recevoir de l'oxygène (n = 4). Les anticorps IgG spécifiques contre le virion complet, la sous-unité S1 de la protéine S, la protéine N et les antigènes contre RBD du SARS-CoV-2 ont été mesurés à l'aide des tests ELISA et ELISpot. L'activité de l'anticorps neutralisant a été mesurée avec un virus actif.	Résultats immunitaires obtenus de 6 à 9 mois après l'apparition des symptômes : - Une réduction importante des titres d'anticorps neutralisants (réduction médiane de 4 fois, EI 2,7 à 10,7) a été observée chez les cas graves. Les titres d'anticorps neutralisant des patients non hospitalisés ont légèrement diminué (réduction médiane de 2,8 fois, EI 1,9 à 6). - Les anticorps neutralisants étaient indétectables (c.-à-d. séroréversion) dans 13,16 % (n = 5 sur 38) des cas non hospitalisés, mais tous les cas graves sont demeurés positifs pour les anticorps neutralisants de 6 à 9 mois après l'apparition des symptômes. - La sous-unité S1 de la protéine S et les anticorps IgG spécifiques contre la protéine N ont diminué, alors que les anticorps IgG spécifiques contre le RBD sont demeurés stables (ou ont même augmenté) pendant la période de suivi. - Les anticorps IgG contre la protéine N ont démontré une faible corrélation avec l'activité des anticorps neutralisants. - Les taux d'anticorps IgG contre la sous-unité S1 de la protéine S et l'activité des anticorps neutralisants étaient tous corrélés. Une corrélation positive significative entre la gravité de l'infection aiguë et les taux médians d'anticorps IgG pour tous les anticorps testés a été observée à tous les temps de mesure.
Levi (2021) (88) *Prépublication* Cohorte prospective	Mesure des changements dans les niveaux d'anticorps sériques dans une période de cinq mois, effectuée chez un échantillon de travailleurs de la santé provenant de	- Les concentrations d'IgG étaient plus élevées chez les travailleurs de la santé dont la COVID-19 était symptomatique, comparativement aux travailleurs de la santé asymptomatiques et paucisymptomatiques.

Italie Avril à août 2020	multiples établissements de soins de santé (n = 4 534). Les concentrations d'IgG spécifiques aux protéines S (S1 et S2) ont été mesurées par des dosages biologiques (dans lesquels le seuil a été fixé à 12 AU/ml pour l'IgG). Parmi les travailleurs de la santé dont les taux d'IgG étaient supérieurs au seuil, 14 % (n = 91 sur 613) étaient asymptomatiques. Les facteurs associés à la dynamique des anticorps ont été déterminés au moyen d'une analyse de régression logistique.	- Les symptômes associés à des taux d'IgG soutenus et plus élevés (évalués après cinq mois) incluaient de la fièvre, de la toux, des douleurs musculaires, de l'asthénie, de la tachycardie et de l'anosmie/dysgueusie. - L'analyse de régression a révélé un lien important entre un taux d'IgG constant et la présence d'anosmie ou de dysgueusie (RC 2,75, IC à 95 %, 1,753 à 4,301). Remarque : Les résultats de l'étude peuvent être biaisés, puisque des augmentations des niveaux d'anticorps des travailleurs de la santé ont été observées dans les régions les plus touchées par la SRAS-CoV-2 alors qu'elles étaient plus faibles dans les régions les moins touchées (c.-à-d. que les niveaux d'anticorps pourraient augmenter en raison des réinfections).
Dobaño (2021) (43) *Prépublication* Cohorte prospective Espagne Mars à décembre 2020	On a évalué les niveaux d'anticorps et la séropositivité dans un échantillon d'agents de soins de santé primaires (n = 173) de 149 à 270 jours après l'apparition des symptômes grâce à des prélèvements de sérum effectués à trois moments distincts. Les infections ont été confirmées par des tests PCR. La majorité des cas de l'échantillon comprenaient des travailleurs ayant eu des symptômes légers à moyens dont 14 % ont dû être hospitalisés. Les niveaux d'IgM, d'IgA et d'IgG contre la protéine S et le RBD ont été mesurés par dosage biologique (non précisé). Les	La dynamique des anticorps effectuée entre cinq et neuf mois après l'apparition des symptômes, comme cela est indiqué dans l'étude, a permis d'obtenir les résultats suivants : - 92,49 % des participants étaient positifs pour au moins un isotype d'immunoglobuline, ce qui indique une immunité très stable et persistante. - 60 % des participants étaient positifs pour l'IgM contre la protéine S et le RBD, 76,30 % pour l'IgA contre la protéine S et le RBD, et 90,17 % pour l'IgG contre la protéine S et le RBD. - Les facteurs associés à des niveaux plus élevés d'anticorps établis pendant le suivi incluaient l'admission à l'hôpital, de la fièvre, de l'anosmie ou de l'hypogueusie, et des allergies antérieures.

	facteurs associés à des niveaux plus élevés d'anticorps ont été déterminés par des analyses de régression multivariables par étapes.	
Wagner (2020) (60) *Prépublication* Cohorte prospective Autriche Avril à octobre 2020	Une importante étude sur la séroprévalence (n = 1 655) a permis de déterminer les personnes positives aux anticorps IgG ou IgA contre la protéine S (n = 168). Seulement 42 % des participants ont déclaré avoir éprouvé des symptômes compatibles avec l'infection au cours des trois mois précédant le recrutement. Des échantillons de sérum provenant de personnes séropositives ont été prélevés trois et six mois après les résultats initiaux du test (n = 1 292 sur 1 655). Les anticorps contre la sous-unité S1 de la protéine S, la protéine N et le RBD et les anticorps neutralisants ont été détectés par des tests sérologiques.	La dynamique des anticorps a été évaluée six mois après les résultats initiaux des tests séropositifs identifiés dans l'étude et a permis d'obtenir les résultats suivants : - les niveaux d'IgG contre la région S1, qui suggèrent une exposition plutôt qu'une immunité protectrice, ont persisté dans 90 % des cas séropositifs (9 sur 10). - Les niveaux d'IgG contre la protéine N n'étaient plus détectables dans 55,5 % de l'échantillon. - Après trois mois, le taux d'IgM contre le RBD avait diminué (par rapport aux résultats séropositifs initiaux) dans 53,3 % de l'échantillon, mais il est demeuré stable de 3 à six mois. - Au départ, 50 % des personnes ayant obtenu un résultat positif pour l'IgM contre le RBD et pour l'IgG contre la protéine N étaient séronégatifs à six mois. - Après six mois, l'IgA contre la protéine S1 avait diminué par rapport au niveau de référence. - Les anticorps totaux RBD avaient une meilleure corrélation avec les anticorps neutralisants (un marqueur substitut pour la protection contre le virus) et le niveau des deux était stable après six mois. - Les niveaux d'anticorps RBD n'ont révélé aucun lien avec les symptômes et de la gravité attribués à l'infection. - Les auteurs ont conclu que les dosages biologiques spécifiques aux anticorps RBD peuvent détecter de façon fiable des anticorps spécifiques au SRAS-CoV-2 pendant au moins six mois après l'infection.

Zhou (2020) (81) Cohorte prospective Chine Printemps 2020*	Les concentrations d'anticorps IgM et IgG contre la protéine S ont été testées dans des échantillons sériques de convalescence prélevés chez des participants ayant eu la COVID-19 (n = 165). Tous les participants avaient été hospitalisés et leurs infections confirmées par test RT-PCR. Le test ELISA a été utilisé pour mesurer les niveaux d'anticorps dans les échantillons de sérum. Tous les échantillons ont été prélevés entre le jour 1 et 7 mois après l'apparition des symptômes dont 28 échantillons de sérum ont été utilisés pour obtenir des données sept mois après l'infection.	La dynamique des anticorps a été évaluée jusqu'à sept mois après l'hospitalisation initiale, comme cela est indiqué dans l'étude et a permis d'obtenir les résultats suivants : - L'IgM contre la protéine S a diminué après avoir atteint un sommet aux alentours de 22 à 28 jours et 79 % des personnes étaient négatives pour ces anticorps sept mois après l'infection. - Les taux d'IgG contre la protéine S ont augmenté du jour 1 au jour 28, les niveaux de pointe se sont maintenus jusqu'à quatre mois après l'apparition des symptômes, mais ont fortement diminué après sept mois.
Vanshylla (2021) (89) *Prépublication* Cohorte prospective Allemagne Avril à décembre 2020	Concentrations d'anticorps dans un échantillon de personnes rétablies (n = 131 sur 963), détectées dans des échantillons sériques prélevés jusqu'à 10 mois après l'apparition des symptômes ou le diagnostic de confirmation. De ce nombre, 41,8 % des personnes convalescentes pour la COVID-19 avaient été hospitalisées et leur infection avait été confirmée par un test RT-PCR. Les concentrations d'IgG dans les anticorps neutralisants et dans la protéine S mesurées	La dynamique des anticorps effectuée entre quatre et dix mois après l'apparition des symptômes ou le diagnostic de confirmation, comme cela est indiqué dans l'étude, a permis d'obtenir les résultats suivants : - Les taux d'IgG contre la protéine S ont diminué entre un et quatre mois après l'infection, puis sont restés constants pendant le reste du suivi. - Alors qu'un mois après l'infection 86 % des personnes étaient encore positives à l'IgG contre la S1, ce pourcentage a atteint 73 % neuf à dix mois après l'infection. - La demi-vie de l'IgG a été estimée à 8,7 mois. Les niveaux et l'activité des anticorps neutralisants ont rapidement diminué au cours des deux premiers mois après l'infection, mais les fonctions neutralisantes des anticorps IgG purifiés, y compris contre la protéine S, ont été maintenues jusqu'à sept mois après l'infection. Ces résultats suggèrent

	par de multiples dosages biologiques ont permis de créer par modélisation une régression linéaire avec effets mixtes comprenant les estimations des demi-vies des anticorps.	un répertoire de cellules IgG et de lymphocytes B mémoires plus stable, ainsi que des niveaux stables d'IgG chez la majorité des individus qui se sont rétablis d'une infection.
Whitcombe (2020) (59) Série de cas Nouvelle-Zélande Printemps 2020*	Des échantillons de sérum tirés de tests RT-PCR effectués chez des convalescents ayant été atteints d'une forme bénigne ou modérée de la COVID-19 (n = 112) ont été recueillis. Des 80 des 189 échantillons prélevés à plusieurs reprises auprès de 50 participants ont permis d'avoir plus de détails sur les quatre à huit mois qui ont suivi l'apparition de l'infection. Une épreuve Triplex a été effectuée à l'interne pour analyser les échantillons et déterminer la présence des anticorps IgG, IgM et IgA et de leurs sous-catégories (IgG1, 2, 3 et 4) spécifiques à la protéine N, à la protéine S et au RBD, ainsi que des anticorps neutralisants.	La dynamique des anticorps dans les quatre à huit mois après l'apparition de l'infection par rapport aux niveaux de référence a permis de constater ce qui suit : - 99 % (79 sur 80) des prélèvements contenaient de l'IgG anti-RBD et 96 % (77 sur 80) contenaient de l'IgG anti-protéine S. - Les anticorps contre le RBD se sont maintenus dans 64 % (51 sur 80), tout comme les IgG1 contre la protéine S qui ont persisté dans 59 % (47 sur 80) des cas alors que les anticorps IgG3 contre la protéine S étaient encore présents dans 60 % (48 sur 80) des cas. - Moins de 30 % des participants ont continué à avoir des résultats positifs pour les anticorps contre la protéine N, avant que le niveau de ces derniers ne diminue rapidement. - 90 % (72 sur 80) des anticorps neutralisants étaient détectables. Pendant toute l'étude, ils étaient relativement stables et ont été corrélés avec l'IgA contre RBD (r ≥ 0,87 de Pearson). À l'aide d'échantillons de sérum appariés (n = 50 participants), on a pu estimer le taux de désintégration des anticorps neutralisants à 146 jours (IC à 95 % : 100 à 199), ce qui est considérablement plus court que les résultats prévus par les modèles de décroissance exponentielle (625 jours) ou de croissance-désintégration (425 jours).
Han (2021) (90) Cohorte prospective	Du plasma provenant de convalescents et de personnes en phase aiguë ayant été atteints d'une forme grave de COVID-19 confirmée	La dynamique des anticorps effectuée entre six et sept mois après l'apparition des symptômes a permis d'obtenir les résultats suivants : - Comparativement aux témoins sains, tous les anticorps spécifiques aux antigènes viraux

Chine Décembre 2019 à mars 2020	par test RT-PCR a été testé pour déterminer la présence d'IgG contre le RBD, la protéine S et la protéine N (n = 104). Le suivi a été effectué environ six à sept mois (médiane de 195 jours; intervalle de 188 à 201 jours) après l'infection. Des échantillons de sérum provenant de 31 témoins sains, sans suivi, ont également été inclus. Le taux d'anticorps a été mesuré à l'aide du test ELISA et par des épreuves de microneutralisation. Les corrélations entre les taux d'anticorps des convalescents et l'activité de neutralisation du virus ont été estimées par ANOVA.	mesurés étaient significativement plus élevés chez les personnes infectées qui en étaient au stade aigu et convalescentes. - Les anticorps spécifiques aux antigènes viraux ne présentaient pas de différences significatives selon l'âge ou le sexe des participants. - Les taux d'IgG contre le RBD et la protéine N étaient beaucoup plus bas pendant la convalescence ($p < 0,000$) que pendant la phase aiguë, mais aucune réduction significative n'a été décelée pour le taux d'IgG contre la protéine S. - Les réductions médianes pour le sérum de phase aiguë et celui de la convalescence ont été estimées à 15,90 % (EI, 7,83 à 30,91 %) pour l'IgG contre la protéine S, à 51,63 % (EI, 31,25 à 66,30 %) pour l'IgG contre la protéine N et à 58,98 % (EI, 48,15 à 68,25 %) pour l'IgG contre le RBD, - Des corrélations significatives ($p < 0,0001$) et fortes ont été effectuées entre l'activité de neutralisation du virus et les niveaux d'anticorps neutralisant avec les niveaux d'IgG contre le RBD, alors que des corrélations significatives ($p < 0,0001$) et modérées entre les niveaux d'IgG contre le RBD et contre la protéine N ont été notées dans le sérum de convalescence.
Choe (2021) (61) Étude transversale Corée du Sud Février à octobre 2020	Des échantillons de sérum provenant de personnes (n = 58) atteintes de COVID-19, dont 7 personnes asymptomatiques et 51 légèrement symptomatiques ont été prélevés huit mois après l'infection. Les niveaux d'anticorps ont été étudiés	Huit mois après l'infection, la dynamique des anticorps était la suivante : - 91,4 % des participants ont continué à avoir des résultats positifs pour les anticorps Ig contre la protéine N. - 25,9 % des participants ont continué à avoir des résultats positifs pour les anticorps Ig contre la protéine N. - 86 % des participants obtenaient des résultats positifs pour les anticorps IgG contre la protéine S alors que 69 % étaient positifs pour les anticorps IgG contre la protéine S1.

	grâce à de multiples essais immunologiques.	- 53,4 % des participants ont obtenu un résultat positif pour l'activité des anticorps neutralisants. On a confirmé que la détection des anticorps variait selon les méthodes d'immuno-essais utilisées.
Zhang (2020) (66) Série de cas Chine Janvier à juillet 2020	Des échantillons sériques ont été prélevés chez des convalescents (n = 54 sur 112) pour la COVID-19 entre 158 et 194 jours après l'apparition des symptômes et ils ont été comparés au niveau d'anticorps pendant la phase d'infection aiguë. L'infection chez tous les participants a été confirmée par un test RT-PCR et a indiqué que 77,7 % étaient des cas bénins et que 22,3 % étaient graves. Les taux d'anticorps IgG et IgM contre la protéine N et le RBD ont été mesurés à l'aide du test ELISA.	La dynamique des anticorps effectuée entre cinq et six mois après l'apparition des symptômes a permis d'obtenir les résultats suivants : - Tous les participants étaient positifs pour les anticorps contre la protéine N (catégorie d'Ig non précisée) et les niveaux des anticorps avaient diminué par rapport aux titres effectués pendant la phase d'infection aiguë. Tant les groupes atteints d'une forme bénigne de l'infection (médiane de 46,31 % (EI de 5,37 % à 68,96 %) que ceux qui avaient une forme grave (médiane de 46,02 % (EI de 11,01 % à 65,75 %) ont vu des réductions semblables dans les titres d'anticorps contre la protéine N.
Kwada (2020) (91) *Prépublication* Série de cas Japon Avril à novembre 2020	Des échantillons de sérum prélevés chez des travailleurs de la santé séropositifs à la suite d'une éclosion dans un hôpital, dont 42 sur 45 ont été confirmés par test RT-PCR et dont la gravité n'a pas été déclarée, ont fait l'objet d'un suivi mensuel jusqu'à sept mois après le diagnostic (n = 45). Les concentrations totales d'anticorps contre les protéines N et S ont été	La dynamique des anticorps effectuée environ sept mois après le diagnostic de l'infection a permis d'obtenir les résultats suivants : - chez 33 % (n = 15) des travailleurs, les taux d'Ig contre la protéine N ont augmenté de façon significative et se sont maintenus à ce niveau; chez 33 % (n = 16) d'entre eux, le taux qui avait augmenté à l'origine a ensuite diminué, alors que chez 31 % (n = 14) des travailleurs, ils n'ont augmenté que de peu et sont restés à ce niveau. - Les personnes qui avaient des taux élevés d'anticorps Ig contre la protéine N qui se sont ensuite maintenus, présentaient également des taux plus élevés d'anticorps contre la

	mesurées jusqu'à sept mois après l'infection (n = 45).	protéine S sept mois après le diagnostic. Les concentrations d'anticorps contre la protéine N n'ont montré aucune corrélation apparente avec le contact avec la COVID-19 ou avec les symptômes. - Les auteurs suggèrent que les niveaux d'anticorps pan-Ig contre la protéine N ne sont peut-être pas liés au rétablissement après la maladie.
Dehgani-Mobaraki (2020) (31) Cohorte prospective Italie Mars à janvier 2021	Des échantillons de sérum ont été prélevés à cinq points dans le temps, soit entre un et dix mois après le diagnostic chez des participants (n = 114) dont l'infection par la COVID-19 avait été confirmée par test RT-PCR. Les six échantillons de sang en série qui devaient être obtenus dans les 10 mois suivant l'infection (mois 2, 3, 5, 7, 8 et 10) n'ont pu être prélevés que chez 30 personnes. Dosages : Test MAGLUMI® 2019-nCoV IgM/IgG CLIA pour les cinq premiers tests et MAGLUMI® SARS-CoV-2 S-RBD IgG CLIA pour le dernier.	L'analyse effectuée sur les 30 personnes incluait différents points de données obtenus dans les dix mois qui ont suivi l'infection. - L'IgG contre la protéine S et RBD a été détecté dans 76,7 % des cas après 8 mois et dans 63,3 % des cas après 10 mois. - Dans l'ensemble, l'IgM était inférieur au seuil (> 83 %) alors que l'IgG était supérieur au seuil (> 63 %) de 1,10 pendant la période d'échantillonnage. Les niveaux de ces anticorps n'ont pas changé de façon significative pendant les points d'échantillonnage. Aucune différence n'a été notée en ce qui concerne la gravité, l'âge, le sexe, le groupe sanguin de type O ou le fait qu'il s'agissait d'un travailleur de la santé.
Pradenas (2020) (58) Cohorte prospective Espagne Avril à octobre 2020	Des échantillons de sérum ont été prélevés au moment du diagnostic, puis à trois et à six mois, chez 210 cas confirmés de COVID-19 par test RT-PCR (106 cas bénins et 104 hospitalisations). Seulement 28 participants sur 210 ont contribué aux données longitudinales. Les anticorps IgG contre le RBD, la protéine S S2, la	La dynamique des anticorps effectuée jusqu'à six mois après l'apparition des symptômes ou l'obtention du diagnostic, comme cela est indiqué dans l'étude, a permis d'obtenir les résultats suivants : - Plus de 30 jours après l'apparition de l'infection, l'on a estimé la demi-vie de l'IgG contre le RBD à 86 jours, celle de l'IgG contre la protéine S 2 à 108 jours et celle de l'IgG contre la protéine N à 59 jours. - Chez les participants atteints d'une forme bénigne ou asymptomatique de l'infection, les

	protéine N, ainsi que les concentrations d'anticorps neutralisant, ont été mesurées à l'aide du protocole ELISA et avec une épreuve de pseudovirus.	niveaux d'anticorps neutralisant étaient 10 fois inférieurs à ceux que l'on retrouvait chez les personnes atteintes d'une forme grave, et sont demeurés stables avec une désintégration négligeable jusqu'à six mois. - Comparativement aux participants ayant eu la forme bénigne ou asymptomatique de l'infection, les participants hospitalisés ont obtenu des titres d'anticorps neutralisant plus élevés jusqu'à la fin du suivi. Ces niveaux d'anticorps ont subi un déclin rapide initial qui s'est ensuite ralenti pour se stabiliser après 80 jours. - Les auteurs, en se fondant sur un seuil d'activité présumé de 1:250 pour prévenir la réinfection, suggèrent que les participants hospitalisés ont une plus grande capacité de neutralisation à long terme et de prévention de l'infection.
Hachim (2021) (67) *Prépublication* Cohorte prospective Hong Kong Avril à novembre 2020	Des échantillons de sérum d'enfants (n = 122) et d'adultes (n = 36) infectés, dont les infections ont été confirmées par test RT-PCR, ont été comparés à des échantillons de participants jamais infectés (n = 33). Parmi les échantillons, 36 % provenaient d'enfants et 25 % provenaient d'adultes asymptomatiques. Les échantillons de sérum ont été prélevés de 0 à 206 jours après l'apparition des symptômes (écart-type moyen de +/- 39±47 jours) chez les enfants alors qu'ils ont été prélevés de 24 à 123 jours après l'apparition des symptômes (écart-type moyen de +/- 54±20 jours) chez les adultes.	- Le modèle d'anticorps spécifiques obtenu pour les échantillons pédiatriques (n = 58 sur 122) jusqu'à six mois indique que les anticorps des deux protéines structurales (S1, S2, S2', M, E et N) et non structurales (NSP1, ORF3a, ORF3b et ORF7a ORF6, ORF8 et ORF10) étaient à un niveau stable ou avaient augmenté. - Les anticorps spécifiques à la protéine accessoire ORF7b ont diminué considérablement.

	Le suivi à long terme a été effectué de 58 à 122 jours jusqu'à 206 jours après l'apparition du symptôme. Seuls 16 échantillons sur 122 avaient des points de données entre quatre et six mois après l'apparition du symptôme et ont été utilisés pour orienter un modèle linéaire à effets mixtes. Les échantillons de sérum ont subi les tests LIPS et ELISA qui ciblent la protéine S, les sous-unités S1 et S2, la protéine N, la protéine E, la protéine M, alors que les anticorps spécifiques aux protéines non structurelles et accessoires, soit les protéines NSP1, et aux ORF ont été mesurés.	

AIM = marqueur induit par activation, ELISA = technique de dosage d'immunoabsorption par enzyme liée, protéine E = enveloppe, Ig = anticorps immunoglobulines, LTE = lettre, LIPS = dosage du système d'immunoprécipitation de la luciférase, protéine M = membrane, protéine N = nucléocapside, ORF = cadre de lecture ouvert, S = protéine de spicule ou Spike, RBD = domaine de liaison du récepteur

REVUE DE LA LITTÉRATURE

Les revues indiquées présentent des sommaires des données connues sur les marqueurs d'immunité à long terme disponibles entre juin et décembre 2020. Les études incluses dans ces revues comprennent également des recherches préliminaires sur les résultats immunitaires pertinents obtenus moins de 6 mois après le diagnostic initial de COVID-19.

Tableau 4 : Revue systématique et revue rapide concernant l'immunité (n = 4)

STUDY	METHOD	KEY OUTCOMES
Arkhipova-Jenkins (2021) (5) *nouvelle*	Une revue rapide qui vise à synthétiser les données probantes sur la prévalence, les taux et la durabilité	- Les données probantes indiquent que la plupart des adultes développent des taux détectables d'anticorps (c.-à-d. IgM, IgG et anticorps neutralisants) qui culminent entre 20 et 30 jours après l'apparition des symptômes.

Revue rapide en direct S.O. Mars 2021*	des anticorps détectables après l'infection par le SRAS-CoV-2 afin de déterminer si les anticorps contre le SRAS-CoV-2 confèrent une immunité naturelle. La documentation pertinente diffusée entre le 1er janvier et le 15 décembre 2020 a été incluse dans la revue. 444 études d'observation ont été incluses dans la revue.	- La durée estimée était de 115 jours pour l'IgM, de 120 jours pour l'IgG et de 140 jours pour l'IgA. - La plupart des adultes ont produit des anticorps neutralisants (à 99 % d'anticorps neutralisants, 95 % d'IgG et 80 % d'IgM) qui ont persisté plusieurs mois après l'infection. - L'âge, la gravité de la maladie et la présence de symptômes peuvent être associés à des niveaux d'anticorps plus élevés (éléments de preuve de bas niveau). - Certains adultes n'ont pas développé d'anticorps après l'infection par le SRAS-CoV-2, pour des raisons qui ne sont pas claires. - La qualité des éléments de preuve résumés a été jugée être de faible à modérée.
Poland (2020) (1) Examen S.O. Octobre 2020*	Cet examen porte sur ce que l'on savait au sujet des réponses immunitaires humorales et cellulaires humaines au SRAS-CoV-2 à la date de la recherche, soit le 24 septembre 2020.	- L'article examine l'immunité humorale et cellulaire et présente certaines données sur la cinétique et la durabilité de la réponse des anticorps et la corrélation avec la réponse des lymphocytes T. De nombreuses incohérences ont été relevées lors de la recherche initiale. - Les lacunes dans les connaissances incluent des études de grande qualité sur la durée de la protection par les anticorps neutralisants et une bonne compréhension de la façon dont les mesures immunologiques sont utilisées pour établir une corrélation avec la protection.
Post (2020) (63) Revue systématique S.O. Juin 2020	Revue systématique sur la réponse des anticorps au SRAS-CoV-2 à la date de la recherche, soit le 26 juin 2020. 150 documents ont été inclus. Les critères d'inclusion comprenaient un suivi de plus de 28 jours et les titres des anticorps mesurés. L'auteur a indiqué une forte variabilité entre les études et plans d'étude.	- Des incohérences dans les corrélats d'anticorps ont été observées dans l'ensemble de la littérature. - L'IgM (séroconversion de 4 à 14 jours, pic à 2 à 5 semaines et baisse jusqu'à des niveaux indétectables autour de 6 semaines) a été systématiquement détecté avant l'IgG. - L'IgG (séroconversion de 12 à 15 jours, pic à 3 à 7 semaines, plateau jusqu'à au moins 8 semaines avec le suivi le plus long (12 semaines) pendant lequel les anticorps étaient encore détectés). - L'IgA, qui est rarement étudiée, a montré une séroconversion entre 4 et 11 jours, avec des valeurs aberrantes à 24 jours. - Les anticorps neutralisants ont été détectés de 7 à 15 jours après l'apparition des symptômes, ont atteint un sommet entre 14 et 22 jours, avant de diminuer pendant 6 semaines. Au jour 39, 79 % des participants à l'étude avaient un faible taux d'anticorps neutralisants alors que 3 % avaient encore un taux élevé. Les personnes qui avaient été atteintes d'une

	Voir à l'annexe 2 pour un graphique sur la cinétique des anticorps au fil du temps.	forme bénigne présentaient des anticorps moins neutralisants. - Les études sur les animaux montrent des résultats initiaux prometteurs en ce qui concerne l'immunité protectrice; toutefois, les études étaient de petite envergure et de courte durée. Des études ont démontré des corrélations avec la gravité de la maladie. Une relation inverse avec la charge virale n'a pas été déclarée de façon uniforme et aucun lien avec la redétection n'a été signalé. Les études ne peuvent pas parler d'immunité durable.
Shrotri (2021) (74) Revue systématique S.O. Juin 2020	Une revue systématique qui évalue de façon critique et synthétise la documentation publiée et préimprimée de janvier 2020 au 26 juin 2020 sur l'immunité induite par les lymphocytes T après l'infection à SRAS-CoV-2. 61 publications ont été incluses dans cette revue.	- Les cas d'adultes symptomatiques montrent constamment une réduction du nombre de lymphocytes T périphériques pendant la phase d'infection aiguë, ce qui correspond positivement à une augmentation de la gravité de la maladie, de la durée de la positivité de l'ARN et du fait que le virus ne survit pas. Les réductions relatives observées dans les lymphocytes T CD4+ et CD8+ variaient. - Les cas asymptomatiques et pédiatriques affichent des nombres préservés de lymphocytes T. - Les personnes ayant eu des formes graves ou critiques de COVID-19 ont développé des réactions de lymphocytes T spécifiques d'un virus plus robustes. Des concentrations élevées de cytokines pro-inflammatoires, d'interleukine-6 (IL-6), à un degré moindre, d'interleukine-10 (IL-10) et de facteur alpha de nécrose tumorale (TNF-α) ont été identifiées dans les cas graves. - Le suivi longitudinal (14 à 44 jours après l'infection) a suggéré le rétablissement des sous-ensembles de cellules T ainsi que le rétablissement clinique et la clairance virale. - Le lymphocyte T mémoire et son effet sur les personnes qui débutent leur convalescence (jusqu'à environ 3 mois après l'apparition des symptômes) ont été démontrés contre les antigènes viraux S, M et N. La portée et l'ampleur de la réponse des lymphocytes T étaient généralement plus importantes chez les personnes qui se rétablissaient de formes graves de l'infection. L'activité productrice de cytokine des lymphocytes T CD 8+ spécifiques aux protéines M et N affichait de plus vastes fonctions que celles ciblant la protéine S chez les personnes atteintes d'une forme bénigne

		de l'infection. Les lymphocytes T CD3+ étaient moins nombreux dans les formes graves de l'infection. - Les lymphocytes T à réaction croisée chez les personnes n'ayant pas été exposées à d'autres coronavirus ou ayant déjà été exposées à d'autres formes de ce virus (p. ex., souches de coronavirus saisonniers prépandémiques, SRAS-CoV-1) ont souvent été détectés et semblent être présents à long terme puisque dans certains cas, ils sont restés dans le sang jusqu'à 17 ans après l'infection. Les lymphocytes T à réaction croisée ciblant les protéines virales S et N sont ceux qui ont été détectés comme cellules immunitaires à réaction croisée. L'impact de la réactivité croisée sur les infections par le SRAS-CoV-2 demeure en grande partie incertain, mais on suppose qu'il est faible en raison de la variabilité des épitopes du coronavirus.

Méthodologies :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Trois recherches distinctes ont été effectuées pour déterminer les citations relatives à la réinfection, aux infections ayant percé et à l'immunité. Les termes de recherche utilisés comprenaient : TERMES ASSOCIÉS À LA RÉINFECTION (reinfect* ou re-infect* ou recurren* ou re-positive).
TERMES associés à RÉVOLUTION (efficacy OU effective* OU breakthrough) dans les études qui utilisent la balise Vaccine
TERMES ASSOCIÉS À L'IMMUNITÉ (month* ou longitudinal) dans les études qui utilisent la balise Immunology.
La présente revue contient des recherches publiées jusqu'au 9 avril 2021.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

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ANNEXE 1 :

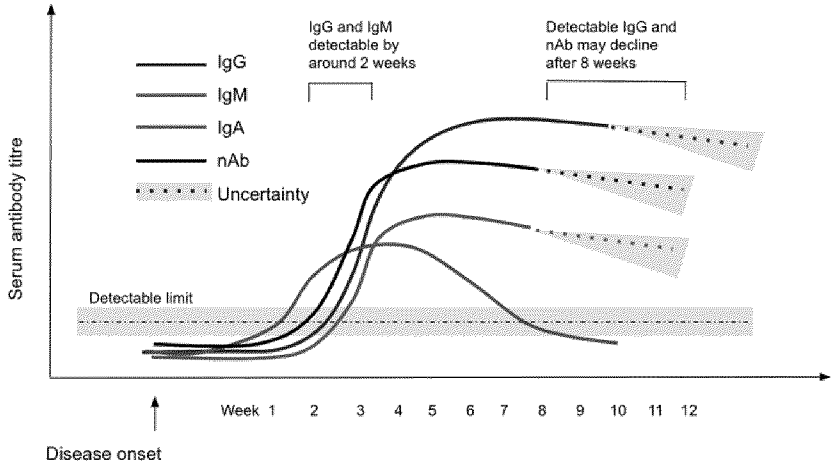

Figure 3 Post (2020) (63)

Emerging Evidence on COVID-19

Evidence Brief on the Risk of COVID-19 and Non-Professional Sports

Introduction

What evidence is available on the risk of transmission of SARS-CoV-2 from playing non-professional sports and has research been conducted on modified play to mitigate the transmission risk?

Governments and health authorities across the globe implemented lockdown and social distancing practices in an effort to mitigate SARS-CoV-2 spread within populations. These included closing of workplaces, schools, and other public venues, as well as the cancelling of sporting events and games. As public health measures to curb the pandemic are cautiously relaxed, many consider retuning to physical activity and sports. This evidence brief provides an overview of the published literature on SARS-CoV-2 transmission risks associated with playing non-professional sports up to August 18, 2020.

Key Points

- Two published investigations of SARS-CoV-2 outbreaks associated with recreational physical activity appear in the literature (Table 1). These transmission events were linked to indoor fitness facility settings and aerobic activities (one a Zumba class, the other playing squash) and occurred in March 2020.
- An additional 10 transmission events related to sports or exercise were identified in a COVID-19 Superspreading Events database (Swinkles, 2020).
    - Several transmission events have been reported in gyms associated with indoor classes, bonspiels, square dancing, and football. Many of these are considered high contact activities within the reporting news articles.
    - The actual sources of infection and transmission within these clusters arising from team sports events have not been identified. For example, in two curling bonspiels and one road hockey game, social activities also occurred before and/or after the game. Similarly, the source of an outbreak in a soccer team in Japan that is on-going has not been identified.
    - Activities such as running do no appear to be at high risk of transmission, a single cluster between running partners was identified.
- Computer simulations of SARS-CoV-2 aerodynamics concluded that respiratory droplets will ride a runner's slip steam and thus, one should avoid running or walking directly behind another person (Blocken, Malizia, van Druenen, & Marchal, 2020).

- Wong et al., report findings from two independent investigations applicable to participation in sports and SARS-CoV-2 transmission (Wong et al., 2020).
    - Analysis of professional soccer game video footage estimates a semi-professional soccer player spends on average 20% of the game within close contact of another player.
    - Experimental simulations of physical activity among athletes found individuals who wore a face mask recorded higher heartrates and perceived exertion compared to those not wearing a face mask.
- Helpful strategies to reduce the risk of SARS-CoV-2 transmission during sports can be found in World Health Organization (WHO) guidance documents, risk assessment tools, and published commentaries (Table 2).
    - WHO guidance outlines key considerations, risks, and mitigation based on the type of sport (i.e. the level of contact among players), size of the event, indoor/outdoor locations, venue facilities, demographics of competitors and spectators, and risk communication, and provides guidance on managing SARS-CoV-2 cases that may be identified at a sporting event (WHO, 2020a). The document is to be used in conjunction with the Key Planning Recommendations for Mass Gatherings in the Context of the Current COVID-19 Outbreak (WHO, 2020b), and Mass Gathering COVID-19 Risk Assessment Tool – Sports Events (WHO, 2020c).
    - Commentary by Carmody et al. proposes a risk assessment matrix to support decision makers on restarting sports events that is based on WHO guidance and consideration of local community transmission of SARS-CoV-2 (Carmody, Murray, Borodina, Gouttebarge, & Massey, 2020).
    - A technical note by Blocken et al. considers the process of reopening indoor exercise facilities while minimizing SARS-CoV-2 transmission. Based on the application of limited indirect evidence, the authors conclude deep exhalation and inhalation from exercise can increase respiratory aerosol emission and inhalation. As such, they advocate for the use of displacement (vs. mixing) ventilation systems, HEPA filters, and limited occupancy within indoor facilities where physical exercise is frequent (B. Blocken et al., 2020).
    - Guidance for physical educators at Chinese schools reinitiating after the COVID-19 lockdown, proposes various strategies, such as the use of drills and staggered physical activity periods, that can be adopted by non-professional sports teams to mitigate transmission risks.

Overview of the Evidence

Publications that directly report on SARS-CoV-2 and non-professional sports is sparse. As such, we applied the available evidence from indoor sports facility settings (i.e. gyms) and professional sports to deduce transmission risks. Fifteen relevant publications and guidance documents on physical activity and sports informed this review.

Among the included publications are two detailed outbreak investigations and 10 reports of SARS-CoV-2 outbreaks associated with sports or exercise from the COVID-19 Superspreading Events Database (Table 1). Although outbreak investigations can be sensitive to high risk of bias the two published investigations appear to have been carefully conducted, with robust case finding and contact tracing activities that minimize sampling bias. The Superspreading Events Databased includes COVID-19 case clusters (n>5 cases) identified from national COVID-19 dashboards and news articles, none of which provide detailed information about the transmission event. As such the information included in this database is noted to be incomplete and imperfect, and highly sensitive to multiple biases and confounders.

The observational analyses scored video footage of a soccer game and has moderate risk of investigator bias, but the reported physiologic measurements were less sensitive to such bias; it simply compared heart rate and rate of perceived exertion in those who wore masks or not. The computer simulation study to observe air flow dynamics in runners is largely theoretical and would have a low risk of bias.

The literature on strategies to mitigate infection transmission risk in non-professional sports is largely limited to commentaries and expert guidance (Table 3). This literature is grounded in available public health evidence and adopts strategies commonly used to minimize SARS-CoV-2 transmission in public settings.

Overall, there remains considerable knowledge gaps in this literature, as such current guidance largely depends on the general principles of risk assessment and mitigation and COVID-19 public health guidance.

CONTENTS

OUTBREAKS ASSOCIATED WITH PARTICIPATION IN SPORTS/PHYSCIAL ACTIVITY

There are few transmission events associated with sports in the current COVID-19 literature. This may largely be due to the public health measures that stopped most sporting activities since early in the pandemic. With the exception of the Zumba outbreak describe by Jang et al., other outbreaks lack detailed investigation or were also associated with social activities before or after the sports activity that make it difficult to attribute transmission to participation in the sport itself.

The outbreak currently on-going within a Japanese soccer team underscores how SARS-CoV-2 infections can travel within a team, and infection control guidelines and precautions should be part of return to sports plans (Swinkles, 2020).

Table 1. Twelve Outbreaks of COVID-19 Linked to Sports and Exercise

Reference	Publication Title	Key Outcomes
(Jang, Han, & Rhee, 2020)	Cluster of Coronavirus Disease Associated with Fitness Dance Classes, South Korea	Summarizes the investigation of 112 COVID-19 cases associated with Zumba classes at 12 different fitness/sports facility locations in South Korea. The primary attack rate was estimated to be 26.3% (95% CI 20.9%–32.5%) and the secondary attack rate was 4.10% (95% CI 2.95%–5.67%). The initial transmission event is assumed to have occurred among fitness instructors at a workshop, where eight of the twenty seven attendees tested positive for SARS-CoV-2. Over the following weeks the infection transmissions occurred among dance class attendees, household contacts, colleagues and acquaintances of instructors and students. 50.9% (n=63) of cases were the result of transmission from instructors and 52 cases were identified among to dance class attendees. The instructors and students met only during classes, which lasted for 50 minutes 2 times per week, and did not have contact outside of class. No cases were observed among Pilates and yoga class participants, also taught by an infected instructor in the same sports/fitness facility setting. These observations suggest the lower intensity of Pilates and yoga did not lead to the same transmission effects as those that occurred during the dance classes, whether that is due to less respiratory droplets or less air movement was not determined.
(Brlek, Vidovič, Vuzem, Turk, & Simonović, 2020)	Possible Indirect Transmission of COVID-19 at a Squash Court, Slovenia, March 2020: Case Report	A SARS-CoV-2 case cluster (n=6) linked to playing squash at a sports venue in Maribor, Slovenia is described. The index case (person A), assumed to have acquired the infection during travel to Italy developed symptoms (i.e. tiredness and fatigue) during the game of squash. Epidemiological investigations link additional cases (four confirmed and one suspect) to the same squash hall and change rooms. Case B had direct contact with the index case, as they spent time in the change room and played a squash match together. Case C and D do not report direct contact with the index case (or Case B), and are epidemiologically linked through the use of change rooms and playing in the same squash court within 20 minutes of case A and B. The remaining two cases, Case E and Case F, arrived at the sports facility approximately 1.5 hr after index case's departure. This pair of cases spoke with Case C and D outside the squash court, used the same change room and the same squash court.

		None of the cases shared sport equipment or had contact with the facility staff. No additional cases were identified.
(Swinkles, 2020)	SARS-CoV-2 Super Spreading Events Around the World	An additional 10 sports events linked to transmission have been reported in news articles, as listed in the database of COVID-19 Superspreading Events (SSE) from around the world. This information source often lacks details of the outbreak or activities that likely resulted in transmission: - 2 curling bonspiels (multiday tournament and social) in Edmonton, Canada March 14-15. 24/72 attendees developed COVID-19 and in Maryland USA March 27, ~20 cases, - Outdoor ball hockey and they "shared a drink" Racine, QC, Canada, Feb 29. 15/21 were infected with COVID-19 - Running, an infected marathon runner transmitted the virus to his running partner, in Italy, February, - Soccer team, Sagan Tosu J1, outbreak, Japan August. 11 players and coaches infected to date, - Square dancing, Lynnwood, WA, USA, February, there was little testing and no investigation. Only anecdotal information that some who were tested were COVID-19 positive (>15 people), - Two gym and one table tennis school outbreak is recorded in Japan without further details and 1 gym outbreak is recorded in Singapore.

TRANSMISSION RISK WHEN PLAYING SPORTS

Two studies provide evidence applicable to COVID-19 transmission risk during sports. One study was a video analysis of a professional football (soccer) game. It identified there was close player-to-player contact for ~19/90minutes game and approximately 52 episodes of high risk interactions (Wong et al., 2020). The use of face masks during exercise was studied under laboratory conditions and this small study concluded heart rate and perceived exertion were significantly elevated after six minutes of moderate exercise with a mask compared to not wearing a mask (Wong et al., 2020).

The other study examined aerodynamic dispersion of droplets when someone is running to assess the transmission risk if an individual is following an infected runner (Bert Blocken et al., 2020). If the individuals are running or walking fast even at 1.5 meters apart there is some risk of infectious particle exposure if the trailing person is directly behind the leading person (positioned in the slipstream). This exposure can be avoided if two runners are beside each other (1.5 meters apart) or are staggered.

Table 2. COVID-19 Transmission Risk When Playing Sports

Reference	Publication Title	Key Outcomes
(Wong et al., 2020)	Impact of the COVID-19 Pandemic on Sports and Exercise.	Video footage of professional Soccer players in Hong Kong was analysed to track players' time engaged in close body contact and frequency of behaviours that increase infection transmission risk. The analysis finds the average duration of close contact between players to be a mean of 19 minutes (range 5.9-35.5)/ 90 minute game, and each player engaged in an average of 52 episodes of increased infection transmission risk behaviour (touching eyes, mouth or nose), during a 90 minute game. The physiological effects of wearing a mask during play was also examined in laboratory settings. The heart rate and rate of perceived exertion (RPE) of participants wearing a face mask were significantly elevated compared to those without a face mask after 6 minutes of moderate exercise (heart rate of 128 beats per minute and 12.7 RPE when masked, heart rate of 124 beats per minute and a RPE of 10.8 when unmasked). Values were statistically significant, but they may not be biologically significant. The investigation concludes infection transmission risk to be high among players during a game, even without spectators. Donning of face masks during physical exercise increases the physiological burden of the body, with implications for those with multiple underlying comorbidities.
(Bert Blocken et al., 2020)	Towards Aerodynamically Equivalent COVID19 1.5 m Social Distancing for Walking and Running	Computer Fluid Dynamics study informed by previous data on droplet dispersion around a runner takes into account the potential aerodynamic effects introduced by individual movements (e.g., walking fast, running and cycling) on droplet travel distance. The study investigates whether a leading infectious person standing still and moving nearby a second susceptible person at a distance of 1.5 meters or more can pose any infection transmission risk. Although particle exposure is negligible when two people are standing 1.5 meters apart, if the individuals are running or walking fast even at 1.5 meters apart there is some risk of infectious particle exposure. The study results suggest the greatest exposure to the trailing person occurs if they are directly behind the leading person (positioned in the slipstream). Substantial droplet exposure risk reduction can be achieved by 1) avoiding to walk or run in the slipstream of the leading person,

		2) keeping the 1.5 meters distance in staggered or side by side arrangement, or 3) by keeping social distances greater than 1.5 meters when moving fast or running.

STRATEGIES AND GUIDANCE

The literature on strategies to mitigate infection transmission risk in non-professional sports includes two WHO interim guidance documents, two risk assessment tools and several expert commentaries (Table 2). Considerations of local SARS-CoV-2 transmission and case rates, risk assessments to identify potential levels of contact among players, limiting the number of players, prioritizing outdoor play and social distancing, prohibiting the shared use of sports equipment, enhanced cleaning and disinfection practices, and screening of participants to effectively identify and isolate SARS-CoV-2 cases are overarching strategies. The WHO recommends refraining from direct contact sports as they increased risk of direct exposure to infection.

Two tools for assessing COVID-19 risk in sports among spectators and participants were identified. The WHO Mass Gathering COVID-19 Risk Assessment Tool - Sports Events, provides a decision tree, risk evaluation, risk mitigation, decision matrix, and risk communication that mass sports event organizers and host countries can apply to determine infection spread associated with an event. An alternative risk matrix is presented by Carmody et al. This risk assessment tool is based on WHO interim guidance, applies local community transmission rates, and mitigation measures to calculate residual risk associated with various professional sports. The commentary by Timpka note the importance of trust, that if players think that other players are not going to abide by COVID-19 restrictions, they are also unlikely to adhere to them. This points to the importance of an excellent communication plan.

Some indirect evidence predating SARS-CoV-2, as presented in the technical note by Blocken, suggest physical activity can increase the emission and inhalation of respiratory aerosols with the potential to cause infection (B. Blocken et al., 2020). Although much of the evidence on aerosol transmission of SARS-CoV-2 is currently evolving the available evidence and outbreaks do point to elevated risks of infection transmission when performing intense physical activity in crowded indoor settings. This evidence should be weighted appropriately when considering the return to non-professional sports in indoor settings.

Table 3. Strategies to Reduce COVID-19 Transmission During Sports

Reference	Publication Title	Key Statements
(WHO, 2020a)	Considerations for Sports Federations/Sports Event Organizers when Planning Mass Gatherings in the Context of COVID-19	Provides key considerations and risk factor mitigating techniques. Recommendations are based on the consideration of contact and transmission risk within a sport, size of the event (i.e. number of attendees), the location of the event, venue facilities, the demographics of participating players, and the adoption of relevant public health guidance.

		Recommendations include daily health check for competitors, distance (at least 1 meter) separation of competitors, officials, spectators and support staff, thorough disinfection and cleaning, the prohibition of sharing equipment, utilization of outdoor venues where possible, the use of designated and physically separated seating and isolation areas to support potential case management and contact tracing activities and effective risk communication and advising individuals at increased risk of SARS-CoV-2 mortality and morbidity to not attend the sports event. Interim guidance, April 14, 2020
(WHO, 2020c)	WHO Mass Gathering COVID-19 Risk Assessment Tool – Sports Events	A formal risk assessment and risk communication tool to be used in conjunction with the, Considerations for Sports Federations/Sports Event Organizers when Planning Mass Gatherings in the Context of COVID-19, document (above). Updated July 10, 2020
(WHO, 2020b)	Key Planning Recommendations for Mass Gatherings in the Context of COVID-19	Provides guidance to host governments, health authorities and national or international organizers of mass gatherings on containing risks of COVID-19 transmission associated with mass gathering events. Interim guidance, May 29, 2020
(Carmody et al., 2020)	When Can Professional Sport Recommence Safely During the COVID-19 Pandemic? Risk Assessment and Factors to Consider	Presents a risk assessment matrix to support decision makers on restarting professional sports when COVID-19 public health measures begin to relax. In addition to leveraging the considerations outlined by WHO guidance (i.e. WHO Guidelines for Mass Gatherings, Considerations for Sports Events, and WHO Sporting Risk Assessment) the risk assessment takes local community transmission of COVID-19 into account. The basic approach is to assess risk, then consider mitigation measures, and then calculate residual risk. Based on the application of this risk assessment, professional soccer is identified to be of high residual risk, while professional golf is considered low residual risk, if appropriate infection mitigation measures are applied. Based on the application of this risk matrix the authors suggest overall risk of restarting sporting events can be low, if local community transmission is low and adequate risk mitigation

		procedures are in place. Professional soccer is assessed at high residual risk, while professional golf is considered to be of low residual risk.
(Timpka, 2020)	Sports Health During the SARS-Cov-2 Pandemic	Written prior to release of WHO guidelines, this commentary states sports organisations should address the athletes and coaches needs, while complying with social distancing and regional public health guidance on COVID-19, when developing a pandemic response strategy. Highlights the importance of trust: "If sportspeople do not believe that most others are going to play by the temporary restrictive rules, they are unlikely to adhere to them. The authors suggest sports activities should be performed outdoors in small groups and physical contact among players avoided as much as possible. Virtual competitions encouraged among athletes of individual sports.
(B. Blocken et al., 2020)	Can Indoor Sports Centers be Allowed to Re-open During the COVID-19 Pandemic based on a Certificate of Equivalence?	Identifies evidence (predating the emergence of COVID-19) that found deep exhalation (as with physical exercise) produces higher concentrations of aerosols and deep inhalation increases exposure to aerosols. Based on this the authors identify the need for good ventilation (displacement of air from floor to ceiling better than mixing), HEPA filters, applying public health measures to visitors and staff, cleansing surfaces for fomites and ensuring no contact activities. The authors also proposed the idea of a Certificate for indoor sports centers prior to reopening.
(Chen et al., 2020)	Returning Chinese School-Aged Children and Adolescents to Physical Activity in the Wake of COVID-19: Actions and Precautions	Summarizes precautions that can be taken by school administrators, physical educators and parents for physical activity as schools in China begin to come back post COVID-19 lockdown that include: - Encouraging proper social distancing (at least 1 meter), - Staggering time tables to avoid crowding, - Making hand-washing or hand sanitizer stations readily accessible, - Sanitizing all surfaces and equipment regularly, - Restricting physical activities that involve body contact and the sharing of sports equipment and water bottles.
(Peter, 2020)	Return to Play After COVID-19: A Sport Cardiologist's View	The article outlines the need for a cardiac assessment prior to a return to sports for adult COVID-19 cases noting sub-clinical cardiac injuries can occur following SARS-CoV-2 infection.

(Dores & Cardim, 2020)	Returning to Play After Coronavirus Infection: A Perspective From Pediatric Cardiologists	The article outlines the need for a cardiac assessment prior to a return to sports for pediatric COVID-19 cases following SARS-CoV-2 infection, as sub-clinical cardiac injury may be present post infection.

Methods

All of the literature on COVID-19 has been compiled and organized by the Emerging Science Group of the Public Health Agency of Canada since the beginning of the outbreak. This involves a daily scan of the literature for all published and pre-published articles. Searches to retrieve relevant COVID-19 literature are conducted in PubMed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, and Research Square. These are cross-referenced with the literature on the World Health Organization COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier, and Wiley. The daily summary and full scan results are maintained in a RefWorks database and a searchable Excel file. Each article is tagged using various foci to identify the focus of the article (e.g., epidemiology, clinical data, therapeutics etc.). Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. The search terms included in this review were sports, exercise and physical fitness/activity. Each potentially relevant reference was analyzed to confirm its relevance and data was extracted into the review. This review contains research published up until August 18, 2020.

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Emerging Evidence on COVID-19

Rapid Review on the Risk of COVID-19 Outbreaks in the Workplace

Introduction

What is the evidence on COVID-19 clusters associated with the workplace, characteristics of workplace settings and factors that may increase the risk of SARS-CoV-2 transmission, and evidence of successful infection prevention and control measures in the workplace?

Sub-Questions:

Is there evidence that employer provided accommodations result in clusters of COVID-19 cases?
Is there evidence that transportation or commuting to the workplace results in clusters of COVID-19 cases?
Is there evidence of work-related travel resulting in clusters of COVID-19 cases?
Is there evidence that social gatherings of co-workers have resulted in COVID-19 clusters?

Mitigation of the current pandemic has involved social-distancing policies that have had an important impact on workplaces (Corrin, 2020). This includes closing workplaces, encouraging telework, changing business flow to minimize individual employee contacts with others and developing enhanced infection prevention and control procedures to reduce the risk of SARS-CoV-2 transmission. The definition of workplace in this review is meant to be all encompassing, thus workplace ranges from, but may not be limited to office, production, retail, service, and public services. Transmissions within healthcare workplaces were not included in this review. In addition to transmission occurring directly at a workplace, evidence was sought for work-related transmission situations including employer provided accommodation or transportation, commuting, work-related travel, and social gatherings of co-workers. This evidence brief identifies and summarizes literature until August 21, 2020.

Key Points

- Outbreaks have been associated with many types of workplaces and occupations (Table 1).
    - In addition to the known risk to healthcare professionals, the occupations most at risk of SARS-CoV-2 infection include drivers and transport workers, service and sales workers, food industry, personal care occupations, food production workers, preschool occupations, community and social services occupations (e.g. social workers, counselors), construction and related trades occupations, and public safety workers (e.g. correction officers, police, firefighters).

  - The majority of these require workers to have frequent contact with clients, work on customers' premises, or in public spaces. Many of these occupations do not allow employees to work from home.

- Workplace clusters have occurred across a wide range of workplaces and circumstances that resulted in transmission (Table 2).
  - Most of the workplace clusters were traced to an asymptomatic or very mild symptomatic index case.
  - Thirty-seven publications describe one or more transmission events considered to have occurred in a workplace involving workers broadly captured under the categories: office environment, meat processing facilities, other factories, migrant work, fitness centers, ships, other service related occupation, and transportation (Table 2).
  - Eight COVID-19 clusters in workplaces with employer-provided accommodations were identified (Table 3). Shared accommodation results in close contact of workers for long durations of time.
  - There is limited evidence on COVID-19 clusters resulting from transportation or commuting to the workplace (Table 4). Shared transportation to and from the workplace was determined as a risk factor for exposure to SARS-CoV-2 in outbreaks at meat processing facilities.
  - COVID-19 clusters resulting from work-related travel were identified in five publications (Table 5). Risk factors identified related to the proximity and length of time secondary cases spent with the primary cases (e.g. sitting at the same table during a meal or meeting).
  - Three COVID-19 clusters resulting from social gatherings of co-workers outside of the workplace were identified (Table 6). In all three scenarios, the infections acquired during the social gathering of co-workers resulted in additional infections in the workplace.
- Risk factors for SARS-CoV-2 infection identified in the workplace include difficulties adhering to physical distancing, lack of hand hygiene, poor ventilation/air circulation design, and crowded working, transportation and/or accommodation conditions (Tables 1-6).
  - The main facilitators for SARS-CoV-2 transmission in an office setting include close contact, duration of interaction, shared common areas, and work-related travel.
  - Socio-demographic factors and occupation were examined to explore determinants of SARS-CoV-2 exposure (Table 1). Being female, a visible minority, and being in a low-income bracket were associated with employment in occupations associated with significantly higher risk of exposure to COVID-19 which typically do not allow working from home and involves working in close proximity to other people. Conversely, increasing age and higher education was associated with lower risk of exposure occupations.

- The risk factors for infection in meat processing facilities were identified as difficulties with physical distancing, prolonged close contact with coworkers for long periods of time, hand hygiene, shared accommodation, shared transportation to and from work, and frequent community contact with fellow workers. These risk factors were also identified for outbreaks on ships.
- In addition to SARS-CoV-2 activity in the community, the activities a worker engages in outside of the workplace will determine the individual risk that a person brings to the organization.
- Several studies report increased risk of exposure to SARS-CoV-2 proportional to the number of contacts related to the workers job. For example grocery store employees with direct customer exposure were five times more likely to test positive for SARS-CoV-2 (OR 4.7; 95% CI: 1.2-32.0). A similar finding was reported for firefighters and paramedics in a second study.
- Shared accommodation or facilities (e.g. bathroom) and a lack of preventative measures (e.g. face mask) have been suggested to contribute to several outbreaks in shopping malls, retail stores, bars, nightclubs, restaurants, concerts, and overnight camps.
- Outbreaks are more likely to occur in an indoor environment OR 18.7 (95%CI 6.0-57.9).

- Two risk assessments explored the attributes of workplaces and potential for SARS-CoV-2 transmission.
  - In a risk assessment a 1% increase in the density of super spreading businesses (SSB - based on the frequency, duration, and square footage of businesses pre-pandemic) equated to a 5% increase in cases. The most common SSBs were full service restaurants, limited service restaurants, and hotels/motels.
  - The potential health risks of SARS-CoV-2 in sewage to wastewater treatment plant workers (WWTPs) was investigated using a quantitative microbial risk assessment (QMRA). Duties close to sewage tanks were considered high risk of exposure and protection such as face mask, eye protection, and/or face shields were recommended.
- Strategies to reduce the risk of SARS-CoV-2 transmission in the workplace were identified in 21 publications (Table 7).
  - Successful prevention strategies included limiting social contact (restricting activities in the workplace, cohorting or staggering employees, and telework), policies on exclusion of sick workers from the work environment, providing workplace guidelines, and provision of personal protective equipment.
  - Monitoring strategies explored the mode (worker or environmental sampling) and frequency of sampling for effective identification of transmission or circulating SARS-CoV-2 in the workplace and how the level of SARS-CoV-2 in the community impact sampling strategies.

- Lifting public health measures were explored to minimize a resurgence, while allowing the economy to slowly re-open.
- Management of migrant workers, particularly their movement from place to place was discussed in three publications from China and India. Strategies included screening and quarantine protocols to limit the importation of SARS-CoV-2 into an unaffected area.

Overview of the Evidence

Seventy-seven publications pertaining to the risk of COVID-19 outbreaks in the workplace and risk reduction in the workplace were identified and included in this review. Of these, 33 are preprints and have not completed the peer-review process. Observational study designs can be affected by several categories of biases including reporting, information, and selection bias which can bias the data and conclusions of a study (Murad, Asi, Alsawas, & Alahdab, 2016). A formal risk of bias assessment is outside of the scope of this rapid review. Bias ratings are based on the study design where observational studies are considered to have moderate to high risk of bias depending on the design. For observational study designs, this places large prospective cohorts at the top as the design has the potential to have a low risk of bias and high confidence in the results and case reports are considered very weak confidence in the results.

The largest proportion of research underpinning this review consists mainly of small epidemiological outbreak and cluster investigations, which generally have a high risk of bias due to their retrospective nature. Although there is a lot of variability in the completeness of the investigations and reporting, there is good consistency across these investigations which improves our confidence in the evidence.

Several ecological studies were captured; these studies are susceptible to a range of biases and ecological fallacy due to their inability to characterize within-group variability in exposures and confounders. Cross-sectional studies were used to provide a snap shot of individual risk factors and exposure to SARS-CoV-2, but cannot make inferences about causality. Prospective cohort design was used in two studies evaluating mitigation strategies in the workplace. The prospective cohort has a lower risk of bias than other observational study designs, although the two captured in this review had small sample sizes.

Predictive models and risk assessments do not predict a future reality, but rather present a range of plausible outcomes within the scenarios being studied. Their results are useful to compare different options as part of a decision-making process, however the results should be interpreted with caution as the models will vary on their assumptions and input values based on the epidemic period and region specific parameters used.

Due to the nature of the evidence in this review (observational studies and predictive models) and their associated biases, this rapid review provides weak evidence on the workplace conditions that lead to higher risk of SARS-CoV-2 transmission and risk reduction strategies. Based on the study designs of included studies there is low confidence that additional research will not change the conclusions of this review. The COVID-19 literature is evolving rapidly and this review should be periodically updated with new research.

CONTENTS

OCCUPATIONAL RISKS

Occupational risks associated with COVID-19 infection were identified in 20 publications (Table 1). These included two reviews and three risk assessments. The publications in this section focused on both occupations and attributes of those occupations that lead to higher or lower risk of transmission in the workplace.

- Across publications occupations identified as most at risk of SARS-CoV-2 exposure aside from healthcare professionals are listed below (Table 1). Healthcare workers (HCWs) are considered outside the scope of this review, however in papers looking at occupational risk factors, HCWs are frequently included in the analysis and results.
    - Transportation: drivers and transport workers, couriers, bus drivers
    - Retail/Service: service and sales workers, hotel/resort staff
    - Food Industry: restaurant, food processing, abattoirs and meat processing plants
    - Office Administration and Sales: occupations with a high client contact rate.
    - Personal care: working in nursing homes, daycares, preschool, religious professionals, personal care workers, associated health professionals (e.g. dentist), salon staff
    - Community and social services: social workers and counselors, community health workers, daycare providers
    - Construction, extraction and related trades: plumbers, septic tank installers, elevator repair, grounds and facility maintenance
    - Public Safety workers: fire, police, correctional officers
    - Wastewater workers
- Occupations at lower risk of SARS-CoV-2 exposure included occupations that could telework and/or socially distance from others (Table 1). Examples of the latter were farmers, machine operators, business that have minimal interaction with the public or clients (Sierpiński et al., 2020).
- Essential workers (includes many of the categories listed as high risk above) are at an increased risk of COVID-19 infection compared to the general population (Table 1). This risk is increased with increasing interaction with co-workers, clients or the public.
- Socio-demographic factors and their association with high risk of SARS-CoV-2 exposure were examined in several studies (Table 1). Being female, a visible minority, and being in a low-income bracket are more likely to be employed in occupations associated with significantly

higher risk of exposure to COVID-19 as their occupation does not allow them to work at home and involves working closely with people. Conversely, increasing age and higher education was associated with lower risk of exposure occupations.

- Staff in pre-school, primary school, and high school do not have a higher relative prevalence of COVID-19 compared to other professions (Swedish Public Health Agency, 2020).
- One study indicated commuting to work on public transport was positively associated with risk of SARS-CoV-2 infection. A result that was considerably stronger in the U.S. then the UK sample, which the authors hypothesize may be related to the uniformity and stringency of the UK lockdown (Anand et al., 2020).
- Two risk assessments explored the attributes of workplaces and mobility for their potential for SARS-CoV-2 transmission.
    - A risk assessment scored businesses for their potential to be super-spreading business (SSBs) based on the frequency, duration, and square footage of businesses pre-pandemic across 8 U.S. states. A positive association between SSBs (the top 5% of scores were considered SSBs) and the cumulative weekly cases of COVID-19 was reported where a 1% increase in the number of SSBs in an area equated to a 5% increase in cases. The most common SSBs were full service restaurants, limited service restaurants, and hotels/motels (Donoghue et al., 2020).
    - The potential health risks of SARS-CoV-2 in sewage to wastewater treatment plant workers (WWTPs) was investigated using a quantitative microbial risk assessment (QMRA). The estimated viral loads in sewage at the entrance of WWTPs was higher than the safe cut-off values suggested by the World Health Organization (WHO) (Zaneti et al., 2020).

Table 1. Twenty Publications on Occupational Risks for COVID-19 Infection.

Reference	Publication Title	Study Details	Key Outcomes
Observational Studies			
(Lan, Wei, & Hsu, 2020)	Work-related COVID-19 transmission in six Asian countries/areas: a follow-up study	• This retrospective observational study which identified possible work-related cases from government investigation reports in Hong Kong, Japan, Singapore, Taiwan, Thailand and Vietnam that were reported between January 23 – March 14, 2020. • The authors have declared that no competing interests exist.	• After excluding all imported cases, 103 possible work-related transmissions were identified from 690 local transmission events investigated. • Apart from HCW, the occupational groups most commonly implicated were: drivers and transport workers (18%), services and sales workers (18%), cleaning and domestic workers 22 (9%) and public safety workers (7%) and religious professionals (6%).

			• A shift in occupations implicated in clusters during the initial phase of the outbreaks (predominantly services and sales workers, and construction laborers) to later in the outbreak (predominantly HCWs, cleaning and domestic workers and police officers).
(Sierpiński et al., 2020)	Occupational risks for SARS-CoV-2 infection: the Polish experience	• This cross-sectional study analyzed the sources and occupational risk factors for SARS-CoV-2 infections on 2122 patients infected with SARS-CoV-2 who remained in home isolation in Poland. • The survey was conducted on April 17–18, 2020 using a structured interview. • No conflict of interest statement available.	• Among the 2,122 participants with SARS-CoV-2 infection, 75% became infected at work and 70% were currently employed (occupationally active). • Of the occupationally active cases, 48% worked in healthcare, 3% worked in public administration or defense, 3% worked in transportation, and 2% worked in education. • 65% of the occupationally active cases worked in companies with >100 employees.
(Torres Martínez, Diaque García, Rubio Salas, & et al., 2020) *preprint*	IgG seroprevalence against SARS-CoV-2 in a cohort of 449 non-hospitalized, high-risk exposure individuals	• This cross-sectional study estimated the seroprevalence on 449 individuals in Madrid, Spain with one of the inclusion criteria: having symptoms of COVID-19, being in contact with a COVID-19 case, or belonging to essential occupations including healthcare workers, firefighters or public safety personnel such as police. • Study conducted April 15 – June 15, 2020. • Authors declare that 3 of their authors are founders, board members and shareholders of EMPIREO Diagnóstico Molecular.	• The overall seroprevalence was 33.69% (95% CI: 29.27-38.21). • Of the 449 individuals tested, 9.58% were healthcare workers, 4.01% were firefighters, and 6.46% worked preserving public safety. The remainder did not belong to these professions. • With respect to these high risk of exposure occupations, there was no significant difference in seroprevalence. Nor was there a difference in IgG seroprevalence between groups of suspected, exposed or high risk occupation groups suggesting a high level of exposure in high risk of exposure occupations.

(Koh, 2020b)	Occupational risks for COVID-19	• This retrospective observational study describes 17 cases that were likely due to occupational exposure in Singapore during the period of February 4-11, 2020 prior to any public health measures. • No conflict of interest statement available.	• Occupational exposures included retail personnel primarily selling to tourists and company staff attending an international business meeting in Singapore. • Transportation drivers, construction workers, and people that work in tourism were implicated (e.g. casino worker, resort employee).
(Anand et al., 2020) *preprint*	Work-related and personal predictors of COVID-19 transmission	• This cross-sectional study analyzes work and personal predictors of COVID-19 transmission experience in the U.S. and UK. • An online survey of 2,000 participants was conducted the first week of June, 2020. • No conflict of interest statement available.	• The findings for the U.S. were different from the UK, the authors theorize this has to do with the stringency of the public health measures. The results indicate occupation, personal traits, circumstance and behaviours all impact risk of COVID-19 exposure and ability to physically distance. • The UK analysis indicated higher risk of having had a COVID-19 diagnosis for those who had no income, lower-middle income status, shared a kitchen and occupations where interactions with customers and staff were on-going. • The U.S. analysis indicated higher risk of having had COVID-19 was related to low income (OR=5.8-6.3), shared kitchen (3.6), having a university degree (2.7), working in a transport related occupation (8.5), belonging to a trade union (4.8), having had a consultation on COVID-19 transmission at work (2.5) and having to take public transportation to work (3.2).

(Swedish Public Health Agency, 2020) *preprint*	Prevalence of COVID-19 in different occupational groups	• Article in Swedish.
		• This cross-sectional study analyzes prevalence of COVID-19 between different occupational groups using data on occupational classification from Statistics Sweden and cases
			• Compared to other occupational groups, taxi drivers were ~5 times more likely to become infected with SARS-CoV-2 (RR: 4.8, 95% CI: 3.9-6).
			• Other high risk occupational groups include:
			  • Pizza bakers – RR 4.5, 95% CI: 3.2-6.3
			  • Bus and tram drivers – RR 4.3, 95% CI: 3.6-5.1
			  • Translators and linguists – RR 2.9, 95% CI: 1.8 - 4.7

		diagnosed during the period of March 13 – May 27, 2020. • Healthcare professionals were excluded from the analysis. • No conflict of interest statement available.	• Restaurant and kitchen managers – RR 2.5, 95% CI: 1.7-3.8 • Other services workers (e.g. workers who refill vending machines, read electrical and gas metres etc.) – RR 2.3, 95% CI: 2.1-3 • Firefighters – RR 2.2, 95% CI: 1.4-3.5 • Cleaning professionals (e.g. car cleaner, window cleaner) – RR 1.7, 95% CI: 1.1-2.7 • Property manager - RR 1.6, 95% CI: 1.3-2 • Restaurant and kitchen assistants – RR 1.4, 95% CI: 1.2-1.7 • Staff in pre-school, primary school, and high school do not have a higher relative prevalence of COVID-19 compared to other professions. • High school teacher – RR 0.7, 95% CI: 0.5-1 • Primary school teacher – RR 1.1, 95% CI: 0.9-1.3 • Leisure educators – RR 0.8, 95% CI: 0.5-1.3 • Pre-school teacher – RR 0.7, 95% CI: 0.6-0.9 • Other educators with specialist competence – RR 1.0, 95% CI: 0.7-1.5 • Nanny – RR 1.0, 95% CI: 0.8-1.2 • Student assistants – RR 1.1, 95% CI: 0.8-1.4 •
Ecological Studies			
(Lewandowski, 2020) *preprint*	Occupational exposure to contagion and the spread of COVID-19 in Europe	• This ecological study measured country-specific levels of occupational exposure to contagion index derived from a combination of data in O*NET (exposure to disease or infection and physical proximity at work) and the European Working Condition Survey (dealing with people, work in public, work at client's premises and no ability	• In countries with higher proportions of highly exposed workers, these workers tended to be older was the reason for a strong correlation between age 45-64 and the occupational exposure to contagion index. • 20-25% of the cross-country variance in numbers of COVID-19 cases and deaths can be attributed to cross-country differences in levels of occupational exposure to contagion in European countries.

		to work at home). HCWs were excluded from the analysis. • No conflict of interest statement available.	• The occupations most at risk include personal service workers, protective service workers, sales workers, and building and related trade workers. • The occupations with the least amount of risk include farm and agriculture workers, plant and machine operators who do not have close proximity to each other, and businesses that do not interact with the public or clients and have the capacity to allow employees to work from home.
(Baker, Peckham, & Seixas, 2020)	Estimating the burden of United States workers exposed to infection or disease: a key factor in containing risk of COVID-19 infection	• This pre-COVID-19 analysis aimed to quantify the number of workers who are frequently exposed to infection and disease in the workplace in the U.S., and understand which occupational groups they represent by combining data on occupational work activities from the Occupation Information Network (O*Net) (from partial update in 2018) with data from the Bureau of Labor Statistics (BLS) Occupational Employment Statistics database (from May 2018). • No conflict of interest statement available.	• Based on self-reported estimates from O*Net in 2018 and extrapolated based on data from BLS, ~10% (14.4 million) workers in the U.S. are employed in occupations where exposure to disease or infection occurs at least once per week. Additionally, 18.4% (26.7 million) are employed in occupations where exposure to disease or infection occurs at least once per month. • Occupations with a higher risk of exposure include those in the healthcare sectors, protective service occupations (e.g. police officers, correctional officers, firefighters), office and administrative support occupations (e.g. couriers and messengers, patient service representatives), education occupations (e.g. preschool and daycare teachers), community and social services occupations (community health workers, social workers, counselors), and construction and extraction occupations (e.g. plumbers, septic tank installers, elevator repair).
(St-Denis, 2020)	Sociodemographic determinants of occupational risks of exposure to COVID-19 in Canada	• This pre-COVID-19 analysis identified which groups of the labor force are at greater risk of exposure to COVID-19 based on the characteristics of their occupation and assessed them against sociodemographic data.	• The results highlight the association between socioeconomic status and occupational-level work activities that may increase the risk of exposure among women, immigrants, and members of visible minority groups.

		• Data on occupational work activities was derived from the O*Net database (level of physical proximity to other people, and the frequency of exposure to diseases and infections) Canadian 2016 census data. • No conflict of interest statement available.	• ~45% of Canadian workers are in occupations that require working in relatively close physical proximity to others (at arm's length or closer). • Women work in occupations associated with significantly higher average risks of exposure to COVID-19 than men. • Those with a Bachelor's degree or higher tend to face significantly lower occupational risks of exposure. • Workers in low-income occupations are more likely to be employed in occupations with high exposure risk scores. • Occupations held by older workers (65+) were characterized by a lower level of physical proximity to others than their younger colleagues.
(Barbieri, Basso, & Scicchitano, 2020) *preprint*	Italian workers at risk during the COVID-19 epidemic	• This ecological study uses synthetic indexes that proxy for physical proximity in the workplace, exposure to diseases and infections, and the possibility to work remotely at the occupational level were created using data from the Italian Sample Survey on Professions (ICP) and the ISTAT Italian labour force survey (LFS). • Authors state that the views expressed in the paper are those of the authors and do not necessarily reflect those of the Bank of Italy nor those of INAPP.	• Several sectors require physical proximity to operate: the workers employed in Italy in sectors whose physical proximity index is above the national average are more than 6.5 million (most of them in retail trade). • Groups at risk of contagion and complications from COVID-19 (mainly male above the age of 50) work in sectors that have little exposure to other people, are currently under lockdown, or can work remotely. • The sectors with the highest physical index are hotel and restaurants, education, healthcare and trade (mainly retail).
(Lewandowski, Lipowska, & Magda, 2020)	The gender dimension of occupational exposure to contagion in Europe	• This ecological study aimed to measure the occupational exposure to contagious diseases using data from O*Net 2018 and the European Working Conditions Survey ('EWCS' 2015).	• Women are 26% more likely to work in highly exposed occupations that require contact with diseases, frequent contact with clients, and high levels of physical proximity at work. • Women are more likely than men to be unable to work from home due to their occupation. Older women and

		• Authors specifically analyze the gender dimension of occupational exposure. • No conflict of interest statement available.	women with higher education were less likely to be in a high exposure occupation. • Occupations with a high exposure to contagions were personal care workers, HCWs, associate health professionals, personal service workers and protective service workers. With the exception of the last category the former categories are female dominated. Accounting for the economic sector of work sex is not a significant predictor of exposure to contagions. However within some sectors younger women were significantly more likely to be in high exposure occupations.
(Hawkins, 2020)	Differential occupational risk for COVID-19 and other infection exposure according to race and ethnicity	• This ecological study aimed to assess how occupational segregation according to race and ethnicity contributes to the risk of COVID-19. • Data from the Bureau of Labor Statistics Current Population Survey was used for the analysis. • The authors have declared that no competing interests exist.	• This article identifies that some high risk of exposure occupations are disproportionately occupied by certain ethnic groups. • Black workers were more likely to be employed in essential industries and in occupations frequently requiring close proximity to others (HCWs, social assistance, hospital, bus drivers, personal care aids, food industry). • Black and Hispanic workers were more than twice as likely to be employed in the animal slaughtering and processing industry, where there have been many outbreaks of COVID-19.
(Rogers et al., 2020)	Racial disparities in COVID-19 mortality among essential workers in the United States	• This ecological study analyses used data from the American Community Survey and Current Population Survey to examine the correlation between COVID-19 deaths and occupational differences across racial/ethnic groups across U.S. states. • COVID-19 death data up to April 24, 2020 was included.	• Non-Hispanic (NH) Black individuals disproportionately occupy the top 9 essential occupations, which increases their risk of exposure to COVID-19 including the 3 highest disparities: transportation and material moving, healthcare support, food preparation and serving. • Hispanic ethnicity was disproportionately more likely to work in food preparation and serving, building and grounds cleaning and maintenance and production.

		• Authors acknowledge an individual, who provided editorial assistance, and Data for Black Lives (http://d4bl.org/) who indirectly supported the investigation as one of the first organizations to compile a list of states that publicly shared COVID-19 incidence and mortality data. The research was partially supported by a grant from the National Institutes of Health.	• Asian ethnicity was disproportionately more likely to work in personal care and service, HCW and in food preparation and service.
(Peters, 2020)	Community susceptibility and resiliency to COVID-19 across the rural-urban continuum in the United States	• In this ecological study, a COVID-19 susceptibility scale is generated at the country level using data from the U.S. Census Bureau and CDC. Authors then assess the health and socioeconomic resiliency of susceptible places across the rural-urban continuum in the U.S. • The study was supported by USDA Agricultural Experiment Station Multistate Research Project W4001. Authors declare there are no conflicts of interest.	• Based on employment data, meat-processing facilities drive risk of infection in rural areas. • Outbreaks of COVID-19 in rural meat packing communities disproportionally impact Hispanic and other minority workers.
Predictive Models			
(Milligan et al., 2020) *preprint*	Impact of essential workers in the context of social distancing for epidemic control	• This SEIR model examined scenarios with 3 different groups of essential workers to determine their risk of contracting COVID-19: 1) public-facing essential workers (cashiers, retail, transportation), 2) non-public facing essential workers (factory, warehouse,	• Essential workers are at an increased risk of COVID-19 infection compared to the general population. • Non-public-facing essential workers are susceptible to outbreaks in the workplace even after social distancing practices, while public-facing essential workers have a high contact rate with people and thus a higher risk of being exposed to an infected person compared to those who stay at home.

		and agriculture employees), and 3) healthcare workers. • No conflict of interest statement available.	• It was found that different types of essential workers (cashiers, factory employees, and HCWs) had different impacts on transmission scenarios. Similarly, mitigation efforts (e.g. masks, physical distancing etc.) had an impact on transmission.
Reviews			
(Rafeeman esh, Ahmadi, & Memarzad eh, 2020)	A Review of the strategies and studies on the prevention and control of the new Coronavirus in workplaces	• Literature Review published in April, 2020, no search date or methods section. • Authors aimed to review the required strategies to prevent and control COVID-19 in the workplace. • Search strategy and dates of the search not reported. • The authors have declared that no competing interests exist.	• High Risk of exposure occupations: o CDC has identified occupations that are more exposed to COVID-19: 1) health care workers (HCWs), 2) staff of the cemeteries and the funeral houses, 3) officials and staff of airports, airlines, railways, subways and all public transport (buses, taxis, etc.), 4) border guards, 5) solid waste and wastewater workers, and 6) employees who travel regularly, especially to contaminated areas o Dentists and makeup artists are also at high risk due to face-to-face communication with clients and exposure to saliva, blood, and exhaled breath o Flight and ship crews are at risk of contact with infected passengers • Control solutions: o Engineering controls (isolation of symptomatics, ventilation, barriers between people, disposable tools) o Administrative controls (exclusion of sick workers, hygiene training, reduced staff hours, teleworking, cohorting, continuous cleaning and disinfection, restrict staff gatherings) o Personal Protective Equipment (proper face mask, eye protection, gloves and special clothing – as needed) • Key Barriers:

			○ Continuing to work despite being sick (presenteeism) is a major issue. Extended sick leave policies will help
(Peng et al., 2020)	Transmission routes of 2019-nCov and controls in dental practice	• Literature review published in April, 2020, no search date or methods section • Authors aim to provide an overview of the transmission routes and risk of exposure to those working in the dental industry. • The authors have declared that no competing interests exist.	• Routes of transmission ○ There is a high risk of direct transmission in dental practice due to working directly with the mouth and contact with the oral/nasal mucous membranes, as well as exposure to saliva, blood, and other respiratory fluids ○ Airborne transmission to susceptible people in the clinic ○ Indirect transmission via fomites may also be a risk as handling of sharp instruments that are in direct contact with potentially virus laden bodily fluids could occur • Infection control measures ○ Patient evaluation, temperature check ○ Hand hygiene ○ Barrier protection including face mask, eye protection, face shield, work clothes (e.g. lab coat) ○ Antimicrobial mouth rinse before dental procedure, rubber dam may minimize blood and saliva spatter. ○ Use of anti-retraction high-speed hand pieces may reduce the risk of cross contamination. ○ Strict and continuous disinfection
Risk Assessments			
(Donoghue et al., 2020) *preprint*	Super-spreader businesses and risk of COVID-19 transmission	• This risk assessment explores the attributes of super-spreading businesses (SSBs). SSBs were those businesses within the top 5% of the COVID-19 Business Transmission Risk Index which is based on the frequency,	• The negative binomial analysis found a positive association between SSBs and the cumulative weekly cases of COVID-19 where a 1% increase in SSB equated to a 5% increase in cases.

		duration and square footage of businesses pre-pandemic across 8 U.S. states. • No conflict of interest statement available.	• Common business types classified as SSBs included full service restaurants, limited service restaurants and hotels/motels. • SSB attributes in this study were typically businesses where visitors stay for longer and are more densely packed.
(Zaneti et al., 2020) *preprint*	QMRA of SARS-CoV-2 for workers in wastewater treatment plants	• A quantitative microbial risk assessment (QMRA) was used to investigate the potential health risks of SARS-CoV-2 in sewage to wastewater treatment plants (WWTPs) workers. • QMRA was applied for 3 COVID-19 scenarios (moderate, aggressive and extreme) to study the risk during different stages of the pandemic. • No conflict of interest statement available.	• Estimated viral loads in sewage at the entrance of WWTPs ranged from $1.03x10^2$ to $1.31x10^4$ GC/mL (GC= genome copies) assumed to equate to 0.1 to 13.06 PFU/mL (PFU= plaque forming units). • The exposure dosage was assumed to be 1mL that were contaminated at concentrations ranging from 1.03×10^2 GC/mL to 1.31×10^4 GC/mL across moderate to extreme scenarios. • The outcome was estimated risk for which WHO suggests a cut-off of 1 x 10-3 (based in the tolerable risk for rotavirus infection from drinking water): The extreme 3.1 x 10-2. Aggressive 6.5 x 10-3 and moderate 3.0 x 10-4 scenarios report risk 31, 6.5 and 0.3 time higher than the WHO cut-off. • WWTP workers exposed to bioaerosols and airborne particles are an occupational risk, few studies have examined this risk. • Infection control could include use of face mask and face shield when performing manual cleaning work and minimizing the time spent in treatment tank areas • Viral loads in sewage could be used as an early-warning tool for the community and aid in prioritizing enhanced infection control strategies in the sanitation sector.
(Zachreson, Mitchell, Lydeamor	Risk mapping for COVID-19 outbreaks using mobility data	• A heuristic approach to estimating transmission risk based only on qualitative information about epidemiological factors and informed	• Workplace (context) specific factors: o Common location (travel into/out of an outbreak area)

e, & et al., 2020) *preprint*		by near-real-time estimates of mobility patterns. • Gathering related outbreaks are particularly well suited to this method. • They validate their estimates using 3 well documented COVID-19 outbreak scenarios in Australia. These include an outbreak at an abattoir, a hotel, and within a community. • Mobility data was used from Facebook and case data was obtained through the Australian state health authorities. • No conflict of interest statement available.	○ Was in the outbreak location prior to identification of the outbreak ○ Occupation statistics for the area or location being studied (aids in identification of a common type of business in the outbreak area) Note: the above method could be applied to anywhere with habitual travel patterns. • Example: Cedar Meats outbreak April, 2020, Australia ○ A mobility risk map and Spearman's correlation coefficient indicates that with limited case data and mobility data, the location of the outbreak associated with Cedar meats in Brimbank could have been identified very early on. This result was further improved with the addition of occupation data for the area. ○ These results also demonstrate how mobility data can be a useful tool in the estimation of COVID-19 transmission risk diffusion from epidemic locations early in an outbreak. This can be used to intensify public health measures early and aid in containment of an outbreak or community transmission (as demonstrated in the other examples) particularly when we have few cases and are working on preventing a resurgence of cases. • 2 other examples are presented related to a social gathering and community transmission. These are not summarized here.

TRANSMISSION IN THE WORKPLACE

A wide range of workplaces have been implicated in transmission events for SARS-CoV-2 and many transmission events despite being identified have not been fully investigated or published. An ongoing publicly available project to compile COVID-19 super spreading events (>5 cases) was identified and the 1500 events reported in this list underscores the magnitude of under-reporting on transmission events (Swinkels, 2020). Transmission events omitted from the published and preprint literature were recorded on country dashboards and by the media. The latter was excluded from this review as they are often not reported with sufficient details to assess the transmission event or investigation.

- Table 2 lists 37 publications that describe one or more transmission events considered to have occurred in a workplace involving workers broadly captured under the categories: office environment, meat processing facilities, other factories, migrant work, fitness centers, ships, other service related occupation, transportation, and studies with multiple clusters.
- Four outbreaks in office settings (call center, administrative office, meetings) were identified. The main facilitators for SARS-CoV-2 transmission in an office setting include activity (e.g. talking), proximity to an infected person (e.g. sitting next to each other) and duration of being in close proximity to an infected person.
- Outbreaks in meat processing facilities in Germany and across the U.S. are described in five publications. The risk factors for infection were identified as: difficulties with physical distancing, prolonged close contact with coworkers, environmental factors such as cooled re-circulated air, hand hygiene, shared accommodation, shared transportation to and from work, and frequent community contact with fellow workers.
    - The cluster investigation on the largest meat processing complex in Germany reports a high attack rate for workers within eight meters of the index cases fixed work station (Guenther et al., 2020).
- A seroprevalence study of a factory in Croatia reported antibodies were detected in 1.27% of participants (95% CI: 0.77–1.98%, n=1,494). However, no outbreak had been detected in the plant, and none of the workers from employer provided accommodations had antibodies. The employer had adopted enhanced protective measures (e.g. hand disinfection stations, regular workstation cleaning, closed communal coffee and food vending stations, temperature checks, self-isolation for those returning from abroad, and work from home for part of the business and administrative staff) (Jerkovic et al., 2020).
- Migrant workers housed in shared accommodations were associated with a large outbreak in Singapore (Koh, 2020a).

- In three outbreaks that occurred on boats (Diamond Princess cruise ship, a fishing vessel and U.S. naval ship), shared accommodation and working in close proximity were identified as risk factors for acquisition of SARS-CoV-2.
- A large multi-center gym related outbreak was traced to a workshop where several instructors were infected and proceeded to transmit SARS-CoV-2 to other employees and clients at centers where they were employed (Jang, Han, & Rhee, 2020).
- A cross-sectional study estimated the seroprevalence of 104 individuals employed at one grocery retail store in Massachusetts, U.S. Results from multivariate analysis reveal that employees with direct customer exposure were five times more likely to test positive for SARS-CoV-2 (OR 4.7; 95% CI: 1.2-32.0) (Lan, Suharlim, Kales, & Yang, 2020). A similar finding was reported for firefighters and paramedics in a second study (Caban-Martinez et al., 2020).
- Employment in transportation was shown to be a risk factor for taxi drivers and bus drivers in three studies, however a transmission event to a flight attendant has not been documented to date.
- Shared accommodation or facilities (e.g. bathroom) and a lack of preventative measures (e.g. face mask) have been suggested to contribute to several outbreaks in shopping malls, retail stores, bars, nightclubs, restaurants, concerts and overnight camps.
- Outbreaks are more likely to occur in an indoor environment OR 18.7 (95%CI 6.0-57.9) (Nishiura et al., 2020).
- Key protective measures identified include practicing exemplary infection control within closed environments, policies on exclusion of ill workers from the work environment, and adherence to personal infection control precautions when working.

Table 2. Thirty-Seven Publications on Transmission Events in the Workplace.

Reference	Publication Title	Study Details	Key Outcomes
Office Environment			
(Park et al., 2020)	Coronavirus Disease Outbreak in Call Center, South Korea	• Aggregated data from retrospective epidemiological investigations. • Conducted on an outbreak of COVID-19 at a call center in Seoul, South Korea in March, 2020. • No conflict of interest statement available.	• The first confirmed case was identified at the call center on March 8, 2020. The call center is located on floors 7-9 and 11 of a 19 storey building. In general, employees do not travel between floors, and they do not have an in-house restaurant for meals. Both residents and employees in in the building had frequent contact in the lobby or elevators. • The building was closed on March 9, 2020 and testing was offered to all occupants of the building.

			• Of 1,143 individuals tested for COVID-19, 97 (8.5%) were positive. The majority of these (94/97) were working on the 11th floor at the call center with 216 employees. This translates to an attack rate of 43.5% (95% CI: 36.9-50.4%). In addition, most of the cases on the 11th floor were on the same side of the building. • The household secondary attack rate among symptomatic cases was 16.2% (95% CI: 11.6-22%). • Duration of interaction (or contact) was most likely the main facilitator for transmission.
(Zhang et al., 2020)	Epidemiological survey of a new coronavirus pneumonia cluster epidemic in collective units in Tianjin	• Article in Chinese. • Retrospective epidemiological investigation conducted in January, 2020. • The outbreak occurred in the administrative office of a plant that has 906 employees in Tianjin, China. • Authors declare there is no conflict of interest.	• The first case was identified on January 15, 2020 and spread to 10 other coworkers before control measures were put in place on January 24, 2020. • The index case and initial case exposures are linked to work related travel to Wuhan. • Secondary and tertiary cases either travelled with, participated in meetings, or sat close to infected cases.
(Böhmer et al., 2020; Rothe et al., 2020)	Transmission of 2019-nCoV infection from an asymptomatic contact in Germany Investigation of a COVID-19 outbreak in Germany resulting from a single travel-associated	• Retrospective epidemiological investigation • 2 studies describing the transmission of SARS-CoV-2 from a Chinese resident who visited Germany for professional reasons to her colleagues in January, 2020. • Böhmer et al. provide detailed outbreak investigation. • Authors declare there is no conflict of interest.	• Patient 0 was an employee of the Chinese branch of a German company based in Munich. She travelled from Shanghai to Munich by airplane on January 19, 2020 to facilitate workshops and attend meetings in the company building. She returned on an overnight flight back to Shanghai on January 22, 2020 and tested positive for SARS-CoV-2 infection on January 26, 2020. • The German company was informed of the infection on January 27, 2020. Initial testing of high-risk contacts identified patients 1-4 as first generation cases. The company site was closed on February 11, 2020. By February 19, 2020, 16 subsequent cases were identified. • The median serial interval was 4.0 days (IQR 3.0–5.0).

	primary case: a case series		• Ten patients in addition to patient 0 were employees of the company. The other 5 were household contacts. Investigation revealed that transmission from patient 0 to the 10 others likely occurred during the following scenarios: ○ Accompanying patient 0 in multiple activities in Germany traveling back on the same plane ○ In business meetings (60-90 minutes) where colleagues sat close together ○ Colleagues worked simultaneously on the same computer for a short period of time ○ After sitting closely for a 90 minute meeting during the day, 2 colleagues also spent the evening together one of their homes. However, the partner of the colleague hosting who was also there that evening did not test positive ○ 2colleagues met during a canteen visit where they sat back to back. One of them turned to the other to borrow the salt shaker
(Hall, Bui, Rowe, & Do, 2020)	COVID-19 case and contact Investigation in an office workspace	• Retrospective epidemiological investigation conducted in March, 2020, • The outbreak occurred in a combined military and civilian office workspace in the U.S. • No conflict of interest statement available	• The index case unintentionally exposed 150 coworkers to SARS-CoV-2 through participation in carpools, conferences, and small meetings over a period of 3 days. • Of the 150 exposures, 37 were considered medium risk and 113 were considered low risk. 5 people reported COVID-19 like symptoms and 5 developed symptoms during the 14 day quarantine. None of the contacts tested positive for SARS-CoV-2 infection. • None of the coworkers who were exposed during the carpool developed symptoms and despite the close contact were believed to not have been infected. • The rapid identification of those at risk of infection and subsequent implementation of mitigation and control

			efforts was successful in controlling the spread of SARS-CoV-2.
Meat Processing Facilities			
(Dyal et al., 2020)	COVID-19 among workers in meat and poultry processing facilities — 19 states, April 2020	• Aggregated data from retrospective epidemiological investigations. • The report provides aggregate data of positive COVID-19 cases among 115 meat and poultry processing facilities across 19 U.S. states through April 27, 2020. • No potential conflicts of interest were disclosed.	• Among approximately 130,000 workers at these facilities, 4,913 cases (~3.0%) and 20 deaths occurred. • These numbers reflect inadequate infection control practices followed within these facilities including poor social distancing, source control measures (e.g., the use of cloth face covers), and increased workload. • The risk factors for infection were identified as difficulties with physical distancing, hygiene, and crowded living and transportation conditions (many workers live in crowded, multigenerational settings and sometimes share transportation to and from work).
(Waltenburg et al., 2020)	Update: COVID-19 among workers in meat and poultry processing facilities — 19 states, April-May 2020	• Aggregated data from retrospective epidemiological investigations. • This is an update to the report above. • The report provides aggregate data of positive COVID-19 cases among 239 meat and poultry processing facilities across 23 US states through May 31, 2020. • No potential conflicts of interest were disclosed.	• Within 239 facilities, there has been 16,233 COVID-19 cases and 86 COVID-19 related deaths among workers (264 facilities / 17,358 cases/ 91 deaths across both publications (Dyal et al., 2020; Waltenburg et al., 2020)). • Among 14 states reporting the total number of workers in affected meat and poultry processing facilities (112,616), COVID-19 was diagnosed in 9.1% of workers. • Of 9,919 (61%) cases with reported race/ethnicity, 87% were among racial and ethnic minority workers. • Factors that increase risk of exposure for these workers include prolonged close workplace contact with coworkers (within 6 feet for ≥15 minutes) for long time periods (8–12 hour shifts), shared work spaces, shared transportation to and from the workplace, congregate housing, and frequent community contact with fellow workers. • Data from 111 facilities across 14 states reveals the implementation of the following prevention and

			control strategies: screening workers on entry (89/111), required all workers to wear face coverings (86/111), increased the availability of hand hygiene stations (72/111), educated workers on community spread (70/111), installed physical barriers between workers (69/111), offered testing to employees (41/111, and closing temporarily (24/111). • Using data from 7 facilities that implemented facility-wide testing, the crude prevalence of asymptomatic or presymptomatic infections among 5,572 workers who tested positive for SARS-CoV-2 infection was 14.4%.
(Steinberg et al., 2020)	COVID-19 Outbreak among employees at a meat processing facility – South Dakota, March – April 2020	• Retrospective epidemiological investigation • Conducted between March 16 - April 25, 2020 in a meat processing facility (facility A). • No potential conflicts of interest were disclosed.	• A total of 929/3,635 (25.6%) COVID-19 cases were diagnosed among facility A employees, of which 39 were hospitalized and 2 died. • An additional 210/2,408 (8.7%) cases were identified among contacts of employees with diagnosed COVID-19. 9 of these were hospitalized. • The attack rate at facility A during March 16 – April 25, 2020 was 25.6%. Department-groups where employees worked in close proximity (i.e., <6 feet) to one another on the production line had the highest attack rates (department groups: cut – 30.2%, conversion – 30.1%, and harvest – 29.4%). • The attack rate was higher among non-salaried employees (26.8%) compared to salaried employees (14.8%). • The attack rate increased ~fivefold during the first 3 weeks of the outbreak. On average 67 employee COVID-19 cases were occurring per day during the fourth week. Cases among employees declined to ~ 10 per day within 7 days of facility closure.
(Richmond, Sabin,	Interregional SARS-CoV-2	• Molecular epidemiology study.	• Results from phylogenetic analysis reveal a large cluster from a single SARS-CoV-2 strain among

Jobe, Lovrich, & Kenny, 2020) *preprint*	spread from a single introduction outbreak in a meat-packing plant in northeast Iowa	• This study describes a phylogenetic analysis of COVID-19 cases identified in 3 neighbouring states in the U.S. (Wisconsin, Iowa, and Minnesota). • No conflict of interest statement available.	individuals associated with a meatpacking plant in Postville, Iowa. • Since April 6, 2020, 27 viral cases attributed to this sub-strain have been identified. Authors believe this only represents a sample of the cases arising from this outbreak. • Cases traceable to this outbreak have been detected in 7 counties in 3 states, affecting a total of 13 municipalities. This region spans 185 square miles.
(Guenther et al., 2020) *preprint*	Investigation of a superspreading event preceding the largest meat processing plant-related SARS-Coronavirus 2 outbreak in Germany	• Retrospective epidemiological investigation. • Conducted March 16 - April 25, 2020 the largest meat processing complex in Germany. • There are 2 facilities MPP-R and MPP-D. MPP-R performs slaughter and fine processing as well as packaging of beef and pork and MPP-D is a processing plant specialized on sow deboning which is located 30 km away from MPP-R.	• Serial testing by health authorities performed a month after the initial encounter identified more than 1,400 positive cases. • Assessment of viral sequences shows that all cases share a set of 8 single nucleotide mutations representing a novel sub-branch in the SARS-CoV-2 C20 clade. • Initial transmission occurred in a confined area of a beef processing plant in which air is constantly recirculated and cooled to 10°C. The index case transmitted the virus to more than 60% (17/26) of their co-workers in a radius of more than 8 meters during work-shifts on 3 consecutive days. • Statistical relationships were also identified for a single shared apartment, bedroom and carpool groups. Correlations between working within 8 meters of the index case and the infection rate in the apartment, bedroom or carpool groups indicate the majority of transmission events are thought to have occurred within the beef processing facility. • Findings indicate that a physical distance of 2 meters is not sufficient to prevent transmission in this environment of low fresh air exchange and continuous cooling, which may favour transmission. Authors

			recommend additional measures such as improved ventilation and airflow, installation of filtering devices, and the use of high-quality face masks to reduce the infection risk in these environments.
Other Factory			
(Jerkovic et al., 2020) *preprint*	SARS-CoV-2 antibody seroprevalance in industry workers in Split-Dalmatia and Šibenik-Knin County, Croatia	• This cross-sectional study estimated the seroprevalence on 1,494 factory employees living in the Split-Dalmatia and Šibenik-Knin County (Croatia) and was conducted between April 23 - 28, 2020. • The factory (DIV Group) specializes in the production and trade of screws and other mechanical parts and metal with 2 major production sites located in Split (Split-Dalmatia County), and Knin (Šibenik-Knin County) employing around 2,200 people and around 400 people, respectively, • Authors declare there is no conflict of interest.	• As of February 25, 2020 the DIV group implemented protective measures such as providing hand disinfection stations in all rooms, regular workstation cleaning protocols, closing communal coffee and food vending stations, temperature checks, self-isolation for those returning from abroad, and work from home for part of the business and administrative staff. The total number of employees working at the facilities was reduced to around 1,300 and 300, respectively, • In a total sample of tested employees (n=1,494), antibodies were detected in 1.27% of participants (95% CI: 0.77–1.98%). • At the facility in Split, some of the employees live at the facility premises. • In the Split facility 13/1,316 (0.99%, 95% CI: 0.53–1.68%) of participants tested positive, of which 13/1,079 (1.20%, 95% CI: 0.64–2.05%) of those were living outside the facility and 0/237 (0%, 95% CI: 0–1.26%) of those were living inside the facility. In the Knin facility, 6/178 (3.37%, 95% CI: 1.25–7.19%) participants tested positive for antibodies. • All participants living inside facility premises, and with limited mobility during the lockdown measures, tested negative for antibodies. Therefore exposure was likely not related to workplace accommodation in this outbreak.
Migrant Work			

(Koh, 2020a)	Migrant workers and COVID-19	• Retrospective epidemiological investigation. • The daily numbers of COVID-19 cases in Singapore from March to May 2020 were analyzed to determine the cause of a surge in cases in April, 2020. Regulations on migrant worker accommodation were studied. • Authors declare there is no conflict of interest.	• The majority of cases associated with a peak in April, 2020 occurred among low-skilled migrant workers living in foreign worker dormitories. As of May 6, 2020 there were 17,758 confirmed COVID-19 cases among dormitory workers (88% of 20,198 nationally confirmed cases). • One dormitory housing with ~ 13,000 workers had 2,526 confirmed cases, which accounted for 12.5% of all cases in the country. • The national response included extensive testing of workers in dormitories, segregation of healthy and infected workers, and daily observation for fever and symptoms. In addition, 24 dormitories were declared as 'isolation areas' for residents to quarantine for 14 days. Vacant public housing flats, military camps, exhibition centres, and floating hotels have been provided to workers that will allow for appropriate social distancing.
Fitness Center			
(Jang et al., 2020)	Cluster of Coronavirus Disease associated with fitness dance classes, South Korea	• Retrospective epidemiological investigation. • An outbreak associated with a nationwide fitness dance instructor workshop held on February 15, 2020 in Cheonan, South Korea. • No conflict of interest statement available.	• At the nationwide fitness dance instructor workshop, instructors trained intensely for 4 hours. Of the 27 instructors who participated, 8 had positive RT-PCR) results for SARS-CoV-2 infection. All were asymptomatic on the day of the workshop. • On March 9, 2020, 112 COVID-19 cases associated with fitness dance classes in 12 different sports facilities were identified. Of these, 82 (73.2%) were symptomatic and 30 (26.8%) were asymptomatic. • Transmission from instructors to fitness class participants accounted for 57 (50.9%) cases. In-family transmission from instructors and students resulted in 38 cases (33.9%) and 17 cases (15.2%) were from

			transmission during meetings with coworkers or acquaintances. • Prior to closing the sports facilities, 217 students were exposed in 12 facilities, an attack rate of 26.3% (95% CI: 20.9-32.5%). • Close contacts of fitness instructors and students were followed up on (n=830) and 34 cases of COVID-19 were identified, translating to a secondary attack rate of 4.10% (95% CI: 2.95-5.67%). From these 34 cases, 418 close contacts were followed and 10 quaternary cases were identified, resulting in a tertiary attack rate of 2.39% (95% CI: 1.30-4.35%). • Fitness classes from which secondary COVID-19 cases were identified included 5–22 students in a room ≈60 m2 during 50 minutes of intense exercise. Cases among classes with <5 participants were not identified. • One of the infected instructors taught Pilates and yoga for classes of 7–8 students in the same facility at the same time as another infected instructor, but none of her students tested positive for the virus. • Authors speculate that the lower intensity of Pilates and yoga did not cause the same transmission effects as the more intense fitness dance classes.
Ships			
(Kakimoto et al., 2020)	Initial investigation of transmission of COVID-19 among crew members during quarantine of a cruise ship — Yokohama, Japan, February 2020	• Retrospective epidemiological investigation of an outbreak on a the Diamond Princess cruise ship of 3,700 passengers and crew that began on February 3, 2020. • Authors declare there is no conflict of interest.	• The investigation of SARS-CoV-2 spread among staff concluded that infection had apparently spread among persons whose cabins were on the same deck (deck 3) and who worked in the same occupational group (food service), probably through contact or droplet spread, which is consistent with current understanding of COVID-19 transmission. • 8 of 20 positive crew members had cabin mates, of which 5/8 became COVID-19 positive.

(Addetia et al., 2020)	Neutralizing antibodies correlate with protection from SARS-CoV-2 in humans during a fishery vessel outbreak with high attack rate	• Retrospective epidemiological investigation. • This study describes an outbreak of SARS-CoV-2 on a fishing vessel that departed from Seattle, Washington in May, 2020. • Prior to the ship's departure, crew members were screened for active SARS-CoV-2 infection by RT-PCR and for serological evidence of prior or ongoing infection. • Authors declare there is no conflict of interest.	• The attack rate on board was 85.2% (104/122 individuals). • 3 crew members tested positive prior to the boat's departure in initial serological screening and had neutralizing and spike-reactive antibodies in follow-up assays. None of these crew members showed evidence of viral infection or experienced any symptoms during the outbreak. • The crew members with neutralizing antibodies from prior infection were protected against re-infection.

(Payne et al., 2020)	SARS-CoV-2 infections and serologic responses from a sample of U.S. Navy service members - USS Theodore Roosevelt, April 2020	• Retrospective epidemiological investigation of an outbreak that occurred on the USS Theodore Roosevelt in March/April 2020 with approximately 1,000 service men onboard.
		• The investigation occurred April 20-24, 2020 once the ship docked in Guam.
		• A convenience sample of 382 (27% of the total service members on the ship or at the Guam naval base).
		• Questionnaires, serology and RT-PCR tests were done to develop the dataset.
			• Previous or current infection was higher among participants who reported contact with someone known to have COVID-19 (64.2%), compared with those who did not (41.7%) (OR = 2.5; 95% CI = 1.1–5.8).
			• Prevalence was also higher among persons who reported sharing the same sleeping berth with a crewmember who had positive test results (65.6%), compared with those who did not (36.4%) (OR = 3.3; 95% CI = 1.8–6.1).
			• Taking protective measures was associated with lower risk of being COVID-19 positive:
			  • Face covering (55.8% versus 80.8%; OR = 0.3; 95% CI = 0.2–0.5)
			  • Avoiding common areas (53.8% versus 67.5%; OR = 0.6; 95% CI = 0.4–0.9)
			  • Social distancing (54.7% versus 70.0%; OR=0.5; 95% CI = 0.3-0.8)

Other Service-Related Occupations			
(Liu et al., 2020)	Analysis on cluster cases of	• Aggregated data from retrospective epidemiological investigations.	• There were family clusters (28 cases, 71 cases), unit clusters (1 case, 10 cases), transportation clusters (3

	COVID-19 in Tianjin	• This study describes all clusters of confirmed COVID-19 cases Tianjin as of February 22, 2020. • Authors declare there is no conflict of interest.	cases, 8 cases), and a public place cluster (1 case, 26 cases). • A cluster in the passenger section of a train involved 10 cases. After epidemiological investigations, it was finally determined that 2 employees with a history of going out in Wuhan were first-generation cases. • The department store outbreak was an infected sales person that infected 26 customers and coworkers.
(Wu et al., 2020)	Investigation and analysis on characteristics of a cluster of COVID-19 associated with exposure in a department store in Tianjin	• Article in Chinese. • Retrospective epidemiological investigation • An outbreak associated with exposure in a department store. • Authors declare there is no conflict of interest.	• The first confirmed case of department employee was on January 31, 2020. • There are 40 cases associated with a department store, which accounted for 75.47% of the number of confirmed cases (53 cases) in the jurisdiction. • The analysis revealed that 6 cases (15%) involved department store employees, 19 cases (47.5%) were customers of the department store, and 15 cases (37.5%) were close contacts.
(Leffler & Hogan, 2020) *preprint*	Age-dependence of mortality from novel coronavirus disease (COVID-19) in highly exposed populations: New York transit workers and residents and Diamond Princess passengers	• Cross-sectional data from several sources and settings were obtained and mortality data was compared. • Authors used publicly available sources to estimate COVID-19 mortality for each age group on the Diamond Princess cruise ship, in the U.S., in New York City and state, and among New York Metropolitan Transit Authority (MTA) workers. • Authors declare there is no conflict of interest.	• In New York transit workers, mortality was estimated to be 1 in 7,329 for those ages 30-39 years, 1 in 1,075 for ages 40-49 yrs, 1 in 343 for ages 50-59 yrs, and 1 in 178 for ages 60-69 yrs. • Of the MTA workers who had died of COVID-19 (106/109 individuals) as of May 6, 2020 were in the subways and buses division, which has 55,000 employees. • Unclear if transmission of these workers occurred at the workplace or outside of the workplace. • Among New York MTA workers, over 6,000 workers (8%) have either tested positive (over 2,000), or entered quarantine (4,000 workers).

(Lan et al., 2020b) *preprint*	Association between SARS-CoV-2 infection, exposure risk and mental health among a cohort of essential retail workers in the United States	• This cross-sectional study estimated the seroprevalence of 104 individuals employed at one grocery retail store in the greater Boston area in Massachusetts, U.S. and was conducted on 3 consecutive days in early May 2020. • No conflict of interest statement available.	• Of the workers tested, 21/104 (20%) had positive viral assays. Among these, 76% of the cases were asymptomatic. • Results from multivariate analysis reveal that employees with direct customer exposure were 5 times more likely to test positive for SARS-CoV-2 (OR 4.7; 95% CI: 1.2-32.0). Smokers were 90% less likely to test positive (OR 0.1; 95% CI: 0.01-0.8).
(Yang et al., 2020)	The preliminary analysis on the characteristics of the cluster for the COVID-19	• Article in Chinese. • Aggregated data from retrospective epidemiological investigations. • This study describes 377 retrospective cluster investigations of SARS-CoV-2 infections involving 1,719 cases in non-medical institutions from January 1-February 20, 2020. • Authors declare there is no conflict of interest.	• Of the 377 clusters the likely setting where SARS-CoV-2 was acquired was attributed to: family clusters accounted for 79%, meals together accounted for 10%, shopping malls or supermarkets accounted for 6%, workplaces accounted for 3%, and transportation vehicles accounted for 2%. • Details of workplace transmission clusters were not presented.
(Hendrix, Walde, Findley, & Trotman, 2020)	Absence of apparent transmission of SARS-CoV-2 from two Stylists after exposure at a hair salon with a universal face covering policy – Springfield, Missouri, May 2020	• Retrospective epidemiological investigation. • 2 hair stylists as a single salon in Missouri, U.S. interacted with approximately 139 clients while they were infected with SARS-CoV-2 in May, 2020. • Both clients and hair stylists were wearing face masks. • Authors declare there is no conflict of interest.	• Of the 139 clients who were exposed, 67 were tested. • There were no symptomatic secondary cases reported, which was most likely due to the use of face masks. • Attack rate: 0/139

(Cai et al., 2020)	Indirect virus transmission in cluster of COVID-19 cases, Wenzhou, China, 2020	• Retrospective epidemiological investigation of an outbreak associated with a shopping mall in Wenzhou, China. • Authors declare there is no conflict of interest.	• After identifying a positive case, the mall was shut down on January 22, 2020. • During January 19 – February 9, 2020, COVID-19 was diagnosed for 7 mall employees and 10 mall customers. • Close contacts associated with the mall were traced, and COVID-19 was confirmed for 11 persons. • A sole common source was not identified, some common spaces were used by infected employees, thus exposure to aerosolized virus or fomite transmission is suspected, possibly from using a common bathroom or elevator.
(Szablewski et al., 2020)	SARS-CoV-2 transmission and infection among attendees of an overnight camp - Georgia, June 2020	• Retrospective epidemiological investigation of an outbreak associated with an overnight camp in Georgia, U.S.. • There was an overnight camp (camp A) for orientation for 138 trainees and 120 staff members during June 17-20, 2020 • The staff members remained for the first camp session, scheduled during June 21–27, 2020, and were joined by 363 campers and 3 senior staff members on June 21, 2020. • Authors declare there is no conflict of interest.	• 597 Georgia residents attended camp A. Of those tested, 260/344 (76%) tested positive for SARS-CoV-2 infection. • The overall attack rate was 44% (260/597), with staff members having the highest attack rate (56%). Attack rates increased with increasing length of time spent at the camp. • The occupancy of the 31 cabins averaged 15 persons per cabin (range = 1–26). The median cabin attack rate was 50% (range = 22–70%) among 28 cabins that had 1 or more cases. • The camp followed all CDC recommendations except opening windows and doors for increased ventilation in buildings and campers wearing cloth masks (but staff wore masks).
(Caban-Martinez et al., 2020)	Epidemiology of SARS-CoV-2 antibodies among firefighters/paramedics of a US fire department: a	• This cross-sectional study estimated seroprevalence of SARS-CoV-2 antibodies among 203 frontline firefighters/paramedics in Florida, U.S. collected on April 16 - 17, 2020.	• Of the 203 firefighters/paramedics tested, 18 were positive for SARS-CoV-2 (8.9%). • The average number of COVID-19 case contacts (i.e. within 6 feet of an infected person ≥15min) was significantly higher (13.3 ± 4.8 case contacts vs 7.31 ± 4.8 contacts; p=0.022) among firefighters/paramedics

	cross-sectional study	• Research was funded in part by the State of Florida, the Federal Emergency Management Administration, and the National Cancer Institute of the National Institutes of Health. • Authors declare there are no conflicts of interest.	who were SARS-CoV-2 antibody positive compared with firefighters who tested negative for antibodies. • Of the firefighters/paramedics who tested positive, none reported receipt of the annual influenza vaccine compared with firefighters/paramedics who tested negative for SARSCoV-2 antibodies (0.0% vs 21.0%; p=0.027).
(Valencia et al., 2020) *preprint*	Asymptomatic and presymptomatic transmission of 2019 novel Coronavirus (COVID-19) infection: an estimation from a cluster of confirmed cases in Ho Chi Minh City, Vietnam	• Retrospective epidemiological investigation from a bar gathering in Ho Chi Minh City, Vietnam. • Demographic, clinical, and laboratory information of all COVID-19 confirmed cases and contacts from a bar gathering on March 14, 2020 were collected. • Authors declare there are no conflicts of interest.	• Of the 298 individuals who attended a bar gathering in Ho Chi Minh City, 13 tested positive for SARS-CoV-2. • Contact tracing of 4,466 individuals identified another 6 cases. • The cluster specific R0 was 2.64 (90% CI: 1.41−3.68). • 3 contexts of transmission coming from field investigations were identified (bar, household, workplace). The bar constituted 68%, workplace 21%, and household 11% of transmissions. • Within the second generation, 3 (50%) of the transmissions were workplace-related, of which 2 (67%) reported symptoms after being exposed to a case that did not report symptoms.
(Bao et al., 2020)	COVID-19 outbreak following a single patient exposure at an entertainment site: An epidemiological study	• Retrospective epidemiological investigation of an outbreak associated with a bathing pool at an entertainment venue in Wuhan, China. • Demographic, clinical, and laboratory information of all COVID-19 confirmed cases and contacts were collected during January-February, 2020. • Authors declare there are no conflicts of interest.	• A COVID-19-infected worker who returned home from Wuhan caused an outbreak by visiting a bathing pool on January 20 where he infected some workers and customers. • The infection was then spread by a pool worker who continued to work and by a customer who attended a family party and dinner with colleagues. • The pool worker who continued to work until January 26 caused SARS-CoV-2 infections in 12 customers. • The dinner party with colleagues was comprised of 36 colleagues on January 22. The infected individual sang together in a closed space with 7 colleagues. All 7 colleagues were later confirmed to be infected

			• The secondary attack rate for the dinner party with colleagues was 20.5 (95% CI: 7.8–33.2). • Overall, 56 cases were confirmed across 8 districts with a resident population of 3.9 million.
Transportation			
(Yang et al., 2020)	In-flight transmission cluster of COVID-19: a retrospective case series	• Retrospective epidemiological investigation. • This study describes an in-flight transmission cluster of COVID-19. • Data was collected from January 25 – February 28, 2020. • Face mask policies were not implemented at the time of this cluster. • Authors declare there is no conflict of interest.	• After a flight, 12 COVID-19 cases were identified and associated with the flight. • No flight attendants were infected, thus demonstrating a lack of transmission to the flight attendants.
(Pongpirul , Pongpirul, Ratnarathon, & Prasithsirikul, 2020)	Journey of a Thai taxi driver and novel Coronavirus	• This case report describes a SARS-CoV-2 infection in a taxi driver in Thailand in January 2020. • No conflict of interest statement available.	• The taxi driver became ill on January 20, 2020 and went to a primary care clinic on January 23, 2020. • He reported contact with Chinese tourist passengers in his taxi who had had frequent coughing but who wore masks. He had no history of travel to China.
Other or Combined			
(Qian et al., 2020) *preprint*	Indoor transmission of SARS-CoV-2	• Aggregated data from retrospective epidemiological investigations. • This study analyzed all outbreaks involving 3 or more cases reported to the municipal health commissions in China during the January 4 – February 11, 2020. • The work was funded by the Research Grants Council of Hong and the National	• 318 indoor outbreaks are described across 120 cities. • 80% of the outbreaks involved <5 people. • The venues in which the outbreaks occurred were divided into 6 categories: 79.9% occurred within a home, followed by 34.0% transportation, 4.4% at restaurant, 2.2% shopping venue, and 9.7% at other venues. Many outbreaks involved more than one venue category.

		Natural Science Foundation of China. The authors declare no conflict of interest.	
(Nishiura et al., 2020) *preprint*	Closed environments facilitate secondary transmission of Coronavirus Disease 2019 (COVID-19)	• Aggregated data from retrospective epidemiological investigations. • This study reports the epidemiological data on 11 clusters of 110 cases total that occurred in Japan as of February 26, 2020: 4 in Tokyo and 1 each in Aichi, Fukuoka, Hokkaido, Ishikawa, Kanagawa and Wakayama prefectures. • Authors declare there is no conflict of interest.	• All clusters were associated with indoor environments: gym, restaurant, hospital, and a festival where eating occurred in tents. • Details on whether the cases were employees or customers was not provided. • This study estimated the odds of transmitting in a closed environment vs. open air environment OR 18.7 (95%CI 6.0-57.9). • There was no control for confounders or potential interaction with other predictors in this analysis. The definition of "open-air environment" was not described
(Pung et al., 2020)	Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures	• Retrospective epidemiological investigation of 3 clusters linked to a tour group from China, a company conference, and a church in Singapore in February, 2020. • Authors declare there is no conflict of interest.	• The analysis revealed that 36 individuals with confirmed COVID-19 were linked to 3 local clusters, consisting of 11, 20, and 5 individuals. • The first outbreak involved 11 individuals in a tour group from China. 5 shop assistants from one of the tour stops tested positive for SARS-CoV-2. The assistants reported that they would assist customers to apply samples of medicinal oil on their bodies, and handwashing was not usually done between customers. • The second cluster was a conference attended by at least 111 participants from 19 different countries on January 20–22, 2020. Twenty individuals were infected. 5 of the cases were seated at the same table for a 3hr banquet-style dinner and another 4 cases attended a 4hr breakout session.
(Furuse et al., 2020)	Clusters of Coronavirus Disease in	• Retrospective epidemiological investigation of 3,184 cases in Japan reported during January 15 – April 4, 2020.	• During the time period, 61 case-clusters were identified in healthcare facilities (18 clusters), other care facilities such as nursing homes and day care centers (10),

	communities, Japan, January-April 2020	• Authors declare there is no conflict of interest.	restaurants and bars (10), workplaces (8), music events (7), gymnasiums (5); ceremonial functions (2), and a transportation-related incident in an airplane (1). • The largest non–healthcare-related cluster observed involved >30 persons who attended a live music concert, including performers, audience members, and event staff. • Authors identify 22 probable primary-case patients responsible for the clusters. Most were 20-39 years of age and were pre-symptomatic or asymptomatic at the time of transmission.
(Ministry of Health Manatū Hauora, 2020)	COVID-19 – significant clusters	• The government of New Zealand compiled a list of significant clusters in New Zealand as of August 17, 2020. • No epidemiological details on the clusters provided.	• Clusters reported in potential workplace settings include: wedding, hospitality venue, conference, and cruise ship.
(Colorado Department of Public Health & Environment, 2020)	Outbreak data	• List of all confirmed outbreaks of COVID-19 reported in Colorado, U.S. as of August 12, 2020. • No epidemiological details on the clusters provided.	• Clusters reported in multiple potential workplace settings in Colorado, U.S. A few examples include construction sites, prison, distribution center, laundry services, potato warehouse, meat processing plant, dog food plant, grocery store etc.
(Kim, 2020)	Social distancing and public health guidelines at workplaces in Korea: responses to Coronavirus Disease-19	• Aggregated data from retrospective epidemiological investigations. • This study summarizes public and workplace policies in response to COVID-19 in Korea. • An overview of workplace outbreaks during the period of January 20 - May 15, 2020 are described using data from the Korean	Workplace Transmission in Korea: • Of the 11,018 COVID-19 cases identified as of May 15, 2020, 15.7% occurred in workplaces including such as health-care facilities, call centers, sports clubs, coin karaoke, and nightlife destinations • 111 cases were associated with fitness clubs after instructors were infected at a workshop (Jang et al., 2020) • 192 cases were associated with the call center outbreak

		Center for Disease Control and the Central Disaster Management Headquarters.
		• Authors declare there is no conflict of interest.
			• 95 cases are related to public service (e.g. health department, correctional officers, fire department and police). However, the reason for their exposure has not been identified.
			• Guidelines were developed by February 29, 2020 and are considered to have been effective at limiting workplace transmission after implementation. The Ministry of Employment and Labor workplace guidelines for COVID-19 included:
			  • Social distancing, flexible working schedules, early identification of workers with suspected infections, and disinfection of workplaces
			  • To prevent the spread of workplace infection, the guidelines suggest avoiding face-to-face meetings, business trips, and education and training

Review			

(Prakash, 2020) *preprint*	Eat, pray, work: a meta-analysis of COVID-19 transmission risk in common activities of work and leisure	• Literature review.
		• The author aggregated data from case studies (20 situations and 425 cases) captured through a literature review to identify transmission patterns and estimate attack rates.
		• Author aimed to investigate the social activities that may carry a risk of COVID-19 transmission after the government's ease of the lockdown measures.
		• Methods of literature review and analysis are lacking detail and clarity. No conflict of interest statement available.
			• Events such as family dinners and work meetings, have higher attack rates and, hence, carry significant risks.
			• Overall, 20 situations that resulted in 418 infections across 32 instances from 44 individuals are described below.
			• Situation (transmission rate):
			  ○ Meals/ family events (15.7% to 66.7%)
			  ○ Meetings – 1 hour private meeting (72.7%, 95% CI: 43.6-98.0%)
			  ○ Open work space with people movement (78.7%, 95% CI: 70.3-85.3%)
			  ○ Singing – 2 hour practice (86.7%, 95% CI: 76.2-93.2%)
			  ○ Prayer service (resulted in 1-7 secondary infections per infected individual)
			  ○ Travelling in a car (closed environment) and talking had a higher risk (100%, 95% CI: 20-100%)

			○ Public transportation, wearing a mask with no talking (0%) ○ Hotels (53.3%, 95% CI: 30.1-75.2%)/Cruise ships (28.1%, 95% CI: 27.3-29.0%) where space is shared for days ○ Direct interaction with an infected sales agent (25%, 95% CI: 10.2-49.5%) ○ Nightclub, attack rate among direct contacts >50%, among patrons of the nightclub (6.27%, 95% CI: 5.15-7.61%) ○ Restaurant overall attack rate (9.9%, 95% CI: 5.3-17.7% vs those down wind of the infected individual (45%, 95% CI: 25.8-65.8%) • Across all these super spreading events, the number of infections caused depends on the number of close contacts and in most cases the index case had no symptoms of COVID-19 at the time of transmission.

EVIDENCE OF COVID-19 CLUSTERS FROM EMPLOYER PROVIDED ACCOMMODATIONS

In some occupations, accommodations are provided to workers. In general, shared accommodation results in close contact of workers for long durations of time. Eight COVID-19 publications of workplaces with employer provided accommodations were identified (Table 3). In most of these investigations it is not possible to separate the risk of transmission due to congregate living from activities in the workplace, however the high attack rates among workers in congregate living facilities underscores that transmission occurs in situations where people spend time together and the number of contacts (or density of people) is associated with the number of transmission events that may occur in a given setting.

- Two sequential outbreak summaries of 264 outbreaks in meat processing facilities that have occurred up to May 31, 2020 in the U.S. indicated shared accommodation was a risk factor for the transmission of SARS-CoV-2, however specific data on the number of outbreaks where shared accommodation was a potential factor or the resulting investigations is not provided in these summaries (Dyal et al., 2020; Waltenburg et al., 2020).
- An outbreak associated with shared accommodation of employees on a cruise ship (Diamond Princess cruise ship) where roommates and people that worked with infected cases were more likely to become infected. Another outbreak on a fishing vessel had an attack rate of 85% (N=122) on the small vessel during its 16 days at sea despite pre-screening for SARS-CoV-2 infection. The third outbreak was on a U.S. naval ship, the investigation reported a higher odds of testing positive among persons who reported sharing the same sleeping berth with a crewmember who had positive test results OR = 3.3; 95% CI = 1.8–6.1 (Payne et al., 2020).
- During the initial outbreak peak of COVID-19 cases in Singapore, 88% (17,758/20,198 as of May 6, 2020) of the national cases were attributed to low-skilled migrant workers living in foreign worker dormitories.
- In an outbreak at an overnight summer camp with shared accommodations, staff member attack rates increased with increasing length of time spent at the camp. People stayed in cabins; there was an average of 15 people per cabin (range = 1–26). The median cabin attack rate was 50% (range = 22–70%) among 28 cabins that had one or more cases suggesting an association between transmission risk and staying in a cabin.
- A seroprevalence study in a facility that specializes in the production of mechanical parts and has 237/1,316 employees living at the facility determined that none of the 13 workers with IgG antibodies (history of SARS-CoV-2 infection) were among those living at the facility.

Table 3. Eight COVID-19 publications of Workplaces with Employer Provided Accommodations.

Reference	Publication Title	Study Details	Key Outcomes
(Jerkovic et al., 2020) *preprint*	SARS-CoV-2 antibody seroprevalance in industry workers in Split-Dalmatia and Šibenik-Knin County, Croatia	• This cross-sectional study estimated the seroprevalence on 1494 factory employees living in the Split-Dalmatia and Šibenik-Knin County (Croatia) and was conducted between April 23-28, 2020. • The factory (DIV Group) specializes in the production and trade of screws and other mechanical parts and metal with 2 major production sites located in Split (Split-Dalmatia County), and Knin (Šibenik-Knin County) employing around 2200 people and around 400 people, respectively. • Authors declare there is no conflict of interest.	• As of February 25, 2020 the DIV group implemented protective measures such as providing hand disinfection stations in all rooms, regular workstation cleaning protocols, closing communal coffee and food vending stations, temperature checks, self-isolation for those returning from abroad, and work from home for part of the business and administrative staff. The total number of employees working at the facilities was reduced to around 1,300 and 300, respectively. • In a total sample of tested employees (n=1,494), antibodies were detected in 1.27% of participants (95% CI: 0.77–1.98%). • At the facility in Split, some of the employees live at the facility premises. • In the Split facility 13/1316 (0.99%, 95% CI: 0.53–1.68%) of participants tested positive, of which 13/1079 (1.20%, 95% CI: 0.64–2.05%) of those were living outside the facility and 0/237 (0%, 95% CI: 0–1.26%) of those were living inside the facility. In the Knin facility, 6/178 (3.37%, 95% CI: 1.25–7.19%) participants tested positive for antibodies. All participants living inside facility premises, and with limited mobility during the lockdown measures, tested negative for antibodies. Therefore exposure was likely not related to workplace accommodation in this outbreak,
(Koh, 2020a)	Migrant workers and COVID-19	• Retrospective epidemiological investigation.	• The majority of cases associated with a peak in April occurred among low-skilled migrant workers living in foreign worker dormitories. As of May 6, 2020 there

		• The daily numbers of COVID-19 cases in Singapore from March to May 2020 were analyzed to determine the cause of a surge in cases in April. Regulations on migrant worker accommodation were studied. • Authors declare there is no conflict of interest.	were 17,758 confirmed COVID-19 cases among dormitory workers (88% of 20,198 nationally confirmed cases). • One dormitory housing with ~ 13,000 workers had 2,526 confirmed cases, which accounted for 12.5% of all cases in the country. • The national response included extensive testing of workers in dormitories, segregation of healthy and infected workers, and daily observation for fever and symptoms. In addition 24 dormitories were declared as 'isolation areas' for residents to quarantine for 14 days. Vacant public housing flats, military camps, exhibition centres, and floating hotels have been provided to workers that will allow for appropriate social distancing.
(Dyal et al., 2020)	COVID-19 among workers in meat and poultry processing facilities — 19 States, April 2020	• Aggregated data from retrospective epidemiological investigations. • The report provides aggregate data of positive COVID-19 cases among 115 meat and poultry processing facilities across 19 US states through April 27, 2020. • No potential conflicts of interest were disclosed.	• Among approximately 130,000 workers at these facilities, 4,913 cases (~3.0%) and 20 deaths occurred. • These numbers reflect inadequate infection control practices followed within these facilities including poor social distancing, source control measures (e.g. the use of cloth face covers), and increased workload. • The risk factors for infection were identified as difficulties with physical distancing, hygiene, and crowded living and transportation conditions (many workers live in crowded, multigenerational settings and sometimes share transportation to and from work).
(Waltenburg et al., 2020)	Update: COVID-19 Among Workers in Meat and Poultry Processing Facilities — 19	• Aggregated data from retrospective epidemiological investigations. • This is an update to the report above. • The report provides aggregate data of positive COVID-19 cases among 239 meat and poultry processing facilities across 23 US states through May 31, 2020.	• Within 239 facilities there has been 16,233 COVID-19 cases and 86 COVID-19 related deaths among workers (264 facilities/17,358 cases/91 deaths across both publications (Dyal et al., 2020; Waltenburg et al., 2020)). • Among 14 states reporting the total number of workers in affected meat and poultry processing facilities (112,616), COVID-19 was diagnosed in 9.1% of workers.

	States, April-May 2020	• No potential conflicts of interest were disclosed.	• Of 9,919 (61%) cases with reported race/ethnicity, 87% were among racial and ethnic minority workers. • Factors that increase risk of exposure for these workers include prolonged close workplace contact with coworkers (within 6 feet for ≥15 minutes) for long time periods (8–12 hour shifts), shared work spaces, shared transportation to and from the workplace, congregate housing, and frequent community contact with fellow workers. • Data from 111 facilities across 14 states reveals the implementation of the following prevention and control strategies: screening workers on entry (89/111), required all workers to wear face coverings (86/111), increased the availability of hand hygiene stations (72/111), educated workers on community spread (70/111), installed physical barriers between workers (69/111), offered testing to employees (41/111, and closing temporarily (24/111). • Using data from 7 facilities that implemented facility-wide testing, the crude prevalence of asymptomatic or presymptomatic infections among 5,572 workers who tested positive for SARS-CoV-2 infection was 14.4%.
(Kakimoto et al., 2020)	Initial investigation of transmission of COVID-19 among crew members during quarantine of a cruise ship — Yokohama, Japan, February 2020	• Retrospective epidemiological investigation of an outbreak on a the Diamond Princess cruise ship of 3,700 passengers and crew that began on February 3, 2020. • Authors declare there is no conflict of interest.	• The investigation of SARS-CoV-2 spread among staff concluded that infection had apparently spread among persons whose cabins were on the same deck (deck 3) and who worked in the same occupational group (food service), probably through contact or droplet spread, which is consistent with current understanding of COVID-19 transmission. • 8 of 20 positive crew members had cabin mates, of which 5/8 became COVID-19 positive.

(Addetia et al., 2020)	Neutralizing antibodies correlate with protection from SARS-CoV-2 in humans during a fishery vessel outbreak with high attack rate	• Retrospective epidemiological investigation. • This study describes an outbreak of SARS-CoV-2 on a fishing vessel that departed from Seattle, Washington in May, 2020. • Prior to the ship's departure, crew members were screened for active SARS-CoV-2 infection by RT-PCR and for serological evidence of prior infection. • Authors declare there is no conflict of interest.	• The attack rate on board was 85.2% (104/122 individuals) and metagenomics suggests the outbreak originated from a single source. • The outbreak reports minimal information of the likely transmission dynamics on the boat, but the high attack rate indicates most people were likely exposed. • 3 individuals with neutralizing antibodies prior to departure of the ship did not get re-infected based on the evidence presented, indicating they likely had some protection.

(Payne et al., 2020)	SARS-CoV-2 infections and serologic responses from a sample of U.S. Navy service members - USS Theodore Roosevelt, April 2020	• Retrospective epidemiological investigation of an outbreak that occurred on the USS Theodore Roosevelt in March/April 2020 with approximately 1,000 service men onboard.
		• The investigation occurred April 20-24, 2020 once the ship docked in Guam.
		• A convenience sample of 382 (27% of the total service members on the ship or at the Guam naval base).
		• Questionnaires, serology and RT-PCR tests were done to develop the dataset.
		• Authors declare there is no conflict of interest.
			• Previous or current infection was higher among participants who reported contact with someone known to have COVID-19 (64.2%), compared with those who did not (41.7%) (OR = 2.5; 95% CI = 1.1–5.8).
			• Prevalence was also higher among persons who reported sharing the same sleeping berth with a crewmember who had positive test results (65.6%), compared with those who did not (36.4%) (OR = 3.3; 95% CI = 1.8–6.1).
			• Taking protective measures was associated with lower risk of being COVID-19 positive:
			  • Face covering (55.8% versus 80.8%; OR = 0.3; 95% CI = 0.2–0.5)
			  • Avoiding common areas (53.8% versus 67.5%; OR = 0.6; 95% CI = 0.4–0.9)
			  • Social distancing (54.7% versus 70.0%; OR = 0.5; 95% CI = 0.3–0.8)

(Szablewski et al., 2020)	SARS-CoV-2 transmission and infection among attendees of an overnight camp -	• Retrospective epidemiological investigation of an outbreak associated with an overnight camp in Georgia, U.S.	• 597 Georgia residents attended camp A. Of those tested, 260/344 (76%) tested positive for SARS-CoV-2 infection. • The overall attack rate was 44% (260/597), with staff members having the highest attack rate (56%). Attack

	Georgia, June 2020	• There was an overnight camp (camp A) for orientation for 138 trainees and 120 staff members during June 17-20, 2020. • The staff members remained for the first camp session, scheduled during June 21–27, 2020, and were joined by 363 campers and 3 senior staff members on June 21, 2020. • Authors declare there is no conflict of interest.	rates increased with increasing length of time spent at the camp. • The occupancy of the 31 cabins averaged 15 persons per cabin (range = 1–26). The median cabin attack rate was 50% (range = 22–70%) among 28 cabins that had one or more cases. • The camp followed all CDC recommendations except opening windows and doors for increased ventilation in buildings and campers wearing cloth masks. Staff were supposed to use cloth masks and campers were cohorted, however adherence to these prevention measures could not be assessed.

EVIDENCE OF COVID-19 CLUSTERS FROM TRANSPORTATION OR COMMUTING TO THE WORKPLACE

There is limited evidence on COVID-19 clusters resulting from transportation or commuting to the workplace. Five COVID-19 publications were identified on this topic (Table 4).

- Two publications summarize 264 outbreaks associated with meat processing facilities in the U.S. up to May 31, 2020, shared transportation to and from the workplace was determined as a risk factor for exposure to SARS-CoV-2 (Dyal et al., 2020; Waltenburg et al., 2020). However no specific data is presented.
- In an outbreak in a combined military and civilian office workspace, none of the 150 coworkers who were exposed over three days during carpooling developed symptoms or were considered to have been infected (Hall et al., 2020).
- A study of risk factors for becoming infected with COVID-19 in the UK and U.S. reported a significant higher odds of infection among U.S. workers who use public transportation to get to work. This finding was in the same direction but not significant for UK respondents. Reasons for this difference may be related to difference in public health measures implemented in the study areas (Anand et al., 2020).

Table 4. Five COVID-19 Publications Related to Transportation or Commuting to the Workplace.

Reference	Publication Title	Study Details	Key Outcomes
(Hall et al., 2020)	COVID-19 case and contact investigation in an office workspace	• Retrospective epidemiological investigation conducted in March, 2020. • The outbreak occurred in a combined military and civilian office workspace in the U.S. • No conflict of interest statement available.	• The index case unintentionally exposed 150 coworkers to SARS-CoV-2 through participation in carpools, conferences, and small meetings over a period of 3 days. • Of the 150 exposures, 37 were considered medium risk and 113 were considered low risk. 5 people reported COVID-19 like symptoms and 5 developed symptoms during the 14 day quarantine. None of the contacts tested positive for SARS-CoV-2 infection. • None of the coworkers who were exposed during the carpool developed symptoms and were not believed to have been infected. • The rapid identification of those at risk of infection and subsequent implementation of mitigation and control

			efforts was successful in controlling the spread of SARS-CoV-2.
(Dyal et al., 2020)	COVID-19 among workers in meat and poultry processing facilities — 19 states, April 2020	• Aggregated data from retrospective epidemiological investigations. • The report provides aggregate data of positive COVID-19 cases among 115 meat and poultry processing facilities across 19 US states through April 27, 2020. • No potential conflicts of interest were disclosed.	• Among approximately 130,000 workers at these facilities, 4,913 cases (~3.0%) and 20 deaths occurred. • These numbers reflect inadequate infection control practices followed within these facilities including poor social distancing, source control measures (e.g., the use of cloth face covers), and increased workload. • The risk factors for infection were identified as difficulties with physical distancing, hygiene, and crowded living and transportation conditions (many workers live in crowded, multigenerational settings and sometimes share transportation to and from work).
(Waltenburg et al., 2020)	Update: COVID-19 among workers in meat and poultry processing facilities — 19 states, April - May 2020	• Aggregated data from retrospective epidemiological investigations. • This is an update to the report above. • The report provides aggregate data of positive COVID-19 cases among 239 meat and poultry processing facilities across 23 US states through May 31, 2020. • No potential conflicts of interest were disclosed.	• Within 239 facilities, there has been 16,233 COVID-19 cases and 86 COVID-19 related deaths among workers (264 facilities/17,358 cases/91 deaths across both publications (Dyal et al., 2020; Waltenburg et al., 2020)). • Among 14 states reporting the total number of workers in affected meat and poultry processing facilities (112,616), COVID-19 was diagnosed in 9.1% of workers. • Of 9,919 (61%) cases with reported race/ethnicity, 87% were among racial and ethnic minority workers. • Factors that increase risk of exposure for these workers in include prolonged close workplace contact with coworkers (within 6 feet for ≥15 minutes) for long time periods (8–12 hour shifts), shared work spaces, shared transportation to and from the workplace, congregate housing, and frequent community contact with fellow workers. • Data from 111 facilities across 14 states reveals the implementation of the following prevention and control strategies: screening workers on entry (89/111), required all workers to wear face coverings (86/111),

			increased the availability of hand hygiene stations (72/111), educated workers on community spread (70/111), installed physical barriers between workers (69/111), offered testing to employees (41/111, and closing temporarily (24/111.) • Using data from 7 facilities that implemented facility-wide testing, the crude prevalence of asymptomatic or presymptomatic infections among 5,572 workers who tested positive for SARS-CoV-2 infection was 14.4%.
(Anand et al., 2020) *preprint*	Work-related and personal predictors of COVID-19 transmission	• This cross-sectional study analyzes work and personal predictors of COVID-19. transmission experience in the U.S. and UK • An online survey of 2,000 participants was conducted the first week of June, 2020. • No conflict of interest statement available.	• The findings for the U.S. were different from the UK, the authors theorize this has to do with the stringency of the public health measures. The results indicate occupation, personal traits, circumstance and behaviours all impact risk of COVID-19 exposure and ability to physically distance. • The UK analysis indicated higher risk of having had a COVID-19 diagnosis for those who had no income, lower-middle income status, shared a kitchen and occupations where interactions with customers and staff were on-going. • The U.S. analysis indicated higher risk of having had COVID-19 was related to low income (OR=5.8-6.3), shared kitchen (3.6), having a university degree (2.7), working in a transport related occupation (8.5), belonging to a trade union (4.8), having had a consultation on COVID-19 transmission at work (2.5) and having to take public transportation to work (3.2).
(Leffler & Hogan, 2020) *preprint*	Age-dependence of mortality from novel coronavirus disease (COVID-19) in highly exposed	• Cross-sectional data from several sources and settings were obtained and mortality data was compared. • Authors used publicly available sources to estimate COVID-19 mortality for each age group on the Diamond Princess cruise ship,	• In New York transit workers, mortality was estimated to be 1 in 7,329 for those ages 30-39 years, 1 in 1,075 for ages 40-49 yrs, 1 in 343 for ages 50-59 yrs, and 1 in 178 for ages 60-69 yrs. • Of the MTA workers who had died of COVID-19 (106/109 individuals) as of May 6, 2020 were in the

	populations: New York transit workers and residents and Diamond Princess passengers	in the U.S., in New York City and state, and among New York Metropolitan Transit Authority (MTA) workers. • Authors declare there is no conflict of interest.	subways and buses division, which has 55,000 employees. • Unclear if transmission of these workers occurred at the workplace or outside of the workplace. • Among New York MTA workers, over 6,000 workers (8%) have either tested positive (over 2,000), or entered quarantine (4,000 workers).

EVIDENCE OF COVID-19 CLUSTERS FROM WORK RELATED TRAVEL

Five COVID-19 publications resulting from work related travel were identified (Table 5).

- The first published cluster started with an infected employee who travelled between the China and Germany branches of an organization to facilitate workshops and attend meetings.
- In the second outbreak, the index case and initial case exposures were linked to work related travel to Wuhan, China. Employees infected while on business travel sparked an outbreak in their workplace.
- The last two studies report on clusters of cases that have been linked to conferences, which are often social and networking events (Ministry of Health Manatū Hauora, 2020; Pung et al., 2020). Risk factors identified related to the proximity and length of time secondary cases spent with the primary cases (e.g. sitting at the same table during a meal).

Table 5. Five COVID-19 Publications with Documented Clusters Associated with Work Related Travel.

Reference	Publication Title	Study Details	Key Outcomes
(Böhmer et al., 2020; Rothe et al., 2020)	Transmission of 2019-nCoV infection from an asymptomatic contact in Germany Investigation of a COVID-19 outbreak in Germany resulting from a single travel-associated primary case: a case series	• Retrospective epidemiological investigation. • 2 studies describing the transmission of SARS-CoV-2 from a Chinese resident who visited Germany for professional reasons to her colleagues in January, 2020. • Böhmer et al provide detailed outbreak investigation. • Authors declare there is no conflict of interest.	• Patient 0 was an employee of the Chinese branch of a German company based in Munich. She travelled from Shanghai to Munich by airplane on January 19, 2020 to facilitate workshops and attend meetings in the company building. She returned on an overnight flight back to Shanghai on January 22, 2020 and tested positive for SARS-CoV-2 infection on January 26, 2020. • The German company was informed of the infection on January 27, 2020. Initial testing of high-risk contacts identified patients 1-4 as first generation cases. The company site was closed on February 11, 2020. By February 19, 2020, 16 subsequent cases were identified. • The median serial interval was 4.0 days (IQR 3.0–5.0). • 10 patients in addition to patient 0 were employees of the company. The other 5 were household contacts. Investigation revealed that transmission from patient 0

			to the 10 others likely occurred during the following scenarios: ○ Accompanying patient 0 in multiple activities in Germany traveling back on the same plane ○ In business meetings (60-90 minutes) where colleagues sat close together ○ Colleagues worked simultaneously on the same computer for a short period of time ○ After sitting closely for a 90-minute meeting during the day, 2 colleagues also spent the evening together at one of their homes. However, the partner of the colleague hosting who was also there that evening did not test positive ○ 2 colleagues met during a canteen visit where they sat back-to-back. One of them turned to the other to borrow the salt shaker
(Zhang et al., 2020)	Epidemiological survey of a new coronavirus pneumonia cluster epidemic in collective units in Tianjin	• Article in Chinese. • Retrospective epidemiological investigation conducted in January, 2020. • The outbreak occurred in the administrative office of a plant that has 906 employees in Tianjin, China. • Authors declare there is no conflict of interest.	• The first case was identified on January 15 and spread to 10 other coworkers before control measures were put in place on January 24, 2020. • The index case and initial case exposures are linked to work related travel to Wuhan. • Secondary and tertiary cases either travelled with, participated in meetings, or sat close to infected cases.
(Pung et al., 2020)	Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures	• Retrospective epidemiological investigation of 3 clusters linked to a tour group from China, a company conference, and a church in Singapore in February, 2020. • Authors declare there is no conflict of interest.	• The analysis revealed that 36 individuals with confirmed COVID-19 were linked to 3 local clusters, consisting of 11, 20, and 5 individuals. • The first outbreak involved 11 individuals in a tour group from China. 5 shop assistants from one of the tour stops tested positive for SARS-CoV-2. The assistants reported that they would assist customers to apply samples of medicinal oil on their bodies, and

			handwashing was not usually done between customers. • The second cluster was a conference attended by at least 111 participants from 19 different countries on January 20–22, 2020. 20 individuals were infected. 5 of the cases were seated at the same table for a 3hr banquet-style dinner and another 4 cases attended a 4hr breakout session.
(Ministry of Health Manatū Hauora, 2020)	COVID-19 – significant clusters	• The government of New Zealand compiled a list of significant clusters in New Zealand as of August 17, 2020. • No epidemiological details on the clusters provided.	• Clusters reported in potential workplace settings include: wedding, hospitality venue, conference, and cruise ship.

EVIDENCE OF COVID-19 CLUSTERS RESULTING FROM SOCIAL GATHERINGS OF CO-WORKERS

In addition to SARS-CoV-2 activity in the community, the activities a worker engages in outside of the workplace will determine the individual risk that person brings to the organization. Three COVID-19 clusters resulting from social gatherings of co-workers outside of the workplace were identified (Table 6). All three clusters involved a group of colleagues socializing outside of the workplace and becoming infected. One group socialized in a bar, the other a dinner party which involved singing in an enclosed space, and the third group had "a history of going out in Wuhan". In all three scenarios, the infections acquired through social gatherings of co-workers resulted in additional infections in the workplace.

Table 6. Three COVID-19 Clusters Associated with Social Gatherings of Co-Workers Outside of the Workplace.

Reference	Publication Title	Study Details	Key Outcomes
(Valencia et al., 2020) *preprint*	Asymptomatic and presymptomatic transmission of 2019 Novel Coronavirus (COVID-19) infection: an estimation from a cluster of confirmed cases in Ho Chi Minh City, Vietnam	• Retrospective epidemiological investigation from a bar gathering in Ho Chi Minh City, Vietnam. • Demographic, clinical, and laboratory information of all COVID-19 confirmed cases and contacts from a bar gathering on March 14, 2020 were collected. • Authors declare there are no conflicts of interest.	• Of the 298 individuals who attended a bar gathering in Ho Chi Minh City, 13 tested positive for SARS-CoV-2. • Contact tracing of 4,466 individuals identified another 6 cases. • The cluster specific R0 was 2.64 (90% CI: 1.41−3.68). • 3 contexts of transmission coming from field investigations were identified (bar, household, workplace). The bar constituted 68%, workplace 21%, and household 11% of transmissions. o Within the second generation, 3 (50%) of the transmissions were workplace-related, of which 2 (67%) reported symptoms after being exposed to a case that did not report symptoms
(Bao et al., 2020)	COVID-19 outbreak following a single patient exposure at an entertainment	• Retrospective epidemiological investigation of an outbreak associated with a bathing pool at an entertainment venue in Wuhan, China. • Demographic, clinical, and laboratory information of all COVID-19 confirmed	• A COVID-19-infected worker who returned home from Wuhan caused an outbreak by visiting a bathing pool on January 20, 2020 where he infected workers and patrons of the facility.

	site: An epidemiological study	cases and contacts were collected during January-February, 2020. • Authors declare there are no conflicts of interest.	• The infection was then spread by a pool worker who continued to work and by a customer who attended a family party and dinner with colleagues. • The pool worker who continued to work until January 26, 2020 caused SARS-CoV-2 infections in 12 customers. • The dinner party with colleagues was comprised of 36 colleagues on January 22, 2020. The infected individual sang together in a closed space with 7 colleagues. All 7 colleagues were later confirmed to be infected. • The secondary attack rate for the dinner party with colleagues was 20.5% (95% CI: 7.8–33.2).
(Liu et al., 2020)	Analysis on cluster cases of COVID-19 in Tianjin	• Aggregated data from retrospective epidemiological investigations. • This study describes all clusters of confirmed COVID-19 cases Tianjin as of February 22, 2020. • Authors declare there is no conflict of interest.	• There were family clusters (28 cases, 71 cases), unit clusters (1 case, 10 cases), transportation clusters (3 cases, 8 cases), and a public place cluster (1 case, 26 cases). • A cluster in the passenger section of a train involved 10 cases. After epidemiological investigations, it was finally determined that 2 employees with a history of going out in Wuhan were first-generation cases. • The department store outbreak was an infected sales person that infected 26 customers and coworkers.

EVIDENCE OF SUCCESSFUL RISK REDUCTION STRATEGIES IN THE WORKPLACE

There were 21 publications on strategies to reduce the risk of SARS-CoV-2 infection in the workplace (Table 7). The majority (75%) of these are mathematical models. These studies covered prevention strategies, impact and lifting of public health measures, and management of migrant workers (Table 7).

- Encouraging individuals not to go to work while sick was demonstrated to be effective in five studies through the implementation of an income support program (ISP), furlough policies, and quarantine policies (Brotherhood & Jerbashian, 2020; Coleman, 2020).
- Limiting social contact through a gradual reintroduction of people to the workplace, and reduced people and time in the workplace overall are effective in slowing the spread of SARS-CoV-2 infections (Kim, 2020; Koralnik & Tyler, 2020; Shaw et al., 2020; Yilmazkuday, 2020).
- Availability of guidelines and measures for personal protection at work improved individual personal protective behaviour (Wang, Yi Wong, & Ho, 2020).
- The effectiveness of workplace testing strategies was examined as a way to identify an outbreak. The strategies explored included environmental testing and worker testing.
    - Environmental testing was explored in a study of workplaces in the UK and U.S., findings from environmental testing concluded that workplaces with positive environmental samples were 10 times more likely to have an infected person within the workplace (Marshall et al., 2020).
    - Testing workers was explored across different R0: if R0=2.4, workers would have to be tested at least every 3-4 days to prevent an outbreak in the workplace whereas if R0=3.0, testing would have to take place every 2 days (Chin, Lo, Huynh, Murrill, & Basu, 2020). Less frequent strategies such as once per week or upon return to work were less likely to prevent an outbreak.

Table 7. Twenty-one Publications on Strategies for Risk Reduction in the Workplace.

Reference	Publication Title	Study Details	Key Outcomes
Limiting Social Contact			
(Shaw et al., 2020) *preprint*	Lessons from movement ecology for the	• 2 SEIR models are used: 1) a movement model to explore movement between home and work environments, and 2) a	• Results from the models show that limiting social contact, via reduced people or reduced time in the

	return to work: modeling contacts and the spread of COVID-19	network model to explore contact patterns within the work environment. • A network case study of 1 academic laboratory and office building to explore trade-offs between limiting contact, people, or time on campus. • No conflict of interest statement available.	workplace are equivalent strategies to slow pathogen spread • Restricting on-campus activities to labs (rather than labs and offices) could dramatically alter (modularize) contact network structure and thus, potentially reduce relative risk of pathogen spread. • If commuting specifically increase transmission risk (i.e., shared transport), reducing the number of people on campus is the most effective strategy to reduce the infection spread rate.
(Brotherhood & Jerbashian, 2020) *preprint*	Firm behavior during an epidemic	• Authors derive a mathematical model in which a representative firm operates in an epidemic environment. • The strategies of the firm for reducing the infections and the associated costs include allocation of employees into teleworking and leave, and their rotation between on-site work, teleworking, and leave. • No conflict of interest statement available.	• Simulation results show that the fight against infections in firms has significant effect on the dynamics of the epidemic. Strategies that are successful include increasing teleworking, rotating/cohorting on-site employees and having appropriate leave options. • A 3% subsidy to teleworking reduces the peak of the epidemic by ~ 3% and the total number of symptomatic infections and death rate by nearly 9%. • Furlough policies are successful in reducing infections and death. • When compared to a hypothetical situation where a firm does not fight against infections, the choices of employee allocations and rotation in firms reduce the peak number of sick employees with symptoms by 5%. These choices also flatten the infections curve by reducing the total number of symptomatic infections by 18%. As a consequence, the death rate also declines by 18%.
(Gallardo, de Arroyabe, & Arranz, 2020)	Preventing internal COVID-19 outbreaks within businesses and	• This study applies Social Networks Analysis (SNA) techniques to support Occupational Health and Safety Services in the design and selection of	• The methodology was demonstrated in a real case, a Spanish Research Center, providing promising results. • Authors use the concept of a network of employees whose interaction is caused by triggers, which are defined as common circumstances between 2 workers

	institutions: a methodology based on social networks analysis for supporting occupational health and safety services decision making	preventive measures to reduce the risk of outbreaks among employees. • Authors declare there is no conflict of interest.	that may result in contagion, like sharing an office or participating in the same management board. • As an example, a shared location with enlarged space between people, which is disinfected daily, is less likely to be a contagion trigger than the same location crowded and without regular disinfection.
(Kim, 2020)	Social distancing and public health guidelines at workplaces in Korea: responses to Coronavirus Disease-19	• Aggregated data from retrospective epidemiological investigations. • This study summarizes public and workplace policies in response to COVID-19 in Korea. • An overview of workplace outbreaks during the period of January 20 - May 15, 2020 are described using data from the Korean Center for Disease Control and the Central Disaster Management Headquarters. • Authors declare there is no conflict of interest.	• Workplace Transmission in Korea: o Of the 11,018 COVID-19 cases identified as of May 15, 2020, 15.7% occurred in workplaces including such as health-care facilities, call centers, sports clubs, coin karaoke, and nightlife destinations. o 111 cases were associated with fitness clubs after instructors were infected at a workshop (Jang et al., 2020). o 192 cases were associated with the call center outbreak. o 95 cases are related to public service (e.g. health department, correctional officers, fire department and police). However, the reason for their exposure has not been identified. • Guidelines were developed by February 29, 2020 and are considered to have been effective at limiting workplace transmission after implementation. The Ministry of Employment and Labor workplace guidelines for COVID-19 included: o Social distancing, flexible working schedules, early identification of workers with suspected infections, and disinfection of workplaces

			○ To prevent the spread of workplace infection, the guidelines suggest avoiding face-to-face meetings, business trips, and education and training ○ Small group gatherings, club activities, and social dinner at workplaces were restricted and a culture of returning home right after work was encouraged
Stay-at-Home/Quarantine Policies			
(Coleman, 2020) *preprint*	Economically-motivated interactions and disease spread	• This SIR model analyzed the movement of people throughout the day to match data on the distribution of households by size and age of occupants, the distribution of K-12 schools and colleges by size and staff-student ratios, and office and retail establishments by number of employees. The model was then used to assess large-scale compliance to a mitigation policy directing symptomatic individuals to stay at home. • No conflict of interest statement available.	• Simulations reveal that a mitigation policy where all symptomatic people stay home is sufficient to control the spread of COVID-19 without any noticeable employment effects. • This holds true even if up to 60% of the population is asymptomatic.
(Yilmazkuday, 2020) *preprint*	Stay-at-home works to fight against COVID-19: international evidence from Google mobility Data	• Ecological study. • Used daily Google mobility data covering 130 countries over the period between February 15 – May 2, 2020. • No conflict of interest statement available.	• A 1% weekly reduction in visits to workplaces was equated to about (SE 6.3, $p<0.01$) less COVID-19 cases and 2.0 (0.5, $P<0.01$) less COVID-19 deaths.
(Koo et al., 2020)	Interventions to mitigate early spread of SARS-CoV-2 in	• This influenza epidemic simulation model published in March 2020 investigated options for early	• Modelling in the early days of the pandemic suggested that if community transmission occurred, implementing the combined intervention of quarantining infected individuals and their family members, workplace

	Singapore: a modelling study	intervention in Singapore should local containment be unsuccessful. • Authors declare there is no conflict of interest.	distancing, and school closure could substantially reduce the number of SARS-CoV-2 infections.
Testing and Contact Tracing			
(Chin et al., 2020) *preprint*	Frequency of routine testing for SARS-CoV-2 to reduce transmission among workers	• This SEIR model simulated different testing frequencies required in the workforce to control the epidemic after shelter-in-place policies are lifted. • No conflict of interest statement available.	• If R0=2.4, workers would have to be tested at least every 3-4 days to reduce R0<1 and prevent an outbreak in the workforce. • With a higher R0 (3.0), testing would have to take place every 2 days. Since this is likely unrealistic, other strategies such as social distancing and contact tracing should also be implemented.
(Foncea, Mondschein, & Massouh, 2020) *preprint*	Safer working spaces at Coronavirus time: a novel use of antibody tests	• A Monte Carlo simulation model was used to analyze the efficacy of periodic SARS-CoV-2 antibody testing to reduce the risk of infection in the workplace. • No conflict of interest statement available.	• This preliminary simulation model suggests that with antibody testing twice a week and quarantine of workers suspected of SARS-CoV-2 infection can reduce the number of infections while improving the productivity of the company. • Authors are currently in the process of applying some combinations of the protocols within the model with specific firms and government agencies and will report on these when results become available.
(Bicher, Rippinger, Urach, Brunmeir, & Popper, 2020) *preprint*	Agent-based simulation for evaluation of contact-tracing policies against the spread of SARS-CoV-2	• This agent-based model quantifies the impact of contact tracing and relaxing lockdown measures on the spread of the disease. The impact of the location tracing for households and for workplaces were evaluated separately and in combination with different compliance levels. • No conflict of interest statement available.	• In workplace tracing, the workplace of a confirmed COVID-19 patient is temporarily closed and all the coworkers are put into quarantine. • Location tracing based on shared workspaces reduces the peak by 30% regardless of compliance level, whereas household tracing performs better as compliance increases. • These measures combined achieves the greatest peak reduction and performs best with a high level of compliance. Additional individual tracing would result in a higher reduction.

(Meng et al., 2020) *preprint*	The effect of control measures on COVID-19 transmission and work resumption: international evidence	• Ecological study, the causal effect of different control measures on COVID-19 transmission and work resumption in 5 countries: China, Italy, Germany, the United Kingdom, and the United States was quantified. • Authors acknowledge financial supports from the National Natural Science Foundation of China, Chinese National Social Science Foundation, and the Humanities and Social Sciences grant of the Chinese Ministry of Education. No conflict of interest statement available.	• The 2 most effective policy measures for disease containment and work resumption are digital contact tracing and delegating clear responsibility to the local community. • Population-wide contact tracing contributes to the largest effect on work resumption, encouraging work resumption by 2.4%. • A 1% increase in the strictness of social distancing encouraged work resumption by 1.2%. • Public information campaigns, delegating clear responsibility to the local community encouraged work resumption of approximately 0.9-1.0%. • Fiscal measures such as loans, tax deduction, and factor price deduction contribute less to work resumption (~0.5%) while the strictness of health care does not directly help at all.
(Way, Champneys, Dyson, & et al., 2020) *preprint*	The benefits of peer transparency in safe workplace operation post pandemic lockdown	• An SEIR model was used to investigate workplace transmission in 2 different groups of workers under the assumption that all workers are regularly tested for SARS-CoV-2 infection: 1) those that are transparent about testing, share their results with colleagues, and isolate as soon as a contact tests positive for the disease, 2) opaques who do none of these. • The workplaces considered in the analysis were back offices, or factory settings where employees are assumed to have a static network of coworkers they regularly interact with and all other interactions in the workplace would be socially distanced.	• The greater the connectivity among coworkers, the smaller the opacity must be among employees to reduce transmission. • There is a double benefit of transparency among employees in maximising productivity and minimizing overall infection rates.

		• No conflict of interest statement available.	
De-Escalation of Public Health Measures			
(Asfaw, 2020) *preprint*	The effect of Income support program on workplace mobility, COVID-19 case and mortality growth	• Ecological study on the income support program (ISP) aims to mitigate the economic consequences of the pandemic while increasing compliance with social distancing measures. This study analyzes the effect of ISP on workplace mobility, and COVID-19 case and mortality growth using a multi-event analysis model. • No conflict of interest statement available.	• Workplace mobility was reduced in the range of 4.4-8.29% 1 week after the introduction of ISP and 21.8-47.7% after 3 weeks. • 5 weeks after the implementation of the program, there was a 21.8-47.0% and 17.1-29.7% reduction on COVID-19 case growth and mortality growth, respectively. • In the absence of ISP programs, authors estimate the global cumulative number of COVID-19 cases and mortality would have been 3.69 million and 160, 000 more than the observed COVID-19 cases and deaths registered by May 15, 2020.
(Koralnik & Tyler, 2020) *preprint*	COVID-19 epidemic study II: phased emergence from the lockdown in Mumbai	• An agent-based city-scale simulator was used to model scenarios for phased emergence from lockdown in Mumbai, India starting on June 1, 2020. • Study was funded by IISc-Cisco Centre for Networked Intelligence, the Robert Bosch Centre for CyberPhysical Systems, the Indian Institute of Science, and the Department of Atomic Energy, Government of India. • No conflict of interest statement available.	• Results demonstrate that a phased opening of workplaces, at a conservative attendance level of 20-33% is a good way to restart economic activity while ensuring that the city's medical care capacity remains adequate to handle the possible rise in the number of COVID-19 patients in June and July 2020. • This will keep the occupancy on the suburban trains and buses at a similar low level, thereby reducing infection spread in crowded public transit systems. • For trains, occupancy should be restricted to about 20% for the first few weeks with enforcement of strict physical distancing and compulsory wearing of face covers.
(López & Rodó, 2020)	The end of the social confinement in Spain and the COVID-19 re-emergence risk	• This SEIR model simulates various potential post-confinement strategies in Spain such as instant massive liberation of different populations and a gradual incorporation of people to work.	• Results show that the current lockdown should be extended at least 2 more weeks to prevent a new escalation in cases and deaths, as well as a second wave in a few months. • Of all the scenarios modeled, the best case involves gradually incorporating workers back into society in a

		• Authors declare there is no conflict of interest.	daily proportion of at most 30% higher than that of previous confinement. This will lower incidence and casualties. To maximize the positive impacts, this strategy should not begin earlier than the end of April 2020.
Surveillance and Environmental Monitoring			
(Marshall et al., 2020) *preprint*	Sentinel Coronavirus environmental monitoring can contribute to detecting asymptomatic SARS-CoV-2 virus spreaders and can verify effectiveness of workplace COVID-19 Controls	• Prospective cohort study aimed to assess the efficacy of using SARS-CoV-2 environmental monitoring as a tool to detect asymptomatic and pre-symptomatic spreaders and conducting clinical and environmental surface testing at work locations to minimize infections. • 9 workplaces in Europe and the U.S. were enrolled in the study. Of these, 3 locations had 1 or more employees infected with SARS-CoV-2. • Authors state that funding for the study was provided by the participating locations and laboratories.	• The locations which had surfaces contaminated with SARS-CoV-2 were 10 times more likely to have employees who tested positive for SARS-CoV-2 infection compared to locations with no or very few positive surfaces. • The most frequently contaminated surfaces were break room chairs, work benches, and door handles. • Since locations with numerous environmental positive detections had an infected employee during the study period, environmental monitoring appears to be a useful tool to inform clinical testing required to detect asymptomatic or pre-symptomatic virus spreaders and implement appropriate control measures.
(Gunawardana et al., 2020) *preprint*	Longitudinal COVID-19 surveillance and characterization in the workplace with public health and diagnostic endpoints	• Prospective cohort was conducted to assess if longitudinal workplace disease surveillance would be an effective approach to controlling SARS-CoV-2 among employees and their household members. Results between March 23-June 22, 2020 are presented. • From a small Southern California organization (Oak Crest), 54 volunteers (27 employees and 27 household members) provided frequent samples	• Using the current prevalence in Los Angeles County, the model predicted without surveillance intervention, up to 7 employees (95% CI: 3-10) would have become infected with at most 1 of them requiring hospitalizations and 0 deaths. • During the study period, 2 study participants were found to be infected with SARS-CoV-2. 1 was an employee and the other a household member. • The employee was not allowed entry to the safe zone workplace until testing negative 3 consecutive times over a period of 7 days. No other employee or

		for SARS-CoV-2 testing. Only participants with a negative test result were able to enter the "safe zone" workplace facility. • A combination of an SEIR model and Bayesian non-linear mixed model were used to predict the number of employees and household members that would have been infected in the absence of the surveillance program. • Authors state that the study was funded entirely through discretional, institutional funds.	household member contracted SARS-CoV-2 over the course of the study.
Workplace Guidance			
(Wang et al., 2020) *preprint*	Availability of workplace policy for prevention of coronavirus disease 2019 and its relationship with personal protective behaviors: a survey of employees	• Cross-sectional study using an online questionnaire assessing the workplace guidelines and personal protection behavior of employed Hong Kong residents (n=1,048) was conducted between February 17-27, 2020. • Authors declare there is no conflict of interest.	• 1,048 questionnaires across 5 occupational groups were analyzed. • In most occupations, the availability of workplace guidelines and measures for the prevention of COVID-19 improved personal protection behaviors such as hand hygiene, wearing a face mask, and social distancing.
Management of Migrant Workers			
(Maji, Choudhari, & Sushma, 2020)	Implications of repatriating migrant workers on	• This SEIR model investigated the potential surge in confirmed and active cases of COVID-19 infection in India and assessed the train and bus fleet size	• Results indicate that reducing the daily arrival rate of migrant workers for states with a very high out flux of migrants (i.e., Uttar Pradesh and Bihar) can help to lower the surge in confirmed and active cases.

	COVID-19 spread and transportation requirements	required for the repatriating migrant workers. • By forecasting the 2011 census data and comparing it with the information reported in the media, the expected repatriate migrant worker population was obtained. • No conflict of interest statement available.	• However, it could create a disparity in the number of days needed to transport all repatriating migrant workers to the home states. Travel arrangements for about 100,000 migrant workers per day to Uttar Pradesh and Bihar, about 50,000 per day to Rajas-than and Madhya Pradesh, 20,000 per day to Maharashtra and less than 20,000 per day to other states of India was recommended. • Authors suggest that stringent measures in screening migrant workers before boarding and strict isolation policy after arrival might control the surge in confirmed and active cases.
(Han & Jia, 2020) *preprint*	Reductions of migrant population reduces the number of COVID-19 epidemic: a case study in China	• A generalized additive model (GAM) was utilized to model the relationship between migrant population and the number of confirmed cases of COVID-19 in China. • The study was funded by the Peking University Start-up Grant. Authors declare there is no conflict of interest.	• Using China as a case study, results show that the number of confirmed COVID-19 cases were correlated with the population migration and regional population density (R2adj = 0.873, deviance explained = 89.6%). The number of confirmed cases will increase with the growth of these variables. • Therefore, restricting population travel can greatly reduce the number of confirmed cases and limit the expansion of the disease. • Once the migrant population returns to work increasing population movement, the number of confirmed cases will reach 27,483 (95% CI: 16,074-48,097). The average increase in 73 cities was 85.53% (95% CI: 19.53-189.81%).
(Maji, Sushma, & Choudhari, 2020) *preprint*	Implication of inter-state movement of migrant workers during COVID-19 lockdown using	• This SEIR model evaluates the effect of inter-state migrant worker transportation during the lockdown in India. Starting on May 5, 2020 it is assumed that migrant workers will start arriving at their respective destinations and the model analyzed the daily arrival	• The states with significant migrant workers are estimated to have a rise in confirmed and active cases • Authors suggest that stringent measures in screening migrant workers prior to boarding and strict isolation after arrival can help to keep the rise in confirmed and active cases under control.

	modified SEIR model	rate of 20,000-100,000 migrant workers per state. • No conflict of interest statement available.	

Methods

All of the literature on COVID-19 has been compiled and organized by the Emerging Science Group of the Public Health Agency of Canada since the beginning of the outbreak. This involves a daily scan of the literature for all published and pre-published articles. Searches to retrieve relevant COVID-19 literature are conducted in PubMed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, and Research Square. These are cross-referenced with the literature on the World Health Organization COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier, and Wiley. The daily summary and full scan results are maintained in a RefWorks database and a searchable Excel file. Each article is tagged using various foci to identify the focus of the article (e.g. epidemiology, clinical data, therapeutics etc.). Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. The search terms included in this review were workplace, work*, occupation, colleague, manufacturing, factory, and employee, gathering, and super spread*. There were no language restrictions. Each potentially relevant reference was analyzed to confirm its relevance and data was extracted into the review. Additional articles and grey literature reports were added to the database as they were identified. Grey literature was limited to government and public health institution reports. Media sources and news briefs were not considered reliable or detailed enough for inclusion. A snowball search was conducted which included cross-checking the reference lists of published reviews and relevant articles for relevant research omitted by the search. As this is a rapid review, double screening or extraction from articles and a formal quality (risk of bias) assessment was not conducted on the included studies. This review contains research published up until August 21, 2020.

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Nouveaux éléments de preuve sur la COVID-19

Revue rapide du risque d'éclosion de la COVID-19 sur le lieu de travail

Introduction

Quels sont les éléments de preuve de l'existence de grappes de COVID-19 associées au lieu de travail, les caractéristiques des lieux de travail et les facteurs susceptibles d'augmenter le risque de transmission du SRAS-CoV-2, et les preuves de la réussite des mesures de prévention et de contrôle de l'infection sur le lieu de travail?

Sous-questions :

Existe-t-il des éléments de preuve que les aménagements fournis par l'employeur entraînent des grappes de cas de COVID-19?
Existe-t-il des éléments de preuve que le transport ou les déplacements vers le lieu de travail entraînent des grappes de cas de COVID-19?
Existe-t-il des éléments de preuve de voyages liés au travail entraînant des grappes de cas de COVID-19?
Existe-t-il des éléments de preuve que les rassemblements sociaux de collègues ont donné lieu à des grappes de COVID-19?

L'atténuation de la pandémie actuelle a impliqué des politiques de distanciation sociale qui ont eu un impact important sur les lieux de travail (Corrin, 2020). Il s'agit notamment de fermer des lieux de travail, d'encourager le télétravail, de modifier le flux des activités pour réduire au minimum les contacts entre les employés avec d'autres personnes et de mettre au point des procédures améliorées de prévention et de contrôle des infections pour réduire le risque de transmission du SRAS-CoV-2. La définition du lieu de travail dans cette étude est censée être globale, c'est-à-dire que le lieu de travail comprend, sans s'y limiter, les bureaux, la zone de production, les commerces de détail, les services et les services publics. Les transmissions sur les lieux de travail des soins de santé n'ont pas été incluses dans cette revue. En plus de la transmission se produisant directement sur les lieux de travail, des éléments de preuve ont été recherchés pour les situations de transmission liées au travail, notamment le logement ou le transport fourni par l'employeur, les trajets domicile-travail, les déplacements liés au travail et les réunions sociales de collègues. Cette synthèse en bref identifie et résume la littérature jusqu'au 21 août 2020.

Points clés

- Les éclosions ont été associées à de nombreux types de lieux de travail et de professions (tableau 1).
    - Outre le risque connu des professionnels de la santé, les professions les plus exposées au risque d'infection par le SRAS-CoV-2 sont les suivantes : les conducteurs et les travailleurs du transport, les travailleurs des services et de la vente, l'industrie alimentaire, les professions des

soins personnels, les travailleurs de la production alimentaire, les professions du secteur préscolaire, les professions des services communautaires et sociaux (par exemple, les travailleurs sociaux, les conseillers), les professions du bâtiment et des métiers connexes, et les travailleurs de la sécurité publique (par exemple, les agents correctionnels, la police, les pompiers).

- La majorité d'entre eux exige que les travailleurs aient des contacts fréquents avec les clients, travaillent dans les locaux des clients ou dans les espaces publics. Nombre de ces professions ne permettent pas aux employés de travailler à domicile.

- Des grappes sur le lieu de travail se sont produites dans un large éventail de lieux et de circonstances qui ont entraîné une transmission (tableau 2).
    - La plupart des grappes sur le lieu de travail ont été attribuées à un cas index asymptomatique ou très légèrement symptomatique.
    - Trente-sept publications décrivent un ou plusieurs événements de transmission considérés comme s'étant produits sur un lieu de travail impliquant des travailleurs, classés en gros dans les catégories suivantes : environnement de bureau, usines de transformation de la viande, autres usines, travail des migrants, centres de remise en forme, navires, autres professions liées aux services et transports (tableau 2).
    - Huit grappes de COVID-19 ont été identifiées dans les lieux de travail où l'employeur fournit le logement (tableau 3). Le partage du logement entraîne un contact étroit entre les travailleurs pendant de longues périodes.
    - Il existe peu de données sur les grappes de COVID-19 résultant du transport ou du déplacement vers le lieu de travail (tableau 4). Le transport partagé vers et depuis le lieu de travail a été déterminé comme un facteur de risque d'exposition au SRAS-CoV-2 dans les éclosions des usines de transformation de la viande.
    - Les grappes de COVID-19 résultant de déplacements liés au travail ont été identifiées dans cinq publications (tableau 5). Les facteurs de risque identifiés sont liés à la proximité et à la durée de la période passée avec les cas primaires (par exemple, s'asseoir à la même table pendant un repas ou une réunion).
    - Trois grappes de COVID-19 résultant de rassemblements sociaux de collègues en dehors du lieu de travail ont été identifiées (tableau 6). Dans les trois scénarios, les infections transmises lors des réunions sociales des collègues ont entraîné des infections supplémentaires sur le lieu de travail.
- Les facteurs de risque d'infection par le SRAS-CoV-2 identifiés sur le lieu de travail comprennent les difficultés à respecter les distances physiques, le manque d'hygiène des mains, une mauvaise conception de la ventilation/circulation de l'air et des conditions de travail, de transport et/ou de logement surpeuplées (tableaux 1-6).

- Les principaux facteurs facilitant la transmission du SRAS-CoV-2 dans un bureau sont les contacts étroits, la durée des interactions, les zones communes partagées et les déplacements professionnels.
- Les facteurs sociodémographiques et la profession ont été examinés pour étudier les facteurs communs de l'exposition au SRAS-CoV-2 (tableau 1). Le fait d'être une femme, d'appartenir à une minorité visible et d'avoir un faible revenu était lié aux professions associées à un risque considérablement plus élevé d'exposition à la COVID-19 qui ne permettent généralement pas de travailler à domicile et qui impliquent de travailler à proximité d'autres personnes. À l'inverse, l'augmentation de l'âge et une éducation supérieure étaient associées à un risque plus faible d'exposition liée à la profession.
- Les facteurs de risque d'infection dans les usines de transformation de la viande ont été identifiés comme étant les difficultés de distanciation physique, le contact étroit prolongé avec les collègues de travail pendant de longues périodes, l'hygiène des mains, le partage du logement, le transport partagé pour se rendre au travail et en revenir, et les contacts fréquents communautaires avec les collègues de travail. Ces facteurs de risque ont également été identifiés dans les éclosions sur les navires.
- En plus de l'activité liée au SRAS-CoV-2 dans la communauté, les activités qu'un travailleur exerce en dehors du lieu de travail détermineront le risque individuel qu'une personne apporte à son entreprise.
- Plusieurs études font état d'un risque accru d'exposition au SRAS-CoV-2 proportionnel au nombre de contacts liés à l'emploi des travailleurs. Par exemple, les employés d'une épicerie directement exposés aux clients avaient cinq fois plus de chances d'obtenir un résultat positif au test de dépistage du SRAS-CoV-2 (RC de 4,7; IC de 95 % : de 1,2 à 32,0). Une deuxième étude a fait état d'un résultat similaire pour les pompiers et les ambulanciers.
- Le partage des logements ou des installations (par exemple, les toilettes) et l'absence de mesures préventives (par exemple, un masque facial) ont été suggérés comme contribuant à plusieurs éclosions dans les centres commerciaux, les magasins de détail, les bars, les boîtes de nuit, les restaurants, les concerts et les camps de nuit.
- Les éclosions sont plus susceptibles de se produire dans un environnement intérieur (RC de 18,7; IC de 95 % : de 6,0 à 57,9).

- Deux évaluations des risques ont examiné les caractéristiques des lieux de travail et le potentiel de transmission du SRAS-CoV-2.
  - Dans une évaluation des risques, une augmentation de 1 % de la densité des entreprises à super-propagation (ESP – basée sur la fréquence, la durée et la superficie des entreprises avant la pandémie) équivaut à une augmentation de 5 % des cas. Les ESP les plus courantes sont les restaurants à service complet, les restaurants à service limité et les hôtels/motels.

  - Les risques sanitaires potentiels du SRAS-CoV-2 dans les eaux usées pour les travailleurs des stations d'épuration ont été étudiés à l'aide d'une évaluation quantitative des risques microbiens (EQRM). Les tâches à proximité des réservoirs d'eaux usées ont été considérées comme présentant un risque élevé d'exposition et une protection telle qu'un masque facial, une protection oculaire et/ou des écrans faciaux ont été recommandés.

- Des stratégies visant à réduire le risque de transmission du SRAS-CoV-2 sur le lieu de travail ont été identifiées dans 21 publications (tableau 7).
  - Parmi les stratégies de prévention réussies, citons la limitation des contacts sociaux (limitation des activités sur le lieu de travail, cohorte ou échelonnement des employés et télétravail), les politiques d'exclusion des travailleurs malades du milieu de travail, la fourniture de directives sur le lieu de travail et la mise à disposition d'équipements de protection individuelle.
  - Les stratégies de surveillance ont exploré le mode (échantillonnage des travailleurs ou de l'environnement) et la fréquence d'échantillonnage permettant une identification efficace de la transmission ou de la circulation du SRAS-CoV-2 sur le lieu de travail et la manière dont le niveau de SRAS-CoV-2 dans la communauté a un impact sur les stratégies d'échantillonnage.
  - La levée des mesures de santé publique a été envisagée pour minimiser une résurgence, tout en permettant une lente réouverture de l'économie.
  - La gestion des travailleurs migrants, en particulier leur déplacement d'un endroit à l'autre, a été abordée dans trois publications de Chine et d'Inde. Les stratégies comprenaient des protocoles de dépistage et de quarantaine pour limiter l'importation du SRAS-CoV-2 dans une zone non touchée.

Vue d'ensemble des éléments de preuves

Soixante-dix-sept publications relatives au risque d'éclosions de la COVID-19 sur le lieu de travail et à la réduction des risques sur le lieu de travail ont été identifiées et incluses dans cette revue. Parmi celles-ci, 33 sont des prépublications et n'ont pas encore été soumis à l'examen des pairs. Les plans d'étude par observation peuvent être affectés par plusieurs catégories de biais, notamment les biais de déclaration, d'information et de sélection, qui peuvent biaiser les données et les conclusions d'une étude (Murad, Asi, Alsawas et Alahdab, 2016). Un risque formel d'évaluation de la partialité est hors du champ de cette revue rapide. Les cotes de biais sont fondées sur le plan d'étude, les études par observation étant considérées comme présentant un risque de biais de modéré à élevé selon le plan. Dans le cas des plans d'étude par observation, cela place les grandes cohortes prospectives en tête, car le plan d'étude peut présenter un faible risque de biais et une grande confiance dans les résultats et les rapports de cas sont considérés comme ayant une très faible confiance dans les résultats.

La plus grande partie des recherches qui sous-tendent cette revue consiste principalement d'investigations épidémiologiques de petite envergure sur les grappes et les éclosions, qui présentent généralement un risque

élevé de biais en raison de leur nature rétrospective. Bien que l'exhaustivité des investigations et des rapports varie beaucoup, il existe une bonne cohérence entre ces investigations, ce qui contribue à notre confiance dans les éléments de preuve.

Plusieurs études écologiques ont été saisies; ces études sont susceptibles d'une série de biais et d'erreurs écologiques en raison de leur incapacité à caractériser la variabilité des expositions et des facteurs de confusion au sein d'un groupe. Des études transversales ont été utilisées pour fournir un aperçu des facteurs de risque individuels et de l'exposition au SRAS-CoV-2, mais ne permettent pas de tirer des conclusions sur la causalité. Le plan de cohortes prospectives a été utilisé dans deux études évaluant les stratégies d'atténuation sur le lieu de travail. La cohorte prospective présente un risque de biais plus faible que les autres plans d'étude par observation, bien que les deux études retenues dans cette revue aient des échantillons de petite taille.

Les modèles prédictifs et les évaluations des risques ne prédisent pas une réalité future, mais présentent plutôt une série de résultats plausibles dans les scénarios étudiés. Leurs résultats sont utiles pour comparer différentes options dans le cadre d'un processus décisionnel, mais ils doivent être interprétés avec prudence, car les modèles varient en fonction de leurs hypothèses et de leurs valeurs d'entrée selon la période épidémique et les paramètres spécifiques à la région utilisés.

En raison de la nature des éléments de preuve présentés dans cette étude (études d'observation et modèles prédictifs) et des biais qui y sont associés, cette revue rapide fournit peu d'éléments sur les conditions de travail qui entraînent un risque plus élevé de transmission du SRAS-CoV-2, et sur les stratégies de réduction des risques. Sur la base des plans d'étude portant sur les études incluses, il est peu probable que des recherches supplémentaires ne modifient pas les conclusions de cette revue. La littérature existante sur la COVID-19 évolue rapidement et cette revue devrait être périodiquement mise à jour afin d'intégrer les nouvelles recherches.

TABLE DES MATIÈRES

RISQUES PROFESSIONNELS

Les risques professionnels associés à l'infection par la COVID-19 ont été identifiés dans 20 publications (tableau 1). Il s'agissait notamment de deux revues et de trois évaluations des risques. Les publications de cette section ont porté sur les professions et les caractéristiques des professions qui entraînent un risque plus ou moins élevé de transmission sur le lieu de travail.

- Dans les publications, les professions identifiées comme les plus exposées au risque d'exposition au SRAS-CoV-2, en dehors des professionnels de la santé, sont énumérées ci-dessous (tableau 1). Les travailleurs de la santé (TS) sont considérés comme n'entrant pas dans le cadre de cette revue, mais dans les documents portant sur les facteurs de risques professionnels, les TS sont fréquemment inclus dans l'analyse et les résultats.
    - Transport : conducteurs et travailleurs du transport, coursiers, chauffeurs de bus
    - Commerce de détail/services : travailleurs des services et de la vente, personnel des hôtels et des centres de villégiature
    - Industrie alimentaire : restaurant, transformation des aliments, abattoirs et usines de transformation de la viande
    - Administration de bureau et vente : professions avec un taux élevé de contacts avec la clientèle.
    - Soins personnels : travail dans les maisons de soins infirmiers, les garderies, les établissements préscolaires; professionnels religieux; travailleurs de soins personnels; professionnels de la santé associés (par exemple, les dentistes), le personnel des instituts et salons
    - Services sociaux et communautaires : travailleurs sociaux et conseillers, agents de santé communautaires, prestataires de services de garde
    - Construction, extraction et métiers connexes : plombiers, installateurs de fosses septiques, réparation d'ascenseurs, entretien des terrains et des installations
    - Travailleurs de la sécurité publique : pompiers, policiers, agents pénitentiaires
    - Travailleurs des eaux usées
- Les professions à faible risque d'exposition au SRAS-CoV-2 comprenaient les professions qui pouvaient faire du télétravail et/ou s'éloigner socialement des autres (tableau 1). Parmi ces derniers, on peut citer les agriculteurs, les opérateurs de machines, les entreprises qui ont une interaction minimale avec le public ou les clients (Sierpiński et coll., 2020).

- Les travailleurs essentiels (qui comprennent un grand nombre des catégories à haut risque énumérées ci-dessus) sont plus exposés au risque d'infection par la COVID-19 que la population générale (tableau 1). Ce risque est accru par l'interaction croissante avec les collègues, les clients ou le public.
- Les facteurs sociodémographiques et leur association avec un risque élevé d'exposition au SRAS-CoV-2 ont été examinés dans plusieurs études (tableau 1). Les femmes, les minorités visibles et les personnes à faible revenu sont plus susceptibles d'occuper des emplois associés à un risque considérablement plus élevé d'exposition à la COVID-19, car leur profession ne leur permet pas de travailler à domicile et implique de travailler de façon très rapprochée d'autres personnes. À l'inverse, l'augmentation de l'âge et une éducation supérieure étaient associées à un risque plus faible d'exposition liée à la profession.
- Le personnel des écoles maternelles, primaires et secondaires n'a pas une prévalence relative de COVID-19 plus élevée que les autres professions (Agence suédoise de santé publique, 2020).
- Une étude a indiqué que les trajets entre le domicile et le lieu de travail dans les transports publics étaient positivement associés au risque d'infection par le SRAS-CoV-2. Un résultat qui était considérablement plus évident dans l'échantillon américain que dans l'échantillon britannique, ce qui, selon les auteurs, pourrait être lié à l'uniformité et à la rigueur du confinement britannique (Anand et coll., 2020).
- Deux évaluations des risques ont exploré les attributs des lieux de travail et de la mobilité quant à leur potentiel de transmission du SRAS-CoV-2.
    - Une évaluation des risques a évalué les entreprises en fonction de leur potentiel de super-propagation (ESP) sur la base de la fréquence, de la durée et de la superficie des entreprises avant la pandémie dans 8 États américains. Une association positive entre les ESP (5 % des entreprises avec les taux les plus élevés étaient considérées comme des ESP) et les cas hebdomadaires cumulés de COVID-19 a été signalée, montrant qu'une augmentation de 1 % du nombre d'ESP dans une zone équivalait à une augmentation de 5 % des cas. Les ESP les plus courantes étaient les restaurants à service complet, les restaurants à service limité et les hôtels/motels (Donoghue et coll., 2020).
    - Les risques sanitaires potentiels du SRAS-CoV-2 dans les eaux usées pour les travailleurs des stations d'épuration ont été étudiés à l'aide d'une évaluation quantitative des risques microbiens (EQRM). Les charges virales estimées dans les eaux usées à l'entrée des stations d'épuration étaient supérieures aux valeurs seuils de sécurité suggérées par l'Organisation mondiale de la santé (OMS) (Zaneti et coll., 2020).

Tableau 1. Vingt publications sur les risques professionnels liés à l'infection par la COVID-19.

Référence	Titre de la publication	Détails de l'étude	Résultats pertinents
Études d'observation			
(Lan, Wei et Hsu, 2020)	Transmission de la COVID-19 liée au travail dans six pays/régions d'Asie : une étude de suivi	• Cette étude d'observation rétrospective a identifié des cas possibles liés au travail à partir de rapports d'investigation gouvernementaux à Hong Kong, au Japon, à Singapour, à Taiwan, en Thaïlande et au Vietnam qui ont été signalés entre le 23 janvier et le 14 mars 2020. • Les auteurs ont déclaré qu'ils n'avaient pas d'intérêts concurrents.	• Après exclusion de tous les cas importés, 103 transmissions possibles liées au travail ont été identifiées à partir des 690 transmissions locales ayant fait l'objet d'une investigation. • En dehors des travailleurs de la santé, les groupes professionnels les plus souvent impliqués sont les suivants : conducteurs et travailleurs du transport (18 %), travailleurs des services et de la vente (18 %), agents d'entretien et femmes de ménage – 22 (9 %), travailleurs de la sécurité publique (7 %) et professionnels du secteur religieux (6 %). • Un changement entre les professions trouvées dans les grappes pendant la phase initiale de l'éclosion (principalement les travailleurs des services et de la vente, et les ouvriers de la construction) et celles trouvées à la phase ultérieure de l'éclosion (principalement les travailleurs de la santé, les agents d'entretien et femmes de ménage et les agents de police).
(Sierpiński et coll., 2020)	Risques professionnels liés à l'infection par le SRAS-CoV-2 : l'expérience polonaise	• Cette étude transversale a analysé les sources et les facteurs de risque professionnels des infections par le SRAS-CoV-2 sur 2122 patients infectés par le SRAS-CoV-2 qui sont restés isolés chez eux en Pologne. • L'investigation a été menée les 17 et 18 avril 2020 au moyen d'une interview structurée.	• Parmi les 2122 participants atteints du SRAS-CoV-2, 75 % ont été infectés au travail et 70 % avaient un emploi (activité professionnelle). • Parmi les cas d'activité professionnelle, 48 % travaillaient dans le secteur des soins de santé, 3 % dans l'administration publique ou la défense, 3 % dans les transports et 2 % dans l'éducation. • 65 % des cas ayant une activité professionnelle travaillaient dans des entreprises de plus de 100 salariés.

		• Aucune déclaration de conflit d'intérêts n'est disponible.	
(Torres Martínez, Diaque García, Rubio Salas et coll., 2020) *prépublication*	Séroprévalence des IgG contre le SRAS-CoV-2 dans une cohorte de 449 personnes non hospitalisées et exposées à un risque élevé	• Cette étude transversale a estimé la séroprévalence sur 449 personnes à Madrid, en Espagne, avec l'un des critères d'inclusion suivants : avoir des symptômes de la COVID-19, être en contact avec un cas de COVID-19, ou appartenir à des professions essentielles, notamment les travailleurs de la santé, les pompiers ou le personnel de sécurité publique comme la police. • Étude réalisée du 15 avril au 15 juin 2020. • Les auteurs déclarent que 3 de leurs auteurs sont fondateurs, membres du conseil d'administration et actionnaires de EMPIREO Diagnóstico Molecular.	• La séroprévalence globale était de 33,69 % (IC de 95 % : de 29,27 à 38,21). • Sur les 449 personnes testées, 9,58 % étaient des travailleurs de la santé, 4,01 % des pompiers et 6,46 % travaillaient dans la sécurité publique. Les autres n'appartenaient pas à ces professions. • En ce qui concerne ces professions à haut risque d'exposition, il n'y a pas eu de différence significative dans la séroprévalence. Il n'y avait pas non plus de différence dans la séroprévalence des IgG entre les groupes de professions suspectes, exposées ou à haut risque, ce qui suggère un niveau élevé d'exposition dans les professions à haut risque d'exposition.
(Koh, 2020b)	Risques professionnels liés à la COVID-19	• Cette étude d'observation rétrospective décrit 17 cas qui étaient probablement dus à une exposition professionnelle à Singapour pendant la période du 4 au 11 février 2020, avant toute mesure de santé publique. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les expositions professionnelles comprenaient du personnel du commerce de détail vendant principalement aux touristes et du personnel d'entreprises qui participait à une réunion d'affaires internationale à Singapour. • Des chauffeurs de transport, des ouvriers du bâtiment et des personnes travaillant dans le secteur du tourisme ont été impliqués (par exemple, un employé de casino ou de station balnéaire).
(Anand et coll., 2020) *prépublication*	Prédicteurs professionnels et personnels de la	• Cette étude transversale analyse les prédicteurs professionnels et personnels de l'expérience de	• Les résultats aux États-Unis étaient différents de ceux au Royaume-Uni, les auteurs théorisent que cela est dû à la rigueur des mesures de santé publique. Les résultats indiquent que la profession, les traits personnels, les

	transmission de la COVID-19	transmission de la COVID-19 aux États-Unis et au Royaume-Uni. • Une enquête en ligne a été menée auprès de 2000 participants la première semaine de juin 2020. • Aucune déclaration de conflit d'intérêts n'est disponible.	circonstances et les comportements ont tous une incidence sur le risque d'exposition à la COVID-19 et sur la capacité à s'éloigner physiquement. • L'analyse britannique a indiqué un risque plus élevé d'être testé positif à la COVID-19 pour les personnes sans revenu, à revenu moyen inférieur, qui partageaient une cuisine et avaient un emploi où les interactions avec les clients et le personnel étaient permanentes. • L'analyse américaine a indiqué que le risque plus élevé d'être infecté par la COVID-19 était lié à un faible revenu (CR entre 5,8 et 6,3), à une cuisine partagée (3,6), à un diplôme universitaire (2,7), à une profession liée au transport (8,5), à l'appartenance à un syndicat (4,8), à une consultation sur la transmission de la COVID-19 au travail (2,5) et au fait d'avoir dû prendre les transports publics pour se rendre au travail (3,2).

(Agence suédoise de la santé publique, 2020) *prépublication*	Prévalence de la COVID-19 dans différents groupes professionnels	• Article en suédois.
		• Cette étude transversale analyse la prévalence de la COVID-19 entre différents groupes professionnels en utilisant les données sur la classification des professions de Statistics Sweden et les cas diagnostiqués pendant la période du 13 mars au 27 mai 2020.
		• Les professionnels de la santé ont été exclus de l'analyse.
		• Aucune déclaration de conflit d'intérêts n'est disponible.
			• Par rapport aux autres groupes professionnels, les chauffeurs de taxi avaient environ 5 fois plus de risques d'être infectés par le SRAS-CoV-2 (RR : 4,8, IC de 95 % : de 3,9 à 6).
			• Parmi les autres groupes professionnels à haut risque, on peut citer :
			  • Les préparateurs de pizzas – RR 4,5, IC de 95 % : de 3,2 à 6,3
			  • Les conducteurs d'autobus et de tramways – RR 4,3, IC de 95 % : de 3,6 à 5,1
			  • Les traducteurs et linguistes – RR 2,9, IC de 95 % : de 1,8 à 4,7
			  • Les responsables de restaurant et de cuisine – RR 2,5, IC de 95 % : de 1,7 à 3,8
			  • Les autres travailleurs des services (par exemple, les travailleurs qui remplissent les distributeurs

			automatiques, qui lisent les compteurs électriques et de gaz, etc.) – RR 2,3, IC de 95 % : de 2,1 à 3 • Les pompiers – RR 2,2, IC de 95 % : de 1,4 à 3,5 • Les professionnels du nettoyage (par exemple, nettoyeurs de voitures, laveurs de vitres) – RR 1,7, IC de 95 % : de 1,1 à 2,7 • Les gestionnaires immobiliers – RR 1,6, IC de 95 % : de 1,3 à 2 • Les assistants de restaurant et de cuisine – RR 1,4, IC de 95 % : de 1,2 à 1,7 • Le personnel des écoles maternelles, primaires et secondaires n'a pas une prévalence relative de COVID-19 plus élevée que les autres professions. • Les professeurs de lycée – RR 0,7, IC de 95 % : de 0,5 à 1 • Les enseignants du primaire – RR 1,1, IC de 95 % : de 0,9 à 1,3 • Les éducateurs en loisirs – RR 0,8, IC de 95 % : de 0,5 à 1,3 • Les enseignants de maternelle – RR 0,7, IC de 95 % : de 0,6 à 0,9 • Les autres éducateurs ayant des compétences spécialisées – RR 1,0, IC de 95 % : de 0,7 à 1,5 • Les gardes d'enfants – RR 1,0, IC de 95 % : de 0,8 à 1,2 • Les assistants d'élèves – RR 1,1, IC de 95 % : de 0,8 à 1,4 •
Études écologiques			
(Lewandowski, 2020)	Exposition professionnelle à la contagion et à la	• Cette étude écologique a mesuré les niveaux d'exposition professionnelle à l'indice de contagion spécifique à chaque pays, dérivé d'une combinaison	• Dans les pays où la proportion de travailleurs fortement exposés est plus élevée, le fait que ces travailleurs aient tendance à être plus âgés explique la forte corrélation

prépublication	propagation de la COVID-19 en Europe	de données d'O*NET (exposition à la maladie ou à l'infection et proximité physique au travail) et de l'Enquête européenne sur les conditions de travail (traiter avec les gens, travailler en public, travailler dans les locaux du client et ne pas pouvoir travailler à domicile). Les travailleurs de la santé ont été exclus de l'analyse. • Aucune déclaration de conflit d'intérêts n'est disponible.	entre l'âge de 45 à 64 ans et l'indice d'exposition professionnelle à la contagion. • Dans les pays européens, de 20 à 25 % de la variance entre ces pays dans le nombre de cas et de décès liés à la COVID-19 peuvent être attribués aux différences entre pays dans les niveaux d'exposition professionnelle à la contagion. • Les professions les plus à risque sont les travailleurs des services personnels, les travailleurs des services de protection, les travailleurs de la vente et les travailleurs du bâtiment et des métiers connexes. • Les professions qui présentent le moins de risques sont notamment les ouvriers agricoles et les travailleurs agricoles, les opérateurs d'usines et de machines qui ne sont pas à proximité les uns des autres, et les entreprises qui n'ont pas d'interaction avec le public ou les clients et qui ont la capacité de permettre à leurs employés de travailler à domicile.
(Baker, Peckham et Seixas, 2020)	Estimation de la charge de travail des travailleurs américains exposés à une infection ou à une maladie : un facteur clé pour contenir le risque d'infection par la COVID-19	• Cette analyse préalable à l'épidémie de COVID-19 visait à quantifier le nombre de travailleurs qui sont fréquemment exposés à des infections et des maladies sur leur lieu de travail aux États-Unis, et à comprendre quels groupes professionnels ils représentent en combinant les données sur leurs activités professionnelles du réseau Occupation Information Network(O*Net) (à partir d'une mise à jour partielle en 2018) avec les données de la base de données Occupational Employment Statistics du	• Selon les estimations autodéclarées par O*Net en 2018 et extrapolées à partir des données du BLS, environ 10 % (14,4 millions) des travailleurs aux États-Unis exercent des professions où l'exposition à la maladie ou à l'infection se produit au moins une fois par semaine. En outre, 18,4 % (26,7 millions) sont employés dans des professions où l'exposition à la maladie ou à l'infection se produit au moins une fois par mois. • Les professions présentant un risque d'exposition plus élevé sont celles du secteur des soins de santé, des services de protection (par exemple, policiers, agents correctionnels, pompiers), des bureaux et du soutien administratif (par exemple, messagers et coursiers, représentants des services aux patients), de l'éducation (par exemple, éducateurs préscolaires et de garderie),

		Bureau of Labor Statistics (BLS) (à partir de mai 2018). • Aucune déclaration de conflit d'intérêts n'est disponible.	des services sociaux et de proximité (agents de santé communautaires, travailleurs sociaux, conseillers), et de la construction et de l'extraction (par exemple, plombiers, installateurs de fosses septiques, réparateurs d'ascenseurs).
(St-Denis, 2020)	Facteurs sociodémographiques des risques professionnels d'exposition à la COVID-19 au Canada	• Cette analyse préalable à l'épidémie de COVID-19 a permis d'identifier les groupes de la population active les plus exposés à la COVID-19 en fonction des caractéristiques de leur profession et de les évaluer par rapport aux données sociodémographiques. • Les données sur les activités professionnelles ont été extraites de la base de données O*Net (niveau de proximité physique avec d'autres personnes, et fréquence d'exposition aux maladies et aux infections) du recensement canadien de 2016. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les résultats mettent en évidence l'association entre le statut socioéconomique et les activités professionnelles qui peut augmenter le risque d'exposition chez les femmes, les immigrants et les membres des minorités visibles. • Environ 45 % des travailleurs canadiens exercent des professions qui exigent de travailler à proximité physique relativement étroite d'autres personnes (à distance d'un bras ou moins). • Les femmes travaillent dans des professions où les risques moyens d'exposition à la COVID-19 sont considérablement plus élevés que chez les hommes. • Les personnes titulaires d'une licence ou d'un diplôme supérieur sont généralement confrontées à des risques d'exposition professionnelle considérablement plus faibles. • Les travailleurs exerçant des professions à faible revenu sont plus susceptibles d'exercer des professions présentant des risques d'exposition plus élevés. • Les professions exercées par les travailleurs âgés (65 ans et plus) se caractérisent par un niveau de proximité physique avec les autres inférieur à celui de leurs collègues plus jeunes.
(Barbieri, Basso et Scicchitano, 2020)	Les travailleurs italiens en danger pendant l'épidémie de la COVID-19	• Cette étude écologique utilise des indices artificiels qui représentent la proximité physique sur le lieu de travail, l'exposition aux maladies et aux infections, et la possibilité de travailler	• Plusieurs secteurs nécessitent une proximité physique pour fonctionner : les travailleurs employés en Italie dans les secteurs dont l'indice de proximité physique est supérieur à la moyenne nationale sont plus de

prépublication		à distance au niveau professionnel et qui ont été créés à partir des données de l'Enquête italienne par échantillonnage sur les professions (ICP) et de l'Enquête sur la population active italienne de l'ISTAT. • Les auteurs déclarent que les opinions exprimées dans le document sont celles des auteurs et ne reflètent pas nécessairement celles de la Banque d'Italie ni celles de l'INAPP.	6,5 millions (la plupart d'entre eux travaillent dans le commerce de détail). • Les groupes à risque de contagion et de complications en raison de la COVID-19 (principalement des hommes de plus de 50 ans) travaillent dans des secteurs peu exposés à d'autres personnes, sont actuellement confinés ou peuvent travailler à distance. • Les secteurs présentant l'indice physique le plus élevé sont l'hôtellerie et la restauration, l'éducation, la santé et le commerce (principalement le commerce de détail).
(Lewandowski, Lipowska et Magda, 2020)	Le facteur sexe de l'exposition des professions à la contagion en Europe	• Cette étude écologique visait à mesurer l'exposition des professions aux maladies contagieuses en utilisant les données de O*Net 2018 et de l'Enquête européenne sur les conditions de travail (« EECS »), 2015). • Les auteurs analysent spécifiquement le facteur sexe dans l'exposition des professions. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les femmes sont 26 % plus susceptibles de travailler dans des professions très exposées qui nécessitent un contact avec des maladies, des contacts fréquents avec des clients et une grande proximité physique au travail. • Les femmes sont plus susceptibles que les hommes de ne pas pouvoir travailler à domicile en raison de leur profession. Les femmes plus âgées et les femmes ayant un niveau d'éducation supérieur étaient moins susceptibles d'exercer une profession très exposée. • Les professions où l'exposition aux contagions est élevée sont les travailleurs de soins personnels, les travailleurs de santé, les professionnels de santé associés, les travailleurs des services personnels et les travailleurs des services de protection. À l'exception de la dernière catégorie, les catégories antérieures sont à prédominance féminine. La prise en compte du secteur économique du sexe au travail n'est pas un prédicteur significatif de l'exposition aux contagions. Toutefois, dans certains secteurs, les jeunes femmes sont nettement plus susceptibles d'exercer des professions très exposées.

(Hawkins, 2020)	Risque professionnel différentiel der l'exposition au COVID-19 et à d'autres infections selon la race et l'origine ethnique	• Cette étude écologique visait à évaluer comment la ségrégation professionnelle selon la race et l'ethnicité contribue au risque de la COVID-19. • Les données de l'enquête Current Population Survey du Bureau of Labor Statistics ont été utilisées pour l'analyse. • Les auteurs ont déclaré qu'ils n'avaient pas d'intérêts concurrents.	• Cet article identifie que certaines professions à haut risque d'exposition emploient de manière disproportionnée certains groupes ethniques. • Les travailleurs noirs étaient plus susceptibles d'être employés dans des secteurs essentiels et dans des professions nécessitant fréquemment une grande proximité avec les autres (travailleurs de la santé, aide sociale, hôpital, chauffeurs de bus, aides aux soins personnels, industrie alimentaire). • Les travailleurs noirs et hispaniques avaient plus de deux fois plus de chances d'être employés dans le secteur de l'abattage et de la transformation des animaux, où de nombreuses éclosions de la COVID-19 se sont déclarées.
(Rogers et coll., 2020)	Disparités raciales dans la mortalité due à la COVID-19 chez les travailleurs essentiels aux États-Unis	• Cette étude écologique analyse les données de l'American Community Survey et de la Current Population Survey pour examiner la corrélation entre les décès dus à la COVID-19 et les différences professionnelles entre les groupes raciaux/ethniques dans les États américains. • Les données sur les décès dus à la COVID-19 jusqu'au 24 avril 2020 ont été incluses. • Les auteurs remercient une personne, qui a fourni une assistance éditoriale, et Data for Black Lives (http://d4bl.org/) qui a indirectement soutenu l'investigation en étant l'une des premières organisations à dresser une liste d'États ayant partagé publiquement les données d'incidence et de mortalité connexes à la COVID-	• Les personnes noires non hispaniques (NH) occupent de manière disproportionnée les 9 premiers emplois essentiels, ce qui augmente leur risque d'exposition à la COVID-19, y compris les 3 plus grandes disparités : transport et déplacement de matériel, soutien aux soins de santé, préparation et service des aliments. • Les personnes d'origine hispanique étaient proportionnellement plus nombreuses à travailler dans la préparation et le service des aliments, le nettoyage et l'entretien des bâtiments et des terrains et la production. • Les personnes d'origine asiatique sont plus susceptibles de travailler dans le secteur des soins et services personnels, des soins de santé et de la préparation et du service des aliments.

		19. La recherche a été partiellement soutenue par une subvention de National Institutes of Health.	
(Peters, 2020)	Sensibilité et résilience de la communauté à la COVID-19 dans le continuum rural-urbain aux États-Unis	• Dans cette étude écologique, une échelle de sensibilité à la COVID-19 est générée au niveau du pays en utilisant des données provenant du Census Bureau des États-Unis et du CDC. Les auteurs évaluent ensuite la santé et la résilience socio-économique des lieux sensibles dans le continuum rural-urbain aux États-Unis. • L'étude a été soutenue par le projet de recherche multi-états W4001 de la station d'expérimentation agricole de l'USDA. Les auteurs déclarent qu'il n'y a pas de conflits d'intérêts.	• Sur la base des données sur l'emploi, les usines de transformation de la viande augmentent le risque d'infection dans les zones rurales. • Les éclosions de COVID-19 dans les communautés rurales de conditionnement de la viande ont une incidence disproportionnée sur les travailleurs hispaniques et d'autres minorités.
Modèles prédictifs			
(Milligan et coll., 2020) *prépublication*	Incidence des travailleurs essentiels dans le contexte de la distanciation sociale pour le contrôle des épidémies	• Ce modèle SEIR a examiné des scénarios avec 3 groupes différents de travailleurs essentiels pour déterminer leur risque de contracter la COVID-19 : 1) les travailleurs essentiels en contact avec le public (caissiers, commerce de détail, transport), 2) les travailleurs essentiels en contact avec le public (employés d'usine, d'entrepôt et d'agriculture), et 3) les travailleurs de la santé. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les travailleurs essentiels courent un risque accru d'infection par la COVID-19 par rapport à la population générale. • Les travailleurs essentiels qui ne sont pas en contact avec le public sont susceptibles d'être exposés à des éclosions sur leur lieu de travail même après des pratiques de distanciation sociale, tandis que les travailleurs essentiels en contact avec le public ont un taux de contact élevé avec d'autres personnes et donc un risque plus élevé d'être exposés à une personne infectée que ceux qui restent à la maison. • Il a été constaté que différents types de travailleurs essentiels (caissiers, employés d'usine et travailleurs de santé) avaient des incidences différentes sur les

			scénarios de transmission. De même, les efforts d'atténuation (par exemple les masques, la distanciation physique, etc.) ont eu une incidence sur la transmission.
Revues			
(Rafeeman esh, Ahmadi et Memarzad eh, 2020)	Une revue des stratégies et des études sur la prévention et le contrôle du nouveau coronavirus sur les lieux de travail	• Revue documentaire publiée en avril 2020, pas de date de recherche ni de section sur la méthodologie. • Les auteurs ont voulu examiner les stratégies nécessaires pour prévenir et contrôler la COVID-19 sur le lieu de travail. • Stratégie de recherche et dates de la recherche non communiquées. • Les auteurs ont déclaré qu'ils n'avaient pas d'intérêts concurrents.	• Professions à haut risque d'exposition : o Le CDC a identifié les professions qui sont plus exposées à la COVID-19 : 1) les travailleurs de la santé (TS), 2) le personnel des cimetières et des pompes funèbres, 3) les fonctionnaires et le personnel des aéroports, des compagnies aériennes, des chemins de fer, des métros et de tous les transports publics (bus, taxis, etc.), 4) les gardes-frontières, 5) les travailleurs du secteur des déchets solides et des eaux usées, et 6) les employés qui se déplacent régulièrement, notamment dans les zones contaminées o Les dentistes et les maquilleurs sont également exposés à un risque élevé en raison de la communication en face à face avec les clients et de l'exposition à la salive, au sang et à l'haleine expirée o Les équipages des avions et des navires risquent d'être en contact avec des passagers infectés • Solutions de contrôle : o Contrôles techniques (isolement des symptômes, ventilation, barrières entre les personnes, outils jetables) o Contrôles administratifs (exclusion des travailleurs malades, formation à l'hygiène, réduction des heures de travail du personnel, télétravail, mise en cohorte, nettoyage et désinfection continus, restriction des rassemblements de personnel)

			○ Équipement de protection individuelle (masque facial approprié, protection des yeux, gants et vêtements spéciaux – selon les besoins) • Obstacles clés : ○ Le fait de continuer à travailler malgré la maladie (présentéisme) est un problème majeur. Des politiques de congé de maladie étendues aideront dans ce sens
(Leng et coll., 2020)	Voies de transmission du coronavirus nCov-2019 et contrôles en cabinet dentaire	• Revue documentaire publiée en avril 2020, pas de date de recherche ni de section sur la méthodologie • Les auteurs visent à donner un aperçu des voies de transmission et du risque d'exposition pour les personnes travaillant dans l'industrie dentaire. • Les auteurs ont déclaré qu'ils n'avaient pas d'intérêts concurrents.	• Voies de transmission ○ Il existe un risque élevé de transmission directe dans les cabinets dentaires en raison du travail direct avec la bouche et du contact avec les muqueuses buccales/nasales, ainsi que de l'exposition à la salive, au sang et à d'autres liquides respiratoires ○ Transmission par voie aérienne aux personnes sensibles dans la clinique ○ La transmission indirecte par des fomites peut également constituer un risque, car la manipulation d'instruments tranchants en contact direct avec des fluides corporels potentiellement chargés de virus peut se produire • Mesures de lutte contre les infections ○ Évaluation du patient, contrôle de la température ○ Hygiène des mains ○ Protection des barrières, notamment masque facial, protection des yeux, écran facial, vêtements de travail (par exemple, blouse de laboratoire) ○ Rinçage de bouche antimicrobien avant l'intervention dentaire, la digue en caoutchouc peut minimiser les éclaboussures de sang et de salive.

			○ L'utilisation de pièces à main anti-retrait à grande vitesse peut réduire le risque de contamination croisée. ○ Une désinfection stricte et continue
Évaluation des risques			
(Donoghue et coll., 2020) *prépublication*	Entreprises de super-propagation et risque de transmission de COVID-19	• Cette évaluation des risques explore les attributs des entreprises à super-propagation (ESP). Les ESP étaient les entreprises se situant dans les 5 % supérieurs de l'indice de risque de transmission de la COVID-19 en entreprise (Business Transmission Risk Index), qui est basé sur la fréquence, la durée et la superficie des entreprises avant la pandémie dans huit États américains. • Aucune déclaration de conflit d'intérêts n'est disponible.	• L'analyse binomiale négative a révélé une association positive entre les ESP et les cas hebdomadaires cumulés de COVID-19, où une augmentation de 1 % des ESP équivaut à une augmentation de 5 % des cas. • Les types d'entreprises les plus courants classés comme ESP comprennent les restaurants à service complet, les restaurants à service limité et les hôtels/motels. • Les attributs des ESP dans cette étude sont généralement des entreprises où les visiteurs restent plus longtemps et où les espaces sont plus bondés.
(Zaneti et coll., 2020) *prépublication*	EQRM du SRAS-CoV-2 pour les travailleurs dans les stations d'épuration des eaux usées	• Une évaluation quantitative des risques microbiens (EQRM) a été utilisée pour étudier les risques sanitaires potentiels du SRAS-CoV-2 dans les eaux usées pour les travailleurs des stations d'épuration des eaux usées (SEEU). • L'EQRM a été appliquée pour 3 scénarios de COVID-19 (modéré, agressif et extrême) afin d'étudier le risque pendant les différentes phases de la pandémie. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les charges virales estimées dans les eaux usées à l'entrée des stations d'épuration variaient de 1,03x102 à 1,31x104 CG/mL (GC= copies du génome), ce qui équivaut à 0,1 à 13,06 UFP/mL (UFP= unités formatrices de plaques). • On a supposé que la dose d'exposition était de 1mL et que la contamination se produisait à des concentrations allant de 1,03 x 10^2 GC/mL à 1,31 x 10^4 GC/mL dans des scénarios modérés à extrêmes. • Le résultat a été un risque estimé pour lequel l'OMS suggère un seuil de 1 x 10^{-3} (basé sur le risque tolérable d'infection par le rotavirus de l'eau potable) : Les scénarios extrêmes (3,1 x 10^{-2}), agressifs (6,5 x 10^{-3}) et

			modérés ($3,0 \times 10^{-4}$) rapportent un risque 31, 6,5 et 0,3 fois supérieur au seuil de l'OMS. • Les travailleurs des stations d'épuration exposés aux bioaérosols et aux particules en suspension dans l'air sont exposés à un risque professionnel que peu d'études ont examiné. • La lutte contre l'infection pourrait inclure l'utilisation d'un masque et d'un écran facial lors des travaux de nettoyage manuel et la réduction du temps passé dans les zones de traitement • Les charges virales dans les eaux usées pourraient être utilisées comme un outil d'alerte précoce pour la communauté et aider à prioriser des stratégies de contrôle des infections améliorées dans le secteur de l'assainissement.
(Zachreson, Mitchell, Lydeamore et coll., 2020) *prépublication*	Cartographie des risques d'éclosions de COVID-19 à l'aide de données sur la mobilité	• Une approche heuristique de l'estimation du risque de transmission basée uniquement sur des informations qualitatives concernant les facteurs épidémiologiques et éclairée par des estimations en temps quasi réel des schémas de mobilité. • Les éclosions liées aux rassemblements sont particulièrement bien adaptées à cette méthode. • Elles valident leurs estimations en utilisant 3 scénarios bien documentés d'éclosions de COVID-19 en Australie. Il s'agit notamment d'éclosions dans un abattoir, un hôtel et au sein d'une communauté. • Les données sur la mobilité ont été utilisées à partir de Facebook et les	• Facteurs spécifiques au lieu de travail (contexte) : o Localisation commune (entrée et sortie d'une zone d'éclosion) o Se trouvait sur le lieu de l'éclosion avant l'identification de l'éclosion o Statistiques des professions dans la zone ou le lieu étudié (aide à identifier un type d'activités communes dans la zone de l'éclosion) Remarque : la méthode ci-dessus peut être appliquée à tout endroit où les déplacements sont habituels. • Exemple : Éclosion de Cedar Meats en avril 2020, Australie o Une carte des risques de mobilité et le coefficient de corrélation de Spearman indiquent qu'avec des données de cas et de mobilité limitées, la localisation de l'éclosion associée à Cedar Meats à Brimbank aurait pu être identifiée très tôt. Ce résultat a encore

		données sur les cas ont été obtenues par l'intermédiaire des autorités sanitaires de l'État australien. • Aucune déclaration de conflit d'intérêts n'est disponible.	été amélioré grâce à l'ajout de données processionnelles pour la région. o Ces résultats montrent également comment les données sur la mobilité peuvent être un outil utile à l'estimation de la diffusion du risque de transmission de la COVID-19 à partir des lieux de l'éclosion et au début d'une éclosion. Cela peut être utilisé pour intensifier les mesures de santé publique à un stade précoce et aider à contenir une éclosion ou une transmission communautaire (comme le montrent les autres exemples), en particulier lorsque nous avons peu de cas et que nous nous efforçons de prévenir une résurgence des cas. • 2 autres exemples sont présentés concernant un rassemblement social et une transmission communautaire. Ils ne sont pas résumés ici.

TRANSMISSION SUR LE LIEU DE TRAVAIL

Un large éventail de lieux de travail ont été impliqués dans des cas de transmission du SRAS-CoV-2 et de nombreux cas de transmission, bien qu'ils aient été identifiés, n'ont pas fait l'objet d'une investigation approfondie ni d'une publication. Un projet en cours, accessible au public, visant à compiler les événements de super-propagation de la COVID-19 (>5 cas) a été identifié et les 1500 événements signalés dans cette liste soulignent l'ampleur de l'insuffisance de signalement des événements de transmission (Swinkels, 2020). Les événements de transmission omis dans la littérature publiée et préimprimée ont été enregistrés sur les tableaux de bord des pays et par les médias. Ces derniers ont été exclus de cette revue, car ils ne sont souvent pas signalés avec suffisamment de détails pour évaluer l'événement de transmission ou l'investigation.

- Le tableau 2 énumère 37 publications qui décrivent un ou plusieurs événements de transmission considérés comme s'étant produits sur un lieu de travail impliquant des travailleurs, classés en gros dans les catégories suivantes : environnement de bureau, usines de transformation de la viande, autres usines, travail des migrants, centres de remise en forme, navires, autres professions liées aux services, transports et études de grappes multiples.

- Quatre éclosions ont été identifiées dans des bureaux (centre d'appels, bureau administratif, réunions). Les principaux facteurs facilitant la transmission du SRAS-CoV-2 dans un bureau sont l'activité (par exemple, parler), la proximité d'une personne infectée (par exemple, s'asseoir à côté d'elle) et la durée pendant laquelle la personne infectée est proche.
- Les éclosions dans les usines de transformation de la viande en Allemagne et aux États-Unis sont décrites dans cinq publications. Les facteurs de risque d'infection ont été identifiés comme suit : difficultés d'éloignement physique, contact étroit prolongé avec des collègues de travail, facteurs environnementaux tels que l'air recyclé refroidi, l'hygiène des mains, le logement partagé, le transport partagé pour se rendre au travail et en revenir, et les contacts communautaires fréquents avec les collègues de travail.
    - L'investigation sur le plus grand complexe de transformation de la viande en Allemagne fait état d'un taux d'attaque élevé des travailleurs se trouvant à moins de huit mètres du poste de travail fixe des cas index (Guenther et coll., 2020).
- Une étude de séroprévalence menée dans une usine en Croatie a révélé que des anticorps ont été détectés chez 1,27 % des participants (IC de 95 % : de 0,77 à 1,98 %, n=1,494). Cependant, aucune éclosion n'a été détectée dans l'usine et aucun des travailleurs hébergés dans les logements fournis par l'employeur ne présentait d'anticorps. L'employeur avait adopté des mesures de protection renforcées (par exemple, des stations de désinfection des mains, le nettoyage régulier des postes de travail, la fermeture des stations communes de vente de café et de nourriture, le contrôle de la température, l'auto-isolement pour les personnes revenant de l'étranger et le travail à domicile pour une partie du personnel commercial et administratif) (Jerkovic et coll., 2020).
- Les travailleurs migrants logés dans des logements partagés ont été associés à une importante éclosion à Singapour (Koh, 2020a).
- Dans trois éclosions survenues sur des bateaux (le navire de croisière Diamond Princess, un navire de pêche et un navire de la marine américaine), le partage de logement et le travail à proximité immédiate ont été identifiés comme des facteurs de risque de transmission du SRAS-CoV-2.
- Une importante éclosion liée à une salle de sport multicentrique a été retracée jusqu'à un atelier où plusieurs instructeurs ont été infectés et ont transmis le SRAS-CoV-2 à d'autres employés et clients dans les centres où ils étaient employés (Jang, Han et Rhee, 2020).
- Une étude transversale a estimé la séroprévalence de 104 personnes employées dans une épicerie du Massachusetts, aux États-Unis. Les résultats d'une analyse multivariée révèlent que les employés directement exposés aux clients avaient cinq fois plus de chances d'obtenir un résultat positif au test de dépistage du SRAS-CoV-2 (RC 4,7; IC de 95 % : de 1,2 à 32,0) (Lan, Suharlim, Kales et Yang, 2020). Une deuxième étude (Caban-Martinez et coll., 2020) a fait état d'un résultat similaire chez les pompiers et les ambulanciers.

- Trois études ont montré que l'emploi dans le secteur des transports constituait un facteur de risque chez les chauffeurs de taxi et les chauffeurs de bus, mais aucun cas de transmission à une hôtesse de l'air n'a été documenté à ce jour.
- Il a été suggéré que le partage des logements ou des installations (par exemple, les toilettes) et l'absence de mesures préventives (par exemple, un masque facial) ont contribué à plusieurs éclosions dans les centres commerciaux, les magasins de détail, les bars, les boîtes de nuit, les restaurants, les salles de concert et les camps de nuit.
- Les éclosions sont plus susceptibles de se produire dans un environnement intérieur (RC de 18,7; IC de 95 % : de 6,0 à 57,9) (Nishiura et coll., 2020).
- Les principales mesures de protection identifiées comprennent la pratique d'un contrôle exemplaire des infections dans les environnements fermés, des politiques d'exclusion des travailleurs malades du lieu de travail et le respect des précautions personnelles de contrôle des infections au travail.

Tableau 2. Trente-sept publications sur les événements de transmission sur le lieu de travail.

Référence	Titre de la publication	Détails de l'étude	Résultats pertinents
Environnement du bureau			
(Park et coll., 2020)	Éclosion de coronavirus dans un centre d'appel, Corée du Sud	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Menée sur une éclosion de COVID-19 dans un centre d'appel à Séoul, en Corée du Sud, en mars 2020. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Le premier cas confirmé a été identifié au centre d'appel le 8 mars 2020. Le centre d'appel est situé aux étages 7 à 9 et 11 d'un immeuble de 19 étages. En général, les employés ne se déplacent pas d'un étage à l'autre et ils ne disposent pas d'un restaurant interne pour les repas. Les résidents et les employés de l'immeuble avaient des contacts fréquents dans le hall ou les ascenseurs. • Le bâtiment a été fermé le 9 mars 2020 et des tests ont été proposés à tous les occupants du bâtiment. • Sur 1143 personnes testées pour la COVID-19, 97 (8,5 %) étaient positives. La majorité des employés (94/97) travaillaient dans un centre d'appel du 11^{e} étage comprenant 216 employés. Le taux d'attaque était donc de 43,5 % (IC de 95 % : de 36,9 à 50,4 %). En

			outre, la plupart des cas au 11e étage se trouvaient du même côté du bâtiment. • Le taux d'attaque secondaire à domicile parmi les cas symptomatiques était de 16,2 % (IC de 95 % : de 11,6 à 22 %). • La durée de l'interaction (ou du contact) a très probablement été le principal facteur facilitant la transmission.
(Zhang et coll., 2020)	Enquête épidémiologique sur une nouvelle épidémie de pneumonie à coronavirus en grappe dans des unités collectives de Tianjin	• Article en chinois. • Investigation épidémiologique rétrospective menée en janvier 2020. • L'éclosion s'est produite dans le bureau administratif d'une usine qui compte 906 employés à Tianjin, en Chine. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Le premier cas a été identifié le 15 janvier 2020 et s'est propagé à 10 autres collègues avant que des mesures de contrôle ne soient mises en place le 24 janvier 2020. • Le cas index et le cas initial sont liés à des voyages professionnels à Wuhan. • Les cas secondaires et tertiaires ont soit voyagé ou participé à des réunions avec les cas infectés, soit se sont assis à proximité d'eux.
(Böhmer et coll., 2020; Rothe et coll., 2020)	Transmission de l'infection au coronavirus nCoV-2019 à partir d'un contact asymptomatique en Allemagne Enquête sur une éclosion de COVID-19 en Allemagne résultant d'un seul cas primaire associé à un	• Investigation épidémiologique rétrospective • 2 études décrivant la transmission du SRAS-CoV-2 d'une résidente chinoise qui s'est rendue en Allemagne pour des raisons professionnelles à ses collègues en janvier 2020. • Böhmer et coll. fournissent une investigation détaillée de l'éclosion. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Le patient 0 était une employée de la branche chinoise d'une société allemande basée à Munich. Elle s'est rendue de Shanghai à Munich en avion le 19 janvier 2020 pour animer des ateliers et assister à des réunions dans le bâtiment de l'entreprise. Elle a pris un vol de nuit pour retourner à Shanghai le 22 janvier 2020 et a été testée positive à l'infection par le SRAS-CoV-2 le 26 janvier 2020. • L'entreprise allemande a été informée de l'infection le 27 janvier 2020. Les premiers tests effectués sur les contacts à haut risque ont permis d'identifier les patients 1 à 4 comme des cas de première génération. Le site de la société a été fermé le 11 février 2020. Au 19 février 2020, 16 cas ultérieurs ont été identifiés. • L'intervalle sériel médian était de 4,0 jours (IQR de 3,0 à 5,0).

	voyage : une série de cas		• Dix patients en plus du patient 0 étaient des employés de l'entreprise. Les 5 autres étaient des contacts familiaux. L'investigation a révélé que la transmission du patient 0 aux 10 autres s'est probablement produite au cours des scénarios suivants : ○ Accompagnement du patient 0 dans ses activités multiples en Allemagne et retour par le même avion ○ Dans les réunions de travail (de 60 à 90 minutes) où les collègues étaient assis à proximité les uns des autres. ○ Les collègues ont travaillé simultanément sur le même ordinateur pendant une courte période. ○ Après s'être assis ensemble au cours d'une réunion de 90 minutes pendant la journée, deux collègues ont également passé la soirée ensemble dans l'une de leurs maisons. Cependant, la partenaire du collègue hôte qui était également présent ce soir-là n'a pas été testée positive. ○ Deux collègues se sont rencontrés lors d'une visite à la cantine où ils se sont assis dos à dos. L'un d'eux s'est tourné vers l'autre pour lui emprunter la salière.
(Hall, Bui, Rowe et Do, 2020)	Investigation des cas de COVID-19 et des cas contacts dans un espace de travail de bureau	• Investigation épidémiologique rétrospective menée en mars 2020, • L'éclosion s'est produite aux États-Unis dans un espace de travail comprenant à la fois des bureaux militaires et des bureaux civils. • Pas de déclaration de conflit d'intérêts disponible	• Le cas index a involontairement exposé 150 collègues au SRAS-CoV-2 en participant à des covoiturages, des conférences et de petites réunions sur une période de 3 jours. • Sur les 150 expositions, 37 ont été considérées comme un risque moyen et 113 comme un risque faible. 5 personnes ont signalé des symptômes de type COVID-19 et 5 ont développé des symptômes pendant la quarantaine de 14 jours. Aucun des contacts n'a été testé positif à une infection par le SRAS-CoV-2.

			• Aucun des collègues exposés pendant le covoiturage n'a développé de symptômes et malgré le contact étroit, il semble qu'ils n'ont pas été infectés. • L'identification rapide des personnes exposées au risque d'infection et la mise en œuvre ultérieure d'efforts d'atténuation et de contrôle ont permis de contrôler la propagation du SRAS-CoV-2.
Usines de transformation de la viande			
(Dyal et coll., 2020)	Présence de la COVID-19 au sein des travailleurs d'usines de transformation de la viande et de la volaille — 19 États, avril 2020	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Le rapport fournit des données globales sur les cas positifs de COVID-19 dans 115 usines de transformation de la viande et de la volaille dans 19 États américains jusqu'au 27 avril 2020. • Aucun conflit d'intérêts potentiel n'a été révélé.	• Parmi les quelque 130 000 travailleurs de ces installations, 4 913 cas (environ 3,0 %) et 20 d'entre eux sont décédés. • Ces chiffres reflètent les pratiques inadéquates de contrôle des infections suivies dans ces installations, notamment une faible distance sociale, des mesures de contrôle à la source (par exemple, l'utilisation de couvre-visages en tissu) et une charge de travail accrue. • Les facteurs de risque d'infection identifiés sont les difficultés liées à l'éloignement physique, à l'hygiène et aux conditions de vie et de transport surpeuplées (de nombreux travailleurs vivent dans des lieux surpeuplés et multigénérationnels et partagent parfois le transport pour se rendre au travail et en revenir).
(Waltenburg et coll., 2020)	Mise à jour : Présence de la COVID-19 au sein des travailleurs d'usines de transformation de la viande et de la volaille — 19	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Ceci est une mise à jour du rapport ci-dessus. • Le rapport fournit des données agrégées sur les cas positifs de COVID-19 parmi 239 usines de transformation de la viande	• Dans 239 usines, il y a eu 16 233 cas de COVID-19 et 86 décès liés à la COVID-19 parmi les travailleurs (264 usines / 17 358 cas / 91 décès dans les deux publications (Dyal et coll., 2020; Waltenburg et coll., 2020)). • Parmi les 14 États ayant déclaré le nombre total de travailleurs dans les usines de transformation de la viande et de la volaille touchées (112 616), la COVID-19 a été diagnostiquée chez 9,1 % des travailleurs.

	États, avril à mai 2020	et de la volaille dans 23 États américains jusqu'au 31 mai 2020. • Aucun conflit d'intérêts potentiel n'a été révélé.	• Sur 9919 (61 %) cas dont la race/ethnicité a été signalée, 87 % concernaient des travailleurs issus de minorités raciales et ethniques. • Les facteurs qui augmentent le risque d'exposition pour ces travailleurs comprennent un contact étroit et prolongé sur le lieu de travail avec des collègues (à moins de 1,80 m pour une durée ≥15 minutes) pendant de longues périodes (équipes de travail de 8 à 12 heures), des espaces de travail partagés, un transport partagé pour se rendre au lieu de travail et en revenir, un logement collectif et des contacts communautaires fréquents avec des collègues. • Les données provenant de 111 usines dans 14 États révèlent la mise en œuvre des stratégies de prévention et de contrôle suivantes : dépistage des travailleurs à l'entrée (89 sur 111), obligation pour tous les travailleurs de porter un couvre-visage (86 sur 111), augmentation de la disponibilité des postes d'hygiène des mains (72 sur 111), sensibilisation des travailleurs à la propagation communautaire (70 sur 111), installation de barrières physiques entre les travailleurs (69 sur 111), offre de tests aux employés (41 sur 111) et fermeture temporaire (24 sur 111). • En utilisant les données de 7 usines qui ont mis en place des tests à l'échelle de l'usine, la prévalence brute des infections asymptomatiques ou présymptomatiques parmi les 5572 travailleurs qui ont été testés positifs à l'infection par le SRAS-CoV-2 était de 14,4 %.
(Steinberg et coll., 2020)	Éclosion de COVID-19 parmi les employés d'une usine de	• Investigation épidémiologique rétrospective	• Au total, 929 sur 3635 cas (25,6 %) de COVID-19 ont été diagnostiqués parmi les employés de l'usine A, dont 39 ont été hospitalisés et 2 sont décédés.

	transformation de la viande – Dakota du Sud, mars à avril 2020	• Effectuée entre le 16 mars et le 25 avril 2020 dans une usine de transformation de la viande (usine A). • Aucun conflit d'intérêts potentiel n'a été révélé.	• De plus, 210 sur 2408 cas (8,7 %) ont été identifiés parmi les contacts des employés ayant reçu un diagnostic de COVID-19. 9 d'entre eux ont été hospitalisés. • Le taux d'attaque de l'usine A entre le 16 mars et le 25 avril 2020 était de 25,6 %. Les groupes de services où les employés travaillaient à proximité (c.-à-d. < 1,8 m) les uns des autres sur la chaîne de production avaient les taux d'attaque les plus élevés (groupes de services : découpe – 30,2 %, conversion – 30,1 % et collecte – 29,4 %). • Le taux d'attaque était plus élevé chez les employés non salariés (26,8 %) que chez les salariés (14,8 %). • Le taux d'attaque a été multiplié par cinq environ au cours des trois premières semaines de l'éclosion. En moyenne, 67 cas de COVID-19 se sont produits par jour parmi les employés au cours de la quatrième semaine. Le nombre de cas parmi les employés est tombé à environ 10 par jour dans les 7 jours suivant la fermeture de l'usine.
(Richmond, Sabin, Jobe, Lovrich et Kenny, 2020) *prépublication*	Diffusion interrégionale du SRAS-CoV-2 à partir d'une seule éclosion d'introduction dans une usine de conditionnement de viande dans le nord-est de l'Iowa	• Étude d'épidémiologie moléculaire. • Cette étude décrit une analyse phylogénétique des cas de COVID-19 identifiés dans 3 États voisins des États-Unis (Wisconsin, Iowa et Minnesota). • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les résultats de l'analyse phylogénétique révèlent une grande grappe d'une seule souche de SRAS-CoV-2 parmi les individus associés à une usine de conditionnement de viande à Postville, dans l'Iowa. • Depuis le 6 avril 2020, 27 cas viraux attribués à cette sous-souche ont été identifiés. Les auteurs pensent que cela ne représente qu'un échantillon des cas résultant de cette éclosion. • Des cas liés à cette éclosion ont été détectés dans 7 comtés de 3 États, touchant au total 13 municipalités. Cette région s'étend sur une superficie de 480 kilomètres carrés.

(Guenther et coll., 2020) *prépublication*	Investigation d'un événement de super-propagation précédant la plus grande éclosion de SRAS-CoV-2 liée à une usine de transformation de la viande en Allemagne	• Investigation épidémiologique rétrospective. • Réalisée du 16 mars au 25 avril 2020, dans le plus grand complexe de transformation de la viande en Allemagne. • Le complexe comprend 2 usines MPP-R et MPP-D. MPP-R effectue l'abattage et la transformation fine ainsi que le conditionnement de la viande bovine et porcine et MPP-D est une usine de transformation spécialisée dans le désossage des truies qui se trouve à 30 km de MPP-R.	• Les tests sériels effectués par les autorités sanitaires un mois après le premier cas ont permis d'identifier plus de 1400 cas positifs. • L'évaluation des séquences virales montre que tous les cas partagent un ensemble de 8 mutations de nucléotides uniques représentant une nouvelle sous-branche dans le clade C20 du SRAS-CoV-2. • La transmission initiale s'est produite dans une zone confinée d'une usine de transformation de viande bovine dans laquelle l'air est constamment recyclé et refroidi à 10°C. Le cas index a transmis le virus à plus de 60 % (17 sur 26) de leurs collègues dans un rayon de plus de 8 mètres pendant les postes de travail de 3 jours consécutifs. • Des relations statistiques ont également été identifiées pour un appartement partagé, une chambre à coucher et des groupes de covoiturage. Les corrélations entre le fait de travailler à moins de 8 mètres du cas index et le taux d'infection dans l'appartement, la chambre ou le groupe de covoiturage indiquent que la majorité des cas de transmission se seraient produits dans l'usine de transformation de viande bovine. • Les résultats indiquent qu'une distance physique de 2 mètres n'est pas suffisante pour empêcher la transmission dans cet environnement de faible échange d'air frais et de refroidissement continu, ce qui peut favoriser la transmission. Les auteurs recommandent des mesures supplémentaires telles que l'amélioration de la ventilation et de la circulation d'air, l'installation de dispositifs de filtrage et l'utilisation de masques faciaux de haute qualité pour réduire le risque d'infection dans ces environnements.
Autre usine			

(Jerkovic et coll., 2020) *prépublication*	Séroprévalence des anticorps anti-SRAS-CoV-2 chez des travailleurs d'usine en Split-Dalmatie et dans le comté de Šibenik-Knin, en Croatie	• Cette étude transversale a estimé la séroprévalence sur 1494 employés d'usine vivant dans la région de Split-Dalmatie et le comté de Šibenik-Knin (Croatie) et a été menée entre le 23 et le 28 avril 2020. • L'usine (groupe DIV) est spécialisée dans la production et le commerce de vis et d'autres pièces mécaniques et métalliques. Elle possède deux sites de production importants situés à Split (comté de Split-Dalmatie) et à Knin (comté de Šibenik-Knin), qui emploient respectivement environ 2200 et 400 personnes. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• À partir du 25 février 2020, le groupe DIV a mis en place des mesures de protection telles que la mise en place de stations de désinfection des mains dans toutes les pièces, des protocoles de nettoyage régulier des postes de travail, la fermeture des stations communes de vente de café et de nourriture, des contrôles de température, l'auto-isolation pour les personnes revenant de l'étranger et le travail à domicile pour une partie du personnel commercial et administratif. Le nombre total d'employés travaillant dans les usines a été réduit à environ 1300 et 300, respectivement. • Dans un échantillon total d'employés testés (n=1 494), des anticorps ont été détectés chez 1,27 % des participants (IC de 95 % : de 0,77 à 1,98 %). • Une partie des employés de l'usine de Split vivent sur la propriété de l'usine. • À l'usine de Split 13 sur 1316 (0,99 %, IC de 95 % : de 0,53 à 1,68 %) des participants ont été testés positifs, dont 13 sur 1079 (1,20 %, IC de 95 %) : de 0,64 à 2,05 %) des personnes qui vivaient en dehors de l'usine et 0 sur 237 (0 %, IC de 95 % : de 0 à 1,26 %) des personnes qui vivaient à l'intérieur des installations. À l'usine de Knin, 6 sur 178 (3,37 %, IC de 95 % : de 1,25 à 7,19 %) des participants ont été testés positifs aux anticorps. • Tous les participants vivants dans les locaux de l'usine et dont la mobilité était limitée pendant les mesures de confinement ont obtenu un résultat négatif au test de dépistage des anticorps. Par conséquent, l'exposition n'était probablement pas liée au logement sur le lieu de travail dans le cas de cette éclosion.
Travail des migrants			

(Koh, 2020a)	Les travailleurs migrants et la COVID-19	• Investigation épidémiologique rétrospective. • Les chiffres quotidiens des cas de COVID-19 à Singapour de mars à mai 2020 ont été analysés afin de déterminer la cause de l'augmentation des cas en avril 2020. La réglementation sur le logement des travailleurs migrants a été étudiée. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• La majorité des cas associés à un pic en avril 2020 se sont produits chez des travailleurs migrants peu qualifiés vivant dans des dortoirs de travailleurs étrangers. Au 6 mai 2020, il y avait 17 758 cas confirmés de COVID-19 parmi les travailleurs vivant en dortoirs (88 % des 20 198 cas confirmés au niveau national). • Dans un dortoir de 13 000 travailleurs environ, 2526 cas ont été confirmés, ce qui représente 12,5 % de tous les cas dans le pays. • La réponse nationale a consisté à soumettre les travailleurs vivant en dortoirs à des tests approfondis, à séparer les travailleurs sains des travailleurs infectés et à observer quotidiennement la fièvre et les symptômes. En outre, 24 dortoirs ont été déclarés « zones d'isolement » pour que les résidents soient mis en quarantaine pendant 14 jours. Des logements publics, des camps militaires, des centres d'exposition et des hôtels flottants ont été mis à la disposition des travailleurs, afin de permettre une distanciation sociale appropriée.
Centre de remise en forme			
(Jang et coll., 2020)	Grappe de maladies à coronavirus associée aux cours de danse de remise en forme, Corée du Sud	• Investigation épidémiologique rétrospective. • Une éclosion associée à un atelier national de professeurs de danse de remise en forme qui s'est tenu le 15 février 2020 à Cheonan, en Corée du Sud. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Dans le cadre de l'atelier national des instructeurs de danse de remise en forme, les instructeurs se sont entraînés intensément pendant 4 heures. Sur les 27 instructeurs qui ont participé, 8 ont eu des résultats positifs à la RT-PCR pour l'infection par le SRAS-CoV-2. Tous étaient asymptomatiques le jour de l'atelier. • Le 9 mars 2020, 112 cas de COVID-19 associés à des cours de danse de remise en forme dans 12 installations sportives différentes ont été identifiés. Parmi eux, 82 (73,2 %) étaient symptomatiques et 30 (26,8 %) étaient asymptomatiques.

			• La transmission des instructeurs aux participants des cours de remise en forme a représenté 57 cas (50,9 %). La transmission au sein des familles des instructeurs et des élèves a donné lieu à 38 cas (33,9 %) alors que 17 cas (15,2 %) étaient dus à une transmission lors de réunions avec des collègues ou des connaissances. • Avant la fermeture des installations sportives, 217 élèves ont été exposés dans 12 installations, soit un taux d'attaque de 26,3 % (IC de 95 % : de 20,9 à 32,5%). • Les contacts étroits des instructeurs de remise en forme et des élèves ont fait l'objet d'un suivi (n=830) et 34 cas de COVID-19 ont été identifiés, ce qui se traduit par un taux d'attaque secondaire de 4,10 % (IC de 95 % : de 2,95 à 5,67%). Sur ces 34 cas, 418 contacts étroits ont été suivis et 10 cas quaternaires ont été identifiés, ce qui donne un taux d'attaque tertiaire de 2,39 % (IC de 95 % : de 1,30 à 4,35%). • Les cours de remise en forme à partir desquels les cas de COVID-19 secondaires ont été identifiés comprenaient de 5 à 22 élèves faisant 50 minutes d'exercice intense dans une salle d'environ 60 m^2. Aucun cas parmi les classes de moins de 5 participants n'a été identifié. • Un des instructeurs infectés a enseigné le Pilates et le yoga à des classes de 7 à 8 élèves dans le même établissement en même temps qu'un autre instructeur infecté, mais aucun de ses élèves n'a été testé positif pour le virus. • Les auteurs spéculent que la faible intensité du Pilates et du yoga n'a pas provoqué les mêmes effets de transmission que les cours de danse de remise en forme plus intenses.
Navires			

(Kakimoto et coll., 2020)	Investigation initiale sur la transmission de la COVID-19 parmi les membres d'équipage pendant la quarantaine d'un navire de croisière – Yokohama, Japon, février 2020	• Investigation épidémiologique rétrospective d'une éclosion sur le navire de croisière Diamond Princess de 3700 passagers et membres d'équipage qui a débuté le 3 février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• L'investigation sur la propagation du SRAS-CoV-2 parmi le personnel a conclu que l'infection s'était apparemment propagée parmi les personnes dont les cabines se trouvaient sur le même pont (pont 3) et qui travaillaient dans le même groupe professionnel (restauration), probablement par contact ou par propagation de gouttelettes, ce qui est conforme à la compréhension actuelle de la transmission de la COVID-19. • Huit des 20 membres d'équipage positifs avaient des compagnons de cabine, dont 5 sur 8 sont devenus positifs à la COVID-19.
(Addetia et coll., 2020)	Des anticorps neutralisants en corrélation avec la protection contre le SRAS-CoV-2 chez l'homme lors d'une éclosion sur un navire de pêche avec un taux d'attaque élevé	• Investigation épidémiologique rétrospective. • Cette étude décrit une éclosion de SRAS-CoV-2 sur un navire de pêche qui a quitté Seattle, Washington, en mai 2020. • Avant le départ du navire, les membres de l'équipage ont été soumis à un test de dépistage d'une infection active par le SRAS-CoV-2 par RT-PCR et à un test sérologique pour détecter les signes d'une infection antérieure ou en cours. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Le taux d'attaque à bord était de 85,2 % (104 sur 122 individus). • Trois membres de l'équipage ont été testés positifs avant le départ du bateau lors du dépistage sérologique initial et ont présenté des anticorps neutralisants et réactifs aux pics lors des tests de suivi. Aucun de ces membres d'équipage n'a présenté de signes d'infection virale ou n'a éprouvé de symptômes pendant l'éclosion. • Les membres de l'équipage ayant des anticorps neutralisants provenant d'une infection antérieure ont été protégés contre la réinfection.
(Payne et coll., 2020)	Infections par le SRAS-CoV-2 et réponses sérologiques d'un échantillon de membres des services de la	• Enquête épidémiologique rétrospective sur une éclosion survenue sur le USS Theodore Roosevelt en mars/avril 2020 avec environ 1000 militaires à bord. • L'investigation s'est déroulée du 20 au 24 avril 2020, une fois le navire amarré à Guam.	• L'infection antérieure ou actuelle était plus élevée chez les participants qui ont déclaré avoir été en contact avec une personne connue comme ayant la COVID-19 (64,2 %), par rapport à ceux qui ne l'ont pas fait (41,7 %) (RC = 2,5; IC de 95 % = de 1,1 à 5,8). • La prévalence était également plus élevée chez les militaires qui ont déclaré avoir partagé la même

	marine américaine – USS Theodore Roosevelt, avril 2020	• Un échantillon commode de 382 (27 % du total des membres du service sur le navire ou à la base navale de Guam).
		• questionnaires, tests sérologiques et tests RT-PCR a été réalisé pour créer l'ensemble de données.
			couchette avec un membre d'équipage dont le test de dépistage était positif (65,6 %), par rapport à ceux qui ne l'ont pas fait (36,4 %) (RC = 3,3; IC de 95 % = de 1,8 à 6,1).
			• Le fait de prendre des mesures de protection était associé à un risque plus faible d'être positif à la COVID-19 :
			  • Revêtement du visage (55,8 % contre 80,8 %; RC = 0,3; IC de 95 % = de 0,2 à 0,5)
			  • Éviter les zones communes (53,8 % contre 67,5 %; RC = 0,6; IC de 95 % = de 0,4 à 0,9)
			  • Éloignement social (54,7 % contre 70,0 %; RC = 0,5; IC de 95 % = de 0,3 à 0,8)

Autres professions liées aux services			
(Liu et coll., 2020)	Analyse des cas de grappe de COVID-19 à Tianjin	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Cette étude décrit toutes les grappes de cas de COVID-19 confirmés à Tianjin en date du 22 février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Il y avait des grappes de familles (28 cas, 71 cas), des grappes d'unités (1 cas, 10 cas), des grappes de transport (3 cas, 8 cas) et une grappe de lieux publics (1 cas, 26 cas). • Une grappe dans la section passagers d'un train a impliqué 10 cas. Après des investigations épidémiologiques, il a finalement été déterminé que 2 employés ayant des antécédents de sorties à Wuhan étaient des cas de première génération. • L'éclosion dans un grand magasin était due à un vendeur infecté qui a contaminé 26 clients et collègues.
(Wu et coll., 2020)	Investigation et analyse sur les caractéristiques d'une grappe de COVID-19 associée à l'exposition dans	• Article en chinois. • Investigation épidémiologique rétrospective • Une éclosion associée à une exposition dans un grand magasin. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Le premier cas confirmé d'employé du magasin a été enregistré le 31 janvier 2020. • Il y a 40 cas associés à un grand magasin, ce qui représente 75,47 % du nombre de cas confirmés (53 cas) dans la juridiction. • L'analyse a révélé que 6 cas (15 %) concernaient des employés d'un grand magasin, 19 cas (47,5 %) étaient

	un grand magasin de Tianjin		des clients du grand magasin et 15 cas (37,5 %) étaient des contacts étroits.
(Leffler et Hogan, 2020) *prépublication*	Dépendance de la mortalité due aux nouvelles maladies à coronavirus (COVID-19) en fonction de l'âge dans les populations fortement exposées : Travailleurs et résidents des transports en commun de New York et passagers du Diamond Princess	• Des données transversales provenant de plusieurs sources et milieux ont été obtenues et les données de mortalité ont été comparées. • Les auteurs ont utilisé des sources accessibles au public pour estimer la mortalité due à la COVID-19 pour chaque groupe d'âge sur le bateau de croisière Diamond Princess, aux États-Unis, dans la ville et l'État de New York, et parmi les travailleurs de la New York Metropolitan Transit Authority (MTA). • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• À New York, la mortalité des travailleurs des transports en commun était estimée à 1 sur 7329 pour les 30 à 39 ans, 1 sur 1075 pour les 40 à 49 ans, 1 sur 343 pour les 50 à 59 ans et 1 sur 178 pour les 60 à 69 ans. • Parmi les travailleurs de la MTA décédés des suites de la COVID-19, 106 sur 109 personnes au 6 mai 2020, faisaient partie de la division des métros et des bus, qui compte 55000 employés. • Il n'est pas clair si la transmission de ces travailleurs s'est produite sur le lieu de travail ou en dehors du lieu de travail. • Parmi les travailleurs de la MTA de New York, plus de 6000 travailleurs (8 %) ont soit été testés positifs (plus de 2000), soit mis en quarantaine (4000 travailleurs).
(Lan et coll., 2020b) *prépublication*	Association entre l'infection par le SRAS-CoV-2, le risque d'exposition et la santé mentale au sein d'une cohorte de travailleurs essentiels du commerce de détail aux États-Unis	• Cette étude transversale a estimé la séroprévalence de 104 personnes employées dans une épicerie de détail de la région métropolitaine de Boston dans le Massachusetts, aux États-Unis, et a été menée pendant 3 jours consécutifs au début du mois de mai 2020. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Parmi les travailleurs testés, 21 sur 104 (20 %) ont eu des tests viraux positifs. Parmi ceux-ci, 76 % des cas étaient asymptomatiques. • Les résultats d'une analyse multivariée révèlent que les employés directement exposés aux clients avaient cinq fois plus de chances d'obtenir un résultat positif au test de dépistage du SRAS-CoV-2 (RC de 4,7; IC de 95 % : de 1,2 à 32,0). Les fumeurs avaient 90 % de chances en moins d'être testés positifs (RC 0,1; IC de 95 % : de 0,01 à 0,8).

(Yang et coll., 2020)	L'analyse préliminaire sur les caractéristiques de la grappe pour la COVID-19	• Article en chinois. • Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Cette étude décrit 377 investigations en grappes rétrospectives sur des infections par le SRAS-CoV-2 impliquant 1719 cas dans des établissements non médicaux entre le 1er janvier et le 20 février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Sur les 377 grappes, le lieu probable où le SRAS-CoV-2 a été contracté a été attribué aux facteurs suivants : les grappes familiales représentaient 79 %, les repas pris ensemble 10 %, les centres commerciaux ou les supermarchés 6 %, les lieux de travail 3 % et les véhicules de transport 2 %. • Les détails des grappes de transmission sur le lieu de travail n'ont pas été présentés.
(Hendrix, Walde, Findley et Trotman, 2020)	Absence de transmission apparente du SRAS-CoV-2 par deux stylistes après une exposition dans un salon de coiffure appliquant une politique de couverture universelle du visage – Springfield, Missouri, mai 2020	• Investigation épidémiologique rétrospective. • Deux coiffeurs dans un seul salon au Missouri, aux États-Unis, ont interagi avec environ 139 clients alors qu'ils étaient infectés par le SRAS-CoV-2 en mai 2020. • Les clients et les coiffeurs portaient des masques. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Sur les 139 clients qui ont été exposés, 67 ont été testés. • Aucun cas secondaire symptomatique n'a été signalé, ce qui est très probablement dû à l'utilisation de masques faciaux. • Taux d'attaque : 0/139
(Cai et coll., 2020)	Transmission indirecte du virus dans une grappe de cas de COVID-	• Investigation épidémiologique rétrospective sur une éclosion associée à un centre commercial à Wenzhou, en Chine.	• Après avoir identifié un cas positif, le centre commercial a été fermé le 22 janvier 2020. • Du 19 janvier au 9 février 2020, la COVID-19 a été diagnostiquée chez 7 employés et 10 clients du centre commercial.

	19, Wenzhou, Chine, 2020	• Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Des contacts étroits associés au centre commercial ont été retracés, et la COVID-19 a été confirmée chez 11 personnes. • Une seule source commune n'a pas été identifiée, certains espaces communs ont été utilisés par des employés infectés, on soupçonne donc une exposition à la transmission de virus ou de fomites sous forme d'aérosol, peut-être en utilisant des toilettes ou un ascenseur commun.
(Szablewski et coll., 2020)	Transmission du SRAS-CoV-2 et infection parmi les participants à un camp de nuit – Géorgie, juin 2020	• Investigation épidémiologique rétrospective d'une éclosion associée à un camp de nuit en Géorgie, aux États-Unis. • Un camp de nuit (camp A) a été organisé pour l'orientation de 138 stagiaires et 120 membres du personnel du 17 au 20 juin 2020 • Les membres du personnel sont restés pour la première session du camp, prévue du 21 au 27 juin 2020, et ont été rejoints par 363 campeurs et 3 membres de la direction le 21 juin 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• 597 résidents de Géorgie ont fréquenté le camp A. Parmi ceux qui ont été testés, 260 sur 344 (76 %) ont été déclarés positifs au SRAS-CoV-2. • Le taux d'attaque global était de 44 % (260/597), les membres du personnel ayant le taux d'attaque le plus élevé (56 %). Le taux d'attaque a augmenté avec la durée du séjour au camp. • L'occupation des 31 cabines était en moyenne de 15 personnes par cabine (fourchette de 1 à 26). Le taux d'attaque médian des cabines était de 50 % (fourchette de 22 à 70 %) parmi les 28 cabines qui ont connu un ou plusieurs cas. • Le camp a suivi toutes les recommandations du CDC, à l'exception de l'ouverture des fenêtres et des portes afin d'accroître la ventilation des bâtiments et du port de masques en tissu par les campeurs (mais le personnel portait des masques).
(Caban-Martinez et coll., 2020)	Épidémiologie des anticorps anti-SRAS-CoV-2 chez les pompiers et les paramédicaux d'un service	• Cette étude transversale a estimé la séroprévalence des anticorps anti-SRAS-CoV-2 chez 203 pompiers de première ligne/paramédicaux de Floride, aux États-Unis, données recueillies les 16 et 17 avril 2020.	• Sur les 203 pompiers/paramédicaux testés, 18 étaient positifs au SRAS-CoV-2 (8,9 %). • Le nombre moyen de contacts de cas de COVID-19 (c'est-à-dire à moins de 1,80 m d'une personne infectée pendant une durée ≥ 15 min) était significativement plus élevé (13,3 ±4,8 contacts de cas contre 7,31 ±4,8 contacts; p = 0,022) chez les pompiers

	d'incendie américain : étude transversale	• La recherche a été financée en partie par l'État de Floride, l'Administration fédérale de gestion des urgences et l'Institut national du cancer des National Institutes of Health. • Les auteurs déclarent qu'il n'y a pas de conflits d'intérêts.	et les paramédicaux qui étaient positifs aux anticorps du SRAS-CoV-2 que chez les pompiers dont les tests de dépistage aux anticorps étaient négatifs. • Parmi les pompiers/paramédicaux ayant obtenu un résultat positif, aucun n'a déclaré avoir reçu le vaccin annuel contre la grippe, comparé aux pompiers/paramédicaux ayant obtenu un résultat négatif aux anticorps du SRAS-CoV-2 (0,0 % contre 21,0 %; p = 0,027).
(Valencia et coll., 2020) *prépublication*	Transmissions asymptomatique et présymptomatique de l'infection du nouveau coronavirus 2019 (COVID-19) : une estimation à partir d'une grappe de cas confirmés à Hô Chi Minh Ville, au Vietnam	• Investigation épidémiologique rétrospective d'un rassemblement dans un bar à Hô Chi Minh Ville, au Vietnam. • Les informations démographiques, cliniques et de laboratoire de tous les cas confirmés de COVID-19 et les contacts d'un rassemblement de bar le 14 mars 2020 ont été recueillies. • Les auteurs déclarent qu'il n'y a pas de conflits d'intérêts.	• Sur les 298 personnes qui ont assisté à un rassemblement dans un bar à Hô Chi Minh Ville, 13 ont été testées positives au SRAS-CoV-2. • La recherche de contacts parmi 4466 personnes a permis d'identifier 6 autres cas. • Le R0 spécifique de la grappe était de 2,64 (IC de 90 % : de 1,41 à 3,68). • 3 contextes de transmission après une investigation sur le terrain ont été identifiés (bar, ménage, lieu de travail). Le bar constituait 68 %, le lieu de travail 21 %, et le ménage 11 % des transmissions. • Dans la deuxième génération, 3 (50 %) des transmissions étaient liées au lieu de travail, dont 2 (67 %) ont signalé des symptômes après avoir été exposés à un cas qui n'a pas signalé de symptômes.
(Bao et coll., 2020)	Éclosion de COVID-19 suite à l'exposition d'un seul patient sur un site de divertissement : Une étude épidémiologique	• Investigation épidémiologique rétrospective d'une éclosion associée à une piscine dans un lieu de divertissement à Wuhan, en Chine. • Les informations démographiques, cliniques et de laboratoire de tous les cas et contacts confirmés de COVID-19 ont été recueillies en janvier et février 2020.	• Un travailleur infecté par la COVID-19qui est rentré chez lui après avoir quitté Wuhan, a provoqué une éclosion en se rendant dans une piscine le 20 janvier, où il a infecté certains travailleurs et clients. • L'infection a ensuite été transmise par un employé de la piscine qui a continué de travailler et par un client qui a participé à une fête familiale et à un dîner avec des collègues.

		• Les auteurs déclarent qu'il n'y a pas de conflits d'intérêts.	• L'employé de piscine qui a continué de travailler jusqu'au 26 janvier a causé des infections par le SRAS-CoV-2 chez 12 clients. • Un dîner avec des collègues a réuni 36 collègues le 22 janvier. La personne infectée a chanté avec 7 collègues dans un espace fermé. L'infection des 7 collègues a été confirmée par la suite • Le taux d'attaque secondaire pour le dîner avec les collègues était de 20,5 (IC de 95 % : de 7,8 à 33,2). • Au total, 56 cas ont été confirmés dans 8 districts avec une population résidente de 3,9 millions de personnes.
Transport			
(Yang et coll., 2020)	Grappe de transmission de la COVID-19 en vol : une série de cas rétrospectifs	• Investigation épidémiologique rétrospective. • Cette étude décrit une grappe de transmission de la COVID-19 en vol. • Les données ont été collectées du 25 janvier au 28 février 2020. • Les politiques de masques faciaux n'ont pas été mises en œuvre à l'époque de cette grappe. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Après un vol, 12 cas de COVID-19 ont été identifiés et associés au vol. • Aucun agent de bord n'a été infecté, ce qui démontre l'absence de transmission aux agents de bord.
(Pongpirul , Pongpirul, Ratnarathon et Prasithsirikul, 2020)	Voyage d'un chauffeur de taxi thaïlandais et nouveau Coronavirus	• Cette étude de cas décrit une infection par le SRAS-CoV-2 chez un chauffeur de taxi en Thaïlande en janvier 2020. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Le chauffeur de taxi est tombé malade le 20 janvier 2020 et s'est rendu dans une clinique de soins primaires le 23 janvier 2020. • Il a rapporté avoir été en contact avec des touristes chinois dans son taxi qui toussaient fréquemment, mais qui portaient des masques. Il n'avait aucun antécédent de voyage en Chine.
Autre ou combiné			

(Qian et coll., 2020) *prépublication*	Transmission du SRAS-CoV-2 à l'intérieur	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Cette étude a analysé toutes les éclosions impliquant trois cas ou plus signalées par les commissions sanitaires municipales en Chine du 4 janvier au 11 février. • Les travaux ont été financés par le Conseil des bourses de recherche de Hong et la Fondation nationale des sciences naturelles de Chine. Les auteurs ne déclarent aucun conflit d'intérêts.	• 318 éclosions intérieures sont décrites dans 120 villes. • 80 % des éclosions ont concerné moins de 5 personnes. • Les lieux où les éclosions sont apparues ont été divisés en 6 catégories : 79,9 % se sont produits dans un ménage, suivis de 34 % dans les transports, 4,4 % au restaurant, 2,2 % dans un centre commercial et 9,7 % dans d'autres lieux. De nombreuses éclosions ont impliqué plus d'une catégorie de lieux.
(Nishiura et coll., 2020) *prépublication*	Les environnements fermés facilitent la transmission secondaire de la maladie à coronavirus 2019 (COVID-19)	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Cette étude rapporte les données épidémiologiques de 11 grappes de 110 cas au total qui se sont produites au Japon à partir du 26 février 2020 : 4 à Tokyo et 1 dans chacune des préfectures de Aichi, Fukuoka, Hokkaido, Ishikawa, Kanagawa et Wakayama. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Toutes les grappes étaient associées à des environnements intérieurs : gymnase, restaurant, hôpital et un festival où l'on mangeait sous des tentes. • Les informations quant à savoir si les cas étaient des employés ou des clients n'ont pas été fournies. • Cette étude a estimé que la probabilité de transmettre dans un environnement fermé par rapport à un environnement en plein air avait un OR de 18,7 (IC de 95 % de 6,0 à 57,9). • Cette analyse n'a pas permis de contrôler les facteurs de confusion ou l'interaction potentielle avec d'autres indicateurs. La définition d'« environnement en plein air » n'a pas été décrite
(Pung et coll., 2020)	Investigation sur trois grappes de COVID-19 à Singapour : implications pour les mesures de surveillance et de réaction	• Investigation épidémiologique rétrospective de 3 grappes liées à un groupe de touristes chinois, une conférence d'entreprise et une église à Singapour en février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• L'analyse a révélé que 36 cas de COVID-19 confirmés ont été liés à 3 grappes locales, composées de 11, 20 et 5 personnes. • La première éclosion a touché 11 personnes d'un groupe de touristes venus de Chine. Cinq assistants d'un magasin où le groupe de touristes s'est arrêté ont été testés positifs au SRAS-CoV-2. Les assistants ont indiqué qu'ils aidaient les clients à appliquer des

			échantillons d'huile médicinale sur leur corps, et que le lavage des mains n'était généralement pas effectué entre les clients. • La deuxième grappe a été une conférence à laquelle ont assisté au moins 111 participants de 19 pays différents, du 20 au 22 janvier 2020. Vingt personnes ont été infectées. Cinq des cas ont été assis à la même table lors d'un dîner de type banquet durant trois heures et quatre autres cas ont participé à une réunion de quatre heures.
(Furuse et coll., 2020)	Grappes de maladies à coronavirus dans les communautés, Japon, de janvier à avril 2020	• Investigation épidémiologique rétrospective de 3184 cas au Japon signalés entre le 15 janvier et le 4 avril 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Pendant cette période, 61 grappes de cas ont été identifiées dans des établissements de soins de santé (18 grappes), d'autres établissements de soins tels que des maisons de repos et des centres de soins de jour (10), des restaurants et des bars (10), des lieux de travail (8), des événements musicaux (7), des gymnases (5), des fonctions cérémonielles (2) et un incident lié au transport dans un avion (1). • La plus grande grappe non liée aux soins de santé observée concernait plus de 30 personnes ayant assisté à un concert de musique en direct, y compris les artistes, les membres du public et le personnel de l'événement. • Les auteurs identifient 22 patients primaires probables responsables de ces grappes. La plupart d'entre eux étaient âgés de 20 à 39 ans et étaient présymptomatiques ou asymptomatiques au moment de la transmission.
(Ministère de la Santé Manatū	COVID-19 – grappes importantes	• Le gouvernement néo-zélandais a dressé une liste des grappes importantes en Nouvelle-Zélande en date du 17 août 2020. • Aucun détail épidémiologique sur les grappes n'a été fourni.	• Les grappes signalées dans les lieux de travail potentiels sont les suivants : mariage, lieu d'accueil, conférence et bateau de croisière.

Hauora, 2020)			
(Département de la santé publique et de l'environnement du Colorado, 2020)	Données sur les éclosions	• Liste de toutes les éclosions confirmées de COVID-19 signalées dans le Colorado, aux États-Unis, au 12 août 2020. • Aucun détail épidémiologique sur les grappes n'a été fourni.	• Des grappes ont été signalées dans de multiples lieux de travail potentiels dans le Colorado, aux États-Unis. Quelques exemples : sites de construction, prison, centre de distribution, services de blanchisserie, entrepôt de pommes de terre, usine de transformation de la viande, usine d'aliments pour chiens, épicerie, etc.
(Kim, 2020)	Distanciation sociale et directives de santé publique sur les lieux de travail en Corée : réponses à la maladie à coronavirus-19	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Cette étude résume les politiques publiques et du lieu de travail en réponse à la COVID-19 en Corée. • Une vue d'ensemble des éclosions sur le lieu de travail pendant la période du 20 janvier au 15 mai 2020 est décrite à l'aide des données du Centre coréen de contrôle des maladies et du siège central de gestion des catastrophes. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	Transmission sur le lieu de travail en Corée : • Sur les 11 018 cas de COVID-19 identifiés au 15 mai 2020, 15,7 % se sont produits sur des lieux de travail tels que des établissements de soins de santé, des centres d'appel, des clubs sportifs, des karaokés et des lieux de vie nocturne • 111 cas ont été associés à des clubs de remise en forme après l'infection des instructeurs lors d'un atelier (Jang et coll., 2020) • 192 cas ont été associés à l'éclosion dans un centre d'appel • 95 cas sont liés au service public (par exemple, le service de santé, les agents correctionnels, les pompiers et la police). Cependant, la raison de leur exposition n'a pas été identifiée. • Des lignes directrices ont été élaborées avant le 29 février 2020 et sont considérées comme ayant été efficaces pour limiter la transmission sur le lieu de travail après leur mise en œuvre. Le ministère de l'Emploi et du Travail a inclus des directives sur le lieu de travail portant sur la COVID-19 :

			• Distanciation sociale, horaires de travail flexibles, identification précoce des travailleurs suspectés d'être infectés et désinfection des lieux de travail • Pour prévenir la propagation de l'infection sur le lieu de travail, les lignes directrices suggèrent d'éviter les réunions en face à face, les voyages d'affaires, l'éducation et la formation
Revue			
(Prakash, 2020) *prépublication*	Manger, prier, travailler : une méta-analyse du risque de transmission de la COVID-19 dans les activités communes de travail et de loisirs	• Revue documentaire. • L'auteur a rassemblé des données provenant d'études de cas (20 situations et 425 cas) recueillies par le biais d'une revue documentaire afin d'identifier les schémas de transmission et d'estimer les taux d'attaque. • L'auteur a voulu étudier les activités sociales qui pourraient comporter un risque de transmission de COVID-19 après l'assouplissement des mesures de confinement par le gouvernement. • Les méthodes de revue et d'analyse documentaires manquent de détails et de clarté. Aucune déclaration de conflit d'intérêts n'est disponible.	• Les événements tels que les dîners de famille et les réunions de travail ont un taux d'attaque plus élevé et, par conséquent, comportent des risques importants. • Au total, 20 situations ayant entraîné 418 infections dans 32 cas pour 44 personnes sont décrites ci-dessous. • Situation (taux de transmission) : o Repas/événements familiaux (de 15,7 % à 66,7 %) o Réunions – réunion privée d'une heure (72,7 %, IC de 95 % : de 43,6 à 98,0 %) o Espace de travail ouvert avec mouvement de personnes (78,7 %, IC de 95 % : de 70,3 à 85,3%) o Chant – pratique de 2 heures (86,7 %, IC de 95 % : de 76,2 à 93,2%) o Service de prière (a entraîné 1 à 7 infections secondaires par personne infectée) o Voyager en voiture (environnement fermé) et parler présentait un risque élevé (100 %, IC de 95 % : de 20 à 100%) o Transports publics, port d'un masque sans parler (0 %) o Hôtels (53,3 %, IC de 95 % : de 30,1 à 75,2 %)/Bateaux de croisière (28,1 %, IC de 95 % : de 27,3 à 29,0 %) où l'espace est partagé pendant des jours

			○ Interaction directe avec un agent de vente infecté (25,0 %, IC de 95 % : de 10,2 à 49,5%) ○ Discothèque, taux d'attaque parmi les contacts directs >50 %, parmi les clients de la discothèque (6,27 %, IC de 95 % : de 5,15 à 7,61%) ○ Taux d'attaque global dans les restaurants (9,9 %, IC de 95 % : de 5,3 à 17,7 %) par rapport à ceux des personnes infectées ensuite (45 %, IC de 95 % : de 25,8 à 65,8%) • Parmi tous ces événements de super-propagation, le nombre d'infections causées dépend du nombre de contacts étroits et dans la plupart des cas, le patient zéro n'était pas détectable au moment de la transmission.

ÉLÉMENTS DE PREUVE DE GRAPPES DE COVID-19 DANS DES LOGEMENTS FOURNIS PAR L'EMPLOYEUR

Dans certaines professions, le logement est fourni aux travailleurs. En général, le logement partagé entraîne un contact étroit des travailleurs pendant de longues périodes. Huit publications sur la COVID-19 dans des lieux de travail où l'employeur a fourni un logement ont été identifiées (tableau 3). Dans la plupart de ces investigations, il n'est pas possible de séparer le risque de transmission dû à la vie en communauté du risque lié aux activités sur le lieu de travail. Cependant, les taux d'attaque élevés parmi les travailleurs dans les lieux de vie en communauté soulignent que la transmission se produit dans des situations où les gens passent du temps ensemble et où le nombre de contacts (ou la densité de personnes) est associé au nombre d'événements de transmission qui peuvent se produire dans un cadre donné.

- Deux résumés séquentiels de 264 éclosions survenues dans des usines de transformation de la viande jusqu'au 31 mai 2020 aux États-Unis ont indiqué que le partage des locaux était un facteur de risque de transmission du SRAS-CoV-2, mais ces résumés ne fournissent pas de données spécifiques sur le nombre d'éclosions où le partage des locaux était un facteur potentiel ou sur les investigations qui en ont résulté (Dyal et coll., 2020; Waltenburg et coll., 2020).

- Une éclosion associée à l'hébergement partagé des employés sur un bateau de croisière (le Diamond Princess) où les colocataires et les personnes qui travaillaient avec des cas infectés étaient plus susceptibles d'être infectés. Une autre éclosion sur un bateau de pêche a eu un taux d'attaque de 85 % (N=122) sur le petit bateau pendant ses 16 jours en mer malgré un dépistage préalable de l'infection par le SRAS-CoV-2. La troisième éclosion s'est produite sur un navire de la marine américaine. L'investigation a révélé une probabilité plus élevée de résultats positifs chez les personnes ayant déclaré avoir partagé la même couchette avec un membre d'équipage dont les résultats étaient positifs, RC = 3,3; IC de 95 % = de 1,8 à 6,1 (Payne et coll., 2020).
- Lors du pic initial de l'éclosion de cas de COVID-19 à Singapour, 88 % (17 758 sur 20 198 au 6 mai 2020) des cas nationaux ont été attribués à des travailleurs migrants peu qualifiés vivant dans des dortoirs pour travailleurs étrangers.
- Lors d'une éclosion dans un camp d'été avec hébergement partagé, le taux d'attaque des membres du personnel a augmenté avec la durée du séjour dans le camp. Les gens séjournaient dans des cabines; il y avait en moyenne 15 personnes par cabine (fourchette entre 1 et 26). Le taux d'attaque médian des cabines était de 50 % (fourchette de 22 à 70 %) parmi les 28 cabines qui présentaient un ou plusieurs cas suggérant une association entre le risque de transmission et le fait de séjourner dans une cabine.
- Une étude de séroprévalence réalisée dans une usine spécialisée dans la production de pièces mécaniques où 237 sur 1316 employés vivaient dans les installations de l'usine a déterminé qu'aucun des 13 travailleurs présentant des anticorps IgG (antécédents d'infection par le SRAS-CoV-2) ne faisait partie des personnes vivant dans les installations de l'établissement.

Tableau 3. Huit publications sur la COVID-19 dans un lieu de travail où l'employeur fournissait l'hébergement.

Référence	Titre de la publication	Détails de l'étude	Résultats pertinents
(Jerkovic et coll., 2020) *prépublication*	Séroprévalence des anticorps anti-SRAS-CoV-2 chez des travailleurs d'usine en Split-Dalmatie et dans le comté de	• Cette étude transversale a estimé la séroprévalence sur 1494 employés d'usine vivant dans la région de Split-Dalmatie et le comté de Šibenik-Knin (Croatie) et a été menée entre le 23 et le 28 avril 2020. • L'usine (groupe DIV) est spécialisée dans la production et le commerce de vis et d'autres pièces mécaniques et métalliques. Elle possède deux sites de production	• À partir du 25 février 2020, le groupe DIV a mis en place des mesures de protection telles que la mise en place de stations de désinfection des mains dans toutes les pièces, des protocoles de nettoyage régulier des postes de travail, la fermeture des stations communes de vente de café et de nourriture, des contrôles de température, l'auto-isolation pour les personnes revenant de l'étranger et le travail à domicile pour une partie du personnel commercial et

	Šibenik-Knin, en Croatie	importants situés à Split (comté de Split-Dalmatie) et à Knin (comté de Šibenik-Knin), qui emploient respectivement environ 2200 et 400 personnes. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	administratif. Le nombre total d'employés travaillant dans les usines a été réduit à environ 1300 et 300, respectivement. • Dans un échantillon total d'employés testés (n=1 494), des anticorps ont été détectés chez 1,27 % des participants (IC de 95 % : de 0,77 à 1,98 %). • Une partie des employés de l'usine de Split vivent sur la propriété de l'usine. • À l'usine de Split 13 sur 1316 (0,99 %, IC de 95 % : de 0,53 à 1,68 %) des participants ont été testés positifs, dont 13 sur 1079 (1,20 %, IC de 95 % : de 0,64 à 2,05 %) des personnes qui vivaient en dehors de l'usine et 0 sur 237 (0 %, IC de 95 % : de 0 à 1,26 %) des personnes qui vivaient à l'intérieur des installations. À l'usine de Knin, 6 sur 178 (3,37 %, IC de 95 % : de 1,25 à 7,19 %) des participants ont été testés positifs aux anticorps. Tous les participants vivants dans les locaux de l'usine et dont la mobilité était limitée pendant les mesures de confinement ont obtenu un résultat négatif au test de dépistage des anticorps. Par conséquent, l'exposition n'était probablement pas liée au logement sur le lieu de travail dans le cas de cette éclosion,
(Koh, 2020a)	Les travailleurs migrants et la COVID-19	• Investigation épidémiologique rétrospective. • Les chiffres quotidiens des cas de COVID-19 à Singapour de mars à mai 2020 ont été analysés afin de déterminer la cause de l'augmentation des cas en avril. La réglementation sur le logement des travailleurs migrants a été étudiée. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• La majorité des cas associés à un pic en avril se sont produits chez des travailleurs migrants peu qualifiés vivant dans des dortoirs de travailleurs étrangers. Au 6 mai 2020, il y avait 17 758 cas confirmés de COVID-19 parmi les travailleurs vivant en dortoirs (88 % des 20 198 cas confirmés au niveau national). • Dans un dortoir de 13 000 travailleurs environ, 2526 cas ont été confirmés, ce qui représente 12,5 % de tous les cas dans le pays. • La réponse nationale a consisté à soumettre les travailleurs vivant en dortoirs à des tests approfondis, à

			séparer les travailleurs sains des travailleurs infectés et à observer quotidiennement la fièvre et les symptômes. En outre, 24 dortoirs ont été déclarés « zones d'isolement » pour que les résidents soient mis en quarantaine pendant 14 jours. Des logements publics, des camps militaires, des centres d'exposition et des hôtels flottants ont été mis à la disposition des travailleurs, afin de permettre une distanciation sociale appropriée.
(Dyal et coll., 2020)	Présence de la COVID-19 au sein des travailleurs d'usines de transformation de la viande et de la volaille — 19 États, avril 2020	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Le rapport fournit des données agrégées sur les cas positifs de COVID-19 parmi 115 usines de transformation de la viande et de la volaille dans 19 États américains jusqu'au 27 avril 2020. • Aucun conflit d'intérêts potentiel n'a été révélé.	• Parmi les quelque 130 000 travailleurs de ces installations, 4 913 cas (environ 3,0 %) et 20 d'entre eux sont décédés. • Ces chiffres reflètent les pratiques inadéquates de contrôle des infections suivies dans ces installations, notamment une faible distance sociale, des mesures de contrôle à la source (par exemple, l'utilisation de couvre-visages en tissu) et une charge de travail accrue. • Les facteurs de risque d'infection identifiés sont les difficultés liées à l'éloignement physique, à l'hygiène et aux conditions de vie et de transport surpeuplées (de nombreux travailleurs vivent dans des lieux surpeuplés et multigénérationnels et partagent parfois le transport pour se rendre au travail et en revenir).
(Waltenburg et coll., 2020)	Mise à jour : Présence de la COVID-19 au sein des travailleurs d'usines de transformation de la viande et de la volaille — 19	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Ceci est une mise à jour du rapport ci-dessus. • Le rapport fournit des données agrégées sur les cas positifs de COVID-19 parmi 239 usines de transformation de la viande	• Dans 239 usines il y a eu 16 233 cas de COVID-19 et 86 décès liés à la COVID-19 parmi les travailleurs (264 usines / 17 358 cas / 91 décès dans les deux publications (Dyal et coll., 2020; Waltenburg et coll., 2020)). • Parmi les 14 États ayant déclaré le nombre total de travailleurs dans les usines de transformation de la viande et de la volaille touchées (112 616), la COVID-19 a été diagnostiquée chez 9,1 % des travailleurs.

	États, avril à mai 2020	et de la volaille dans 23 États américains jusqu'au 31 mai 2020. • Aucun conflit d'intérêts potentiel n'a été révélé.	• Sur 9919 (61 %) cas dont la race/ethnicité a été signalée, 87 % concernaient des travailleurs issus de minorités raciales et ethniques. • Les facteurs qui augmentent le risque d'exposition pour ces travailleurs comprennent un contact étroit et prolongé sur le lieu de travail avec des collègues (à moins de 1,80 m pour une durée ≥15 minutes) pendant de longues périodes (équipes de travail de 8 à 12 heures), des espaces de travail partagés, un transport partagé pour se rendre au lieu de travail et en revenir, un logement collectif et des contacts communautaires fréquents avec des collègues. • Les données provenant de 111 usines dans 14 États révèlent la mise en œuvre des stratégies de prévention et de contrôle suivantes : dépistage des travailleurs à l'entrée (89 sur 111), obligation pour tous les travailleurs de porter un couvre-visage (86 sur 111), augmentation de la disponibilité des postes d'hygiène des mains (72 sur 111), sensibilisation des travailleurs à la propagation communautaire (70 sur 111), installation de barrières physiques entre les travailleurs (69 sur 111), offre de tests aux employés (41 sur 111) et fermeture temporaire (24 sur 111). • En utilisant les données de 7 usines qui ont mis en place des tests à l'échelle de l'usine, la prévalence brute des infections asymptomatiques ou présymptomatiques parmi les 5572 travailleurs qui ont été testés positifs à l'infection par le SRAS-CoV-2 était de 14,4 %.
(Kakimoto et coll., 2020)	Investigation initiale sur la transmission de la COVID-19 parmi	• Investigation épidémiologique rétrospective d'une éclosion sur le navire de croisière Diamond Princess de 3700	• L'investigation sur la propagation du SRAS-CoV-2 parmi le personnel a conclu que l'infection s'était apparemment propagée parmi les personnes dont les cabines se trouvaient sur le même pont (pont 3) et qui

	les membres d'équipage pendant la quarantaine d'un navire de croisière – Yokohama, Japon, février 2020	passagers et membres d'équipage qui a débuté le 3 février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	travaillaient dans le même groupe professionnel (restauration), probablement par contact ou par propagation de gouttelettes, ce qui est conforme à la compréhension actuelle de la transmission de la COVID-19. • Huit des 20 membres d'équipage positifs avaient des compagnons de cabine, dont 5 sur 8 sont devenus positifs à la COVID-19.
(Addetia et coll., 2020)	Des anticorps neutralisants en corrélation avec la protection contre le SRAS-CoV-2 chez l'homme lors d'une éclosion sur un navire de pêche avec un taux d'attaque élevé	• Investigation épidémiologique rétrospective. • Cette étude décrit une éclosion de SRAS-CoV-2 sur un navire de pêche qui a quitté Seattle, Washington, en mai 2020. • Avant le départ du navire, les membres de l'équipage ont été soumis à un test de dépistage d'une infection active par le SRAS-CoV-2 par RT-PCR et à un test sérologique pour détecter les signes d'une infection antérieure. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Le taux d'attaque à bord était de 85,2 % (104 sur 122 individus) et la métagénomique suggère que l'éclosion provient d'une seule source. • Les données de l'éclosion ne donnent que peu d'informations sur la dynamique probable de la transmission sur le bateau, mais le taux d'attaque élevé indique que la plupart des personnes ont probablement été exposées. • 3 personnes ayant des anticorps neutralisants avant le départ du navire n'ont pas été réinfectées sur la base des éléments de preuve présentés, indiquant qu'elles avaient probablement une certaine protection.
(Payne et coll., 2020)	Infections par le SRAS-CoV-2 et réponses sérologiques d'un échantillon de membres des services de la marine américaine – USS Theodore Roosevelt, avril 2020	• Enquête épidémiologique rétrospective sur une éclosion survenue sur l'USS Theodore Roosevelt en mars/avril 2020 avec environ 1000 militaires à bord. • L'investigation s'est déroulée du 20 au 24 avril 2020, une fois le navire amarré à Guam. • Un échantillon commode de 382 (27 % du total des membres du service sur le navire ou à la base navale de Guam).	• L'infection antérieure ou actuelle était plus élevée chez les participants qui ont déclaré avoir été en contact avec une personne connue comme ayant la COVID-19 (64,2 %), par rapport à ceux qui ne l'ont pas fait (41,7 %) (RC = 2,5; IC de 95 % = de 1,1 à 5,8). • La prévalence était également plus élevée chez les militaires qui ont déclaré avoir partagé la même couchette avec un membre d'équipage dont le test de dépistage était positif (65,6 %), par rapport à ceux qui ne l'ont pas fait (36,4 %) (RC = 3,3; IC de 95 % = de 1,8 à 6,1).

		• questionnaires, tests sérologiques et tests RT-PCR a été réalisé pour créer l'ensemble de données.
		• Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.
			• Le fait de prendre des mesures de protection était associé à un risque plus faible d'être positif à la COVID-19 :
			  • Revêtement du visage (55,8 % contre 80,8 %; RC = 0,3; IC de 95 % = de 0,2 à 0,5)
			  • Éviter les zones communes (53,8 % contre 67,5 %; RC = 0,6; IC de 95 % = de 0,4 à 0,9)
			  • Distanciation sociale (54,7 % contre 70,0 %; RC = 0,5; IC de 95 % = de 0,3 à 0,8)

(Szablewski et coll., 2020)	Transmission du SRAS-CoV-2 et infection parmi les participants à un camp de nuit – Géorgie, juin 2020	• Investigation épidémiologique rétrospective d'une éclosion associée à un camp de nuit en Géorgie, aux États-Unis • Un camp de nuit (camp A) a été organisé pour l'orientation de 138 stagiaires et 120 membres du personnel du 17 au 20 juin 2020. • Les membres du personnel sont restés pour la première session du camp, prévue du 21 au 27 juin 2020, et ont été rejoints par 363 campeurs et 3 membres de la direction le 21 juin 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• 597 résidents de Géorgie ont fréquenté le camp A. Parmi ceux qui ont été testés, 260 sur 344 (76 %) ont été déclarés positifs au SRAS-CoV-2. • Le taux d'attaque global était de 44 % (260/597), les membres du personnel ayant le taux d'attaque le plus élevé (56 %). Le taux d'attaque a augmenté avec la durée du séjour au camp. • L'occupation des 31 cabines était en moyenne de 15 personnes par cabine (fourchette de 1 à 26). Le taux d'attaque médian des cabines était de 50 % (fourchette de 22 à 70 %) parmi les 28 cabines qui ont connu un ou plusieurs cas. • Le camp a suivi toutes les recommandations du CDC, à l'exception de l'ouverture des fenêtres et des portes afin d'accroître la ventilation des bâtiments et du port de masques en tissu par les campeurs. Le personnel était censé utiliser des masques en tissu et les campeurs étaient en cohorte, mais le respect de ces mesures de prévention n'a pas pu être évalué.

ÉLÉMENTS DE PREUVE DE GRAPPES DE COVID-19 DANS LE TRANSPORT OU LES DÉPLACEMENTS VERS LE LIEU DE TRAVAIL

Il existe peu de données sur les grappes de COVID-19 résultant du transport ou des déplacements vers le lieu de travail. Cinq publications relatives à la COVID-19 ont été identifiées sur ce sujet (tableau 4).

- Deux publications résument 264 éclosions associées à des usines de transformation de la viande aux États-Unis jusqu'au 31 mai 2020. Le transport partagé vers et depuis le lieu de travail a été déterminé comme un facteur de risque d'exposition au SRAS-CoV-2 (Dyal et coll., 2020; Waltenburg et coll., 2020). Cependant, aucune donnée spécifique n'est présentée.
- Lors d'une éclosion dans un espace de travail combiné de bureau militaire et civil, aucun des 150 collègues qui ont été exposés pendant trois jours au cours du covoiturage n'a développé de symptômes ou n'a été considéré comme infecté (Hall et coll., 2020).
- Une étude sur les facteurs de risque d'infection par la COVID-19 au Royaume-Uni et aux États-Unis a révélé que les risques d'infection étaient nettement plus élevés chez les travailleurs américains qui utilisent les transports publics pour se rendre au travail. Ce résultat va dans le même sens, mais n'est pas significatif pour les répondants britanniques. Les raisons de cette différence peuvent être liées à la différence des mesures de santé publique mises en œuvre dans les zones étudiées (Anand et coll., 2020).

Tableau 4. Cinq publications sur la COVID-19 relatives au transport ou aux déplacements du domicile au travail.

Référence	Titre de la publication	Détails de l'étude	Résultats pertinents
(Hall et coll., 2020)	Investigation des cas de COVID-19 et des cas contacts dans un espace de travail de bureau	• Investigation épidémiologique rétrospective menée en mars 2020. • L'éclosion s'est produite aux États-Unis dans un espace de travail comprenant à la fois des bureaux militaires et des bureaux civils. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Le cas index a involontairement exposé 150 collègues au SRAS-CoV-2 en participant à des covoiturages, des conférences et de petites réunions sur une période de 3 jours. • Sur les 150 expositions, 37 ont été considérées comme un risque moyen et 113 comme un risque faible. 5 personnes ont signalé des symptômes de type COVID-19 et 5 ont développé des symptômes pendant la quarantaine de 14 jours. Aucun des contacts n'a été testé positif à une infection par le SRAS-CoV-2.

			• Aucun des collègues exposés pendant le covoiturage n'a développé de symptômes et malgré le contact étroit, il semble qu'ils n'ont pas été infectés. • L'identification rapide des personnes exposées au risque d'infection et la mise en œuvre ultérieure d'efforts d'atténuation et de contrôle ont permis de contrôler la propagation du SRAS-CoV-2.
(Dyal et coll., 2020)	Présence de la COVID-19 au sein des travailleurs d'usines de transformation de la viande et de la volaille — 19 États, avril 2020	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Le rapport fournit des données agrégées sur les cas positifs de COVID-19 parmi 115 usines de transformation de la viande et de la volaille dans 19 États américains jusqu'au 27 avril 2020. • Aucun conflit d'intérêts potentiel n'a été révélé.	• Parmi les quelque 130 000 travailleurs de ces installations, 4 913 cas (environ 3,0 %) et 20 d'entre eux sont décédés. • Ces chiffres reflètent les pratiques inadéquates de contrôle des infections suivies dans ces installations, notamment une faible distance sociale, des mesures de contrôle à la source (par exemple, l'utilisation de couvre-visages en tissu) et une charge de travail accrue. • Les facteurs de risque d'infection identifiés sont les difficultés liées à l'éloignement physique, à l'hygiène et aux conditions de vie et de transport surpeuplées (de nombreux travailleurs vivent dans des lieux surpeuplés et multigénérationnels et partagent parfois le transport pour se rendre au travail et en revenir).
(Waltenburg et coll., 2020)	Mise à jour : Présence de la COVID-19 au sein des travailleurs d'usines de transformation de la viande et de la volaille — 19 États, avril à mai 2020	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Ceci est une mise à jour du rapport ci-dessus. • Le rapport fournit des données agrégées sur les cas positifs de COVID-19 parmi 239 usines de transformation de la viande et de la volaille dans 23 États américains jusqu'au 31 mai 2020.	• Dans 239 usines, il y a eu 16 233 cas de COVID-19 et 86 décès liés à la COVID-19 parmi les travailleurs (264 usines / 17 358 cas / 91 décès dans les deux publications (Dyal et coll., 2020; Waltenburg et coll., 2020)). • Parmi les 14 États ayant déclaré le nombre total de travailleurs dans les usines de transformation de la viande et de la volaille touchées (112 616), la COVID-19 a été diagnostiquée chez 9,1 % des travailleurs.

		• Aucun conflit d'intérêts potentiel n'a été révélé.	• Sur 9919 (61 %) cas dont la race/ethnicité a été signalée, 87 % concernaient des travailleurs issus de minorités raciales et ethniques. • Les facteurs qui augmentent le risque d'exposition pour ces travailleurs comprennent un contact étroit et prolongé sur le lieu de travail avec des collègues (à moins de 1,80 m pour une durée ≥15 minutes) pendant de longues périodes (équipes de travail de 8 à 12 heures), des espaces de travail partagés, un transport partagé pour se rendre au lieu de travail et en revenir, un logement collectif et des contacts communautaires fréquents avec des collègues. • Les données provenant de 111 usines dans 14 États révèlent la mise en œuvre des stratégies de prévention et de contrôle suivantes : dépistage des travailleurs à l'entrée (89 sur 111), obligation pour tous les travailleurs de porter un couvre-visage (86 sur 111), augmentation de la disponibilité des postes d'hygiène des mains (72 sur 111), sensibilisation des travailleurs à la propagation communautaire (70 sur 111), installation de barrières physiques entre les travailleurs (69 sur 111), offre de tests aux employés (41 sur 111) et fermeture temporaire (24 sur 111). • En utilisant les données de 7 usines qui ont mis en place des tests à l'échelle de l'usine, la prévalence brute des infections asymptomatiques ou présymptomatiques parmi les 5572 travailleurs qui ont été testés positifs à l'infection par le SRAS-CoV-2 était de 14,4 %.
(Anand et coll., 2020) *prépublication*	Prédicteurs professionnels et personnels de la	• Cette étude transversale analyse les prédicteurs professionnels et personnels de l'expérience de transmission de la COVID-19 aux États-Unis et au Royaume-Uni	• Les résultats aux États-Unis étaient différents de ceux au Royaume-Uni, les auteurs théorisent que cela est dû à la rigueur des mesures de santé publique. Les résultats indiquent que la profession, les traits

	transmission de la COVID-19	• Une enquête en ligne a été menée auprès de 2000 participants la première semaine de juin 2020. • Aucune déclaration de conflit d'intérêts n'est disponible.	personnels, les circonstances et les comportements ont tous une incidence sur le risque d'exposition à la COVID-19 et sur la capacité à s'éloigner physiquement. • L'analyse britannique a indiqué un risque plus élevé d'être testé positif à la COVID-19 pour les personnes sans revenu, à revenu moyen inférieur, qui partageaient une cuisine et avaient un emploi où les interactions avec les clients et le personnel étaient permanentes. • L'analyse américaine a indiqué que le risque plus élevé d'être infecté par la COVID-19 était lié à un faible revenu (CR entre 5,8 et 6,3), à une cuisine partagée (3,6), à un diplôme universitaire (2,7), à une profession liée au transport (8,5), à l'appartenance à un syndicat (4,8), à une consultation sur la transmission de la COVID-19 au travail (2,5) et au fait d'avoir dû prendre les transports publics pour se rendre au travail (3,2).
(Leffler et Hogan, 2020) *prépublication*	Dépendance de la mortalité due aux nouvelles maladies à coronavirus (COVID-19) en fonction de l'âge dans les populations fortement exposées : Travailleurs et résidents des transports en commun de New York et passagers	• Des données transversales provenant de plusieurs sources et milieux ont été obtenues et les données de mortalité ont été comparées. • Les auteurs ont utilisé des sources accessibles au public pour estimer la mortalité due à la COVID-19 pour chaque groupe d'âge sur le bateau de croisière Diamond Princess, aux États-Unis, dans la ville et l'État de New York, et parmi les travailleurs de la New York Metropolitan Transit Authority (MTA). • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• À New York, la mortalité des travailleurs des transports en commun était estimée à 1 sur 7329 pour les 30 à 39 ans, 1 sur 1075 pour les 40 à 49 ans, 1 sur 343 pour les 50 à 59 ans et 1 sur 178 pour les 60 à 69 ans. • Parmi les travailleurs de la MTA décédés des suites de la COVID-19, 106 sur 109 personnes au 6 mai 2020, faisaient partie de la division des métros et des bus, qui compte 55000 employés. • Il n'est pas clair si la transmission de ces travailleurs s'est produite sur le lieu de travail ou en dehors du lieu de travail. • Parmi les travailleurs de la MTA de New York, plus de 6000 travailleurs (8 %) ont soit été testés positifs (plus de 2000), soit mis en quarantaine (4000 travailleurs).

	du Diamond Princess		

ÉLÉMENTS DE PREUVE DE L'EXISTENCE DE GRAPPES DE CAS DE COVID-19 PROVENANT DE VOYAGES LIÉS AU TRAVAIL

Cinq publications sur la COVID-19 résultant de voyages liés au travail ont été identifiées (tableau 5).

- La première grappe publiée a débuté avec un employé infecté qui se déplaçait entre les branches chinoise et allemande d'une organisation pour animer des ateliers et assister à des réunions.
- Lors de la deuxième éclosion, le cas index et les expositions initiales ont été liés à des voyages professionnels à Wuhan, en Chine. Les employés infectés lors d'un voyage d'affaires ont déclenché une éclosion sur leur lieu de travail.
- Les deux dernières études font état de grappes de cas liées à des conférences, qui sont souvent des événements sociaux et de réseautage (ministère de la Santé Manatū Hauora, 2020; Pung et coll., 2020). Les facteurs de risque identifiés sont liés à la proximité et à la durée de la période passée avec les cas primaires (par exemple, s'asseoir à la même table pendant un repas).

Tableau 5. Cinq publications sur la COVID-19 comprenant des grappes documentées associées aux voyages liés au travail.

Référence	Titre de la publication	Détails de l'étude	Résultats pertinents
(Böhmer et coll., 2020; Rothe et coll., 2020)	Transmission de l'infection au coronavirus nCoV-2019 à partir d'un contact asymptomatique en Allemagne Enquête sur une éclosion de COVID-19 en	• Investigation épidémiologique rétrospective. • 2 études décrivant la transmission du SRAS-CoV-2 d'une résidente chinoise qui s'est rendue en Allemagne pour des raisons professionnelles à ses collègues en janvier 2020. • Böhmer et coll. fournissent une investigation détaillée de l'éclosion. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Le patient 0 était une employée de la branche chinoise d'une société allemande basée à Munich. Elle s'est rendue de Shanghai à Munich en avion le 19 janvier 2020 pour animer des ateliers et assister à des réunions dans le bâtiment de l'entreprise. Elle a pris un vol de nuit pour retourner à Shanghai le 22 janvier 2020 et a été testée positive à l'infection par le SRAS-CoV-2 le 26 janvier 2020. • L'entreprise allemande a été informée de l'infection le 27 janvier 2020. Les premiers tests effectués sur les contacts à haut risque ont permis d'identifier les patients 1 à 4 comme des cas de première génération.

	Allemagne résultant d'un seul cas primaire associé à un voyage : une série de cas		Le site de la société a été fermé le 11 février 2020. Au 19 février 2020, 16 cas ultérieurs ont été identifiés. • L'intervalle sériel médian était de 4,0 jours (IQR de 3,0 à 5,0). • Dix patients en plus du patient 0 étaient des employés de l'entreprise. Les 5 autres étaient des contacts familiaux. L'investigation a révélé que la transmission du patient 0 aux 10 autres s'est probablement produite au cours des scénarios suivants : ○ Accompagnement du patient 0 dans ses activités multiples en Allemagne et retour par le même avion ○ Dans les réunions de travail (de 60 à 90 minutes) où les collègues étaient assis à proximité les uns des autres. ○ Les collègues ont travaillé simultanément sur le même ordinateur pendant une courte période. ○ Après s'être assis ensemble au cours d'une réunion de 90 minutes pendant la journée, deux collègues ont également passé la soirée ensemble dans l'une de leurs maisons. Cependant, la partenaire du collègue hôte qui était également présent ce soir-là n'a pas été testée positive. ○ Deux collègues se sont rencontrés lors d'une visite à la cantine où ils se sont assis dos à dos. L'un d'eux s'est tourné vers l'autre pour lui emprunter la salière.
(Zhang et coll., 2020)	Enquête épidémiologique sur une nouvelle épidémie de pneumonie à coronavirus en	• Article en chinois. • Investigation épidémiologique rétrospective menée en janvier 2020.	• Le premier cas a été identifié le 15 janvier et s'est propagé à 10 autres collègues avant que des mesures de contrôle ne soient mises en place le 24 janvier 2020. • Le cas index et le cas initial sont liés à des voyages professionnels à Wuhan.

	grappe dans des unités collectives de Tianjin	• L'éclosion s'est produite dans le bureau administratif d'une usine qui compte 906 employés à Tianjin, en Chine. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Les cas secondaires et tertiaires ont soit voyagé ou participé à des réunions avec les cas infectés, soit se sont assis à proximité d'eux.
(Pung et coll., 2020)	Investigation sur trois grappes de COVID-19 à Singapour : implications pour les mesures de surveillance et de réaction	• Investigation épidémiologique rétrospective de 3 grappes liées à un groupe de touristes chinois, une conférence d'entreprise et une église à Singapour en février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• L'analyse a révélé que 36 cas de COVID-19 confirmés ont été liés à 3 grappes locales, composées de 11, 20 et 5 personnes. • La première éclosion a touché 11 personnes d'un groupe de touristes venus de Chine. Cinq assistants d'un magasin où le groupe de touristes s'est arrêté ont été testés positifs au SRAS-CoV-2. Les assistants ont indiqué qu'ils aidaient les clients à appliquer des échantillons d'huile médicinale sur leur corps, et que le lavage des mains n'était généralement pas effectué entre les clients. • La deuxième grappe a été une conférence à laquelle ont assisté au moins 111 participants de 19 pays différents, du 20 au 22 janvier 2020. Vingt personnes ont été infectées. Cinq des cas ont été assis à la même table lors d'un dîner de type banquet durant trois heures et quatre autres cas ont participé à une réunion de quatre heures.
(Ministère de la Santé Manatū Hauora, 2020)	COVID-19 – grappes importantes	• Le gouvernement néo-zélandais a dressé une liste des grappes importantes en Nouvelle-Zélande en date du 17 août 2020. • Aucun détail épidémiologique sur les grappes n'a été fourni.	• Les grappes signalées dans les lieux de travail potentiels sont les suivants : mariage, lieu d'accueil, conférence et bateau de croisière.

ÉLÉMENTS DE PREUVE DE L'EXISTENCE DE GRAPPES DE COVID-19 RÉSULTANT DE RASSEMBLEMENTS SOCIAUX DE COLLÈGUES

En plus de l'activité liée au SRAS-CoV-2 dans la communauté, les activités qu'un travailleur exerce en dehors du lieu de travail détermineront le risque individuel qu'une personne apporte son entreprise. Trois grappes de COVID-19 résultant de rassemblements sociaux de collègues en dehors du lieu de travail ont été identifiées (tableau 6). Dans les trois grappes, un groupe de collègues se sont rencontrés en dehors du lieu de travail et ont été infectés. Un groupe s'est réuni dans un bar, l'autre a organisé un dîner au cours duquel il a chanté dans un espace clos, et le troisième groupe a « des antécédents de sorties à Wuhan ». Dans les trois scénarios, les infections acquises lors de réunions sociales de collègues ont entraîné des infections supplémentaires sur le lieu de travail.

Tableau 6. Trois grappes de COVID-19 associées à des rassemblements sociaux de collègues en dehors du lieu de travail.

Référence	Titre de la publication	Détails de l'étude	Résultats pertinents
(Valencia et coll., 2020) *prépublication*	Transmissions asymptomatique et présymptomatique de l'infection du nouveau coronavirus 2019 (COVID-19) : une estimation à partir d'une grappe de cas confirmés à Hô Chi Minh Ville, au Vietnam	• Investigation épidémiologique rétrospective d'un rassemblement dans un bar à Hô Chi Minh Ville, au Vietnam. • Les informations démographiques, cliniques et de laboratoire de tous les cas confirmés de COVID-19 et les contacts d'un rassemblement de bar le 14 mars 2020 ont été recueillies. • Les auteurs déclarent qu'il n'y a pas de conflits d'intérêts.	• Sur les 298 personnes qui ont assisté à un rassemblement dans un bar à Hô Chi Minh Ville, 13 ont été testées positives au SRAS-CoV-2. • La recherche des contacts parmi 4466 personnes a permis d'identifier 6 autres cas. • Le R0 spécifique de la grappe était de 2,64 (IC de 90 % : de 1,41 à 3,68). • 3 contextes de transmission après une investigation sur le terrain ont été identifiés (bar, ménage, lieu de travail). Le bar constituait 68 %, le lieu de travail 21 %, et le ménage 11 % des transmissions. o Dans la deuxième génération, 3 (50 %) des transmissions étaient liées au lieu de travail, dont 2 (67 %) ont signalé des symptômes après avoir été exposés à un cas qui n'a pas signalé de symptômes
(Bao et coll., 2020)	Éclosion de COVID-19 suite à	• Investigation épidémiologique rétrospective	• Un travailleur infecté par la COVID-19 qui est rentré chez lui après avoir quitté Wuhan, a provoqué une

	l'exposition d'un seul patient sur un site de divertissement : Une étude épidémiologique	d'une éclosion associée à une piscine dans un lieu de divertissement à Wuhan, en Chine. • Les informations démographiques, cliniques et de laboratoire de tous les cas et contacts confirmés de COVID-19 ont été recueillies en janvier et février 2020. • Les auteurs déclarent qu'il n'y a pas de conflits d'intérêts.	éclosion en se rendant dans une piscine le 20 janvier 2020, où il a infecté certains travailleurs et clients de l'établissement. • L'infection a ensuite été transmise par un employé de la piscine qui a continué de travailler et par un client qui a participé à une fête familiale et à un dîner avec des collègues. • L'employé de piscine qui a continué de travailler jusqu'au 26 janvier 2020 a causé des infections par le SRAS-CoV-2 chez 12 clients. • Un dîner avec des collègues a réuni 36 collègues le 22 janvier 2020. La personne infectée a chanté avec 7 collègues dans un espace fermé. L'infection des 7 collègues a été confirmée par la suite. • Le taux d'attaque secondaire pour le dîner avec les collègues était de 20,5% (IC de 95 % : de 7,8 à 33,2).
(Liu et coll., 2020)	Analyse des cas de grappe de COVID-19 à Tianjin	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Cette étude décrit toutes les grappes de cas de COVID-19 confirmés à Tianjin en date du 22 février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Il y avait des grappes de familles (28 cas, 71 cas), des grappes d'unités (1 cas, 10 cas), des grappes de transport (3 cas, 8 cas) et une grappe de lieux publics (1 cas, 26 cas). • Une grappe dans la section passagers d'un train a impliqué 10 cas. Après des investigations épidémiologiques, il a finalement été déterminé que 2 employés ayant des antécédents de sorties à Wuhan étaient des cas de première génération. • L'éclosion dans un grand magasin était due à un vendeur infecté qui a contaminé 26 clients et collègues.

ÉLÉMENTS DE PREUVE DE STRATÉGIES DE RÉDUCTION DES RISQUES RÉUSSIES SUR LE LIEU DE TRAVAIL

Il y a eu 21 publications sur les stratégies visant à réduire le risque d'infection par le SRAS-CoV-2 sur le lieu de travail (tableau 7). La majorité (75 %) d'entre elles sont des modèles mathématiques. Ces études ont porté sur les stratégies de prévention, l'incidence et la levée des mesures de santé publique, et la gestion des travailleurs migrants (tableau 7).

- Cinq études ont démontré l'efficacité de l'incitation à ne pas travailler pendant la maladie par la mise en place d'un programme de soutien au revenu (PSR), de politiques de congé et de politiques de quarantaine (Brotherhood et Jerbashian, 2020; Coleman, 2020).
- La limitation des contacts sociaux par une réintroduction progressive des personnes sur le lieu de travail, ainsi que la réduction du nombre de personnes et du temps passé sur le lieu de travail en général, sont efficaces pour ralentir la propagation des infections par le SRAS-CoV-2 (Kim, 2020; Koralnik et Tyler, 2020; Shaw et coll., 2020; Yilmazkuday, 2020).
- La disponibilité de lignes directrices et de mesures de protection personnelle au travail a amélioré le comportement individuel de protection personnelle (Wang, Yi Wong et Ho, 2020).
- L'efficacité des stratégies de dépistage sur le lieu de travail a été examinée comme moyen d'identifier une éclosion. Les stratégies explorées comprenaient des tests environnementaux et des tests sur les travailleurs.
    - Une étude des lieux de travail au Royaume-Uni et aux États-Unis a examiné les tests environnementaux. Les résultats de ces tests ont conclu que les lieux de travail dont les échantillons environnementaux étaient positifs étaient dix fois plus susceptibles d'avoir une personne infectée sur le lieu de travail (Marshall et coll., 2020).
    - Les tests des travailleurs ont été étudiés pour différents R0 : si R0=2,4, les travailleurs devraient être testés au moins tous les 3 à 4 jours pour prévenir une éclosion sur le lieu de travail alors que si R0=3,0, les tests devraient avoir lieu tous les 2 jours (Chin, Lo, Huynh, Murrill et Basu, 2020). Des stratégies moins fréquentes, comme une fois par semaine ou lors du retour au travail, étaient moins susceptibles de prévenir une éclosion.

Tableau 7. Vingt et une publications sur les stratégies de réduction des risques sur le lieu de travail.

Référence	Titre de la publication	Détails de l'étude	Résultats pertinents
Limiter les contacts sociaux			

(Shaw et coll., 2020) *prépublication*	Leçons de l'écologie des déplacements pour le retour au travail : modélisation des contacts et de la diffusion de la COVID-19	• 2 modèles SEIR sont utilisés : 1) un modèle des déplacements pour explorer les mouvements entre le domicile et le lieu de travail, et 2) un modèle de réseau pour explorer les modèles de contact dans l'environnement de travail. • Une étude de cas de réseau d'un laboratoire universitaire et d'un immeuble de bureaux pour explorer les compromis entre la limitation des contacts, des personnes ou du temps sur le campus. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les résultats des modèles montrent que les limitations des contacts sociaux, par la réduction du nombre de personnes ou du temps passé sur le lieu de travail, sont des stratégies équivalentes pour ralentir la propagation des agents pathogènes • Restreindre les activités sur le campus aux laboratoires (plutôt qu'aux laboratoires et aux bureaux) pourrait modifier considérablement (modulariser) la structure du réseau de contacts et donc, potentiellement, réduire le risque relatif de propagation des agents pathogènes. • Si les déplacements domicile-travail augmentent spécifiquement le risque de transmission (c'est-à-dire le partage des transports), la réduction du nombre de personnes sur le campus est la stratégie la plus efficace pour réduire le taux de propagation de l'infection.
(Brotherhood et Jerbashian, 2020) *prépublication*	Comportement en entreprise pendant une épidémie	• Les auteurs en déduisent un modèle mathématique dans lequel une entreprise représentative opère dans un environnement épidémique. • Les stratégies de l'entreprise pour réduire les infections et les coûts associés comprennent l'affectation des employés au télétravail et aux congés, et leur rotation entre le travail sur site, le télétravail et les congés. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les résultats des simulations montrent que la lutte contre les infections dans les entreprises a un effet significatif sur la dynamique de l'épidémie. Parmi les stratégies qui ont fait leurs preuves, citons le développement du télétravail, la rotation/mise en cohortes des employés sur site et la mise en place de possibilités de congé appropriées. • Une subvention de 3 % au télétravail réduit le pic de l'épidémie d'environ 3 % et le nombre total d'infections symptomatiques et le taux de mortalité de près de 9 %. • Les politiques de congé sont efficaces pour réduire les infections et les décès. • Par rapport à une situation hypothétique où une entreprise ne lutte pas contre les infections, les choix d'affectation et de rotation des employés dans les entreprises réduisent de 5 % le nombre maximum d'employés malades présentant des symptômes. Ces choix aplatissent également la courbe des infections en

			réduisant de 18 % le nombre total d'infections symptomatiques. En conséquence, le taux de mortalité diminue également de 18 %.
(Gallardo, de Arroyabe et Arranz, 2020)	Prévention des éclosions internes de COVID-19 dans les entreprises et les établissements publics : une méthodologie basée sur l'analyse des réseaux sociaux pour soutenir la prise de décision des services de santé et de sécurité au travail	• Cette étude applique les techniques d'analyse des réseaux sociaux pour aider les services de santé et de sécurité au travail à concevoir et à sélectionner des mesures préventives pour réduire le risque d'épidémies parmi les employés. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• La méthodologie a été démontrée dans un cas réel, un centre de recherche espagnol, fournissant des résultats prometteurs. • Les auteurs utilisent le concept de réseau d'employés dont l'interaction est causée par des déclencheurs, qui sont définis comme des circonstances communes entre 2 travailleurs qui peuvent entraîner une contagion, comme le fait de partager un bureau ou de participer au même conseil d'administration. • Par exemple, un lieu partagé avec un espace élargi entre les personnes, qui est désinfecté quotidiennement, est moins susceptible d'être un déclencheur de contagion qu'un même lieu encombré et sans désinfection régulière.
(Kim, 2020)	Distanciation sociale et directives de santé publique sur les lieux de travail en Corée : réponses à la maladie à coronavirus-19	• Données agrégées provenant d'investigations épidémiologiques rétrospectives. • Cette étude résume les politiques publiques et du lieu de travail en réponse à la COVID-19 en Corée. • Une vue d'ensemble des éclosions sur le lieu de travail pendant la période du 20 janvier au 15 mai 2020 est décrite à l'aide des données du Centre coréen de contrôle des maladies et du siège central de gestion des catastrophes. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Transmission sur le lieu de travail en Corée : o Sur les 11 018 cas de COVID-19 identifiés au 15 mai 2020, 15,7 % se sont produits sur des lieux de travail tels que des établissements de soins de santé, des centres d'appel, des clubs sportifs, des karaokés et des lieux de vie nocturne. o 111 cas ont été associés à des clubs de remise en forme après l'infection des instructeurs lors d'un atelier (Jang et coll., 2020). o 192 cas ont été associés à l'éclosion dans un centre d'appel. o 95 cas sont liés au service public (par exemple, le service de santé, les agents correctionnels, les

			pompiers et la police). Cependant, la raison de leur exposition n'a pas été identifiée. • Des lignes directrices ont été élaborées avant le 29 février 2020 et sont considérées comme ayant été efficaces pour limiter la transmission sur le lieu de travail après leur mise en œuvre. Le ministère de l'Emploi et du Travail a inclus des directives sur le lieu de travail portant sur la COVID-19 : o Distanciation sociale, horaires de travail flexibles, identification précoce des travailleurs suspectés d'être infectés et désinfection des lieux de travail o Pour prévenir la propagation de l'infection sur le lieu de travail, les lignes directrices suggèrent d'éviter les réunions en face à face, les voyages d'affaires, l'éducation et la formation o Les réunions en petits groupes, les activités de club et les dîners sociaux sur le lieu de travail ont été limités et une culture du retour à la maison juste après le travail a été encouragée
Politiques « rester à la maison »/de quarantaine			
(Coleman, 2020) *prépublication*	Interactions motivées par l'économie et propagation des maladies	• Ce modèle SIR a analysé les déplacements de personnes tout au long de la journée pour faire correspondre les données à la répartition des ménages selon la taille et l'âge des occupants, à la répartition des écoles et collèges de la maternelle à la 12e année selon la taille et les ratios personnel-élève, et aux établissements de bureaux et de vente au détail selon le nombre d'employés. Le modèle a ensuite été utilisé pour évaluer le respect à grande échelle d'une	• Les simulations révèlent qu'une politique d'atténuation où toutes les personnes symptomatiques restent chez elles est suffisante pour contrôler la propagation de la COVID-19 sans effets perceptibles sur l'emploi. • Cela est vrai même si jusqu'à 60 % de la population est asymptomatique.

		politique d'atténuation des symptômes obligeant les personnes symptomatiques à rester chez elles. • Aucune déclaration de conflit d'intérêts n'est disponible.	
(Yilmazkuday, 2020) *prépublication*	« Rester à la maison » est efficace pour lutter contre la COVID-19 : éléments de preuve internationaux de données de mobilité de Google	• Étude écologique. • A utilisé les données quotidiennes de Google sur la mobilité couvrant 130 pays entre le 15 février et le 2 mai 2020. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Une réduction hebdomadaire de 1 % des visites sur les lieux de travail a été assimilée à environ (SE de 6,3, $p < 0,01$) moins de cas de COVID-19 et 2,0 (0,5, $P < 0,01$) moins de décès dus à la COVID-19.
(Koo et coll., 2020)	Interventions visant à atténuer la propagation précoce du SRAS-CoV-2 à Singapour : une étude de modélisation	• Ce modèle de simulation d'épidémie de grippe publié en mars 2020 a étudié les possibilités d'intervention précoce à Singapour en cas d'échec du confinement local. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• La modélisation effectuée dans les premiers jours de la pandémie a suggéré que si une transmission communautaire se produisait, la mise en œuvre de l'intervention combinée de la mise en quarantaine des personnes infectées et des membres de leur famille, de la distanciation sur le lieu de travail et de la fermeture des écoles pourrait réduire considérablement le nombre d'infections par le SRAS-CoV-2.
Dépistage et recherche des contacts			
(Chen et coll., 2020) *prépublication*	Fréquence du dépistage routinier du SRAS-CoV-2 afin de réduire la transmission	• Ce modèle SEIR a simulé différentes fréquences de tests nécessaires au sein de la population active pour contrôler l'épidémie après la levée des politiques d'hébergement sur place. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Si R0=2,4, les travailleurs devraient être testés au moins tous les 3 à 4 jours pour réduire $R0 < 1$ et empêcher une éclosion parmi les travailleurs. • Avec un R0 plus élevé (3,0), les tests devraient avoir lieu tous les 2 jours. Comme cela est probablement irréaliste, d'autres stratégies telles que la distanciation

	parmi les travailleurs		sociale et la recherche des contacts devraient également être mises en œuvre.
(Foncea, Mondscheinet Massouh, 2020) *prépublication*	Des espaces de travail plus sûrs à l'heure du coronavirus : une nouvelle utilisation des tests d'anticorps	• Un modèle de simulation de Monte-Carlo a été utilisé pour analyser l'efficacité du dépistage périodique des anticorps anti-SRAS-CoV-2 afin de réduire le risque d'infection sur le lieu de travail. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Ce modèle de simulation préliminaire suggère qu'avec un dépistage d'anticorps deux fois par semaine et la mise en quarantaine des travailleurs suspectés d'être infectés par le SRAS-CoV-2, il est possible de réduire le nombre d'infections tout en améliorant la productivité de l'entreprise. • Les auteurs sont actuellement en train d'appliquer certaines combinaisons des protocoles du modèle avec des entreprises et des agences gouvernementales spécifiques et feront rapport à ce sujet lorsque les résultats seront disponibles.
(Bicher, Rippinger, Urach, Brunmeir et Popper, 2020) *prépublication*	Simulation basée sur des agents pour l'évaluation des politiques de recherche des contacts contre la propagation du SRAS-CoV-2	• Ce modèle basé sur les agents quantifie l'incidence de la recherche des contacts et du relâchement des mesures de confinement sur la propagation de la maladie. L'incidence de la localisation des ménages et des lieux de travail a été évaluée séparément et en combinaison avec différents niveaux de conformité. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Dans le cadre de la recherche des contacts sur le lieu de travail, le lieu de travail d'un cas confirmé de COVID-19 est temporairement fermé et tous les collègues sont mis en quarantaine. • La recherche des contacts dans les espaces de travail partagé réduit le pic de 30 %, quel que soit le niveau de conformité, tandis que la recherche des cas contacts dans les ménages est plus performante à mesure que la conformité augmente. • Ces mesures combinées permettent d'atteindre la plus grande réduction de pointe et donnent les meilleurs résultats avec un niveau élevé de conformité. Une recherche des contacts individuels supplémentaire entraînerait une réduction plus importante.
(Leng et coll., 2020) *prépublication*	L'effet des mesures de contrôle sur la transmission de la	• Étude écologique, l'effet causal de différentes mesures de contrôle sur la transmission de la COVID-19 et la reprise du travail dans 5 pays : La Chine,	• Les deux mesures politiques les plus efficaces pour l'endiguement de la maladie et la reprise du travail sont la recherche numérique des contacts et la délégation de responsabilités claires à la communauté locale.

	COVID-19 et la reprise du travail : preuves internationales	l'Italie, l'Allemagne, le Royaume-Uni et les États-Unis ont été quantifiés. • Les auteurs reconnaissent le soutien financier de la Fondation nationale des sciences naturelles de Chine, de la Fondation nationale des sciences sociales de Chine et de la bourse des sciences humaines et sociales du ministère de l'Éducation chinois. Aucune déclaration de conflit d'intérêts n'est disponible.	• La recherche des contacts à l'échelle de la population contribue à l'effet le plus important sur la reprise du travail, en encourageant la reprise du travail de 2,4 %. • Une augmentation de 1 % de la rigueur de la distanciation sociale a encouragé la reprise du travail de 1,2 %. • Des campagnes d'information du public, déléguant clairement la responsabilité à la communauté locale, ont encouragé la reprise du travail à environ de 0,9 à 1,0 %. • Les mesures fiscales telles que les prêts, la déduction fiscale et la déduction du prix des facteurs contribuent moins à la reprise du travail (environ 0,5 %), alors que la rigueur des soins de santé n'apporte aucune aide directe.
(Way, Champneys, Dyson et coll., 2020) *prépublication*	Les avantages de la transparence entre pairs dans le fonctionnement sûr du lieu de travail après un confinement dû à une pandémie	• Un modèle SEIR a été utilisé pour étudier la transmission sur le lieu de travail dans deux groupes différents de travailleurs, en supposant que tous les travailleurs sont régulièrement testés pour une infection par le SRAS-CoV-2 : 1) ceux qui sont transparents sur les tests, qui partagent leurs résultats avec leurs collègues et qui s'isolent dès qu'un contact est positif, 2) ceux qui sont opaques et qui ne font rien de tout cela. • Les lieux de travail considérés dans l'analyse sont les services administratifs, ou les usines où les employés sont supposés avoir un réseau statique de collègues avec lesquels ils interagissent régulièrement et où toutes les autres	• Plus la connectivité entre collègues est grande, plus l'opacité doit être faible entre employés pour réduire la transmission. • La transparence des employés présente un double avantage : elle permet de maximiser la productivité et de minimiser le taux d'infection global.

		interactions sur le lieu de travail seraient socialement distantes. • Aucune déclaration de conflit d'intérêts n'est disponible.	
Réduction des mesures de santé publique			
(Asfaw, 2020) *prépublication*	L'effet du programme de soutien du revenu sur la mobilité professionnelle, les cas de COVID-19 et la croissance de la mortalité	• L'étude écologique sur le programme de soutien au revenu (PSR) vise à atténuer les conséquences économiques de la pandémie tout en augmentant le respect des mesures de distanciation sociale. Cette étude analyse l'effet du PSR sur la mobilité au travail, ainsi que la croissance des cas et de la mortalité due à la COVID-19 à l'aide d'un modèle d'analyse multi-événement. • Aucune déclaration de conflit d'intérêts n'est disponible.	• La mobilité sur le lieu de travail a été réduite dans une fourchette de 4,4 à 8,29 % une semaine après l'introduction du PSR et de 21,8 à 47,7 % après trois semaines. • 5 semaines après la mise en œuvre du programme, on a constaté une réduction de 21,8 à 47,0 % et de 17,1 à 29,7 % de la croissance des cas et de la mortalité due à la COVID-19, respectivement. • En l'absence de programmes PSR, les auteurs estiment que le nombre cumulé mondial de cas et de mortalité due à la COVID-19 aurait été de 3,69 millions et 160 000 de plus que les cas et décès dus à la COVID-19 observés et enregistrés au 15 mai 2020.
(Koralnik et Tyler, 2020) *prépublication*	Étude épidémiologique II sur la COVID-19 : sortie progressive du confinement à Mumbai	• Un simulateur de ville à base d'agents a été utilisé pour modéliser des scénarios de sortie progressive du confinement à Mumbai, en Inde, à partir du 1er juin 2020. • L'étude a été financée par le centre IISc-Cisco Centre pour l'intelligence réseautée, le centre Robert Bosch pour les systèmes cyberphysiques, l'Institut indien de la Science et le ministère de l'Énergie atomique du gouvernement indien. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les résultats montrent qu'une ouverture progressive des lieux de travail, à un niveau de fréquentation conservateur de 20 à 33 %, est un bon moyen de relancer l'activité économique tout en garantissant que la capacité de soins médicaux de la ville reste suffisante pour faire face à l'augmentation possible du nombre de cas de COVID-19 en juin et juillet 2020. • Cela permettra de maintenir le taux d'occupation des trains et des bus de banlieue à un niveau bas similaire, réduisant ainsi la propagation de l'infection dans les systèmes de transport public surchargés. • Dans le cas des trains, l'occupation devrait être limitée à environ 20 % pendant les premières semaines, avec

			l'application d'une distance physique stricte et le port obligatoire de masques de protection.
(López et Rodó, 2020)	Fin du confinement social en Espagne et risque de réémergence de la COVID-19	• Ce modèle SEIR simule diverses stratégies potentielles post-confinement en Espagne, telles que le déconfinement massif instantané de différentes populations et le retour progressif des personnes au travail. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• Les résultats montrent que le confinement actuel devrait être prolongé d'au moins 2 semaines supplémentaires pour éviter une nouvelle escalade des cas et des décès, ainsi qu'une deuxième vague dans quelques mois. • Parmi tous les scénarios modélisés, le meilleur scénario consiste à réintégrer progressivement les travailleurs dans la société dans une proportion quotidienne supérieure de 30 % au maximum à celle du confinement précédent. Cela permettra de réduire l'incidence et le nombre de victimes. Pour maximiser les effets positifs, cette stratégie ne devrait pas commencer avant la fin avril 2020.
Surveillance et contrôle de l'environnement			
(Marshall et coll., 2020) *prépublication*	La surveillance environnementale du coronavirus sentinelle peut contribuer à détecter les propagateurs asymptomatiques du virus du SRAS-CoV-2 et peut vérifier l'efficacité des contrôles contre la COVID-19 sur le lieu de travail	• Une étude de cohorte prospective visait à évaluer l'efficacité de l'utilisation de la surveillance environnementale du SRAS-CoV-2 comme outil de détection des agents de propagation asymptomatiques et présymptomatiques et de la réalisation de tests cliniques et environnementaux de surface sur les lieux de travail pour minimiser les infections. • Neuf lieux de travail en Europe et aux États-Unis ont participé à l'étude. Sur ces trois sites, un ou plusieurs employés étaient infectés par le SRAS-CoV-2.	• Les endroits dont les surfaces étaient contaminées par le SRAS-CoV-2 étaient dix fois plus susceptibles d'avoir des employés dont le test de dépistage du SRAS-CoV-2 était positif que les endroits dont les surfaces n'étaient pas ou très peu contaminées. • Les surfaces les plus fréquemment contaminées étaient les chaises des salles de détente, les bancs de travail et les poignées de porte. • Comme les lieux où l'on a détecté de nombreux prélèvements positifs dans l'environnement avaient un employé infecté pendant la période d'étude, la surveillance de l'environnement semble être un outil utile pour informer les tests cliniques nécessaires à la détection de propagateurs de virus asymptomatiques ou présymptomatiques et à la mise en œuvre de mesures de contrôle appropriées.

		• Les auteurs indiquent que le financement de l'étude a été assuré par les lieux et les laboratoires participants.	
(Gunawardana et coll., 2020) *prépublication*	Surveillance et caractérisation longitudinale de la COVID-19 sur le lieu de travail avec des points de contrôle de santé publique et de diagnostic	• Une cohorte prospective a été menée pour évaluer si la surveillance longitudinale des maladies sur le lieu de travail serait une approche efficace pour contrôler le SRAS-CoV-2 chez les employés et les membres de leur ménage. Les résultats entre le 23 mars et le 22 juin 2020 sont présentés. • Dans une petite organisation du sud de la Californie (Oak Crest), 54 volontaires (27 employés et 27 membres de ménages) ont fourni des échantillons fréquents pour le dépistage du SRAS-CoV-2. Seuls les participants ayant obtenu un résultat négatif au test pouvaient entrer dans la « zone de sécurité » du lieu de travail. • Une combinaison d'un modèle SEIR et d'un modèle mixte non linéaire bayésien a été utilisée pour prédire le nombre d'employés et de membres de ménages qui auraient été infectés en l'absence du programme de surveillance. • Les auteurs affirment que l'étude a été entièrement financée par des fonds institutionnels discrétionnaires.	• En utilisant la prévalence actuelle dans le comté de Los Angeles, le modèle prévoyait, sans intervention de surveillance, jusqu'à 7 employés (IC de 95 % : de 3 à 10) auraient été infectés avec au maximum 1 d'entre eux nécessitant une hospitalisation et 0 décès. • Pendant la période d'étude, deux participants à l'étude ont été très infectés par le SRAS-CoV-2. L'un était un employé et l'autre un membre du ménage. • L'employé n'a pas été autorisé à entrer sur le lieu de travail de la zone de sécurité avant d'avoir été testé négatif 3 fois consécutives sur une période de 7 jours. Aucun autre employé ou membre du ménage n'a contracté le SRAS-CoV-2 au cours de l'étude.
Orientation sur le lieu de travail			

(Wang et coll., 2020) *prépublication*	Disponibilité d'une politique de prévention des maladies à coronavirus 2019 sur le lieu de travail et son lien avec les comportements de protection personnelle : une enquête menée auprès des employés	• Une étude transversale utilisant un questionnaire en ligne évaluant les directives sur le lieu de travail et le comportement en matière de protection personnelle des résidents de Hong Kong ayant un emploi (n=1048) a été menée entre le 17 et le 27 février 2020. • Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• 1048 questionnaires ont été analysés dans 5 groupes professionnels. • Dans la plupart des professions, l'existence de directives et de mesures de prévention contre la COVID-19 sur le lieu de travail a permis d'améliorer les comportements de protection personnelle tels que l'hygiène des mains, le port d'un masque facial et la distanciation sociale.
Gestion des travailleurs migrants			
(Maji, Choudhari et Sushma, 2020)	Implications du rapatriement de travailleurs migrants sur la diffusion de la COVID-19 et les exigences de transport	• Ce modèle SEIR a permis d'étudier l'augmentation potentielle des cas confirmés et actifs d'infection par la COVID-19 en Inde et d'évaluer la taille du parc de trains et d'autobus nécessaire au rapatriement des travailleurs migrants. • En faisant des prévisions à partir des données du recensement de 2011 et en les comparant avec les informations rapportées dans les médias, on a pu estimer la population de travailleurs migrants rapatriés. • Aucune déclaration de conflit d'intérêts n'est disponible.	• Les résultats indiquent que la réduction du taux d'arrivée quotidien de travailleurs migrants dans les États où le flux sortant de migrants est très élevé (c'est-à-dire l'Uttar Pradesh et le Bihar) peut contribuer à diminuer la hausse des cas confirmés et actifs. • Cependant, cela pourrait créer une disparité dans le nombre de jours nécessaires pour transporter tous les travailleurs migrants rapatriés vers leur État d'origine. Il a été recommandé d'organiser le voyage d'environ 100 000 travailleurs migrants par jour vers l'Uttar Pradesh et le Bihar, d'environ 50 000 par jour vers le Rajasthan et le Madhya Pradesh, de 20 000 par jour vers le Maharashtra et de moins de 20 000 par jour vers les autres États de l'Inde. • Les auteurs suggèrent que des mesures strictes de contrôle des travailleurs migrants avant l'embarquement et une politique d'isolement stricte

			après l'arrivée pourraient contrôler la hausse des cas confirmés et actifs.
(Han et Jia, 2020) *prépublication*	La réduction de la population migrante réduit le nombre de cas de COVID-19 : une étude de cas en Chine	• Un modèle additif généralisé (MAG) a été utilisé pour modéliser la relation entre la population migrante et le nombre de cas confirmés de COVID-19 en Chine. • L'étude a été financée par la Bourse pour start-up de l'université de Pékin. Les auteurs déclarent qu'il n'y a pas de conflit d'intérêts.	• En utilisant la Chine comme étude de cas, les résultats montrent que le nombre de cas de COVID-19 confirmés était corrélé avec la migration de la population et la densité régionale de la population (R2aj = 0,873, déviance expliquée = 89,6 %). Le nombre de cas confirmés augmentera avec la croissance de ces variables. • Par conséquent, la restriction des déplacements de la population peut réduire considérablement le nombre de cas confirmés et limiter l'expansion de la maladie. • Une fois que la population migrante retournera au travail, le nombre de cas confirmés atteindra 27 483 (IC de 95 % : de 16 074 à 48 097). L'augmentation moyenne dans 73 villes était de 85,53 % (IC de 95 % : de 19,53 à 189,81%).
(Maji, Sushma et Choudhari, 2020) *prépublication*	Implication des mouvements interétatiques de travailleurs migrants pendant le confinement dû à la COVID-19 en utilisant le modèle SEIR modifié	• Ce modèle SEIR évalue l'effet du transport interétatique des travailleurs migrants pendant la période de confinement en Inde. À partir du 5 mai 2020, on suppose que les travailleurs migrants commenceront à arriver à leurs destinations respectives et le modèle a analysé le taux d'arrivée quotidien de 20 000 à 100 000 travailleurs migrants par État. • Aucune déclaration de conflit d'intérêts n'est disponible.	• On estime que les États comptant un nombre important de travailleurs migrants connaissent une augmentation des cas confirmés et actifs • Les auteurs suggèrent que des mesures strictes de contrôle des travailleurs migrants avant l'embarquement et un isolement strict après l'arrivée peuvent contribuer à maîtriser la hausse des cas confirmés et actifs.

Méthodologies

Toute la littérature sur la COVID-19 a été compilée et organisée par le Groupe des sciences émergentes de l'Agence de la santé publique du Canada depuis le début de l'éclosion. Cela implique une analyse documentaire quotidienne de tous les articles publiés et prépubliés. Les recherches visant à retrouver la littérature pertinente à la COVID-19 sont menées dans PubMed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square. Les résultats sont recoupés avec la littérature figurant sur la liste documentaire sur la COVID de l'Organisation mondiale de la santé et les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et un fichier Excel consultable. Chaque article est étiqueté en fonction de divers critères permettant d'identifier le thème central de l'article (par exemple, épidémiologie, données cliniques, thérapeutiques, etc.). Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche inclus dans cette revue étaient : lieu de travail, travail*, profession, collègue, fabrication, usine, et employé, rassemblement, et super-propagation*. Il n'y avait pas de restrictions linguistiques. Chaque référence potentiellement pertinente a été analysée pour confirmer sa pertinence et les données ont été extraites dans la revue. Des articles supplémentaires et des rapports de littérature grise ont été ajoutés à la base de données au fur et à mesure qu'ils ont été identifiés. La littérature grise se limitait aux rapports du gouvernement et des établissements de santé publique. Les sources médiatiques et les bulletins d'information n'ont pas été jugés suffisamment fiables ou détaillés pour être inclus. Une recherche en boule de neige a été effectuée, qui comprenait le recoupement des listes de référence des revues publiées et des articles pertinents pour les recherches pertinentes omises par la recherche. Comme il s'agit d'une revue rapide, les études incluses n'ont pas fait l'objet d'un double filtrage ou d'une extraction d'articles et d'une évaluation formelle de la qualité (risque de biais). Cette revue contient les recherches publiées jusqu'au 21 août 2020.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse sur la désescalade des bulles sociales

Introduction

Quelles sont les données probantes disponibles à propos de la désescalade des « bulles des ménages »? Y a-t-il des suggestions sur la façon dont nous pouvons réduire la segmentation des communautés en réseaux plus importants?

Cet examen portera sur les données probantes relatives au concept de segmentation des réseaux mis en œuvre pour le grand public sous forme de « bulles sociales ». Ce concept fait référence aux limitations des interactions individuelles avec les personnes en dehors de leur réseau fermé (par exemple, la famille proche). Alors que nous passons à différentes phases de l'épidémie, il est intéressant de comprendre quelle incidence l'augmentation de la taille de la bulle sociale ou la segmentation des réseaux peut avoir sur l'épidémie. Cette note d'information comprend la littérature jusqu'au 15 juin 2020.

Points clés

- On a défini une prépublication qui modélise directement les bulles sociales et les options du monde réel en utilisant le Royaume-Uni comme étude de cas. L'étude indique que les bulles familiales ont réduit le nombre de cas de 17 %. Dans son modèle, on étudie la possibilité d'assouplir la bulle du ménage unique pour différents scénarios de ménages multiples en utilisant trois taux d'attaque secondaire différents et le taux de reproduction de base (R0) comme résultat. Il est démontré que le R0 augmente à mesure que les restrictions sont assouplies, mais certaines des options limitées semblent présenter une augmentation minimale du risque.
- Trois modèles de réseaux sociaux prouvent également que des réseaux plus vastes, mais toujours fermés et segmentés, offrent un effet protecteur contre l'introduction du SRAS-CoV-2. Plus un réseau segmenté est grand, plus il y a de contacts en dehors de ce réseau, plus le risque d'introduction du virus est élevé.
- Il existe de nombreuses études qui examinent l'incidence de l'éloignement social de manière plus générale et en combinaison avec d'autres interventions. Elles ne sont pas résumées dans cette note d'information, mais elles sont disponibles sur demande, car elles sont recueillies dans le cadre de l'examen permanent sur les interventions de santé publique.
- On a également défini un protocole pour une étude systématique sur les interventions d'éloignement physique, mais il ne sera pas déployé avant octobre 2020.

Vue d'ensemble des éléments de preuve

Le concept de réduction de la transmission du SRAS-CoV-2 en limitant les interactions étroites à un petit réseau très strict (c'est-à-dire une seule famille) est une intervention efficace. Il est important d'augmenter la

taille du réseau ou de désamorcer l'intervention avec prudence et pas trop rapidement afin de maintenir le contrôle sur l'épidémie tout en levant lentement les restrictions. Comme il y a peu d'observations dans la littérature, les données probantes se trouvent majoritairement dans quelques prépublications récentes qui font état de modèles prédictifs. Ces modèles sont basés sur des scénarios et sont paramétrés à partir des données d'observation de l'épidémie. La mesure dans laquelle les résultats peuvent être généralisés au contexte local est variable et doit être utilisée avec prudence.

TABLE DES MATIÈRES

BULLES SOCIALES

Quatre modèles prédictifs ont étudié les concepts de bulles sociales en utilisant des modèles basés sur les agents et d'autres modèles de réseau pour démontrer l'incidence protectrice du fait d'avoir des réseaux de contacts fermés et limités pendant l'épidémie de COVID-19 (Block *et al.*, 2020; leng *et al.*, 2020; Sneppen et Simonsen, 2020; St-Onge, Thibeault, Allard, Dube et Hebert-Dufresne, 2020). Un modèle étudie directement une gamme d'options d'assouplissement des restrictions de contact et en étudie les implications à l'aide du R0 (Leng *et al.*, 2020). Ces modèles étudient et expliquent le concept de réseaux communautaires à petits segments offrant une résistance accrue à l'introduction du virus dans des réseaux plus petits. Ils explorent également les activités qui dégradent la protection d'un réseau segmenté. Cela se produit lorsqu'un individu issu d'un réseau fermé interagit avec d'autres réseaux, et cela est particulièrement plus risqué lorsque l'interaction se fait dans le cadre d'un événement de rassemblement fortuit où se mêlent des inconnus, par exemple dans les transports publics, lors de déplacements vers un lieu de travail en dehors du réseau segmenté, dans les lieux de socialisation tels que les bars et les restaurants, ou lors d'événements sportifs. Cependant, on ne sait pas dans quelle mesure on peut utiliser ces estimations, car elles sont basées sur la dynamique de l'épidémie dans un endroit précis.

Tableau 1 : Études de modélisation sur les bulles sociales ou les réseaux sociaux restreints

Référence	Description de l'étude	Résultats pertinents
(Leng *et al.*, 2020) Prépublication	Modèle basé sur l'individu : En utilisant le Royaume-Uni comme étude de cas, on a utilisé un modèle mathématique pour évaluer l'efficacité de diverses stratégies de bulles sociales dans le cadre d'une stratégie de sortie de déconfinement progressive.	Maintenir le taux d'attaque secondaire = 20 % constant. Le scénario de base est celui du R0 = 0,8 dans les bulles unifamiliales. Les scénarios suivants montrent la manière dont le Ro devrait évoluer avec un assouplissement modéré des restrictions de contact :

	En utilisant un cas de base où les boutiques et les écoles non essentielles sont fermées, le taux d'attaque des ménages est de 20 % et R0 = 0,8, on simule un certain nombre de stratégies de bulles sociales. Les résultats montrent que dans le scénario de ce cas de base, les bulles sociales ont réduit les cas et les décès de 17 % par rapport à une augmentation non groupée des contacts. Le regroupement des contacts en dehors du ménage dans des bulles sociales exclusives est une stratégie efficace pour augmenter les contacts tout en limitant une partie de l'augmentation du risque d'épidémie qui y est associée.	1. Autoriser tous les ménages ayant des enfants d'âge scolaire à se réunir, R0= 0,85 2. Autoriser tous les ménages ayant des enfants de tous âges à se réunir, R0 = 0,90 3. Autoriser tous les ménages individuels à se réunir avec d'autres ménages individuels, R0 = 0,85 4. Autoriser tous les ménages individuels à se réunir avec tout autre ménage, R0 = 1,00 5. Scénarios 1 et 3, Ro = 0,90 6. Tous les ménages se réunissent, Ro = 1,11
(Block *et al.*, 2020)	Modèle stochastique : en adoptant une approche de réseau social, nous évaluons l'efficacité de trois stratégies d'éloignement conçues pour garder la courbe plate et aider à la conformité dans un monde d'après-confinement. Nous démontrons qu'une réduction stratégique des contacts basée sur les réseaux sociaux renforce fortement l'efficacité des mesures d'éloignement social tout en maintenant les risques à un niveau plus bas.	Trois scénarios d'éloignement social - « renforcer la communauté et rechercher des stratégies de similarité ». - Les individus choisissent leurs contacts en fonction de la similarité d'une caractéristique individuelle prédéterminée. Cela facilite la formation de petits groupes, par exemple dans le quartier ou dans une petite organisation. - Les individus tiennent compte des interactions de leurs contacts et ne voient personne d'autre en dehors d'un réseau de contacts défini. Créer des bulles par des contacts répétés. Les individus décident avec qui ils veulent interagir. On peut également utiliser ce système avec les unités de travail. Il est difficile pour le virus de pénétrer dans ces microcommunautés.
(St-Onge *et al.*, 2020) Prépublication	Modèles SIS-SIR d'auteurs canadiens (Université Laval) utilisant un cadre scientifique de réseau pour examiner l'incidence de structures telles que les rassemblements (groupes/classes/équipes sportives, etc.).	- Ils démontrent que les épidémies localisées peuvent être mises en échec si la taille du groupe ou du rassemblement reste en dessous d'un certain seuil. - Le seuil pour le régime de localisation mésoscopique, avec un taux de transmission β = 0,07, était de 23 personnes et moins.

(Sneppen et Simonsen, 2020) *Prépublication*	Ce modèle à base d'agents a étudié l'incidence des événements de superpropagation. Dans le modèle de base, les événements de superpropagation ont eu peu d'effet sur l'épidémie, mais selon diverses stratégies d'intervention, la limitation des contacts sociaux diffus – lors de rassemblements fortuits – dans les milieux tels que les bars, les transports, les restaurants, les fêtes, les concerts et les salles de conférence est bien plus efficace que la limitation du même nombre d'événements de contact à la maison et au travail.	- La limitation des rassemblements fortuits a eu une incidence importante sur le risque de super propagation des événements dans ce modèle dans le cadre de scénarios où diverses stratégies d'intervention sont mises en œuvre.

PROTOCOLE DE RECHERCHE EN COURS

On a défini un protocole d'examen systématique qui résumera les données probantes sur les stratégies d'isolement, de quarantaine et d'éloignement social.

Tableau 2 : Protocoles de recherche

Référence	Description de l'étude	
(Regmi et Lwin, 2020)	Quelle a été l'incidence des mesures d'éloignement social pour la prévention de la maladie à coronavirus 2019 [COVID-19]?	Les études seront ciblées de juillet à octobre 2020 et se limiteront à des articles en anglais évalués par des pairs.

Méthodologies

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'Agence de la santé publique du Canada (ASPC). L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés étaient les suivants : social ET (bulle ou bulles ou réseau). Les résultats ont été recoupés avec l'examen permanent sur les interventions de santé publique. La présente revue contient des recherches publiées jusqu'au 15 juin 2020.

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

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Emerging Evidence on COVID-19

Evidence Brief on viral load and the likelihood of transmission during the infectious period of SARS-CoV-2

Introduction

What is the relationship between viral load and the likelihood of transmission during the infectious period of SARS-CoV-2? Does this vary by presence of symptoms, severity of symptoms, risk factors (e.g., age, chronic health conditions) or by infection with the currently circulating SARS-CoV-2 variants of concern?

The correlation between viral load and likelihood of transmission has been studied throughout the pandemic in order to characterize when during an infection with SARS-CoV-2 a person may be more infectious and most likely to transmit the virus. Research has also attempted to characterize the attributes of individuals or characteristics of infection that may be associated with higher risk of transmission. During Winter 2021 new research has indicated that variants of concern (e.g., B.1.1.7, B.1.351, and P.1) may have different transmission dynamics and virulence than wild-type strains that were circulating earlier in the pandemic. This could be due to a multitude of interlacing factors (e.g., longer persistence of viral RNA shedding, decreased immune response, or lower binding energy between the SARS-CoV-2 spike protein and human receptors). The current evidence base is conflicting on whether variants of concern have higher viral loads. Some studies have reported higher viral loads in variant cases (B.1.1.7 and P.1) compared to wild-type (1-5), while three new studies reported no significant difference (6-8). Further investigations are necessary to determine what factors are contributing to the increased transmission observed with the circulating variants of concern. On the other hand, recent vaccination studies indicate that vaccination may prevent against symptomatic infection and may reduce viral load by 1.6 times to 20 times in infections occurring after the first dose of vaccine (9-11). Thus, even if vaccines do not fully prevent infection, reducing viral load during infection will also likely reduce transmission. This evidence brief focuses on research that investigates the relationship between viral load and likelihood of transmission during the infectious period of SARS-CoV-2 published up to March 31, 2021.

The most common proxy measurement of SARS-CoV-2 viral load is the cycle threshold (Ct) value, which is the number of cycles during reverse transcription polymerase chain reaction (RT-PCR) required to reach a threshold of detection for a certain gene target. Within this model, lower Ct values indicate a higher viral load and where provided, an estimate of viral load, copies/mL, can be calculated. The calculation of copies/mL requires a standardization process based on the amplification target in the extract and the Ct value. There are several downsides to using Ct values as a proxy of viral load. First, amplification efficiency is influenced by the assay itself and factors associated with sample collection (e.g., amount of sample material collected) (12, 13). Studies are often highly heterogeneous in the sampling methods, detection assay, and gene targets used. Second, the Ct value upper bound cut-off that determines a positive PCR result has been inconsistent among

studies, though most reported positive values at Ct ≤35. It is recommended that a standard curve using reference materials or in-house plasmid controls with known viral copy numbers be utilized to interpret Ct values as viral loads – this would allow for appropriate quantification (e.g., copies/mL) (14). However, there has been wide heterogeneity and inconsistency of the standard curves calculated across studies, so precaution is necessary when interpreting viral load results in the COVID-19 literature.

Detection of viral RNA by RT-PCR does not provide proof of infectivity as this test also gives positive results when non-infectious virus particles are present. Recovery of replication-competent virus has been used as a measure of infectiousness (i.e., transmission potential). This is most often accomplished using cell culture. The detection of subgenomic RNA has also been recommended as a potential proxy for shedding of replication-competent virus (15), although consensus on this application is lacking (16). While viral RNA shedding is often observed in respiratory samples collected more than 15-17 days post symptom onset (17), replicative virus has in most instances not been isolated past 10 days in mild cases (18-22). The correlation of SARS-CoV-2 viral loads and Ct values with isolation of replicative virus is an important topic of interest when investigating transmission potential and is explored in this review.

Key Points

- The evidence brief identified 27 studies including 2 systematic reviews, 5 prospective cohorts, 5 retrospective cohorts, 1 case-control, 7 cross-sectional studies, 1 surveillance study, 4 case series, 1 contact tracing study, and 2 modelling studies.

- Across all studies, transmission is most likely to occur when, samples contained replicative virus, which occurred when Ct values were low (<30) and the sample was taken less than 8-10 days from symptom onset.

Studies that investigate an association between viral load and evidence of replicative virus (Culture/subgenomic RNA) (n=15):

- Replicative virus was most likely to be isolated from samples with Ct values <30 or viral loads >1x 10^6 copies/mL. Samples with Ct values ≤25 demonstrated replicative virus at a rate >90%.

- The most recently published systematic review on this topic reported significant correlation between Ct value and culture positivity rates. The probability of recovery of virus from specimens with Ct > 35 was 8.3% (95% CI: 2.8% to 18.4%). Further, the odds for culturing replicative virus has been reported to decrease by 0.64 for every one unit increase in Ct (95% CI 0.49 to 0.84, p<0.001).

- Recovery of replicative virus was unlikely in samples collected >8-10 days post symptom onset, even in samples with Ct values <35. Thus, Ct value and days post symptom onset assessed in tandem may be an effective method for deciding the likelihood an individual is still infectious.

- Cases with positive culture identified at greater than 8-10 days or at Ct values >35 were more likely to be severe or immunocompromised cases.

- There was heterogeneity in the sampling and detection methods used across studies. The overall association between Ct value and isolation of replicative virus did not appear to differ depending on SARS-CoV-2 gene target (e.g., Nucleocapsid (N), Envelope (E), Spike protein (S)) used for the PCR test.

Studies that investigate an association between viral load and likelihood of transmission (n=12):

- Modelling studies demonstrated that viral loads peak on average 5 days post expsoure and 1-2 days post symptom onset, with a short period (<2 days) of high transmission risk after which the likelihood of transmission quickly diminishes by 7-10 days post symptom onset. Highly infectious cases can shed tens to thousands of SARS-CoV-2 virions/min, especially between 1-5 days post symptom onset.

- Index cases with high viral loads (>10^6 copies/mL or Ct values <30) were more likely to transmit SARS-CoV-2 to household contacts.

- Transmission from index cases with high Ct values (>35) have occurred, but the transmission risk is much lower (8%).

- The majority of secondary household cases were detected within 10 days post symptom onset of the index case.

- High viral loads have been reported during the pre-symptomatic period and up to 8-10 days post symptom onset. It is during this time when Ct values are low (<30) that there is a high probability of transmission.

Overview of the Evidence

A total of 27 studies were included in this review, including several observational studies. Multiple studies are pre-prints and have not undergone a peer-review process. Prospective cohorts are at lower risk of bias than retrospective cohorts and cross-sectional analyses of medical record data or routinely collected surveillance data on COVID-19. Some of these studies appeared to have good generalizability as they represented large or national databases. However, retrospective cohorts and cross-sectional studies are at higher risk of bias due to their retrospective nature, as well as the increased risk of having missing and confounding data. Case series suffer from low sample size, selection bias and recall bias (e.g., self-report symptom onset) and lack of generalizability. Predictive models were also included in this review, and their analyses represent an approximation of a real situation and can be used to compare options or scenarios, keeping in mind the limitations of the models used. Case reports and studies/reviews published prior to the latest relevant systematic reviews on this topic (search conducted up to September 2020) were excluded from this review, as it was expected they would be captured in the systematic reviews (23, 24).

Studies were highly heterogeneous in the designs, sampling methods, detection tests, and gene targets used. Thus, results cannot be directly compared across studies. The RT-PCR test results depend on the quality of the sample as well as the assay used (i.e., the chosen primers, reagents, and gene targeted) which determine the accuracy of the test. These technical differences in how the tests were conducted also made comparisons across studies difficult.

While many studies reported that viral loads differed by symptoms or risk factors, very few actually reported on this relationship in the context of transmission potential. Similarly, evidence to date on the potential relationship between viral load and increased transmissibility of SARS-CoV-2 variants of concern such as B.1.1.7 and P.1 are currently assumed to be related based on surveillance data reporting lower Ct values among infections (1-5) and recent models of rising VOC cases (25). However, the evidence is currently conflicting on whether B.1.1.7 and P.1 do in fact result in higher viral loads than wild-type SARS-CoV-2 (6-8). Evidence on whether other variants of concern, such as B.1.351, might be associated with higher viral loads has not yet been substantiated by primary data. Future empirical research will hopefully help close these knowledge gaps. No studies were identified that directly analyzed how the relationship between viral load and likelihood of transmission varied by infection with the currently circulating SARS-CoV-2 variants of concern. As such, the evidence presented below reflects wild-type strains as opposed to variants of concern.

CONTENTS

ASSOCIATION BETWEEN VIRAL LOAD AND EVIDENCE OF REPLICATIVE VIRUS

- Thirteen studies reported detection of replicative virus via cell culture and three studies reported detection via subgenomic RNA.
- Across all studies, replicative virus was more likely to be isolated from samples with lower Ct values than samples with high Ct values. Detection of replicative virus varied by viral load and timing of collection post symptom onset. No studies reported whether the association between viral load and evidence of replicative virus varied by risk factors (e.g., age, sex) or by infection with SARS-CoV-2 variants of concern.
    - Replicative virus was most likely to be isolated from samples with Ct values <30 (26-34) or viral loads >1x 10^6 copies/mL (23, 35).
        - A systematic review estimated that the probability of recovery of virus from specimens with Ct > 35 was 8.3% (95% CI: 2.8% to 18.4%) (23). Further, the odds for culturing live

virus has been reported to decrease by 0.64 for every one unit increase in Ct (95% CI 0.49 to 0.84, p<0.001) (23).
    - At Ct=25, up to 70% of patients remain positive in culture. At Ct=30 this value drops to 20%. At Ct=35 only <3% of cultures are positive (30).
    - In both mild and severe groups, viral replication was significantly more likely to be detected for samples with lower Ct values (p<0.001) (36). Samples with Ct values ≤ 25 demonstrated replicative virus at a rate >90% (36).
- Recovery of replicative virus was unlikely in samples collected >8-10 days post symptom onset, even in samples with Ct values <35 (34, 37-39). Thus, the probability of isolating replicative virus is highest prior to 8-10 days post symptom onset when Ct levels are low.
- Evidence of replicative virus has been detected in immunocompetent asymptomatic/mild cases with high Ct values (>35) (26, 33, 36), but such instances appear to be rare. In general, cases with positive culture identified at greater than 8-10 days or at Ct values >35 were more likely to be severe or immunocompromised cases (36, 39).

- There was heterogeneity in the sampling and detection methods used across studies.
    - RT-PCR gene targets reported across studies included the SARS-CoV-2 N gene (28, 29, 31, 37), E gene (27, 28, 30, 32, 36), S gene (26, 29), and ORF1ab (29). The overall association between viral load and isolation of replicative virus did not appear to differ depending on gene target.
    - The majority of studies were conducted using nasopharyngeal swabs (26-30, 30, 33-38, 38). However, oropharyngeal (34, 35, 37), sputum (34, 37), bronchial aspirate (36), serum (37), urine (37) and stool (37) swabs were also reported. Culture was more likely to be positive in nasopharyngeal, oropharyngeal, and sputum swabs than other specimen types (37).

Table 1: Studies that investigate association between viral load and evidence of replicative virus (n=15)

STUDY	METHOD	KEY OUTCOMES
Culture studies (n=13)		
Jefferson (2020) (23) Systematic review UK* Dec 2020*	Searched databases for studies attempting to culture or observe SARS-CoV-2 in specimens with RT-PCR positivity published up to September 10, 2020. Twenty-nine studies were captured, ten of which analysed the relationship between Ct values and virus culture.	- 5 studies reported no growth in specimens based on Ct cut-offs >24 to 35. The estimated probability of recovery of virus from specimens with Ct > 35 was 8.3% (95% CI: 2.8% to 18.4%). All donors with Ct > 35 (n=5) producing live culture were symptomatic. - One study reported the odds for culturing live virus decreased by 0.64 for every one unit increase in Ct (95% CI 0.49 to 0.84, p<0.001). - One study reported similar results in line with empirical evidence of an increased Ct of 0.58 per day since symptoms started.

		- One study reported that no successful viral culture was obtained from samples with viral loads less than 1x 10^6 copies/mL. - Viral load and probability of growing live virus of SARS-CoV-2 appears to peak much sooner than that of SARS CoV-1 or MERS-CoV.
Killerby (2021) (37) Prospective cohort study USA Mar 2021*	Nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, sputum (if available), serum, urine and stool specimens were collected every 2–3 days from the first 14 symptomatic patients detected in the USA and tested by rRT-PCR (targeting the N1, N2, or N3 gene). For a sample to be positive, all three gene targets had to be detected. Inconclusive results meant two gene targets were detected. Viral culture (Vero CCL-81 cells) was attempted on rRT-PCR positive and inconclusive specimens (n=131) collected during days 0-29 post illness onset.	- Virus was not recovered from respiratory specimens collected more than 8 days post symptom onset. - Successful culture was observed in 14% (8/57) of NP swabs, 10% (4/92) of OP swabs, and 14% (2/14) of sputum specimens with nucleocapsid (N)1, N2, and N3 Cts ranging from 16.5–32.5, 17.7–32.6, and 16.7–31.4 respectively. - Ct values were all significantly lower ($p<0.0001$ for all 3 gene targets) among specimens from which virus was successfully recovered in culture versus not. - Live virus was not recovered from serum or stool specimens, from inconclusive respiratory specimens, or from specimens collected after symptom resolution, despite continued detection of viral RNA.
Antar (2021) (34) *Preprint* Prospective cohort study USA Apr-July 2020	Outpatients (n=95) self-collected mid-turbinate nasal, oropharyngeal (OP), and oral fluid a median of 6 times over 1-3 months. Samples were tested for viral RNA using the RT-PCR Abbott m2000 platform targeting. Ct values < 31.5 were considered positive. Positive nasal-OP samples by RT-PCR were tested for propagation of SARS-CoV-2 in cell culture (methods not described). Also analyzed whether oral fluid anti-SARS-CoV-2 IgG could be used to predict which	- No samples collected more than 11 days post symptom onset tested positive for viral culture, even in an immunocompromised case who had positive RT-PCRs with low Ct values two months post symptom onset. - Virus culture was positive only in samples with Ct values <17. - Mean Ct values were all significantly lower among specimens from which virus was successfully recovered in culture versus culture negative samples ($p<0.00001$). - 14/15 positive for oral fluid anti-S-RBD IgG, with Ct values <20, were negative for virus culture. The one culture positive sample was collected on day 11 post symptom onset, which is around the time of expected first detection of this antibody.

	samples with low Ct values were negative for virus culture.	
Owusu (2021) (38) Prospective cohort study USA Mar-May 2020	Collected serial nasopharyngeal specimens at various time points from individuals (n=109) with rRT-PCR-confirmed COVID-19. Viral culture (Vero CCL-81 cells) was attempted for rRT-PCR-positive nasopharyngeal specimens (n=35) collected ≥10 days after symptom onset. Participants were classified into three categories based on their viral RNA shedding duration: Persistent (≥14 days), not persistent (<14 days), or indeterminate.	- The Ct values of the 35 specimens collected ≥10 days after symptom onset ranged from 26.3-38.4. - Culture was not successful for any of these specimens.
Folgueira (2021) (36) Cross-sectional study Spain Feb 2021*	Respiratory samples (186 nasopharyngeal exudates and seven bronchial aspirates) were processed by rRT-PCR (targeting the E gene) and cell culture (Vero E6 cells) from asymptomatic (n=11), mild (n=91) and severe (n=87) patients, obtained at various times from clinical diagnosis to follow-up.	- In both the mild and severe groups, the samples that showed viral replication had significantly lower median Ct values than the samples without viable virus: 23.3 (IQR: 20.5–28.0) vs. 36.4 (IQR: 31.8–39.1), respectively, for mild COVID-19 and 27.7 (IQR: 23.2–30.0) vs. 33.0 (IQR: 30.4–38.0), respectively, for severe COVID-19) ($p < 0.001$). - The samples with Ct ≤ 25 in both patient groups showed viable virus at a rate >90%. However, even the samples with Ct ≥ 35 could harbour viable virus (5% for mild COVID-19 and 15% for severe illness).
Felix (2021) (26) *Preprint* Cross-sectional study Brazil Feb 2021*	Patients with confirmed mild COVID-19 were invited to participate by providing nasopharyngeal (NP) samples at the day 10 if illness (n=53). Cell-cultured SARS-COV-2 RT-PCR (targeting the S gene) positive respiratory samples (n=29) at 10 days post symptom onset in VeroE6 cells. After two passages, cytopathic effect and cycle threshold lower than that obtained in the original sample were used to determine positivity of culture.	- Forty patients (79%) were SARS-CoV-2 positive by RT-PCR at day 10 (79%) with the median Ct of 25.7 (range 12-32). Of these, 29 were submitted for culture testing. - Culture was successful for 24% (7/29) of the samples tested. - The positivity in cell culture was strongly associated with low Ct values in clinical samples. Mean Ct value was 20 (IQR 16.5-21) in culture positive samples vs. 29 (IQR, 24-32.3) in culture negative samples, $p<0.0001$. - Two patients for which culture was successful reported having no symptoms on day 10.

Marot (2021) (27) LTE Cross-sectional study France Aug-Sept 2020	Conducted real-time RT-PCR assays to detect the presence of the viral E (envelope) subgenomic RNA and E negative-strand RNA in clinical samples. Also attempted to isolate virus via culture (Vero CCL-81 cells, incubated 2-7 days) from samples to associate the presence of positive-stranded replicative intermediate RNAs (RIs) with the detection of viable virus. Data were obtained from 61 immunocompetent healthcare workers (HCWs) diagnosed with SARS-CoV-2 infection by RT-PCR on nasopharyngeal samples.	- No isolate was recovered via culture when Ct > 28 (i.e., viral load below 5.83 log_{10} copies/mL).
Piralla (2020) (28) Cross-sectional study Italy Apr-Aug 2020	A series of nasal swabs collected from convalescent patients positive for SARS-CoV-2 RNA detected by rRT-PCR (targeting the E or N gene) with Ct >30 were included in the study (n=387). Cell culture (Vero E6 cells incubated up to 7 days) was conducted to investigate the infectious potential of samples. Note: No time point (i.e., day of illness) was provided for when samples were collected, however it is specified that all samples were drawn from clinically recovered patients.	- The median Ct value of convalescent samples was 36.8 (range: 30.0–39.4). For the E gene, the median Ct value was 36.9 (range 30.0–39.4) while the N gene was 35.5 (range 32.0–39.4). - Culture of convalescent specimens was successful for only 9 samples (2.3%, 9/387). - The median Ct value of culture-positive samples was not significantly different from that observed in culture-negative samples (35.6 vs. 36.9, p = 0.37).
Romero-Gómez (2020) (29) LTE	Investigated samples obtained from patients with SARS-CoV-2, comparing the results obtained by RT-PCR with the growth capacity of the virus via cell culture (Vero E6 cells, incubated for 4 days). 72	- Culturable samples had significantly lower Ct values (<30) than those with non-culturable samples (>30) (p<0.0001, see figures 1&2 in article). - Isolation of virus in culture was successful in samples with Ct between 21.54 and 37.73. - The highest Ct values in samples with positive cultures were found to be 36.08, 37.73 and 37.41 for

Cross-sectional study Spain Feb-June 2020	nasopharyngeal specimens taken at various time points of infection from 66 patients were analysed in this study. 17 samples were successfully isolated.	the ORF1ab, N and S genes, respectively, taken 1 day post symptom onset from a patient with a cough and fever.
Jaafar (2020) (30) LTE Cross-sectional study France* May 2020	Performed 250,566 SARS-CoV-2 RT-PCR tests on nasopharyngeal samples (Ct values based on the E gene). 13,161 were positive and 1,941 isolates were obtained via culture (Vero E6 cells).	- At Ct = 25, up to 70% of patients remain positive in culture. At Ct = 30 this value drops to 20%. At Ct = 35, the value used to report a positive result for PCR, <3% of cultures are positive.
Kim (2021) (31) LTE Case series South Korea Feb-Jun 2020	Clinical and virological characterization of 21 hospitalized patients. Viral RNA was quantitated using rtRT-PCR (targeting the N gene) and viral cultures were conducted via plaque assay (vero cells) until at least two consecutive cultures showed no growth.	- Viable SARS-CoV-2 was cultured in 29/89 samples. - Viral culture was positive only in samples with a CT ≤ 28.4. - Median time from symptom onset to viral clearance in culture was 7 days. - The incidence of culture positivity decreased with an increasing time from symptom onset and with an increasing cycle-threshold value.
Vetter (2020) (35) Case series Switzerland Feb 2020	Clinical, virological, and immunological characterization of the first five patients assessed at the Geneva University Hospital (HUG), from the day of diagnosis until convalescence. SARS-CoV-2 was detected by rtRT-PCR in both the oropharyngeal swabs (OPS) and the nasopharyngeal swabs (NPS) of each patient. Viral culture was conducted using Vero E6 cells.	- Isolation of virus in culture was successful from both NPS and OPS during the first week of illness for four mild cases. - The mean viral load in samples affording successful isolation was $1.2x10^9$ copies/ml. SARS-CoV-2 could not be isolated in clinical specimens containing less than $1.4x10^6$ viral RNA copies/ml.
Lewis (2020) (39)	Investigated household transmission in 5 households with daily specimen collection.	- In multiple patients, low Ct values (<20) on days 2-4 post symptom onset coincided with onset of additional symptoms (chest pain, myalgia, and loss

Contact tracing study USA Apr 2020	During days 1–4, if a household contact had an inconclusive result (1 of 2 target gene regions positive for SARS-CoV-2 by rRT-PCR) or positive result (both target gene regions positive) the associated specimen and all subsequent daily specimens from the person were submitted for viral culture to evaluate infectiousness. Specimens positive by rRT-PCR that were collected on day 14 with Ct values<35 were also cultured. Gene targets for rRT-PCR and methods for culture were not described.	of taste and smell) and positive viral cultures on both days. - Culture was not successful among specimens collected 14 days post symptom onset, despite positive rRT-PCR and Ct values <35.
Subgenomic RNA Studies (n=3)		
Rodríguez-Grande (2021) (32) Case series Spain Jan 2021*	Assessed samples of persistent RT-PCR positive cases (n=60) with >21 days since the first diagnostic RT-PCR for evidence of replicative virus as determined by subgenomic E gene RNA (SG RNA).	- SG RNA was detected in 12/60 cases (20%). Collection dates ranged from 28-79 days after onset in these samples. - In all cases with detectable SG RNA, Ct values for genomic RNA were <30, consistent with the values expected for an active virus. - The age range of subjects with prolonged viral shedding and SG viral RNA was quite wide and equally distributed between males and females. Seven were immunosuppressed. The severities of the COVID-19 episodes were mild (40%), intermediate (20%), and severe (40%). One case with SG RNA at day 25 was asymptomatic.
Marot (2021) (27) LTE Cross-sectional study France Aug-Sept 2020	Conducted real-time RT-PCR assays to detect the presence of the viral E (envelope) subgenomic RNA and E negative-strand RNA in clinical samples. Also attempted to isolate virus via culture (Vero CCL-81 cells, incubated 2-7 days) from samples to associate the presence of positive-stranded replicative intermediate RNAs (RIs) with	- No RIs were detectable in samples when the Ct > 33 (viral load below 4.34 $\log_{10}$ copies/mL) - The ratios of mean normalized RIs per genome indicate a high level of viral replication during the first 5 days from symptom onset, followed by a significant decline.

	the detection of viable virus. Data were obtained from 61 immunocompetent healthcare workers (HCWs) diagnosed with SARS-CoV-2 infection by RT-PCR on nasopharyngeal samples.	
Hogan (2021) (33) Prospective and retrospective cohort studies USA Mar-Apr 2020 & July-Sep 2020	Developed a novel 2-step rRT-PCR specific to the minus strand of the envelope gene (actively replicating virus produces minus-strand RNA intermediates thus can be used as a proxy for potential infectiousness). Retrospectively collected a convenience set of longitudinal upper respiratory specimens with a broad range of Ct values. For the prospective phase of the study, they collected upper respiratory samples from 53 consecutive patients with confirmed SARS-CoV-2 infection. Samples were collected a median of 9 days (IQR: 4–18 days) after symptom onset.	- Minus-strand RNA was detected in 41 (28.1%) patients. - The median Ct value was significantly lower in samples with detected minus-strand RNA (20.7) than those in which the minus strand was not detected (33.2, $p<0.01$). - Minus-strand RNA was detected in two immunocompentent inpatients >10 days post symptom onset with high Ct values (~39). Minus-strand SARS-CoV-2 RNA was detected up to 30 days after symptom onset in an immunocompromised patient.

LTE= letter to editor

ASSOCIATION BETWEEN VIRAL LOAD AND TRANSMISSION RISK

- Viral loads appear to peak on average 5 days post expsoure and 1-2 days post symptom onset, with a short period (<2 days) of high transmission risk and transmission potential being greatly diminished by 7-10 days post symptom onset (40-42). During peak viral load, highly infectious cases can shed tens to thousands of SARS-CoV-2 virions/min (24).

- Several observational studies were conducted that investigated household/cluster transmission. In line with the culture findings from the section above, cases with higher viral loads (i.e., lower Ct values) were more likely to transmit SARS-CoV-2.
    - Index cases with high viral load (>10^6 copies/uL) were more likely to transmit SARS-CoV-2 to close contacts (OR 4.9, 95% CI: 1.3-18, p=0.02) (43). The secondary attack rate was reported to range from 12% when the index case had a viral load ≤1x10^6 copies/mL to 24% when the index

case had a viral load of ≥1x10^{10} copies/mL (adjusted odds ratio per $\log_{10}$ increase in viral load=1.3, 95% CI: 1.1-1.5) (44).

- Regression models demonstrated that cases resulting in secondary transmission had higher median viral loads than that of cases that did not transmit SARS-CoV-2 (45). Two retrospective cohort studies conducted in US university residences also found that index cases resulting in secondary transmission had higher viral loads (up to 6.5 fold) than cases that did not cause secondary transmission (46, 47). Although both symptomatic and asymptomatic cases exhibited average Ct peaks around Ct 19-22, the Ct values were significantly lower in symptomatic cases (range: 12-36 vs. 14-37), indicative of reduced viral load among asymptomatic cases (47).
- A cross-sectional study comprising the full population of Denmark found that index cases with a Ct <20 had a transmission risk 1.89 times higher than an index case with a Ct >25 (48). The index case had a Ct value of >30 in 39% of secondary cases, but transmission risk was significantly higher if the Ct values were <28. Index cases with high Ct values (>35) did occur, but the transmission risk was much lower (8%).
- The majority of secondary household cases were detected within 10 days post symptom onset of the index case, aligning with the timing of recovery of replicative virus findings noted in section above (43).
- One study found that clusters with high viral loads (>10^6 copies/mL) were considerably larger than clusters with subjects showing a lower viral load (17 infected individuals vs 3 within cluster, p<0.001) (49).

- There were few studies that reported on how the relationship between viral load and transmission risk varied by presence of symptoms, severity of symptoms, or risk factors (e.g., age, chronic health conditions).
  - A systematic review found that adult, pediatric, symptomatic/presymptomatic and asymptomatic COVID-19 cases show similar respiratory viral load distributions during the infectious period (24). Interestingly, a larger population study found that older age was positively associated with transmission risk, even after controlling for viral load (i.e., age was a better predictor of transmission risk than viral load) (48).
  - High viral loads (Ct<20) prior to symptom onset among cases that transmitted SARS-CoV-2 presymptomatically have been reported (50). The longer the incubation period, the larger the fraction of presymptomatic viral load, and thus a higher likelihood of presymptomatic transmission (41).
  - High viral loads have been reported both in the pre-symptomatic period and up to 8-10 post-symptom onset. It is during this time when Ct values are low (<30) that there is a high probability of transmission.

Table 2: Studies that investigate association between viral load and transmission risk (n=12).

STUDY	METHOD	KEY OUTCOMES
Chen (2020) (24) *Preprint* Systematic review and modelling study Canada* Dec 2020*	A systematic review was conducted to capture studies published up to August 7, 2020 (n=64) in order to develop a comprehensive dataset of respiratory viral loads (rVLs) of SARS-CoV-2. A meta-analysis and model was then conducted to investigate individual infectiousness by shedding viable virus via respiratory droplets and aerosols. SARS-CoV-2 rVLs was analyzed across age and symptomatology subgroups as well as disease course.	- At the 90th case percentile (cp) throughout the infectious period, the estimated rVL was 8.91 (95% CI: 8.83-9.00) log10 copies/ml. - Age and symptomatology minimally influenced case variation in SARS-CoV-2 rVL during the infectious period. Adult, pediatric, symptomatic/presymptomatic and asymptomatic COVID-19 cases showed similar rVL distributions, with standard deviations of 2.03, 2.06, 2.00 and 2.01 log10 copies/ml, respectively. - The mechanistic model showed that SARS-CoV-2 rVL increased exponentially after infection, peaked around 1 day post symptom onset and then diminished exponentially. Highly infectious cases can shed tens to thousands of SARS-CoV-2 virions/min, especially between 1-5 days post symptom onset.
Cerami 2021 (43) *Preprint* Prospective cohort study USA Apr-Oct 2020	Enrolled COVID-positive persons (n=102) and their household members (n=213) to study SARS-CoV-2 transmission within households. Households were enrolled a median of 6 days from onset of symptoms in the index case. Secondary cases were detected either by RT-qPCR (targeting N1, N2, and RNase P) of a nasopharyngeal swab on study day 1 and weekly nasal swabs (days 7, 14, 21), or based on seroconversion by day 28.	- The majority of secondary household cases were detected within 10 days post symptom onset of the index case. - Index cases with high viral load (>10^6 viral copies/ul) at enrollment were more likely to transmit virus to household contacts during the study (OR 4.9, 95% CI 1.3-18, p=0.02). - Viral load was correlated within families, meaning persons in the same household were more likely to have similar viral loads, suggesting an inoculum effect. These differences were not attributable to the D614G mutation in the SARS-CoV-2 spike protein, as the vast majority of isolates genotyped contained this mutation (98%).
Bjorkman (2021) (46) Retrospective cohort study USA	Analyzed the transmission of COVID-19 in residence halls based on the weekly RT-qPCR (targeting the E gene) screening of residential	- The average viral load was 6.5-fold higher in rooms with likely transmission (mean Ct=26.2) than in rooms without transmission (mean Ct=28.9).

Aug-Nov 2020	students. Each Ct whole unit is a factor of 2 in RNA copies per ml. Investigated the extent to which the timing of cases supported inter-roommate transmission.	- These cases spanned a range of over 7 orders of magnitude in viral load, with the highest load found in the likely transmission group (Ct=15.4) and the lowest found in the unlikely transmission group (Ct=40.6). The only cases with Ct greater than 34 (22 cases) were found in the unlikely transmission group.
Tian (2021) (47) *Preprint* Retrospective cohort study USA Sept-Oct 2020	Performed a total of 61,982 tests of 7,440 undergraduate students to determine whether the Ct value could differentiate the spreader from the non-spreader. Students were tested multiple times via RT-PCR (targeting the N, S and ORF1ab genes) over the study period and 602 cases were identified.	- 48.2% (94/195) of index cases had at least one contact who became SARS-CoV-2-positive, whereas 51.8% of the index cases (n=101) did not spread SARS-CoV-2 to their contacts. - Mean Ct values of the spreader and the non-spreader were nearly identical (peak at Ct = 18-21) but their median Ct values differed by almost one cycle, suggesting that spreaders had a lower Ct value than the non-spreaders (see Figure 1B&C in article). Ct range was slightly broader for the spreader (12-36) than that for the non-spreader (14-36). - Although both groups exhibited Ct peaks around Ct 19-22, the Ct values were significantly lower in symptomatic than those in asymptomatic cases (range: 12-36 vs. 14-37), indicative of reduced viral load among asymptomatic cases.
Shrestha (2021) (42) Retrospective cohort study USA Mar-Apr 2020	Evaluated transmission potential by examining viral load with respect to time since onset of symptoms in healthcare professionals infected with SARS-CoV-2 (n=230). Nasopharyngeal swabs were tested by RT-PCR (targeting the N1, N2, and N3 genes). The mean of the 3 Ct values from the three gene targets was considered the Ct for the test. Viral loads since symptom onset were predicted using the	- SARS-CoV-2 viral RNA load is very high within 2–3 days post onset of symptoms and falls rapidly by orders of magnitude within a few days (see Figure 1 in article). - Transmission potential of COVID-19 is greatly diminished by 7–10 days post onset of symptoms (see Figure 3 in article). Of the AUC spanning the interval from onset of symptoms to 30 days, 86.3% lie within the first 5 days, 96.9% within the first 7 days, and 99.7% within the first 10 days.

	regression model, with the area under the curve (AUC) representing the distribution of transmission potential over time.	
Marks (2020) (44) Retrospective cohort study Spain Mar-Apr 2020	This study was a post-hoc analysis of data collected in a cluster randomised trial that included individuals with qPCR confirmed COVID-19 and their close contacts. Factors associated with transmission were assessed by linear regression using all clusters of an index case for which quantitative viral load from nasopharyngeal swabs was available.	- The overall secondary attack rate was 17% (125/753 contacts) with a range of 12% when the index case had a viral load $\leq 1x10^6$ copies/mL to 24% when the index case had a viral load of $\geq 1x10^{10}$ copies/mL. - According to multivariate analysis, the odds of transmission were higher when the index case had a high viral load (adjusted odds ratio per $\log_{10}$ increase in viral load=1.3 (95%CI: 1.1-1.5). - 90% of transmission events occurred when the index case had a high viral load (≥5.1 $\log_{10}$ copies/mL). 50% occurred in clusters where the index case had a viral load of ≥8.8 $\log_{10}$ copies/mL. - Other factors associated with an increased risk of transmission were household contact and age of the contact. No association was observed with mask usage, age or sex of index case, or with presence of respiratory symptoms in index case.
Kawasuji (2020) (45) Case-control study Japan Apr-May 2020	COVID-19 patients who transmitted the disease to at least one other patient were analysed as "cases" (index patients, n=14) and compared with patients who were not the cause of secondary transmission (non-index patients, n=14, analysed as "controls"). Cases were confirmed and viral load quantified via RT-qPCR (targeting the N2 gene). The nasopharyngeal viral load time courses were assessed between the index and non-index symptomatic patients using non-linear	- Viral loads peaked soon after symptom onset, and then gradually decreased. Median time to viral clearance did not significantly differ between index and non-index patients: 21 days (IQR: 15–31) vs. 17 days (9-26), p=0.34. - The viral load at the time of initial sample collection was significantly higher in symptomatic vs. asymptomatic patients and in adult vs. children. - Regression models of symptomatic cases only (n=18) demonstrated that the median viral load of the index patients at onset was higher than that of the non-index patients: 6.6 log copies/µL (95%CI: 5.2-8.2) vs. 3.1 (1.5-4.8). This trend continued until 10 days post onset. When asymptomatic cases were also included in this model (n=10), the

	regression employing a standard one-phase decay model.	overall trend stayed the same: 3.3 log copies/µL (95% CI: 1.6-5.2) vs. 1.8 (-0.4-4.6), p=0.015.
Lyngse (2021) (48) *Preprint* Cross-sectional study Denmark Aug 25-Feb 10, 2021	Used comprehensive administrative register data from Denmark, comprising the full population and all SARS-CoV-2 tests, to estimate household transmission risk. RT-PCR (targeting the E-gene) was used and a test for SARS-CoV-2 was defined as positive if the Ct value was ≤38. 66,602 primary cases were identified, from which 99.6% had available Ct values. 103,389 secondary cases were identified.	- 25% of primary cases had a Ct value ≤25, 50% had a Ct value ≤28, and 75% had a Ct value ≤32. Ct value was similar across age groups. - There was an approximately linear decreasing relationship between Ct values and transmission risk. - The index case had a Ct value of >30 in 39% of secondary cases (but this is day of testing vs. an unknown peak viral load point- they did not have data to adjust for this). Primary cases with a Ct value of 38 had a transmission risk of 8% within the household. - Transmission risk was significantly higher if Ct values were <28. - A primary case with a Ct value of 18-20 has a transmission risk 1.89 higher than a primary case with a Ct value of 36-38. - Transmission risk had a negative association with age in children <20 and a positive association with age for those >20 yrs.
Ladoy (2021) (49) *Preprint* Surveillance study Switzerland Jan-Jun 2020	Characterized the dynamics of the first wave of SARS-CoV-2 infection in the canton of Vaud (western Switzerland) through the detection and the location of clusters using the results of SARS-CoV-2 RT-PCR tests (n= 33,651 tested, n=3,317 positive). A spatial scan approach was used to assess the importance of viral load in the evolution of the clusters and a Modified Space-Time DBSCAN algorithm was used to	- 1,684 space-time clusters were identified. - The majority of clusters had at least one person with a high viral load (>1 billion copies/ml). Clusters with such high viral loads were considerably larger (median of 17 infected individuals) than clusters with subjects showing a viral load lower >1 million copies/ml (median of 3 infected individuals, p<0.001). - Clusters involving younger individuals had the highest viral loads, while clusters composed of older individuals had low to medium viral loads. - There were 20 clusters in which the viral load of the three first cases were all below 100,000 copies/ml, suggesting that in some

	characterize the diffusion dynamics of transmission clusters.	instances, even subjects with less than 100,000 copies/ml may still be contagious.
Park (2020) (50) Case series South Korea -> Israel Feb 2020	An outbreak of SARS-CoV-2 among 39 pilgrim travelers was investigated. Ten confirmed cases without symptoms at the first sampling dates (2 post-symptomatic, 4 pre-symptomatic, and 4 asymptomatic) were selected for follow-up respiratory tract sample RT-PCR tests (targeting the E gene).	- Available Ct values from specimens of the lower respiratory tract were significantly lower in cases without symptoms (median, 22.8; IQR, 20.1–25.4) than in cases with symptoms at the first sampling dates (median, 27.9; IQR, 23.4–30.4). The viral loads gradually decreased over time and were not different between symptomatic and asymptomatic cases. - The highest viral load (Ct<20) was observed from the first sample of a case collected 7 days before symptom onset. Transmission occurred from this case to a close contact during the presymptomatic period.
Goyal 2021 (40) Modelling study USA* Feb 2021*	Developed a transmission simulation framework to analyze the contribution of viral load to observed epidemiologic transmission metrics SARS-CoV-2. This process included within-host modeling of viral loads, simulations of exposures and possible transmissions based on various transmission dose response curves, testing of various parameter sets against epidemiologic data and exploratory analyses with the best fitting model.	- Simulations demonstrated an upper airway viral load $<10^4$ SARS-CoV-2 RNA copies is very unlikely (~0.00005%) to lead to transmission. Transmission is much more likely (39%) given an exposure to an infected person who is shedding $>10^7$ RNA copies, and 75% given an exposure to an infected person with a viral load of $>10^8$ RNA copies. - There is an inflection point between 10^6 and 10^7 RNA copies, after which multiple transmission events becomes much more likely from a single person (i.e., super spreading event). - Infected persons are likely to be most infectious (viral load above TD50) for a 0.5–1.0 day period between days 2 and 6 post infection. This variability is likely attributable to heterogeneity in incubation period rather than timing of peak viral load.
Ke (2020) (41) *Preprint* Modelling study USA*	Developed data-driven within-host models of SARS-CoV-2 infection. Analyzed the relationship between viral load in the lower and upper respiratory trans (LRT & URT) and potential	- Respiratory viral load peak on average 5.2 days (SD: ±1.3 days) and 5.4 days (±1 day) post infection in the URT and the LRT, respectively, and on average 2 days (±0.2 day) and 2.1 days (±1.2 days) post symptom onset.

Sep 2020	infectiousness via a probabilistic model using existing epidemiological evidence (from 8 cases). Develop several more models to explain the prolonged period of virus infection in the LRT.	- The longer the incubation period, the larger the fraction of presymptomatic viral load (See Fig. 2; $p<0.001$), and thus leads to a higher fraction of presymptomatic transmission. - Model demonstrates that the logarithm of viral load (rather than absolute viral load) is an appropriate surrogate for infectiousness (i.e., viral growth is a better predictor of presymptomatic transmission than viral load measurement alone). - Spatial dissemination in the lungs is an important process in sustaining prolonged high viral loads in the LRT.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Sciences Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: Shedding, Viral dynamics, Viral RNA dynamics, Viral clearance, Viral RNA clearance, Viable, Culture, Infectivity, Infectious Period, Communicability period, Period of communicability, Viral load, Viral RNA load, Infectiousness. This review contains research published up to March 31, 2021. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur la charge virale et la probabilité de transmission pendant la période infectieuse du SRAS-CoV-2

Introduction

Quel est le lien entre la charge virale et la probabilité de transmission pendant la période infectieuse du SRAS-CoV-2? Varie-t-il selon la présence des symptômes, la gravité des symptômes, les facteurs de risque (p. ex., âge, problèmes de santé chroniques) ou selon l'infection découlant des variants du SRAS-CoV-2 qui circulent actuellement et qui sont préoccupants?

La corrélation entre la charge virale et la probabilité de transmission a été étudiée pendant toute la durée de la pandémie afin de caractériser le moment où, pendant une infection au SRAS-CoV-2, une personne peut être plus infectieuse et plus susceptible de transmettre le virus. La recherche a également tenté de caractériser les attributs des personnes ou les caractéristiques de l'infection qui peuvent être associés à un risque plus élevé de transmission. Pendant l'hiver 2021, de nouvelles recherches ont indiqué que les variants préoccupants (p. ex., B.1.1.7, B.1.351 et P.1) peuvent avoir une dynamique de transmission et une virulence différentes des souches de type sauvage qui circulaient plus tôt pendant la pandémie. Cela pourrait être attribuable à une multitude de facteurs entrelacés (p. ex., persistance plus longue de l'excrétion de l'ARN viral, diminution de la réponse immunitaire ou énergie de liaison plus faible entre la protéine de pointe du SRAS-CoV-2 et les récepteurs humains). La base de données probantes actuelle est contradictoire en ce qui concerne la question de savoir si les variants préoccupants ont une charge virale plus élevée. Certaines études ont signalé des charges virales plus élevées dans les cas de variants (B.1.1.7 et P.1) comparativement aux cas de type sauvage (1 à 5), tandis que trois nouvelles études n'ont signalé aucune différence significative (6 à 8). D'autres études sont nécessaires pour déterminer les facteurs qui contribuent à l'augmentation de la transmission observée avec les variants préoccupants actuellement en circulation. Des études récentes sur la vaccination indiquent par ailleurs que la vaccination peut prévenir les infections symptomatiques et réduire la charge virale de 1,6 fois à 20 fois dans les infections qui se produisent après avoir reçu la première dose du vaccin (9 à 11). Ainsi, même si les vaccins ne préviennent pas entièrement l'infection, la réduction de la charge virale pendant l'infection réduira probablement aussi la transmission. La présente synthèse en bref sur la recherche qui examine le lien entre la charge virale et la probabilité de transmission pendant la période infectieuse du SRAS-CoV-2, publié jusqu'au 31 mars 2021.

La mesure de substitution la plus courante de la charge virale du SRAS-CoV-2 est la valeur de cycle seuil (Ct), qui est le nombre de cycles pendant la réaction en chaîne de la polymérase (RT-PCR) à transcription inversée nécessaire pour atteindre un seuil de détection pour une certaine cible génétique. Dans ce modèle, des valeurs Ct plus faibles indiquent une charge virale plus élevée et, lorsqu'elles sont fournies, une estimation de

la charge virale, copies/ml, peut alors être calculée. Ce calcul nécessite un processus de normalisation basé sur la cible d'amplification dans l'extrait et la valeur Ct. L'utilisation des valeurs Ct comme indicateur de la charge virale comporte plusieurs inconvénients. Premièrement, l'efficacité de l'amplification est influencée par le dosage lui-même et les facteurs associés au prélèvement de l'échantillon (p. ex., quantité de matériel d'échantillonnage prélevé) (12, 13). Les études sont souvent très hétérogènes dans les méthodes d'échantillonnage, les essais de détection et les cibles génétiques utilisées. Deuxièmement, le seuil de la limite supérieure de la valeur Ct qui détermine un résultat PCR positif n'était pas uniforme dans les différentes études, bien que la plupart aient rapporté des valeurs positives à la valeur Ct 35. Il est recommandé d'utiliser une courbe standard avec des matériaux de référence ou des témoins internes du plasmide avec des nombres de copies virales connus pour interpréter les valeurs de Ct comme des charges virales pour ainsi obtenir une quantification appropriée (p. ex., copies/ml) (14). Comme il y a toutefois eu une grande hétérogénéité et une incohérence dans les courbes types calculées entre les différentes études, il faut donc faire preuve de prudence lorsqu'on interprète les résultats de la charge virale dans la documentation sur la COVID-19.

La détection de l'ARN viral par RT-PCR ne fournit pas de preuve d'infectiosité, puisque ce test donne également des résultats positifs en présence de particules de virus non infectieux. La récupération d'un virus capable de se répliquer a été utilisée comme mesure de l'infectiosité (c.-à-d. du potentiel de transmission). Cela se fait le plus souvent au moyen de la culture cellulaire. La détection de l'ARN subgénomique a également été recommandée comme substitut potentiel pour l'élimination du virus capable de se répliquer (15), bien qu'il n'y ait pas de consensus à cet égard (16). Bien que l'excrétion de l'ARN viral soit souvent observée dans les échantillons respiratoires prélevés plus de 15 à 17 jours après l'apparition des symptômes (17), le virus réplicatif n'a pas été isolé au cours des 10 derniers jours dans les formes légères (18 à 22). La corrélation entre les charges virales du SRAS-CoV-2 et les valeurs Ct avec isolement du virus réplicatif est un sujet d'intérêt important dans l'étude du potentiel de transmission et est explorée dans cette synthèse.

Points clés

- L'exposé sur les données probantes a permis de cerner 27 études, dont 2 revues systématiques, 5 cohortes prospectives, 5 cohortes rétrospectives, 1 étude cas-témoin, 7 études transversales, 1 étude de surveillance, 4 séries de cas, 1 étude de dépistage des contacts et 2 études de modélisation.

- Dans toutes les études, la transmission était plus probable lorsque les échantillons contenaient un virus réplicatif, ce qui s'est produit lorsque les valeurs Ct étaient faibles (< 30) et que l'échantillon avait été prélevé moins de 8 à 10 jours après l'apparition des symptômes.

Études qui examinent l'association entre la charge virale et les preuves d'un virus réplicatif (culture/ARN subgénomique) (n = 15) :

- Le virus réplicatif était le plus susceptible d'être isolé à partir d'échantillons dont les valeurs Ct étaient inférieures à 30 ou dont la charge virale était supérieure à 1 x 106 copies/ml. Les échantillons dont la valeur Ct est ≤ 25 ont montré la présence d'un virus réplicatif à un taux supérieur à 90 %.

- La revue systématique la plus récemment publiée sur ce sujet a fait état d'une corrélation importante entre la valeur Ct et les taux de positivité de la culture. La probabilité de récupération du virus dans les spécimens dont la valeur Ct est supérieure à 35 était de 8,3 % (IC à 95 % : 2,8 % à 18,4 %). On a en outre indiqué que les probabilités de propagation du virus réplicatif diminuaient de 0,64 pour chaque augmentation d'une unité de la valeur Ct (IC à 95 % : 0,49 à 0,84, p < 0,001).

- Il était peu probable que l'on récupère un virus réplicatif dans les échantillons prélevés plus de 8 à 10 jours après l'apparition des symptômes, et ce, même dans les échantillons dont les valeurs Ct étaient inférieures à 35. Ainsi, la valeur Ct et le nombre de jours après l'apparition des symptômes évalués en tandem peuvent être une méthode efficace pour déterminer la probabilité qu'une personne soit toujours contagieuse.

- Les cas de culture positive identifiés après plus de 8 à 10 jours ou grâce à des valeurs Ct supérieures à 35 étaient plus susceptibles d'être des cas graves ou immunodéprimés.

- Les méthodes d'échantillonnage et de détection utilisées dans les études étaient hétérogènes. L'association globale entre la valeur Ct et l'isolement du virus réplicatif ne semblait pas différer selon la cible génétique du SRAS-CoV-2 (p. ex., nucléocapside (N), enveloppe (E), protéine de spicule (S)) utilisée pour le test PCR.

Études qui examinent l'association entre la charge virale et la probabilité de transmission (n = 12) :

- Des études de modélisation ont démontré que la charge virale atteignait un sommet en moyenne cinq jours après l'exposition et un à deux jours après l'apparition des symptômes, avec une courte période (< 2 jours) de risque de transmission élevé, après quoi la probabilité de transmission diminue rapidement de 7 à 10 jours après l'apparition des symptômes. Les formes hautement infectieuses peuvent excréter des dizaines à des milliers de virions SARS-CoV-2/min, particulièrement de 1 à 5 jours après l'apparition des symptômes.

- Les cas index présentant une charge virale élevée (> 10^6 copies/ml ou une valeur Ct inférieure à 30) étaient plus susceptibles de transmettre le SRAS-CoV-2 aux contacts du ménage.

- La transmission à partir de cas index ayant des valeurs Ct élevées (> 35) s'est produite, mais le risque de transmission était beaucoup plus faible (8 %).

- La majorité des cas dans des ménages secondaires ont été détectés dans les 10 jours suivant l'apparition des symptômes du cas index.

- Des charges virales élevées ont été signalées pendant la période présymptomatique et jusqu'à 8 à 10 jours après l'apparition des symptômes. C'est pendant cette période où les valeurs Ct sont faibles (< 30) qu'il y a une forte probabilité de transmission.

Vue d'ensemble des éléments de preuve

Au total, 27 études ont été incluses dans la présente synthèse, y compris plusieurs études d'observation. Bon nombre d'études sont des préimpressions et n'ont donc pas fait l'objet d'un processus d'évaluation par les pairs. Les cohortes prospectives présentent un risque plus faible de biais que les cohortes rétrospectives et les analyses transversales des données des dossiers médicaux ou les données de surveillance recueillies régulièrement sur la COVID-19. Certaines de ces études semblaient cependant avoir une bonne capacité de généralisation, car elles utilisaient de grandes bases de données nationales. Toutefois, les cohortes rétrospectives et les études transversales présentent un risque plus élevé de biais en raison de leur nature rétrospective, ainsi que du risque accru de données manquantes et confusionnelles. Les séries de cas comprennent un petit échantillon, en plus de présenter un biais de sélection et un biais de rappel (p. ex., apparition de symptômes autodéclarés) et un manque de généralisable. Des modèles prédictifs ont également été inclus dans cette synthèse en bref, et leurs analyses représentent une approximation d'une situation réelle et peuvent donc être utilisées pour comparer des options ou des scénarios, en gardant à l'esprit les limites des modèles utilisés. Les rapports de cas et les études ou revues publiées avant les plus récentes revues systématiques pertinentes sur ce sujet (recherche effectuée jusqu'en septembre 2020) ont été exclus de cet examen, car on s'attendait à ce qu'ils soient inclus dans les revues systématiques (23, 24).

Les études étaient souvent très hétérogènes dans les méthodes d'échantillonnage, les tests de détection et les cibles génétiques utilisées. Par conséquent, les résultats ne peuvent pas être comparés directement entre les études. Les résultats du test RT-PCR dépendent de la qualité de l'échantillon ainsi que du matériel utilisé (c.-à-d., les amorces, les ensembles de réactifs et le gène ciblés) qui déterminent la précision du test. Ces différences techniques dans la façon dont les tests ont été effectués ont également rendu plus difficiles les comparaisons entre les études.

Bien que de nombreuses études aient indiqué que les charges virales différaient selon les symptômes ou les facteurs de risque, très peu d'entre elles faisaient état de ce lien dans le contexte du potentiel de transmission. De même, les données probantes obtenues jusqu'à maintenant sur le lien potentiel entre la charge virale et la transmissibilité accrue des variants préoccupants du SRAS-CoV-2, comme le B.1.1.7 et le P.1, sont actuellement présumées être liées, comme l'indiquent les données de surveillance qui indiquent des valeurs Ct plus faibles parmi les infections (1 à 5) et les modèles récents portant sur l'augmentation des cas de variants préoccupants (25). Les éléments de preuve sont actuellement contradictoires quant à savoir si les variants B.1.1.7 et P.1 entraînent en fait une charge virale plus élevée que le SARS-CoV-2 de type sauvage (6 à 8). Les données primaires n'ont pas encore permis de déterminer si d'autres variants préoccupants, comme B.1.351, pourraient être associés à des charges virales plus élevées. Nous espérons que les recherches empiriques futures aideront à combler ces lacunes. Aucune étude n'a analysé directement comment variait le lien entre la charge virale et la probabilité de transmission en fonction du type d'infection associé aux variants préoccupants du SRAS-CoV-2 actuellement en circulation. Ainsi, la preuve présentée ci-dessous reflète les souches de type sauvage par opposition aux variants préoccupants.

TABLE DES MATIÈRES

ASSOCIATION ENTRE LA CHARGE VIRALE ET LA PREUVE D'UN VIRUS RÉPLICATIF

- Treize études ont mentionné avoir détecté un virus reproductif par la culture cellulaire alors que trois autres ont fait état de la détection par l'ARN subgénomique.
- Dans toutes les études, le virus réplicatif était plus susceptible d'être isolé dans des échantillons ayant des valeurs Ct plus faibles que dans des échantillons ayant des valeurs Ct élevées. La détection du virus reproductif variait selon la charge virale et le moment de la collecte de l'échantillon après l'apparition des symptômes. Aucune étude n'a permis de déterminer si l'association entre la charge virale et les preuves d'un virus reproductif variait en fonction des facteurs de risque (p. ex., âge, sexe) ou de l'infection par les variants préoccupants du SRAS-CoV-2.
    - Le virus réplicatif était le plus susceptible d'être isolé à partir d'échantillons dont les valeurs Ct étaient inférieures à 30 (26 à 34) ou dont la charge virale était supérieure à 1 x 10^6 copies/ml (23, 35).
        - Une revue systématique a estimé que la probabilité de récupération du virus dans les spécimens dont la valeur Ct était supérieure à 35 était de 8,3 % (IC à 95 % : 2,8 % à 18,4 %) (23). On a en outre indiqué que les probabilités de propagation du virus vivant diminuaient de 0,64 pour chaque augmentation d'une unité de la valeur Ct (IC à 95 % : 0,49 à 0,84, p < 0,001)(0,001) (23).
        - Lorsque Ct = 25, jusqu'à 70 % des patients obtiennent des résultats de culture positifs. Lorsque Ct = 30, ce pourcentage chute à 20 %. Lorsque Ct = 35, seuls < 3 % des cultures sont positives (30).
        - Dans les groupes ayant eu une forme légère et grave de l'infection, la réplication virale était beaucoup plus susceptible d'être détectée pour les échantillons ayant des valeurs Ct plus faibles (p < 0,001) (36). Les échantillons dans lesquels les valeurs de Ct ≤ 25 incluaient un virus réplicatif à un taux supérieur à 90 % (36).
- Il était peu probable que l'on récupère un virus réplicatif dans les échantillons prélevés plus de 8 à 10 jours après l'apparition des symptômes, et ce, même dans les échantillons dont les valeurs Ct étaient inférieures à 35(34, 37 à 39). Ainsi, la probabilité d'isoler le virus réplicatif sera la plus élevée dans les 8 à 10 jours qui suivent l'apparition des symptômes alors que les niveaux de Ct sont faibles.
- Des signes de virus reproductif ont été détectés dans des cas asymptomatiques ou bénins immunocompétents ayant des valeurs Ct élevées (> 35) (26, 33, 36), mais ces cas semblent rares. De façon générale, les cas dans lesquels la culture a donné des résultats positifs après plus de 8 à 10 jours

ou grâce à des valeurs Ct supérieures à 35 étaient plus susceptibles d'être des cas graves ou immunodéprimés (36, 39).

- Les méthodes d'échantillonnage et de détection utilisées dans les études étaient hétérogènes.
    - Les cibles génétiques détectées dans les tests RT-PCR mentionnés dans les études comprenaient le gène N du SARS-CoV-2 (28, 29, 31, 37), le gène E (27, 28, 30, 32, 36), le gène S (26, 29) et le gène ORF1ab (29). L'association globale entre la charge virale et l'isolement du virus réplicatif ne semblait pas différer selon la cible génétique.
    - La majorité des études ont été réalisées à l'aide de sécrétions rhinopharyngées prélevées par écouvillonnage (26-30, 30, 33 à 38, 38). Toutefois, des écouvillons oropharyngés (34, 35, 37), des expectorations (34, 37), des aspirations bronchiques (36), du sérum (37), de l'urine (37) et des selles (37) ont également été signalés. La culture était plus susceptible d'être positive dans les écouvillons nasopharyngés, oropharyngés et dans les expectorations que dans les autres types de spécimens (37).

Tableau 1 : Études qui examinent l'association entre la charge virale et les preuves d'un virus réplicatif (n = 15)

ÉTUDE	MÉTHODOLOGIE	PRINCIPAUX RÉSULTATS
Études portant sur les cultures (n = 13)		
Jefferson (2020) (23) Revue systématique Royaume-Uni* Décembre 2020*	Recherche dans des bases de données afin de trouver des études publiées jusqu'au 10 septembre 2020 qui tentaient de cultiver ou d'observer le SRAS-CoV-2 dans des spécimens ayant obtenu des résultats positifs au test RT-PCR. Vingt-neuf études ont été trouvées, dont dix ont analysé le lien entre les valeurs Ct et la culture du virus.	- Cinq études ont indiqué une croissance nulle des spécimens lorsque les seuils de Ct variaient entre 24 et 35. La probabilité estimative de récupération du virus dans les spécimens dont la valeur Ct est supérieure à 35 était de 8,3 % (IC à 95 % : 2,8 % à 18,4 %). Tous les donneurs dont la valeur Ct était supérieure à 35 (n = 5) a permis d'obtenir une culture vivante étaient symptomatiques. - Une étude a signalé que les probabilités de culture du virus vivant diminuaient de 0,64 pour chaque augmentation d'une unité de la valeur Ct (IC à 95 % de 0,49 à 0,84, p < 0,001). - Une étude a fait état de résultats similaires, en harmonie avec les preuves empiriques d'une augmentation de la valeur Ct de 0,58 par jour depuis le début des symptômes. - Une étude a révélé que les échantillons ayant une charge virale inférieure à 1 x 10^6 copies/ml n'avaient permis de réussir à créer une culture virale.

		- La charge virale et la probabilité de faire croître un virus SRAS-CoV-2 vivant atteignent un sommet beaucoup plus tôt que pour le SRAS-CoV-1 ou le MERS-CoV.
Killerby (2021) (37) Étude de cohorte prospective ÉTATS-UNIS Mars 2021*	Des écouvillons nasopharyngés (NP), des écouvillons oropharyngés (OP), des expectorations (si disponibles), ainsi que des échantillons de sérum, d'urine et de selles ont été prélevés tous les 2 à 3 jours sur les 14 premiers patients symptomatiques détectés aux États-Unis et ayant subi un test rRT-PCR (ciblant le gène N1, N2 ou N3). Pour qu'un échantillon soit positif, le test devait détecter les trois gènes cibles. Les résultats non concluants étaient ceux qui avaient permis de détecter deux gènes cibles. Une culture virale (cellules Vero CCL-81) a été tentée sur des spécimens non concluants ayant donné un résultat positif au test rRT-PCR (n = 131) recueillis pendant les jours 0 à 29 après l'apparition de la maladie.	- Aucun virus n'a pu être récupéré dans les spécimens respiratoires prélevés plus de 8 jours après l'apparition des symptômes. - Une culture réussie a été observée dans 14 % (8 sur 57) des écouvillons NP, 10 % (4 sur 92) des écouvillons OP et 14 % (2 sur 14) des spécimens d'expectorations avec nucléocapsides (N)1, N2 et N3 SEC allant entre 16,5 et 32,5, 17,7 et 32,6 et 16,7 et 31,4 respectivement. - Les valeurs Ct étaient toutes beaucoup plus faibles ($p < 0,0001$ pour les trois gènes cibles) parmi les spécimens dont le virus a pu être récupéré dans les cultures. - Le virus vivant n'a pas été récupéré dans les spécimens de sérum ou de selles, les spécimens respiratoires non concluants ou les spécimens prélevés après la guérison des symptômes, malgré la détection continue de l'ARN viral.
Antar (2021) (34) *Prépublication* Étude de cohorte prospective ÉTATS-UNIS Avril à juillet 2020	Les patients externes (n = 95) ont effectué une autocollecte de liquides nasaux, oropharyngés (OP) et oraux à moyenne turbulence à six reprises en moyenne, en 1 à 3 mois. Les échantillons ont été testés pour détecter l'ARN viral à l'aide de la plateforme ciblée RT-PCR Abbott M2000. Les valeurs Ct inférieures à 31,5 ont été jugées positives. Des échantillons positifs d'OP nasal évalués par RT-PCR ont	- Aucun échantillon prélevé plus de 11 jours après l'apparition des symptômes n'a donné de résultats positifs pour la culture virale, même dans un cas immunodéprimé ayant obtenu un résultat positif au test RT-PCR avec des valeurs Ct faibles deux mois après l'apparition des symptômes. - La culture virale n'était positive que dans les échantillons dont la valeur Ct était inférieure à 17. - Les valeurs Ct moyennes étaient toutes beaucoup plus faibles dans les spécimens dont le virus avait pu être récupéré dans la culture que dans les échantillons négatifs en culture ($p < 0,00001$). - 14 résultats sur 15 positifs pour l'IgG anti-S-RBD dans la salive, avec des valeurs Ct inférieures à 20,

	été testés pour déterminer la propagation du SRAS-CoV-2 dans la culture cellulaire (méthodes non décrites). On a également analysé si l'IgG anti-SARS-CoV-2 présent dans le liquide buccal pouvait être utilisé pour prédire quels échantillons ayant de faibles valeurs Ct seraient négatifs dans la culture virale.	ont donné des résultats négatifs pour ce qui est de la culture virale. Un échantillon de culture positif a été prélevé le 11e jour après l'apparition des symptômes, soit à peu près au moment prévu de la première détection de cet anticorps.
Owusu (2021) (38) Étude de cohorte prospective ÉTATS-UNIS Mars à mai 2020	Prélèvement de spécimens nasopharyngés en série à divers moments chez des personnes (n = 109) dont la COVID-19 a été confirmée par rRT-PCR. Une culture virale (cellules Vero CCL-81) a été tentée sur des spécimens nasopharyngés ayant donné un résultat positif au test rRT-PCR (n = 35) recueillis pendant dix jours et plus après l'apparition des symptômes. Les participants ont été répartis en trois catégories selon la durée d'excrétion d'ARN viral : Persistant (≥ 14 jours), non persistant (< 14 jours) ou indéterminé.	- Les valeurs Ct des 35 spécimens prélevés ≥ 10 jours après l'apparition des symptômes variaient de 26,3 à 38,4. - La culture n'a réussi pour aucun de ces spécimens.
Folgueira (2021) (36) Étude transversale Espagne Février 2021*	Des échantillons de voies respiratoires (186 exsudats nasopharyngés et 7 aspirations bronchiques) provenant de patients asymptomatiques (n = 11), atteints de la forme légère (n = 91) et grave (n = 87), obtenus à divers moments, du diagnostic clinique jusqu'au suivi, ont été traités par rRT-PCR (ciblant le gène E) et par	- Dans les groupes atteints de la forme légère et grave, les échantillons qui montraient une réplication virale présentaient des valeurs Ct médianes beaucoup plus faibles que les échantillons sans virus viable : 23,3 (EI : 20,5 à 28,0) par rapport à 36,4 (EI : 31,8 à 39,1), respectivement, pour la forme légère de la COVID-19 et 27,7 (EI : 23,2 à 30,0) par rapport à 33,0 (EI : 30,4 à 38,0), respectivement, pour la forme grave de la COVID-19 (p < 0,001). - Les échantillons avec valeur Ct ≤ 25 des deux groupes de patients présentaient un virus viable à un taux supérieur à 90 %. Cependant, même les

	culture cellulaire (cellules Vero E6).	échantillons ayant une valeur Ct ≥ 35 pourraient contenir un virus viable (5 % pour la forme légère et 15 % pour la forme grave de la COVID-19).
Felix (2021) (26) *Prépublication* Étude transversale Brésil Février 2021*	Les patients atteints de la forme légère confirmée de la COVID-19 ont été invités à participer en fournissant des échantillons nasopharyngés (NP) au jour 10 de leur maladie (n = 53). Résultat positif au test RT-PCR (ciblant le gène S) (n = 29) pour la culture cellulaire de SARS-COV-2 obtenue 10 jours après l'apparition des symptômes dans les cellules VeroE6. Après deux passages, l'effet cytopathique et un seuil du cycle inférieur à celui obtenu dans l'échantillon original ont été utilisés pour déterminer la positivité de la culture.	- Quarante patients (79 %) présentaient un résultat positif au SRAS-CoV-2 obtenu par test par RT-PCR effectué le jour 10 (79 %), avec une valeur Ct médiane de 25,7 (plage de 12 à 32). De ce nombre, 29 ont été soumis à des cultures microbiennes. - La culture a réussi pour 24 % (7 sur 29) des échantillons analysés. - La positivité de la culture cellulaire était fortement associée à de faibles valeurs Ct dans les échantillons cliniques. La valeur Ct moyenne était de 20 (EI 16,5 à 21) dans les échantillons positifs après la culture par rapport à 29 (EI, 24 à 32,3) dans les échantillons négatifs après la culture, $p < 0,0001$. - Deux patients pour lesquels la culture a réussi ont déclaré n'avoir aucun symptôme le jour 10.
Marot (2021) (27) Lettre à la rédaction Étude transversale France Août et septembre 2020	Exécution de tests RT-PCR en temps réel pour détecter la présence de l'ARN subgénomique viral (enveloppe) et de l'ARN négatif de la chaîne E dans les échantillons cliniques. On a également tenté d'isoler le virus par culture (cellules Vero CCL-81, incubées de 2 à 7 jours) à partir d'échantillons afin d'associer la présence d'ARN intermédiaires réplicatifs à chaînes positives avec la détection d'un virus viable. Les données ont été obtenues auprès de 61 travailleurs de la santé immunocompétents ayant reçu un diagnostic d'infection au SRAS-CoV-2 par RT-PCR	- Aucun isolat n'a été récupéré par culture lorsque la valeur Ct était supérieure à 28 (c.-à-d. charge virale inférieure à 5,83 $\log_{10}$ copies/ml).

	sur des échantillons nasopharyngés.	
Piralla (2020) (28) Étude transversale Italie Avril à août 2020	Une série d'écouvillonnage de sécrétions nasales prélevées sur des patients en convalescence positifs pour l'ARN du SRAS-CoV-2 détecté par rRT-PCR (ciblant les gènes E ou N) avec une valeur Ct supérieure à 30 a été incluse dans l'étude (n = 387). Une culture cellulaire (cellules Vero E6 incubées jusqu'à 7 jours) a été effectuée pour étudier le potentiel infectieux des échantillons. Remarque : Aucun point temporel (c.-à-d. jour de la maladie) n'a été fourni pour le moment où les échantillons ont été prélevés, mais il est précisé que tous les échantillons ont été prélevés sur des patients qui se sont rétablis au niveau clinique.	- La valeur Ct médiane des échantillons des convalescents était de 36,8 (plage de 30,0 à 39,4). Pour le gène E, la valeur Ct médiane était de 36,9 (plage de 30,0 à 39,4) tandis qu'elle était de 35,5 (plage de 32,0 à 39,4) pour le gène N. - La culture de spécimens de convalescents n'a réussi que pour 9 échantillons (2,3 %, 9 sur 387). - La valeur Ct médiane des échantillons positifs pour la culture n'était pas significativement différente de celle observée dans les échantillons négatifs pour la culture (35,6 par rapport à 36,9, p = 0,37).
Romero-Gómez (2020) (29) Lettre à la rédaction Étude transversale Espagne Février à juin 2020	Échantillons prélevés chez des patients atteints du SRAS-CoV-2. L'examen a comparé les résultats obtenus par RT-PCR à la capacité de croissance du virus par culture cellulaire (cellules Vero E6, incubées pendant 4 jours). 72 spécimens nasopharyngés prélevés à différentes étapes de l'infection chez 66 patients ont été analysés dans le cadre de cette étude. 17 échantillons ont été isolés avec succès.	- Les valeurs Ct des échantillons pouvant être mis en culture étaient significativement inférieures (< 30) à celles des échantillons qui ne pouvaient être mis en culture (> 30) (p < 0,0001, voir les figures 1 et 2 de l'article). - L'isolement du virus en culture a été réussi dans les échantillons dont la Ct se situait entre 21,54 et 37,73. - Les valeurs Ct les plus élevées dans les échantillons cultivés ayant obtenu un résultat positif étaient de 36,08, 37,73 et 37,41 pour les gènes ORF1ab, N et S, respectivement, prélevés un jour après l'apparition des symptômes chez un patient qui avait une toux et de la fièvre.
Jaafar (2020) (30)	Réalisation de 250 566 tests RT-PCR pour le SRAS-CoV-2 sur des échantillons	- Lorsque Ct = 25, jusqu'à 70 % des patients ont obtenu des résultats de culture positifs. Lorsque Ct = 30, ce pourcentage chute à 20 %. Lorsque

Lettre à la rédaction Étude transversale France* Mai 2020	nasopharyngés (valeurs Ct basées sur le gène E). 13 161 de ces tests étaient positifs et 1 941 isolats ont pu être obtenus par culture (cellules Vero E6).	Ct = 35, la valeur utilisée pour déclarer un résultat positif pour le test PCR, < 3 % des cultures obtenaient un résultat positif.
Kim (2021) (31) Lettre à la rédaction Série de cas Corée du Sud Février à juin 2020	Caractérisation clinique et virologique de 21 patients hospitalisés. L'ARN viral a été quantifié à l'aide du test rRT-PCR (ciblant le gène N) et les cultures virales ont été réalisées avec la méthode des plages de lyse (cellules Vero) jusqu'à ce qu'au moins deux cultures consécutives n'affichent aucune croissance.	- Du SRAS-CoV-2 viable a pu être mis en culture dans 29 échantillons sur 89. - La culture virale a été positive seulement dans les échantillons ayant une valeur Ct de 28,4. - Le temps médian entre l'apparition des symptômes et la clairance virale en culture était de 7 jours. - L'incidence de positivité de la culture diminuait avec le temps écoulé depuis l'apparition des symptômes et avec l'augmentation de la valeur du seuil de cycle.
Vetter (2020) (35) Série de cas Suisse Février 2020	Caractérisation clinique, virologique et immunologique des cinq premiers patients évalués à l'Hôpital universitaire de Genève (HUG), du jour du diagnostic jusqu'à la convalescence. Le SARS-CoV-2 a été détecté par rRT-PCR dans les écouvillons oropharyngés (OP) et nasopharyngés (NP) de chacun des patients. La culture virale a été effectuée à l'aide de cellules Vero E6.	- L'isolement du virus en culture a réussi tant pour les OP que les NP pendant la première semaine de la maladie pour quatre personnes atteintes d'une forme légère de l'infection. - La charge virale moyenne dans les échantillons ayant permis de réussir l'isolement était de $1,2 \times 10^9$ copies/ml. Le SARS-CoV-2 n'a pas pu être isolé dans des spécimens cliniques contenant moins de $1,4 \times 10^6$ copies virales d'ARN/ml.
Lewis (2020) (39) Étude de recherche des contacts ÉTATS-UNIS	Enquête sur la transmission aux ménages dans cinq ménages ayant participé à une collecte quotidienne de spécimens. Pendant les jours 1 à 4, si un contact avec un ménage a eu un résultat non concluant (1 des 2 régions du	- Chez plusieurs patients, les faibles valeurs de Ct (< 20) les jours 2 à 4 après l'apparition des symptômes coïncidaient avec l'apparition de symptômes supplémentaires (douleur thoracique, myalgie et perte de goût et d'odeur) et de cultures virales positives les deux jours. - La culture n'a rien donné pour les spécimens recueillis 14 jours après l'apparition des

Avril 2020	gène cible est positive pour le SRAS-CoV-2, comme indiqué par le rRT-PCR) ou un résultat positif (les deux régions du gène cible sont positives), le spécimen associé et tous les spécimens quotidiens subséquents de la personne ont été soumis à une culture virale pour en évaluer l'infectiosité. Les spécimens positifs par rRT-PCR recueillis le jour 14 et ayant des valeurs Ct inférieures à 35 ont également été cultivés. Les cibles génétiques pour le rRT-PCR et les méthodes de culture n'ont pas été décrites.	symptômes, malgré des valeurs positives au test rRT-PCR et une valeur Ct inférieure à 35.
Études de l'ARN subgénomique (n = 3)		
Rodríguez-Grande (2021) (32) Série de cas Espagne Janvier 2021*	On a évalué des échantillons de cas persistants avec tests RT-PCR positifs (n = 60) après plus de 21 jours depuis le premier résultat positif au test RT-PCR pour obtenir des preuves de virus réplicatif déterminé par l'ARN du gène E subgénomique (ARN SG).	- L'ARN SG a été détecté dans 12 cas sur 60 (20 %). Les dates de prélèvement de ces échantillons variaient de 28 à 79 jours après l'apparition des symptômes. - Dans tous les cas où l'ARN SG était détectable, les valeurs Ct pour l'ARN génomique étaient inférieures à 30, ce qui correspond aux valeurs attendues pour un virus actif. - L'éventail d'âge des sujets présentant une excrétion virale prolongée et un ARN viral SG était assez large et réparti également entre les hommes et les femmes. Sept personnes étaient immunodéprimées. Les formes de COVID-19 étaient légères (40 %), intermédiaires (20 %) et graves (40 %). Un cas d'ARN SG au jour 25 était asymptomatique.
Marot (2021) (27) Lettre à la rédaction Étude transversale	Exécution de tests RT-PCR en temps réel pour détecter la présence de l'ARN subgénomique viral (enveloppe) et de l'ARN négatif de la chaîne E dans les échantillons cliniques. On a également tenté d'isoler le virus par culture (cellules	- Aucun ARN intermédiaire n'a été détecté dans les échantillons lorsque la valeur Ct était supérieure à 33 (charge virale inférieure à 4,34 $\log_{10}$ copies/ml). - Les rapports de risques normalisés moyens par génome indiquent un niveau élevé de réplication virale au cours des cinq premiers jours suivant

France Août et septembre 2020	Vero CCL-81, incubées de 2 à 7 jours) à partir d'échantillons afin d'associer la présence d'ARN intermédiaires réplicatifs à chaînes positives avec la détection d'un virus viable. Les données ont été obtenues auprès de 61 travailleurs de la santé immunocompétents ayant reçu un diagnostic d'infection au SRAS-CoV-2 par RT-PCR sur des échantillons nasopharyngés.	l'apparition des symptômes, suivi d'une baisse significative.
Hogan (2021) (33) Études de cohorte prospectives et rétrospectives ÉTATS-UNIS Mars et avril 2020 et juillet à septembre 2020	Développement d'un nouveau rRT-PCR à 2 étapes spécifique à la chaîne négative du gène de l'enveloppe (le virus réplicateur activement produit des intermédiaires d'ARN à chaîne négative et peut donc être utilisé comme indicateur d'infectiosité potentielle). Nous avons recueilli rétrospectivement un ensemble pratique d'échantillons longitudinaux des voies respiratoires supérieures avec une large gamme de valeurs Ct. Pour la phase prospective de l'étude, nous avons prélevé des échantillons des voies respiratoires supérieures chez 53 patients consécutifs atteints d'une infection confirmée au SRAS-CoV-2. Les échantillons ont été prélevés sur une période médiane de 9 jours (EI : 4 à 18 jours) après l'apparition des symptômes.	- L'ARN à chaîne négative a été détecté chez 41 patients (28,1 %). - La valeur Ct médiane était significativement plus faible dans les échantillons où l'ARN à chaîne négative a été détecté (20,7) que dans ceux où la chaîne négative n'a pas été détectée (33,2, $p < 0,01$). - L'ARN à chaîne négative a été détecté chez deux patients hospitalisés immunocompétiteurs plus de 10 jours après l'apparition des symptômes avec des valeurs Ct élevées (~39). L'ARN à chaîne négative du SRAS-CoV-2 a été détecté jusqu'à 30 jours après l'apparition des symptômes chez un patient immunodéprimé.

LTE = lettre à la rédaction

ASSOCIATION ENTRE LA CHARGE VIRALE ET LE RISQUE DE TRANSMISSION

- Les charges virales semblent atteindre un sommet en moyenne cinq jours après l'exposition et un à deux jours après l'apparition des symptômes, avec une courte période (< 2 jours) de risque de transmission élevé et un potentiel de transmission grandement réduit de 7 à 10 jours après l'apparition des symptômes (40 à 42). En période de charge virale maximale, les cas hautement infectieux excrètent des dizaines à des milliers de virions SARS-CoV-2/min (24).

- Plusieurs études d'observation ont été effectuées sur la transmission dans les ménages et dans les grappes. Conformément aux constatations culturelles de la section ci-dessus, les cas présentant une charge virale plus élevée (c.-à-d. des valeurs Ct plus faibles) étaient plus susceptibles de transmettre le SRAS-CoV-2.
    - Les cas index ayant une charge virale élevée (plus de 10^6 copies/uL) étaient plus susceptibles de transmettre le SRAS-CoV-2 à des contacts étroits (RC 4,9, IC à 95 % : 1,3 à 18, p = 0,02) (43). Le taux d'attaque secondaire variait de 12 % lorsque le cas index avait une charge virale de 1×10^6 copies/ml à 24 % lorsque ce cas avait une charge virale de 1×10^{10} copies/ml (rapport de cotes ajusté par $\log_{10}$ augmentation de la charge virale = 1,3, IC à 95 % : 1,1 à 1,5) (44).
    - Les modèles de régression ont démontré que les cas entraînant une transmission secondaire présentaient une charge virale médiane plus élevée que les cas qui ne transmettaient pas le SRAS-CoV-2 (45). Deux études de cohorte rétrospectives effectuées dans des résidences universitaires aux États-Unis ont également révélé que les cas index entraînant une transmission secondaire présentaient une charge virale plus élevée (jusqu'à 6,5 fois) que les cas qui n'ont pas causé de transmission secondaire (46, 47). Même si les cas symptomatiques et asymptomatiques présentaient des sommets pour les valeurs Ct moyennes se rapprochant de 19 à 22, les valeurs Ct étaient beaucoup plus faibles dans les cas symptomatiques (plage de 12 à 36 par rapport à 14 à 37), ce qui indique une réduction de la charge virale chez les cas asymptomatiques (47).
    - Une étude transversale portant sur l'ensemble de la population du Danemark a permis de constater que les cas index ayant une valeur Ct inférieure à 20 présentaient un risque de transmission 1,89 fois plus élevé que celui d'un cas index ayant une valeur Ct supérieure à 25 (48). Le cas index avait une valeur Ct supérieure à 30 dans 39 % des cas secondaires, mais le risque de transmission était significativement plus élevé si les valeurs Ct étaient inférieures à 28. Des cas index avec des valeurs Ct élevées (> 35) se sont produits, mais le risque de transmission était beaucoup plus faible (8 %).
    - La majorité des cas associés à des ménages secondaires ont été détectés dans les 10 jours suivant l'apparition des symptômes chez le cas index, ce qui correspond au moment du rétablissement des résultats du virus réplicatif mentionnés à la section précédente (43).

- Une étude a révélé que les grappes ayant une charge virale élevée (supérieure à 10^6 copies/ml) étaient considérablement plus grandes que les grappes dont les sujets présentaient une charge virale plus faible (17 personnes infectées contre 3 au sein de la grappe, $p < 0,001$) (49).

- Peu d'études ont fait état de la façon dont le lien entre la charge virale et le risque de transmission variait selon la présence de symptômes, la gravité des symptômes ou les facteurs de risque (p. ex., âge, problèmes de santé chroniques).
  - Un examen systématique a révélé que les cas de COVID-19 chez les adultes, les enfants, les patients symptomatiques/présymptomatiques et les patients asymptomatiques présentaient des distributions semblables de la charge virale respiratoire pendant la période infectieuse (24). Fait intéressant, une étude sur une population plus importante a révélé qu'un âge plus avancé était associé positivement au risque de transmission, même après contrôle de la charge virale (c.-à-d. que l'âge était un meilleur prédicteur du risque de transmission que la charge virale) (48).
  - Des charges virales élevées (Ct inférieure à 20) avant l'apparition des symptômes parmi les cas qui ont transmis le SRAS-CoV-2 de façon présymptomatique ont été signalées (50). Plus la période d'incubation est longue, plus grande est la fraction de la charge virale présymptomatique, ce qui augmente la probabilité de transmission présymptomatique (41).
  - Des charges virales élevées ont été signalées tant pendant la période présymptomatique que jusqu'à 8 à 10 jours après l'apparition des symptômes. C'est pendant cette période où les valeurs Ct sont faibles (< 30) qu'il y a une forte probabilité de transmission.

Tableau 2 : Études qui étudient l'association entre la charge virale et le risque de transmission (n = 12).

ÉTUDE	MÉTHODOLOGIE	PRINCIPAUX RÉSULTATS
Chen (2020) (24) *Prépublication* Revue systématique et étude de modélisation Canada* Décembre 2020*	Une revue systématique a été effectuée pour tenir compte des études publiées jusqu'au 7 août 2020 (n = 64) et élaborer un ensemble complet de données sur les charges virales respiratoires (CVR) du SRAS-CoV-2. Une méta-analyse et un modèle ont ensuite été utilisés pour étudier l'infectiosité individuelle en excrétion d'un virus viable par des gouttelettes respiratoires et	- Au 90e centile de cas pendant toute la période infectieuse, la CVR estimée était de 8,91 copies/ml (IC à 95 % : 8,83-9,00). - L'âge et la symptomatologie ont eu une influence minimale sur la variation des cas de CVR du SRAS-CoV-2 pendant la période infectieuse. Les cas de COVID-19 adultes, pédiatriques, symptomatiques ou présymptomatiques et asymptomatiques ont montré des distributions de la valeur de référence semblables, avec des écarts-types de 2,03, de 2,06, de 2,00 et de 2,01 copies/ml, respectivement. - Le modèle mécaniste a montré que la valeur de la CVR du SRAS-CoV-2

	des aérosols. Les CVR du SRAS-CoV-2 ont été analysées dans l'ensemble des sous-groupes d'âge et de symptomatologie, ainsi que dans l'évolution de la maladie.	augmentait de façon exponentielle après l'infection, atteignait un sommet environ un jour après l'apparition des symptômes, puis diminuait de façon exponentielle. Les formes hautement infectieuses peuvent excréter des dizaines à des milliers de virions SARS-CoV-2/min, particulièrement de 1 à 5 jours après l'apparition des symptômes.
Cerami 2021 (43) *Prépublication* Étude de cohorte prospective ÉTATS-UNIS Avril à octobre 2020	Inscription de personnes séropositives à la COVID (n = 102) et de membres de leur ménage (n = 213) pour étudier la transmission du SRAS-CoV-2 dans les ménages. Les ménages ont été inscrits en moyenne six jours après l'apparition des symptômes chez le cas index. Des cas secondaires ont été détectés soit par test RT-qPCR (ciblant N1, N2 et RNase P) à la suite d'un écouvillon nasopharyngé effectué le jour 1 de l'étude et d'écouvillons nasaux hebdomadaires (jours 7, 14, 21), ou par séroconversion le jour 28.	- La majorité des cas dans des ménages secondaires ont été détectés dans les 10 jours suivant l'apparition des symptômes du cas index. - Les cas index ayant une charge virale élevée (supérieure à 10^6 copies virales/uL) au moment de l'inscription étaient plus susceptibles de transmettre le virus aux contacts du ménage pendant l'étude (RC 4,9, IC à 95 %, 1,3 à 18, p = 0,02). - La charge virale était corrélée au sein des familles, ce qui signifie que les personnes du même ménage étaient plus susceptibles d'avoir une charge virale semblable, ce qui suggère un effet d'inoculum. Ces différences n'étaient pas attribuables à la mutation D614G dans la protéine spicule SARS-CoV-2, puisque la grande majorité des isolats génotypés contenaient cette mutation (98 %).
Bjorkman (2021) (46) Étude de cohorte rétrospective ÉTATS-UNIS Août à novembre 2020	Analyse de la transmission de la COVID-19 dans les salles de résidence en fonction du dépistage hebdomadaire du RT-qPCR (ciblant le gène E) chez les élèves dans les résidences. Chaque unité Ct complète est un facteur de 2 copies d'ARN par ml. Enquête sur la mesure dans laquelle le moment des cas a favorisé la transmission entre camarades.	- La charge virale moyenne était 6,5 fois plus élevée dans les pièces où la transmission était probable (Ct moyenne = 26,2) que dans les pièces sans transmission (Ct moyenne = 28,9). - Ces cas s'étendaient sur une plage de plus de 7 ordres de grandeur de la charge virale, la charge la plus élevée se trouvant dans le groupe de transmission probable (Ct = 15,4) et la charge la plus faible se trouvant dans le groupe de transmission improbable (Ct = 40,6). Les seuls cas avec Ct supérieur à 34 (22 cas) ont été découverts dans le groupe de transmission improbable.

Tian (2021) (47) *Prépublication* Étude de cohorte rétrospective ÉTATS-UNIS Septembre et octobre 2020	Exécution d'un total de 61 982 tests sur 7 440 étudiants de premier cycle afin de déterminer si la valeur Ct pouvait différencier le propagateur de celui qui ne l'était pas. Les étudiants ont été testés à plusieurs reprises par des tests RT-PCR (ciblant les gènes N, S et ORF1ab) au cours de la période de l'étude et 602 cas ont été déterminés.	- 48,2 % (94 sur 195) des cas index ont eu au moins un contact qui est devenu positif pour le SRAS-CoV-2, tandis que 51,8 % des cas index (n = 101) n'ont pas transmis le SRAS-CoV-2 à leurs contacts. - Les valeurs Ct moyennes du propagateur et de la personne qui n'est pas un propagateur étaient presque identiques (pic de Ct = 18 à 21), mais leurs valeurs Ct médianes différaient de presque un cycle, ce qui suggère que les propagateurs avaient une valeur Ct inférieure à celle des autres (voir les figures 1B et C dans l'article). La plage des Ct était légèrement plus large pour le propagateur (12 à 36) que pour la personne qui n'avait rien propagé (14 à 36). - Même si les deux groupes présentaient des sommets pour les valeurs Ct se rapprochant de 19 à 22, les valeurs Ct étaient beaucoup plus faibles dans les cas symptomatiques que dans les cas asymptomatiques (plage de 12 à 36 par rapport à 14 à 37), ce qui indique une réduction de la charge virale chez les cas asymptomatiques.
Shrestha (2021) (42) Étude de cohorte rétrospective ÉTATS-UNIS Mars et avril 2020	Évaluation du potentiel de transmission obtenue en examinant la charge virale selon le temps qui s'est écoulé depuis l'apparition des symptômes chez les professionnels de la santé infectés par le SRAS-CoV-2 (n = 230). Des tests RT-PCR (ciblant les gènes N1, N2 et N3) ont été effectués sur des écouvillons nasopharyngés. La moyenne des 3 valeurs Ct pour les trois gènes cibles a été jugée être la valeur Ct du test. Les charges virales depuis l'apparition des symptômes ont été prédites à l'aide du modèle de	- La charge virale d'ARN du SRAS-CoV-2 est très élevée dans les 2 à 3 jours suivant l'apparition des symptômes et chute rapidement d'un ordre de grandeur en quelques jours (voir la figure 1 dans l'article). - Le potentiel de transmission de la COVID-19 est grandement réduit de 7 à 10 jours après l'apparition des symptômes (voir la figure 3 dans l'article). Parmi la zone sous la courbe qui couvre l'intervalle entre l'apparition des symptômes et 30 jours, 86,3 % ont eu lieu dans les 5 premiers jours, 96,9 % dans les 7 premiers jours et 99,7 % dans les 10 premiers jours.

	régression, la zone sous la courbe représentant la distribution du potentiel de transmission au fil du temps.	
Marks (2020) (44) Étude de cohorte rétrospective Espagne Mars et avril 2020	Cette étude a consisté en une analyse ponctuelle des données recueillies dans le cadre d'un essai randomisé en grappe auquel ont participé des personnes atteintes de COVID-19 dont le résultat a été confirmé par un test qPCR et leurs contacts étroits. Les facteurs associés à la transmission ont été évalués par régression linéaire à l'aide de toutes les grappes d'un cas index pour lequel la charge virale quantitative provenant des écouvillons nasopharyngés était disponible.	- Le taux d'attaque secondaire global était de 17 % (125 contacts sur 753) avec une plage de 12 % lorsque le cas index avait une charge virale de 1 x 10^6 copies/ml à 24 % lorsque le cas de l'indice avait une charge virale de 1 x 10^{10} copies/ml. - Selon une analyse multivariée, les probabilités de transmission étaient plus élevées lorsque le cas index présentait une charge virale élevée (rapport de cotes ajusté par augmentation par $\log_{10}$ de la charge virale = 1,3 (IC à 95 % : 1,1 à 1,5). - 90 % des événements de transmission se sont produits lorsque le cas index avait une charge virale élevée (≥ 5,1 $\log_{10}$ copies/ml). 50 % se sont produits dans des grappes où le cas index avait une charge virale de ≥ 8,8 $\log_{10}$ copies/ml. - D'autres facteurs associés à un risque accru de transmission étaient le contact avec le ménage et l'âge du contact. Aucun lien n'a été observé avec l'utilisation du couvre-visage, l'âge ou le sexe du cas index, ou avec la présence de symptômes respiratoires dans le cas index.
Kawasuji (2020) (45) Étude cas/témoin Japon Avril et mai 2020	Les patients atteints de COVID-19 qui ont transmis la maladie à au moins un autre patient ont été analysés comme des « cas » (patients de référence, n = 14) et comparés aux patients qui n'étaient pas la cause de la transmission secondaire (patients autres qu'index, n = 14, analysés comme des « témoins »). Les cas ont été confirmés et la charge virale quantifiée par RT-qPCR (ciblant le	- Les charges virales ont atteint un sommet peu après l'apparition des symptômes, puis ont diminué graduellement. Le temps médian avant la clairance virale ne différait pas de façon significative entre les patients index et autres qu'index : 21 jours (EI : 15 à 31) par rapport à 17 jours (9 à 26), p = 0,34. - La charge virale au moment du prélèvement initial de l'échantillon était beaucoup plus élevée chez les patients symptomatiques et asymptomatiques, ainsi que chez les adultes et les enfants. - Les modèles de régression des cas symptomatiques seulement (n = 18) ont démontré que la charge virale médiane des

	gène N2). Les parcours temporels de la charge virale nasopharyngée ont été évalués entre le cas index et les patients non symptomatiques à l'aide d'une régression non linéaire utilisant un modèle standard de désintégration en une phase.	patients index au début était plus élevée que celle des patients autres qu'index : 6,6 copies log/µL (IC à 95 % : 5,2 à 8,2) c. 3,1 (1,5 à 4,8). Cette tendance s'est poursuivie jusqu'à 10 jours après l'apparition des symptômes. Lorsque des cas asymptomatiques ont également été inclus dans ce modèle (n = 10), la tendance globale est demeurée la même : 3,3 copies log/µL (IC à 95 % : 1,6 à 5,2) c. 1,8 (-0,4 à 4,6), p = 0,015.
Lyngse (2021) (48) *Prépublication* Étude transversale Danemark Du 25 août au 10 février 2021	On a utilisé des données complètes du registre administratif du Danemark, comprenant l'ensemble de la population et tous les tests SARS-CoV-2, pour estimer le risque de transmission des ménages. Le test RT-PCR (ciblage du gène E) a été utilisé et un test pour le SARS-CoV-2 a été défini comme positif si la valeur Ct était ≤ 38. 66 602 cas primaires ont été cernés, dont 99,6 % avaient des valeurs Ct disponibles. 103 389 cas secondaires ont été identifiés.	- 25 % des cas primaires avaient une valeur Ct de 25, 50 % avaient une valeur Ct de 28 et 75 % avaient une valeur Ct de 32. La valeur Ct était similaire pour tous les groupes d'âge. - Il y avait un lien décroissant à peu près linéaire entre les valeurs Ct et le risque de transmission. - Le cas index avait une valeur Ct supérieure à 30 dans 39 % des cas secondaires (mais c'est le jour du test par rapport à un point de charge virale de pointe inconnu - ils n'avaient pas de données pour le modifier). Les cas primaires dont la valeur Ct était de 38 présentaient un risque de transmission de 8 % au sein du ménage. - Le risque de transmission était significativement plus élevé si les valeurs Ct étaient inférieures à 28. - Un cas primaire avec une valeur Ct de 18 à 20 présente un risque de transmission de 1,89 plus élevé qu'un cas primaire avec une valeur Ct de 36 à 38. - Le risque de transmission présentait un lien négatif avec l'âge chez les enfants de moins de 20 ans et un lien positif avec l'âge chez ceux de plus de 20 ans.
Ladoy (2021) (49) *Prépublication* Étude de surveillance	Caractérisation de la dynamique de la première vague d'infection par le SRAS-CoV-2 dans le canton	- 1 684 grappes spatio-temporelles ont été identifiées. - La majorité des grappes comptaient au moins une personne ayant une charge

Suisse Janvier à juin 2020	de Vaud (Suisse occidentale) grâce à la détection et à l'emplacement de grappes à l'aide des résultats des tests RT-PCR pour le SARS-CoV-2 (n = 33 651 testés, n = 3 317 positifs). Une approche d'acquisition spatiale a été utilisée pour évaluer l'importance de la charge virale dans l'évolution des grappes et un algorithme DBSCAN espace-temps modifié a été utilisé pour caractériser la dynamique de diffusion des grappes de transmission.	virale élevée (>1 milliard de copies/ml). Les grappes ayant une charge virale aussi élevée étaient considérablement plus importantes (médiane de 17 personnes infectées) que les grappes dont la charge virale était inférieure à plus d'un million de copies/ml (médiane de 3 personnes infectées, p < 0,001). - Les grappes contenant des individus plus jeunes avaient la charge virale la plus élevée, tandis que les grappes composées d'individus plus âgés avaient une charge virale faible à moyenne. - Il y avait 20 grappes dans lesquelles la charge virale des trois premiers cas était inférieure à 100 000 copies/ml, ce qui suggère que dans certains cas, même les sujets ayant moins de 100 000 copies/ml peuvent encore être contagieux.
Park (2020) (50) Série de cas Corée du Sud -> Israël Février 2020	Une éclosion de SRAS-CoV-2 parmi 39 pèlerins a fait l'objet d'une enquête. Dix cas confirmés sans symptômes aux premières dates d'échantillonnage (2 post-symptomatiques, 4 pré-symptomatiques et 4 asymptomatiques) ont été sélectionnés pour les tests RT-PCR de suivi des voies respiratoires (ciblant le gène E).	- Les valeurs Ct disponibles pour les spécimens des voies respiratoires inférieures étaient beaucoup plus faibles dans les cas sans symptômes (médiane, 22,8; EI, 20,1 à 25,4) que dans les cas avec symptômes aux premières dates d'échantillonnage (médiane, 27,9; EI, 23,4 à 30,4). La charge virale a diminué graduellement au fil du temps et n'était pas différente entre les cas symptomatiques et asymptomatiques. - La charge virale la plus élevée (Ct < 20) a été observée à partir du premier échantillon d'un cas prélevé 7 jours avant l'apparition des symptômes. La transmission s'est produite entre ce cas et un contact étroit pendant la période présymptomatique.
Goyal 2021 (40) Étude de modélisation États-Unis* Février 2021*	Élaboration d'un cadre de simulation de la transmission pour analyser la contribution de la charge virale aux paramètres de transmission épidémiologique observée SARS-CoV-2. Ce processus comprenait la	- Les simulations ont démontré qu'une charge virale supérieure des voies aériennes inférieure à 104 copies d'ARN SARS-CoV-2 est très peu probable (~0,00005 %) pour entraîner la transmission. La transmission est beaucoup plus probable (39 %) étant donné l'exposition d'une personne infectée qui

	modélisation des charges virales à l'intérieur de l'hôte, des simulations des expositions et des transmissions possibles en fonction de diverses courbes de la dose-réponse de la transmission, l'essai de divers ensembles de paramètres par rapport aux données épidémiologiques et des analyses exploratoires avec le meilleur modèle d'ajustement.	perd plus de 107 copies d'ARN, et 75 % étant exposée à une personne infectée ayant une charge virale de plus de 108 copies d'ARN. - Il y a un point d'inflexion entre 106 et 107 copies d'ARN, après quoi des événements de transmission multiples deviennent beaucoup plus probables d'une seule personne (c.-à-d. un événement de super propagation). - Les personnes infectées sont susceptibles d'être les plus infectieuses (charge virale supérieure à la dose TD50) pendant une période de 0,5 à 1 jour entre les jours 2 et 6 après l'infection. Cette variabilité est probablement attribuable à l'hétérogénéité de la période d'incubation plutôt qu'au moment du pic de la charge virale.
Ke (2020) (41) *Prépublication* Étude de modélisation États-Unis* Septembre 2020	Élaboration de modèles d'infection au SRAS-CoV-2 à l'intérieur de l'hôte fondés sur des données. Analyse de la relation entre la charge virale dans les voies respiratoires inférieures et supérieures trans (TLR et URT) et l'infectiosité potentielle au moyen d'un modèle probabiliste utilisant les données épidémiologiques existantes (provenant de 8 cas). Élaboration de plusieurs autres modèles pour expliquer la période prolongée d'infection virale dans les VRI.	- Pic de la charge respiratoire virale 5,2 jours en moyenne (ET : ± 1,3 jour) et 5,4 jours (± 1 jour) après l'infection dans les VRS et les VRI, respectivement, et en moyenne 2 jours (± 0,2 jour) et 2,1 jours (± 1,2 jour) après l'apparition des symptômes. - Plus la période d'incubation est longue, plus grande sera la fraction de la charge virale présymptomatique (voir fig. 2; $p < 0,001$), ce qui entraîne une fraction plus élevée de transmission présymptomatique. - Le modèle démontre que le logarithme de la charge virale (plutôt que la charge virale absolue) est un substitut approprié pour l'infectiosité (c.-à-d. que la croissance virale est un meilleur prédicteur de la transmission présymptomatique que la mesure de la charge virale seule). - La dissémination spatiale dans les poumons est un processus important pour maintenir des charges virales élevées prolongées dans les VRI.

Méthodologies :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient : Shedding, Viral dynamics, Viral RNA dynamics, Viral clearance, Viral RNA clearance, Viable, Culture, Infectivity, Infectious Period, Communicability period, Period of communicability, Viral load, Viral RNA load, Infectiousness. La présente revue contient des recherches publiées jusqu'au 31 mars 2021. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

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Public Health Agency of Canada | Agence de la santé publique du Canada

May 27, 2021

Evidence Snapshot:

Evidence Brief on the Therapeutic use of Vitamin D Supplementation for COVID-19

Context

This evidence brief summarizes the evidence of the efficacy of therapeutic or prophylactic supplementation of vitamin D in the treatment or prevention of COVID-19. The immunomodulating effects of vitamin D are complex and not fully understood and research conducted prior to COVID-19 suggested there was limited evidence of vitamin D benefit in lowering risk of acute respiratory infections.

Key Findings

This evidence brief includes five systematic reviews and reports that summarize three randomized controlled trials (RCTs) and one prospective cohort conducted in adults and 2 quasi-experimental conducted in geriatric populations up to May 26, 2021.

The key findings were:

- One of three RCTs found that vitamin D treatment in COVID-19 patients may reduce the risk of severe disease progression (admittance to ICU) (RR 0.04, 95%CI 0.01- 0.29, 1 RCT, 76 observations). A small prospective cohort reported reduced ICU admission (unadjusted OR = 0.13, 95%CI 0.03–0.6) among those that received 1000 IU vitamin D3 per day.
- Two RCTs found that vitamin D treatment did not significantly reduce mortality across 2 RCTs compared to the standard of care control group (RR 0.56; 95%CI 0.05 – 5.85, 2 RCTs, 313 observations), but a significant reduction in mortality was reported across two quasi-experimental studies and one RCT (OR 0.26; 95%CI 0.10-0.71).
- No association was reported with vitamin D treatment and adverse reactions. Across all studies only one trial recorded a single adverse event, vomiting, following a large bolus treatment of 200 000IU of cholecalciferol treatment (RR 2.98; 95%CI 0.12-72.30).
- None of the systematic reviews identified studies on supplementation of vitamin D to prevent COVID-19, although there are on-going trials registered to address this question.
- The overall confidence in these results is low as there was a lot of heterogeneity in the treatment regime, study design and imprecision in outcomes. Several trials have been initiated to further explore this question, which may change the conclusions of this review.

Considerations

There is insufficient evidence at present to determine the benefits and any potential harms of vitamin D supplementation as a treatment of COVID-19 and no evidence on prevention.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evidence Brief of Vitamin D Supplementation for Therapeutic use on COVID-19 Cases. May 27, 2021. Full report available from: **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Aperçu des éléments de preuve :

Synthèse en bref sur l'utilisation thérapeutique d'une supplémentation en vitamine D contre la COVID-19

Contexte

Ce document résume les éléments de preuve en ce qui concerne l'efficacité de la prophylactique supplémentation thérapeutique en vitamine D pour le traitement ou la prévention de la COVID-19. Les effets immunomodulateurs de la vitamine D sont complexes et mal compris, et les recherches effectuées avant la COVID-19 ont indiqué qu'il y avait peu d'éléments de preuve sur les bienfaits de la vitamine D pour réduire le risque d'infections respiratoires aiguës.

Principales constatations

Ce résumé des éléments de preuve comprend cinq revues systématiques et des rapports qui résument trois essais cliniques randomisés (ECR) et une cohorte prospective formée d'adultes, ainsi que deux quasi-expériences effectuées auprès de populations gériatriques jusqu'au 26 mai 2021.

Les principales conclusions sont les suivantes :

- L'un des trois ECR a révélé que le recours à un régime de vitamine D chez les patients atteints de COVID-19 pouvait permettre de réduire le risque de progression plus sévère de la maladie (admission aux SI) (RR = 0,04, IC à 95 % : 0,01 à 0,29, 1 ECR, 1 ECR, 76 observations). Une petite cohorte prospective a indiqué une réduction des admissions aux SI (RC non ajusté = 0,13, IC à 95 % : 0,03 à 0,6) chez les personnes qui ont reçu 1 000 UI de vitamine D3 par jour.
- Deux ECR ont révélé que l'apport d'un régime de vitamine D ne réduisait pas significativement la mortalité comparativement au groupe témoin standard ayant obtenu des soins habituels (RR 0,56; IC à 95 % : 0,05 à 5,85, 2 ECR, 313 observations) (5, 8 à 11). Une réduction importante de la mortalité a cependant été signalée dans deux quasi-expériences et dans un ECR (RC = 0,26; IC à 95 % : 0,10 à 0,71) (11).
- Aucun lien n'a été signalé avec le traitement à la vitamine D et les effets indésirables. Dans toutes les études, un seul essai a enregistré un événement indésirable, soit des vomissements, à la suite d'un important traitement avec bolus de 200 000 UI de cholécalciférol (RR 2,98; IC à 95 % : 0,12 à 72,30).
- Aucune des revues systématiques n'a relevé d'études sur la supplémentation en vitamine D pour prévenir la COVID-19, bien qu'il y ait des essais en cours enregistrés pour répondre à cette question.

- La confiance globale dans ces résultats est faible, car il y avait beaucoup d'hétérogénéité dans le régime de traitement, la conception de l'étude et l'imprécision des résultats. Plusieurs essais ont été entrepris pour approfondir cette question, ce qui pourrait modifier les conclusions de la présente revue systématique.

Facteurs dont il faut tenir compte

À l'heure actuelle, il n'y a pas suffisamment d'éléments de preuve pour déterminer les bienfaits et les méfaits potentiels de la supplémentation en vitamine D comme traitement de la COVID-19, et il n'y a pas non plus d'éléments de preuve en ce qui concerne la prévention.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Synthèse en bref sur l'utilisation thérapeutique d'une supplémentation en vitamine D dans les cas de COVID-19. 27 mai 2021. Rapport complet disponible auprès de : **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur la supplémentation thérapeutique en vitamine D pour des cas de la COVID-19

Introduction

Y a-t-il des preuves de l'efficacité d'une supplémentation thérapeutique en vitamine D pour traiter ou prévenir la COVID-19?

La vitamine D est une prohormone, soit un élément important que l'organisme convertit en hormone avant de l'utiliser dans l'homéostasie du calcium et la santé des os. Cette vitamine joue également un rôle dans d'autres systèmes, y compris la fonction immunitaire (1). Les fonctions immunomodulatrices de la vitamine D sont cependant complexes et mal comprises. Parmi les recherches effectuées avant la pandémie de COVID-19, peu ont montré l'avantage potentiel d'une supplémentation en vitamine D pour réduire le risque de développer des infections respiratoires aiguës (2, 3).

Les normes nutritionnelles canadiennes incluent des recommandations alimentaires sur la vitamine D pour chacun des groupes d'âge, recommandations qui visent à aider à répondre aux besoins nutritionnels habituels et à maintenir des taux sériques de 25-hydroxyvitamine D [25(OH)D] supérieurs à 40 nmol/l pour permettre la santé osseuse (4). Le taux sérique de 25(OH)D est utilisé comme indicateur afin de savoir si la personne a en une quantité suffisante dans son sang (1). Au Canada, une supplémentation en vitamine D est recommandée chez les adultes de plus de 50 ans (4). Les lignes directrices des États-Unis, du Royaume-Uni et de l'Irlande ont, quant à elles, tenu compte des éléments de preuve sur la COVID-19 et recommandent une supplémentation en vitamine D pour la santé des os, mais non pour traiter la COVID-19 ou en prévenir l'apparition (5 à 7).

Les chercheurs ont postulé qu'une carence en vitamine D pourrait augmenter le risque d'infection à la COVID-19, accélérer la progression de la maladie ou entraîner des effets plus sévères. Bien que cette question ne relève pas de la portée de la présente recherche, de nombreuses études d'observation ont porté sur le lien entre l'état nutritionnel en vitamine D et le risque d'infection par la COVID-19, les effets graves et la mortalité. Nous avons relevé dix revues systématiques de qualité faible à élevée qui résument chacune entre 10 et 43 études portant sur les liens entre les effets cliniques de la COVID-19 et l'état nutritionnel en vitamine D (tableau en annexe). Les constatations figurant dans les études incluses dans les revues systématiques n'étaient cependant pas toujours significatives. Les résultats généralement cohérents tirés des revues systématiques ont révélé que la carence en vitamine D était plus importante chez les personnes ayant eu la COVID-19 et que plus le niveau moyen de vitamine D était faible, plus la sévérité de l'infection était grande. En ce qui concerne les résultats associés aux effets de la COVID-19, des associations avec un faible taux sérique en vitamine D ont été mentionnées dans certaines études, notamment en lien avec les hospitalisations, l'admission aux soins intensifs, la ventilation mécanique, l'oxygénothérapie et la mortalité. Les groupes susceptibles de présenter une carence en vitamine D étaient les mêmes à risque d'être atteints

d'une forme grave de COVID-19. La relation entre ces deux éléments est complexe et il est donc difficile d'extrapoler et de trouver une relation de cause à effet entre un faible taux de vitamine D et les effets plus sévères de la COVID-19 (8).

La présente synthèse en bref porte sur les éléments de preuve résumant la recherche sur le lien entre la supplémentation en vitamine D et le traitement ou la prévention de la COVID-19. Les études concernant le traitement ont été effectuées sur des patients atteints de la COVID-19 et incluent généralement des doses élevées de vitamine D (un bolus de grande taille avec un maximum de 200 000 UI ou des doses pouvant aller jusqu'à 60 000 UI par jour pris une fois par semaine, plusieurs fois par semaine ou de façon hebdomadaire) afin de voir si cela permet d'obtenir de meilleurs résultats. Les études concernant la prévention ont porté soit sur une population en santé, soit sur des personnes asymptomatiques ou ayant une forme bénigne de COVID-19 et incluent des doses modérées de vitamine D (entre 1 000 et 9 600 UI par jour pendant 2 à 24 semaines) afin de déterminer si la vitamine prévient la COVID-19 ou en réduit la gravité des effets. Des revues systématiques portant sur le traitement ou sur la prévention de la COVID-19 avec supplémentation en vitamine D ont été recensées. Lorsque de nouvelles données sur les essais ont été publiées depuis les revues systématiques les plus récentes, la recherche primaire ayant été publiée ou en prépublication a également été prise en compte si sa date de publication était postérieure à la plus récente revue systématique, soit jusqu'au 26 mai 2021. À ce jour, aucune étude à ce sujet n'a été réalisée au Canada.

Points clés

- Cinq revues systématiques (deux ayant été publiées, une prépublication et deux rapports inclus dans la littérature grise) sur le traitement avec la vitamine D ont été recensées, ce qui incluait la documentation disponible jusqu'au mars 2021, dont l'une indiquait la date du 15 mai 2021 comme date de vérification des nouvelles recherches. Aucune autre recherche primaire portant sur l'efficacité thérapeutique de la vitamine D pour la COVID-19 n'a été recensée (tableau 1).
- Les schémas posologiques de vitamine D utilisés dans les études étaient hétérogènes, variant d'un bolus unique de 200 000 UI de cholécalciférol à des traitements répartis sur plusieurs jours (jusqu'à 14 jours) comprenant entre 1 000 et 60 000 UI de cholécalciférol ou 532 à 266 µg de calcifédiol par jour (5, 8 à 11).
- Les cinq revues systématiques comprenaient trois essais cliniques randomisés (ECR) publiés, une cohorte prospective effectuée chez des adultes et deux expériences semi-expérimentales menées auprès de populations gériatriques afin d'évaluer la vitamine D comme traitement pour les patients atteints de COVID-19 (tableau 1).
    - L'un des trois ECR a révélé que le recours à un régime de vitamine D chez les patients atteints de COVID-19 pouvait permettre de réduire le risque de progression plus sévère de la maladie (admission aux SI) (RR = 0,04, IC à 95 % : 0,01 à 0,29, 1 ECR, 76 observations) (5, 8 à 11). Une petite cohorte prospective a indiqué une réduction des admissions aux SI (RC non

ajusté = 0,13, IC à 95 % : 0,03 à 0,6) chez les personnes qui ont reçu 1 000 UI de vitamine D3 par jour (10).

  - Deux ECR ont révélé que l'apport d'un régime de vitamine D ne réduisait pas significativement la mortalité comparativement aux résultats du groupe témoin ayant obtenu des soins habituels (RR 0,56; IC à 95 % : 0,05 à 5,85, 2 ECR, 313 observations) (5, 8 à 11). Une réduction importante de la mortalité a cependant été signalée dans deux quasi-expériences sur les populations gériatriques et dans un ECR effectué chez des adultes (RC = 0,26; IC à 95 % : 0,10 à 0,71) (11).
  - Aucun lien n'a été signé entre des événements indésirables et le régime de vitamine D. Dans l'un des essais (n = 237), on a enregistré un épisode de vomissements à la suite d'un grand bolus de 200 000 UI de cholécalciférol, mais aucun lien direct avec le traitement (RR = 2,98; IC à 95 % : 0,12 à 72,30) n'ait pu être établi (9).

- Aucune revue systématique ou étude sur la supplémentation en vitamine D pour prévenir la COVID-19 ou en réduire la gravité n'a été trouvée.
- On trouve 38 essais cliniques inscrits sur clinicaltrials.gov qui incluent une forme de supplémentation en vitamine D (dose de 1 000 à 9 600 UI par jour pendant 2 à 24 semaines chez des populations en santé et des personnes atteintes de la forme bénigne de COVID-19) ou un traitement (fortes doses quotidiennes pouvant aller jusqu'à 60 000 UI par jour dans le cadre de traitements durant une journée, plusieurs jours ou une semaine). Au 28 mai 2021, six de ces études étaient terminées, mais aucun des résultats n'était encore disponible. Ce secteur constitue donc un domaine de recherche actif, et les résultats tirés de ces nouvelles études pourraient modifier les conclusions présentées dans cette synthèse en bref.

Vue d'ensemble des éléments de preuve

Pour ce qui est de la vitamine D utilisée comme traitement contre la COVID-19, quatre revues systématiques avec cote AMSTAR 2 de qualité élevée à faible (ci-après appelés AMSTAR) comprenant trois ECR et deux études semi-expérimentales ont été sélectionnées. Chacune comportait des risques de biais et de l'information manquante en ce qui concerne les protocoles utilisés (12). On pouvait aussi voir des variations dans le traitement en vitamine D et dans les normes de soins (soins donnés au groupe témoin) entre les études. Aucune revue systématique n'a permis de cerner des études sur le lien entre la supplémentation en vitamine D et les effets de la COVID-19. Par conséquent, à l'heure actuelle, il n'y a pas suffisamment d'éléments de preuve pour déterminer les avantages et les inconvénients potentiels de la supplémentation en vitamine D comme traitement de la COVID-19, et on ne retrouve aucune étude publiée sur les avantages et les inconvénients potentiels de la supplémentation en vitamine D pour la prévention de la COVID-19. D'autres essais contrôlés, qui peuvent déjà avoir été entrepris à la suite de l'inscription des essais cliniques dans le registre, seront nécessaires pour évaluer en toute confiance les avantages de la supplémentation en vitamine D pour le traitement ou la prévention de la COVID-19. La confiance globale dans les résultats actuels

des études est faible et des recherches supplémentaires sont susceptibles de modifier les conclusions présentées dans cette revue.

TABLE DES MATIÈRES

SUPPLÉMENTATION EN VITAMINE D OU USAGE THÉRAPEUTIQUE CONTRE LA COVID-19

Tableau 1. Supplémentation en vitamine D ou utilisation comme traitement contre la COVID-19 (n = 5 revues systématiques)

ÉTUDE	PRINCIPAUX RÉSULTATS
Stroehlein (Cochrane) (8) *nouvelle* Revue systématique évolutive (AMSTAR haute qualité) Allemagne* 24 mai 2021 (données de recherche au 11 mars 2021)	- Vitamine D comme traitement contre la COVID-19, évaluée dans des ECR : o Trois ECR avec 356 participants, dont 183 ont reçu un traitement à la vitamine D. Deux études comprenaient des personnes atteintes d'une forme modérée ou grave de COVID-19 et une étude comprenait des personnes asymptomatiques ou atteintes de la forme bénigne de la COVID-19. Un ECR présentait un faible risque de biais et deux étaient associés à des préoccupations en raison des rapports sélectifs. Les traitements consistaient en une seule dose élevée de cholécalciférol par voie orale ou en des doses multiples de calcifédiol par voie orale. o Deux ECR ont constaté que la supplémentation en vitamine D ne faisait aucune différence pour l'ensemble des causes de mortalité alors qu'un ECR n'a trouvé aucune différence dans le besoin de ventilation mécanique. o On pouvait également voir des éléments de preuve contradictoires (RR protecteur de 0,04, RR non significatif de 0,75) en ce qui concerne l'effet protecteur possible contre l'admission aux soins intensifs dans deux ECR.

	○ Une étude sur les cas bénins de COVID-19 n'a signalé aucun effet dont la gravité était jugée prioritaire, mais a plutôt abordé la clairance virale, les marqueurs inflammatoires et les changements des taux sériques de vitamine D. ○ La revue systématique (RS) a cerné 21 essais terminés ou en cours pour lesquels aucun résultat n'avait encore été publié, mais dont le domaine d'étude était pertinent pour la présente revue et pourront donc, une fois publiés, modifier les conclusions présentées dans toute mise à jour de la présente revue. - Les traitements comprenaient : ○ Murai : Cholécalciférol 200 000 UI en une dose ○ Rustogi : Cholécalciférol 60 000 UI par jour pendant 7 jours ○ Castillo : calcifédiol 0,532 mg le jour 1, 0,266 mg les jours 3 et 7, puis une fois par semaine jusqu'au congé ou à l'admission aux SI. - Conclusion : il n'y avait pas suffisamment d'éléments de preuve pour déterminer les bienfaits et les méfaits de la supplémentation en vitamine D comme traitement contre la COVID-19.
Bassatne (Metabolism) (10) *nouvelle* Revue systématique et méta-analyse (cote AMSTAR de qualité faible) Liban* 24 mars 2021 (données de recherche au 18 décembre 2020)	- 31 études d'observation de basse qualité et avec un faible niveau de certitude et 3 ECR ont été inclus. - Études concernant le traitement : ○ Les trois ECR n'ont montré aucune amélioration en ce qui concerne la gravité des effets ou la mortalité, sauf que Castillo a déclaré que la vitamine D était associée à un taux d'admission plus faible aux SI (RC = 0,03 (IC à 95 % : 0,003 à 0,25)). Il s'agissait cependant d'un petit essai comportant un risque incertain de biais. ○ La présente RS a permis de cerner 32 essais en cours qui pourraient être pertinents pour cette revue. ○ Une petite cohorte prospective a constaté qu'un régime de vitamine D3 avec une dose de 1 000 IU par jour pendant 14 jours était associé à un risque plus

	faible d'admission aux SI en raison de la COVID-19 (RC non ajusté = 0,13, IC à 95 % : 0,03 à 0,6). - Liens avec de faibles niveaux de vitamine D : o Le risque de mortalité était plus élevé chez les personnes ayant de faibles taux de vitamine D (RR 2,1, IC à 95 % [0,9 à 4,8]; I^2 = 76 %, 7 études) et trois études utilisant un seuil de 25(OH)D < 30 ng/ml ont montré un risque de mortalité encore plus élevé (RR = 3,1, IC à 95 % [1,4 à 6,8]; I^2 = 0 %, 3 études). o Le risque d'admission aux soins intensifs était plus élevé chez les personnes ayant un faible taux de vitamine D (RR 4,89, IC à 95 % [0,54 à 44,26]; I^2 = 85 %, trois études). o Le risque d'hospitalisation était plus élevé chez les personnes ayant de faibles niveaux de vitamine D dans 2 études sur 3. o Le risque de positivité au SRAS-CoV-2 chez les personnes ayant de faibles taux de vitamine D était significatif pour 25(OH)D < 30 ng/ml (RR = 1,5, IC à 95 % [1,3, 1,8], I^2 = 0 %, 2 études).
National Institute for Health and Care Excellence (NICE), COVID-19 rapid guideline for practitioners on Vitamin D and evidence review (5) (cote AMSTAR de qualité élevée) ROYAUME-UNI 17 décembre 2020 (données de recherche au 29 octobre 2020)	- Supplémentation en vitamine D : o Cette ligne directrice précise que la vitamine D ne devrait pas être recommandée dans le seul but de prévenir la COVID-19, car il n'y avait pas suffisamment de preuves à l'appui. o Les recommandations relatives à la supplémentation pour la population en général portaient sur le maintien de la santé des os et des muscles. L'exposition insuffisante à la lumière du soleil a été associée à des niveaux de vitamine D sous-optimaux, et une supplémentation a été recommandée, particulièrement pendant les mois d'hiver. - Utilisation de la vitamine D pour traiter l'infection à la COVID-19 : o Un ECR (Castillo et coll.) a ajouté du calcifédiol (0,532 mg) au moment de l'admission, puis les jours 3 et 7, ainsi que chaque semaine en plus de la norme de

	soins habituelle. Cette étude présentait un risque élevé de biais et a été jugée comme une preuve très faible. Résultats : 1 personne sur 50 dans le groupe de traitement ayant reçu du calcifédiol et 13 personnes du groupe-témoin sur 26 ont été admis aux SI (RC = 0,03 IC à 95 % : 0,003 à 0,25). La mortalité dans les groupes a touché 0 personne sur 50 et 2 personnes sur 26 respectivement dans le groupe expérimental et dans le groupe témoin (RC = 0,097, IC à 95 % : 0,004 à 2,099). - Lien entre la vitamine D et les effets de la COVID-19 : o 12 études ont été incluses dans cet examen (12 autres n'ont pas été incluses parce qu'elles étaient encore en préimpression). Le lien entre l'infection à la COVID-19 (qu'elle soit ou non présente) et les niveaux de vitamine D était contradictoire (lien négatif et non significatif) et les analyses étaient très variables. Les résultats en ce qui concerne la gravité de l'atteinte étaient également contradictoires pour les soins intensifs, la ventilation mécanique ou l'oxygénothérapie. Une étude a indiqué un lien de protection entre la forme grave de la COVID-19 et la supplémentation en vitamine D.
Nikniaz et coll. (prépublication MedRxiv) (11) Revue systématique et méta-analyse (cote AMSTAR de qualité moyenne) 5 janvier 2021 (données de recherche au 16 décembre 2020)	- Cette revue a examiné 4 essais cliniques (2 ECR (Castillo et Rastogi) et 2 quasi-expériences (Annweiler) ayant porté sur 259 cas de COVID-19 ayant ou non été hospitalisés. Supplémentation orale en vitamine D, y compris avec du cholécalciférol et du calcifédiol (n = 139). - Les études quasi expérimentales ont été effectuées sur des populations de personnes âgées dans les unités de soins de longue durée et de gériatrie de l'hôpital. Le traitement consistait en une dose unique de 80 000 UI de vitamine D3 pour les cas positifs à la COVID-19. L'ECR de Rastogi a porté sur des cas atteints de la forme bénigne de COVID-19 qui ont reçu 60 000 UI par jour de cholécalciférol pendant 7 jours alors que dans l'ECR de Castillo, les personnes hospitalisées en raison de la COVID-19 ont reçu 0,532 mg de calcifédiol le jour 1, 0,266 mg les jours 3 et 7, puis une fois par semaine par la

	suite, jusqu'à ce que la personne obtienne son congé ou soit admise aux soins intensifs. *(Remarque : dans ces études, la dose donnée était supérieure aux limites maximales sécuritaires prévues pour la supplémentation en vitamine D.)* - Dans trois études (deux quasi-expériences et l'ECR de Castillo), les probabilités de mortalité parmi les groupes d'intervention étaient significativement plus faibles comparativement aux groupes témoins (RC = 0,264, IC à 95 % : 0,099 à 0,708, p = 0,008). Les deux quasi-expériences sur les populations gériatriques ont indiqué un effet important sur la survie. - Castillo et coll. a indiqué un taux d'admission aux SI plus faibles, un rapport de cotes (RC) de 0,03 (IC à 95 % : 0,003 à 0,25), alors que deux autres études ont montré une amélioration importante de l'état clinique avec la supplémentation en vitamine D.
COVID-NMA Project (9) Synthèse évolutive (non évaluée) France Mise à jour le 11 mai 2021	- Trois ECR (Castillo, Rastogi et Murai) ont été résumées et le sommaire des constatations indique que la preuve était de très faible qualité. o Le traitement avec vitamine D peut avoir un lien protecteur en ce qui concerne la gravité de l'atteinte (RR : 0,04, IC à 95 % : 0,01 à 0,29, étude (76 observations), très faible certitude). o À ce moment-ci, aucun lien n'a été établi avec la mortalité (très faible certitude) ou les événements indésirables (faible certitude).

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Méthodologies :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été

effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient : (vitamin D, 25(OH)D, 25hydroxyvitaminD, dihydroxyvitamin, calcif*, cholecalcif*) ou (zinc), un filtre supplémentaire pour les revues systématiques a aussi été utilisé pour sélectionner les premières revues.
Une recherche effectuée dans la littérature grise ciblait les principaux sites web des gouvernements et des entreprises de synthèse de données probantes pour obtenir des éléments de preuve à jour sur ces sujets.
La présente revue contient des recherches publiées jusqu'au 26 mai 2021.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle portait sur la question à l'étude et les conclusions clés qui ont été extraites et présentées dans des tableaux, dans la revue.

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

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ANNEXE : VITAMINE D ET LIENS AVEC LES EFFETS CLINIQUES DE LA COVID-19

Tableau dans l'annexe. Niveaux de vitamine D ou supplémentation quotidienne et liens avec les effets cliniques de la COVID-19 (n = 10 revues systématiques)

ÉTUDE	PRINCIPAUX RÉSULTATS
Dramé (Nutrients) (13) *nouvelle* Revue systématique (cote AMSTAR de qualité moyenne) 13 avril 2021 (données de recherche au 5 novembre 2020)	- Comprend 11 études d'observation sur le lien entre les effets associés à la COVID-19 et la vitamine D chez des personnes âgées de plus de 60 ans. Les études ont été évaluées comme étant de qualité élevée à moyenne. o Les quatre études comparant les effets de la COVID-19 dans les groupes qui ont pris une supplémentation en vitamine D et ceux qui n'en ont pas reçu ont indiqué que les groupes qui avaient reçu la supplémentation présentaient des effets moins graves. Aucune description quant à l'importance n'est indiquée. o Sept études ont examiné le lien entre la carence en vitamine D et la gravité des effets et révélé que la fréquence des effets graves était plus basse chez les personnes ayant un taux suffisamment élevé de vitamine D. Aucune description quant à l'importance n'est indiquée.. - Ces données confirment que la supplémentation quotidienne en vitamine D peut avoir un effet protecteur sur le système immunitaire contre les infections respiratoires.
Petrelli (J Steroid Biochem Mol Biol, courte communication) (14) *nouvelle*	- 43 études d'observation (612 601 patients) ont été incluses et ont examiné le lien entre la vitamine D et le risque, la gravité et la mortalité associés à la COVID-19.

Revue systématique et méta-analyse (cote AMSTAR de qualité faible) Italie* 29 mars 2021 (données de recherche au 31 janvier 2021)	○ Une carence en vitamine D était associée à un risque plus élevé de COVID-19 (RC = 1,26; IC à 95 % : 1,19 à 1,34; P < 0,01). Le risque d'infection était plus élevé lorsque les taux de vitamine D étaient inférieurs à 20 ng/ml (RC = 1,5). ○ Une carence en vitamine D a été associée à une forme plus grave de COVID-19 (RC = 2,6; IC à 95 % : 1,84 à 3,67; P < 0,01) ○ Une carence en vitamine D a été associée à un risque plus élevé de COVID-19 (RC = 1,22; IC à 95 % : 1,04 à 1,43; P < 0,01) ○ La supplémentation en vitamine D a été associée à une réduction de la gravité de la COVID-19 (n = 6 études) et du risque de mortalité (n = 7 études) (RC = 0,27; IC à 95 % : 0,11 0,66; P < 0,01 et RC = 0,41; IC à 95 % : 0,21 0,81; P = 0,01).
Bassatne (Metabolism) (10) *nouvelle* Revue systématique et méta-analyse (cote AMSTAR de qualité faible) Liban* 24 mars 2021 (données de recherche au 18 décembre 2020)	- 31 études d'observation de basse qualité et avec un faible niveau de certitude et 3 ECR ont été inclus. - Études concernant le traitement : ○ Les trois ECR n'ont pas montré une amélioration de la gravité ou de la mortalité, sauf que Castillo a déclaré, dans son étude, que la vitamine D protégeait contre l'admission aux SI (RC 0,03, IC à 95 % : 0,003 à 0,25) dans un petit essai comportant un risque incertain de biais. ○ 32 essais en cours ont été recensés dans les registres des essais (janvier 2021). ○ Le traitement avec la vitamine D3 à 1 000 IU par jour pendant 14 jours a eu un effet protecteur (RC non ajusté = 0,13, IC à 95 % [0,03–0,6], 1 étude). - Liens avec de faibles niveaux de vitamine D : ○ Le risque de mortalité était plus élevé chez les personnes ayant de faibles taux de vitamine D (RR 2,1, IC à 95 % [0,9 à 4,8]; I^2 = 76 %, 7 études) et trois études utilisant un seuil de 25(OH)D < 30 ng/ml ont montré un risque de mortalité encore plus élevé (RR = 3,1, IC à 95 % [1,4 à 6,8]; I^2 = 0 %, 3 études).

	○ Le risque d'admission aux soins intensifs était plus élevé chez les personnes ayant un faible taux de vitamine D (RR 4,89, IC à 95 % [0,54 à 44,26]; I^2 = 85 %, trois études). ○ Le risque d'hospitalisation était plus élevé chez les personnes ayant de faibles niveaux de vitamine D dans 2 études sur 3. - Le risque de positivité au SRAS-CoV-2 chez les personnes ayant de faibles taux de vitamine D était significatif pour 25(OH)D < 30 ng/ml (RR = 1,5, IC à 95 % [1,3, 1,8], I^2 = 0 %, 2 études).
Teshome (Frontiers in Public Health) (15) *nouvelle* Revue systématique et méta-analyse (cote AMSTAR de qualité moyenne) Éthiopie* 5 mars 2021 (données de recherche au 20 décembre 2020)	- 14 études (91 120 participants) ont examiné les niveaux de vitamine D et le risque d'infection à la COVID-19. 5 études de cohorte, 5 comparaisons avec témoins et 4 études de prévalence ont été incluses. ○ Une carence en vitamine D était associée à un risque d'infection à la COVID-19 plus élevé (RC = 1,80; IC à 95 % : 1,72 à 1,88, I^2 de 79,1 %, 8 études).
Akbar (Frontiers in Nutr) (16) *nouvelle* Revue systématique et méta-analyse (cote AMSTAR de haute qualité) Indonésie* 29 mars 2021 (données de recherche au 9 décembre 2020)	- De faibles taux sériques de 25-hydroxyvitamine D (25-DHO) associés à la susceptibilité à la COVID-19, à la gravité et à la mortalité liées à la COVID-19 ont été étudiées dans 14 études (999 179 participants) : ○ Un faible taux sérique de vitamine D a été associé à des taux d'infection à la COVID-19 plus élevés (RC = 2,71 [1,72, 4,29], p < 0,001; I^2 : 92,6 %) et à l'âge et au sexe masculin, ce qui augmentait considérablement le lien. ○ Un faible taux sérique de vitamine D a été associé à une forme plus grave de COVID-19 (RC = 1,90 [1,24, 2,93], p = 0,003; I^2 : 55,3 %). ○ Un faible taux sérique de vitamine D a été associé à un taux de mortalité plus élevé (RC = 3,08 [1,35, 7,00], p = 0,011; I^2 : 80,3 %). Les facteurs de risque de mortalité connexes étaient le sexe masculin et le diabète, qui nécessitent un examen plus poussé pour déterminer le lien.

	- Une relation de causalité ne peut être établie avec les études d'observation incluses.
Ghasemian (prépublication MedRxiv) (17) *nouvelle* Revue systématique et méta-analyse (cote AMSTAR de qualité faible) Iran* 3 février 2021 (données de recherche au 18 décembre 2020)	- 23 études (11 901 participants) ont été incluses. o Les probabilités de contracter la COVID-19 étaient plus élevées chez les personnes ayant une carence en vitamine D (RC 3,3., IC à 95 % : 2,5 à 4,3, 3 études). o Les probabilités de contracter une forme grave de COVID-19 étaient plus élevées chez les personnes ayant une carence en vitamine D (RC 5,1, IC à 95 % : 2,6 à 10,3, 13 études). o Selon sept études, il n'y avait aucun lien entre la mortalité et la carence en vitamine D. - Il a été démontré que la positivité du SRAS-CoV-2 était inversement proportionnelle aux concentrations sériques de 25(OH)D.
National Institute for Health and Care Excellence (NICE), COVID-19 rapid guideline for practitioners on Vitamin D and evidence review (5) (AMSTAR high quality) ROYAUME-UNI 17 décembre 2020 (données de recherche au 29 octobre 2020)	- Supplémentation en vitamine D : o Cette ligne directrice précise que la vitamine D ne devrait pas être recommandée dans le seul but de prévenir la COVID-19, car il n'y avait pas suffisamment de preuves à l'appui. o Les recommandations relatives à la supplémentation pour la population en général portaient sur le maintien de la santé des os et des muscles. L'exposition insuffisante à la lumière du soleil a été associée à des niveaux de vitamine D sous-optimaux, et une supplémentation a été recommandée, particulièrement pendant les mois d'hiver. - Utilisation de la vitamine D pour traiter l'infection à la COVID-19 : o Un ECR (Castillo et coll.) a ajouté du calcifédiol (0,532 mg) au moment de l'admission, puis les jours 3 et 7, ainsi que chaque semaine en plus de la norme de soins habituelle. Cette étude présentait un risque élevé de biais et a été jugée comme une preuve très faible. Résultats : 1 personne sur 50 dans le groupe de traitement ayant reçu le calcifédiol et 13 personnes sur 26 dans le groupe-témoin ont été admises aux SI

	(RC = 0,03 IC à 95 % : 0,003 à 0,25). La mortalité dans les groupes a touché 0 personne sur 50 et 2 personnes sur 26 respectivement dans le groupe expérimental et dans le groupe témoin (RC = 0,097, IC à 95 % : 0,004 à 2,099). - Lien entre la vitamine D et les effets de la COVID-19 : o 12 études ont été incluses dans cet examen (12 autres n'ont pas été incluses parce qu'elles étaient encore en préimpression). Les liens entre l'infection à la COVID-19 (présente ou non) et les niveaux de vitamine D étaient contradictoires (lien négatif et non significatif) et les analyses étaient très variables. Les résultats en ce qui concerne la gravité de l'atteinte étaient également contradictoires pour les soins intensifs, la ventilation mécanique ou l'oxygénothérapie. Une étude a indiqué un lien de protection entre la forme grave de la COVID-19 et la supplémentation en vitamine D.
Liu (IJID) (18) Revue systématique et méta-analyse (cote AMSTAR de haute qualité) Chine* 2 janvier 2021 (données de recherche au 25 septembre 2020)	- Dans 10 études d'observation (cotées de qualité moyenne à élevée par l'auteur de la revue) qui comprenaient 361 934 participants (4 178 cas de COVID-19), la carence en vitamine D était associée à un risque accru de contracter l'infection à la COVID-19 (RC = 1,43, IC à 95 % : 1,00 à 2,05) et les personnes atteintes de COVID-19 présentaient des niveaux de vitamine D considérablement plus bas. Il y avait une hétérogénéité importante.
Pereira (Crit Rev Food Sci Nutr) (19) Revue systématique et méta-analyse (cote AMSTAR de qualité faible) Brésil* 2 novembre 2020 (données de recherche au 9 octobre 2020)	- Rapport sur le lien entre la carence en vitamine D et la gravité de la COVID-19 dans une analyse de la prévalence portant sur la carence et l'insuffisance en vitamine D chez les personnes atteintes de la maladie. - On a inclus 27 études d'observation jugées comme présentant un risque de biais faible (n=4) et élevé (n=23). - La probabilité d'une carence en vitamine D était plus élevée dans les formes graves de COVID-19 (RC 1,65 IC à 95 % : 1,30 à 2,09, I^2 35,7 %) et les niveaux de vitamine D étaient beaucoup plus faibles chez les personnes atteintes de la forme grave.

	- Dans le cas d'une carence grave, on a signalé une augmentation de l'hospitalisation (RC 1,81, IC à 95 % : 1,41 à 2,21, I^2 0,0 %) et de la mortalité (RC 1,82, IC à 95 % : 1,06 à 2,58, I^2 59,0 %).
Das (prepublication MedRxiv) (20) Revue systématique (cote AMSTAR de qualité faible) Multiple* 3 décembre 2020 (données de recherche au 3 novembre 2020)	- Onze études d'observation publiées et jugées être de qualité moyenne à élevée selon l'auteur de la revue ont été incluses. Toutes les études ont examiné le lien possible entre la carence en vitamine D et l'incidence ou la gravité de la COVID-19 et ont été incluses. L'analyse est descriptive, aucune méta-analyse n'a été prévue. - Les résultats de chacune des études figurent dans les tableaux. Il y avait constamment des liens entre la carence en vitamine D et la forme plus grave de la COVID-19 ou la mortalité découlant de cette infection.

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Emerging Evidence on COVID-19

Evidence Brief on the Therapeutic use of Vitamin D Supplementation for COVID-19

Introduction

Is there evidence of the efficacy of therapeutic supplementation of vitamin D in the treatment or prevention of COVID-19?

Vitamin D is a prohormone, a substance the body converts to a hormone, important for calcium homeostasis and bone health. It is also implicated in other systems including immune function (1). The immunomodulating functions of vitamin D are complex and not fully understood. Research conducted prior to the COVID-19 pandemic suggests there is limited evidence of a potential benefit of vitamin D supplementation to lower risk of developing acute respiratory infections (2, 3).

Nutrition standards in Canada include dietary recommendations for vitamin D for all age groups to help meet usual nutrient requirements and maintain 25-hydroxyvitamin D [25(OH)D] serum levels above 40 nmol/L in support of bone health (4). Serum 25(OH)D is used as an indicator of vitamin D status (1). In Canada, Vitamin D supplementation is advised for adults over 50 y of age (4). Guidelines from the United States, United Kingdom and Ireland have considered the evidence for COVID-19 and recommend Vitamin D supplementation for bone health, but not for treatment or prevention of COVID-19 (5-7).

Researchers have postulated that vitamin D deficiency could put individuals at higher risk of developing COVID-19 infection or having more serious disease progression/outcomes. Although outside of the scope of this research question, many observational studies have been conducted on the association between Vitamin D status and risk of COVID-19 infection, severe outcomes and mortality. We identified ten systematic reviews of low to high quality that each summarize 10-43 studies related to associations with COVID-19 clinical outcomes and vitamin D status (Appendix Table). Across studies within the systematic reviews, findings were not consistently significant. Overall consistent findings from the systematic reviews identified that vitamin D deficiency was higher among COVID-19 cases, and mean vitamin D levels were lower with increasing severity of COVID-19. For outcomes of COVID-19 severity, associations with low serum vitamin D were reported in some studies for hospitalizations, ICU admittance, mechanical ventilation or oxygen therapy as well as mortality. The groups likely to be vitamin D deficient were the same groups at risk of severe COVID-19. This relationship is complex, and finding an association of low vitamin D levels and more severe COVID-19 outcomes cannot be extrapolated to mean causation (8).

This evidence brief focuses on systematic reviews that summarize research on COVID-19 and vitamin D supplementation for treatment or prevention. Treatment studies are on COVID-19 patients and generally include high doses of vitamin D (large bolus up to 200 000 UI or doses up to 60 000 IU/day as single day, multi-day or weekly treatment) to see if this improves outcome. Prevention studies are either on a healthy

population or asymptomatic/mild cases of COVID-19 and include moderate doses of vitamin D (1000-9600 IU/day for 2-24 weeks) to see if it prevents COVID-19 or reduces the severity outcomes of COVID-19 infection. Systematic reviews on COVID-19 treatment or prevention with vitamin D supplementation were identified and where new trial data have been published since the most recent systematic reviews, primary research in published or prepublication format was also considered for inclusion if it had been published following the most recent systematic review, up to May 26, 2021. To date, no studies have been done in Canada on this topic.

Key Points

- Five systematic reviews (two published, one prepublication and two grey literature reports) on vitamin D treatment were identified and included literature up to March 2021, with one reporting they last checked for new research May 15, 2021. No additional primary research was identified on the therapeutic efficacy of vitamin D for COVID-19 (Table 1).
- Across the studies there was a lot of heterogeneity in treatment regimes from large single bolus of 200 000 IU Cholecalciferol to multi-day treatments (up to 14d) of 1000-60 000 IU cholecalciferol to 532-266 mcg calcifediol per day (5, 8-11).
- The five systematic reviews included three published randomized controlled trials (RCT) and one prospective cohort conducted in adults and 2 quasi-experiments conducted in geriatric populations evaluating Vitamin D as a treatment for patients with COVID-19 (Table 1).
    - One of three RCTs found that vitamin D treatment in COVID-19 patients may reduce the risk of severe disease progression (admittance to ICU) (RR 0.04, 95%CI 0.01- 0.29, 1RCT, 76 observations) (5, 8-11). A small prospective cohort reported reduced ICU admission (unadjusted OR = 0.13, 95%CI 0.03–0.6) among those that received 1000 IU vitamin D3 per day (10).
    - Two RCTs found that vitamin D treatment did not significantly reduce mortality compared to the standard care control group (RR 0.56; 95%CI 0.05 – 5.85, 2 RCTs, 313 observations) (5, 8-11), but a significant reduction in mortality was reported in two quasi-experimental studies on geriatric populations and one RCT on adults (OR 0.26; 95%CI 0.10-0.71) (11).
    - No association with adverse events and vitamin D treatment were reported. In one trial (n=237) one vomiting event was recorded following a large single bolus of 200 000 IU cholecalciferol, however an association with treatment was not found (RR 2.98; 95%CI 0.12-72.30) (9).
- No systematic reviews or studies were found on supplementation of vitamin D to prevent COVID-19 or reduce COVID-19 severity.
- There were 38 clinical trials registered on clinicaltrials.gov that included a form of vitamin D supplementation (dosing 1000-9600 IU/day for 2-24 weeks in healthy population and mild COVID-19

cases) or treatment (large bolus or high daily doses up to 60 000 IU/day as single day or multi-day or weekly treatments) and COVID-19 outcomes, six indicated they were completed as of May 28, 2021, but have not yet posted results. This remains an area of active research and the results of new studies may change the conclusions of this evidence brief.

Overview of the Evidence

For vitamin D as a treatment for COVID-19, four systematic reviews with AMSTAR 2 rating of high to low quality (herein referred to as AMSTAR) included three RCTs and two quasi-experiments, each with some risk of bias concerns and missing information in the study protocols (12). There were also variations in the vitamin D treatment and standard of care (control group care) across studies. No systematic reviews identified studies on supplementation of vitamin D and COVID-19 outcomes. Thus, at present there is insufficient evidence to determine the benefits and any potential harms of vitamin D supplementation as a treatment of COVID-19 and no published evidence on the benefits and potential harms of vitamin D supplementation for prevention of COVID-19. Additional controlled trials, which may already be initiated based on the trials registered, are needed to confidently evaluate whether there are benefits to vitamin D supplementation for treatment or prevention. The overall confidence in the current results is low and additional research is likely to change the conclusions of this review.

CONTENTS

VITAMIN D SUPPLEMENTATION OR THERAPEUTIC USE FOR COVID-19

Table 1. Vitamin D Supplementation or Use as a Therapeutic for COVID-19 (n= 5 systematic reviews)

STUDY	KEY OUTCOMES
Stroehlein (Cochrane) (8) *new* Living Systematic Review (AMSTAR high quality) Germany* May 24, 2021 (search date Mar 11, 2021)	- Vitamin D as a treatment for COVID-19 assessed by RCTs: o 3 RCTs with 356 participants of whom 183 received vitamin D treatment. 2 studies included moderate/severe COVID-19 and 1 included asymptomatic/mild COVID-19. 1 RCT was at low risk of bias and 2 had some concerns due to selective

	reporting. Treatments were a single high dose of oral cholecalciferol or multiple doses of oral calcifediol. o 2 RCTs found vitamin D supplementation made no difference to all cause mortality and 1 RCT found no difference in the need for mechanical ventilation. o There was conflicting evidence (protective RR 0.04, not significant RR 0.75) for a possible protective effect against ICU admission in 2 RCTs. o One study on mild COVID-19 cases did not report any of the prioritized severity outcomes, instead they report on viral clearance, inflammatory markers and changes in vitamin D serum levels. o The SR identified 21 completed or on-going trials without published results that would be relevant to this review, thus future results may change the conclusions of any updates to this review. - The treatments included: o Murai: Cholecalciferol 200 000IU in 1 dose o Rustogi: Cholecalciferol 60 000IU/ day for 7 days o Castillo: Calcifediol 0.532 mg on day 1, 0.266 mg on days 3 and 7, and then weekly until discharge or ICU admission. - Conclusion: there was insufficient evidence to determine the benefits and harms of vitamin D supplementation as a treatment of COVID-19.
Bassatne (Metabolism) (10) *new* Systematic review and meta-analysis (AMSTAR rating low quality) Lebanon* Mar 24, 2021 (search date Dec 18, 2020)	- 31 observational studies, low quality and certainty in the evidence, and 3 RCTs were included. - Treatment studies: o The 3 RCTs did not show an improvement in severity outcomes or mortality except Castillo reported Vitamin D was associated with lower ICU admission OR 0.03 (95% CI: 0.003–0.25), however, this was a small trial with uncertain risk of bias. o This SR identified 32 on-going trials that may be relevant to this review.

	○ 1 small prospective cohort found treatment with vitamin D3 1000IU/day for 14 days was associated with lower risk of COVID-19 ICU admission (unadjusted OR = 0.13, 95% CI 0.03–0.6). - Associations with low Vitamin D levels: ○ Mortality risk was higher for those with low vitamin D levels (RR 2.1, 95% CI [0.9–4.8]; I^2 = 76%, 7 studies) and three studies using a 25(OH)D <30ng/ml cut-off showed a even higher risk of mortality (RR = 3.1, 95% CI [1.4–6.8]; I^2 = 0%, 3 studies). ○ ICU risk was higher for those with low vitamin D levels (RR 4.89, 95%CI [0.54 - 44.26]; I^2 = 85%, 3 studies). ○ Risk of hospitalization was higher for those with low vitamin D levels in 2/3 studies. ○ Risk of SARS-CoV-2 positivity for those with low vitamin D levels was significant for 25 (OH)D <30ng/ml (RR = 1.5, 95% CI [1.3, 1.8], I2 = 0%, 2 studies).
National Institute for Health and Care Excellence (NICE), COVID-19 rapid guideline for practitioners on Vitamin D and evidence review (5) (AMSTAR high quality) UK Dec 17, 2020 (search date Oct 29, 2020)	- Vitamin D supplementation: ○ The guideline states vitamin D should not be recommended for the sole purpose of preventing COVID-19, as there was insufficient evidence to support this. ○ The recommendations for general population supplementation were related to maintenance of bone and muscle health. Insufficient exposure to sunlight has been linked to suboptimal vitamin D levels, and supplementation was recommended, particularly during the winter months. - Vitamin D for treating COVID-19 infection: ○ One RCT (Castillo et al) added Calcifediol (0.532mg) on admission, day 3 and 7 and then weekly in addition to standard of care. This study had serious risk of bias and was considered very low evidence. Results: 1/50 from the calcifediol treatment group and 13/26 controls were admitted to the ICU (OR 0.03 (95%CI 0.003-0.25).

	Mortality occurred in 0/50 and 2/26 in the treatment and control arms (OR 0.097, 95%CI 0.004-2.099). - Vitamin D status associations with COVID-19 outcomes: o 12 studies were included in their review (an additional 12 were not included because they were still in preprint). The association between COVID-19 status and vitamin D levels was conflicting (non-significant and negative association) and analyses were highly variable. Outcomes of severity were also conflicting for ICU, mechanical ventilation or oxygen therapy. One study reported a protective association with severe COVID-19 and supplementing with Vitamin D.
Nikniaz et al (prepublication MedRxiv) (11) Systematic Review and Meta-analysis (AMSTAR moderate quality) Jan 5, 2021 (search date Dec 16, 2020)	- This review included 4 clinical trials (2 RCTs (Castillo and Rastogi) and 2 quasi-experiments (Annweiler x2)), of 259 COVID-19 cases, hospitalized and not-hospitalized. Oral vitamin D supplementation, including cholecalciferol and calcifediol (n=139). - The quasi-experimental studies were conducted on elderly populations in long-term care and geriatric unit in the hospital. The treatment was a single 80 000IU dose of Vitamin D_3 for COVID-19 positive cases. Rastogi RCT was conducted on mild COVID-19 cases and received Cholecalciferol 60 000IU/ day for 7 days and Castillo was on hospitalized COVID-19 cases that received Calcifediol 0.532 mg on day 1, 0.266 mg on days 3 and 7, and then weekly until discharge or ICU admission. *(Note: Dosing in these studies is above upper limits of supplement safety for vitamin D.)* - Across 3 studies (two quasi-experiments and Castillo RCT), a significantly lower odds of mortality among the intervention groups compared with the control groups (OR = 0.264, 95% CI = 0.099–0.708, p-value = 0.008) was reported. Both quasi-experiments on geriatric populations reported a significant impact on survival. - Castillo et al. reported lower ICU admissions, odds ratio (OR) of 0.03 (95% CI: 0.003 - 0.25) and two studies showed significant improvement in clinical status with vitamin D treatment.

COVID-NMA Project (9) Living Synthesis (Not evaluated) France Updated May 11, 2021	- Three RCTs (Castillo, Rastogi, and Murai) were summarized and the summary of findings table indicates the evidence was very low quality. o Treatment with vitamin D may have a protective association with disease severity (RR: 0.04, 95%CI 0.01 - 0.29, 1 study (76 obs),very low certainty). o No association was identified for mortality (very low certainty) or adverse events at this time (low certainty).

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Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: (vitamin D, 25(OH)D, 25hydroxyvitaminD, dihydroxyvitamin, calcif*, cholecalcif*) or (zinc), an additional filter for systematic reviews was used to identify reviews initially.
A grey literature search was conducted targeting key government websites and evidence synthesis organizations for current evidence syntheses on these topics.
This review contains research published up to May 26, 2021.
Each potentially relevant reference was examined to confirm it addressed the review question and key findings were extracted into tables in the review.

Peer-review
This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX: VITAMIN D AND ASSOCIATIONS WITH COVID-19 CLINCIAL OUTCOMES

Appendix Table. Vitamin D Levels or Daily Supplementation and Association with COVID-19 Clinical Outcomes (n=10 systematic reviews)

STUDY	KEY OUTCOMES
Dramé (Nutrients) (13) *new* Systematic review (AMSTAR rating moderate quality) Apr 13, 2021 (search date Nov 5, 2020)	- Includes 11 observational studies on the association between COVID-19 outcomes and vitamin D in populations aged >60 years old. Studies were assessed to be of high – moderate quality. ○ 4 studies comparing COVID-19 outcomes in groups who supplement with vitamin D and those who don't found the supplementation groups had fewer severe outcomes in all 4 studies. Significance not described.

	○ 7 studies looked at the association between vitamin D deficiency and severity outcomes and found lower frequency of severe outcomes among those with sufficient vitamin D. Significance not described. - These data support that daily supplementation of vitamin D may have a protective effect via a positive impact on the immune system against respiratory infections.
Petrelli (J Steroid Biochem Mol Biol, short communication) (14) *new* Systematic review and meta-analysis (AMSTAR rating low quality) Italy* Mar 29, 2021 (search data Jan 31. 2021)	- 43 observational studies (612601 patients) were included and examined the association between vitamin D and risk, severity and mortality from COVID-19. ○ Vitamin D deficiency was associated with higher risk of COVID-19 (OR = 1.26; 95 % CI, 1.19–1.34; P < .01). Infection risk was higher with vitamin D values <20 ng/mL, (OR 1.5). ○ Vitamin D deficiency was associated with more severe COVID-19 (OR = 2.6; 95 % CI, 1.84–3.67; P < .01) ○ Vitamin D deficiency was associated with higher risk of COVID-19 mortality (OR = 1.22; 95 % CI, 1.04–1.43; P < .01) ○ Supplementation with Vitamin D was associated with reduced COVID-19 severity (n=6 studies) and mortality risk (n=7 studies) (OR = 0.27; 95 % CI, 0.11−0.66; P < .01 and OR = 0.41; 95 % CI, 0.21−0.81; P = .01).
Bassatne (Metabolism) (10) *new* Systematic review and meta-analysis (AMSTAR rating low quality) Lebanon* Mar 24, 2021 (search data Dec 18, 2020)	- 31 observational studies, low quality and certainty in the evidence, and 3 RCTs were included. - Treatment studies: ○ The 3 RCTs did not show an improvement in severity outcomes or mortality except Castillo reported Vitamin D was protective against ICU admission OR 0.03 (95% CI: 0.003–0.25) in a small trial with uncertain risk of bias. ○ 32 on-going trials were identified across trial registries (Jan 2021). ○ Treatment with vitamin D3 1000IU/day for 14 days was protective (unadjusted OR = 0.13, 95% CI [0.03–0.6], 1 study). - Associations with low Vitamin D levels:

	○ Mortality risk was higher for those with low vitamin D levels (RR 2.1, 95% CI [0.9–4.8]; I^2 = 76%, 7 studies) and three studies using a 25(OH)D <30ng/ml cut-off showed a even higher risk of mortality (RR = 3.1, 95% CI [1.4–6.8]; I^2 = 0%, 3 studies). ○ ICU risk was higher for those with low vitamin D levels (RR 4.89, 95%CI [0.54 - 44.26]; I^2 = 85%, 3 studies). ○ Risk of hospitalization was higher for those with low vitamin D levels in 2/3 studies. - Risk of SARS-CoV-2 positivity for those with low vitamin D levels was significant for 25 (OH)D <30ng/ml (RR = 1.5, 95% CI [1.3, 1.8], I2 = 0%, 2 studies).
Teshome (Frontiers in Public Health) (15) *new* Systematic review and meta-analysis (AMSTAR rating moderate quality) Ethiopia* Mar 5, 2021 (search data Dec 20, 2020)	- 14 studies (91120 participants) looked at Vitamin D levels and the risk of COVID-19 infection. 5 cohort, 5 case control, and 4 cross-sectional studies were included. ○ Vitamin D deficiency was associated with higher infection rates of COVID-19 (OR = 1.80; 95%CI: 1.72, 1.88, I^2 of 79.1%, 8 studies).
Akbar (Frontiers in Nutr) (16) *new* Systematic review and meta-analysis (AMSTAR rating high quality) Indonesia* Mar 29, 2021 (search data Dec 9, 2020)	- Low serum 25-hydroxyvitamin D (25-OHD) levels associated with susceptibility to COVID-19, severity, and mortality related to COVID-19 was investigated in 14 studies (999 179 participants): ○ Low serum Vitamin D was associated with higher infection rates of COVID-19 (OR = 2.71 [1.72, 4.29], p < 0.001; I^2: 92.6%) and age and male gender significantly increased the association. ○ Low serum Vitamin D was associated with higher severe COVID-19 (OR = 1.90 [1.24, 2.93], p = 0.003; I2: 55.3%). ○ Low serum Vitamin D was associated with higher mortality (OR = 3.08 [1.35, 7.00], p = 0.011; I2: 80.3%), intervening risk factors for mortality were male gender and diabetes, which require further exploration to determine the relationship.

	- A causal relationship cannot be established with the included observational studies.
Ghasemian (prepublication MedRxiv) (17) *new* Systematic review and meta-analysis (AMSTAR rating low quality) Iran* Feb 3, 2021 (search date Dec 18, 2020)	- 23 studies (11901 participants) were included. o The odds of getting COVID-19 were higher among vitamin D deficient persons (OR 3.3., 955CI 2.5-4.3, 3 studies). o The odds of developing severe COVID-19 were higher among vitamin D deficient persons (OR 5.1, 95%CI 2.6-10.3, 13 studies). o There was no association with mortality and vitamin D deficiency, 7 studies. - SARS-CoV-2 positivity has been shown to be inversely proportional to 25(OH) D serum levels.
National Institute for Health and Care Excellence (NICE), COVID-19 rapid guideline for practitioners on Vitamin D and evidence review (5) (AMSTAR high quality) UK Dec 17, 2020 (search date Oct 29, 2020)	- Vitamin D supplementation: o The guideline states vitamin D should not be recommended for the sole purpose of preventing COVID-19, as there was insufficient evidence to support this. o The recommendations for general population supplementation were related to maintenance of bone and muscle health. Insufficient exposure to sunlight has been linked to suboptimal vitamin D levels, and supplementation was recommended, particularly during the winter months. - Vitamin D for treating COVID-19 infection: o One RCT (Castillo et al) added Calcifediol (0.532mg) on admission, day 3 and 7 and then weekly in addition to standard of care. This study had serious risk of bias and was considered very low evidence. Results: 1/50 calcifediol treatment group and 13/26 controls were admitted to the ICU (OR 0.03 (95%CI 0.003-0.25). Mortality occurred in 0/50 and 2/26 in the treatment and control arms (OR 0.097, 95%CI 0.004-2.099). - Vitamin D status associations with COVID-19 outcomes: o 12 studies were included in their review (an additional 12 were not included because they were still in preprint). The associations between COVID-19 status

	and vitamin D levels were conflicting (non-significant and negative associations) and analyses were highly variable. Outcomes of severity were also conflicting for ICU, mechanical ventilation or oxygen therapy. One study reported a protective association with severe COVID-19 and supplementing with Vitamin-D.
Liu (IJID) (18) Systematic Review and Meta-analysis (AMSTAR rating high quality) China* Jan 2, 2021 (search date Sept 25, 2020)	- Across 10 observational studies (rated as medium to high quality by the review author) that included 361 934 participants (4178 COVID-19 cases), vitamin D deficiency was associated with increased risk of COVID-19 (OR = 1.43, 95% CI 1.00 to 2.05) and people with COVID-19 were shown to have significantly lower vitamin D levels. There was significant heterogeneity.
Pereira (Crit Rev Food Sci Nutr) (19) Systematic Review and Meta-analysis (AMSTAR rating low quality) Brazil* Nov 2, 2020 (search date Oct 9, 2020)	- Reports on the association between vitamin D deficiency and COVID-19 severity, via an analysis of the prevalence of vitamin D deficiency and insufficiency in people with the disease. - 27 observational studies considered at low (n=4) and high (n=23) risk of bias were included. - Higher odds of vitamin D deficiency was found in severe COVID-19 cases, OR 1.65 95%CI 1.30–2.09, I^2 35.7% and vitamin D levels were significantly lower among severe cases. - For severe deficiency, increased hospitalization OR 1.81 (95%CI 1.41–2.21, I^2 0.0%) and mortality OR 1.82 (95%CI 1.06–2.58, I^2 59.0%) were reported.
Das (prepublication MedRxiv) (20) Systematic Review (AMSTAR rating low quality) Multiple* Dec 3, 2020 (search date Nov 3, 2020)	- 11 published observational studies considered to be moderate to high quality by the review author were included. All studies examined the possible association between vitamin D deficiency and the incidence or severity of COVID-19 disease and were included. Analysis is descriptive, no meta-analysis was planned. - Individual study results were presented in the tables. Consistently there were associations between vitamin D deficiency and more severe COVID-19 and/or mortality.

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Emerging Evidence on COVID-19

Evidence Brief of vitamin D and zinc supplementation for therapeutic use on COVID-19 cases

Introduction

Is there evidence of the efficacy of therapeutic or prophylactic supplementation of vitamin D or zinc in the prevention or treatment of COVID-19?

Vitamin D and zinc are micronutrients that play various physiological roles, including a role in the immune system (1). Deficiencies of these micronutrients have been postulated to put individuals at higher risk of developing infection or more serious progression of disease, thus data on the association of deficiencies and COVID-19 disease outcomes are also summarized in this review. This evidence brief highlights the most recent systematic reviews on these micronutrients supplementation or status and COVID-19, where systematic reviews were not identified, primary research in published or prepublication format up to Jan 7, 2021 has been included. To date evidence in the Canadian context is pending.

Key Points

Vitamin D

- Vitamin D is a prohormone, a substance the body converts to a hormone, which is important for calcium homeostasis and bone health and is also implicated in other systems including immune function. The immunomodulating functions of vitamin D are complex and not fully understood. Research conducted prior to the pandemic suggests there is limited evidence of a potential benefit of vitamin D supplementation to lower risk of developing acute respiratory infections (2, 3).
- Nutrition standards in Canada include dietary recommendations for vitamin D for all age groups to help maintain 25-hydroxyvitamin D serum levels above 40 nmol/L in support of bone health (4). Vitamin D supplementation is advised for adults over 50 y of age (4). Other guidelines such as one from the United States and United Kingdom that have considered the evidence for COVID-19 continue to recommend supplementation for bone health, but not for treatment or prevention of COVID-19 (5, 6).
- Seven systematic reviews were identified in bibliographic databases, five of which included literature up to Fall 2020 and are summarized below along with three grey literature reports on the therapeutic efficacy of vitamin D for COVID-19 or acute respiratory tract infections.
- Five systematic reviews reported on observational studies that detailed associations between insufficient and/or deficient levels of vitamin D and increased risk of severe COVID-19 and mortality (Table 1). The associations across studies were not consistently significant, however vitamin D deficiency was shown to be high among COVID-19 cases, and mean vitamin D levels were lower with

increasing severity of COVID-19. For outcomes of severity, associations were reported in some studies for ICU admittance, mechanical ventilation or oxygen therapy as well as mortality. Most studies contributing to these outcomes were considered to have a high risk of bias. The groups at risk of vitamin D deficiency are the same groups at risk of severe COVID-19, this relationship is complex and although some studies have reported associations with low vitamin D and COVID-19 outcomes, these data cannot be extrapolated as a cause of the COVID-19 outcomes.

- Vitamin D as a treatment for patients with COVID-19 was assessed in three systematic reviews that collectively include two published and one prepublished randomized controlled trial (RCT) and 2 quasi-experiments conducted in adults (Table 1).
    - Evidence that vitamin D treatment in COVID-19 patients may reduce the risk of severe disease progression (RR 0.04, 95%CI 0.01 -0.29, 1RCT, 76 observations) (7).
    - Evidence that vitamin D treatment reduces mortality was not significant across 2 RCTs (RR 0.56; 95%CI 0.05 – 5.85, 2 RCT, 313 observations) (7), but was significant across two quasi-experimental studies and one RCT (OR 0.26; 95%CI 0.10-0.71) (8).
    - In one trial (n=237) a single adverse event was recorded (RR 2.98; 95%CI 0.12-72.30) (7).
- Several clinical trials were registered on clinicaltrials.gov. Of 45 on vitamin D, four indicated they were completed, but have not posted results. The objectives of these studies varied across treating COVID-19 with vitamin D (n=33) to exploring vitamin D levels (n=12) along with other micronutrients.

Zinc

- Zinc is an essential micronutrient that is required for adaptive and innate immune response (1). It has been used against other respiratory viruses and diarrhea in children with conflicting results across studies (9). Globally up to 20% of people are deficient in zinc, inadequate intake of zinc is more prevalent in low and middle income countries (9).
- Zinc has demonstrated antiviral properties *in vitro* studies have found that zinc inhibit viral RNA-dependent RNA polymerase against SARS-CoV-1 (1). Cellular uptake of zinc has been shown to increase when zinc is combined with a zinc ionophore such as hydroxychoroquine. Thus, many on-going clinical trials are examining the addition of zinc to existing treatments (1).
- One guidance document from the United States addressed zinc supplementation and COVID-19, the recommendation is against supplementation above the current dietary allowances (10).
- Two systematic reviews were identified. One high quality systematic review includes non-SARS-CoV-2 research and indicates moderate evidence for the role of zinc as a therapeutic in the prevention and reduction of severe disease progression across respiratory tract infection literature. The other review identified one retrospective observational study, also summarized in Table 2.

- A high quality systematic review last updated in August did not identify any RCTs related to the therapeutic use of zinc for COVID-19.
- As a therapeutic, two retrospective cohort studies evaluated the impact of adding zinc sulphate to standard of care treatment for COVID-19 cases:
    - Multivariable analysis showed an increased frequency of being discharged home (OR 1.53, 95 % CI 1.12–2.09) and reduction in mortality or transfer to hospice among patients who did not require ICU level of care remained significant (OR 0.449, 95 % CI 0.271–0.744) (11).
    - Zinc sulfate was not significantly associated with a change in risk of in-hospital mortality (adjusted hazard ratio, 0.66; 95% CI, 0.41 to 1.07; P = .09) in one retrospective cohort (12).
- This is an area of active research, 21 registered trials were identified on clinicaltrials.gov, three were completed, but have not posted results. Most registered trials were looking at supplementing or treating with zinc as a monotherapy or in combination with other compounds, others were exploring zinc levels along with other micronutrients.

Overview of the Evidence

For vitamin D as a therapeutic for COVID-19, three systematic reviews of high to low quality based on AMSTAR 2 criteria (herein referred to as AMSTAR) included three RCTs and two quasi-experiments, each with some risk of bias concerns and missing information in the study protocols (13). There were also variations in the vitamin D treatment and standard of care across studies. Thus, the overall confidence in this evidence was low and the conclusions of this review are likely to change with future research.

Five systematic reviews with an AMSTAR quality rating from high to low examined associations between vitamin D levels and COVID-19 infection, severity or mortality (13). The studies included in these reviews were observational studies, frequently retrospective in design and considered at high risk of bias. The outcomes summarized in each review varied as did the inclusion of prepublications, which meant each review examined a different subset of studies. Thus, the overall confidence in these results is low and additional research is likely to change the conclusions of this review.

Limited evidence was identified on the use of zinc in treatment of COVID-19. Two systematic reviews on zinc were identified; the quality ranged from low to high AMSTAR ratings (13). Two retrospective cohorts at high risk of bias due to their retrospective study design were also included. Thus, the overall confidence in these results is very low and additional research is likely to change the conclusions of this review.

CONTENTS

VITAMIN D

Table 1. Vitamin D and COVID-19

STUDY	KEY OUTCOMES
Effect of Vitamin D supplementation or use as a therapeutic	
National Institute for Health and Care Excellence (NICE), COVID-19 rapid guideline for practitioners on Vitamin D and evidence review (AMSTAR high quality) (5) UK Published December 17, 2020	- Vitamin D supplementation • The guideline states vitamin D should not be recommended for the sole purpose of preventing COVID-19, as there was insufficient evidence to support this. • The recommendations for general population supplementation were related to maintenance of bone and muscle health. Insufficient exposure to sunlight has been linked to suboptimal vitamin D levels, and supplementation was recommended, particularly during the winter months. - Vitamin D for treating COVID-19 infection • One RCT (Castillo et al) added Calcifediol (0.532mg) on admission, day 3 and 7 and then weekly in addition to standard of care. This study had serious risk of bias and was considered very low evidence. Results: 1/50 calcifediol treatment group and 13/26 controls were admitted to the ICU (OR 0.03 (95%CI 0.003-0.25). Mortality occurred in 0/50 and 2/26 in the treatment and control arms (OR 0.097, 95%CI 0.004-2.099) - Vitamin D status associations with COVID-19 outcomes • 12 studies were included in their review (an additional 12 were not included because they were still in preprint). The association between COVID-19 status and vitamin D levels were conflicting (non-significant and negative association) and analyses were highly variable. Outcomes of severity were also conflicting for ICU, mechanical ventilation or oxygen therapy. One study reported a protective association with severe COVID-19 and supplementing with Vitamin-D.

Nikniaz et al (prepublication MedRxiv) (8) Systematic Review and Meta-analysis (AMSTAR moderate quality) Jan 5, 2021 (search date Dec 16, 2020)	- This review included 4 clinical trials (2 RCTs (Castillo and Rastogi) and 2 quasi-experiments (Annweiler x2)), of 259 COVID-19 cases, hospitalized and not-hospitalized. Oral vitamin D supplementation, including cholecalciferol and calcifediol (n=139). The therapeutic protocols ranged from 60,000 to 80,000 IU dosing for a duration range of 7 to 14 days. *(Note: Dosing in these studies is above upper limits of supplement safety for vitamin D.)* - Across 3 studies, a significantly lower odds of mortality among the intervention groups compared with the control groups (OR = 0.264, 95% CI = 0.099–0.708, p-value = 0.008) was reported. Both quasi-experiments on geriatric populations reported a significant impact on survival. - Castillo et al. reported lower ICU admissions, odds ratio (OR) of 0.03 (95% CI: 0.003 - 0.25) and two studies showed significant improvement in clinical status with vitamin D treatment.
COVID-NMA Project (7) Living Synthesis (Not evaluated) France Jan 7, 2021 (Search date Dec 4, 2020)	- Three RCTs (Castillo, Rastogi, and Murai) were summarized and the summary of findings table indicates the evidence was very low quality however, treatment with vitamin D may have a protective association with disease severity (very low certainty), but no association was identified for mortality (very low certainty) or adverse events at this time (low certainty).
Association of vitamin D levels and clinical outcomes	
Liu et al. (IJID) (14) Systematic Review and Meta-analysis (AMSTAR rating high quality) Jan 2, 2021 (search date Sept 25, 2020)	- Across 10 observational studies (rated as medium to high quality by review author) included 361 934 participants (4178 COVID-19 cases), vitamin D deficiency was associated with increased risk of COVID-19 (OR = 1.43, 95% CI 1.00 to 2.05) and people with COVID-19 were shown to have significantly lower vitamin D levels. There was significant heterogeneity.
Pereira et al. (Crit Rev Food Sci Nutr) (15) Systematic Review and Meta-analysis (AMSTAR rating low quality)	- Reports on the association between vitamin D deficiency and COVID-19 severity, via an analysis of the prevalence of vitamin D deficiency and insufficiency in people with the disease.

Nov 2, 2020 (search date Oct 9, 2020)	- 27 observational studies considered at low (n=4) and high (n=23) risk of bias were included. - A higher odds of vitamin D deficiency was found in severe COVID-19 cases, OR 1.65 95%CI 1.30–2.09, I^2 35.7% and vitamin D levels were significantly lower among severe cases. - For severe deficiency, increased hospitalization OR 1.81 (95%CI 1.41–2.21, I^2 0.0%) and mortality OR 1.82 (95%CI 1.06–2.58, I^2 59.0%) were reported.
Das et al. (prepublication MedRxiv) (16) Systematic Review (AMSTAR rating low quality) Dec 3, 2020 (search date Nov 3, 2020)	- 11 published observational studies considered to be moderate to high quality by the review author were included. All studies examined the possible association between vitamin D deficiency and the incidence or severity of COVID-19 disease were included. Analysis is descriptive, no meta-analysis was planned. - Individual study results were presented in the tables. Consistently there were associations between vitamin D deficiency and more severe COVID-19 and/or mortality.
Ghasemian et al (prepublication MedRxiv) (17) Systematic Review (AMSTAR rating low quality) Oct 26, 2020 (search date Oct 10, 2020)	- 16 observational studies, rated by the author as fair quality, on possible associations between vitamin D deficiency and COVID-19 were included. - Across included COVID-19 cases the meta-analysis results indicated 48% (33-63) were vitamin D deficient and 29% (8-65) were insufficient and 25% (8-59) had normal levels of vitamin D. A similar analysis of a comparable control group was not presented in the review. - The other summaries reported in this review do not address the review question.
Not on COVID	
The Scientific Advisory Committee on Nutrition (SACN), rapid review on vitamin D and acute respiratory tract infections (ARTI). (2) UK December 2020	- This rapid review was updated from June to December to support the work of the NICE rapid guideline for practitioners on vitamin D. - This review reports a protective association with daily vitamin D supplementation and ARTIs for dosages >400IU and < 1000IU per day in 1-16 year olds (moderate quality evidence).

	ARTI: refers to any infection of the sinuses, throat, airways or lungs. Upper RTIs (URTI) include tonsillitis, laryngitis and the common cold. Lower RTIs (LRTIs) include bronchitis and pneumonia. Influenza affects both upper and lower respiratory tracts.

ZINC

Table 2: Zinc and COVID-19

Study	Key Outcomes
Hunter et al. (prepublication MedRxiv) (18) Systematic Review (AMSTAR rating high quality) Nov 4, 2020 (search date Aug 2020)	- This living systematic review identified 128 RCTs on zinc as a therapeutic, no RCTs specific to SARS-CoV-2 or COVID-19 met the inclusion criteria. - Studies of respiratory tract infections indicate treatment with zinc may prevent infection, reduce severity, and decrease duration of illness (moderate, low, low quality of evidence for these outcomes respectively). Quantitative outcomes available in text. - Adverse events were not higher than active controls and none were serious (moderate quality evidence). - Overall confidence in the results was very low due to risk of bias and indirectness across studies within outcomes.
James et al. (prepublication MedRxiv) (9) Systematic Review (AMSTAR rating low quality) Oct 19, 2020 (search conducted Aug 11, 2020)	- A systematic review of COVID-19 papers on zinc netted 1 prepublication (Carlucci included below) from 79 potentially relevant citations.
Yao et al (Chest, letter to the editor) (12) Retrospective cohort USA January 2021	- Retrospective study that evaluated mortality in COVID-19 patients (n=242) treated with or without zinc sulphate. - Results: Multivariate Cox regression, zinc sulfate was not significantly associated with a change in risk of in-hospital mortality (adjusted hazard ratio, 0.66; 95% CI, 0.41 to 1.07; P = .09).
Carlucci et al. (J Med Micro) (11)	- Retrospective observational study to compare outcomes among hospitalized COVID-19 patients ordered to receive

Retrospective cohort USA Sept 2020 (conducted Mar-Apr 2020)	hydroxychloroquine and azithromycin plus zinc sulphate (n=411) versus hydroxychloroquine and azithromycin alone (n=521). - The addition of zinc sulphate did not impact the length of hospitalization, duration of ventilation or intensive care unit (ICU) duration. - In univariate analyses, zinc sulphate increased the frequency of patients being discharged home, and decreased the need for ventilation, admission to the ICU and mortality or transfer to hospice for patients who were never admitted to the ICU. - After adjusting for the time at which zinc sulphate was added to our protocol, an increased frequency of being discharged home (OR 1.53, 95 % CI 1.12–2.09) and reduction in mortality or transfer to hospice among patients who did not require ICU level of care remained significant (OR 0.449, 95 % CI 0.271–0.744).

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching was conducted within these databases to identify relevant citations on COVID-19 and SARS-COV-2. Search terms used included: (vitamin D, 25(OH)D, 25hydroxyvitaminD, calcitriol*) or (zinc), an additional filter for systematic reviews was used to identify reviews initially.
A grey literature search was conducted targeting key government websites and evidence synthesis organizations for current evidence syntheses on these topics.
This review contains research published up to January 7, 2021
Each potentially relevant reference was examined to confirm it addressed the review question and key findings were extracted into tables in the review.

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Nouveaux éléments de preuve sur la COVID-19

Sommaire des éléments de preuve sur la supplémentation thérapeutique en vitamine D or en zinc pour des cas de la COVID-19

Introduction

Existe-t-il des éléments de preuve sur l'efficacité d'une supplémentation thérapeutique ou prophylactique en vitamine D ou en zinc dans la prévention ou le traitement de la COVID-19 ?

La vitamine D et le zinc sont des micronutriments qui jouent divers rôles physiologiques, notamment un rôle dans le système immunitaire (1). Les carences en ces micronutriments sont présumées exposer les individus à un risque plus élevé de développer une infection ou de faire évoluer la maladie vers une forme plus grave, c'est pourquoi les données sur l'association entre les carences et l'évolution de la maladie COVID-19 sont également résumées dans cette étude. Cette synthèse met en évidence les revues systématiques les plus récentes portant sur le niveau ou les supplémentations en micronutriments et la COVID-19, lorsque des revues systématiques n'ont pas été identifiées, les recherches principales sous forme publiée ou prépubliée jusqu'au 7 janvier 2021 ont été incluses. À ce jour, les éléments de preuve dans le contexte canadien sont en suspens.

Points clés

Vitamine D

- La vitamine D est une prohormone, une substance transformée en hormone par le corps, qui est importante pour l'homéostasie du calcium et la santé des os et qui est également impliquée dans d'autres systèmes, notamment la fonction immunitaire. Les fonctions immunomodulatrices de la vitamine D sont complexes et ne sont pas entièrement comprises. Les recherches menées avant la pandémie suggèrent qu'il existe peu d'éléments de preuve sur un bénéfice potentiel de la supplémentation en vitamine D dans la réduction du risque de développer des infections respiratoires aiguës (2, 3).
- Les normes de nutrition au Canada comprennent des recommandations alimentaires en matière de vitamine D pour tous les groupes d'âge afin de contribuer à maintenir des niveaux sériques de 25-hydroxyvitamine D supérieurs à 40 nmol/L en faveur de la santé des os (4). Une supplémentation en vitamine D est conseillée aux adultes de plus de 50 ans (4). D'autres lignes directrices, comme celle des États-Unis et du Royaume-Uni, qui ont examiné les éléments de preuve sur la COVID-19, continuent de recommander la supplémentation pour la santé osseuse, mais pas pour le traitement ou la prévention de la COVID-19 (5, 6).

- Sept revues systématiques ont été identifiées dans les bases de données bibliographiques, dont cinq comprenaient de la littérature jusqu'à l'automne 2020 et sont résumées ci-dessous, ainsi que trois rapports de littérature grise sur l'efficacité thérapeutique de la vitamine D pour la COVID-19 ou les infections aiguës des voies respiratoires.
- Cinq revues systématiques ont fait état d'études d'observation qui décrivaient des associations entre des niveaux insuffisants et/ou déficients de vitamine D et un risque accru de COVID-19 grave et de mortalité (Tableau 1). Les associations entre les études n'étaient pas toujours significatives, mais le nombre de carences en vitamine D s'est avéré élevé parmi les cas de COVID-19, et les taux moyens de vitamine D diminuaient de manière proportionnelle au niveau de gravité de la COVID-19. En ce qui concerne l'évolution de la gravité, des associations ont été signalées dans certaines études lors de l'admission en USI, la ventilation mécanique ou l'oxygénothérapie ainsi que la mortalité. La plupart des études contribuant à ces résultats ont été considérées comme présentant un risque de biais élevé. Les groupes présentant un risque de carence en vitamine D sont également ceux qui présentent un risque de COVID-19 grave, cette relation est complexe et bien que certaines études aient rapporté des liens entre le niveau peu élevé en vitamine D et la COVID-19, ces données ne peuvent pas être extrapolées comme cause de l'évolution de la COVID-19.
- La vitamine D en tant que traitement pour les patients atteints de COVID-19 a été évaluée dans trois revues systématiques qui comprenaient collectivement deux essais contrôlés randomisés (ECR) publiés et un prépublié, ainsi que deux quasi-expériences menées chez des adultes (Tableau 1).
    - Éléments de preuve confirmant que le traitement à la vitamine D chez les patients atteints de COVID-19 peut réduire le risque d'évolution de la maladie vers une forme grave (RR 0,04, 95 % IC 0,01 -0,29, 1RCT, 76 observations) (7).
    - Les éléments de preuve indiquant que le traitement à la vitamine D réduit la mortalité n'étaient pas significatifs dans 2 ECR (RR 0,56; 95 %CI 0,05 - 5,85, 2 ECR, 313 observations) (7), mais étaient significatifs dans deux études quasi-expérimentales et un ECR (OR 0,26; 95 %CI 0,10-0,71) (8).
    - Dans un essai (n=237), un seul événement indésirable a été enregistré (RR 2,98; 95 %CI 0,12-72,30) (7).
- Plusieurs essais cliniques ont été enregistrés sur clinicaltrials.gov. Sur les 45 personnes sous vitamine D, quatre ont indiqué qu'elles avaient été jusqu'au bout, mais n'ont pas communiqué les résultats. Les objectifs de ces études variaient du traitement de la COVID-19 avec de la vitamine D (n=33) à l'exploration des niveaux de vitamine D (n=12) ainsi que d'autres micronutriments.

Zinc

- Le zinc est un micronutriment essentiel nécessaire à la réponse immunitaire adaptative et innée (1). Il a été utilisé contre d'autres virus respiratoires et contre la diarrhée chez les enfants, avec des résultats

contradictoires d'une étude à l'autre (9). À l'échelle mondiale, jusqu'à 20 % des individus présentent une carence en zinc, l'apport insuffisant en zinc étant plus fréquent dans les pays à faibles et moyens revenus (9).

- Le zinc a démontré des propriétés antivirales; des études *in vitro* ont indiqué que le zinc inhibe l'ARN polymérase virale dépendante de l'ARN contre le SRAS-CoV-1 (1). Il a été démontré que l'absorption du zinc par les cellules augmente lorsque le zinc est combiné avec un ionophore de zinc tel que l'hydroxychoroquine. Ainsi, de nombreux essais cliniques en cours examinent l'ajout de zinc aux traitements existants (1).
- Un document d'orientation américain traite de la supplémentation en zinc et de la COVID-19, la recommandation est contre une supplémentation supérieure aux apports alimentaires actuels (10).
- Deux revues systématiques ont été identifiées. Une revue systématique de haute qualité inclut des recherches ne portant pas sur le SARS-CoV-2 et indique des éléments de preuve modérés sur le rôle du zinc comme thérapeutique dans la prévention et la réduction de l'évolution de la maladie vers une forme grave dans la littérature sur les infections des voies respiratoires. L'autre examen a identifié une étude d'observation rétrospective, également résumée dans le Tableau 2.
- Une revue systématique de haute qualité, mise à jour pour la dernière fois en août, n'a identifié aucun ECR lié à l'utilisation thérapeutique du zinc pour la COVID-19.
- Sur le plan thérapeutique, deux études de cohorte rétrospectives ont évalué l'impact de l'ajout de sulfate de zinc au traitement standard des cas de COVID-19:
    - L'analyse à plusieurs variables a révélé une augmentation de la fréquence des renvois à domicile (OR 1,53, 95 % CI 1,12-2,09) et la réduction de la mortalité ou du transfert dans un centre de soins palliatifs chez les patients qui n'avaient pas besoin du niveau de soins administré par une USI est restée significative (OR 0,449, 95 % CI 0,271-0,744) (11).
    - Le sulfate de zinc n'a pas été associé de manière significative à une modification du risque de mortalité hospitalière (rapport de risque ajusté, 0,66; IC à 95 %, 0,41 à 1,07; P = 0,09) dans une cohorte rétrospective (12).
- Il s'agit d'un domaine de recherche active, 21 essais enregistrés ont été identifiés sur clinicaltrials.gov, trois ont été achevés, mais n'ont pas encore publié de résultats. La plupart des essais enregistrés ont porté sur la supplémentation ou le traitement au zinc en monothérapie ou en association avec d'autres composés, d'autres ont exploré les niveaux de zinc en même temps que d'autres micronutriments.

Vue d'ensemble des éléments de preuve

Concernant la vitamine D en tant que thérapeutique pour COVID-19, trois revues systématiques de haute à basse qualité basées sur les critères AMSTAR 2 (ci-après dénommées AMSTAR) ont inclus trois ECR et deux quasi-expériences, chacune présentant un certain risque de biais et de manque d'informations dans les

protocoles d'étude (13). Dans les études, il existe également des variations dans le traitement à la vitamine D et dans la qualité des soins. Ainsi, le niveau de confiance générale dans ces éléments de preuve était peu élevé et les conclusions de cette étude sont susceptibles de changer selon les recherches futures.

Cinq revues systématiques avec une cote de qualité AMSTAR variant d'élevée à faible ont examiné les associations entre les niveaux de vitamine D et l'infection, la gravité ou la mortalité par COVID-19 (13). Les études incluses dans ces revues étaient des études d'observation, souvent de conception rétrospective et considérées comme présentant un risque élevé de biais. Les résultats résumés dans chaque étude étaient variables, de même que l'inclusion des prépublications, ce qui signifie que chaque étude a examiné un sous-ensemble différent d'études. Ainsi, le niveau de confiance générale dans ces résultats est peu élevé et d'autres recherches sont susceptibles de modifier les conclusions de cette étude.

Des éléments de preuve limités ont été identifiés concernant l'utilisation du zinc dans le traitement du COVID-19. Deux revues systématiques sur le zinc ont été identifiées; la qualité variait de faible à élevée selon le classement AMSTAR (13). Deux cohortes rétrospectives présentant un risque élevé de biais en raison de la conception des études rétrospectives ont également été incluses. Ainsi, le niveau de confiance générale dans ces résultats est très faible et d'autres recherches sont susceptibles de modifier les conclusions de cette étude.

TABLE DES MATIÈRES

VITAMINE D

Tableau 1. Vitamine D et COVID-19

ÉTUDE	PRINCIPAUX RÉSULTATS
Effet d'une utilisation ou d'une supplémentation en vitamine D à des fins thérapeutiques	
National Institute for Health and Care Excellence (NICE), COVID-19 rapid guideline for practitioners on Vitamin D and evidence review (AMSTAR, qualité élevée) (5) ROYAUME-UNI Publié le 17 décembre 2020	- Supplémentation en vitamine D • La directive stipule que la vitamine D ne doit pas être recommandée dans le seul but de prévenir la COVID-19, car il n'y avait pas suffisamment d'éléments de preuve pour l'étayer. • Les recommandations en faveur de la supplémentation de la population générale étaient liées au maintien de la santé des os et des muscles. Une exposition insuffisante au soleil a été liée à des taux de vitamine D

	sous-optimaux, et une supplémentation a été recommandée, en particulier pendant les mois d'hiver. - La vitamine D comme traitement de l'infection par COVID-19 • Un ECR (Castillo et al) a ajouté du Calcifediol (0,532 mg) à l'admission, le troisième et le septième jour, puis chaque semaine, en plus des soins standard. Cette étude présentait un risque sérieux de partialité et a été considérée comme un élément de preuve très peu fiable. Résultats : 1/50 du groupe de traitement au calcifédiol et 13/26 du groupe de contrôle ont été admis en USI (OR 0,03 (95 % IC 0,003-0,25). La mortalité observée était de 0/50 et 2/26 dans les groupes de traitement et de contrôle (OR 0,097, 95 %CI 0,004-2,099) - Associations entre le niveau de vitamine D et l'évolution de la COVID-19 • 12 études ont été incluses dans leur revue (12 autres n'ont pas été incluses, car elles étaient encore en phase de préimpression). L'association entre l'état de la COVID-19 et les taux de vitamine D était contradictoire (association non significative et négative) et les analyses étaient très variables. Les résultats des formes graves étaient également contradictoires pour les soins intensifs, la ventilation mécanique ou l'oxygénothérapie. Une étude a fait état d'une association protectrice entre une forme grave de la COVID-19 et la supplémentation en vitamine D.
Nikniaz et al (prépublication MedRxiv) (8) Revue systématique et méta-analyse (AMSTAR, qualité moyenne) 5 janvier 2021 (date de recherche, 16 décembre 2020)	- Cette revue a porté sur 4 essais cliniques (2 ECR (Castillo et Rastogi) et 2 quasi-expériences (Annweiler x2)), sur 259 cas de COVID-19, hospitalisés et non hospitalisés. Supplémentation orale en vitamine D, y compris cholécalciférol et calcifediol (n=139). Les protocoles thérapeutiques variaient de 60 000 à 80 000 UI de dosage pendant une durée de 7 à 14 jours. *(Note : le dosage dans ces études est supérieur aux limites maximales de sécurité des compléments en vitamine D)*

	- Dans trois études, une probabilité de mortalité significativement plus faible dans les groupes d'intervention que dans les groupes de contrôle (OR = 0,264, 95 % IC = 0,099-0,708, valeur p = 0,008) a été constatée. Les deux quasi-expériences sur des populations gériatriques ont fait état d'un impact significatif sur la survie. - Les essais Castillo et al. ont indiqué une baisse des admissions en USI, avec un rapport de cotes (RC) de 0,03 (IC à 95 %: 0,003 - 0,25) et deux études ont révélé une amélioration significative de l'état clinique avec le traitement à la vitamine D.
Projet COVID-NMA (7) Synthèse vivante (non évaluée) France 7 janvier 2021 (Date de recherche: 4 décembre 2020)	- Trois ECR (Castillo, Rastogi et Murai) ont été résumés et le tableau de synthèse des résultats indique que les éléments de preuve sont de très mauvaise qualité; toutefois, le traitement à la vitamine D peut avoir une association protectrice avec la gravité de la maladie (très faible certitude), mais aucune association n'a été établie concernant la mortalité (très faible certitude) ou les événements indésirables pour le moment (faible certitude).
Association des taux de vitamine D et des résultats cliniques	
Liu et al. (IJID) (14) Revue systématique et méta-analyse (AMSTAR, qualité élevée) 2 janvier 2021 (date de recherche, 25 septembre 2020)	- Dans 10 études d'observation (classées de qualité moyenne à élevée par l'auteur de la revue) portant sur 361 934 participants (4 178 cas de COVID-19), la carence en vitamine D était associée à un risque accru de COVID-19 (OU = 1.43, 95 % IC 1,00 à 2,05) et les personnes atteintes de COVID-19 présentaient des taux de vitamine D significativement plus faibles. Il y avait une forte hétérogénéité.
Pereira et al. (Crit Rev Food Sci Nutr) (15) Revue systématique et méta-analyse (AMSTAR, qualité faible) 2 nov. 2020 (date de recherche, 9 oct. 2020)	- Rapport sur l'association entre la carence en vitamine D et la gravité de la COVID-19, via une analyse de la prévalence de la carence et de l'insuffisance en vitamine D chez les personnes atteintes de la maladie. - 27 études d'observation considérées comme présentant un risque de biais faible (n=4) et élevé (n=23) ont été incluses.

	- Une probabilité plus élevée de carence en vitamine D a été constatée dans les cas graves de COVID-19, OU 1,65 95 %CI 1,30-2,09, I2 35,7 % et les niveaux de vitamine D étaient significativement plus faibles chez les cas graves. - Pour les carences graves, une augmentation du taux d'hospitalisation OU 1,81 (95 % IC 1,41-2,21, I2 0,0 %) et de la mortalité OU 1,82 (95 %CI 1,06–2,58, I2 59,0 %) ont été rapportés.
Das et al. (prépublication MedRxiv) (16) Examen systématique (évaluation AMSTAR, qualité faible) 3 déc. 2020 (date de recherche, 3 nov. 2020)	- 11 études d'observation publiées, considérées comme de qualité moyenne à élevée par l'auteur de la revue, ont été incluses. Toutes les études ayant étudié l'association possible entre une carence en vitamine D et l'incidence ou la gravité de la maladie COVID-19 ont été incluses. L'analyse est descriptive, aucune méta-analyse n'a été prévue. - Les résultats des études individuelles ont été présentés dans les tableaux. Des associations entre la carence en vitamine D et une forme plus grave de COVID-19 et/ou la mortalité ont systématiquement été observées.
Ghasemian et al (prépublication MedRxiv) (17) Examen systématique (évaluation AMSTAR, qualité faible) 26 oct. 2020 (date de recherche, 10 oct. 2020)	- 16 études d'observation, jugées de qualité moyenne par l'auteur, sur les associations possibles entre la carence en vitamine D et la COVID-19 ont été incluses. - Sur l'ensemble des cas COVID-19 inclus, les résultats de la méta-analyse ont indiqué que 48 % (33-63) présentaient une carence en vitamine D, 29 % (8-65) avaient un niveau insuffisant et 25 % (8-59) avaient un taux normal de vitamine D. Aucune analyse similaire d'un groupe témoin comparable n'a été présentée dans la revue. - Les autres résumés présentés dans cette revue ne traitent pas de la question de la revue.
Ne concerne pas la COVID	
Le Scientific Advisory Committee on Nutrition (SACN), rapid review on vitamin D and acute respiratory tract infections (ARTI). (2) ROYAUME-UNI	- Cette revue rapide a été mise à jour entre juin et décembre afin de soutenir le travail de la ligne directrice rapide du NICE sur la vitamine D et destinée aux praticiens. - Cette étude fait état d'une association protectrice entre une supplémentation quotidienne en vitamine D et les

Décembre 2020	ARTI pour les dosages >400 UI et < 1000 UI par jour chez les 1-16 ans (éléments de preuve de qualité modérée). *ARTI : désigne toute infection des sinus, de la gorge, des voies respiratoires ou des poumons. Les infections des voies respiratoires supérieures (IVRS) comprennent l'amygdalite, la laryngite et le rhume. Les infections des voies respiratoires inférieures (IVRI) comprennent la bronchite et la pneumonie. La grippe affecte les voies respiratoires supérieures et inférieures.*

ZINC

Tableau 2: Zinc et COVID-19

Étude	Principaux résultats
Hunter et al. (prépublication MedRxiv) (18) Revue systématique (AMSTAR, qualité élevée) 4 novembre 2020 (date de recherche, août 2020)	- Cette revue systématique vivante a identifié 128 ECR sur le zinc thérapeutique, aucun ECR spécifique au SRAS-CoV-2 ou à la COVID-19 ne remplissait les critères d'inclusion. - Des études sur les infections des voies respiratoires indiquent que le traitement au zinc peut prévenir l'infection, réduire la gravité et diminuer la durée de la maladie (qualité des éléments de preuve respectivement modérée, faible, faible pour ces résultats). Les résultats quantitatifs sont disponibles dans le texte. - Les événements indésirables n'étaient pas plus nombreux que dans le groupe de contrôle actif et aucun n'était grave (éléments de preuve de qualité moyenne). - La confiance générale dans les résultats était très faible en raison du risque de biais et du caractère indirect des études au sein des résultats.
James et al. (prépublication MedRxiv) (9) Examen systématique (évaluation AMSTAR, qualité médiocre) 19 octobre 2020 (recherche effectuée le 11 août 2020)	- Une revue systématique des articles sur la COVID-19 traitant du zinc a identifié 1 prépublication (Carlucci incluse ci-dessous) à partir de 79 citations potentiellement pertinentes.

Yao et al (Chest, letter to the editor) (12) Cohorte rétrospective ÉTATS-UNIS Janvier 2021	- Étude rétrospective ayant évalué la mortalité chez les patients atteints de COVID-19 (n=242) et traités avec ou sans sulfate de zinc. - Résultats : après analyse par régression de Cox à plusieurs variables, le sulfate de zinc n'a pas été associé de manière significative à une modification du risque de mortalité hospitalière (rapport de risque ajusté, 0,66; IC à 95 %, 0,41 à 1,07; P = 0,09).
Carlucci et al. (J Med Micro) (11) Cohorte rétrospective ÉTATS-UNIS Sept 2020 (effectuée en mars-avril 2020)	- Étude d'observation rétrospective visant à comparer les résultats chez les patients hospitalisés pour la COVID-19 à qui on a administré de l'hydroxychloroquine et de l'azithromycine plus du sulfate de zinc (n=411) par rapport à de l'hydroxychloroquine et l'azithromycine seules (n=521). - L'ajout de sulfate de zinc n'a pas eu d'incidence sur la durée de l'hospitalisation, la durée de la ventilation ou la durée du séjour en soins intensifs (USI). - Dans les analyses à variable simple, le sulfate de zinc a augmenté la fréquence des renvois de patients chez eux et a réduit le besoin de ventilation, l'admission en soins intensifs et le taux de mortalité ou le transfert dans un centre de soins palliatifs pour les patients qui n'ont jamais été admis en soins intensifs. - Après ajustement de l'heure à laquelle le sulfate de zinc a été ajouté à notre protocole, l'analyse multivariable a révélé une augmentation de la fréquence des renvois à domicile (OR 1,53, 95 % CI 1,12-2,09) et une réduction de la mortalité ou du transfert dans un centre de soins palliatifs chez les patients qui n'avaient pas besoin du niveau de soins administré par une USI est restée significative (OR 0,449, 95 % CI 0,271-0,744) (11).

Méthodes:

Un balayage quotidien de la littérature (publiée et prépubliée) est effectué par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont effectuées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et croisées avec les centres

d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste excel qui peut être consultée. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour identifier les citations pertinentes sur COVID-19 et SARS-COV-2. Les termes de recherche utilisés comprenaient: (vitamin D, 25(OH)D, 25hydroxyvitaminD, calcitriol*) ou (zinc), un filtre supplémentaire pour les revues systématiques a d'abord été utilisé pour identifier les revues.
Une recherche de littérature grise a été effectuée en ciblant les principaux sites web gouvernementaux et les organisations de synthèse des éléments de preuve pour obtenir des synthèses d'éléments de preuve actuels sur ces sujets.
Cette étude contient les recherches publiées jusqu'au 7 janvier 2021
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle répondait à la question de la revue et les principales conclusions ont été extraites dans des tableaux la revue.

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Emerging Evidence on COVID-19

Rapid Review of Multisystem Inflammatory Syndrome in Children (MIS-C)

INTRODUCTION

What are the epidemiological characteristics of multisystem inflammatory syndrome in children (MIS-C)?

The goal of this review is to summarize the epidemiological characteristics of multisystem inflammatory syndrome in children (MIS-C), which is also referred to as Paediatric Inflammatory Multisystem Syndrome (PIMS). MIS-C is an emerging condition that has been identified during the COVID-19 pandemic. Children presenting with Kawasaki-like illness following positive COVID-19 tests were first reported in the UK on April 27, 2020 (1). Case definitions have since been released by World Health Organization (2), the Centers for Disease Control in the United States (USA) (3), and the Royal College of Paediatrics and Child Health in the United Kingdom (4). As illustrated in the appendix, the three case definitions are similar, but not the same.

In this review, the term MIS-C is used for consistency, but broadly refers to the syndrome known as PIMS or MIS-C. There is no definitive diagnostic test for MIS-C. MIS-C is considered a separate, but related, syndrome to incomplete, complete or atypical Kawasaki disease (KD), Kawasaki disease shock syndrome (KDSS), toxic shock syndrome (TSS), and macrophage activated syndrome (MAS), with many overlapping features (5).This review includes evidence from articles where one of the three definitions were applied, or Kawasaki Disease or an inflammatory syndrome following COVID-19 was diagnosed.

The vast majority of the MIS-C articles were case reports and cohort studies. To give a rough indication of the strength of the evidence, the articles were then organized as large, medium, and small based on the number of MIS-C patients presented in the article ≥50, 6-49, and ≤5, respectively. Outcomes related to the epidemiology of MIS-C were summarized, including: demographics of MIS-C patients (age, sex, ethnicity/race and comorbidities), common severity outcomes (intensive care unit (ICU) admission, mechanical ventilation and extracorporeal membrane oxygenation (ECMO) utilization), mortality and the timing of MIS-C compared to acute COVID-19 infection. Note that similar cases of multisystem inflammatory syndrome have been reported in adults (known as MIS-A), which is the topic of a separate review available upon request: phac.evidence-donnees.probantes.aspc@canada.ca

KEY POINTS

There were 102 articles identified. Eleven articles were large cohort studies, describing more than 50 cases of MIS-C each. Forty-three articles were medium-sized, describing 6-49 cases of MIS-C each. Forty-eight articles were case reports where the number of cases of MIS-C described ranged from one to five.

Prevalence among Paediatric COVID-19 Cases

A large, international, multi-site study estimated that MIS-C affected between 0.5%-3.1% of all diagnosed pediatric COVID-19 patients and between 0.9%-7.6% of hospitalized pediatric COVID-19 patients aged less than 18 years (6). Three other articles looked at the frequency of MIS-C amongst hospitalized pediatric COVID-19 cases, with estimates varied from 6% in Peru (7) to 9% and 11% in the USA (8,9).

Age

MIS-C can affect children of any age as indicated by the ranges across articles. However, the median age of cases was in the range of 7-11 years. This was consistent in the large, medium and small articles.

Sex

In the large, medium and small articles, 57-58% of cases were male.

Comorbidities

In the articles that reported on comorbidities, the definition of comorbidity was inconsistent. The most commonly reported comorbidity was obesity. Obesity rates were consistent, but lower in small articles (8%) compared with medium (22%) and large (24-29%) articles. Another common comorbidity was asthma (6-18%). Patients with at least one comorbidity ranged from 19% when excluding obesity to 29% with obesity included. Few articles made comparisons of the rates of a given comorbidity to the prevalence of that comorbidity in the general pediatric population. One article found that the proportion of MIS-C patients with obesity is slightly higher than reported in the underlying population (10).

No articles attempted to disentangle the relationship between any given condition, COVID-19 infection and the development of MIS-C. For example, children with obesity or asthma could be more likely to contract COVID-19, and would therefore be overrepresented in MIS-C cases, without being specifically predisposed to MIS-C. This relationship is largely unexplored and needs to be studied further.

Ethnicity

Although some articles reported on ethnicity or race, few articles provided comparisons to the composition of the underlying population. However, in 14 medium-sized articles from the USA, Black and Hispanic children were the largest portion of patients at 36% and 29% respectively. A large article from the USA reported similar demographics (33% Hispanic and 27% Black) (10). The USA CDC states that, compared with White people, Black people are 2.6 times more likely and Hispanic people 2.8 times more likely to be infected with COVID-19 (11). This may partially or wholly explain any disproportionately high rates of MIS-C among these populations. This complex relationship needs to be studied further.

Onset of MIS-C relative to SARS-CoV-2 infection

Clinical case data suggests that there is a delay in the onset of MIS-C after acute infection with SARS-CoV-2. In three articles that documented the timing of acute COVID-19 infection for each MIS-C patient, the onset of MIS-C occurred 15-24 days after the onset of acute COVID-19 symptoms. A handful of articles (n=6) determined the time between the peak of MIS-C cases was approximately two to five weeks after the peak of

COVID-19 cases at the state or country level. The delay in onset is further supported by low positivity rates (<50%) using RT-PCR compared to IgG serology (>75%). This suggests that MIS-C is often a post-infection syndrome, having a delayed onset after the acute COVID-19 infection.

Severity Outcomes

The evidence suggests MIS-C patients often need intensive care, but that the overall survival rate is high. Eight large articles reported ICU admission rates of 21-80%; this was consistent with the medium-sized articles reporting 65% and the small articles reporting 74%. In addition, between 25-40% of MIS-C cases were intubated and 5-11% required ECMO. In the large articles, fatality rates ranged from 0 to 2.2% of hospitalized patients and 2.6% of MIS-C patients admitted to the ICU. This was consistent with the medium-sized articles that reported a 2% mortality rate but was lower than the 7% mortality reported in the small articles. There may be duplicate cases and deaths included in these totals, but the number of deaths could also be an underestimation as not all cases were resolved at the time of publication of the papers.

OVERVIEW OF THE EVIDENCE

In a literature search up to November 10, 2020, 102 articles were found that contain information on the epidemiological characteristics of MIS-C. Nearly all of these articles were case reports or retrospective cohorts.

There were 11 large articles that were mostly retrospective cohorts. These included two multi-national studies, four articles from the USA, three from the UK, and two from mainland Europe (Table 1).

There were 43 medium-sized articles (with a total of 861 cases of MIS-C) included in this review. These included both case series and retrospective cohort studies. In total, 18 were from the USA (379 cases), 13 from Europe (314 cases), four were from South America (50 cases), two from the Middle East (53 cases), two from India (42 cases) and one from South Africa (23 cases) (Table 2).

Case reports tend to be published when a new condition has been identified. They are good for generating hypotheses but are generally considered weak evidence. These 48 case reports are keeping with this trend as they capture some of the earlier case reports of MIS-C, prior to official recognition of the syndrome and to highlight the range of countries that have reported cases of MIS-C: 20 were from the USA, 13 from Europe, and the rest were from India (6 articles), the Middle East (5 articles), South America (2 articles), Africa (1 article) and Canada (1 article) (Table 3).

Limitations

- The majority of articles in this review are from the USA and Europe. In contrast, only two articles are from Africa, and only a portion of one review drew data from Asia. There is only one case report from Canada.

- There is an issue with double counting patients, as some articles were drawing from the same hospitals, regions or data sources. This could bias the results. When reported by the author, this is identified in the tables below. To avoid the extensive double counting, systematic and other reviews were not included.
- Many articles had incomplete data, especially co-morbidity and ethnicity data, which were often collected from only a portion of the cases.
- Because this is an emerging syndrome, case definitions and inclusion criteria have evolved over time. Each case may or may not meet one of the three standard case definitions, or the requirements for Kawasaki disease.
- None of the articles provide any follow-up to patients after they recover from acute MIS-C. Therefore, sequelae or further complications are still unknown.

CONTENTS

For each study contained in the evidence tables below, the following information on MIS-C is provided when available: Age, sex, ethnicity/race, comorbidities, severity outcomes (ICU admission, intubation, ECMO and death), PCR and serology testing results for SARS-CoV-2, and interval between acute COVID-19 infection and MIS-C onset. These variables are not included when they were not reported.

LARGE ARTICLES

Table 1: Articles describing 50 or more cases of MIS-C, by descending order of size

Study	Method	Key Findings
Godfred-Cato (2020) (10) Retrospective cohort USA Mar-Jul, 2020	Data on 570 MIS-C cases was collected from 40 state health departments in the District of Columbia and New York City	- Median age = 8 years (range = 2 weeks – 20 years) - 316/570 (55%) male - 187 (33%) were Hispanic, 153 (27%) Black, 61 (11%) White, 13 (2%) Asian, 48 (8%) other ethnicity and 108 (19%) unknown ethnicity. This study finds that the proportion of Hispanic, Black and White MIS-C patients with obesity is slightly higher than reported in the population.

		- 146 (26%) were obese, 48 (8%) had a chronic lung disease - 364 (64%) admitted to ICU, 69 (12%) required mechanical ventilation - 10 (2%) died - All but 5 tested positive for COVID-19 by either or both PCR or serological testing and the other 5 had an epidemiological link to a known COVID-19 case
Feldstein (2020) (12) Retrospective cohort USA Mar-May, 2020	Prospective and retrospective surveillance of 186 patients with MIS-C admitted to participating health centers in 26 states in the USA	- Median age = 8.3 years (IQR = 3.3-12.5 years) - 115/186 (62%) male - 57 (31%) were Hispanic, 46 (25%) Black, 35 (19%) Asian, 9 (5%) other ethnicity, 41 (22%) unknown ethnicity - 45 (24%) were obese. In addition, 51 (27%) had a comorbidity, including 33 (18%) with respiratory conditions, 5 (3%) with cardiac conditions, 10 (5%) with immune-related conditions and 20 (11%) with other conditions. - 148 (80%) admitted to ICU, 37 (20%) required mechanical ventilation, 8 (4%) required ECMO - 4 (2%) died - 131 tested positive for COVID-19 by either or both PCR or serological testing and the other 55 had an epidemiological link to a known COVID-19 case - MIS-C cases occurred a median of 25 days (range = 6-51 days) after acute COVID-19 infection
Deep (2020) (13) Retrospective cohort UK Mar-May, 2020 Note: 78 of the children in this study had been previously reported.	116 children admitted to 24 PICUs in the UK were assessed for acute kidney injury Patients with existing kidney problems were excluded	- Median age = 11 years (IQR = 7-14 years) - 76/116 (66%) male - 51 (45%) were Black, 29 (26%) Asian, 24 (21%) White, 9 (8%) other ethnicity - 20 (17%) had a comorbidity, including 5 (4%) with asthma, 3 (3%) with cystic fibrosis, 1 (1%) with chronic lung disease, 1 (1%) with autism, 10 (9%) others - 116 (100%) admitted to ICU (as required by the study design), 41 (35%) required mechanical ventilation, 3 (3%) required ECMO - 2 (2%) died

Belot (2020) (14) Retrospective cohort France Mar-May, 2020	All paediatric departments in France reported 108 cases of MIS-C diagnosed after March 1, 2020, to estimate the burden of this condition in France	- Median age = 8 years (IQR = 5-11 years) - 53/108 (49%) male - 72 (67%) admitted to ICU, 46 (43%) required mechanical ventilation - 1 (1%) died - 79 tested positive for COVID-19 by either or both PCR or serological testing. 16 had proven contact with COVID-19 cases and 13 were suspected to have had COVID-19 based upon symptoms and history. - MIS-C cases peaked 4-5 weeks after local COVID-19 cases peaked
Dufort (2020) (15) Retrospective cohort USA Mar-May, 2020	Hospitals in New York State that provide pediatric care reported 99 potential cases of MIS-C	- Age categories were given: 31 (31%) were aged 0 to 5 years, 42 (42%) were aged 6 to 12 years, and 26 (26%) were aged 3 to 20 years - 53/99 (54%) male - 31 (31%) were Black, 29 (29%) White, 4 (4%) Asian, 14 (14%) other ethnicity, 21 (21%) unknown ethnicity - 36 (36%) had a comorbidity, including 29 (29%) with obesity and 14 (14%) with chronic lung disease - 79 (80%) admitted to ICU, 10 (10%) required mechanical ventilation, 1 (1%) required ECMO - 2 (2%) died - 76/77 (99%) tested serology positive while 50/99 (56%) tested PCR positive - MIS-C cases peaked 31 days after local COVID-19 cases peaked
Antunez-Montes (2020) (16) Ambidirectional cohort Mexico, Colombia, Peru, Costa Rica and Brazil Jul-Aug, 2020	A physician group in Central and South America collected 95 MIS-C cases from 409 confirmed pediatric SARS-CoV-2 infections	- 95 cases of MIS-C were identified from 409 pediatric patients admitted to hospital with a positive COVID-19 test (23%) - Median age = 7 years (range = 1 month - 17 years). The MIS-C patients were significantly older than non-MIS-C pediatric patients admitted to hospital with COVID-19. - 52/95 (55%) male - 11 (12%) had comorbidities, and had significantly lower socioeconomic status than pediatric patients admitted with acute COVID-19

		- 20 (21%) admitted to ICU, 9 (9%) required mechanical ventilation - 2 (2%) died - All tested positive for COVID-19 by either or both PCR or serological testing
Davies (2020) (17) Retrospective cohort UK Apr-May, 2020 Note: Eight of the children included in this study had been reported previously	A description of 78 PIMS cases, aged 17 and under, admitted to PICUs in the UK	- Prior to COVID-19, historical data for similar inflammatory disease averaged 1 ICU admission per week (95% CI 0.85–1.22). In comparison, there was an average of 14 cases per week for PIMS, and a peak of 32 admissions per week during the study period. - Median age = 11 years (IQR = 8-14 years) - 52/78 (67%) male - 37 (47%) were Black, 22 (28%) Asian, 17 (22%) White, 2 (3%) other ethnicity - 17 (22%) had comorbidities, including 2 (3%) with major pre-existing conditions - 78 (100%) admitted to ICU (as it was required for inclusion in the study), 36 (46%) required mechanical ventilation, 3 (4%) required ECMO - 2 (3%) died - 33/35 (94%) tested serology positive while 17/78 (22%) tested PCR positive
Jonat (2020) (18) Retrospective cohort USA Mar-Jun, 2020	A description of all 54 cases of MIS-C identified in a single hospital in the given date range	- Median age = 7 years (range = 10 months - 20 years) - 25/54 (46%) male - 19 (35%) were White, 10 (19%) Black, 8 (15%) other ethnicity, 17 (31%) unknown ethnicity - 7 had pre-existing conditions (excluding obesity) - 31 (57%) admitted to the ICU. No patients required mechanical ventilation or ECMO - None died - 41/54 (97%) tested serology positive while 20/54 (34%) tested PCR positive
Cattalini (2020) (19) *(preprint)* Retrospective cohort	A survey sent to the Italian Pediatric Society and 53 patients	- Median age of KawaCOVID cases = 7 years (IQR: 4.5-11 years), while the median age of Kawasaki cases = 2 years

Italy Feb-May, 2020	met the diagnosis of "KawaCOVID" (equivalent to MIS-C)	(IQR: 1-4 years). Median age is significantly different (p<0.0001). - There was no significant difference in the sex ratio of KawaCOVID compared to Kawasaki disease - ICU admission was more common in KawaCOVID compared to Kawasaki cases (23.1% vs 1.1%; p<0.0001) - KawaCOVID cases had more serious cardiac involvement than Kawasaki cases - myocarditis (60.4% vs 3.1%; p<0.0001), pericarditis (26.4% vs 7.3%; p=0·0013), heart failure (35.8% vs 1%; p<0.00001) and others - All KawaCOVID patients tested positive for COVID-19 by either or both PCR or serological testing (31 tested serology positive while 14 tested PCR positive) - None died
Whittaker (2020) (20) Retrospective survey UK Mar-May, 2020 Note: Eight of the children included in this study have previously been reported	An online survey with data on 58 children who had been admitted to 8 hospitals in England with PIMS (MIS-C)	- Median age = 9 years (IQR = 5.7-14 years, range = 3 months – 17 years) - 38/58 (66%) male - 7 (12%) had comorbidities, including 3 (5%) with asthma, and 1 each (2%) with neurodisability, epilepsy, sickle cell trait, and alopecia - 29 (50%) of patients were admitted to ICU, 25 (43%) required mechanical ventilation, 2 (3%) required ECMO - 1 (2%) died - 40/46 (87%) tested serology positive while 15/58 (26%) tested PCR positive
Duarte-Salles (2020) (6) *(preprint)* Retrospective cohort US, Spain, France, Germany and South Korea Jan-Jun, 2020	Based on medical records, hospital billing data and insurance claims data from the US, Europe, and Asia, children diagnosed or hospitalized with COVID-19 were compared with a	- This study includes 55,270 children and adolescents diagnosed with COVID-19, including 3,693 hospitalized with COVID-19 and were compared with a historical cohort of 1,952,693 children diagnosed with influenza. - MIS-C was relatively uncommon, affecting between 0.5% and 3.1% of patients diagnosed with COVID-19, and between 0.9% and 7.6% of patients hospitalized with COVID-19. - MIS-C was thought to be linked with COVID-19, as similar syndromes are much less common in the historical influenza cohort.

	previous seasonal influenza cohort	

MEDIUM-SIZED ARTICLES

Table 2: Articles describing 6 to 49 cases of MIS-C, by descending order of size

STUDY	METHOD	KEY OUTCOMES
Mamishi (2020) (21) Retrospective cohort Iran Mar-Jun 2020	45 cases of MIS-C are described	- Median age = 7 years (range = 10 months – 17 years) - 24/45 (46%) male - 6 (13%) had pre-existing conditions - 5 (11%) died - 4 of them had underlying diseases (acute lymphocytic leukaemia, chronic kidney disease, cerebral palsy and Budd–Chiari syndrome) - 35 tested serology positive, 10 tested PCR positive
Miller (2020) (22) Retrospective cohort USA Apr-May 2020	44 cases of MIS-C are described	- Median age = 7.3 years (SD = 4.98 years, range = 7 months – 20 years) - 20/44 (45%) male - 15 (34%) were Hispanic, 9 (20%) Black, 9 (20%) White, 11 (25%) unknown ethnicity - 16 (36%) were overweight - 1 (2%) required mechanical ventilation - None died - 31/32 tested serology positive while 15/44 tested PCR positive
Belhadjer (2020) (23) Retrospective cohort France Mar-Apr 2020	35 cases of MIS-C that had cardiac involvement and required ICU admission are described	- Median age = 10 years (range = 2-16 years) - 18/35 (51%) male - 6 (17%) were overweight, 3 (9%) had asthma, 1 (3%) had lupus - 35 (100%) admitted to ICU, 22 (63%) required mechanical ventilation, 10 (29%) required ECMO - None died - 14 tested PCR positive, while 30 patients tested serology positive (28 IgG positive and 2 IgM positive)

Hameed (2020) (24) Retrospective cohort UK Apr-May 2020 Note: 8 patients were reported in other studies	35 cases of MIS-C under the age of 17 are described	- Median age = 11 (IQR = 8 years) - 27/35 (77%) male - 24 (69%) admitted to ICU, 7 (20%) required mechanical ventilation, 2 (6%) required ECMO - 1 (3%) died - 25 tested IgG positive and 23 IgM positive.
Sethuraman (2020) (25) Retrospective cohort USA Apr-Jul 2020	34 cases of MIS-C are described	- Median age = 6 years (IQR = 8 years) - 16/34 (47%) male - 23 (68%) were Black, other ethnicity/race not reported - 2 (6%) were obese and 9 (26%) had asthma 24 (71%) admitted to ICU, 8 (24%) required mechanical ventilation, 2 (6%) required ECMO - None died - 18/25 tested IgG positive, 8/34 tested PCR positive - MIS-C cases peaked 3 weeks after local COVID-19 cases peaked
Minocha (2020) (26) Retrospective cohort USA Mar-Jun 2020	33 cases of MIS-C are described	- Median age = 2.8 years (IQR = 1.4-9 years) - 19/33 (56%) male - 12 (36%) Hispanic, 10 (30%) White, 7 (21%) Black, 4 (12%) Asian - 7 (21%) were obese, 5 (15%) had asthma, 1 (3%) was born prematurely - 11 (33%) admitted to ICU - None died - 14/23 tested IgG positive, while 11/33 tested PCR positive
Kaushik, Aydin, (2020) (27) Retrospective cohort USA Apr-May 2020	33 cases of MIS-C that were admitted to ICU are described	- Median age = 10 years (IQR = 6-13 years) - 20/33 (61%) male - 15 (45%) were Hispanic, 13 (39%) Black, 3 (9%) White, 1 (3%) Asian, 1 (3%) other ethnicity - 16 (48%) of patients had comorbidities - 4 (12%) were obese, 2 (6%) were overweight, 5 (15%) had asthma, 3 (9%) had allergies/eczema, 2 (6%) had cardiac issues, 2 (6%) had hematological issues

Note: 4 patients were reported in other studies		- 33 (100%) admitted to ICU, 5 (15%) required mechanical ventilation, 1 (3%) required ECMO - 1 (3%) died - 11 tested PCR positive while 27 tested serology positive
Capone (2020) (28) Retrospective cohort USA Apr-May 2020	33 cases of MIS-C are described	- Median age = 8.6 years (IQR = 5.5-12.6 years) - 20/33 (61%) male - 8 (24%) were Black, 3 (9%) White, 3 (9%) Asian, 19 (58%) other/mixed/unknown. The ethnic rates of MIS-C were similar to the ethnic rates of the in-hospital population. - 12 (36%) were obese, 2 (6%) were overweight. The childhood obesity rate in the region is 18%, so obese patients are overrepresented in MIS-C cases in this study. - 26 (79%) admitted to ICU, 6 (18%) required mechanical ventilation - None died - 30 tested IgG positive - MIS-C cases peaked 5 weeks after local COVID-19 hospitalization peaked
Moraleda (2020) (29) Retrospective cohort Spain Mar-Jun 2020	31 cases of MIS-C are described	- Median age = 7.6 years (IQR = 4.5-11.5 years) - 18/31 (58%) male - 3 (10%) were obese, 4 (13%) had asthma, and 1 each (3%) had chronic cardiac disease, hematological disease and cancer - 20 (65%) admitted to ICU, 6 (19%) required mechanical ventilation - 1 (3%) died - 17 tested PCR positive, 10 IgM positive and 19 IgG positive - MIS-C cases peaked 1 month after local COVID-19 hospitalizations peaked
Alders (2020) (30) Retrospective cohort UK Mar-May 2020	31 cases of MIS-C are described	- Median age = 10.1 years (range = 8.7-13.9 years) - 21/31 (68%) male - 14 (45%) were Black, 9 (29%) Asian, 4 (13%) White, 3 (10%) mixed, 1 (3%) unknown ethnicity - 5 (16%) were overweight and 7 (23%) were obese

		- 14 (45%) required mechanical ventilation, 1 (3%) required ECMO - None died - 20 tested PCR positive while 28 tested serology positive
Felsenstein (2020) (31) Retrospective cohort UK Mar-Jun 2020	29 cases of MIS-C are described	- Median age = 6 years (IQR = 3.8-9.9 years) - 20/29 (69%) male - 12 (41%) were Caucasian, 6 (21%) South East Asian, 4 (14%) Black, 2 (7%) East Asian, 5 (17%) unknown ethnicity - None died - 14 tested serology positive, 3 tested PCR positive - MIS-C cases peaked 4 weeks after local COVID-19 cases peaked
Lee (2020) (32) Retrospective cohort USA Mar-Jun 2020	28 cases of MIS-C are described	- Median age = 9 years (range = 1 month - 17 years) - 16/28 (57%) male - 12 (43%) Hispanic, 10 (36%) were White, 5 (18%) Black - 14 (50%) of had comorbidities; 4 (14%) were obese, 3 (11%) had asthma, and 1 (4%) each had congenital heart disease, sickle cell anemia, and mitochondrial disorder - 17 (61%) admitted to ICU, none required mechanical ventilation or ECMO - None died - 17 tested PCR positive while 18 tested serology positive
Matsubara (2020) (33) Retrospective cohort USA Apr-Jun 2020	28 cases of MIS-C are described	- Median age = 11.4 years (IQR = 8-13.7 years) - 14/28 (50%) male - 13 (46%) were Black, 7 (25%) White, 4 (14%) Hispanic, 1 (4%) Asian, 3 (11%) unknown ethnicity - 8 tested IgG positive
Torres (2020) (34) Retrospective cohort Chile May-Jun 2020	27 cases of MIS-C in children up to age 14 are described	- Median age = 6 (range = 0-14 years) - 14/27 (52%) male - 23 (85%) parents were Chilean, 2 (7%) Venezuelan, 1 (4%) Haitian, 1 (4%) Peruvian - 4 (15%) were overweight or obese, 1 (4%) had asthma, 1 (4%) was immunocompromised

		- 16 (59%) of were admitted to ICU, 12 (44%) required mechanical ventilation - None died - 14 tested PCR positive, 10 tested serology positive
Carter (2020) (35) Prospective cohort UK Apr-May 2020	25 cases of MIS-C are described	- Median age = 12.5 years (range = 7.7-14.4 years) - 15/25 (60%) male - 10 (40%) were White, 9 (36%) Black, 5 (20%) Asian, 1 (4%) other ethnicity - 5 (20%) had comorbidities, including 2 (8%) with asthma (1 also with autism and 1 with eczema), 1 (4%) food allergy, 1 (4%) with hemoglobin C trait, and 1 (4%) with aplastic anemia and immunosuppression - 21 (84%) admitted to ICU, 2 (8%) required mechanical ventilation - None died - 18 tested serology positive and 1 tested PCR positive
Dionne (2020) (36) Retrospective cohort USA Mar-May 2020	25 cases of MIS-C are described	- Median age = 9.7 years (IQR = 2.7-15.0 years) - 15/25 (60%) male - 4 (16%) were obese, 4 (16%) had asthma, and 1 (4%) each had sickle cell anemia, mitochondrial disease, prematurity/respiratory failure - 14 (56%) admitted to ICU, 1 (4%) required mechanical ventilation - None died - 15 tested PCR positive, while 13 tested serology positive
Jain (2020) (37) Retrospective cohort India May-Jul 2020	23 cases of MIS-C are described	- Median age = 7.2 years (range = 0.8-14 years) - 11/23 (48%) male - 9 (39%) required mechanical ventilation - 1 died (4%) - 7 tested serology positive, 9 tested PCR positive - MIS-C cases peaked 2-4 weeks after local COVID-19 cases peaked
Webb (2020) (38) Retrospective cohort	23 suspected cases of MIS-C are described in	- Mean age = 6.6 years (95% CI = 4.8-8.4 years) - 17/23 (74%) male

South Africa Jun-Jul 2020	an area where COVID-19 testing is limited	- 18 (78%) were Black, 5 (22%) were South African coloured - 2 (9%) were obese, 4 (17%) prenatal exposure to HIV, but HIV-, 1 (4%) had asthma, 1 (4%) had leukemia - 12 (52%) admitted to ICU, 6 (26%) required mechanical ventilation - None died - 4 tested PCR positive - MIS-C cases occurred on average 24 days after acute COVID-19 infection (95% CI = 9-39 days)
Toubiana (2020) (39) Ambidirectional cohort France Apr-May 2020	21 cases of MIS-C are described	- 21 cases of MIS-C are described - Median age = 7.9 years (range = 3.7-16.6 years) - 24 (57%) parents of the patients were Black, 12 (29%) White, 4 (10%) Asian, 2 (5%) Middle Eastern - 24% of patients weighed above the 75th percentile - 17 (81%) admitted to ICU, 11 (53%) required mechanical ventilation - None died - 19 tested IgG positive, 8 tested PCR positive
Grimaud (2020) (40) Retrospective cohort France Apr 2020	20 cases of MIS-C admitted to ICU are described	- Median age = 10 years (range = 2.9-15 years) - 10/20 (50%) male - 20 (100%) admitted to ICU, 8 (40%) required mechanical ventilation, none required ECMO - None died - 15 tested serology positive, 10 tested PCR positive
Dhanalakshmi (2020) (41) Retrospective cohort India May-Jul 2020	19 cases of MIS-C are described	- Median age = 6 years (range = 13 months – 16 years) - 8/19 (42%) male - 1 (5%) had developmental delays - 12 (63%) admitted to ICU, none required mechanical ventilation or ECMO - None died - 8 tested serology positive, 4 tested PCR positive
Blumfield & Levin (42)	19 cases of MIS-C are described	- Median age = 8 years (range = 2 months – 18 years) - 10/19 (53%) male

Retrospective cohort USA Feb-Mar 2020		- 3 (16%) were obese, 5 (26%) had existing neurological impairment, and 1 (5%) each had congenital heart disease, cardiomyopathy, cancer, asthma, hypertension, sickle cell disease, prior thromboembolic events and Fragile X syndrome - 14 (74%) admitted to ICU, 8 (42%) required mechanical ventilation - 2 died (11%) – both had comorbidities - 18 tested PCR positive
Yonker (2020) (8) Retrospective cohort USA Aug 2020*	18 cases of MIS-C are described from a total of 192 hospitalized pediatric COVID-19 cases	- 18/192 (9%) children presenting to urgent care or hospitalized related to COVID-19 had MIS-C - Mean age = 7.7 years (SD = 7 years) - 14/18 (78%) male - 9 (50%) were White, 6 (33%) Hispanic, 2 (11%) White, and 1 (6%) Asian - 2 (11%) were obese, 1 each (6%) had inflammatory bowel disease, ADHD and autism
Cheung (2020) (43) Retrospective cohort USA Apr-May 2020	17 cases of MIS-C are described	- Median age = 8 years (range = 1.8-16 years) - 8/17 (47%) male - 3 (18%) had asthma - 1 (6%) admitted to ICU, none required mechanical ventilation or ECMO - None died - 9 tested serology positive, while 8 tested PCR positive
Pouletty (2020) (44) Retrospective cohort France Apr 2020	16 cases of MIS-C are described	- Median age = 12 years (range = 4.7-12.5 years) - 8/16 (50%) male - 4 (25%) were overweight, 2 (13%) had asthma - 7 (44%) admitted to ICU, 2 (13%) required mechanical ventilation, none required ECMO - None died - 7/8 tested IgG positive, while 11/16 tested PCR positive
Ramcharan (2020) (45) Retrospective cohort UK	15 cases of MIS-C are described	- Median age = 8.8 years (IQR = 6.4-11.2 years) - 11/15 (73%) male - 6 (40%) were Black, 6 (40%) South Asian, 3 (20%) other ethnicity

Apr-May 2020		- 4 (27%) required mechanical ventilation, none required ECMO - None died - 12 tested serology positive, 2 tested PCR positive
Riollano-Cruz (2020) (46) Retrospective cohort USA Apr-Jun 2020	15 cases of MIS-C are described	- Median age = 12 years (range = 3-20 years) - 11/15 (73%) male - 10 (67%) were Hispanic, 2 (13%) Black, 2 (13%) White, and 1 (7%) unknown ethnicity - 2 (13%) were obese, 2 (13%) were overweight, 4 (27%) had asthma, and 1 (7%) had hypothyroidism - 15 (100%) admitted to ICU, 3 (20%) required mechanical ventilation, 1 (7%) required ECMO - 1 (7%) died - 15 tested serology positive while 9 tested PCR positive - MIS-C onset began 21 days after acute COVID-19 infection (IQR= 21-24 days)
Rosat Consiglio (2020) (47) Retrospective cohort Italy, Sweden Mar-May, 2020	13 cases of MIS-C are described	- Median age = 106 months (IQR = 71-165 months) - 8/11 (73%) male (2 missing) - 3/4 (75%) tested IgG positive
Gaitonde (2020) (48) Case-control USA Mar-Jun 2020	12 cases of MIS-C are described	- Median age = 8 years (IQR = 5.5-11.5 years) - 9/12 (75%) male - 8 (80%) were Black, 3 (30%) White, 1 (10%) other ethnicity - None died
de Farias (2020) (49) Prospective cohort Brazil Apr-Jun 2020	11 cases of MIS-C are described	- Median age = 4 years (range = 7 months - 11 years) - 9/11 (82%) male - 2 (18%) were malnourished, 3 (27%) were obese, 3 (27%) were overweight - 11 admitted to ICU – required for inclusion (100%), 3 (27%) required mechanical ventilation - 2 (18%) died– both were malnourished. - 9 tested serology positive, 2 tested PCR positive

		- MIS-C onset began 15 days after acute COVID-19 infection (range = 7-60 days)
Ouldali (2020) (50) Natural experiment France Dec 2005-May 2021	10 cases of MIS-C are described after the onset of the COVID-19 pandemic, and compared to Kawasaki cases prior to April 2020	- Prior to April 2020, Kawasaki Disease hospitalization rate was 1.2 cases per month. In April 2020, this spiked to 6 cases per month (497% increase). Another peak in December 2009 reached 6 cases per month (365% increase) around the time of the influenza A H1N1 pandemic. - Median age = 11.5 years (range = 1-15 years) - 4/10 (40%) male - 6 (60%) admitted to ICU, none required mechanical ventilation or ECMO - None died - 5/10 tested IgG positive, 5/9 tested PCR positive - MIS-C cases peaked 2 weeks after local COVID-19 cases peaked
Verdoni (2020) (51) Natural experiment Italy Feb-Apr 2020	10 cases of MIS-C are described after the onset of the COVID-19 pandemic, compared to Kawasaki cases prior to Feb 2020	- This is an early study that compared Kawasaki disease rates between Jan 1, 2015, and Feb 17, 2020 (19 patients) with Feb 18, 2020 and April 20, 2020 (10 patients). The study found a 30 fold increase in Kawasaki like disease in early 2020 in Italy - Median age = 7.5 years (SD = 3.5 years) - 7/10 (70%) male - 8 tested IgG positive, 2 tested IgM positive, 2 tested PCR positive
Rostad (2020) (52) Ambidirectional cohort USA Mar-May 2020	10 cases of MIS-C are described	- Median age = 106 months (range = 71-165 months) - 6/10 (60%) male - 6 (60%) were Black, 3 (30%) White, 1 (10%) other ethnicity - 3 (30%) had underlying respiratory conditions - 10 (100%) admitted to ICU - All tested IgG and IgM positive, 2 tested PCR positive
Gruber (2020) (53) Retrospective cohort USA	9 cases of MIS-C are described	- Median age = 11.5 years - 4/9 (44%) male

Apr-Jun 2020		- 6 (67%) were Hispanic, 2 (22%) Black, 1 (11%) unknown ethnicity - 2 (22%) had asthma, 1 (11%) PTSD - None died - 9 tested serology positive, 3 tested PCR positive
Kim (2020) (9) Retrospective cohort USA Mar-Jul 2020	9 cases of MIS-C are described from a total of 83 hospitalized pediatric COVID-19 cases	- Of 83 hospitalized COVID-19 pediatric patients, 9 were diagnosed with MIS-C (11% of hospitalized children with COVID-19) - Age: 0-2 years (1), 2-4 years (5), 5-17 years (3)
Khan & Ullah (2020) (54) Case series Pakistan Aug 2020*	8 cases of MIS-C are described with data derived from news reports	- Age range = 5-15 years - All tested serology positive
Riphagen (2020) (55) Retrospective cohort UK Apr 2020	8 cases of MIS-C are described	- Median age = 8 years (range = 4-14 years) - 5/8 (63%) male - 6 (75%) were Black, 1 (13%) Asian, 1 (13%) Middle Eastern - 2 (25%) were obese, 1 (13%) overweight, 1 (13%) had autism, 1 (13%) hayfever - 8 (100%) admitted to ICU, 5 (63%) required mechanical ventilation, 1 (13%) required ECMO - 1 died (13%)
Perez-Toledo (2020) (56) *(preprint)* Retrospective cohort UK Apr-May 2020	8 cases of MIS-C are described, where patients tested PCR negative but serology positive	- Median age = 9 years (range 7-14 years) - 5/8 (63%) male - 6 (75%) admitted to the ICU - None died
Syrimi (2020) (57) *(preprint)* Retrospective cohort UK	7 cases of MIS-C are described	- Ages: <5 years (1), 5-10 years (3), 10-15 years (3) - 4/7 (57%) male - 4 (57%) were Black, 2 (29%) Asian, 1 (14%) White - 6 (86%) admitted to the ICU

Apr-May 2020		
Pereira (2020) (58) Retrospective cohort Brazil Apr-Jun 2020	6 cases of MIS-C are described, from a group of 66 hospitalized pediatric COVID-19 patients	- Of 66 hospitalized COVID-19 pediatric patients, 6 were diagnosed with MIS-C (9% of hospitalized children with COVID-19) - Median age = 7.8 years (range = 0.01-17.6 years) - 5/6 (83%) male - 5 (83%) had a pre-existing condition, 4 were immunocompromised, 3 had cancer, 1 had chronic kidney disease - 6 (100%) admitted to ICU, 5 (83%) required mechanical ventilation - 4 (67%) died
Chiara-Chilet (2020) (7) *(preprint)* Retrospective cohort Peru Mar-Jul 2020	6 cases of MIS-C are described, from a total of 91 hospitalized pediatric COVID-19 cases	- Of 91 hospitalized COVID-19 pediatric patients, 6 were diagnosed with MIS-C (7% of hospitalized children with COVID-19) - 2 (33%) admitted to ICU
Chiotos (2020) (59) Case series USA May 2020*	6 cases of MIS-C that were admitted to the ICU are described	- Median age = 7.5 years (range = 5-14 years) - 1/6 (17%) male - 2 (33%) were Black, 2 (33%) White, 2 (33%) unknown ethnicity - 6 (100%) admitted to ICU, 3 (50%) required mechanical ventilation, and none required ECMO - None died - 5 tested IgG positive, while 2 tested PCR positive
Diorio (2020) (60) Prospective cohort USA Apr-May 2020	6 cases of MIS-C are described	- Median age = 6 years (IQR = 5-7 years) - 2/6 (33%) male - 4 (66%) were White, 1 (17%) Black, 1 (17%) other ethnicity - 5 (83%) admitted to ICU, 2 (33%) required mechanical ventilation, and none required ECMO - None died

* Article publication date because case date(s) unavailable

SMALL ARTICLES

Table 3: Articles describing of one to five cases of MIS-C, by country and study size

STUDY	METHOD	KEY OUTCOMES
CASE SERIES		
Blondiaux (2020) (61) Case series France Apr 2020	Descriptive case series of 4 MIS-C patients	- 3 girls aged 6, 8 and 11; 1 boy aged 12 - All 4 admitted to ICU, 1 was intubated, none were placed on ECMO - None died - All tested PCR negative and IgG positive, 1 tested IgM positive
Labé (2020) (62) Case series France May 2020*	Descriptive case series of 2 MIS-C patients	- 2 boys aged 3 and 6 - No ICU admission, intubation or ECMO - None died - 1 tested PCR positive, no serology results
Licciardi (2020) (63) Case series Italy Arp 2020	Descriptive case series of 2 MIS-C patients	- 2 boys, aged 7 and 12, neither with comorbidities - Both admitted to ICU; neither intubated and no ECMO - None died - Both tested PCR negative, but IgG and IgM positive
Pang (2020) (64) Case series UK Mar-May 2020	Descriptive case series of 5 MIS-C patients	- 3 boys aged 8, 12 and 14; 2 girls aged 5 and 15 - 2 were Asian, 1 was Black, 1 was White and 1 was mixed-race - 2 had seizure disorders - 4 were admitted to ICU and intubated - None died - All tested PCR positive, no serology results
Ng (2020) (65) Case series UK Apr-May 2020	Descriptive case series of 3 MIS-C patients	- 2 boys aged 13 and 17; 1 girl aged 16 - 2 were Black, 1 was Asian - 1 was obese - All 3 admitted to ICU; 1 was intubated; no ECMO - None died - All 3 tested IgG positive, 1 tested PCR positive
Del Greco (2020) (66) Case series USA Oct 2020*	Descriptive case series of 4 MIS-C patients	- 3 girls aged 4, 10 and 16; 1 boy aged 13 - 1 had asthma, the rest had no comorbidities - 2 admitted to ICU; none intubated and no ECMO - None died - All 4 tested serology positive, 1 tested PCR positive

Rogo (2020) (67) Case series USA Apr-May 2020	Descriptive case series of 4 MIS-C patients	- 3 boys aged 5, 17 and 20; 1 girl aged 3 - 4 admitted to ICU, 2 intubated, 1 placed on ECMO - 1 died - All 4 tested PCR negative and IgG positive
Waltuch (2020) (68) Case series USA May 2020	Descriptive case series of 4 MIS-C patients	- 3 boys aged 5, 10, and 13; 1 girl aged 12 - 1 had hypothyroidism, another had asthma - 4 admitted to ICU; none intubated and no ECMO - None died - All 4 tested serology positive, 1 tested PCR positive
Heidemann (2020) (69) Case series USA Aug 2020*	Descriptive case series of 3 MIS-C patients	- 2 boys aged 5 and 7; 1 girl aged 6, with no comorbidities - 2 admitted to ICU and intubated; 1 was placed on ECMO - 1 died - 1 tested PCR positive, 3 tested serology positive
Schupper (2020) (70) Case series USA Jun 2020*	Descriptive case series of 2 MIS-C patients	- 2 boys aged 2 months, 5 years - 1 had tracheomalacia - Both admitted to ICU, intubated and placed on ECMO - 1 died - 1 tested serology positive, no PCR results
Spencer (2020) (71) Case series USA Sep 2020*	Descriptive case series of 2 MIS-C patients	- 1 girl aged 7; 1 boy aged 11 - 1 had seizure disorder - 1 admitted to ICU, none intubated and no ECMO - None died - Both tested PCR positive, no serology results
CASE REPORTS		
Khesrani (2020) (72) Case report Algeria Aug 2020*	Descriptive case report of 1 MIS-C patient	- 9 year-old girl with idiopathic medullar aplasia - Admitted to ICU and intubated, no ECMO - Patient died - Patient tested PCR positive, no serology results
De Paulis (2020) (73) Case report Brazil May 2020	Descriptive case report of 1 MIS-C patient	- 4 year-old girl with no comorbidities - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR and IgM negative, but IgG positive
Tam (2020) (74) Case report Canada Sep 2020*	Descriptive case report of 1 MIS-C patient	- 10 years old boy with no comorbidities - Admitted to ICU, not intubated and no ECMO - Patient survived - Patient tested PCR negative, serology positive

Klocperk (2020) (75) Case report Czechia Jul 2020*	Descriptive case report of 1 MIS-C patient	- 8 year-old girl with no comorbidities - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR positive and IgG positive
Acharyya (2020) (76) *(preprint)* Case report India May 2020*	Descriptive case report of 1 MIS-C patient	- 4 month-old boy with no comorbidities - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR positive, no serology results
Balasubramanian (2020) (77) Case report India Jul 2020*	Descriptive case report of 1 MIS-C patient	- 8 year-old boy with no comorbidities - Admitted to ICU; not intubated and no ECMO - Patient survived - Patient tested PCR positive, no serology results
Gupta (2020) (78) *(preprint)* Case report India Sep 2020*	Descriptive case report of 1 MIS-C patient	- 2 year-old boy - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR negative, parents IgG positive
Rauf (2020) (79) Case report India Apr 2020	Descriptive case report of 1 MIS-C patient	- 5 year-old boy with no comorbidities - Admitted to ICU; not intubated and no ECMO - Patient survived - Patient tested PCR and serology negative
Singhi (2020) (80) Case report India Oct 2020*	Descriptive case report of 1 MIS-C patient	- 8 year-old girl - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR negative, serology positive
Tiwari (2020) (81) Case report India Oct 2020*	Descriptive case report of 1 MIS-C patient	- 9 year-old girl - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR and serology positive
Bahrami (2020) (82) Case report Iran Jul 2020*	Descriptive case report of 1 MIS-C patient	- 5 year-old girl with no comorbidities - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR negative and serology positive
Parvaneh & Rahmani (2020) (83) *(preprint)* Case report	Descriptive case report of 1 MIS-C patient	- 7 year-old boy - Patient survived - Patient tested PCR positive, no serology results

Iran May 2020		
Regev (2020) (84) Case report Israel Aug 2020*	Descriptive case report of 1 MIS-C patient	- 16 year-old boy with no comorbidities - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR and IgG positive
Schnapp (2020) (85) Case report Israel Jun 2020*	Descriptive case report of 1 MIS-C patient	- 16 year-old boy with no comorbidities - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR negative, IgG positive
Buonsenso (2020) (86) Case report Italy Apr 2020	Descriptive case report of 1 MIS-C patient	- 11 year-old girl - Patient tested PCR positive, no serology results
Giannattasio (2020) (87) Case report Italy Jun 2020*	Descriptive case report of 1 MIS-C patient	- 9 year-old boy - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR negative, IgG and IgM positive
Yáñez (2020) (88) Case report Peru Jun 2020	Descriptive case report of 1 MIS-C patient	- 3 year-old girl - No other information provided
Tracewski (2020) (89) Case report Poland May 2020	Descriptive case report of 1 MIS-C patient	- 2 year-old boy - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR and IgM negative, IgG positive
Rodriguez-Gonzalez (2020) (90) Case report Spain Jun 2020*	Descriptive case report of 1 MIS-C patient	- 6 month-old boy with short bowel syndrome - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR negative, IgG positive
Bapst (2020) (91) Case report Switzerland Apr 2020	Descriptive case report of 1 MIS-C patient	- 13 year-old boy with no comorbidities - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR negative, serology positive
Yozgat (2020) (92) *(preprint)* Case report Turkey	Descriptive case report of 1 MIS-C patient	- 3 year-old girl - Patient survived - Patient tested PCR negative, no serology results

Jul 2020*		
Domico (2020) (93) Case report UK Apr 2020	Descriptive case report of 1 MIS-C patient	- 11 year-old boy with no comorbidities - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR and IgM negative, IgG positive
Chiu (2020) (94) Case report USA Jun 2020*	Descriptive case report of 1 MIS-C patient	- 10 year-old boy with no comorbidities - Admitted to ICU - Patient tested PCR positive, no serology results
Choi (2020) (95) Case report USA Aug 2020*	Descriptive case report of 1 MIS-C patient	- 19 years-old Hispanic man with sleep apnea and obesity - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR positive, no serology results
Clouser (2020) (96) Case report USA May 2020	Descriptive case report of 1 MIS-C patient	- 11 year-old Black girl with obesity - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR positive, no serology results
Dasgupta (2020) (97) Case report USA Jun 2020*	Descriptive case report of 1 MIS-C patient	- 8 year-old mixed race girl with no comorbidities - Admitted to ICU - Patient survived - Patient tested PCR and IgG negative
Deza Leon (2020) (98) Case report USA May 2020*	Descriptive case report of 1 MIS-C patient	- 6 year-old girl with no comorbidities - Admitted to ICU, intubated and was placed on ECMO - Patient survived - Patient tested PCR positive, no serology results
Dolhnikoff (2020) (99) Case report USA Aug 2020*	Descriptive case report of 1 MIS-C patient	- 11 year-old Black girl with no comorbidities - Admitted to ICU and intubated, no ECMO - Patient died - Patient tested PCR positive, no serology results
Dolinger (2020) (100) Case report USA May 2020*	Descriptive case report of 1 MIS-C patient	- 14 year-old boy with Crohn's disease - Patient survived - Patient tested PCR positive, no serology results
Greene (2020) (101) Case report USA Jun 2020*	Descriptive case report of 1 MIS-C patient	- 11 year-old girl with no comorbidities - Admitted to ICU; not intubated and no ECMO - Patient survived - Patient tested PCR positive, no serology results

Jones (2020) (102) Case report USA Jun 2020*	Descriptive case report of 1 MIS-C patient	- 6 month-old girl with no comorbidities - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR positive, no serology results
Kaushik, Ahluwalia, (2020) (103) Case report USA Sep 2020*	Descriptive case report of 1 MIS-C patient	- 5 year-old boy with no comorbidities - Admitted to ICU, intubated and placed on ECMO - Patient died - Patient tested PCR negative, serology positive
Nelson (2020) (104) Case report USA Oct 2020*	Descriptive case report of 1 MIS-C patient	- 15 year-old girl with no comorbidities - No ICU admission, intubation or ECMO - Patient survived - Patient tested PCR negative, no serology results
Rivera-Figueroa (2020) (105) Case report USA Jul 2020*	Descriptive case report of 1 MIS-C patient	- 5 year-old Black boy with no comorbidities - Admitted to ICU; not intubated and no ECMO - Patient survived - Patient tested PCR positive, no serology results
Stevens (2020) (106) Case report USA Apr 2020	Descriptive case report of 1 MIS-C patient	- 10 year-old Black girl with asthma - Admitted to ICU; not intubated and no ECMO - Patient survived - Patient tested PCR negative, IgG positive
Vari (2020) (107) Case report USA Apr 2020	Descriptive case report of 1 MIS-C patient	- 14 year-old boy - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR negative, IgG positive
Verkuil (2020) (108) Case report USA Aug 2020*	Descriptive case report of 1 MIS-C patient	- 14 year-old girl with no comorbidities - Admitted to ICU and intubated, no ECMO - Patient survived - Patient tested PCR negative, IgG positive

* Article publication date because case date(s) unavailable

Methods

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group at the Public Health Agency of Canada (PHAC). The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The

daily summary and full scan results are maintained in a Refworks database and an Excel list that can be searched.

Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: "MIS-C", "PIMS", "Kawasaki", "multisystem inflam", "multi-system inflam", "inflammatory multisystem", "inflammatory multi-system".

382 papers were identified on the topic of MIS-C, after the removal of duplicates. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review. 102 studies identified as relevant to the study question. This review contains research published up to November 10, 2020.

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APPENDIX

The case definition of MIS-C published by the USA Centers for Disease Control (CDC) (3) states:

- An individual aged <21 years presenting with fever (>38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours), laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological);

AND

- No alternative plausible diagnoses;

AND

- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

The definition of MIS-C published by the World Health Organization (WHO) (2) states:

- Children and adolescents 0–19 years of age with fever > 3 days

AND

- two of the following:
    - Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
    - Hypotension or shock.
    - Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
    - Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
    - Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

- Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

AND

- No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

AND

- Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

Finally, the definition of PIMS released by the UK Royal College of Paediatrics and Child Health (RCPCH) (4) states:

- A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopaenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki disease.

AND

- Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice).

AND

- SARS-CoV-2 PCR testing may be positive or negative.

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Preuve émergente sur la COVID-19

Revue rapide sur l'utilisation du couvre-visage pour prévenir la propagation de la COVID-19 en milieu communautaire, mise à jour 1

Introduction

Quelles sont les données probantes sur l'utilisation des couvre-visages pour prévenir la propagation de la COVID-19 en milieu communautaire?

Parmi toutes les mesures de santé publique qui ont été utilisées pendant la pandémie de COVID-19, le port du couvre-visage dans la collectivité est une mesure simple sur le plan technique, qui a également eu peu d'incidence sur l'économie (1). Mais est-elle efficace? Cette revue rapide résume les preuves empiriques sur l'efficacité des couvre-visages pour prévenir la propagation de la COVID-19 en milieu communautaire. Il s'agit d'une mise à jour de la précédente *Synthèse en bref sur le port du masque pour prévenir la COVID-19 en milieu communautaire, juillet 2020* (2). Cette revue ne comporte aucune donnée expérimentale sur la filtrabilité des différents types de masques ou de couvre-visages, des matériaux ou des combinaisons de matériels non médicaux, puisque cette question fait l'objet d'une revue distincte. Elle ne comprend pas non plus de modèles prédictifs visant à estimer les effets d'atténuation associés au port d'un couvre-visage seul ou en combinaison avec d'autres interventions de santé publique. La présente revue contient la documentation disponible jusqu'au 19 novembre 2020.

Points clés

- Quarante-neuf études portant sur l'efficacité des couvre-visages pour prévenir la propagation de la COVID-19 en milieu communautaire ont été recensées, soit une étude expérimentale, 15 études d'observation, 27 études écologiques et 6 revues.
- La majorité d'entre elles démontrent que le fait de porter un couvre-visage en milieu communautaire (études d'observation) et la mise en œuvre d'une politique sur le port du couvre-visage dans la communauté (études écologiques) assurent une protection contre la COVID-19, mais que la portée de cette protection varie. Cette variabilité de la protection peut être attribuable tant au moment où l'étude a été effectuée qu'aux facteurs de confusion et aux taux d'observance sur le port du couvre-visage.
- Les études d'observation effectuées au niveau individuel (n = 15) et lors d'un essai clinique randomisé (n = 1) ont permis d'établir les principales constatations suivantes :
    - Dans sept études d'observation, le port d'un couvre-visage a été associé à une diminution de 7,0 à 79 % du taux d'infection par la COVID-19.

- Un important essai clinique randomisé (DANMASK-19) effectué au Danemark a révélé des résultats non significatifs sur le port du couvre-visage (RC 0,82, IC à 95 %, de 0,54 à 1,23, P = 0,33), bien que cet essai ait comporté un bas niveau d'adhésion dans le groupe de personnes qui devaient porter le couvre-visage probablement en raison de la faible quantité de gens qui portaient un couvre-visage dans la communauté au moment où l'étude a été effectuée (3).
- Les enquêtes sur les grappes et les éclosions ont toujours indiqué un plus petit nombre de cas secondaires lorsque les cas de référence ou leurs contacts portaient des couvre-visages.
- Aucune preuve n'a été trouvée à propos des différences dans l'efficacité des couvre-visages chez les adultes et les enfants.

- Vingt-six études écologiques ont démontré que les politiques sur les couvre-visages étaient associées à une diminution des infections par la COVID-19 et des décès dus à ce coronavirus. On trouvait cependant une certaine variabilité dans le type de politique sur les couvre-visages mise en œuvre puisque bon nombre d'entre elles exigeaient le port universel du couvre-visage dans tous les lieux publics alors que trois autres portaient spécifiquement sur le port du couvre-visage pour les employés.
  - Neuf études ont calculé l'effet des différentes politiques sur le port universel du couvre-visage, ce qui a permis de voir que la diminution des infections par la COVID-19 variait de 3,2 à 48 %. On trouvait cependant une certaine variabilité dans le type de politique sur les couvre-visages mise en œuvre puisque bon nombre d'entre elles exigeaient le port universel du couvre-visage dans tous les lieux publics alors que trois autres portaient spécifiquement sur le port du couvre-visage pour les employés.
  - Une étude canadienne a démontré que les politiques sur le port du couvre-visage mises en œuvre en juin et en juillet en Ontario avaient entraîné une diminution de 25 à 31 % des cas de COVID-19 par semaine, réduction qui fut visible deux semaines après la mise en œuvre de la politique (4).
  - Une étude sur la réduction du nombre de cas de COVID-19 pendant le premier mois ayant suivi l'entrée en vigueur d'une politique sur le port de couvre-visage universel à New York a montré des différences associées à l'âge. Ainsi, on a pu voir une réduction de 20,8 % des cas chez les 65 à 74 ans et chez les 75 ans et plus pendant le premier mois, alors que cette réduction n'a atteint que 4,5 % chez les 25 à 44 ans et 8,1 % chez les 45 à 64 ans (5).
  - Trois études sur les politiques qui exigeaient le port du couvre-visage pour tous les employés dans tous les milieux de travail d'une région (comté ou État) ont révélé une diminution des infections et des décès liés à la COVID-19 (1, 6, 7), bien que ces résultats

n'aient pas été cohérents quant à l'ampleur ou à la signification statistique dans les différents modèles (1).

- Une étude menée aux États-Unis a révélé que les politiques sur le port du couvre-visage, qu'elles aient été adoptées de façon précoce ou tardive, étaient efficaces pour réduire l'infection par la COVID-19 (8).
- Avec un résultat de -1 % (IC à 95 %, de -13 à 8 %), la seule étude qui n'a pas montré de répercussions significatives en lien avec la politique sur le port du couvre-visage a été réalisée dans des conditions de confinement (9).
- Une étude a révélé que les pays qui avaient déjà adopté une norme en vertu de laquelle toute personne malade devait porter un couvre-visage affichaient un taux de croissance quotidien des cas de COVID-19 et des décès plus faible que les pays qui n'avaient aucune norme préexistante à cet effet (10).

- La mise en œuvre d'une politique sur le port du couvre-visage dans la communauté plutôt que le fait de simplement recommander aux gens de porter un couvre-visage a eu une grande incidence sur l'adhésion au port du couvre-visage dans les établissements publics. L'étude menée en Ontario a révélé une augmentation de 30 % du port du couvre-visage après la mise en œuvre des politiques à cet égard (4). Une étude similaire menée en Australie a révélé qu'une politique sur les couvre-visages augmentait de près de 50 % le port de ceux-ci (11). En revanche, une étude américaine a montré que les recommandations sur le port du couvre-visage n'avaient eu aucune incidence sur le taux de mortalité lié à la COVID-19 (1).

Vue d'ensemble des éléments de preuve

Quarante-neuf articles portant sur l'efficacité des couvre-visages pour prévenir la transmission de la COVID-19 dans les milieux communautaires ont été déterminés et inclus dans la présente revue. De ce nombre, 23 sont des préimpressions ou des rapports pour lesquels le processus d'examen par les pairs n'est pas terminé. Les publications qui indiquent l'efficacité des couvre-visages comprennent un essai clinique randomisé (n = 1), des études longitudinales (n = 2), des études de cohorte (n = 2), une expérience naturelle (n = 1), une étude cas/témoin (n = 1), des études transversales (n = 5), des enquêtes sur les grappes et les éclosions (n = 4), des études écologiques (n = 27), ainsi que des examens systématiques ou des revues rapides (n = 6).

Les études qui permettent de tirer des déductions à propos des individus incluent des essais cliniques randomisés qui constituent la norme de référence pour mesurer les répercussions d'une intervention, sachant que dans un tel essai, le processus de randomisation contrôle les variables confusionnelles et permet de présumer que l'échantillon est représentatif de la population. Les essais cliniques randomisés devraient donc,

de par leur conception, isoler l'effet de l'intervention. L'essai clinique randomisé inclus dans cette revue a été réalisé dans une communauté dans laquelle aucune politique sur le port universel du couvre-visage n'avait été adoptée. Il y a donc eu un manque en ce qui concerne l'adhésion au port du couvre-visage dans le groupe visé, les données et l'aveuglement des auteurs de l'essai. Cet essai clinique randomisé présente donc un certain risque de biais qui ébranle la confiance selon laquelle les recherches futures ne modifieront pas les conclusions obtenues.

Les quinze études d'observation ont évalué les données au niveau de l'individu. Les études de cohorte, les expériences naturelles, les études longitudinales et les études cas/témoin peuvent présenter un risque de biais modéré à élevé selon que la stratégie d'échantillonnage utilisée a permis ou non d'obtenir un échantillon représentatif de la population cible. Les études transversales donnent une image ponctuelle d'un problème, mais ne peuvent établir de lien de cause à effet, ce qui fait qu'elles fournissent des données probantes de basse qualité. Les enquêtes rétrospectives sur les grappes et les éclosions présentent également un risque élevé de biais. Puisque les résultats et facteurs de risque de nombreuses études étaient autodéclarés, ces études pourraient donc comporter un biais de rappel et de désirabilité sociale. De façon générale, les études d'observation ne peuvent pas établir le lien de causalité, mais elles peuvent cependant être utiles pour formuler des hypothèses ou comprendre les facteurs de transmission observés.

Les 27 études écologiques ont évalué les données au niveau de la population. Ces études sont peu coûteuses et peuvent être réalisées rapidement, puisqu'elles tirent largement parti des données accessibles au public. Elles présentent cependant un risque élevé de biais en raison de données disparates au niveau de la population, en plus d'être assujetties à des erreurs écologiques (puisque ce qui est vrai au niveau de la population pourrait ne pas s'appliquer au niveau individuel).

Les six revues ont été évaluées à l'aide de l'outil AMSTAR conçu pour les revues systématiques et visant à déterminer si l'exécution d'un examen pourrait minimiser les biais. Les revues rapides et systématiques étaient de qualité variable (de faible à élevée) en fonction du nombre de rapports et de questions inclus dans chacune. Malgré cela, les résultats étaient généralement les mêmes dans l'ensemble des documents examinés.

La documentation sur la COVID-19 évolue rapidement et, avec le temps, les études présentant un faible risque de biais peuvent être utilisées pour combler les lacunes existantes dans les connaissances. Une lacune importante en ce qui concerne les connaissances est le manque d'études qui permettent de tirer des conclusions sur l'adhésion au port du masque au niveau individuel (tant l'adhésion au port du couvre-visage que la façon appropriée de le porter) et ses effets sur l'infection par SRAS-CoV-2 en milieu communautaire. Il existe également peu de preuves de l'efficacité des couvre-visages ou des politiques sur les masques pour les employés, ainsi que dans les milieux scolaires.

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ÉTUDES EXPÉRIMENTALES ET D'OBSERVATION ÉVALUANT LA PRÉVENTION

Seize études, soit une étude expérimentale et 15 études d'observation, ont utilisé des données individuelles (tableau 1) pour évaluer l'efficacité des couvre-visages pour prévenir la propagation de la COVID-19 en milieu communautaire.

- L'étude expérimentale était un essai clinique randomisé de grande envergure (DANMASK-19) effectué au Danemark. Il a montré que lorsqu'il n'y avait pas de politique sur les couvre-visages déjà en place dans la communauté, le fait de recommander le port du masque n'était pas efficace. Même si les personnes qui portaient un couvre-visage étaient 18 % moins susceptibles d'être infectées par le SRAS-CoV-2 que celles qui n'en portaient pas, ces résultats n'étaient cependant pas significatifs (RC 0,82, IC à 95 %, de 0,54 à 1,23, P = 0,33). Le niveau variable d'adhésion au port du couvre-visage, les données manquantes et le manque d'aveuglement des auteurs de l'essai sont les principales limites de cette étude (3).
- Les 15 études d'observation comprenaient, quant à elles, deux études longitudinales, deux études de cohorte, une étude cas/témoin, cinq études transversales, quatre enquêtes sur les grappes et éclosions, et une expérience naturelle. La majorité de ces études ont démontré que le port d'un couvre-visage protégeait contre la COVID-19, mais l'ampleur variait cependant d'une étude à l'autre.
    - Une étude longitudinale effectuée dans 24 pays montre que le port généralisé du couvre-visage par 100 % des personnes dans un pays est associé à une réduction de 7 % (IC à 95 %, de 3,94 à 9,99 %) des cas quotidiens actifs de COVID-19. En 30 jours, ce taux cumulatif a permis d'obtenir une réduction des cas actifs de 88,5 % (IC à 95 %, de 68,7 à 89,2 %) (12).
    - Une diminution de 7,0 à 7,9 % des cas de COVID-19 associée à l'utilisation de couvre-visage a également été observée dans trois études transversales, deux études de cohorte, une étude longitudinale et une étude cas/témoin (12 à 18).
    - Une étude cas/témoin menée en Thaïlande a montré que le fait de porter un couvre-visage en tout temps, comparativement au fait de ne jamais en porter, était associé à une diminution du risque d'infection par le SRAS-CoV-2 (RCA 0,23, IC à 95 %, de 0,09 à 0,60), alors que le port

irrégulier du couvre-visage n'était associé à aucune diminution du risque (RCA 0,87, IC à 95 %, de 0,41 à 1,84) (18).

- Quatre enquêtes sur les grappes et les éclosions ont continuellement indiqué moins de cas secondaires lorsque les cas de référence ou leurs contacts portaient des couvre-visages (19 à 22).

Tableau 1. Études expérimentales et d'observation sur l'efficacité des couvre-visages pour se protéger contre la COVID-19 en milieu communautaire (n = 16)

RÉFÉRENCE	DESCRIPTION DE L'ÉTUDE	RÉSULTATS PERTINENTS
Essais cliniques randomisés (n = 1)		
Bundgaard (2020) (3) Essai clinique randomisé Danemark Avril et mai 2020	Cet essai clinique randomisé visait à déterminer si le port d'un masque chirurgical à l'extérieur du domicile réduisait le risque d'infection par le SRAS-CoV-2. L'étude a été menée dans une collectivité où le port du couvre-visage ne faisait pas partie des habitudes, mais était recommandé par la santé publique. 4 862 participants ont pris part à l'essai (3 030 personnes choisies au hasard devaient porter un couvre-visage alors que 2 994 ne devaient pas en porter). Limites de l'essai clinique : données manquantes, adhésion variable au port du couvre-visage, résultats déclarés par les patients lors des vérifications à domicile, absence d'aveuglement et aucune évaluation de la possibilité à savoir si les couvre-visages pouvaient réduire la transmission de la maladie entre les personnes qui portent un couvre-visage et les autres.	• Parmi les participants à qui l'on avait recommandé de porter un couvre-visage, 42 (1,8 %) ont attrapé l'infection associée au SRAS-CoV-2 tout comme et 53 participants témoins (2,1 %). • La différence entre les groupes était de 0,3 point de pourcentage (IC à 95 %, de 1,2 à 0,4 point de pourcentage, p = 0,38) (RC 0,82, IC à 95 %, de 0,54 à 1,23, p = 0,33). • L'adhésion au port du couvre-visage était autodéclarée. Selon le plus faible niveau d'adhésion indiqué pendant la période de suivi, 46 % des participants auraient porté le couvre-visage de la façon recommandée, 47 % l'auraient porté majoritairement de la façon recommandée et 7 % l'auraient porté d'une façon autre que celle qui avait été recommandée.
Études longitudinales (n = 2)		

Aravindakshan (2020) *préimpression* (12) Étude longitudinale À l'échelle mondiale Février à juillet 2020	Une analyse économétrique avec modèle de forme réduite a été utilisée pour mesurer les liens entre le port déclaré d'un couvre-visage et la propagation du SRAS-CoV-2 dans 24 pays. Une enquête longitudinale a été effectuée tous les 7 jours pour recueillir des informations sur les interventions non pharmaceutiques (INP) et l'adhésion au port du couvre-visage dans 24 pays.	• Le port généralisé d'un couvre-visage par 100 % des personnes dans un pays a été associé à une réduction de 7 % (IC à 95 %, de 3,94 à 9,99 %) des cas quotidiens actifs de COVID-19. En 30 jours, ce taux cumulatif a permis d'obtenir une réduction des cas actifs de 88,5 % (IC à 95 %, de 68,7 à 89,2 %).
Rader (2020) *préimpression* (23) Étude longitudinale États-Unis Juin et juillet 2020	Des enquêtes en série ont été effectuées du 3 juin au 27 juillet aux États-Unis (n = 378 207) afin de recueillir des données sur le port du couvre-visage dans la communauté et sur les comportements de distanciation sociale dans différentes collectivités. Ces données ont été combinées au Rt local, aux données sur la mobilité et aux informations sur les politiques mises en œuvre avant d'être analysées avec des analyses de régression multivariées afin de déterminer les facteurs associés au contrôle de la transmission communautaire du SRAS-CoV-2 aux États-Unis.	• Un lien important a été établi entre la proportion de personnes qui ont déclaré porter un couvre-visage et le contrôle de la transmission dans la collectivité (Rt < 1) : RC = 1,14 (IC à 95 %, de 1,07 à 1,20). • Le rapport de contrôle de transmission (Rt < 1) a augmenté (RC 3,53, IC à 95 %, de 2,03 à 6,43) pour chaque hausse de 10 % dans le port du couvre-visage en collectivité signalée dans l'enquête. • Dans toutes les analyses, le port d'un couvre-visage s'est révélé être un facteur de protection robuste dans le contrôle de la transmission dans la collectivité. • L'on avait prédit que le contrôle de la transmission dans la communauté serait plus élevé lorsque les gens porteraient le couvre-visage et respecteraient les mesures de distanciation sociale. Lorsque la distanciation sociale était basse malgré la forte utilisation du couvre-visage, le contrôle de transmission communautaire est descendu jusqu'à atteindre 35 %.

		• L'analyse n'a pas révélé d'augmentation importante dans l'utilisation des couvre-visages à la suite de la mise en œuvre de la politique sur le port du couvre-visage ni abordé les raisons pour ce faire. • L'adhésion au port du couvre-visage était plus élevée chez les femmes, les personnes âgées, les groupes ethniques non blancs ou hispaniques et les personnes à faible revenu. • Le couvre-visage était plus fréquemment porté dans les régions le long de la côte, à la frontière sud et dans les zones urbaines des États-Unis.
Études de cohorte (n = 2)		
Kwon (2020) *préimpression* (15) Étude de cohorte prospective États-Unis Mars à juillet 2020	Cette cohorte prospective d'étude des symptômes de la COVID-19 a été effectuée du 29 mars au 16 juillet et comprenait des participants des États-Unis ayant utilisé une application. Ces participants ont fourni des informations de base et sur la santé, avant d'être invités à enregistrer quotidiennement leurs informations relatives à la santé et à la COVID-19. 139 690 participants ont fourni des informations afin d'établir un lien entre l'utilisation autodéclarée d'un couvre-visage et le risque prévisible d'avoir la COVID-19. En raison du petit nombre d'utilisateurs de l'application ayant reçu un résultat positif à la COVID-19 pendant la période de l'étude, cette dernière a utilisé le risque	• Les personnes qui ont dit avoir porté un couvre-visage dans la communauté (parfois, la plupart du temps ou toujours) ont obtenu un RR ajusté de 0,35 (IC à 95 %, de 0,30 à 0,42) pour le risque prévisible d'être atteintes de la COVID-19 comparativement à celles qui ont déclaré n'avoir jamais porté de couvre-visage. • Le port autodéclaré du couvre-visage a été associé à une réduction de 69 %, de 71 % et de 63 %, respectivement, du risque prévisible d'être atteint de la COVID-19 pour les personnes qui vivent dans des collectivités où le respect de la distanciation sociale a été jugé excellent, passable et faible, respectivement. • Les résultats confirment l'efficacité du port du couvre-visage pour réduire la transmission de la COVID-19, même dans les milieux où le respect de la distanciation sociale est faible.

	prévisible d'être atteint de la COVID-19 comme approximation pour le nombre de tests positifs. L'analyse de survie a été ajustée pour l'âge, le sexe, l'origine ethnique, la condition, le tabagisme, les travailleurs de première ligne et les comorbidités.	
Wang (2020) (17) Étude de cohorte rétrospective Chine Février et mars 2020	Cette étude de cohorte rétrospective comprenait 335 personnes de 124 familles ayant eu au moins un cas de COVID-19 confirmé par un laboratoire à Beijing, en Chine, entre le 28 février et le 27 mars 2020.	• Le taux d'attaques secondaires dans les familles était de 23,0 % (77/335). • L'utilisation d'un couvre-visage par le cas primaire et les contacts de la famille avant l'apparition des symptômes chez le cas primaire a permis de réduire de 79 % la transmission (RC = 0,21, IC à 95 %, de 0,06 à 0,79). • Toutefois, le port du couvre-visage après l'apparition de la maladie chez le cas primaire ne s'est pas révélé très protecteur.
Études cas/témoin (n = 1)		
Doung-ngern (2020) (18) Étude cas/témoin Thaïlande Mars 2020	Cette étude cas/témoin rétrospective a utilisé les registres de recherche de contacts en Thaïlande pour établir son échantillon. 1 050 contacts de patients atteints de la COVID-19 entre le 1er et le 31 mars 2020 ont pris part à des entrevues rétrospectives. Les cas (n = 211) ont été définis comme des contacts asymptomatiques de patients atteints de la COVID-19 qui ont ensuite obtenu un résultat positif au test de dépistage de l'infection à SRAS-CoV-2, alors que les témoins (n = 839) étaient des contacts	• Le port d'un couvre-visage en tout temps (RCA de 0,23; IC à 95 %, de 0,09 à 0,60) était associé de façon indépendante à un risque plus faible d'infection par la COVID-19 que le fait de ne pas en porter. Toutefois, le port du couvre-visage à l'occasion (RCA de 0,87, IC à 95 %, de 0,41 à 1,84) n'a pas eu le même effet. • Les personnes qui portaient un couvre-visage en tout temps étaient plus susceptibles de se laver les mains et de mettre en œuvre les pratiques de distanciation sociale.

	asymptomatiques qui n'ont jamais obtenu de résultat positif.	
Études transversales (n = 5)		
Lopez (2020) *préimpression* (14) Étude transversale États-Unis Juillet 2020	Dans cette étude, on a déterminé la séroprévalence du SRAS-CoV-2 chez 753 membres du personnel des écoles publiques et analysé les corrélations entre la séropositivité, les antécédents autodéclarés (p. ex., port d'un couvre-visage) et les données démographiques.	• La séroprévalence a été estimée à 1,7 % (IC à 90 %, de 0,27 à 3,3). • Après avoir contrôlé six facteurs de confusion, les résultats de l'analyse multivariée ont révélé que les antécédents autodéclarés de port de couvre-visage réduisaient le risque de séropositivité (RR de 0,83, IC à 95 %, de 0,18 à 3,8).
Rodríguez-Barranco (2020) (24) Étude transversale Espagne Avril et mai 2020	Cette étude a examiné les voies possibles d'exposition au SRAS-CoV-2, les facteurs de risque et l'efficacité des mesures d'hygiène recommandées. Des renseignements autodéclarés ont été recueillis auprès de 2 086 personnes dans un sondage en ligne.	• 73,4 % des personnes ont dit avoir porté un couvre-visage, une fois le confinement terminé (34,9 % ont porté des masques FFP2/FFP3, 64,4 % des masques chirurgicaux et 0,7 % des couvre-visages maison). • La prévalence estimée de COVID-19 était de 4,7 % (49 cas confirmés et 50 cas soupçonnés). • Lorsqu'on ne tient compte d'aucune autre variable, on ne peut établir de lien entre le fait d'être ou non atteint de la COVID-19 et le port du couvre-visage (p = 0,205) puisque 3,9 % (masque FFP2/FFP3), 5,7 % (masque chirurgical), 0 % (couvre-visage maison), 3,1 % (aucun couvre-visage) et 5,8 % (ne pas être sorti de chez elles) respectivement, des personnes ont dit avoir été infectées de manière présumée ou confirmée par la COVID-19.
Payne (2020) (13) Étude transversale États-Unis	Une enquête a été menée auprès de membres de la Marine américaine (échantillon de commodité, n =382) associés à une éclosion de COVID-19 dans un porte-avions afin de recueillir des	• Les participants qui ont déclaré porter un couvre-visage (55,8 %) présentaient une plus faible probabilité d'être atteint de la COVID-19 (RC de 0,3, IC à 95 %, de 0,2 à 0,5) comparativement à ceux qui ont déclaré ne pas en porter (80,8 %).

Mars et avril 2020	renseignements sur l'utilisation autodéclarée du couvre-visage et d'autres mesures de protection (p. ex., éviter les aires communes, distanciation sociale). Les résultats ont été analysés afin de déterminer les liens avec le risque d'infection. Dans l'échantillon, 284 personnes avaient obtenu un résultat positif pour le SRAS-CoV-2 au moment de l'analyse du sérum ou avant celle-ci.	
Clipman (2020) (16) Étude transversale États-Unis Juin 2020	Les associations avec la positivité autodéclarée au SRAS-CoV-2 et l'adoption des INP ont été analysées par un sondage en ligne effectué auprès de 1 030 résidents du Maryland. La régression logistique a été utilisée pour déterminer les variables associées à des tests positifs pour le SRAS-CoV-2.	• Parmi l'échantillon de l'étude, 5 % (n = 55) ont déclaré avoir déjà obtenu un résultat positif au test de dépistage du SRAS-CoV-2. • 53 % des participants ont déclaré toujours porter un couvre-visage à l'intérieur et à l'extérieur. • Un petit lien a été établi entre le fait de porter un masque (toujours) et un résultat positif au test de dépistage du SRAS-CoV-2, soit un RCA de 0,63 (IC à 95 %, de 0,36 à 1,09).
van den Broek (2020) *préimpression* (25) Étude transversale États-Unis Avril à juin 2020	Cette étude a sondé des résidents (n = 454) de la collectivité, avant de leur offrir de passer des tests RT-PCR et sérologiques pour le SARS-CoV-2. Une analyse multivariée a ensuite été effectuée avec des probits pour établir de possibles liens.	• Ainsi, 2,2 % (IC à 95 %, de 0,8 à 3,6 %) des répondants qui faisaient partie de l'échantillon de l'étude ont obtenu un résultat positif au test sérologique du SRAS-CoV-2. • Le fait de porter un couvre-visage à l'extérieur du lieu de travail n'a pas créé de différence statistique importante entre les résidents qui ont obtenu un résultat positif (0,5 %, ET 0,189) ou un résultat négatif (0,7 %, ET 0,230) au test de dépistage de la COVID-19.

Enquêtes sur les grappes et les éclosions (n = 4)		
Hendrix (2020) (19) Enquête sur les grappes États-Unis Mai 2020	Cette enquête épidémiologique rétrospective a permis d'analyser les résultats de 139 clients qui ont été exposés à deux coiffeurs infectés par le SRAS-CoV-2 au Missouri, aux États-Unis. Les clients comme les coiffeurs portaient tous un couvre-visage.	• Des 139 clients ayant été exposés, 67 ont été testés. • Aucun cas secondaire symptomatique n'a été signalé, probablement en raison de l'utilisation des couvre-visages.
Cheng (2020) (20) Enquête sur les grappes Hong Kong Janvier à avril 2020	Cette enquête décrit les résultats des recherches effectuées à Hong Kong au cours des 100 premiers jours de la pandémie. On y a comparé le nombre de grappes de COVID-19 et le fait de porter ou non un couvre-visage. Hong Kong avait mis en place une politique sur le port obligatoire des couvre-visages, ce qui a permis d'obtenir un taux de respect estimé à 96,6 % (IC à 95 %, de 95,7 à 97,2 %).	• Au 100e jour de l'épidémie, 961 cas confirmés de COVID-19 avaient été déclarés à Hong Kong. De ces cas, 11 groupes de 113 personnes participaient de façon active à des activités sans couvre-visage, comme manger et boire dans un restaurant ou un bar, faire du karaoké et faire de l'exercice dans des centres d'entraînement, comparativement à 3 groupes de 11 personnes qui prenaient part à des activités avec couvre-visage dans leur lieu de travail (chi carré p = 0,036).
Hong (2020) (22) Enquête sur les grappes Chine Janvier à mars 2020	Les données cliniques et épidémiologiques ont été extraites rétrospectivement du 23 janvier au 1er mars 2020 des dossiers médicaux électroniques et des questionnaires individuels valides de 127 patients atteints de la COVID-19 à Zhejiang, en Chine.	• Avant leur diagnostic, 41 patients présymptomatiques avaient eu des contacts étroits avec les résidents locaux. • De ces personnes, 28 ont porté un couvre-visage et été en contact étroit avec 123 résidents, ce qui a entraîné 10 infections secondaires au SRAS-CoV-2. • Les 13 autres personnes, qui ne portaient pas de couvre-visage, ont été en contact étroit avec 74 résidents, ce qui a entraîné 14 infections secondaires au SRAS-CoV-2. • Le pourcentage de résidents locaux infectés par le SRAS-CoV-2 était beaucoup plus faible dans le groupe qui

		est entré en contact avec des personnes infectées portant un masque que dans celui des personnes qui sont entrées en contact avec des personnes infectées ne portant pas de masque (8,1 % contre 19,0 %; p < 0,001).
Liu (2020) (21) Enquête sur l'épidémie Chine 2020	Il s'agit d'une enquête épidémiologique rétrospective sur l'exposition au SRAS-CoV-2 dans les transports en commun. Elle décrit deux trajets d'autobus successifs effectués par une personne infectée et symptomatique au départ de Chongqing, le premier sans couvre-visage et le second avec un couvre-visage.	• Pendant le trajet en autobus où la personne infectée portait un masque, aucune personne n'a été infectée (14 passagers). • Au cours du trajet en autobus où la personne infectée ne portait pas de masque, 5 personnes sur 39 ont été infectées.
Expérience naturelle (n = 1)		
Pletz (2020) *préimpression* (26) Expérience naturelle Allemagne Avril 2020	Les effets du port universel d'un couvre-visage dans les lieux publics ont été comparés dans deux villes proches dont la taille et la structure communautaires étaient semblables. En ce qui concerne les INP, la ville de Jena a adopté une politique sur le port des couvre-visages au début d'une période de confinement de quatre semaines alors que la ville d'Erfurt n'a adopté sa politique sur le port du masque qu'à la fin de la période de confinement. Remarque : les couvre-visages en tissu et les foulards étaient acceptables tant qu'ils couvraient la bouche et le nez.	• Aucun nouveau cas de SRAS-CoV-2 n'a été observé à Jena 5 jours après la mise en œuvre de la politique obligeant le port du couvre-visage. • À Erfurt cependant, l'infection a continué de se propager au sein de la communauté pendant le confinement, jusqu'à ce que la politique sur le port obligatoire du couvre-visage dans la collectivité soit mise en œuvre, une fois le confinement levé. • Puisque ces observations peuvent être liées à d'autres facteurs, les conclusions tirées de cette étude sont limitées, mais cette étude offrait une occasion unique d'examiner les répercussions d'une politique sur le port du couvre-visage dans deux collectivités semblables.

IC = intervalle de confiance, RR = rapport de risque, INP = intervention non pharmaceutique, RC = rapport de cotes, Rt = nombre de reproduction effectif

ÉTUDES ÉCOLOGIQUES ÉVALUANT LES RÉPERCUSSIONS DES POLITIQUES ET DES NORMES SOCIÉTALES

Vingt-sept études écologiques sur l'incidence des recommandations et des politiques sur le port du couvre-visage afin de prévenir la propagation de la COVID-19 en milieu communautaire ont été recensées (tableau 2). Elles ont toutes analysé des données agrégées au niveau de la population afin d'estimer l'incidence des politiques sur le port du couvre-visage sur la réduction de la propagation de la COVID-19. Diverses approches et analyses de sensibilité ont été utilisées dans toutes les études et ne sont pas détaillées ici. Les lecteurs sont encouragés à consulter les études individuelles pour en savoir plus sur la méthodologie utilisée.

- La majorité (n = 26) de ces études écologiques ont démontré que les politiques sur le port du couvre-visage protégeaient contre la COVID-19, mais que l'ampleur de la protection variait d'une étude à l'autre.
    - Neuf études associées à la mise en œuvre de politiques communautaires sur le port du couvre-visage ont montré une diminution de 3,2 à 48 % de l'infection par la COVID-19 (4 à 7, 9, 27 à 30).
    - Cinq études ont montré une réduction de 17 à 23 % du Rt après la mise en œuvre des politiques sur le port du couvre-visage (11, 29, 31 à 33).
    - Dans une étude ontarienne, les politiques sur le port du couvre-visage ont entraîné une réduction hebdomadaire de 25 à 31 % des cas de COVID-19 deux semaines après leur mise en œuvre (4).
    - Comme l'a démontré une étude menée aux États-Unis, que les politiques sur le port du couvre-visage aient été mises en œuvre de façon précoce ou tardive, elles ont toutes été efficaces pour réduire la propagation de la COVID-19 (8).
    - Une étude qui a comparé l'efficacité des couvre-visages dans les pays ayant des normes préexistantes et dans ceux qui n'en avaient pas a révélé que dans les pays où toutes les personnes malades portaient généralement un couvre-visage, le taux quotidien d'augmentation des cas et des décès liés à la COVID-19 était inférieur (10).
- La seule étude qui n'a pas démontré que la politique sur le port du couvre-visage avait eu des répercussions importantes a été effectuée pendant le confinement et donné un résultat de -1 % (IC à 95 %, de -13 à 8 %) (9).
- Une étude a évalué l'efficacité d'une politique sur le port universel du couvre-visage selon l'âge. La réduction du nombre de cas de COVID-19 liés à l'âge, combinée à une politique universelle sur le port du couvre-visage à New York, a permis de réduire de 20,8 % le nombre de cas chez les 65 à 74 ans et les

75 ans et plus au cours du premier mois, alors que cette réduction a atteint 4,5 % chez les 25 à 44 ans et 8,1 % chez les 45 à 64 ans (5).

- Les politiques sur le port du couvre-visage par les employés ont également été associées à une diminution des infections et des décès liés à la COVID-19 dans trois études (1, 6, 7). Cette association n'est cependant pas aussi forte ni aussi cohérente d'une analyse à l'autre que les politiques universelles sur le port du couvre-visage (7).
- Les recommandations relatives au port du couvre-visage dans la collectivité ne sont pas aussi efficaces que les politiques sur le port du couvre-visage (1). Il a été démontré dans deux études que la mise en œuvre de politiques sur le port du couvre-visage augmentait l'utilisation de ces deniers de 30 à 54 % (4, 11).
- Le respect de l'une ou de l'autre de ces INP est essentiel à la réussite. Une étude a notamment indiqué qu'un taux de respect de 75 % était nécessaire pour que le couvre-visage soit efficace en milieu communautaire et que si plus de 85 % des gens le portaient, les politiques de distanciation sociale n'avaient aucun effet supplémentaire sur l'atténuation du nombre de cas de COVID-19 (34).

Tableau 2. Études écologiques sur l'efficacité des politiques sur le port du couvre-visage ou des normes sociétales pour se protéger contre la COVID-19 en milieu communautaire (n = 27)

RÉFÉRENCE	DESCRIPTION DE L'ÉTUDE	RÉSULTATS PERTINENTS
À l'échelle mondiale (n = 8)		
Haug (2020) (32) Étude écologique À l'échelle mondiale Mars à août 2020	Cette étude visait à évaluer l'efficacité des INP pour atténuer la propagation du SRAS-CoV-2. Elle a utilisé quatre approches statistiques différentes et un ensemble de données codées portant sur 6 068 INP mises en œuvre entre mars et avril 2020 dans 79 territoires pour évaluer l'incidence des interventions gouvernementales sur le Rt. Les résultats ont ensuite été validés à l'aide de deux ensembles de données externes contenant 42 151 INP supplémentaires provenant de 226 pays.	• Trois méthodes différentes (ΔRt entre -0,018 et -0,12) ont établi un lien important entre le port du couvre-visage et une incidence importante sur le Rt. • Les résultats indiquent notamment qu'une combinaison appropriée d'INP est nécessaire pour freiner la propagation du virus.
Miyazawa (2020) *préimpression* (35)	L'étude visait à identifier le lien entre le taux de port du couvre-visage et le nombre cumulatif de	• En mars, le taux de gens qui ne portaient pas le couvre-visage a été associé positivement au nombre cumulatif de

Étude écologique 22 pays Mars à mai 2020	décès causés par la COVID-19 dans les pays. Les taux de port du couvre-visage ont été calculés à partir des réponses au sondage effectué entre le 9 et le 18 mars et entre le 26 avril et le 1er mai 2020, respectivement.	décès (β 0,0048, ET 0,011, R2 ajusté 0,680), mais pas en avril et en mai (β 0,0020, ET 0,011, R2 ajusté 0,466) • Les modèles de régression expliquaient 69 % de la variation du nombre cumulatif de décès par million dans 22 pays et ont déterminé que le taux de port du couvre-visage en mars était un prédicteur important.
Brauner (2020) *préimpression* (9) Étude écologique À l'échelle mondiale Janvier à mai 2020	Dans cette étude, un modèle hiérarchique bayésien a été utilisé pour estimer l'efficacité de huit INP dans 41 pays en établissant un lien entre les dates de mise en œuvre des INP et le nombre total de cas et de décès. Ces modèles ont examiné les politiques sur le port obligatoire du couvre-visage, le fait de limiter les rassemblements à moins de 1 000, à moins de 100 ou à moins de 10 personnes, le fait de fermer des entreprises à risque élevé de propagation, des entreprises non essentielles, des écoles et des universités et le fait de diffuser des ordres de confinement.	• Pendant les périodes où les gens étaient confinés, l'obligation de porter un couvre-visage en public n'a pas vraiment eu d'incidence. La réduction de la moyenne proportion associée au port obligatoire du couvre-visage dans (certains) lieux publics a atteint -1 % (IC à 95 %, de -13 à 8 %). • L'étude a donc voulu examiner les répercussions de l'adoption des politiques sur le port obligatoire du couvre-visage, même si celles-ci ont été mises en œuvre après les mesures de distanciation sociale et la fermeture de toutes les écoles et entreprises, mais elle a pris fin avant la levée de ces différentes restrictions.
Esra (2020) *préimpression* (29) Étude écologique À l'échelle mondiale Janvier à mai 2020	En utilisant les cas de SRAS-CoV-2 déclarés à l'échelle mondiale pour les inscrire dans un cadre de modèle bayésien, cette étude visait à estimer la transmission associée aux INP dans 26 pays et 34 États américains. Les INP examinées comprenaient l'obligation de rester à la maison, les limites imposées aux	• La réduction moyenne du Rt en ce qui concerne l'infection par le SRAS-CoV-2 a atteint 17 % (IC à 95 %, de 6 à 28 %) avec les politiques sur le port du couvre-visage.

	rassemblements, les fermetures d'école et les politiques sur le port du couvre-visage.	
Zhang (2020) (36) Étude écologique Chine, Italie, États-Unis Janvier à mai 2020	Cette analyse des tendances quotidiennes sur l'infection par le SRAS-CoV-2, effectuée du 23 janvier au 9 mai, porte spécifiquement sur la trajectoire linéaire des cas de COVID-19 et les changements qui se sont produits après la mise en œuvre des politiques sur le port du couvre-visage en Italie et à New York.	• On estime que le port du couvre-visage a permis d'éviter plus de 75 000 infections en Italie (entre le 6 avril et le 9 mai) et plus de 66 000 à New York (entre le 17 avril et le 9 mai). • Alors que d'autres régions du monde affichaient une augmentation linéaire, cette étude montre que la mise en œuvre des politiques sur le port du couvre-visage en Italie et à New York a réduit la propagation de la COVID-19.
Leffler (2020) (37) Étude écologique 196 pays Janvier à mai 2020	Cette étude utilise les données sur la mortalité dans 196 pays pour évaluer l'incidence du port du couvre-visage sur la mortalité par COVID-19 par habitant (des données jusqu'au 9 mai 2020 ont été fournies).	• La durée du port du couvre-visage par le public avait un lien négatif indépendant avec la mortalité ($p < 0,001$). • Dans les pays où les normes culturelles ou les politiques publiques favorisaient le port du couvre-visage, la mortalité par habitant due au coronavirus n'a augmenté en moyenne que de 16,2 % chaque semaine, contre 61,9 % chaque semaine dans les autres pays.
Abaluck (2020) *préimpression* (10) Étude écologique À l'échelle mondiale Février et mars 2020	Cette étude analyse donc l'incidence du port du couvre-visage en tenant compte du lien entre les normes d'utilisation des couvre-visages et la propagation de la COVID-19 au niveau national. Les pays qui ont des normes préexistantes en vertu desquelles toutes les personnes malades doivent porter un couvre-visage ont été comparés aux pays qui n'avaient pas adopté de telle	• Les pays qui ont des normes préexistantes en vertu desquelles les personnes malades doivent porter un couvre-visage (Corée du Sud, Japon, Hong Kong et Taïwan) ont été parmi les pays les plus efficaces pour contenir la propagation de l'épidémie. • Le taux de croissance quotidien moyen de cas confirmés est de 18 % dans les pays qui n'avaient aucune norme préexistante sur le port du couvre-visage et de

	obligation, mais ont ensuite décidé d'obliger les personnes infectées à porter un couvre-visage, ainsi qu'aux pays qui n'ont ni norme ni recommandation officielle en ce qui concerne le port du couvre-visage. Les pays qui comptent au moins 5 millions d'habitants et ont au moins 8 jours de données disponibles après le premier jour où 100 cas ont été signalés ont été inclus dans l'étude.	10 % dans les pays ayant déjà adopté de telles normes. • Le taux de croissance quotidien moyen de décès est de 21 % dans les pays qui n'avaient aucune norme préexistante sur le port du couvre-visage et de 11 % dans les pays ayant déjà adopté de telles normes. • Après correction pour les interventions simultanées, l'incidence des normes sur le port du couvre-visage (β [ET]) était de 0,076 [0,030], p < 0,05 pour les cas et de 0,107 [0,024], p < 0,01 pour les décès.
Kenyon (2020) *préimpression* (38) Étude écologique 49 pays Janvier à mars 2020	Le lien entre les cas de COVID-19 et la promotion nationale du port des couvre-visages en public a été analysé, en tenant notamment compte de l'âge de l'épidémie et de l'intensité des tests effectués. Seuls les pays ayant au moins 500 cas cumulatifs et dont le premier cas a été signalé avant le 7 mars 2020 ont été inclus. Ainsi, 8 pays sur 49 préconisaient le port de couvre-visage en public (Chine, Tchéquie, Hong Kong, Japon, Singapour, Corée du Sud, Thaïlande et Malaisie).	• Les résultats de l'analyse multivariée montrent que le port du couvre-visage en public avait un lien négatif avec le nombre de cas de COVID-19 par habitant (β -326, IC à 95 %, de -601 à -51, P = 0,021).
Amérique du Nord (n = 13)		
Karaivanov (2020) *préimpression* (4) Étude écologique Canada	L'incidence des INP a été évaluée à l'aide de données accessibles au public portant notamment sur les politiques sur le port des couvre-visages en Ontario, sur d'autres INP mises en œuvre au Canada et sur le nombre de cas de COVID-19.	• Après un délai de deux semaines, les politiques sur le port des couvre-visages ont entraîné une réduction hebdomadaire de 25 à 31 % des cas de COVID-19. • Les politiques sur le port du couvre-visage ont également augmenté de 30 % l'utilisation de ces derniers.

Juillet et août 2020		
Spiegel (2020) *préimpression* (1) Étude écologique États-Unis Mars à octobre 2020	Cette analyse de régression a porté sur l'augmentation du nombre de décès attribuables à la COVID-19 et sur l'incidence des politiques sur le port obligatoire du couvre-visage dans chacun des comtés américains entre mars et octobre.	• Les politiques sur le port obligatoire du couvre-visage ont entraîné pendant 4 et 6 semaines un taux d'augmentation des décès inférieur de 1 % au taux obtenu lorsqu'aucune politique sur le port du couvre-visage n'était en vigueur, $p < 0,01$. • Les politiques sur le port du couvre-visage se sont révélées efficaces dans chacune des spécifications du modèle, en plus de s'accompagner de coûts économiques et sociaux relativement faibles. Ce résultat était à la fois significatif sur le plan statistique et important sur le plan de la portée. • Les politiques sur le port du couvre-visage présentées dans les analyses n'offraient pas toutes la même protection aux employés. • Les recommandations relatives aux couvre-visages n'ont pas eu d'effet protecteur constant comparativement au taux de mortalité.
Shacham (2020) *préimpression* (28) Étude écologique États-Unis Juin à septembre 2020	Cette étude a analysé l'incidence sur les cas de COVID-19, pendant une période de trois mois, d'une politique sur le port des couvre-visages mise en œuvre dans deux comtés d'une région métropolitaine qui en comptait cinq.	• Les politiques des comtés sur le port du couvre-visage ont été associées à une croissance beaucoup plus faible avec le temps du nombre de cas de COVID-19 comparativement aux comtés voisins qui n'avaient pas mis de telles politiques en œuvre. • La modélisation brute avec un indicateur de différence dans la différence a montré que trois semaines après la mise en œuvre de la politique sur le port du couvre-visage, les comtés qui avaient adopté une telle politique avaient un taux de croissance quotidien de COVID-19 de

		1,32 fois inférieur (diminution de 32 %) à celui des comtés n'ayant pas adopté ce type de politique. • Douze semaines après la mise en œuvre de la politique, la croissance quotidienne moyenne des cas de COVID-19 dans les pays n'ayant pas adopté ce type de politique était de 2,42 % (± 1,92), ce qui veut dire qu'elle était beaucoup plus élevée que la croissance quotidienne moyenne des cas de COVID-19 dans les pays ayant une politique sur le port du couvre-visage (1,36 % [± 0,96 %]) (p < 0,001).
Yilmazuday (2020) *préimpression* (34) Étude écologique États-Unis Février à août 2020	Les données au niveau du comté sur les changements dans le nombre de cas ou de décès liés à la COVID-19 ont été analysées en utilisant un plan de différence dans la différence et les interactions sociales mesurées par les données de Google sur la mobilité. Les comtés ont été répartis en deux catégories, soit ceux dans lesquels les gens portaient un couvre-visage et ceux dans lesquels les gens n'en portaient pas, en fonction des données fournies par Mask-Wearing Survey Data. L'incidence du port du masque sur la relation causale entre les cas de COVID-19 et les interactions sociales a ensuite été analysée.	• Il faut que plus de 75 % des gens d'un comté portent un couvre-visage pour que cela réduise le nombre de cas et de décès liés à la COVID-19. Les effets de l'interaction sociale sur la COVID-19 ont été éliminés de façon statistique lorsque plus de 85 % des habitants d'un comté portaient « toujours » un masque dans les établissements publics.
Matzinger (2020) *préimpression* (8) Étude écologique	Une analyse de régression a été effectuée pour évaluer l'incidence des INP sur les cas de COVID-19, ainsi que sur les hospitalisations et	• L'analyse de régression a montré que la fermeture des écoles et des bars et le port du couvre-visage ont eu des effets très importants sur le niveau d'infection, les

États-Unis Mars à juillet 2020	les décès liés à ce virus. Les politiques sur le port du couvre-visage ont ensuite été mises en œuvre entre mars et juillet, ce qui a permis d'évaluer l'effet tant des politiques précoces que des politiques tardives.	hospitalisations et les taux de mortalité aux États-Unis pendant la pandémie de COVID-19. • On a observé dans quatre États (IL, NJ, MA, MD) une baisse des taux d'infection après la mise en œuvre d'une politique sur le port du couvre-visage, baisse qui a été suivie d'une diminution des hospitalisations et des décès deux fois supérieure. • Les données présentées dans l'étude sont liées à des politiques sur le port du couvre-visage mises en œuvre à différents moments et les auteurs montrent de façon prévisible les réductions de taux qui ont suivi. Les politiques mises en œuvre plus tard sont liées à des points d'inflexion ultérieurs. Cela appuie la preuve que ces réductions de taux étaient attribuables au port de couvre-visage plutôt qu'à d'autres changements potentiels dans la mobilité ou le comportement. • Les politiques sur le port du couvre-visage, qu'elles aient été mises en œuvre de façon précoce ou tardive, ont toutes deux été efficaces pour réduire la propagation de la COVID-19. • Le délai entre la mise en œuvre des politiques sur le port du couvre-visage et la réduction des infections par la COVID-19 variait de 16 à 23 jours. • Une exception en ce qui concerne l'effet des politiques précoces sur le port du couvre-visage est apparue dans les données de l'État de New York, qui a rendu les couvre-visages obligatoires

		après avoir déjà transformé en nombre décroissant un nom de cas d'infections auparavant en croissance rapide. La politique sur le port du couvre-visage n'a pas eu d'autre effet suppresseur sur le taux d'infection. Cependant, lorsque l'économie de l'État de New York a repris et que le nombre d'infections a recommencé à augmenter, le niveau de l'augmentation a été très inférieur à celui que l'on trouvait dans les États qui ont rouvert les entreprises et écoles sans avoir mis en œuvre de politiques sur le port du couvre-visage et montre donc que les effets de cette politique se sont poursuivis lorsque les autres INP ont été levées.
Kaufman (2020) (39) Étude écologique États-Unis Janvier à juillet 2020	Cette étude a estimé le fardeau excessif associé à la COVID-19 pour deux types d'États américains, soit ceux qui avaient adopté une stratégie de réouverture fondée sur des preuves, incluant la réouverture des salles à manger intérieures après la mise en œuvre d'une politique sur le port du couvre-visage dans l'ensemble de l'État, et ceux qui n'avaient pas établi de stratégie de réouverture fondée sur des preuves et avaient donc décidé de rouvrir les salles à manger intérieures sans mettre en œuvre de politique sur le port du couvre-visage dans tout l'État.	• On estime que plus de 50 000 décès supplémentaires ont été évités en six semaines dans les 13 États qui ont mis en œuvre des politiques sur le port du couvre-visage avant la réouverture. • Huit semaines après la réouverture, on peut voir que dans les États qui ont rouvert sans avoir adopté de politique sur le port du couvre-visage, le nombre de cas excédentaires par 100 000 résidents est dix fois plus élevé que dans les États qui ont adopté de telles politiques (643,1 cas; IC à 95 %, de 406,9 à 879,2 comparativement à 62,9 cas; IC à 95 %, de 12,6 à 113,1). • Après six semaines, les cas excédentaires auraient pu diminuer de 90 %, passant de 576 371 à 63 062, et les décès excédentaires auraient aussi pu être réduits de 80 %, passant de 22 851 à 4858, si les États avaient mis en œuvre

		des politiques sur le port du couvre-visage avant la réouverture.
Yang (2020) *préimpression* (31) Étude écologique États-Unis Janvier à juillet 2020	Cette étude a analysé les valeurs de Rt au niveau du comté au fil du temps grâce à un modèle de métapopulation mécaniste avant de les associer à des caractéristiques au niveau du comté et à des INP comme la fermeture des écoles et des garderies, l'interdiction des visites dans les maisons de soins infirmiers, les ordres de confinement et le port d'un couvre-visage. À l'exception de la politique sur le port du couvre-visage qui était claire, les fermetures ont engendré une certaine confusion puisque les gens continuaient à se rendre sur leur lieu de travail. Le nombre d'employés sur les lieux de travail a cependant diminué au fur et à mesure que le nombre de fermetures augmentait.	• Alors que les répercussions des interventions individuelles ont pu être mesurées par des stratégies d'intervention à plusieurs niveaux, il n'est pas possible d'estimer les répercussions potentielles lorsque seules ces interventions sont effectuées. • Les politiques sur le port du couvre-visage ont cependant été associées à une réduction de 18 % du Rt (IC à 95 %, de 16 à 20 %).
Tchernozhukov (2020) (6) Étude écologique États-Unis Mars à juin 2020	Cette étude utilise des données sur les cas et des renseignements sur les modifications apportées aux INP pour évaluer l'incidence de ces INP sur le taux de croissance des cas confirmés de COVID-19 et des décès associés. La politique sur le port du couvre-visage évaluée dans cette étude obligeait les employés à porter un masque. Les INP examinées incluaient les ordres de confinement, ainsi que	• Les résultats obtenus attribuent une réduction de 9 % du taux hebdomadaire de cas et de 15 % du taux de décès à la période de 14 jours qui s'est écoulée avant que le port du couvre-visage soit imposé aux employés, $p < 0,01$. Plusieurs types d'analyse ont donné des chiffres semblables.

	des fermetures d'entreprises et d'écoles.	
Maloney (2020) *préimpression* (40) Étude écologique États-Unis Mars à juin 2020	Cette étude a utilisé un algorithme d'apprentissage machine non paramétrique pour vérifier l'hypothèse selon laquelle les politiques sur le port du couvre-visage étaient associées à des réductions du nombre de nouveaux cas de COVID-19. Les données sur les nouveaux cas COVID-19 dans 38 États américains ont été analysées dans le mois qui précédait et suivait la date de mise en œuvre de la politique.	• Analyse de tous les États : le nombre total moyen de nouveaux cas de COVID-19 avant et après l'entrée en vigueur de la politique sur le port du couvre-visage était de 654 (N = 1 138, ET = 1 357) comparativement à 639 (N = 1 177, ET = 975), respectivement. Dans 13 États, le nombre moyen de cas était plus élevé avant qu'après l'adoption de cette politique. • Analyse à l'échelle de l'État : à l'exception de la Géorgie et du Wyoming, les États dont la moyenne était plus élevée avant la mise en œuvre de la politique sur le port du couvre-visage se sont révélés statistiquement significatifs puisque la mise en œuvre de la politique dans onze États a permis de réduire de fortement à modérément le nombre de cas de COVID-19. • Il a été démontré que la cohésion sociale et les liens sociaux étroits étaient les meilleurs facteurs de prédiction pour savoir dans quels États les politiques sur le port du couvre-visage donnaient de bons résultats, sans oublier qu'ils indiquent également le niveau de conformité entre les différents États.
Li (2020) (30) Étude écologique États-Unis	L'analyse du nombre total d'infections et du nombre d'infections quotidiennes dans les 15 États les plus infectés des États-Unis a été menée afin d'étudier les répercussions des INP, comme la distanciation sociale, les ordres de	• L'analyse révèle que, malgré les ordres de confinement, la plupart des États ont vu une tendance à la hausse dans le nombre de nouvelles infections quotidiennes. Huit États ont vu une tendance à la baisse ou un ralentissement du nombre d'infections

Mars à mai 2020	confinement et les politiques sur le port du couvre-visage (six États n'avaient pas d'ordonnance en ce qui concerne le port du couvre-visage, neuf États avaient des politiques sur le port du couvre-visage) entre le 1er mars et le 18 mai 2020. Les variations dans les pentes de régression après la mise en œuvre des INP ont été mesurées et comparées entre les États.	après l'adoption de politiques sur le port du couvre-visage. • En revanche, dans les États où ces couvre-visage n'étaient pas obligatoires, la tendance à la hausse dans le nombre de cas s'est prolongée jusqu'à deux mois de plus. • L'analyse estime qu'environ 252 000 infections ont été évitées dans les sept États qui ont adopté des politiques sur le port obligatoire du couvre-visage avec une proportion prévue de cas évités variant entre 3,2 % et 48 % jusqu'au 18 mai.
Lyu (2020) (7) Étude écologique États-Unis Mars à mai 2020	Cette étude a mesuré les effets des politiques gouvernementales des États sur le port du couvre-visage par le public, en fonction des données publiées par 15 États (et DC) du 8 avril au 15 mai 2020. Les données utilisées sur les cas au niveau du comté portaient sur la période entre le 31 mars (sept jours avant que le premier État n'adopte de politique port du couvre-visage) et le 22 mai. Entre le 17 avril et le 9 mai 2020, l'étude a également évalué l'incidence dans les 20 États qui exigeaient que certains employés portent un couvre-visage.	• Il y a eu une baisse importante du taux de croissance quotidien du nombre de cas de COVID-19 après l'imposition du port du couvre-visage, un effet qui a augmenté avec le temps. • Le taux de croissance quotidien du nombre de cas de COVID-19 a diminué de 0,9 (1 à 5 jours), de 1,1 (6 à 10 jours), de 1,4 (11 à 15 jours), de 1,7 (16 à 20 jours) et de 2,0 % (21 jours et plus) après la mise en œuvre des politiques obligatoires sur le port du couvre-visage. • On a estimé que l'imposition de ces politiques avait pu permettre d'éviter entre 230 000 et 450 000 cas d'ici au 22 mai. • L'incidence de l'utilisation obligatoire d'un couvre-visage par les employés était cependant faible et non statistiquement significative.

Yang (2020) *préimpression* (5) Étude écologique États-Unis Avril 2020	Cette étude a utilisé une régression linéaire qui tenait compte des données sur la mobilité à New York pour estimer l'efficacité des INP, tant pour l'ensemble de la population que par groupe d'âge.	• Les politiques sur le port du couvre-visage ont entraîné une réduction de 6,6 % (IC à 95 %, de 0,8 à 12,4 %) des cas au cours du premier mois et une réduction de 3,4 % (IC à 95 %, de -1,9 à 8,6 %) pour l'ensemble des huit semaines de confinement. • Cet effet variait selon l'âge. Il a atteint 20,8 % (IC à 95 %, de -0,1 à 41,6 %) pour les 65 à 74 ans et 20,8 % (IC à 95 %, de -0,9 à 42,5 %) pour les 75 ans et plus pendant le premier mois, avant de se maintenir à des niveaux semblables par la suite. Chez les 25 à 44 ans et les 45 à 64 ans, l'efficacité s'est chiffrée à 4,5 % (IC à 95 %, de -0,6 à 9,7 %) et à 8,1 % (IC à 95 %, de -0,1 à 16,1 %) au cours du premier mois, respectivement. Elle a toutefois considérablement diminué par la suite, probablement en raison du comportement inversé face au risque.
Xu (2020) (41) Étude écologique États-Unis Mars et avril 2020	Cette étude a analysé les liens entre les ordres de confinement et la recommandation de porter un couvre-visage en lien avec la pandémie de COVID-19. Les tendances temporelles pour les nouveaux cas et les décès quotidiens de COVID-19 et de Rt ont été modélisées. Le CDC a recommandé aux gens de porter un couvre-visage le 3 avril 2020.	• Les changements globaux dans la pente des nouveaux décès quotidiens masqués ont atteint 0,13 (IC à 95 %, de 0,25 à 0,07). • Quant aux changements globaux dans la pente des nouveaux cas quotidiens attribuables au port du couvre-visage, ils se chiffraient à 0,10 (IC à 95 %, de 0,18 à 0,08).
Australie (n = 1)		
Scott (2020) *préimpression* (11) Étude écologique	En raison d'une résurgence de la COVID-19 à Melbourne, une politique sur le port obligatoire du couvre-visage a été mise en œuvre le 22 juillet, ce qui a donné lieu à	• L'introduction d'une politique sur le port obligatoire du couvre-visage a été associée à une réduction du nombre de

Australie Juillet et août 2020	une expérience naturelle qui a permis d'évaluer l'indice de la politique sur le taux de croissance de l'épidémie, puisque l'introduction de la politique s'est faite sans que d'autres changements aux restrictions ne soient apportés.	cas estimée à 23 % du Rt, qui est ainsi passé de 1,18 à 0,91. • Le changement dans la croissance de l'épidémie a été observé huit jours après la mise en œuvre de la politique, ce qui est conforme au temps d'incubation de la COVID-19 auquel s'ajoute le temps nécessaire pour tester et signaler de nouveaux cas. • L'analyse des images des personnes qui circulent dans les espaces publics a révélé que le port du couvre-visage est passé d'environ 43 % à 97 %. Les données du sondage ont quant à elles révélé qu'avant l'adoption de la politique, 44 % des participants avaient déclaré porter « souvent » ou « toujours » un masque alors qu'après la mise en œuvre de la politique, 100 % d'entre eux ont déclaré « toujours » le faire.
Europe (n = 4)		
Sruthi (2020) *préimpression* (33) Étude écologique Suisse Mars à septembre 2020	Cette étude visait à développer une relation systématique entre les niveaux d'INP mis en œuvre dans les 26 cantons en Suisse et leurs contributions respectives au Rt. La politique sur le port du couvre-visage ne s'appliquait que dans les transports en commun et les écoles secondaires.	• La politique sur le port du couvre-visage dans les transports en commun et les écoles secondaires a contribué à réduire le Rt de 0,025 (IC : 0,018 à 0,03) comparativement au niveau de référence obtenu alors qu'aucune politique n'était en vigueur. • Lorsque ces données ont été analysées séparément, l'on a pu estimer une réduction de 0,011 (IC : 0,008 à 0,0127) et de 0,0139 (IC : 0,0132 à 0,0144) respectivement grâce au port du couvre-visage dans les écoles secondaires et les transports en commun. • Certains endroits ont également obligé les employés dans les ateliers à porter le

		couvre-visage, mais cela n'a donné lieu à aucune autre réduction du Rt.
Mergel (2020) *préimpression* (42) Étude écologique Allemagne Avril à juillet 2020	Cette étude a étudié l'impact du port du couvre-visage sur le Rt quotidien pour la COVID-19 et sur le taux de mortalité en raison de la COVID-19. L'étude s'est également penchée sur la mise en œuvre et la levée des INP (rassemblements en groupe interdits, restriction en ce qui concerne la fréquentation des lieux publics et les contacts privés, obligation de porter le couvre-visage dans les espaces publics et levée partielle du confinement).	• Dans le cadre de cette étude, le port du couvre-visage est devenu obligatoire à compter du 27 avril, après toutes les autres restrictions. • Il n'a cependant pas été possible de faire de distinction entre l'effet positif potentiel du printemps et de l'été sur la trajectoire de la pandémie et l'effet positif associé à la mise en œuvre de la politique sur le port du couvre-visage. • Les auteurs de l'étude n'ont détecté aucun impact sur le Rt attribuable à la politique sur le port du couvre-visage. • Pendant la période pendant laquelle la politique sur le port du couvre-visage a été mise en œuvre, le niveau de fatalité des cas a diminué, passant de 7 % le 27 avril à 1 % en juillet.
Pedersen (2020) *préimpression* (43) Étude écologique Italie Février à juillet 2020	Pour déterminer quelles mesures de la santé publique ont modifié la dynamique des maladies, des données régionales et nationales ont été utilisées pour estimer certains points de changement associés à la dynamique de la COVID-19. Un point de virage se définit comme le point temporel déterminé à partir duquel un changement se produit dans le nombre quotidien de cas confirmés en raison d'une intervention publique effectuée entre 7 et 11 jours auparavant.	• En Vénétie, un point de virage a été défini le 21 avril (IC à 95 %, de 14 à 28), ce qui correspond au délai comparativement à la date à laquelle la politique sur le port obligatoire du couvre-visage est entrée en vigueur le 14 avril. • En Toscane, un point de virage a été défini le 16 avril (IC à 95 %, de 8 à 24), ce qui correspond au délai comparativement à la date à laquelle la distribution de couvre-visage a débuté, soit le 7 avril. • Les points de virage dans les nombres régionaux de cas de COVID-19 correspondent bien aux dates d'entrée en vigueur des politiques sur le port des couvre-visages.

Mitze (2020) *non publié* (27) Étude écologique Allemagne Janvier à mai 2020	Une méthode de contrôle synthétique a utilisé des données sur l'épidémie provenant de l'Allemagne pour évaluer l'effet des couvre-visages sur la propagation de la COVID-19. La ville de Jena a mis en œuvre une politique sur le port couvre-visage du couvre-visage le 6 avril 2020. Jena a ensuite été comparée à un emplacement témoin synthétique qui suivait de près la tendance pour la COVID-19 avant la mise en place des couvre-visages obligatoires à Jena.	• Dix jours après que les masques soient devenus obligatoires en Allemagne, le nombre cumulatif de cas enregistrés de COVID-19 a diminué de 2,3 à 13 %. • Une fois la politique sur le port des couvre-visages mise en œuvre, le taux de croissance quotidien des infections signalées a baissé de 18,94 %. Après avoir tenu compte de l'effet du traitement dans les grandes villes, les auteurs ont conclu à une réduction d'environ 40 % du taux de croissance des infections.
Moyen-Orient (n = 1)		
Saki (2020) *préimpression* (44) Étude écologique Iran Juin et juillet 2020	Cette étude a examiné les effets de la mise en œuvre d'une politique sur la distanciation sociale et de sa levée, ainsi que les effets des politiques sur le port du couvre-visage sur la tendance temporelle des nouveaux cas de COVID-19. Les données ont été recueillies pendant deux semaines avant et après la mise en œuvre de chacune des politiques.	• Avant la mise en œuvre de la politique sur le port du couvre-visage dans la collectivité, environ 2 491,97 nouveaux cas confirmés s'ajoutaient chaque jour et on pouvait voir la pente ascendante des cas ($p < 0,001$). • Après la mise en œuvre de la politique sur le port du couvre-visage, une tendance à la baisse est apparue dans le nombre de cas confirmés au quotidien, ce qui a entraîné un changement de -25,84 ($p < 0,001$) de la pente de la courbe de l'épidémie.

IC = intervalle de confiance, RR = rapport de risque, INP = intervention non pharmaceutique, NYC = New York, RR = rapport de cotes, Rt = nombre de reproduction effectif, ET = erreur type

RECHERCHE DE SYNTHÈSE VISANT À ÉVALUER L'EFFICACITÉ

Six études de synthèse sur l'effet protecteur associé au port des couvre-visages en milieu communautaire ont été recensées, dont quatre revues systématiques et deux revues rapides (tableau 3). La première revue a été effectuée en avril 2020. Deux des examens ultérieurs incluaient des études publiées jusqu'au début d'octobre. Ces revues permettent de discerner une progression dans la preuve entre avril et octobre. Bon nombre des

études incluses dans ces revues sont jugées pertinentes dans le cadre de la présente revue rapide et figurent donc dans les tableaux de données présentés ci-dessus.

Tableau 3. Recherche de synthèse sur le port des couvre-visages pour prévenir la propagation de la COVID-19 en milieu communautaire (n = 6)

RÉFÉRENCE	DESCRIPTION DE L'ÉTUDE	RÉSULTATS PERTINENTS
Examens systématiques (n = 4)		
Li (2020) *préimpression* (45) Examen systématique et méta-analyse Chine, Inde, Thaïlande, États-Unis Octobre 2020	Cet examen visait à évaluer l'efficacité du port des couvre-visages comme mesure de protection contre l'infection par le SRAS-CoV-2. Six études cas/témoins ont été incluses. Cinq portaient sur les travailleurs de la santé et une sur la population en général. L'examen contient les documents disponibles jusqu'en octobre 2020. Cote AMSTAR : haute qualité Remarque : une méta-analyse (MA) a été effectuée. Dans cette étude, un modèle d'effets aléatoires a été utilisé lorsque I^2, la mesure de l'hétérogénéité de l'étude, était supérieure à 50 % alors qu'un modèle à effet fixe a plutôt été utilisé lorsqu'elle était inférieure à ce niveau.	• Dans l'ensemble, le port d'un masque a réduit considérablement le risque d'infection par le SRAS-CoV-2 (RC de la méta-analyse : 0,38, IC à 95 %, de 0,21 à 0,69, I^2 = 54,1 %). • Dans une analyse de sous-groupe, les travailleurs de la santé qui portaient un couvre-visage avaient environ 70 % moins de risques d'attraper la COVID-19 (RC de la méta-analyse : 0,29, IC à 95 %, de 0,18 à 0,44, I^2 = 11 %). • En ce qui concerne la seule étude effectuée sur la population en général, le port d'un couvre-visage a réduit le risque d'infection par le SRAS-CoV-2 d'environ 28 % (RC 0,72, IC à 95 %, de 0,46 à 1,12) et donné les résultats suivants, après ajustement pour tenir compte des facteurs de confusion (RCA 0,23, IC à 95 %, de 0,09 à 0,59) (18). • Des études menées en Chine ont montré un effet protecteur plus élevé que dans d'autres pays : Chine (RC de la méta-analyse : 0,21, IC à 95 %, de 0,09 à 0,53, I^2 = 26,1 %) comparativement aux autres pays (RC de la méta-analyse : 0,55, IC à 95 %, de 0,32 à 0,95, I^2 = 39,3 %).
Coclite (2020) (46)	Cet examen visait à résumer les données probantes sur l'efficacité du port du couvre-visage dans la collectivité pour réduire la	• Aucune étude d'observation sur le port du couvre-visage dans la collectivité pour réduire la propagation de la COVID-19 n'a été relevée.

Examen systématique et méta-analyse Chine, Hong Kong, Iran, Israël, Italie, Japon, Malaisie, Pays-Bas, Arabie saoudite, Corée du Sud, Taiwan, Royaume-Uni, États-Unis Avril 2020	propagation de la maladie. Trente-cinq études ont été incluses (3 ECR, 13 modèles prédictifs, 10 études d'observation et 9 expériences en laboratoire). Sept modèles prédictifs et une étude de laboratoire étaient propres au SRAS-CoV-2. L'examen contient la documentation disponible jusqu'au 22 avril 2020. Cote AMSTAR : haute qualité	• Les modèles mathématiques indiquent une diminution de la mortalité lorsque le port du couvre-visage dans la population est presque universel, peu importe l'efficacité du couvre-visage. • Tous les types de masques peuvent réduire l'exposition aux aérosols. Cependant, les respirateurs personnels sont plus efficaces que les masques chirurgicaux, qui sont plus efficaces que les couvre-visages maison. • Les ECR ont montré une tendance vers l'effet protecteur du port du couvre-visage comparativement à l'absence de couvre-visage (RCA 0,90, IC à 95 %, de 0,78 à 1,05), mais ces résultats n'étaient pas significatifs. Des conclusions semblables ont été indiquées dans des études d'observation.
Chou (2020) (47) Chou (2020) (mise à jour 1) (48) Chou (2020) (mise à jour 2) (49) Chou (2020) (mise à jour 3) (50) Revue rapide en direct Chine, Thaïlande, États-Unis Octobre 2020	L'efficacité des masques N95, des masques chirurgicaux et des masques en tissu dans la communauté et les établissements de soins de santé pour prévenir les infections respiratoires virales a été évaluée dans cet examen systématique en direct. Dates des recherches : Recherche originale : 2002 - 2 juin 2020 Mise à jour 1 : 2 juin au 2 juillet 2020 Mise à jour 2 : 3 juillet au 2 août 2020 Mise à jour 3 : 3 août au 2 octobre 2020	• Dans la première version et la deuxième mise à jour de cette revue, aucune étude visant à évaluer l'efficacité des couvre-visages pour prévenir les infections par le SRAS-CoV-2 dans les milieux communautaires n'a été indiquée. • La première mise à jour a présenté une étude de cohorte comprenant 124 ménages avec un cas de référence de SRAS-CoV-2 et 355 contacts familiaux non infectés. Les ménages dans lesquels les couvre-visages ont été portés par au moins un membre de la famille (y compris le cas de référence) avant l'apparition des symptômes ont été associés à une diminution du risque d'infections accidentelles (RCA 0,21, IC à 95 %, de 0,06 à 0,79). Il n'y a pas eu d'association

	Cote AMSTAR : qualité modérée à élevée (aucun protocole *a priori*, l'évaluation de la qualité n'a pas été effectuée avec un instrument officiel, rapport sous-optimal, par exemple, incertitude quant à la présence de responsables du double examen pour l'évaluation de la qualité).	entre le port du couvre-visage après l'apparition de la maladie dans le cas de référence et le risque d'infection par le CoV-2 du SRAS chez les membres de la famille (17). • La troisième mise à jour comprenait une étude cas/témoins en Thaïlande. Le fait de porter un couvre-visage en tout temps a été associé à une diminution du risque d'infection par le SRAS-CoV-2 (RCA 0,23, IC à 95 %, de 0,09 à 0,60), alors que le port non uniforme d'un couvre-visage n'a pas été associé à une diminution du risque (RCA 0,87, IC à 95 %, de 0,41 à 1,84). Le type de masque (masque médical seulement, masque non médical seulement, ou les deux) n'était pas lié de manière indépendante au risque d'infection par le SRAS-CoV-2 (p = 0,54) (18).
Chaabna (2020) (51) Examen systématique et méta-analyse Australie, Chine, France, Allemagne, Hong Kong, Thaïlande, États-Unis Mai 2020	Les données probantes sur l'efficacité des masques en tissu et des masques médicaux pour prévenir la transmission des infections respiratoires dans les milieux communautaires ont été évaluées dans le cadre de cet examen. Douze études ont été incluses, dont une seule portait sur le SRAS-CoV-2. L'examen contient les documents disponibles jusqu'au 12 mai 2020. Cote AMSTAR : qualité médiocre (absence de protocole *a priori* et de responsables du double examen, examen effectué seulement dans	• Aucune étude primaire sur l'efficacité du couvre-visage en tissu pour prévenir la transmission des infections respiratoires n'a été relevée. • La méta-analyse a révélé que le port d'un masque médical réduisait considérablement le risque de transmission d'infections respiratoires (RC combiné = 0,66, IC à 95 %, de 0,54 à 0,81). • Une étude portant spécifiquement sur le SRAS-CoV-2 a été sélectionnée. Cette étude de cohorte rétrospective a démontré que les masques médicaux sont efficaces pour réduire la transmission du SRAS-CoV-2 lorsqu'ils sont utilisés avant que les personnes infectées ne développent des symptômes (17).

	deux bases de données, aucune évaluation officielle de la qualité).	
Revues rapides (n = 2)		
Warkentin (2020) *non publiée* (52) Revue rapide Canada, Chine, Allemagne, Israël, Japon, Afrique du Sud, Thaïlande, Ouganda, Royaume-Uni, États-Unis Août 2020	Cette revue rapide visait à évaluer les données probantes sur l'incidence du port du couvre-visage en milieu communautaire en ce qui concerne la susceptibilité à la COVID-19 et la transmission de ce virus, ainsi que les répercussions sur l'efficacité du couvre-visage selon la façon de porter le couvre-visage, qu'elle soit uniforme ou non. Trente et une études ont été incluses (21 modèles principaux, 10 modèles sur l'efficacité des masques et 5 sur la conformité dans le port du couvre-visage). Les 17 études primaires sur l'efficacité des couvre-visages comprenaient 9 études écologiques, 1 étude de cohorte, 1 étude cas/témoin et 6 études de rapport de cas/épizootie. La recherche documentaire portait sur la période entre décembre 2019 et août 2020. Cote AMSTAR : qualité médiocre (absence de protocole *a priori*, de responsables du double examen et d'évaluation officielle de la qualité).	• Il n'y avait pas suffisamment de preuves pour quantifier l'efficacité de l'utilisation du couvre-visage. • Dans l'ensemble, le port du couvre-visage dans la collectivité a réduit le nombre de cas de COVID-19 au sein d'une population. • Les rapports de cas ont toujours indiqué moins de cas secondaires lorsque les cas de référence ou leurs contacts portaient des couvre-visages. • Des études de modélisation ont révélé que le port d'un couvre-visage, combiné à d'autres stratégies d'atténuation, pouvait réduire la mortalité causée par la COVID-19 et éviter une résurgence des cas dans les endroits où les mesures de confinement avaient déjà réduit le nombre de cas. • Aucune étude n'a été menée sur l'incidence du port du couvre-visage dans les écoles.
The Royal Society (2020)) *non publiée* (53) Revue rapide Chine	Cette revue rapide visait à évaluer l'efficacité des masques en tissu et des couvre-visages dans le grand public et dans les établissements de soins de santé. Elle comprenait notamment une comparaison internationale du moment où la politique sur les couvre-visages a	• Les résultats ont révélé qu'aucun examen systématique et aucune méta-analyse n'avaient encore été effectués sur l'efficacité des types de masques en tissu autres que les masques chirurgicaux et les masques N95.

Juin 2020	été introduite. Une seule étude sur le SRAS-CoV-2 était incluse. La revue contient la documentation disponible jusqu'au 26 juin 2020. Cote AMSTAR : qualité médiocre (peu de détails sur la façon d'effectuer l'étude : recherche, sélection, évaluation ou extraction des données ou de l'analyse).	• Les données empiriques et expérimentales sur le port du couvre-visage dans la collectivité ou sur le port du couvre-visage en tissu sont limitées. • Une étude portant spécifiquement sur le SRAS-CoV-2 a été sélectionnée. Cette étude de cohorte rétrospective a démontré que les masques médicaux sont efficaces pour réduire la transmission du SRAS-CoV-2 lorsqu'ils sont utilisés avant que les personnes infectées ne développent des symptômes (17). • La méta-analyse fondée sur la littérature non liée au SRAS-CoV-2 dans le milieu des soins de santé a indiqué que les masques en gaze ou en tissu (RR = 0,46; IC à 95 %, de 0,22 à 0,97; N = 746) et les masques en papier (RR = 0,61; IC à 95 %, de 0,41 à 0,90; N = 166) assuraient une certaine protection comparativement au fait de ne pas porter de masque.

RCC = rapport de cotes corrigé, IC = intervalle de confiance, ECR = essai clinique randomisé

Méthodologie

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'Agence de la santé publique du Canada. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et dans les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Les résultats cumulatifs de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Des détails sur cette stratégie de recherche sont disponibles sur demande. Une recherche ciblée par mot-clé dans les titres et les résumés des articles a été effectuée dans ces bases de données et dans la liste en Excel. Les termes de recherche utilisés comprenaient : mask* OU (face ET cover*). Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue. La présente revue contient des recherches publiées jusqu'au 19 novembre 2020.

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Nouveaux éléments de preuve sur la COVID-19

Note d'information sur le risque lié à la COVID-19 et les sports non professionnels

Introduction

Quelles sont les données probantes accessibles sur le risque de transmission du SRAS-CoV-2 par la pratique de sports non professionnels et des recherches ont-elles été menées sur les modifications apportées au jeu pour atténuer le risque de transmission?

Les gouvernements et les autorités sanitaires du monde entier ont mis en œuvre des pratiques de confinement et de distanciation sociale afin d'atténuer la propagation du SRAS-CoV-2 au sein des populations. Il s'agissait notamment de la fermeture de lieux de travail, d'écoles et d'autres lieux publics, ainsi que de l'annulation d'événements sportifs et de jeux. Alors que les mesures de santé publique visant à endiguer la pandémie sont prudemment assouplies, beaucoup envisagent de reprendre l'activité physique et le sport. Cette note d'information donne un aperçu de la littérature publiée sur les risques de transmission du SRAS-CoV-2 associés à la pratique de sports non professionnels en date du 18 août 2020.

Points clés

- Deux enquêtes publiées sur les épidémies de SRAS-CoV-2 associées à l'activité physique récréative apparaissent dans la littérature (tableau 1). Ces événements de transmission ont été liés à des installations sportives intérieures et à des activités aérobiques (l'une étant un cours de Zumba, l'autre un match de squash) et se sont produits en mars 2020.
- Dix autres cas de transmission liés au sport ou à l'exercice ont été relevés dans une base de données de cas de superpropagation de la COVID-19(Swinkles, 2020).
    - Plusieurs cas de transmission ont été signalés dans des gymnases associés à des cours en salle, des tournois de curling, des danses carrées et du football. Bon nombre de ces activités sont considérées comme des activités à contact élevé dans les articles de presse.
    - Les sources réelles d'infection et de transmission au sein de ces groupes s'adonnant à des sports d'équipe n'ont pas été identifiées. Par exemple, dans le cas de deux tournois de curling et d'un match de hockey sur la route, des activités sociales avaient également eu lieu avant et/ou après le match. Dans le même ordre d'idées, la source d'une éclosion dans une équipe de football au Japon n'a pas été identifiée.
    - Par ailleurs, des activités telles que la course à pied ne semblent pas présenter un risque élevé de transmission; un seul groupe de partenaires de course à pied a été identifié.

- Des simulations informatiques des caractéristiques aérodynamiques du SRAS-CoV-2 ont conclu que les gouttelettes respiratoires suivront le sillage d'un coureur et qu'il faut donc éviter de courir ou de marcher directement derrière une autre personne (Blocken, Malizia, van Druenen, & Marchal, 2020).
- Wong et coll., rapportent les conclusions de deux enquêtes indépendantes applicables à la participation aux sports et à la transmission du SRAS-CoV-2 (Wong et al., 2020).
    - Selon une analyse de séquences vidéo de matchs de football professionnel, on estime qu'un joueur de football semi-professionnel passe en moyenne 20 % du match en contact étroit avec un autre joueur.
    - Des simulations expérimentales de l'activité physique chez les athlètes ont révélé que les personnes qui portaient un masque enregistraient des fréquences cardiaques et des efforts perçus plus élevés que celles qui ne portaient pas de masque.
- Les documents d'orientation de l'Organisation mondiale de la santé (OMS), les outils d'évaluation des risques et les commentaires publiés comprennent des stratégies utiles pour réduire le risque de transmission du SRAS-CoV-2 lors de la pratique d'un sport (tableau 2).
    - Les orientations de l'OMS décrivent les principales considérations, les risques et les mesures d'atténuation en fonction du type de sport (c'est-à-dire le niveau de contact entre les joueurs), de la taille de l'événement, des lieux intérieurs et extérieurs, des installations du site, des données démographiques des concurrents et des spectateurs, et de la communication des risques, et fournissent des conseils sur la gestion des cas de SRAS-CoV-2 qui peuvent être détectés lors d'un événement sportif (WHO, 2020a). Le document doit être utilisé de pair avec les Key Planning Recommendations for Mass Gatherings in the Context of the Current COVID-19 Outbreak [recommandations clés pour la planification des rassemblements de masse dans le contexte de l'épidémie actuelle de COVID-19](WHO, 2020b) (en anglais seulement) et le Mass Gathering COVID-19 Risk Assessment Tool – Sports Events [outil d'évaluation des risques liés à la COVID-19 lors de rassemblements de masse – événements sportifs] (en anglais seulement) (WHO, 2020c).
    - Carmody et coll. proposent une matrice d'évaluation des risques pour aider les décideurs à redémarrer les événements sportifs, basée sur les orientations de l'OMS et tenant compte de la transmission du SRAS-CoV-2 dans les communautés locales (Carmody, Murray, Borodina, Gouttebarge, & Massey, 2020).
    - Dans une note technique, Blocken et coll. examinent le processus de réouverture des installations sportives intérieures tout en réduisant au minimum la transmission du SRAS-CoV-2. S'appuyant sur l'application de preuves circonstancielles limitées, les auteurs concluent que l'inspiration et l'expiration profondes résultant de l'exercice physique peuvent augmenter l'émission et l'inhalation d'aérosols respiratoires. À ce titre, ils préconisent l'utilisation de systèmes de ventilation par déplacement d'air (plutôt que par mélange d'air), de filtres HEPA et

d'une occupation limitée dans les installations intérieures où l'exercice physique est fréquent (B. Blocken et al., 2020).

- Les directives destinées aux éducateurs physiques des écoles chinoises qui rouvrent après le confinement imposé par la COVID-19 proposent diverses stratégies, telles que des exercices et l'échelonnement des périodes d'activité physique, qui peuvent être adoptées par des équipes sportives non professionnelles pour atténuer les risques de transmission.

Vue d'ensemble des éléments de preuve

Les publications qui traitent directement du SRAS-CoV-2 et des sports non professionnels sont rares. Nous avons donc appliqué les données disponibles sur les installations sportives intérieures (p. ex. les gymnases) et les sports professionnels pour déduire les risques de transmission. Quinze publications et documents d'orientation pertinents sur l'activité physique et le sport ont été utilisés pour étayer cette revue.

Parmi les publications incluses figurent deux enquêtes détaillées sur des foyers d'éclosion et dix rapports sur des foyers d'éclosion de SRAS-CoV-2 associés à des sports ou à des exercices physiques, tirés de la base de données de cas de superpropagation de la COVID-19 (tableau 1). Bien que les enquêtes sur les épidémies puissent être sensibles à un risque élevé de biais, les deux enquêtes publiées semblent avoir été menées avec soin, avec de solides activités de recherche de cas et de recherche de contacts afin de réduire au minimum les biais d'échantillonnage. La base de données de cas de superpropagation comprend des groupes de cas de COVID-19 (n>5 cas) identifiés à partir des tableaux de bord sur la COVID-19 du Canada et d'articles de presse, dont aucun ne fournit de renseignements détaillés sur l'événement de transmission. Les renseignements contenus dans cette base de données sont donc incomplets et imparfaits, et très sensibles aux multiples biais et facteurs confusionnels.

Les analyses de données d'observation portaient sur des séquences vidéo d'un match de football. Elles présentent un risque modéré de biais de la part des chercheurs, mais les mesures physiologiques rapportées étaient moins sensibles à ce biais; il s'agissait simplement de comparer la fréquence cardiaque et la mesure de la perception de l'effort chez ceux qui portaient un masque et chez ceux qui n'en portaient pas. L'étude par simulation informatique pour observer la dynamique des flux d'air chez les coureurs est largement théorique et aurait un faible risque de biais.

La littérature sur les stratégies visant à atténuer le risque de transmission des infections dans les sports non professionnels se limite en grande partie à des commentaires et à des conseils d'experts (tableau 3). Cette littérature se fonde sur les données de santé publique disponibles et adopte des stratégies couramment utilisées pour réduire au minimum la transmission du SRAS-CoV-2 dans les lieux publics.

Dans l'ensemble, les connaissances contenues dans cette littérature présentent toujours d'importantes lacunes, car les orientations actuelles dépendent largement des principes généraux d'évaluation et d'atténuation des risques ainsi que des orientations de la santé publique en matière de COVID-19.

TABLE DES MATIÈRES

ÉCLOSIONS ASSOCIÉES À LA PARTICIPATION À DES ACTIVITÉS SPORTIVES/PHYSIQUES

Il y a peu de cas de transmission associés au sport dans la littérature actuelle sur la COVID-19. Cela pourrait être dû en grande partie aux mesures de santé publique qui ont mis fin à la plupart des activités sportives depuis le début de la pandémie. À l'exception de l'éclosion liée à la pratique de la Zumba décrite par Jang et coll., d'autres éclosions n'ont pas fait l'objet d'une enquête détaillée ou ont été associées à des activités sociales s'étant déroulées avant ou après l'activité sportive, ce qui rend difficile d'attribuer la transmission à la participation au sport lui-même.

La flambée de cas observée actuellement au sein d'une équipe de soccer japonaise montre comment les infections par le SRAS-CoV-2 peuvent se propager au sein d'une équipe, et les directives et précautions de lutte contre l'infection devraient faire partie des plans de reprise des sports (Swinkles, 2020).

Tableau 1. Douze éclosions de COVID-19 liées au sport et à l'exercice

Référence	Titre de la publication	Résultats pertinents
(Jang, Han, & Rhee, 2020)	Cluster of Coronavirus Disease Associated with Fitness Dance Classes, South Korea	Résume l'enquête portant sur 112 cas de COVID-19 associés aux classes de Zumba dans 12 installations sportives différentes en Corée du Sud. Le taux d'attaque primaire a été estimé à 26,3 % (IC 95 % 20,9 % à 32,5 %) et le taux d'attaque secondaire à 4,10 % (IC 95 % 2,95 % à 5,67 %). On suppose que la transmission initiale a eu lieu chez les instructeurs de conditionnement physique lors d'un atelier, où huit des vingt-sept participants ont reçu un diagnostic positif pour le SRAS-CoV-2. Au cours des semaines suivantes, l'infection a été transmise aux participants aux cours de danse, aux contacts familiaux, aux collègues et aux connaissances des instructeurs et des participants. Selon l'étude, 50,9 % (n=63) des cas provenaient d'une transmission par les instructeurs et 52 cas ont été identifiés parmi les participants aux cours de danse. Les instructeurs et les participants se rencontraient uniquement pendant les cours, qui duraient 50 minutes, à raison de 2 fois par semaine, et n'avaient pas de contact en dehors des cours.

		Aucun cas n'a été observé chez les participants aux cours de Pilates et de yoga, également dispensés par un instructeur infecté dans le même établissement de sport ou de conditionnement physique. Ces observations suggèrent que la plus faible intensité du Pilates et du yoga n'a pas entraîné les mêmes effets de transmission que dans le cas des cours de danse, bien qu'il n'ait pas été déterminé que cela puisse être dû à une moins grande quantité de gouttelettes respiratoires ou à une circulation d'air moins importante.
(Brlek, Vidovič, Vuzem, Turk, & Simonović, 2020)	Possible Indirect Transmission of COVID-19 at a Squash Court, Slovenia, March 2020: Case Report	Cette publication décrit un groupe de cas de SRAS-CoV-2 (n=6) liés à la pratique du squash dans un centre sportif à Maribor, en Slovénie. Le cas index (personne A), supposé avoir contracté l'infection lors d'un voyage en Italie, a développé des symptômes (c'est-à-dire fatigue et épuisement) pendant une partie de squash. Les enquêtes épidémiologiques relient des cas supplémentaires (quatre cas confirmés et un suspect) à la même salle de squash et aux mêmes vestiaires. Le cas B a eu un contact direct avec le cas index, car ils ont passé du temps dans les vestiaires et ont joué un match de squash ensemble. Les cas C et D ne signalent pas de contact direct avec le cas index (ou le cas B), et sont épidémiologiquement liés par l'utilisation de vestiaires et le fait de jouer sur le même court de squash dans les 20 minutes après que les cas A et B y aient joué. Les deux autres cas, le cas E et le cas F, sont arrivés au centre sportif environ 1,5 heure après le départ du cas index. Ces deux cas ont discuté avec les cas C et D à l'extérieur du court de squash, et ils ont utilisé le même vestiaire et le même court de squash. Aucun des cas n'a partagé d'équipements sportifs ou n'a eu de contact avec le personnel de l'installation. Aucun autre cas n'a été identifié.
(Swinkles, 2020)	SARS-CoV-2 Super Spreading Events Around the World	Dix autres événements sportifs liés à la transmission ont été signalés dans des articles de presse, tels qu'ils figurent dans la base de données de cas de superpropagation de la COVID-19 du monde entier. Dans cette source d'information, les renseignements sur l'éclosion ou les activités qui ont probablement entraîné la transmission ne sont souvent pas mentionnés : - 2 tournois de curling (tournoi de plusieurs jours et activités sociales) à Edmonton, au Canada, les 14 et 15 mars. 24/72 participants ont développé la COVID-19 et dans le Maryland aux É.-U. le 27 mars, il y a eu environ 20 cas, - Hockey-balle en plein air « sur une même patinoire » Racine, Québec, Canada, 29 février. 15/21 ont été infectés par la COVID-19

		- En février, en Italie, un marathonien infecté a transmis le virus à son partenaire de course - Équipe de soccer, Sagan Tosu J1, éclosion, Japon, août. 11 joueurs et entraîneurs infectés à ce jour - Danse carrée, Lynnwood, Washington, É.-U., février, il y a eu peu de tests et aucune enquête. Seules des informations anecdotiques indiquent que certaines personnes testées étaient bel et bien atteintes de la COVID-19 (>15 personnes), - Des foyers d'éclosion dans deux écoles de gymnastique et une école de tennis de table sont enregistrés au Japon sans autre précision et un foyer dans une école de gymnastique est enregistré à Singapour.

RISQUE DE TRANSMISSION LORS DE LA PRATIQUE D'UN SPORT

Deux études fournissent des preuves applicables au risque de transmission de la COVID-19 pendant la pratique d'un sport. L'une des études consistait en une analyse vidéo d'un match de soccer professionnel. Elle a révélé qu'il avait eu contact étroit entre les joueurs pendant environ 19 minutes sur 90 minutes de jeu et environ 52 épisodes d'interactions à risque élevé (Wong et al., 2020). Le port d'un masque pendant l'exercice a été étudié en laboratoire et cette petite étude a conclu que la fréquence cardiaque et la perception de l'effort étaient significativement plus élevées après six minutes d'exercice modéré avec un masque que sans masque (Wong et al., 2020).

L'autre étude a examiné la dispersion aérodynamique des gouttelettes lorsqu'une personne court afin d'évaluer le risque de transmission lorsqu'une personne suit un coureur infecté (Bert Blocken et al., 2020). Si les personnes courent ou marchent rapidement, même à 1,5 mètre l'une de l'autre, il existe un risque d'exposition aux particules infectieuses si la personne qui suit est directement derrière la personne qui précède (placée dans son sillage). Cette exposition peut être évitée si deux coureurs sont côte à côte (1,5 mètre de distance) ou sont décalés.

Tableau 2. Risque de transmission de la COVID-19 lors de la pratique d'un sport

Référence	Titre de la publication	Principaux résultats
(Wong et al., 2020)	Impact of the COVID-19 Pandemic on sports and exercise	Des séquences vidéo de joueurs de soccer professionnels à Hong Kong ont été analysées pour suivre le temps passé par les joueurs en contact physique étroit et la fréquence des comportements qui augmentent le risque de transmission de l'infection. L'analyse révèle que la durée moyenne des contacts étroits entre les joueurs est de 19 minutes (plage de 5,9 à 35,5) par partie de 90 minutes, et que chaque joueur s'est commis en moyenne 52 fois des gestes à risque accru de transmission d'infection (toucher des yeux, de la bouche ou du nez) au cours d'une partie de 90 minutes.

		Les effets physiologiques du port d'un masque pendant le jeu ont également été examinés en laboratoire. La fréquence cardiaque et la perception de l'effort (RPE) des participants portant un masque étaient significativement élevées par rapport à celles des participants sans masque après 6 minutes d'exercice modéré (fréquence cardiaque de 128 battements par minute et RPE à 12,7 pour les participants portant le masque, et fréquence cardiaque de 124 battements par minute et RPE à 10,8 pour les participants sans masque). Les valeurs étaient statistiquement significatives, mais elles ne sont pas nécessairement significatives sur le plan biologique. L'enquête conclut que le risque de transmission de l'infection est élevé entre les joueurs pendant un match, même sans spectateurs. Le port du masque pendant l'exercice physique augmente la charge physiologique du corps, avec des répercussions pour ceux qui présentent de multiples comorbidités sous-jacentes.
(Bert Blocken et al., 2020)	Towards aerodynamically equivalent COVID-19 1.5 m social distancing for walking and running	L'étude de la dynamique des fluides par ordinateur, éclairée par des données antérieures sur la dispersion des gouttelettes autour d'un coureur, prend en compte les effets aérodynamiques potentiels introduits par les mouvements individuels (par exemple, marcher rapidement, courir et faire du vélo) sur la distance de déplacement des gouttelettes. L'étude vise à déterminer si une personne infectieuse principale qui se tient immobile et se déplace à proximité d'une deuxième personne sensible à une distance de 1,5 mètre ou plus peut présenter un risque de transmission de l'infection. Bien que l'exposition aux particules soit négligeable lorsque deux personnes se tiennent à 1,5 mètre l'une de l'autre, si les personnes courent ou marchent rapidement même à 1,5 mètre de distance, il existe un certain risque d'exposition aux particules infectieuses. Les résultats de l'étude suggèrent que la plus grande exposition de la personne qui suit se produit si elle se trouve directement derrière la personne qui précède (positionnée dans son sillage). Une réduction substantielle du risque d'exposition aux gouttelettes peut être obtenue en 1) évitant de marcher ou de courir dans le sillage de la personne en tête, 2) gardant la distance de 1,5 mètre en se décalant ou en se tenant côte à côte, ou 3) gardant des distances sociales supérieures à 1,5 mètre lorsqu'on se déplace rapidement ou qu'on court.

STRATÉGIES ET ORIENTATIONS

La littérature sur les stratégies visant à atténuer le risque de transmission des infections dans les sports non professionnels comprend deux documents d'orientation provisoires de l'OMS, deux outils d'évaluation des risques et plusieurs commentaires d'experts (tableau 2). La prise en compte des taux locaux de transmission et de cas de SRAS-CoV-2, l'évaluation des risques pour déterminer les niveaux potentiels de contact entre les joueurs, la limitation du nombre de joueurs, la priorité donnée au jeu en plein air et à la distanciation sociale, l'interdiction de l'utilisation partagée des équipements sportifs, l'amélioration des pratiques de nettoyage et de désinfection, et le dépistage des participants pour identifier et isoler efficacement les cas de SRAS-CoV-2 sont des stratégies globales. L'OMS recommande de s'abstenir de pratiquer des sports de contact direct, car ils augmentent le risque d'exposition directe à l'infection.

Deux outils d'évaluation du risque de contracter la COVID-19 chez les spectateurs et les participants à un événement sportif ont été relevés. Le WHO Mass Gathering COVID-19 Risk Assessment Tool [outil d'évaluation des risques liés à la COVID-19 lors de rassemblements de masse – événements sportifs] (en anglais seulement), fournit un arbre décisionnel et des outils pour l'évaluation des risques, l'atténuation des risques, ainsi qu'une matrice de décision et un outil pour la communication des risques que les organisateurs d'événements sportifs de masse et les pays hôtes peuvent appliquer pour déterminer la propagation des infections associées à un événement. Une autre matrice de risque est présentée par Carmody et coll. Cet outil d'évaluation des risques est fondé sur les orientations provisoires de l'OMS, applique les taux locaux de transmission communautaire et les mesures d'atténuation afin de calculer le risque résiduel associé à divers sports professionnels. Le commentaire de Timpka souligne l'importance de la confiance, en ce sens que si les joueurs pensent que les autres joueurs ne respecteront pas les restrictions pour se protéger contre la COVID-19, il est également peu probable qu'ils y adhèrent, d'où l'importance d'un excellent plan de communication.

Certaines preuves circonstancielles antérieures à la pandémie de SRAS-CoV-2, telles que présentées dans la note technique de Blocken, suggèrent que l'activité physique peut augmenter l'émission et l'inhalation d'aérosols respiratoires susceptibles de provoquer une infection (B. Blocken et al., 2020). Bien qu'une bonne partie des données sur la transmission du SRAS-CoV-2 par aérosol continuent d'évoluer, les données probantes et l'information sur les éclosions qui sont accessibles révèlent des risques élevés de transmission de l'infection lors d'une activité physique intense dans un environnement intérieur bondé. Ces données probantes doivent être pondérées de manière appropriée lorsque l'on envisage le retour à des sports non professionnels en salle.

Tableau 3. Stratégies pour réduire la transmission de la COVID-19 pendant la pratique d'un sport

Référence	Titre de la publication	Déclarations clés
(WHO, 2020a)	Considerations for sports federations/sports event organizers when planning mass gatherings in the context of COVID-19	Fournit des considérations clés et des techniques d'atténuation des facteurs de risque. Les recommandations sont fondées sur la prise en compte du risque de contact et de transmission dans le cadre de la pratique d'un sport, la taille de l'événement (c'est-à-dire le nombre de participants), l'emplacement de l'événement, les installations du site, les données démographiques des joueurs participants et l'adoption de directives de santé publique pertinentes. Les recommandations comprennent un examen de santé quotidien pour les concurrents; la distance (au moins 1 mètre) entre les concurrents, les officiels, les spectateurs et le personnel de soutien; une désinfection et un nettoyage approfondis; l'interdiction de partager l'équipement; l'utilisation de sites extérieurs lorsque cela est possible; l'utilisation de sièges désignés et physiquement séparés ainsi que de zones d'isolement au soutien des éventuelles activités de gestion des cas et de recherche des contacts; une communication efficace des risques; et la communication d'information aux personnes présentant un risque accru de mortalité et de morbidité liées au SRAS-CoV-2 leur conseillant de ne pas assister à l'événement sportif. Orientations provisoires, 14 avril 2020
(WHO, 2020c)	WHO mass gathering COVID-19 risk assessment tool – sports events	Un outil formel d'évaluation et de communication des risques à utiliser de pair avec le document intitulé « Considerations for Sports Federations/Sports Event Organizers when Planning Mass Gatherings in the Context of COVID- » (ci-dessus). Mis à jour le 10 juillet 2020
(WHO, 2020b)	Key planning recommendations for mass gatherings in the context of COVID-19	Fournit des conseils aux gouvernements hôtes, aux autorités sanitaires et aux organisateurs nationaux ou internationaux de rassemblements de masse sur la manière de contenir les risques de transmission de la COVID-19 associés aux rassemblements de masse. Orientations provisoires, 29 mai 2020
(Carmody et al., 2020)	When can professional sport	Présente une matrice d'évaluation des risques pour aider les décideurs à redémarrer les activités de sport professionnel

	recommence safely during the COVID-19 Pandemic? Risk assessment and factors to consider	lorsque les mesures de santé publique relatives à la COVID-19 commenceront à s'assouplir. En plus de s'appuyer sur les considérations exposées dans les lignes directrices de l'OMS (c'est-à-dire celles concernant les rassemblements de masse, les considérations relatives aux événements sportifs et l'évaluation des risques liés aux activités sportives), l'évaluation des risques tient compte de la transmission communautaire de la COVID-19 à l'échelle locale. L'approche de base consiste à évaluer le risque, puis à envisager des mesures d'atténuation, et enfin à calculer le risque résiduel. Sur la base de l'application de cette évaluation des risques, le soccer professionnel est considéré comme présentant un risque résiduel élevé, tandis que le golf professionnel est considéré comme présentant un risque résiduel faible, si des mesures appropriées d'atténuation des risques d'infection sont appliquées. Sur la base de l'application de cette matrice des risques, les auteurs suggèrent que le risque global de reprise des événements sportifs peut être faible, si la transmission au sein de la communauté locale est faible et si des procédures adéquates d'atténuation des risques sont en place. Selon les évaluations faites, le soccer professionnel est considéré comme présentant un risque résiduel élevé, tandis que le golf professionnel est considéré comme présentant un risque résiduel faible.
(Timpka, 2020)	Sports health during the SARS-Cov-2 pandemic	Rédigé avant la publication des lignes directrices de l'OMS, ce commentaire indique que les organisations sportives doivent répondre aux besoins des athlètes et des entraîneurs, tout en se conformant aux mesures de distanciation sociale et aux orientations régionales de santé publique sur la COVID-19, lorsqu'elles élaborent une stratégie de réponse à une pandémie. Souligne l'importance de la confiance : « Si les sportifs ne croient pas que la plupart des autres respecteront les restrictions temporaires, il est également peu probable qu'ils y adhèrent. Les auteurs suggèrent que les activités sportives doivent être pratiquées en plein air, en petits groupes, et le contact physique entre les joueurs doit être évité autant que possible. Les compétitions virtuelles sont encouragées entre les athlètes des sports individuels.
(B. Blocken et al., 2020)	Can indoor sports centers be allowed	Ce document présente les preuves (antérieures à l'émergence de la COVID-19) qui montrent que l'expiration profonde

	to re-open during the COVID-19 Pandemic based on a certificate of equivalence?	(comme lors d'un exercice physique) produit des concentrations plus élevées d'aérosols et que l'inhalation profonde augmente l'exposition aux aérosols. À la lumière de cette constatation, les auteurs indiquent qu'il est nécessaire d'assurer une bonne ventilation (le déplacement de l'air du sol au plafond est préférable au mélange d'air), d'utiliser des filtres HEPA, d'appliquer des mesures de santé publique pour les visiteurs et le personnel, de nettoyer les surfaces afin d'éliminer les vecteurs passifs et de s'assurer que les activités se font sans contact. Les auteurs ont également proposé l'idée de délivrer un certificat aux centres sportifs intérieurs avant leur réouverture.
(Chen et al., 2020)	Returning Chinese school-aged children and adolescents to physical activity in the wake of COVID-19: Actions and precautions	Résume les précautions qui peuvent être prises par les directeurs d'écoles, les éducateurs physiques et les parents concernant l'activité physique, alors que les écoles en Chine commencent à rouvrir après le confinement imposé par la COVID-19. Ces précautions comprennent : - Encourager une bonne distanciation sociale (au moins 1 mètre), - Décaler les horaires pour éviter que trop de personnes se retrouvent en même temps au même endroit, - Rendre les stations de lavage ou de désinfection des mains facilement accessibles, - Désinfecter régulièrement toutes les surfaces et tous les équipements, - Limiter les activités physiques qui impliquent un contact physique et le partage d'équipements sportifs et de bouteilles d'eau.
(Peter, 2020)	Return to play after COVID-19: a sport cardiologist's view	L'article souligne la nécessité de subir un examen cardiaque avant un retour au sport pour les cas de COVID-19 chez les adultes, soulignant que des lésions cardiaques subcliniques peuvent survenir à la suite d'une infectionpar le SRAS-CoV-2.

(Dores & Cardim, 2020)	Returning to play after coronavirus infection: a perspective from pediatric cardiologists	L'article souligne la nécessité de procéder à un examen cardiaque avant un retour au sport pour les cas de COVID-19 chez les enfants à la suite d'une infectionpar le SRAS-CoV-2, car une lésion cardiaque subclinique peut être présente après l'infection.

Méthodologies

Toute la littérature sur la COVID-19 a été compilée et classée par le Groupe des sciences émergentes de l'Agence de la santé publique du Canada depuis le début de l'épidémie. Cela suppose une recension quotidienne de la littérature pour tous les articles publiés et prépubliés. Les recherches pour trouver de la littérature pertinente sur la COVID-19 sont menées dans PubMed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square. Elles sont mises en correspondance avec les publications figurant sur la liste de littérature de l'Organisation mondiale de la santé au sujet de la COVID et les centres d'information COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de la recension sont conservés dans une base de données Refworks et un fichier Excel qui peut être consulté. Chaque article est étiqueté en fonction de divers critères permettant de déterminer le thème central de l'article (p. ex. épidémiologie, données cliniques, thérapeutique, etc.) Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour y relever des citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche inclus dans cet examen étaient « sports », « exercise » et « physical fitness/activity ». Chaque référence potentiellement pertinente a été analysée pour confirmer sa pertinence, et des données ont été extraites et incluses dans la recension de la littérature. Cette revue contient des recherches publiées jusqu'au 18 août 2020.

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Preuve émergente sur la COVID-19

Synthèse en bref sur le risque d'infection à la suite du contact oculaire pour orienter les précautions à prendre en cas de contact et d'exposition aux gouttelettes

Introduction

Quelles sont les données disponibles en ce qui concerne la protection des yeux (en plus des masques médicaux et des respirateurs standard) pour prévenir la transmission de l'infection à la COVID-19 chez les travailleurs de la santé?

La COVID-19 est une infection respiratoire qui se transmet principalement par des gouttelettes, et peut-être par des aérosols, lors d'interactions non protégées (Vuorinen et al., 2020). La parole, la toux et les éternuements des patients symptomatiques sont tous des vecteurs de transmission de l'infection puisqu'ils génèrent des gouttelettes chargées de virus (et peut-être d'aérosols) qui se retrouveront ensuite dans l'air, dans le milieu des soins de santé (Liu et al., 2020; Loh et al., 2020; Ong et al., 2020; Vuorinen et al., 2020). L'équipement de protection individuelle efficace et approprié fournit cependant une barrière qui empêche la transmission de l'infection des patients aux travailleurs de la santé.

Cette synthèse en bref met donc en évidence les données probantes disponibles à l'appui de l'utilisation d'une protection oculaire chez les travailleurs de la santé pour ainsi réduire l'infection par la COVID-19 publiées jusqu'au 18 juin 2020.

Points clés

- À ce jour, aucune étude n'a porté spécifiquement sur l'infection par le SRAS-CoV-2 à la suite de l'exposition des surfaces oculaires. Le tableau 1 présente les données probantes à l'appui de l'utilisation d'une protection oculaire par les travailleurs de la santé pour réduire au minimum la transmission des coronavirus par l'infection.
    - Le récepteur ACE-2, un récepteur cellulaire pour la fixation du virus SRAS-CoV-2, se trouve dans les tissus oculaires humains. De nombreuses études, y compris une revue systématique, fournissent des preuves biologiques moléculaires que le SRAS-CoV-2 peut utiliser les tissus oculaires (c.-à-d. l'œil) comme portail d'entrée pour infecter les

hôtes humains (Aiello et al., 2020; Lange et al., 2020; Ma et al., 2020; Zhang, Jin, & Lei, 2020; Zhou et al., 2020).

  - Les données sur l'exposition provenant de plusieurs hôpitaux pendant l'éclosion de SRAS en Ontario, au Canada, fournissent des données d'observation indiquant que la protection des yeux a réduit l'incidence des infections par le SRAS chez les travailleurs de la santé qui l'ont utilisée (Raboud et al., 2010).

- Dans sa dernière mise à jour le 19 mai 2020, le document Prévention et contrôle de la maladie COVID-19 : Lignes directrices provisoires pour les établissements de soins actifs de l'Agence de la santé publique du Canada sur la prévention et le contrôle des infections à l'intention des travailleurs de la santé recommande : (PHAC & Canada, 2020)
  - Les précautions à prendre en cas de contact ET d'exposition aux gouttelettes (c.-à-d. gants, masques, écrans faciaux et lunettes de protection) lorsque les travailleurs de la santé interagissent avec des patients soupçonnés d'être infectés par la COVID-19 ou dont l'infection a été confirmée;
  - Les précautions à prendre en cas de contact ET d'exposition aux gouttelettes qui doivent être utilisées par les travailleurs de la santé 1) en ce qui concerne les patients qui présentent une fièvre ou une toux nouvelle ou qui s'aggrave ou une maladie respiratoire aiguë, 2) qui entrent dans les chambres des patients, ou 3) qui se trouvent à proximité de toute procédure générant des aérosols, indépendamment de l'apparition de symptômes d'infection respiratoire aiguë chez le patient.
  - Des dépistages actifs doivent être mis en œuvre dans les endroits où les travailleurs de la santé et les patients accèdent aux milieux de soins de santé. Les responsables de l'examen doivent être protégés par des barrières transparentes ou porter l'EPI approprié (p. ex., gants, blouse, masque et protection du visage ou des yeux) lorsqu'une barrière transparente ne peut être mise en place.
  - À l'heure actuelle, des évaluations des risques au point d'intervention doivent également être effectuées (en fonction du patient, de l'interaction et de la tâche) afin de déterminer toute précaution supplémentaire nécessaire pour TOUS les patients et visiteurs (PHAC & Canada, 2020).
- De nouvelles données probantes sur les tests sérologiques effectués sur des travailleurs d'hôpitaux révèlent que la positivité de l'IgG est liée à la prévalence géographique de l'infection dans une région (Sandri et al., 2020). Il peut donc être avantageux pour les travailleurs de la santé de tenir compte de la prévalence de la COVID-19 dans les circonscriptions hospitalières des patients lorsqu'ils évaluent le risque de transmission et l'utilisation de la protection oculaire.

Vue d'ensemble des éléments de preuve

Les données d'études d'observation sur les effets protecteurs de la protection oculaire propre à la transmission de la COVID-19 dans les soins de santé sont insuffisantes, et ce, même si les données de biologie moléculaire appuient la plausibilité de l'infection par le SRAS-CoV-2 en utilisant l'œil de l'hôte comme portail d'entrée. Il y a donc des lacunes dans les connaissances de la recherche qui permettent d'estimer les risques de transmission des infections aux travailleurs de la santé associés à la protection des yeux.

CONTENU

INFECTION PAR EXPOSITION OCULAIRE

Tableau 1 : Littérature sur le risque de transmission de l'infection par exposition de la surface oculaire.

Titre de la publication	Principaux résultats	Référence
Littérature primaire		
Enquêtes améliorées sur les contacts pour neuf cas précoces de SRAS-CoV-2 à la suite de déplacements aux États-Unis.	L'étude fait état de l'utilisation de différents types d'équipement de protection individuelle (EPI) chez les travailleurs de la santé qui s'occupent de la grappe de cas précoces de COVID-19 à la suite de déplacements aux États-Unis. Il s'agit de la seule étude (à ce jour) à examiner et à fournir des données sur l'utilisation de l'équipement de protection individuelle sélectif chez les travailleurs de la santé pendant l'épidémie de COVID-19. Le risque relatif d'infection par la COVID-19 fondé sur la protection des yeux par rapport à l'absence de protection des yeux ne peut cependant PAS être estimé, car aucun cas secondaire chez les travailleurs de la santé n'a été relevé.	(Burke et al., 2020)

Expression du récepteur ACE2 du SRAS-CoV-2et TMPRSS2 dans la conjonctive primaire humaine et les lignées cellulaires du ptérygium, ainsi que dans la cornée des souris Expression de la COVID-19 récepteur ACE2 dans la conjonctive humaine Répartition et importance clinique de l'ACE2, un récepteur clé du 2019-nCoV dans les tissus oculaires ACE2 et TMPRSS2 sont exprimés sur la surface oculaire de l'être humain, ce qui suggère une susceptibilité à l'infection par le SRAS-CoV-2	Les tissus oculaires humains expriment donc les récepteurs ACE-2, les récepteurs cellulaires du SRAS-CoV-2, ce qui confirme la capacité du virus à infecter un hôte par son œil.	(Ma et al., 2020), (Lange et al., 2020), (Zhang et al., 2020), (Zhou et al., 2020)
Facteurs de risque de transmission du SRAS par des patients qui doivent être intubés : une enquête multicentrique effectuée à Toronto, au Canada	Selon une enquête multicentrique effectuée sur une éclosion antérieure de SRAS à Toronto, le manque d'uniformité des lunettes de protection portées par les travailleurs de la santé lorsqu'ils entraient dans la chambre des patients augmentait le risque d'infection chez ces travailleurs (n=624). Un lien statistiquement significatif entre la protection des yeux et l'infection a été identifié, ce qui suggère que la conjonctive aurait pu être un portail d'entrée pour les agents pathogènes.	(Raboud et al., 2010)

Titre de la publication	Principaux résultats	Référence
Commentaires clés et revues		
Interventions physiques visant à interrompre ou à réduire la propagation des virus respiratoires. Partie 1 - Masques faciaux, protection des yeux et distanciation des personnes : revue systématique et méta-analyse	La revue systématique n'a pas permis de relever de rapports associés à l'épidémie de SRAS en 2003 ayant évalué l'utilisation de la protection oculaire et la prévention des infections.	(Jefferson et al., 2020)
Distanciation physique, masques faciaux et protection des yeux pour prévenir la transmission de la COVID-19 d'une personne à l'autre : revue systématique et méta-analyse	Une revue systématique et une méta-analyse effectuées par Chu et coll. examinent les preuves disponibles, tirées des études d'observation sur le risque de transmission des coronavirus (SRAS-CoV-2, MERS-CoV, SRAS), en fonction de la protection des yeux. La revue conclut que la protection des yeux et l'utilisation d'un masque ou d'un respirateur sont associées à une réduction de la transmission du coronavirus (différence de risque de -10,6 % (-12,5 à -7,7, IC à 95 %) et probabilité ajustée de 0,22, -12 à 0,39, IC à 95 % respectivement avec une fiabilité jugée faible). Toutefois, le SRAS-CoV-2 n'a cependant pas été pris en compte dans les estimations des risques liés à la protection des yeux, car cette preuve n'existe pas à l'heure actuelle.	(Chu et al., 2020)
Maladie à coronavirus 2019 (SRAS-CoV-2) et colonisation des tissus oculaires et des sécrétions : une revue systématique	Une revue systématique par Aiello résume l'information disponible sur la présence du SRAS-CoV-2 dans la cornée, la conjonctive, le larmoiement, le sac lacrymal et les larmes. Elle confirme que le SRAS-CoV-2 peut être présent et infecter les tissus oculaires, ce qui veut dire qu'il peut donc utiliser les structures oculaires comme voie de transmission supplémentaire.	(Aiello et al., 2020)
La transmission de 2019-nCoV par l'entremise de la surface oculaire ne doit donc pas être ignorée.	Commentaire dans lequel les auteurs font référence à un reportage médiatique (en chinois) portant sur la transmission d'une infection à un travailleur portant un masque N95, mais aucune protection oculaire.	(Lu, Liu, & Jia, 2020)

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe de science émergente de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont menées par Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont recoupées avec la littérature de la liste de littérature COVID de l'OMS, et les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Une recherche ciblée par mot-clé était effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-COV-2. Une recherche supplémentaire par mot-clé ciblé a été effectuée sur Pubmed pour identifier les citations pertinentes non spécifiques à COVID-19 et à SRAS-CoV-2. Termes de recherche utilisés comprennent : Goggle, ocular, eye, ACE2 Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites dans l'examen.

Cet examen contient des recherches publiées jusqu'au 20 juin 2020.

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Preuve émergente sur la COVID-19

Synthèse en bref sur l'infectiosité et l'apparition des symptômes

Introduction

Existe-t-il une différence de risque de transmission entre les personnes présymptomatiques et asymptomatiques infectées et les cas symptomatiques?

Des études de cas, des séries de cas, des enquêtes sur les contacts et les grappes, ainsi que des études sur de grandes populations, ont démontré que la transmission se produit fréquemment chez des personnes présymptomatiques et asymptomatiques. Cette revue visait à résumer la littérature publiée jusqu'au 29 mai 2020.

Points clés

- La littérature provenant des milieux de soins de santé souligne que la transmission de la COVID-19 est complexe et liée à la situation, à la durée de l'exposition et aux facteurs individuels.
    - La transmission asymptomatique potentielle a été documentée dans les milieux de soins de santé chez les résidents de l'établissement, les travailleurs de la santé et les visiteurs (Arons et coll., 2020; McMichael et coll., 2020). Une épidémie, dans un établissement de soins infirmiers spécialisé de l'État de Washington, a permis de constater que plus de la moitié des résidents qui avaient des résultats positifs étaient asymptomatiques au moment des tests et que des virus viables pouvaient se développer chez des personnes présymptomatiques jusqu'à six jours avant l'apparition des symptômes (Arons et coll., 2020).
    - Une autre étude n'a cependant pas pu démontrer que la transmission asymptomatique se produisait en raison des contacts étroits et dans les établissements de soins (Canova et coll., 2020). Cette étude n'était cependant pas assez puissante et n'aurait donc pas été suffisante pour estimer un risque de transmission.
- Il a été démontré que la transmission asymptomatique se produit et qu'elle peut être liée au temps passé en contact étroit avec une personne infectée, ainsi qu'à d'autres attributs du scénario dans lequel la transmission s'est produite.
    - Dans une méta-analyse de cas bénins (n=8) et asymptomatiques (n=36), on a pu observer des taux élevés de transmission dans des situations de proximité comme lors des repas et dans des événements familiaux, des conversations en voiture, des réunions privées et lors des cérémonies de prière (Prakash, 2020a). Il est probable que dans de telles situations, la

propagation asymptomatique soit facilitée par le contact (contamination des mains et des fomites) ainsi que par la génération de gouttelettes par la parole et le chant.

- La charge virale estimée dans les aérosols émis par les patients qui respirent normalement était en moyenne de 0,34 à 11,5 copies/cm^3, tandis que les chiffres correspondants pour les patients qui présentaient des symptômes respiratoires étaient beaucoup plus élevés, atteignant de 10 900 à 366 000 copies/cm^3 par quinte de toux (Riediker et Tsai, 2020). Une personne qui passait du temps dans une pièce avec une personne respirant normalement (c.-à-d. sans symptômes respiratoires) était tout de même susceptible d'inhaler des dizaines ou des centaines de copies du virus.
- Dans les enquêtes épidémiologiques, la proportion d'événements de transmission chez les personnes présymptomatiques et asymptomatiques est très variable (plage <10 à 73 %) (tableau 1). Les modèles prédictifs estiment que 40 à 80 % des événements de transmission se produisent chez des personnes présymptomatiques et asymptomatiques (Ferretti et coll., 2020; Javid et Balaban, 2020; Li et coll., 2020).
- Les probabilités de transmission pour les cas symptomatiques et asymptomatiques peuvent cependant être très semblables :
    - Une analyse n'a révélé aucune différence significative dans les taux de transmission entre les patients symptomatiques et asymptomatiques (6,3/100 et 4,1/100, respectivement) (Yin et Jin, 2020).
    - Des charges virales dans les voies respiratoires supérieures semblables pour le SRAS-CoV-2 ont été signalées chez les patients asymptomatiques et symptomatiques (Zou et al., 2020).

Vue d'ensemble des éléments de preuve

Peu d'études comparent directement le potentiel de transmission et l'infectiosité entre les personnes qui présentent des symptômes respiratoires et celles qui ne présenteront pas de symptômes respiratoires. Aux fins de cette revue, la majorité des données probantes sur ce sujet ont été extrapolées à partir d'études comparant les cas symptomatiques et présymptomatiques ou asymptomatiques en général, ainsi que dans le contexte des soins de santé.

Les données probantes à ce sujet sont principalement décrites dans des exposés de cas et études de recherche des contacts, qui présentent un risque élevé de biais et sont donc jugés être de basse qualité. De nombreuses études sont des prépublications qui n'ont donc pas fait l'objet d'un examen par les pairs. Dans l'ensemble, il faut donc interpréter les résultats avec prudence.

Aucune évaluation des risques ou étude n'a permis d'estimer le risque d'infection pour les travailleurs de la santé qui s'occupent de patients présymptomatiques ou asymptomatiques par rapport aux patients symptomatiques.

Les estimations changent à mesure que de nouvelles recherches deviennent disponibles puisqu'il y a de nombreuses lacunes dans les connaissances actuelles. De nouvelles recherches visant à combler ces lacunes

pourraient modifier considérablement notre compréhension de l'infectiosité du SRAS-CoV-2 chez les personnes symptomatiques et asymptomatiques. Il faut davantage de données probantes démontrant l'existence d'un virus cultivable provenant d'infections asymptomatiques, présymptomatiques et symptomatiques pour déterminer avec plus de certitude l'infectiosité à différents stades.

CONTENU

SIGNES DE POTENTIEL DE TRANSMISSION PRÉSYMPTOMATIQUE ET ASYMPTOMATIQUE

Il est important de garder à l'esprit que la transmission entre les personnes dépend du contexte et de multiples facteurs. Les personnes qui présentent des symptômes respiratoires sont beaucoup plus susceptibles de s'isoler que les personnes asymptomatiques, ce qui explique les taux élevés de transmission présymptomatique et asymptomatique indiqués dans cette littérature. Des études sur la transmission des cas présymptomatiques et asymptomatiques ont montré que la transmission présymptomatique et asymptomatique atteint des proportions élevées dans cette pandémie, et ce, tant dans la population générale que dans les milieux de soins de santé. Par conséquent, les cas qui ne présentent pas de signes évidents d'infection, y compris des événements générateurs de gouttelettes comme la toux et les éternuements, peuvent quand même se révéler très infectieux.

Tableau 1 : Études fournissant des preuves liées à l'infectiosité et au potentiel de transmission des infections présymptomatiques et asymptomatiques. Un indicateur de la qualité des données probantes est fourni (faible, modéré, élevé) en fonction du risque de biais dans le plan de l'étude et la production de rapports.

Référence	Principaux résultats	Qualité
Estimations de la transmission présymptomatique		
(Arons et coll., 2020)	Enquête sur l'éclosion chez des résidents dans un établissement de soins infirmiers spécialisés à Washington, aux États-Unis Date de fin : 3 avril 2020 - Quarante-huit (63 %) des résidents qui ont participé aux enquêtes sur la prévalence ponctuelle ont obtenu un résultat positif. - Vingt-quatre étaient présymptomatiques et deux étaient asymptomatiques. - Un virus viable a pu être isolé dans les spécimens prélevés 6 jours avant l'apparition des symptômes et 9 jours après.	Faible

	- Cela indique que l'infection présymptomatique et asymptomatique a été un facteur important dans la transmission du SRAS-CoV-2 dans cet établissement.	
(Du et coll., 2020) *Prépublication*	Étude de cas de données accessibles au public en Chine Étude de 468 paires d'infecteur/infecté identifiées par la recherche des contacts 21 janvier au 8 février 2020 - 59 paires d'infecteur/infecté (12,6 %) ont indiqué que l'infecté avait eu des symptômes plus tôt que l'infecteur. - Ces intervalles de série négatifs suggèrent que la transmission présymptomatique s'est probablement produite.	Faible
(Chun, Baek et Kim, 2020) *Prépublication*	Étude de cas de données accessibles au public en Corée du Sud Étude de 72 paires de transmissions entre infecteur et infecté 23 janvier au 31 mars 2020 - La proportion de transmission présymptomatique était de 37 % (16 à 52 %, IC à 95 %).	Faible
(He et coll., 2020) *Prépublication*	Étude de recherche des contacts au Vietnam, en Malaisie, au Japon, en Chine, à Taïwan, aux États-Unis et à Singapour Étude de 77 paires de transmissions entre infecteur et infecté 18 décembre au 5 mars 2020 -On estime que 44 % (25 à 69 %, IC à 95 %) des cas secondaires ont été infectés pendant le stade présymptomatique des cas index.	Faible
(Pham et coll., 2020) *Prépublication*	Étude de cas de données accessibles au public au Vietnam Étude de 33 paires de transmissions entre infecteur et infecté 15 avril au 1er mai 2020 - Les intervalles des séries ont été calculés à partir de paires infecteur/infecté et utilisés pour estimer la proportion d'événements de transmission présymptomatique. - 27,5 % (15,7 % à 40,0 %, IC à 95 %) des transmissions se sont produites de manière présymptomatique.	Faible
(Wei et coll., 2020)	Étude de recherche des contacts pour 243 cas et sept grappes de cas à Singapour 23 janvier au 16 mars 2020 - Sept grappes de cas avec une transmission présymptomatique probable ont été identifiées. - La proportion globale de transmission à partir de cas présymptomatiques représentait 6,3 % de la transmission globale.	Faible
(Xia et coll., 2020) *Prépublication*	Enquête sur 50 grappes de cas en Chine Apparition des symptômes avant le 25 janvier 2020 - Enquête portant sur 124 cas dans lesquels le contact secondaire avec le cas de première génération s'est produit avant l'apparition des symptômes. La courbe infectieuse a montré que chez 73,0 % des personnes infectées, la date d'infection était antérieure à l'apparition	Modérée

	des symptômes de leurs infecteurs, en particulier dans les trois derniers jours de la période d'incubation.	
(Casey et coll., 2020) *Prépublication*	Analyse secondaire des données publiées indiquant l'intervalle de série ou le temps de génération en provenance de Hong Kong, de Tianjin, de Singapour, de la Chine continentale, à l'exception d'Hubei, de sources mixtes, de Shenzhen, du nord de l'Italie et de Wuhan 1 décembre 2019 au 15 avril 2020 - Période d'incubation soustraite de l'intervalle de série ou du temps de génération pour déduire la période d'infection présymptomatique et estimer la proportion de transmission présymptomatique. - La transmission présymptomatique a été estimée à 56,1 % d'après les estimations des intervalles en série et à 65,5 % d'après les estimations du temps de génération.	Faible
(Prakash, 2020b) *Prépublication*	Analyse secondaire des données publiées Comprend 1 251 personnes mentionnées dans la littérature - On estime que 68,4 % (67,0-69,7 %, IC à 95 %) des infections sont causées par des infecteurs présymptomatiques.	Faible
(Nishiura, Linton et Akhmetzhanov, 2020)	Modèle bayésien log-normal basé sur l'examen de cas des rapports de recherche et d'enquête publiés Étude de 28 paires infecteur/infecté Date de fin : 12 février 2020 - En tenant compte de la troncature à droite et en analysant toutes les paires, les auteurs ont estimé un intervalle de série de 4,0 jours (3,1 à 4,9, IC à 95 %). - Cet intervalle est plus court que les estimations préliminaires de la période d'incubation d'environ 5 jours. - Cela suggère que la transmission présymptomatique peut représenter une proportion importante de la transmission secondaire.	Faible
Estimations de la transmission asymptomatique		
(McMichael et coll., 2020)	Enquête sur l'éclosion d'une épidémie dans un établissement de soins de longue durée à Washington, aux États-Unis qui a touché les résidents, les travailleurs de la santé et les visiteurs Date de fin : 18 mars 2020 - Au total, 167 cas confirmés de COVID-19, dont 101 résidents, 50 professionnels de la santé et 16 visiteurs, ont été associés épidémiologiquement à l'établissement. - Aucun symptôme n'a été documenté chez 7 résidents (6,9 %).	Faible
(Yin et Jin, 2020)	Nouvelle analyse des données sur le cas et les contacts à Ningbo, en Chine Analyse de 157 cas symptomatiques et de 30 cas asymptomatiques 21 janvier au 6 mars 2020 -Les taux de transmission pour les patients symptomatiques et asymptomatiques étaient de 0,063 et de 0,041 respectivement (aucune différence significative).	Faible

	- La probabilité de transmission à une personne en bonne santé par un patient symptomatique est de 1,2 fois celle d'un patient asymptomatique (non statistiquement significative).	
(Danis et coll., 2020)	Étude des grappes dans les Alpes françaises avec exportation et diffusion du virus dans plusieurs pays d'Europe. Cas index présymptomatique et 15 contacts dans le chalet; 172 contacts ont été identifiés dans l'ensemble des cas. À compter du 25 janvier 2020 - Taux d'attaque du cas index asymptomatique 12/15 (75 %) pour 4 jours de contact; 1/15 asymptomatique. Seul 1 des 172 contacts subséquents était positif. - Charge virale d'un cas symptomatique similaire à un cas asymptomatique.	Faible
(Wang et coll., 2020)	Étude rétrospective en Chine Étude de 125 patients confirmés par RT-PCR en temps réel. 20 janvier au 18 février 2020. - 22,4 % des cas n'ont pas fait état d'une exposition connue à des personnes malades.	Faible
(Wong et coll., 2020)	Examen du cas des voyageurs et des résidents de retour à Brunei Examen de 53 paires infecteur/infecté symptomatiques. 5 mars au 24 avril 2020 -Vingt et un cas (39,6 %) avaient un SI de 3,0 jours et six (11,3 %) avaient des valeurs SI nulles ou négatives, ce qui suggère une infectiosité potentielle lorsque les personnes sont asymptomatiques.	Faible
(Zou et coll., 2020)	Étude sur la charge virale de 17 patients symptomatiques et d'un patient asymptomatique en Chine 7 au 26 janvier 2020 - Analyse de la charge virale dans les écouvillons dans le nez et dans la gorge. - La charge virale détectée chez le patient asymptomatique était similaire à celle détectée chez les patients symptomatiques. Cela suggère le potentiel de transmission des patients asymptomatiques ou paucisymptomatiques.	Faible
(Li et coll., 2020) *Prépublication*	Modèle mathématique qui simule la dynamique spatiotemporelle des infections en Chine 10 janvier au 8 février 2020 - On estime que 86 % de toutes les infections n'étaient pas documentées avant l'arrêt des voyages à Wuhan, et que par personne, ces infections non documentées (dont bon nombre n'étaient probablement pas gravement symptomatiques) étaient 55 % aussi contagieuses que les infections documentées et la source de l'infection dans 79 % des cas documentés.	Faible
(Riediker et Tsai, 2020) *Prépublication*	Un modèle à un compartiment a été utilisé pour estimer la concentration de charge du virus dans une salle parfaitement mélangée d'un volume de 50 m^3 avec un patient comme source	Faible

	- L'émission totale cumulative par respiration des patients ayant une respiration normale était de 0,34 copie/cm^3 (air) pour un patient moyen, et de 11,5 copies/cm^3 pour les patients dont le niveau d'émission était élevé. - Les émissions virales des patients qui toussaient étaient beaucoup plus élevées, avec une émission totale cumulative par toux de 19 400 copies/cm^3 pour un patient moyen et de 651 315 copies/cm^3 pour les patients dont le niveau d'émission était élevé. Une personne qui passe du temps dans une pièce avec un patient ayant une respiration moyenne a normalement une forte probabilité d'inhaler des dizaines ou des centaines de copies du virus même lorsqu'elle pratique la distanciation. La probabilité est plus grande en présence d'un patient dont le niveau d'émission est élevé ou si le patient a un niveau d'émission élevé et qu'il tousse. - Conclure que les concentrations de virus prédites élevées peuvent expliquer la fréquence de la transmission communautaire des cas asymptomatiques et les taux élevés d'infection chez le personnel médical. - Les auteurs recommandent une protection respiratoire stricte lorsque vous êtes dans une chambre avec un patient, que le patient soit symptomatique ou non.	
(Aguirre-Duarte, 2020) *Prépublication*	Examen systématique et rapport narratif sur les enquêtes dans les grappes/contact. Études primaires sur la capacité des porteurs asymptomatiques d'infecter d'autres personnes. Neuf articles ont porté sur 83 personnes asymptomatiques ou présymptomatiques. Publié dans des revues indexées du 1er janvier au 31 mars 2020. - Bien qu'aucune estimation précise n'ait été indiquée, il existe des preuves que les personnes asymptomatiques et présymptomatiques peuvent infecter d'autres personnes avec la COVID-19.	Modérée
(Prakash, 2020a) *Prépublication*	Cette synthèse n'est pas effectuée à l'aide de la méthode d'examen systématique standard, bien qu'une recherche approfondie ait été effectuée. Vingt situations ont entraîné 418 infections dans 32 instances chez 44 personnes (huit présentaient des symptômes légers, 36 étaient asymptomatiques). Situation (taux de transmission) : • Repas/événements familiaux (15,7 % à 66,7 %) • Réunions (réunion privée d'une heure, 72,7 % (IC de 43,6 à 98,0 %) • Espace de travail ouvert avec circulation des personnes (78,7 % (70,3 à 85,3 %)) • Chant (par exemple, pratique de deux heures 86,7 % (76,2 à 93,2 %)	Modérée

	• Cérémonie de prière (a entraîné une à sept infections secondaires par personne infectée) • Déplacement en voiture (environnement fermé) et discussions présentait un risque élevé (100 % (20 à 100 %)) • Transports publics, port d'un masque sans parler (~0 %) • Hôtels (53,3 % (30,1 à 75,2 %))/bateaux de croisière (28,1 % (27,3 à 29,0 %)) où l'espace est partagé pendant des jours • Interaction directe avec un représentant infecté (25,0 % (10,2 à 49,5 %)) • Boîte de nuit, taux d'attaque pour les contacts directs >50 %, parmi les clients de la boîte de nuit (6,27 % (5,15 à 7,61 %)) • Taux d'attaque global pour le restaurant (9,9 % (5,3 à 17,7 %) contre ceux dans le flux d'air du climatiseur (45,0 % (25,8 à 65,8 %))	

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe de science émergente de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont menées par Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont recoupées avec la littérature de la liste de littérature COVID de l'OMS, et les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Des recherches ciblées par mot-clé ont été effectuées en utilisant une combinaison des termes « outbreak », « hospital », « long-term care » et « nursing ». Des résumés et des notes d'information sur l'infection asymptomatique, les événements de super-diffusion et la période infectieuse ont été utilisés pour rassembler des preuves liées aux symptômes respiratoires et à l'infectiosité. Cet examen contient des recherches publiées jusqu'au 29 mai 2020. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites dans l'examen.

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Preuve émergente sur la COVID-19

Synthèse en bref sur la distance de dispersion du virus SRAS-CoV-2

Introduction

Quel est l'impact d'une distance physique de 1 mètre, de 1,5 mètre et de 2 mètres sur le risque de transmission du virus SRAS-CoV-2?

La physique complexe et la dynamique des particules entourant la dispersion des gouttelettes et des aérosols, ainsi que les preuves limitées sur la dose infectieuse et la viabilité des virus dans les particules expulsées, font qu'il est difficile de quantifier avec certitude le risque d'exposition au SRAS-CoV-2 en fonction de la distance. Cette synthèse en bref met en évidence des documents précis sur la distance de dispersion des gouttelettes expulsées et des particules d'aérosol publiés jusqu'au 22 juin 2020.

Points clés

- L'ensemble des preuves suggère que la vitesse des particules, l'évaporation, la circulation de l'air, l'humidité, la température jouent toutes un rôle dans les distances que les particules respiratoires chargées de virus peuvent parcourir après avoir été libérées par une personne infectieuse. Par conséquent, les effets protecteurs de la distance physique à différentes distances dépendent également des conditions dans lesquelles ils sont pratiqués.
- Les données empiriques et modélisées disponibles indiquent que, dans certaines circonstances, les gouttelettes respiratoires et les aérosols expulsés d'individus infectieux peuvent parcourir des distances supérieures à 2 mètres (tableau 1), mais les masques faciaux sont efficaces pour limiter les distances de dispersion à moins de 0,5 mètre (tableau 2).
- Selon les modèles mathématiques et l'analyse dynamique des fluides, la taille des gouttelettes, l'humidité, la température, le flux d'air et les turbulences de l'air ont tous un impact sur le mouvement et la décomposition des particules en suspension dans l'air contenant le virus (tableau 1).
    - Certains modèles prédisent que les gouttelettes et les aérosols peuvent parcourir des distances allant jusqu'à dix mètres lorsqu'ils sont générés par la toux ou les éternuements et concluent fréquemment qu'une distance sociale de deux mètres n'est pas toujours suffisante pour annuler la transmission du SRAS-CoV-2 par voie

aérienne (Feng, Marchal, Sperry, & Yi, 2020; Guerrero, Brito, & Cornejo, 2020; Zhao, Qi, Luzzatto-Fegiz, Cui, & Zhu, 2020).

- La basse température et l'humidité élevée facilitent la transmission et la dispersion des gouttelettes respiratoires. La température élevée et le faible taux d'humidité favorisent la perte rapide de la masse des gouttelettes respiratoires (due à l'évaporation) réduisant ainsi la distance de déplacement des gouttelettes (Feng et al., 2020; Zhao et al., 2020).
- Un consortium de recherche multidisciplinaire a appliqué des modèles Monte-Carlo fondés sur des données probantes et des simulations en 3D pour étudier la physique de la dispersion des aérosols du SRAS-CoV-2 (Vuorinen et al., 2020). Les chercheurs utilisent des simulations informatiques pour démontrer que les aérosols SRAS-CoV-2 peuvent parcourir des distances allant jusqu'à dix mètres, et que l'inhalation de concentrations suffisantes d'aérosols (on a supposé que 100 particules chargées de virus étaient infectieuses) est possible en une seconde à une heure selon les conditions ambiantes.
- Les résultats d'un modèle basé sur des agents ont révélé une diminution du risque d'un événement de transmission à l'intérieur (p. ex., supermarché) lorsque la distance entre les individus passe de 30 cm à 2 mètres (Hernandez Mejia & Hernandez-Vargas, 2020).
- La vitesse de déplacement a également une incidence sur la distance parcourue par les gouttelettes. Les simulations informatiques de la dynamique des fluides montrent que, bien qu'une distance de 1,5 mètre puisse être suffisante à l'arrêt, des distances supérieures à 1,5 mètre sont nécessaires lorsque deux personnes courent ou se déplacent rapidement, car l'inertie des gouttelettes expulsées a également un impact sur la propagation des gouttelettes (Blocken, Malizia, van Druenen, & Marchal, 2020).

- Des études de simulation en laboratoire indiquent que les gouttelettes de toux produites par les humains et les mannequins peuvent parcourir de un à deux mètres et un maximum de quatre mètres dans certaines simulations (Loh et al., 2020; Rodriguez-Palacios, Cominelli, Basson, Pizarro, & Ilic, 2020; Viola et al., 2020).
- Deux études de simulation ont examiné les effets de la couverture faciale sur la distance de dispersion des particules expulsées. Les deux études révèlent que l'inclusion de masques faciaux, comme des écrans faciaux, des respirateurs filtrants pour masque facial, des masques faciaux chirurgicaux et des masques maison, a réduit la dispersion des gouttelettes expulsées à moins de 0,5 mètre, même lorsqu'elles toussent.
- Une revue systématique récente de Chu et coll. quantifie le risque relatif d'infection par le virus bêta-Corona en fonction de la distance (Chu et al., 2020). Les auteurs signalent que la

transmission des virus est plus faible avec une distance physique de 1 m ou plus, comparativement à une distance de moins de 1 m (n=10 736, probabilités ajustées [aOR] combinées 0 à 18, 0,09 à 0,38, IC à 95 %; différence de risque [DR] de 10 2 %, 11,5 à 7,5, IC à 95 %; fiabilité modérée); la protection augmentait à mesure que la distance s'allongeait (changement du risque relatif [RR] 2,02 par m; *p* interaction=0,041; fiabilité modérée). Il semble y avoir une certaine ambiguïté dans la mesure de la distance physique pour certaines des données probantes incluses dans le présent examen et, à ce titre, elles sont de piètre qualité. Par conséquent, il pourrait être prématuré de quantifier le risque relatif d'infection par le SRAS-CoV-2 en fonction des différences progressives de distance physique, en raison du manque de preuves suffisantes.

- À l'heure actuelle, aucune étude d'observation n'évalue le risque de transmission de l'infection par le SRAS-CoV-2 en fonction d'une distance variable d'une source infectieuse.

Vue d'ensemble des éléments de preuve

Les publications parues dans la littérature émergente jusqu'au 22 juin 2020 ont alimenté cette synthèse en bref. Le corpus de données disponibles est limité et repose en grande partie sur des simulations dans des conditions contrôlées. Ces études sont de bonne qualité, mais la généralisation de ces résultats à des situations réelles est inconnue. Pour cette raison, des recherches supplémentaires sur la transmission du SRAS-CoV-2 dans des situations et des distances variables pourraient modifier les conclusions de cette revue.

CONTENU

DISTANCE DE DISPERSION DU SRAS-COV-2

Tableau 1 : Littérature primaire sur la distance de dispersion des aérosols et gouttelettes

Titre de la publication	Principaux résultats	Référence
Études expérimentales et de simulation		
Impact de la canule nasale à débit élevé (HFNC) sur la distance de toux : répercussions de l'utilisation pendant la nouvelle éclosion de coronavirus	Une étude simulée menée auprès de volontaires en bonne santé (n=5) a révélé que les gouttelettes générées par la toux se propageaient sur une distance moyenne de 2,48 mètres (écart-type de 1,03) au niveau de référence, jusqu'à un maximum de 3,90 mètres. Lorsqu'on portait une canule nasale à débit élevé bien ajustée, la propagation moyenne des gouttelettes générées par la toux était de 2,91 mètres (1,09) avec une distance maximale de 4,50 mètres.	(Loh et al., 2020)
Masques faciaux, dispersion des aérosols et atténuation du risque de transmission du virus	Les chercheurs utilisent une technique Schlieren orientée vers l'arrière-plan pour visualiser le flux d'air et étudier l'efficacité de différents masques faciaux pour atténuer la dispersion des aérosols pendant la respiration et la toux. L'étude rapporte qu'un panache thermique contenant des particules respiratoires était visible à des distances inférieures à 0,5 mètre lors d'une respiration normale simulée par des sujets humains et des mannequins. Des panaches thermiques étaient visibles à environ 1,1 mètre de la bouche source pendant la toux simulée par le mannequin.	(Viola et al., 2020)
Masques textiles et revêtements de surface – Une méthode de simulation de pulvérisation et un « modèle universel de réduction des gouttelettes » contre les pandémies respiratoires	Les distances de dispersion des gouttelettes respiratoires lorsque l'on porte un masque fait de matériaux ménagers courants ont été mesurées à l'aide d'une simulation de pulvérisation en suspension bactérienne (imitant un éternuement). La plupart des gouttelettes porteuses de bactéries ont atterri à moins de 1,2 mètre de la source avec un masque en textile, alors que les gouttelettes ont parcouru des distances supérieures à 1,8 mètre lorsqu'aucune barrière (censée imiter l'absence de protection du visage) n'était en place.	(Rodriguez-Palacios et al., 2020)
Modèles mathématiques et simulations		
Titre de la publication	**Principaux résultats**	**Référence**
Vers une distance sociale de 1,5 m de	L'étude de la dynamique des fluides par ordinateur, éclairée par des données antérieures sur la dispersion des gouttelettes autour d'un	(Blocken et al., 2020)

la COVID19 aérodynamiquement équivalente pour la marche et la course	coureur, prend en compte les effets aérodynamiques potentiels introduits par les mouvements d'une personne (par exemple, marcher rapidement, courir et faire du vélo) sur la distance de déplacement des gouttelettes. L'étude vise à déterminer si une personne infectieuse principale qui se tient immobile et se déplace à proximité d'une deuxième personne sensible à une distance de 1,5 mètre ou plus peut présenter un risque de transmission de l'infection. Bien que l'exposition aux particules soit négligeable lorsque deux personnes se tiennent à 1,5 mètre l'une de l'autre, si les personnes courent ou marchent rapidement même à 1,5 mètre de distance, il existe un certain risque d'exposition aux particules infectieuses. Les résultats de l'étude suggèrent que la plus grande exposition de la personne qui suit se produit si elle se trouve directement derrière la personne qui précède (positionnée dans son sillage). Une réduction substantielle du risque d'exposition aux gouttelettes peut être obtenue en 1) évitant de marcher ou de courir dans le sillage de la personne en tête, 2) gardant la distance de 1,5 m en se décalant ou en se tenant côte à côte, ou 3) gardant des distances sociales supérieures à 1,5 m lorsqu'on se déplace rapidement ou qu'on court.	
À quel moment le SRAS-CoV-2 s'ajoute-t-il à votre liste d'épicerie?	La propagation de la COVID-19 dans un supermarché commercial et le potentiel de contagion sont estimés à l'aide d'une modélisation basée sur les agents. Cette méthode permet de cartographier toutes les caractéristiques souhaitées des clients et du personnel (p. ex., nombre de personnes infectées ou vulnérables, utilisateurs simultanés) et de l'agent infectieux, ainsi que les interactions/trajectoires possibles dans une disposition hypothétique. L'analyse du modèle révèle une augmentation de la distance entre les individus dans un supermarché (les distances testées étaient de 30 cm, de 50 cm, de 1 mètre, de 1,5 mètre et de 2 mètres), ainsi que la limitation du nombre d'individus dans le supermarché ont amélioré le pourcentage d'événements de transmission potentiels évités dans les simulations.	(Hernandez Mejia & Hernandez-Vargas, 2020)
COVID-19 : Effets des conditions météorologiques sur la propagation des gouttelettes respiratoires	Un modèle mathématique complet a été créé pour explorer l'évaporation des gouttelettes générées par la parole, le transfert de chaleur et la cinématique dans différentes conditions (par exemple, la température, l'humidité et la ventilation). La basse température et la forte humidité facilitent la transmission et la dispersion des gouttelettes, mais qu'elles empêchent la formation d'aérosols. D'autre part, une température élevée et une faible humidité favorisent une perte rapide de la masse des gouttelettes respiratoires (par	(Zhao et al., 2020)

	évaporation) et réduisent la distance de parcours des gouttelettes, mais ces conditions augmentent le risque de transmission des particules d'aérosol. L'étude conclut que les recommandations actuelles en matière de distanciation sociale pourraient ne pas être suffisantes pour diminuer tous les risques de transmission par voie aérienne, car les gouttelettes peuvent parcourir des distances allant jusqu'à 6 mètres.	
COVID-19. Transport de gouttelettes respiratoires dans un scénario urbain microclimatologique	Examen de la propagation des gouttelettes respiratoires dans les environnements extérieurs en appliquant un modèle de calcul d'une personne qui éternue dans un scénario urbain sous un vent climatologique d'intensité moyenne. La propagation des gouttelettes respiratoires est caractérisée par la dynamique de la taille des gouttelettes : les gouttelettes les plus grosses (de 400 à 900 µm) se propagent entre 2 et 5 mètres pendant 2,3 secondes tandis que les gouttelettes plus petites (de 100 à 200 µm) sont transportées entre huit et onze mètres en 14,1 secondes lorsqu'elles sont portées par un vent turbulent.	(Guerrero et al., 2020)
Influence du vent et de l'humidité relative sur l'efficacité de la distanciation sociale pour prévenir la transmission aérienne de la COVID-19 : Une étude numérique	La transmission aérienne des gouttelettes de toux avec des effets de condensation et d'évaporation est modélisée entre deux humains virtuels dans des environnements et des vitesses de vent différents. Les microgouttelettes suivent les courants d'air et peuvent être déposées sur des corps humains virtuels (y compris les régions de la tête) à des distances supérieures à 3,05 mètres. Une humidité relative élevée (99,5 %) entraîne également des gouttelettes plus grosses et un dépôt plus important de gouttelettes de toux sur les surfaces (en raison des effets de croissance hygroscopique). Des microgouttelettes en suspension pourraient être transmises entre les deux humains virtuels en moins de 5 secondes. L'étude conclut qu'en raison du vent ambiant, des effets de convection et de l'humidité relative sur les particules respiratoires émises par l'homme, les 1,83 mètre de distance sociale fréquemment recommandés pourraient ne pas être suffisants pour prévenir la transmission d'aérosols entre les personnes.	(Feng et al., 2020)
Modélisation du transport des aérosols et de l'exposition aux virus par des simulations numériques en relation avec la transmission du	Les preuves disponibles sur le transport des aérosols dans l'air sont combinées à des simulations 0D-3D dans des modèles basés sur la physique et des calculs théoriques. Les simulations de Monte-Carlo indiquent que les gouttelettes produites par la parole et la toux (diamètre < 20 µm) peuvent se propager dans l'air et y rester de 20 minutes à 1 heure, et être inhalées par d'autres personnes. La durée d'exposition pour inhaler 100 aérosols (supposée être une dose	(Vuorinen et al., 2020)

SRAS-CoV-2 par inhalation à l'intérieur	infectieuse adéquate) est variable en fonction de la situation et peut aller d'une seconde, à une minute, à une heure. Les simulations 3D de la dynamique des fluides suggèrent que les aérosols (dp <20 µm) peuvent être transportés sur des distances de 10 mètres dans des environnements génériques, en fonction de l'humidité relative et du débit d'air. Enfin, le séchage rapide des gouttelettes de mucus expulsées produirait des noyaux de gouttelettes et des aérosols qui pourraient potentiellement transporter des particules de virus en suspension dans l'air. Ces gouttelettes (diamètre initial des particules de 50 µm à 100 µm) pourraient rester en suspension dans l'air pendant environ 20 secondes à 3 minutes.	
Domaine d'études		
Titre de la publication	**Principaux résultats**	**Référence**
Potentiel de transmission du SRAS-CoV-2 par les aérosols et les surfaces	Des échantillons d'air et de surface provenant d'espaces isolés abritant des cas de COVID-19 aux États-Unis ont été recueillis et testés pour détecter la présence de l'ARN viral du SRAS-CoV-2. Des échantillons d'air de grands espaces et des échantillons d'air d'espaces personnels ont été testés par PCR en temps réel pour détecter la présence du SRAS-CoV-2. 63,2 % des échantillons d'air provenant des zones d'isolement des patients étaient positifs à l'ARN viral, et 58,3 % des échantillons d'air provenant des couloirs en dehors des zones d'isolement des patients ont également été testés positifs au virus. Les conclusions suggèrent que les particules d'aérosol viral peuvent être produites par les personnes infectées même en l'absence de toux, et qu'elles peuvent parcourir des distances supérieures à 1,8 mètre.	(Santarpia et al., 2020)

DISPERSION DU SRAS-COV-2 DISTANCE ET COUVRE-VISAGE

Tableau 2 : Littérature primaire sur l'efficacité du couvre-visage et de la distance

Titre de la publication	Principaux résultats	Référence
Masques textiles et revêtements de surface – Une méthode de simulation de pulvérisation et un « modèle	Les distances de dispersion des gouttelettes respiratoires lorsque l'on porte un masque fait de matériaux ménagers courants ont été mesurées à l'aide d'une simulation de pulvérisation en suspension bactérienne (imitant un éternuement). La plupart des gouttelettes porteuses de bactéries ont atterri à moins de 1,2 mètre de la source, alors que certaines gouttelettes	(Rodriguez-Palacios et al., 2020)

universel de réduction des gouttelettes » contre les pandémies respiratoires	ont parcouru des distances supérieures à 1,8 mètre lorsqu'aucune barrière (censée imiter l'absence de protection du visage) n'était en place. Tous les textiles testés ont réduit le nombre de gouttelettes atteignant les surfaces, limitant leur dispersion à moins de 30 cm, lorsqu'ils sont utilisés comme couches individuelles. Lorsqu'ils étaient utilisés en double couche, les textiles étaient aussi efficaces que les masques médicaux/tissus chirurgicaux, réduisant la dispersion des gouttelettes à moins de 10 cm, et la zone de contamination circonférentielle à environ 0,3 %.	
Masques faciaux, dispersion des aérosols et atténuation du risque de transmission du virus	Les chercheurs utilisent une technique Schlieren orientée vers l'arrière-plan pour visualiser le flux d'air et étudier l'efficacité de différents masques faciaux pour atténuer la dispersion des aérosols pendant la respiration et la toux. L'étude rapporte qu'un panache thermique contenant des particules respiratoires était visible à des distances inférieures à 0,5 mètre lors d'une respiration normale générée par des sujets humains et des mannequins. Des panaches thermiques étaient visibles à environ 1,1 mètre de la bouche source pendant la toux simulée par le mannequin. On a constaté que tous les masques faciaux testés (y compris les masques chirurgicaux, les masques maison, les appareils respiratoires filtrants et les écrans faciaux) réduisaient de plus de 90 % le débit des jets respiratoires à l'avant, et que les panaches thermiques étaient visibles à moins de 0,5 mètre pour la toux. Plusieurs jets de fuite vers l'arrière et vers le bas ont également été détectés à des distances inférieures à 0,2 de la source de la toux.	(Viola et al., 2020)

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe de science émergente de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature pertinente sur la COVID-19 sont menées par Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont recoupées avec la littérature de la liste de littérature COVID de l'OMS, et les centres d'information de la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et

les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour identifier les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Termes de recherche utilisés comprennent : distance.

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes sont extraites dans l'examen. Cet examen contient des recherches publiées jusqu'au 22 juin 2020.

Préparé par : Chatura, Prematunge. Groupe des sciences émergentes, ASPC. phac.emergingsciencesecretariat-secretariatdessciencesemergentes.aspc@canada.ca

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Evidence Snapshot:

Rapid Review on SARS-CoV-2 Aerosol Transmission – Update 2

Context

A wide range of evidence supporting SARS-CoV-2 aerosol transmission potential, in different settings and conditions, appears in the scientific literature. The current update includes 46 new studies, pre-published and published, between November 6, 2020 and March 12, 2021.

New Findings

- Twelve new reports of SARS-CoV-2 outbreaks/cluster investigations attributed to aerosol transmission including: inside a post-travel quarantine hotel, nursing home, hospital hematology unit, passenger bus, restaurant, fitness facilities, department store, and apartments arranged in a vertical line in an apartment building. In most outbreaks/clusters, the index cases were pre-symptomatic or early symptomatic and mask use was infrequent or improper.
- An experimental study on SARS-CoV-2 viability and decay within aerosols reported dependence on environmental conditions in order of influence: simulated sunlight exposure levels (midday summer, midday spring, indoor/night tested) > temperature (10-40°C) > humidity (20-70%). A 90% reduction in infectious virus took 4.8 minutes with midday summer sunlight exposure but took more than 2 hours under no sunlight exposure (i.e., indoors or at night) at 40^0C and 20% relative humidity.
- Viral RNA was detected in exhaled breath samples when COVID-19 patients were oropharyngeal, nasopharyngeal, and/or salivary swab positive at the time of sampling.
- Twenty-eight new biological monitoring studies examined SARS-CoV-2 contamination in environmental air samples. Two notable studies included significant SARS-CoV-2 aerosols produced by a mildly symptomatic individual during a short car ride. The other estimated 8.75 [95% CI 1.21-63.43; p=0.058] greater odds of SARS-CoV-2 in air samples collected from active case households compared to hospital rooms, which was attributable to differences in air exchanges and ventilation between the two settings.

Considerations

Scientific evidence on aerosol transmission of SARS-CoV-2 is increasing. SARS-CoV-2 infectious dose, characterization of case attributes and environmental conditions that change aerosol transmission risk are not well defined within the available literature.

Reference: Emerging Science Group of the Public Health Agency of Canada. Rapid Review on SARS-CoV-2 Aerosol Transmission – Update 2 Full report available from: **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Aperçu des éléments de preuve :

Revue rapide sur la transmission par les aérosols du SRAS-CoV-2 – Mise à jour 2

Contexte

On trouve, dans la littérature scientifique, une vaste gamme d'éléments de preuve qui appuient la transmission potentielle du SRAS-CoV-2 par les aérosols, dans différents contextes et dans différentes conditions. Cette mise à jour inclut 46 nouvelles études, tant publiées qu'en préimpression, diffusées entre le 6 novembre 2020 et le 12 mars 2021.

Nouvelles constatations

- Douze nouveaux rapports associés à des enquêtes sur des éclosions ou des grappes de SRAS-CoV-2 attribuées à la transmission par les aérosols, y compris dans un hôtel où se trouvaient des voyageurs en quarantaine, dans une maison de soins infirmiers, dans l'unité d'hématologie d'un hôpital, dans un autobus avec passagers, dans un restaurant, dans des installations de conditionnement physique, dans un grand magasin et dans des appartements à la verticale dans une tour d'habitation, ont été examinés dans la présente revue rapide. En les regardant, on peut voir que les cas index inclus dans ces rapports en étaient aux stades présymptomatiques ou symptomatiques précoces de l'infection et que le masque ou le couvre-visage avait soit été peu porté ou mis de façon inadéquate.
- Une étude expérimentale sur la viabilité et la désintégration du SRAS-CoV-2 dans les aérosols a révélé une dépendance aux conditions environnementales suivantes, par ordre d'influence : concentrations d'exposition simulées à la lumière du soleil (mi-journée, l'été, mi-journée, au printemps, intérieur/nuit) > température (entre 10 et 40 °C) > humidité (entre 20 et 70 %). Il a ainsi fallu 4,8 minutes à 40 °C avec une exposition à la lumière du soleil en mi-journée pour obtenir une réduction de 90 % des virus infectieux alors que, sans exposition à la lumière du soleil (c.-à-d. à l'intérieur ou la nuit), il a fallu plus de 2 heures à 40 °C, avec une humidité relative de 20 %, pour obtenir la même réduction.
- L'échantillonnage a permis de détecter la présence d'ARN viral dans l'air expiré chez différents patients atteints de COVID-19 ayant reçu des résultats positifs après des prélèvements oropharyngés, nasopharyngés ou salivaires.
- Vingt-huit nouvelles études de suivi biologique ont examiné la contamination par le SRAS-CoV-2 dans des échantillons d'air ambiant. Deux études notables ont également mentionné qu'une personne légèrement symptomatique avait produit une quantité importante d'aérosols du SRAS-CoV-2 alors qu'elle effectuait un court trajet en voiture. Une étude a comparé des échantillons d'air ambiant prélevés dans des chambres d'hôpital et chez des ménages en quarantaine où se trouvaient des cas actifs et estimé à plus de 8,75 [IC à 95 %, 1,21 à 63,43; P = 0,058] la probabilité de résultats positifs dans les échantillons d'air prélevés dans les ménages par rapport aux chambres d'hôpital, un

résultat qui a été attribué aux différences dans les échanges d'air et la ventilation entre les deux milieux.

Facteurs dont il faut tenir compte

Les preuves scientifiques sur la transmission par les aérosols du SRAS-CoV-2 sont de plus en plus nombreuses. La dose infectieuse du SRAS-CoV-2, la caractérisation des caractéristiques des cas et les conditions environnementales qui modifient le risque de transmission par les aérosols ne sont cependant pas bien définies dans la documentation disponible.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Revue rapide sur la transmission par les aérosols du SRAS-CoV-2– Mise à jour 2. Rapport complet disponible auprès de : **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Evidence Snapshot:
SARS-CoV-2 Contact Tracing

Context

Contact tracing is one of several public health measures (PHMs) used to control the COVID-19 pandemic. When cases are too high, there is not enough capacity for contact tracing to contain the epidemic. As regions transition from restrictive PHMs (e.g., lift lockdown), the potential and limits of new and traditional contact tracing techniques to prevent resurgence of the pandemic must be fully understood. The evidence brief identified relevant literature to assess the strategic use of effective and efficient methods for contact tracing.

Key Findings

There were 23 articles in the review: seven rapid or systematic reviews with studies up to December 2020; and two empirical and 14 modelling studies posted November 2020 through February 10, 2021. The key findings were:

- Studies have shown that as transmission decreases and restrictive PHMs (e.g., lockdowns, closures and restricted movement) are lifted, a strong contact tracing system with sufficient capacity is needed to avoid a resurgence (5% vs. <50% chance of a resurgence when sufficient contact tracing capacity is and is not in place, respectively).
- For contact tracing to be effective, timely isolation of cases (≤3 days after onset of symptoms) and quarantine of at least 60-90% of people exposed to the case is necessary.
- Models show decreased effectiveness of contact tracing when system capacity is exceeded, as case contacts are not traced, or there are delays in tracing and initiating quarantine, all of which may lead to ongoing transmission.
- Increasing efficiency and effectiveness of contact tracing can be achieved with bidirectional contact tracing, the use of electronic data management tools and contact tracing apps. Apps require that high proportions of population use the app (estimates from 56% to up to 100%) to result in improved epidemic control.

Considerations

The limitations of the evidence include a lack of empirical studies and high reliance on the findings of modeling studies and reviews based on pre-pandemic experience. Overall, evidence indicates that contact tracing systems can effectively contain the COVID-19 pandemic when they have the capacity to rapidly isolate identified cases and quarantine the majority of their contacts, to limit transmission potential within a community.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evidence Brief of SARS-CoV-2 Contact Tracing. Feb 8, 2021. Full report available from: **phac.evidence-donnees.probantes.aspc@canada.ca**

Aperçu des éléments de preuve : Recherche des contacts pour le SRAS-CoV-2

Contexte

La recherche des contacts est l'une des nombreuses mesures de santé publique qui ont été utilisées pour contrôler la pandémie de COVID-19. Lorsque le nombre de cas est trop élevé, la capacité de dépistage des contacts n'est cependant pas suffisante pour contenir l'épidémie. Ainsi, au fur et à mesure que les régions passent à des mesures de santé publique moins restrictives (p. ex., fin du confinement), il faut s'assurer de bien comprendre le potentiel et les limites des techniques de recherche des contacts pour pouvoir prévenir toute résurgence de la pandémie. La synthèse en bref a permis d'identifier des documents pertinents qui permettront d'utiliser stratégiquement différentes méthodes efficaces et efficientes de recherche des contacts.

Principales constatations

Vingt-trois articles ont été inclus dans cette synthèse, soit sept revues rapides ou systématiques (portant sur des études publiées jusqu'en décembre 2020), deux études empiriques et quatorze études de modélisation publiées entre novembre 2020 et le 10 février 2021. Les principales constatations qui en découlent sont les suivantes :

- Les études ont montré qu'à mesure que la transmission diminue et que les mesures de santé publique restrictives (p. ex., confinement, fermetures et déplacements restreints) sont levées, un système de recherche des contacts solide et suffisamment puissant est nécessaire pour éviter une résurgence de la pandémie (la probabilité de résurgence atteint 5 % les capacités pour effectuer la recherche des contacts sont disponibles comparativement à < 50 % lorsque ces capacités ne sont pas disponibles).
- Pour que la recherche des contacts soit efficace, il faut cependant s'assurer d'isoler rapidement les cas (≤ 3 jours après l'apparition des symptômes) et de mettre en quarantaine au moins 60 à 90 % des personnes exposées à ces cas.
- Les modèles montrent une diminution de l'efficacité de la recherche des contacts lorsque les capacités du système de soins de santé sont dépassées, car la recherche des contacts n'est alors plus effectuée ou est retardée, ce qui entraîne également un retard dans la mise en quarantaine et peut donc permettre une transmission continue du virus.
- Il est cependant possible d'augmenter l'efficience et l'efficacité de la recherche des contacts grâce à la recherche bidirectionnelle, ainsi qu'à l'utilisation d'outils électroniques de gestion des données et d'applications de recherche des contacts. Pour que ces applications puissent être utilisées de façon adéquate et permettre d'obtenir un meilleur contrôle de l'épidémie, il faut cependant s'assurer qu'une importante proportion de la population les utilise (estimations variant entre 56 % et 100 %).

Facteurs dont il faut tenir compte

Les limites associées aux éléments de preuve comprennent un manque de preuves empiriques et une forte dépendance aux conclusions tirées des études de modélisation ou des examens fondés sur l'expérience prépandémique. Dans l'ensemble, les éléments de preuve indiquent que les systèmes de recherche des contacts peuvent permettre de contenir efficacement la pandémie de COVID-19 lorsqu'ils sont utilisés pour isoler rapidement les cas identifiés et mettre la majorité de leurs contacts en quarantaine, ce qui permettra de limiter le potentiel de transmission du virus dans la collectivité.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Synthèse en bref sur la recherche des contacts pour le SRAS-CoV-2. 8 février 2021. Rapport complet disponible auprès de : **phac.evidence-donnees.probantes.aspc@canada.ca**

Evidence Snapshot:

Evidence Brief of COVID-19 Infectious Period in Immunosuppressed/Immunocompromised Individuals

Context

The infectious period is an important clinical and epidemiologic parameter in the management of COVID-19 patients and has been estimated to be approximately 10-13 days in immunocompetent COVID-19 cases. The objective of this brief was to review the evidence on the infectious period for immunosuppressed and immunocompromised COVID-19 cases.

Key Findings

The evidence brief identified 19 studies, including 12 cohort studies and 7 longitudinal case series, published before February 5, 2021. All but two studies relied on RT-PCR testing to monitor viral shedding. The key findings were:

- Patients with immunosuppression due to hematologic cancers have been shown to shed replication-competent SARS-CoV-2 for up to 2 months, median 25 days (range 8-61 days). In cancer patients overall, median time to viral RNA clearance ranged from 12-50 days with an overall range of 9-78 days.
- In solid organ transplant patients undergoing immunosuppressive therapy, time to viral RNA clearance ranged from 9-66 days. Kidney transplant recipients had mean viral RNA shedding of 28.4 ± 9.3 days, similar to another study that reported high viral loads at day 30.
- In patients with HIV, viral RNA clearance occurred over a median of 18 days (IQR 7-28) but remained detectable in some patients >40 days post symptom onset. Lower CD4 cell counts in HIV patients were associated with longer time to viral clearance.
- Overall, longer time to viral clearance was associated with more severe disease and more comorbidities, however this was not significant in all studies.

Considerations

Immunosuppressed and immunocompromised individuals with COVID-19 appear to have longer and highly variable infectious periods compared to immunocompetent individuals. The evidence is limited by the use of RT-PCR to assess infectivity as this test cannot distinguish between infectious and non-infectious viral particles. A gap in research is how infectious period is affected by immune-modulating drugs for non-cancer diseases. Prospective studies and the use of culture are needed to better inform when to de-isolate immunosuppressed and immunocompromised patients recovering from COVID-19 infection.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evidence Brief of COVID-19 Infectious Period in Immunosuppressed/Immunocompromised Individuals. February 17, 2021. Full report available from: **phac.evidence-donnees.probantes.aspc@canada.ca**

février 17, 2021

Aperçu des éléments de preuve :

Synthèse en bref sur la période infectieuse de la COVID-19 chez les personnes immunodéprimées ou immunodéficientes

Contexte

La période infectieuse est un paramètre clinique et épidémiologique qui joue un rôle important dans la prise en charge des patients atteints de COVID-19 et cet état de fait est encore plus vrai dans le cas des patients immunocompétents atteints de COVID-19 puisque leur période infectieuse a une durée estimative de 10 à 13 jours. La présente synthèse vise donc à examiner les éléments de preuve sur la période infectieuse des patients immunodéprimés et immunodéficients atteints de COVID-19.

Principales constatations

La synthèse en bref a identifié 19 études, soit 12 études de cohorte et 7 séries de cas longitudinales, qui ont été publiées avant le 5 février 2021. Toutes ces études, à l'exception de deux, ont utilisé des tests RT-PCR pour surveiller l'excrétion virale. Les principales constatations qui en découlent sont les suivantes :

- Les patients dont l'immunosuppression est due à des cancers hématologiques ont excrété le virus SARS-CoV-2 réplicatif pendant un maximum de deux mois avec une médiane de 25 jours (plage de 8 à 61 jours) Dans l'ensemble, chez les patients atteints de cancer, le délai médian avant la clairance de l'ARN viral variait de 12 à 50 jours, avec une plage globale allant de 9 à 78 jours.
- Chez les patients qui ont subi une greffe d'organe entier et suivent une thérapie immunosuppressive, le temps qui s'est écoulé avant la clairance de l'ARN viral variait entre 9 et 66 jours. Le temps moyen d'excrétion de l'ARN viral du SRAS-CoV-2 dans un groupe de patients ayant subi une greffe de rein était de 28,4 ± 9,3 jours, ce qui est similaire aux données d'une autre étude qui a déclaré des charges virales élevées le jour 30.
- Chez les patients atteints de VIH, la clairance virale de l'ARN a atteint 18 jours en moyenne (EI 7 à 28), mais le virus est demeuré détectable chez certains patients plus de 40 jours après l'apparition des symptômes. Un lien a été établi entre un nombre plus bas de cellules CD4 chez les patients atteints du VIH et une plus longue période avant la clairance virale.
- Dans l'ensemble, une plus longue période de clairance virale est donc associée à une forme plus grave de la maladie et à un plus grand nombre de comorbidités, même si cet élément de preuve n'a pas été jugé significatif dans toutes les études.

Facteurs dont il faut tenir compte

Comparativement aux personnes immunocompétentes, les personnes immunodéprimées et immunodéficientes atteintes de la COVID-19 semblent avoir eu des périodes infectieuses plus longues et beaucoup plus variables. La preuve présentée est cependant limitée par l'utilisation du test RT-PCR pour évaluer l'infectivité, puisque ce test ne permet pas de faire de distinction entre les particules virales infectieuses et non infectieuses. La recherche comporte également une lacune, à savoir la manière dont la période infectieuse est affectée par les médicaments immunomodulateurs utilisés dans les cas de maladies non cancéreuses. Des études prospectives et l'utilisation de cultures seront nécessaires pour mieux savoir à quel moment ne plus isoler les patients immunodéprimés et immunodéficients qui se remettent d'une infection à la COVID-19.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Synthèse en bref sur la période infectieuse de la COVID-19 chez les personnes immunodéprimées ou immunodéficientes. 17 février 2021. Rapport complet disponible auprès de : **phac.evidence-donnees.probantes.aspc@canada.ca**

Aperçu des éléments de preuve : **Synthèse en bref sur la charge virale et la probabilité de transmission pendant la période infectieuse du SRAS-CoV-2**

Contexte

L'identification des personnes infectieuses est essentielle à la prévention et au contrôle efficaces de la COVID-19. La présente synthèse en bref examine le lien entre la charge virale et la probabilité de transmission pendant la période infectieuse du SRAS-CoV-2. La valeur du seuil de cycle (Ct), qui correspond au nombre de cycles requis pendant la RT-PCR pour atteindre le seuil de détection pour une certaine cible génétique, est souvent utilisée comme indicateur de la charge virale (puisqu'une faible valeur Ct correspond à une charge virale plus élevée).

Principales constatations

La synthèse en bref comprend 27 études, soit 2 revues systématiques, 22 études d'observation, 1 étude de surveillance et 2 études de modélisation publiées avant le 31 mars 2021. Il s'agissait d'études portant notamment sur le lien entre la charge virale et la preuve d'un virus réplicatif (n = 15) et l'association entre la charge virale et le risque de transmission (n = 12). Les principales constatations qui en découlent sont les suivantes :

- Des charges virales élevées (Ct inférieur à 30 ou supérieur à 10^6 copies/ml) ont été signalées pendant la période présymptomatique, ainsi que jusqu'à 8 à 10 jours après l'apparition des symptômes. C'est précisément pendant cette période que le risque de transmission est le plus grand. Les échantillons dont la valeur Ct est ≤ 25 ont indiqué la présence d'un virus réplicatif à un taux supérieur à 90 %.
- Les cas index qui avaient une faible charge virale (indiquée par une valeur Ct supérieure à 35) présentaient un faible risque de transmission (environ 8 %).
- Dans de rares cas, on pouvait tout de même détecter un risque de transmission chez ces personnes plus de 10 jours après l'apparition des symptômes ou lorsque leurs valeurs Ct étaient supérieures à 35, mais ces cas sont plus susceptibles d'être atteints de la forme grave de la maladie ou d'être immunodéprimés.

Facteurs dont il faut tenir compte

Dans la plupart des cas, la charge virale et les jours qui ont suivi l'apparition des symptômes sont de bons prédicteurs du potentiel de transmission. Les preuves sont cependant limitées par la grande hétérogénéité des méthodes d'échantillonnage, des tests de détection et des cibles génétiques utilisés dans les différentes études. Une lacune importante dans la recherche porte sur le lien potentiel entre la charge virale et la transmissibilité accrue des variants préoccupants du SRAS-CoV-2. Des recherches futures seront donc nécessaires pour combler ce manque de connaissances.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Synthèse en bref sur la charge virale et la probabilité de transmission pendant la période infectieuse du SRAS-CoV-2. 31 mars 2021. Rapport complet disponible auprès de : **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Evidence Snapshot:

Evidence Brief of SARS-CoV-2 Risks in Arenas

Context

COVID-19 outbreaks related to arenas and ice sports have highlighted the need to understand how transmission is occurring and what environmental and behavioural factors may be altered to lower the risk of transmission. To address this, the available literature was summarized.

Key Findings

Thirteen publications available as of February 12, 2021 were included: four of outbreaks in arena sports (hockey, curling), two cross-sectional studies on transmission in non-arena based sports, four guidance documents for resumption of hockey, and three reviews on SARS-CoV-2 with respect to cold temperatures. The key findings were:

- Hockey provides favourable conditions for SARS-CoV-2 transmission because of both on-ice activities: heavy breathing on ice and the bench due to high intensity physical activity, close proximity of players and coaches, dry and cold air in the arena, and segregated air mass caused by ~10 foot barriers around the ice resulting in poor air circulation. And off-ice activities: due to time spent in close proximity to others before and after on-ice activities.
- Evidence on transmission during non-arena sports found lower risk of COVID-19 among outdoor sports compared to indoor sports, and non-contact sports compared to contact sports. For indoor sports, wearing a mask had a significant protective association.
- Strategies to reduce risk for all indoor ice activities include limiting the number of individuals in the arena, screening of individuals and increasing the use of sanitizers, minimizing the sharing of equipment, and using masks and social distancing when not on the ice, as well as lessening time of both before and after on-ice activities.

Considerations

Published empirical evidence is limited, despite many jurisdictions reporting cases or outbreaks traced to hockey teams or curling, as the nature of these sports makes it difficult to establish with certainty where transmission has occurred. However, it appears basic public health measures can reduce the risk of COVID-19 transmission in ice arenas.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evidence Brief of SARS-CoV-2 Risks in Arenas. Feb 12, 2021. Full report available from: **phac.evidence-donnees.probantes.aspc@canada.ca**

Aperçu des éléments de preuve :

Synthèse en bref sur les risques associés au SRAS-CoV-2 dans les arénas

Contexte

Les éclosions de COVID-19 associées aux arénas et aux sports sur glace ont fait ressortir la nécessité de comprendre comment s'effectue la transmission et les facteurs environnementaux et comportementaux qui peuvent être modifiés pour réduire le risque de transmission. La littérature disponible à cet égard a donc été résumée dans la présente synthèse en bref.

Principales constatations

Treize publications disponibles en date du 12 février 2021 ont été incluses, soit quatre études portant sur des éclosions dans les arénas (hockey, curling), deux études transversales sur la transmission dans des sports pratiqués à l'extérieur des arénas, quatre documents d'orientation sur la reprise du hockey et trois revues sur le lien entre le SRAS-CoV-2 et les températures froides. Les principales constatations qui en découlent sont les suivantes :

- Le hockey offre des conditions favorables à la transmission du SRAS-CoV-2 en raison des activités pratiquées sur la glace, de la respiration forte, tant sur la glace et sur le banc en raison de l'intense activité physique, de la proximité des joueurs et des entraîneurs, de l'air sec et froid que l'on retrouve dans les arénas, ainsi que de la masse d'air séparée que créent les barrières d'environ 3 mètres (10 pieds) de hauteur tout autour de la glace et favorisent une mauvaise circulation de l'air. Les activités en dehors de la glace, notamment le temps passé à proximité d'autres personnes, tant avant qu'après les activités sur glace, sont aussi des conditions favorables à la transmission du virus.
- Les preuves sur la transmission pendant la pratique des sports à l'extérieur des arénas ont révélé un risque plus faible de COVID-19 lorsque les sports étaient pratiqués en plein air plutôt qu'à l'intérieur, et le même type de lien a pu être établi entre les sports sans contact et les sports de contact. En ce qui concerne les sports pratiqués à l'intérieur, le port d'un masque ou d'un couvre-visage a semblé offrir un important niveau de protection.
- Les stratégies visant à réduire le risque de transmission associé à l'ensemble des activités sur glace pratiquées à l'intérieur comprennent le fait de limiter le nombre de personnes pouvant se trouver dans l'aréna, d'effectuer le dépistage des personnes et d'améliorer l'utilisation des désinfectants, de minimiser le partage de l'équipement, de favoriser le port des masques ou des couvre-visages et d'assurer le respect de la distanciation sociale lorsque les personnes ne sont pas sur la glace, ainsi que de réduire le temps passé dans l'aréna, tant avant qu'après les activités sur glace.

Facteurs dont il faut tenir compte

Les données empiriques publiées sont limitées, malgré le fait que de nombreuses administrations signalent des cas ou des éclosions liés aux équipes de hockey ou de curling, car la nature de ces sports ne permet pas d'établir facilement avec certitude le lieu où la transmission s'est produite. Il semble toutefois que le respect des mesures de base en matière de santé publique puisse réduire le risque de transmission de la COVID-19 dans les arénas.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Synthèse en bref sur les risques associés au SRAS-CoV-2 dans les arénas. 12 février 2021. Rapport complet disponible auprès de : **phac.evidence-donnees.probantes.aspc@canada.ca**

Evidence Snapshot:

Evergreen Rapid Review on COVID-19 Vaccine Attitudes and Uptake – Update 8

Context

Vaccination is a key public health strategy for the prevention and control of COVID-19. Update 8 of this living rapid review summarizes 205 studies on COVID-19 vaccine uptake globally, and vaccine attitudes in the Canadian general population and pre-defined priority populations. Evidence on priority populations includes studies from Australia, New Zealand, USA, and the UK to complement areas where there was little Canadian research.

New Findings

There were 40 new studies identified from June 1-July 1, 2021 including 6 new studies from Canada. Key results from studies conducted after January 2021 found that:

- Intention to vaccinate in Canada continues to increase and was 84-88% across the country in June 2021.
- In June, 89% of Canadians reported they intend to receive a second dose, 9% have already had their second dose, 1% probably will not, and 1% were unsure.
- One study indicated that 48% of Canadians were uncomfortable about receiving a different brand of vaccine as their second dose, whereas 46% were comfortable and 6% were unsure.
- Financial incentives were not reported to increase the likelihood of accepting a vaccine in a study conducted in Manitoba, however two studies indicate text messaging reminders are effective.
- Parental and child vaccine intentions continue to be highly correlated with each other, with parents who were intending to take a vaccine more likely to intend to vaccinate their children. In a group of 70 parents or guardians of children aged 12-17 from Manitoba, 15% and 13% were not sure or would not vaccinate their children, respectively. Similar to the general population, parents from lower-income households, who are younger, less educated, have a history of not accepting other vaccines, who are female, and ethnic minorities were more likely to reject a vaccine for their children.
- Vaccine passports have high support in Quebec with 72% of residents in favour.
- In February, Israel implemented the "green pass" which could be acquired post-vaccination or with a recent negative test. This resulted in a 22% increase in vaccine uptake after three days.

Considerations

Since November 2020, Canadians have indicated an increasing intention to vaccinate. Most of the evidence on vaccine intention has been based on self-reported results from surveys, so may be limited by response and social desirability bias. Since the vaccine rollout began, 29 studies on vaccine uptake have been identified. Uptake trends were in line with trends reported in intention to vaccinate studies.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evergreen Rapid Review on COVID-19 Vaccine: Attitudes and Uptake: Update #8. July 2021. Full report available from: **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Aperçu des éléments de preuve

Revue rapide et évolutive sur les attitudes à l'égard des vaccins et de l'adoption des vaccins contre la COVID-19 – Mise à jour 8

Contexte

La vaccination est une stratégie de santé publique clé pour la prévention et le contrôle de la COVID-19. La mise à jour 8 de la présente revue rapide évolutive résume 205 études sur l'adoption du vaccin contre la COVID-19 à l'échelle mondiale et les attitudes à l'égard du vaccin dans la population canadienne en général que dans des populations prioritaires prédéterminées. Les données probantes sur les populations prioritaires en Australie, en Nouvelle-Zélande, aux États-Unis et au Royaume-Uni ont également été incluses pour compléter les domaines dans lesquels il y avait peu de recherche au Canada.

Nouvelles constatations

Entre le 1er juin et le 1er juillet 2021, 40 nouvelles études ont été recensées, dont six nouvelles études provenaient du Canada. Les études effectuées après janvier 2021 ont notamment révélé ce qui suit :

- Au Canada, l'intention de se faire vacciner a continué d'augmenter et se situait entre 84 et 88 % dans l'ensemble du pays en juin 2021.
- En juin, 89 % des Canadiens ont déclaré avoir l'intention de recevoir une deuxième dose, 9 % ont déjà reçu leur deuxième dose, 1 % ne le feront probablement pas et 1 % étaient incertains.
- Une étude a indiqué que 48 % des Canadiens étaient mal à l'aise à l'idée de recevoir une marque différente de vaccin comme deuxième dose, tandis que 46 % étaient à l'aise et 6 % étaient incertains.
- Une étude menée au Manitoba a révélé que les incitations financières n'augmentaient pas la probabilité de se faire vacciner, mais deux études indiquent que les rappels par messagerie texte sont efficaces.
- L'intention de se faire vacciner des parents et des enfants sont fortement corrélées les unes avec les autres, puisque les parents qui avaient l'intention de se faire vacciner étant plus susceptibles de vouloir faire vacciner leurs enfants. Dans un groupe de 70 parents ou tuteurs d'enfants âgés de 12 à 17 ans du Manitoba, 15 % et 13 % n'étaient pas sûrs ou ne feraient pas vacciner leurs enfants, respectivement. Tout comme dans la population en général, les parents qui sont dans des ménages à faible revenu, qui sont plus jeunes et moins instruits, qui ont déjà refusé d'autres vaccins, qui sont des femmes ou des membres de minorités ethniques, sont ceux qui étaient plus susceptibles de refuser un vaccin pour leurs enfants.
- Le passeport vaccinal bénéficie d'un soutien important au Québec, 72 % des résidents y étant favorables.
- En février, Israël a mis en place le « laissez-passer vert » qui peut être acquis après la vaccination ou avec un test négatif récent. Cela a entraîné une hausse de 22 % de l'adoption du vaccin après trois jours.

Facteurs dont il faut tenir compte

Depuis novembre 2020, les Canadiens ont dit être de plus en plus nombreux à vouloir se faire vacciner. La plupart des données probantes sur l'intention de se faire vacciner étaient fondées sur les résultats autodéclarés provenant de sondage, ce qui veut dire qu'elles peuvent être limitées par la réponse et le biais de désirabilité sociale. Depuis le début du déploiement du vaccin, 29 études sur l'adoption du vaccin ont été recensées. Les tendances en ce qui concerne l'adoption du vaccin étaient conformes aux tendances déclarées dans les études sur l'intention de se faire vacciner.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Revue rapide et évolutive sur les attitudes à l'égard des vaccins et de l'adoption des vaccins contre la COVID-19 : mise à jour 8. Juillet 2021. Rapport complet disponible en écrivant à : **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Evidence Snapshot:

Evergreen Rapid Review on COVID-19 Vaccine Attitudes and Uptake in Canada – Update 9

Context

Vaccination is a key public health strategy for the prevention and control of COVID-19. Update 9 of this living rapid review summarizes 62 studies on COVID-19 vaccine uptake and attitudes in Canada. Previous versions of this report (1-8) included vaccine uptake globally, vaccine attitudes in the Canadian general population and pre-defined priority populations from Australia, New Zealand, USA, and the UK to complement areas where there was little Canadian research.

New Findings

There were 9 new studies identified from July 1-August 1, 2021 and key results from studies conducted in the last 4 months were highlighted. This included:

- Two July studies indicated 86-91% of Canadians have either received a vaccine or wish to get a vaccine as soon as possible, a slight increase from May and June.
- A study that explored the relationship between race and intention to vaccinate found that 21% of Canadians were vaccine hesitant with higher levels among Black (33%) and non-Black visible minorities (25%) compared to White Canadians (19%). Black Canadians aged 25-34 had the highest levels of vaccine hesitancy (54%). Drivers of vaccine hesitancy among Black Canadians were the inability to take paid time off, concern that vaccines cause autism, and vaccine safety concerns in general.
- In Saskatchewan, those with Indigenous status were more vaccine hesitant than non-Indigenous (RRR 1.65, 95% CI: 1.01-2.70) and those who were born outside of Canada or who had lived in Canada less than 20 years were more vaccine hesitant than those born in Canada (RRR 3.14, 95% CI: 1.56-6.34).
- A longitudinal study from Quebec demonstrated that 87% of parents intend to vaccinate their children, up 1% from June.
- 76% of those unwilling or unsure about vaccination were planning on resuming everything they did before COVID-19 with no hesitation, compared to 34% of people after their first dose and 27% of people after both doses of vaccine.
- Two studies reported 66% of Canadians want full vaccination as a requirement to allow people to cross the USA-Canada border and 69% want to wait until at least 75% of Canadians are fully vaccinated before opening the border.

Considerations

Since November 2020, Canadians have indicated an increasing intention to vaccinate. This is based on self-reported results from surveys, so may be limited by response and social desirability bias. Since the vaccine rollout began, only one study on vaccine uptake has been identified. Uptake trends were in line with trends reported in intention to vaccinate studies.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evergreen Rapid Review on COVID-19 Vaccine: Attitudes and Uptake: Update #9. August 2021. Full report available from: **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Emerging Evidence on COVID-19

Rapid Review of Infectious Period

Introduction

What is the length of the infectious period for SARS-CoV-2?

The infectious period (also known as the communicability period) is defined as the time during which an infected person can transmit an infectious agent to another person. The infectious period and its relationship to exhibiting symptoms is an important clinical and epidemiologic parameter to understand for the control of any infectious disease.

Infectious period estimates have been determined from a combination of epidemiological and clinical investigations that together inform when an infected person can or is likely to transmit the virus. To establish a person is infected, most studies report the use of RT-PCR to diagnose cases of COVID-19 and to monitor viral shedding over time. However, detection of viral RNA by RT-PCR does not provide proof of infectivity and virus particles are likely to be shed from infected tissue for a period of time after an infection has been cleared by the host immune system (Jefferson et al., 2020). To establish if viable virus has been isolated in a sample, replication of virus is established most commonly in cell culture and indicates that infective virus is present. In this review few studies have employed culture methods (or animal inoculation) because it is slow, costly, and is not as sensitive as RT-PCR. The results of epidemiological studies, RT-PCR, qRT-PCR and culture results together provide evidence on when a case is likely infective and capable of transmitting the virus.

This rapid review covers the evidence for the infectious period of pre-symptomatic, asymptomatic, and symptomatic COVID-19 cases as inferred by culturable virus shedding, viral RNA detection, epidemiological data, and predictive models. Samples studied are most commonly nasopharyngeal swabs, however fecal/rectal swabs and eye swabs have also been studied for the presence of SARS-CoV-2. Respiratory transmission is considered most common, and more evidence is needed to determine importance of other modes of transmission including fecal-oral, fecal-fomite or fecal-respiratory given viable SARS-CoV-2 has been found in feces.

This is an evergreen rapid review of infectious period and contains key studies captured by the PHAC emerging sciences daily COVID-19 literature scan up to August 31, 2020.

Key Points

Overall, the best available evidence indicates infectious period for most symptomatic cases is considered to start on average 2.5 days before developing symptoms, peak around day 4 of symptoms and decrease to low levels within 8-10 days after the start of symptoms for a total of 10-13 days. The asymptomatic infectious period has been found to be similar. Longer infectious periods have been documented in more severe or immunocompromised cases (18-32 days post symptom onset).

Pre-symptomatic Infectious Period, N=25 studies

- Viable virus has been cultured from respiratory samples of pre-symptomatic cases 1-6 days before symptom onset as determined by medical observation (Table 1). Viable virus has also been cultured from gastrointestinal samples; for example a rectal sample showed evidence of active SARS-CoV-2 viral replication three days prior to symptom onset (Qian et al., 2020).
- Studies utilizing RT-PCR to detect viral RNA from respiratory samples also suggest that shedding occurs on average 2.5 days (1-7 range) prior to symptom onset.

Asymptomatic Infectious Period, N=25 studies

- Viable virus and viral RNA detected in a cohort of asymptomatic cases was highest during the first week of infection and declined in subsequent weeks (Quicke et al., 2020). Infectious virus was not detected by plaque assay in nasopharyngeal swabs from individuals with less than 100,000 RNA copies/swab.
- There has been little consensus about whether asymptomatic and mildly symptomatic infections differ in viral shedding time (Table 2). Based on the current evidence, the total infectious period of asymptomatic cases appears to be similar or shorter than that of mildly symptomatic cases. Across studies, similar viral loads have been reported for asymptomatic, pre-symptomatic, and symptomatic cases.

Symptomatic Infectious Period, N=107 studies

- Viable virus, culture results, N=18 primary research studies and 2 systematic reviews:
  - For mild cases, the best estimate for the infectious period, measured from self-reported symptom onset using virus culture from respiratory samples, is 8-10 days with a peak in viral load during the first week of illness (Table 3).
  - Cases of prolonged viable viral shedding (18-32 days) have been documented using virus culture in a few studies. Many of these studies are still in preprints and include single cases or small sample sizes (Table 3). These cases are typically individuals with severe infection, who are either immunocompromised, or have multiple chronic underlying health conditions.
  - There are a few studies that have cultured SARS-CoV-2 from the fecal/rectal samples of a confirmed case (Table 3). A recent study of inoculated ferrets has confirmed the presence of infectious SARS-CoV-2 in fecal and urine specimens from days 11, 13 and 15 of illness (Jeong et al., 2020).
- Viral RNA detection, RT-PCR results, N=88 primary research studies and 6 systematic reviews:
  - Most studies report time from self-reported symptom onset or test positive diagnosis to time viral infection has been cleared, determined via RT-PCR. Positive RT-PCR results are not proof of infectiousness.

- Viral RNA presence varies widely by sample type. Respiratory swabs typically become negative within 14-20 days of self-reported symptom onset, while stool samples remain positive a few days to four weeks longer than respiratory samples. Evidence of SARS-CoV-2 RNA has also been identified in eye swabs up to 22 days post onset of self-reported symptoms.
- Extended periods of viral RNA shedding have been reported (up to 83 days) in respiratory samples, with shedding frequently outlasting the duration of symptoms. However, concentrations of viral RNA measured in upper respiratory samples has been shown to decline after symptom onset and there has been no evidence of transmission in clinically recovered individuals with persistent detection of viral RNA nor has there been viable virus isolated from such cases.
- Prolonged viral RNA shedding has been shown to be positively associated with severity of COVID-19 and older age in multiple studies (Table 3). However, a recent meta-regression identified that the reported average of four days longer duration of viral RNA shedding in severe cases was not statistically significant (Byrne et al., 2020). The length of viral RNA shedding does not significantly differ between male and female.

<u>Recurrence of Viral Shedding in Convalescent Period, N=55 studies</u>

- Recurrence of viral RNA shedding in the convalescent period after meeting discharge criteria (defined at the time as two consecutive negative RT-PCR tests) has been reported in multiple case reports and observational studies (Table 4). These cases are not thought to be re-infection with a new strain of the virus, instead are considered to have not fully cleared the original SARS-CoV-2 infection.
  - Recurrence typically occurs within seven days of discharge.
  - Following recurrence, patients remained viral RNA positive for approximately 1-8 days and typically remained asymptomatic.
  - Although this is an active area of study and numerous new studies have been published, to date, only one study has provided evidence of viable virus in a recurrent case (Quicke et al., 2020). No evidence of transmission during the recurrence of viral RNA detection has been reported.
- Additional research is needed to improve our understanding of RT-PCR results and how to interpret those results with respect to infectious period and risk of transmission. Particularly in cases with prolonged RT-PCR positive test results. As a result, the CDC has stopped recommending two consecutive negative RT-PCR tests to determine when to end isolation and precautions for COVID cases.

<u>Reinfection, N=2 studies</u>

- Since August 25, 2020, good evidence that reinfection can occur has been reported (Table 5):
  - A patient from Hong Kong was reinfected 142 days after initial infection and this was documented with compelling epidemiological, clinical, serological evidence as well as genomic analyses. (To, Hung, et al., 2020).

    - There is also strong evidence for a case of re-infection in the United States (Tillet et al., 2020).
- At this time, knowledge gaps exist on whether clinical course and epidemiological characteristics including infectious period of re-infection cases are different from the initial infection.
- Additional research is needed to understand the role of immunity in protection against SARS-CoV-2 post infection.

Overview of the Evidence

To date, there have been numerous publications related to the infectious period of COVID-19. The majority of these publications are case reports and observational studies based on contact tracing; these study designs are at high risk of bias and thus are considered low quality. Many of these are pre-prints and have not undergone a peer-review process. Prospective cohorts are of lower risk of bias and are considered higher quality research, but there are few of this study design contributing to this question. Overall, the outcomes should be interpreted with caution, estimates are changing as new research becomes available and there are many knowledge gaps that new research addressing these gaps could significantly change our understanding of SARS-CoV-2 infection in humans.

Outcomes from key studies are summarized in the evidence tables: 1) pre-symptomatic, 2) asymptomatic, 3) symptomatic, and 4) recurrence of viral shedding. Within these, key information including study type and specific methods used (e.g. culture, serial RT-PCR results, epidemiological data, or modeling) are specified along with the infectious period estimates and risk factors.

There is substantial variation in the methodological approach utilized and how infectious period was defined across studies. Research based on case series and contact tracing investigations alone is considered very low quality. These study designs suffer from low sample size, selection bias and recall bias (e.g. self-report symptom onset). Their results should be interpreted with caution, as results are likely to change with additional research.

Several knowledge gaps exist for infectious period. Detection or confirmation of viable virus rather than RNA is underpinned by few observations. The relationship between transmission potential and RT-PCR results is not well defined. Additional research on post infection immunity, recurrence of RNA positive tests and the likelihood and epidemiological characteristics of reinfection are needed to understand if and/or when a person is potentially infectious after the initial acute infection. This research is fundamental to understanding the transmission dynamics of SARS-CoV-2.

CONTENTS

BACKGROUND INFECTIOUS PERIOD

The infectious period (also known as the communicability period) is defined as the time during which an infected person can transmit an infectious agent to another person. The infectious period and its relationship to exhibiting symptoms is an important epidemiological parameter to understand for the control of any infectious disease. For COVID-19, there is evidence that SARS-CoV-2 can be shed by an infected person before they exhibit symptoms (pre-symptomatic) (e.g., (Arons et al., 2020; Hoehl et al., 2020; Pan, Zhang, Yang, Poon, & Wang., 2020)) and by infected persons who never develop noticeable symptoms (asymptomatic) (e.g., (Alshami et al., 2020; Y. Lu et al., 2020; Z. Zhang et al., 2020)). There are also studies that suggest viral shedding may persist in the convalescent phase or may re-emerge after the virus has been undetectable for a period of time (e.g., (Hoang, Dao, & Gautret, 2020; Q. Hu et al., 2020)). This report covers the evidence for these different periods and studies that attempt to estimate the entire infectious period for COVID-19. Studies will be further divided by methods for determining viral shedding and the question of how detection of viral RNA by RT-PCR compares to that of culture and what inferences can be made for these different results.

Infectious period estimates have been determined from a combination of epidemiological and clinical investigations that together inform when an infected person can or is likely to transmit the virus. To determine if a person is infected, most studies report the use of RT-PCR to diagnose cases of COVID-19 and to monitor viral RNA shedding over time. However, detection of viral RNA by RT-PCR does not provide proof of infectivity and virus particles are likely to be shed from infected tissue for a period of time after an infection has been cleared by the host immune system (Jefferson et al., 2020). To establish if viable virus has been isolated, replication of virus from the sample is established most commonly in cell culture and indicates that infective virus is present. In this review few studies have utilized culture methods (or animal inoculation) because it is slow, costly, and is not as sensitive as RT-PCR. The results of epidemiological studies, RT-PCR, qRT-PCR and culture results together provide evidence on when a case is likely infective and capable of transmitting the virus.

Variability in the measurement of infectious period is also present across studies. The majority of studies measure time from diagnosis or symptom onset until clearance of viral RNA. Thus, there are no measurements prior to diagnosis. Epidemiological research, mainly in the form of cluster investigations and testing close contacts of cases regardless of their clinical status has provided evidence that virus shedding can occur prior to symptom onset (Z. Du et al., 2020; X. He et al., 2020). The heterogeneity across definitions and how infectious period is determined in each study is summarized in the detailed evidence tables.

PRE-SYMPTOMATIC INFECTIOUS PERIOD

Table 1 lists twenty-five studies that provide estimates of the pre-symptomatic infectious period, identified through case series, contact tracing investigations, and modeling. Many of these case reports and contact tracing studies originate from China and show evidence of COVID-19 transmission from people who are in their incubation period. SARS-CoV-2 has been successfully isolated from pre-symptomatic cases, which further provides evidence that pre-symptomatic transmission occurs. However, the vast majority of evidence is based on case reports and cluster investigations which are subject to recall bias as the cases and their contacts are responsible for providing information about exposure and symptom onset time. Additionally, with widespread transmission of COVID-19 in an epidemic area it is possible that infections described in these studies could have been caused by other unrecognized sources.

Pre-symptomatic infectious period across studies suggests a person likely sheds SARS-CoV-2 on average 2.5 days (1-7 range) prior to symptom onset based on respiratory samples (Hoehl et al., 2020; Z. Liu et al., 2020; Nissen et al., 2020; Pan et al., 2020; Sakurai et al., 2020). Estimates from contact tracing studies also suggest an average pre-symptomatic infectious period of 2-3 days (1-12.3 range) (X. He et al., 2020; S. Hu et al., 2020; R. Huang, Xia, Chen, Shan, & Wu, 2020; Kong et al., 2020; J. Li et al., 2020; Rothe et al., 2020; W. E. Wei et al., 2020). Evidence of active SARS-CoV-2 virus replication from a rectum sample three days prior to symptom onset has also been presented (Qian et al., 2020). A study of long-term care residents found that viable virus could be cultured up to six days before symptom onset and reported similar cycle threshold values (i.e. viral load) for asymptomatic, pre-symptomatic, and symptomatic cases (Arons et al., 2020).

There are few studies that take measurements prior to diagnosis/symptom onset. More evidence is needed to improve the certainty of the estimates for pre-symptomatic infectious period of COVID-19.

Table 1: Studies evaluating the pre-symptomatic infectious period of COVID-19 (N=25)

Reference	Study Type	-Population & Setting -Time Period	IP determined via: Culture, serial RT-PCR results, Epi data, or Model	Key Outcomes
Culture & RT-PCR Studies				
(Arons et al., 2020)	Outbreak investigation	-Residents of a skilled nursing facility in Washington, US -April 3, 2020 end date	Culture & RT-PCR	Nasopharyngeal and oropharyngeal swabs -48 (63%) of residents that participated in point-prevalence surveys tested positive. -24 were pre-symptomatic and 2 were asymptomatic as determined by standardized symptom-assessments completed

				by nurses. -Viable virus was isolated from specimens collected six days before to nine days after onset of symptoms.
(Hoehl et al., 2020)	Case series	-Travelers from Wuhan to Germany - February 1, 2020	Culture & RT-PCR	Throat Swab -2 patients were asymptomatic RT-PCR test positive. One day later 1 of the cases demonstrated a faint rash and minimal pharyngitis. -SARS-CoV-2 was successfully isolated from the 2 cases, indicating potential infectiousness while pre-symptomatic. -These findings suggest that infectiousness may occur at least 1 day before symptom onset.
(Nissen et al., 2020) *Preprint*	Case report	-36 year old healthcare worker in Sweden -April 2 – 17, 2020	Culture & RT-PCR	Nasopharyngeal and oropharyngeal swabs - Observed cytopathic effect via cell culture, immunofluorescence for dsRNA and rRT-PCR determined that the SARS-CoV-2 virus from two samples (taken on day 3 and day 1 before symptom onset) were infectious in two independent experiments.
(Qian et al., 2020)	Case report	-Patient receiving surgery for rectal cancer in China -January 16, 2020 onward	Culture & RT-PCR	Rectal tissue and throat swabs -On January 16, 2020, the patient underwent rectal surgery. On day 3 postoperatively, the patient presented with fever and cough and he was subsequently diagnosed with COVID-19 via RT-PCR. In March, a retrospective study was conducted on the patient's surgically removed tissue. Ultrathin sections of rectal tissues were prepared, and virus particles were found in the cytoplasm of intestinal epithelial cells. To further confirm the SARS-CoV-2 -specific infection and replication in the rectum, immunohistochemistry and immunofluorescence using the rabbit anti-SARS-CoV-2 NP antibody was used. -This is the first report of direct evidence of active replication of SARS-CoV-2 in a patient's rectum during the incubation period.
(Z. Liu et al., 2020)	Prospective cohort	-Pre-symptomatic carriers in China (n=16)	RT-PCR	Sputum and throat swabs -The median period between positive SARS-CoV-2 RNA

		-Timeline not reported		detection and symptom onset was calculated as 2 days (1-5 range).
(Sakurai et al., 2020)	Retrospective cohort	-Asymptomatic (n=90) and pre-symptomatic (n=11) cases hospitalized in Japan from the Diamond Princess cruise ship -February 19 - 26, 2020	RT-PCR	Specimen type not reported -11 patients were pre-symptomatic, and developed symptoms a median of four days (3-7 range) after the first positive RT-PCR test. -The asymptomatic cases experience a median duration of SARS-CoV-2 viral RNA shedding of 9 days (3-21 range) between the first positive PCR test and the first of 2 serial negative PCR tests.
Epidemiological data studies				
(Pan et al., 2020)	Contact tracing study	-Two individuals tracked due to exposure to an infected patient in China -Timeline not reported	RT-PCR & Epi data	Respiratory swab -Cases were serially tested prior to onset of symptoms. -Cases showed positive RT-PCR results one day before onset, suggesting that infectiousness may occur before symptom onset.
(J. Li et al., 2020)	Contact tracing study	-Three family clusters in China -January 21 – February 9, 2020	Epi data	- The three index cases transmitted the infection to 28 family members 2-10 days before illness onset.
(Kong et al., 2020)	Contact tracing study	-Ten cases in China -January 8 – 27, 2020	Epi data	-The last two generations were infected in public places, 3 and 4 days prior to the onset of illness in their infectors.
(R. Huang et al., 2020)	Contact tracing study	-Family cluster of confirmed infection in China -January, 2020	Epi data	-Tracing within a family cluster (n=11) and exposure dates demonstrated a median pre-symptomatic infectious period of four days (3-5 range).
(Rothe et al., 2020)	Contact tracing study	-Cluster of cases from pre-symptomatic contact in Germany -January 19- 29, 2020	Epi data	-Transmission occurred from a pre-symptomatic case to 4 contacts. -The tracing results show a median pre-symptomatic infectious period of two days (1-3 range).
(W. E. Wei et al., 2020)	Contact tracing study	-Seven clusters in Singapore	Epi data	-Pre-symptomatic transmission was evident in 4 clusters with a median infectious period of two days (1-3 range).

		-January 23 – March 16, 2020		-Transmission exposure was not ascertained for the other 3 clusters.
(S. Hu et al., 2020) *Preprint*	Contact tracing study	-1,178 SARS-CoV-2 infected individuals and their 15,648 contacts in China -January 13 – April 2, 2020	Epi data	-Forty-three pre-symptomatic transmission events were recorded in 23 clusters. -Infectiousness was estimated to peak 1.8 days before symptom onset, with 95% of transmission events occurring between 7.6 days before and 7.3 days after the date of symptom onset. -The proportion of pre-symptomatic transmission was estimated to be 62.5%.
(X. He et al., 2020)	Contact tracing study	-77 infector–infectee transmission pairs from Vietnam, Malaysia, Japan, China, Taiwan, USA, Singapore -December 18, 2019 – March 5, 2020	Epi data	-Authors assumed an incubation period distribution of mean 5.2 days to infer that infectiousness started from 12.3 days (5.9-17 95%CI) before symptom onset and peaked at symptom onset (-0.9-0.9 95%CI). -Observed that only <0.1% of transmission would occur before 7 days, 1% of transmission would occur before 5 days and 9% of transmission would occur before 3 days prior to symptom onset. -In a sensitivity analysis, infectiousness was shown to peak at 2 days before to 1 day after symptom onset. -Estimated that 44% (30-57% 95%CI) of secondary cases were infected during the index cases' pre-symptomatic stage.
(Chun, Baek, & Kim, 2020) *Preprint*	Literature review	-72 infector-infectee transmission pairs in South Korea -January 23 – March 31, 2020	Epi data	-The mean and median estimates were 1.31 days (0.38–2.55 95%CI) and 0.68 days (-0.09–1.73 95%CI) after symptom onset, respectively, with the peak at 0.72 days before symptom onset. -The pre-symptomatic transmission proportion was 37% (16–52% 95%CI).
(Z. Du et al., 2020) *Preprint*	Literature review	-468 infector–infectee pairs identified via contact tracing in China -January 21 – February 8,	Epi data	-59 of 468 infector-infectee pairs indicated that the infectee had symptoms earlier than the infector. -These negative serial intervals suggest that pre-symptomatic transmission may have occurred.

		2020		
(Casey et al., 2020) *Preprint*	Literature review	-17 studies reporting serial interval or generation time from Hong Kong, Tianjin, pooled data from Hong Kong and Shenzhen, Singapore, Mainland China excluding Hubei, mixed sources, Shenzhen, northern Italy and Wuhan -December 1 – April 15, 2020	Epi data	-Subtracted incubation period from serial interval or generation time to infer pre-symptomatic infectious period and to estimate the proportion of pre-symptomatic transmission. -The pooling of serial interval estimates for transmission time relative to symptom onset gave a mean pre-symptomatic infectious period of 0.67 days (0.63 median). -The pooling of 5 generation time-based estimates gave a mean pre-symptomatic infectious period of 1.62 days (1.32 median). -Pre-symptomatic transmission was estimated to be 56.1% based on serial interval estimates and 65.5% based on generation time estimates.
(Prakash, 2020) *Preprint*	Literature review	-Individuals reported in the literature (n=1251) -No limit on country -No timeline reported	Epi data	-The peak of infectiousness was 2 days after the infection. -Estimated that 68.4% (67.0-69.7% 95%CI) of infections are caused by pre-symptomatic infectors.
Modeling studies				
(Nishiura, Linton, & Akhmetzhanov, 2020)	Bayesian Predictive Model	-28 infector-infectee pairs -No limit on country -February 12, 2020 end date	Modeled	-Accounting for right truncation and analyzing all pairs, authors estimated a serial interval of 4.0 days (3.1-4.9 95%CI). -This interval is shorter than preliminary estimates of the incubation period of approximately 5.0 days. -This suggests that pre-symptomatic transmission may make up a substantial proportion of secondary transmission.
(Tindale et al., 2020) *Preprint*	Statistical Model	-Outbreak cases in Tianjin, China, and Singapore -January 19 – February 27, 2020	Modeled	-Period of pre-symptomatic transmission was inferred from estimates of serial interval and incubation periods for populations in Tianjin and Singapore. -Average pre-symptomatic infectious periods were 2.55 days (1.2-3.3 range) in Singapore and 2.89 days (2.79-8.2 range) in Tianjin.
(Zhu, 2020) *Preprint*	SEIR model	-Wuhan outbreak in China	Modeled	-Authors propose a new epidemic model called SEIR-HC, with 2 different social circles. Using the model alongside an

		-April 15, 2020 end date		optimization algorithm, the spread process of the outbreak in Wuhan city is reproduced and the propagation characteristics and unknown data are estimated. -A pre-symptomatic infectious period of 1.01 day was estimated by taking the difference between the latent period and the incubation period.
(Siwiak, Szczesny, & Siwiak, 2020) *Preprint*	SIR metapopulation model	-Entire pandemic (Global) -January 22 – March 26, 2020	Modeled	-Built a modified SIR metapopulation transmission mode parameterized analytically according to the literature, and fitted missing parameters to the observed dynamics of the virus spread. -Estimated a pre-symptomatic infectious period of 4.6 days.
(Peak et al., 2020) *Preprint*	SEIR model	-Confirmed cases in Massachusetts, US -Timeline not specified	Modeled	-Pre-symptomatic infectious period was modelled assuming a serial interval of 4.8 -The mean time of infectiousness onset was 0.77 days before symptom onset (1.98 days before, 0.29 days after 95%CI)
(H. Yuan et al., 2020) *Preprint*	Two-layered SEIQR model	-Imported and confirmed local cases in Hong Kong -January 18 – February 29, 2020	Modeled	-Epidemiological parameters of COVID-19 were estimated. -The pre-symptomatic transmission period before symptom onset was 3.49 days (0.48-5.80 95%CI).
(S. Zhao, 2020)	Novel likelihood-based framework	-Confirmed cases -Country and timeline not specified	Modeled	-Estimate the mean pre-symptomatic transmission period to be 2.2 days (95%CI: 1.3−4.7). -Approximate that 32.2% (10.3−73.7 95%CI) of secondary infections may be due to pre-symptomatic transmission.

ASYMPTOMATIC INFECTIOUS PERIOD

Table 2 lists twenty-five studies that provide estimates of the asymptomatic infectious period, identified through case series and contact tracing investigations. Asymptomatic cases can transmit COVID-19 but there have been few studies investigating the infectious period of asymptomatic cases as they rarely undergo testing. Furthermore, there have been few studies that investigate live viral shedding from asymptomatic carriers via culture. The majority of studies identify asymptomatic cases through contact tracing and determine the length of viral RNA shedding via RT-PCR

from the first day of a positive RT-PCR test to the first day of consecutive negative results. Caution is warranted when interpreting these results as RT-PCR positivity is not indicative of infectiousness and the duration of viral detectability likely overestimates the infectious period.

The best available evidence come from a cohort of asymptomatic cases that detected viable virus and viral RNA through infection. The viral load was highest during the first week of infection and declined in subsequent weeks (Quicke et al., 2020). Further, infectious virus was not detected in nasopharyngeal swabs from individuals with less than 100,000 RNA copies/swab, indicating that low levels of viral RNA correspond to low levels of infectious virus.

Some studies comparing asymptomatic and symptomatic cases show that symptomatic cases demonstrate longer viral RNA shedding periods (Alshami et al., 2020; Y. H. Lee et al., 2020; S. Lee et al., 2020; W. Li et al., 2020; Y. Li et al., 2020a; Y. Lu et al., 2020; Noh et al., 2020; Saurabh et al., 2020; Valente et al., 2020; X. Wei et al., 2020; Z. Zhang et al., 2020), while other studies show no difference between the groups (Lombardi et al., 2020; Xiong et al., 2020) or the opposite association (Long et al., 2020). Similar viral loads have been reported for asymptomatic, pre-symptomatic, and symptomatic cases. Thus, the total infectious period of asymptomatic cases is likely similar or shorter than that of symptomatic cases. The length of viral RNA shedding in asymptomatic cases is not significantly associated with age or sex.

Table 2: Studies evaluating the asymptomatic infectious period of COVID-19 (N=25)

Reference	Study Type	-Population & Setting -Time Period	IP determined via: Culture, RT-PCR Serial testing, Epi data, or Model	Key Outcomes
Culture & RT-PCR Studies				
(Quicke et al., 2020) *Preprint*	Longitudinal surveillance study	-Asymptomatic staff (n=454) at 5 skilled nursing facilities (prevalence varied considerable between facilities) in Colorado, USA	Culture (Plaque assay) & RT-PCR	<u>Nasopharyngeal swabs</u> -N1 viral RNA level was positively correlated with the amount of infectious virus detected via plaque assays. -Infection length ranged from 1- 4 weeks, as determined by detection of viral RNA via qRT-PCR for the SARS-CoV-2 N1 gene. -Levels of viral RNA and infectious virus were highest during the first week of infection and declined in subsequent weeks. -Infectious virus was not detected in individuals with less than 100,000 N1 RNA copies/swab. -One staff member had a weak positive result detected via a single passage plaque assay three weeks after initial diagnosis.

		-Timeline not reported		
(Lavezzo et al., 2020)	Prospective cohort	-Survey 1= 2,812 residents and Survey 2 =2,343 residents in Italy -February 21 – March 7, 2020	RT-PCR	Nasopharyngeal swabs -Found no statistically significant difference in the viral load of symptomatic versus asymptomatic infections. -Found that the viral load tends to peak around the day of symptom onset and for most of the subjects tends to decline after symptom onset.
(W. Li et al., 2020)	Prospective cohort	-Asymptomatic (n=3), pre-symptomatic (n=6), and symptomatic (n=9) cases in China -January 29 – February 5, 2020	RT-PCR	Respiratory and anal swabs - The median duration of viral shedding was shorter in pre-symptomatic patients (11.5 days) than in asymptomatic (28 days) and mild symptomatic cases (31 days).
(Y. H. Lee et al., 2020)	Prospective cohort	-Asymptomatic and mild cases (n=632) in South Korea -March 2 – April 12, 2020	RT-PCR	Oral and nasal swabs -Symptomatic patients had a longer period between diagnosis and negative RT-PCR results than asymptomatic patients: 21.8 days (7.6 SD) vs. 19.1 days (7.5 SD), $p<0.0001$. -Respiratory symptoms had statistically significant correlation to the RNA shedding period ($p<0.0001$). However, there were no statistically significant differences related to gastrointestinal symptoms, headache, fever, and other symptoms. There were also no statistically significant differences according to sex, age, or underlying conditions.
(Saurabh et al., 2020)	Prospective cohort	-Asymptomatic (n=44) and symptomatic	RT-PCR	Oropharyngeal and nasopharyngeal swab -The asymptomatic individuals had median virus persistence duration of 8.87 days (95% CI: 7.65–10.27) and 95 percentile duration of 20.70 days (95% CI:

		(n=7) cases in India -March 19 – May 21, 2020		16.08–28.20). -Around one-fourth asymptomatics (10/44) demonstrated SARS-CoV-2 persistence beyond 2 weeks. -The virus persistence duration for symptomatic individuals was 10.98 days (8.38–14.44 95%CI). This was not found to be significantly longer than that of asymptomatic individuals (P = 0.222). -Age (<60 years) and local transmission were found to be significantly associated with longer virus persistence among asymptomatic individuals on univariate regression but not in multivariate analysis.
(Long et al., 2020)	Prospective cohort	-Asymptomatic cases (n=37) and matched symptomatic cases (n=37) in China -April 10, 2020 end date	RT-PCR	Nasopharyngeal swabs -The median duration of viral RNA shedding in the asymptomatic group was 19 days (15-26 IQR). -The asymptomatic group had a significantly longer duration of viral RNA shedding than the symptomatic group (log-rank P = 0.028). -Data suggest that asymptomatic individuals had a weaker immune response to SARS-CoV-2 infection.
(Y. Lu et al., 2020)	Retrospective cohort	-Hospitalized children with mild and ordinary COVID-19 (n=110) in China -January 30 – March 10, 2020	RT-PCR	Respiratory swab -The median duration of viral RNA shedding was 15 days (11–20 IQR, 5-37 range). -The duration of viral shedding in symptomatic patients was statistically longer (p<0.001) than that in asymptomatic patients: 17 days (12-23 IQR) vs. 11 days (9-13 IQR).
(Alshami et al., 2020) *Preprint*	Retrospective cohort	-Laboratory-confirmed COVID-19 subjects who were quarantined in	RT-PCR	Nasopharyngeal and oropharyngeal swab -69 patients (54%) did not exhibit any symptoms. -For the patients that did experience symptoms, the median time to resolution was 5 days. -The median time to viral clearance was significantly longer (p=0.011) in the symptomatic patients than the asymptomatic patients: 17 days (12.4-21.6

		a government-designated facility following travel outside the kingdom (n=128) in Saudi Arabia -March 16 – April 18, 2020		95%CI) vs. 11 days (8.7-13.3 95%CI).
(Noh et al., 2020)	Retrospective cohort	-Hospitalized patients (n=199) in South Korea, 26.6% were asymptomatic -Timeline not reported	RT-PCR	Specimen type not reported -Duration of viral shedding was defined as time from diagnosis to the day before first negative conversion of two consecutive negative results of RT-PCR. -Mean duration of viral shedding was 24.5 days (± 4.8 SD). -Duration of viral shedding was longer in symptomatic patients than in asymptomatic patients: 25.2 days (± 4.9 SD) vs. 22.6 days (± 4.0 SD), $p < 0.01$. -Symptomatic patients with chest pain released the virus significantly longer than those without: 30.0 (± 4.7 SD) days vs. 25.0 days (± 4.8 SD), $p = 0.01$). -Patients who complained of sputum also experienced prolonged viral RNA shedding: 26.8 days (± 4.8 SD) vs. 24.6 days (± 4.8 SD), $p = 0.03$.
(S. Lee et al., 2020)	Retrospective cohort	-Symptomatic and asymptomatic patients (n=303) in Korea -March 6 – 26, 2020	RT-PCR	Nasopharynx, oropharynx, and sputum swab -The median time from diagnosis to the first negative viral RNA conversion was 17 (1.07, SE) days for asymptomatic patients and 19.5 (0.63, SE) days for symptomatic (including pre-symptomatic) patients ($p=0.07$).
(Xiong et al., 2020)	Retrospective cohort	-Hospitalized pediatric cases (n=244) -January 21 –	RT-PCR	Nasopharyngeal aspirate -The duration between positive and negative nasopharyngeal aspirate were similar in patients with COVID-19, regardless of whether they were asymptomatic or symptomatic (mean of 8.2 days vs 8.9 days; $P = 0.434$),

		March 20, 2020		suggesting a similar duration of viral shedding.
(Lombardi et al., 2020) *Preprint*	Retrospective cohort	-Health care workers in Italy -February 24 – March 31, 2020	RT-PCR	Nasopharyngeal swab -Of 138 subjects with a positive viral RNA test, 41/138 (29·7%) were asymptomatic. -Median time from first positive to a negative test did not differ between symptomatic subjects and asymptomatic cases, 23 days (18-26 95%CI) vs. 23 days (19-29 95%CI). -Median time of viral shedding was not statistically associated with gender or age.
(Kim et al., 2020)	Retrospective cohort	-Laboratory-confirmed hospitalized COVID-19 patients in South Korea -February 4 – April 7, 2020	RT-PCR	Nasal-throat swab -10/71 laboratory confirmed cases, as determined by RT-PCR, were asymptomatic. -The median time to first negative RT-PCR test after diagnosis was 4.5 days (2.5–9 range). -Authors suggest that 14-day quarantine at home after diagnosis may be adequate for asymptomatic carriers.
(Y. J. Liu et al., 2020)	Retrospective cohort	-Asymptomatic (n=35) and subclinical (n=18) pediatric cases in China -Timeline not reported	RT-PCR	Nasopharyngeal swabs -The mean time to clearance of SARS-CoV-2 nucleic acid in nasopharyngeal swabs was 9±4 days.
(M.S. Han et al., 2020)	Retrospective cohort	-Mildly symptomatic (n=9) and asymptomatic children (n=3) in South Korea -March 8 –	RT-PCR	Nasopharyngeal, fecal, and saliva swabs -Viral RNA load in the nasopharyngeal swabs peaked early at median 7.56 $\log^{10}$ copies/mL and decreased over time ($p<0.001$ for trend). The positivity of the specimens was 75% during week 2 and 55% during week 3. -In comparison, the median initial fecal RNA load was 7.68 $\log^{10}$ copies/mL and remained steadily high ($p = 0.148$ for trend) for >3 weeks. Fecal positivity remained >80%.

		April 28, 2020		-The median RNA load in fecal samples was significantly higher than that for nasopharyngeal swab specimens during week two (p = 0.006) and week 3 (p = 0.006). -The RNA load in saliva declined rapidly with time (p = 0.003 for trend). Positivity in saliva samples was 80% in week one but dropped sharply to 33% in week 2 and 11% in week 3. -Symptomatic children had higher initial RNA load in nasopharyngeal swab specimens than asymptomatic children (p = 0.048). There was no significant differences in feces or in saliva and no correlation between RNA load and age.
(Shen et al., 2020)	Retrospective cohort	-Pediatric patients (seven mild & two asymptomatic) in China -January 8 – February 26, 2020	RT-PCR	Specimen type not reported -6 children had a family exposure and could provide exact dates of close contract with someone confirmed to have COVID-19. -The time from exposure to negative RT-PCR results in asymptomatic cases (n=2) was 10 days and 14 days.
(Z. Zhang et al., 2020) *Preprint*	Case series	-56 COVID-19 patients without symptoms at admission (33 later displayed symptoms) and 19 age-matched symptomatic patients from China -January 23 – April 1, 2020	RT-PCR	Respiratory and anal swab -Among 56 patients without symptoms at admission, 23 remained asymptomatic throughout the follow-up period. -Infectious period in this study was defined as the period from the first day of positive nucleic acid test to the first day of continuous negative test during hospitalization. -They also provide estimates for the mean days from symptom onset to RNA negative-conversion. -The infectious period of asymptomatic patients (n=19) was statistically shorter than pre-symptomatic patients (n=30) 9.6 days (±5.3 SD) vs. 13.6 (±6.6 SD), p=0.03. -The symptomatic patients also had a shorter infectious period, 9.71 days (±4.3 SD), compared to pre-symptomatic cases (p=0.05), but a similar time between illness onset and negative conversion, 16.6 (±5.6 SD) and 16.6 (±7.5 SD).
(Mesoraca et	Case series	-Asymptomatic	RT-PCR	Respiratory and fecal swabs

al., 2020)		and mild patients (n=15) in Italy -March 4 – April 20, 2020		-Of the 10 patients with fecal sample negative in the first 10 days, 6 samples became positive 2 weeks after their first positive respiratory tract test. -In four cases, fecal samples showed positive viral RNA shedding 25 days more than their respiratory tract samples.
(W. Du et al., 2020)	Case series	-Asymptomatic (n=5) and mild (n=5) pediatric cases in China -January 23 – March 9, 2020	RT-PCR	Respiratory and fecal samples -The median time from onset to negative RT-PCR results in respiratory tract and fecal specimens was 9 days and 34.43 days, respectively.
(Shin et al., 2020)	Case report	-11 year old asymptomatic girl from South Korea -March 12 – May 13, 2020	RT-PCR	Nasopharyngeal swabs -Child had positive SARS-CoV-2 RNA detection for 62+ days with no symptoms during the entire period.
(Mao, Wan, He, Hu, & Chen, 2020)	Case series	-Asymptomatic cases (n=2) in China -January 27 – February 21, 2020	RT-PCR	Throat swab -Discovered that after 14 days of isolation, 2 asymptomatic cases were still viral carriers of COVID-19. -1 case produced positive RT-PCR results up to 19 days post start of isolation.
(Y. Li et al., 2020a) *Preprint*	Case series	-Asymptomatic cases (n=38) in China -February – March, 2020	RT-PCR	Pharyngeal swabs -The median viral shedding time was 6 days with a minimum of 2 days and maximum of 17 days between first nucleic positive test and last nucleic positive test. - The authors note that this shedding period is shorter than that noted in other studies of symptomatic cases, suggesting shorter infectivity for asymptomatic cases.
(Valente et al., 2020)	Case series	-Pediatric hospitalized	RT-PCR	Nasopharyngeal and conjunctival swab -Two asymptomatic cases became negative after three days post symptom

		patients (n=27) in Italy, 4 were asymptomatic, 15 showed respiratory symptoms, and 8 had gastrointestinal symptoms -March 16 – April 15, 2020		onset while a symptomatic case tested negative after 6 days, while remaining positive on nasopharyngeal swabs. -Additionally, the nasopharyngeal swab was negative on average 8 days (range, 2-17 days) from onset of symptoms, whereas conjunctival swab became negative in all patients on average in 4 days (range, 3-6 days).
Epidemiologic studies				
(Z. Hu et al., 2020)	Serial testing and cluster tracing study	-Cases with asymptomatic infection (n=24) in China -January 28 – February 9, 2020	RT-PCR & Epi data	<u>Pharyngeal swab</u> -Observed asymptomatic transmission to the cohabiting family members, which even caused severe COVID-19 pneumonia. -The median asymptomatic communicable period, defined as the interval from the first day of positive nucleic acid tests to the first day of continuous negative tests, was 6 days (2-12 IQR) in cases that did not develop symptoms but had some evidence of COVID-19 in CT scan (n=19), and 4 days (2-15 IQR) in cases that did not develop symptoms and had normal CT scan.
(Ma et al., 2020) *Preprint*	Literature review	-Cases that contained the data that allowed for estimation of at least 1 parameter in China, Japan, Singapore, South Korea, Vietnam, Germany, and	Epi data	-Among 49 asymptomatic cases the median infectious period was 11.66 days (9.9-13.3 range) -Infectious period was approximated as serial interval minus the upper limit of latent period. In these analyses, the date of diagnosis was used as the day of onset for asymptomatic cases.

		Malaysia -February 20, 2020 end date		

SYMPTOMATIC INFECTIOUS PERIOD

Table 3 lists one hundred and seven studies that evaluate the symptomatic infectious period of COVID-19, identified through systematic reviews/meta-analyses, case series, observational studies, and modeling. Key studies report robust evidence of infectiousness via culture, evaluation of risk factors for prolonged viral shedding (e.g., sex, age, severity), evidence of differences in viral RNA shedding between different specimen types (fecal vs. respiratory) and models that estimate the entire infectious period.

Studies that report virus culture only provide measurements from symptom onset and are likely to underestimate the total infectious period, as they do not take pre-symptomatic infectiousness into account. They are also based on limited sample size. For mild cases, the best available estimates for the infectious period measured from symptom onset is 8-10 days determined using virus culture (Arons et al., 2020; Bullard et al., 2020; Folgueira et al., 2020; La Scola et al., 2020; Perera et al., 2020; Singanayagam et al., 2020; van Kampen, Jeroen J. A. et al., 2020; Wölfel et al., 2020), with high viral loads observed in the first five days and a viral peak at four days post onset (Wölfel et al., 2020).

Prolonged viable virus shedding have been reported in a few studies, mainly still in preprint with small sample sizes. Case reports, some of which detail immunocompromised cases, demonstrate viable virus up to 18-22 days self-reported post symptom onset (Decker et al., 2020; Gniazdowski et al., 2020; W. D. Liu et al., 2020; van Kampen, Jeroen J. A. et al., 2020). Even longer durations (up to 32 days) have been reported in a small sample of severe cases (Folgueira et al., 2020). One study confirmed the presence of infectious SARS-CoV-2 in urine and faecal specimens from days 11, 13, and 15 of severe/critical illness by demonstrating infection in inoculated ferrets (Jeong et al., 2020).

There are a few studies that have cultured SARS-CoV-2 from the fecal/rectal samples of confirmed cases (Qian et al., 2020; F. Xiao et al., 2020; Y. Zhang et al., 2020). However, more evidence is needed to determine the likely frequency and duration of shedding viable virus via the fecal route and whether fecal-oral, fecal-fomite or fecal-respiratory transmission occurs.

The majority of serial testing studies measure infectious period via RT-PCR from the date of self-reported symptom onset or first RT-PCR positive result to the first of two negative consecutive RT-PCR results. Caution is warranted when interpreting these results as RT-PCR positivity is not indicative of infectiousness and the duration of viral detectability likely overestimates the infectious period.

Estimates from RT-PCR show prolonged shedding of viral RNA, frequently outlasting the duration of symptoms. A recent meta-analysis estimated that the mean duration of RT-PCR positivity in respiratory samples from symptom onset to recovery or death was 13.4 days (95%CI: 10.9-15.8) (Byrne et al., 2020). Concentration of viral RNA measured in upper respiratory samples are shown to decline after symptom onset (Kujawsk et al., 2020; Lavezzo et al., 2020; Quicke et al., 2020; Wölfel et al., 2020; van Kampen et al., 2020; B. E. Young et al., 2020b; L. Zou et al., 2020). There have also been extended periods of viral RNA shedding reported (up to 83 days) in respiratory samples (e.g. J. Li, Zhang, Liu, & Song, 2020; N. Li, Wang, & Lv, 2020; Park et al., 2020; Shin et al., 2020).

Viral RNA presence has varied widely by sample type. Stool samples initially test positive by RT-PCR several days after the onset of symptoms on average and remain positive longer than respiratory samples (Cai et al., 2020; Z. Chen et al., 2020; Du et al., 2020; Hua et al., 2020; Ling et al., 2020; Lyu et al., 2020; Mesoraca et al., 2020; Santos et al., 2020; F. Xiao et al., 2020; Y. Xing et al., 2020; C. L. H. Xu et al., 2020; N. Zhang et al., 2020). Evidence of SARS-CoV-2 RNA viral shedding has also been identified in eye swabs (Hu et al., 2020; Valente et al., 2020; Xia et al., 2020). In one study, eye swabs were continuously positive for two weeks after nasopharyngeal swabs turned negative on day 22 (Y. Hu et al., 2020). Whereas conjunctival swabs became negative in pediatric patients sooner than nasopharyngeal swabs (4 days vs. 8 days) in another study (Valente et al., 2020). In a study of 17 COVID-19 patients, no evidence of viral RNA shedding was found in tears throughout the course of disease (Seah et al., 2020).

Individual or disease characteristics that determine the length of viral RNA shedding have been investigated, including cancer, severity, age, symptomology. Further, the duration of viral RNA shedding was shown to be inversely correlated with plasma levels of T-cell cytokines IL-1β and IL-17A at the initial phase of infection (P. H. Lee et al., 2020). There is also variable evidence for neutralizing antibodies and the association with COVID-19 severity and viral clearance (Jeewandara, et al., 2020; Ru et al., 2020).

There are three studies that investigate SARS-CoV-2 shedding from animals. An experimental challenge trial in rhesus macaques reported the isolation of viable virus up to three days post infection, while viral RNA shedding continued up to 17 days post infection (Munster et al., 2020). A case series of large felines from the Bronx zoo reported the isolation of viable virus in two animals, five days after clinical signs had ceased (Bartlett et al., 2020). An experimental challenge trial of cats found that nasal swabs were positive for viral RNA at days 1 through 10 post challenge, with maximal quantities observed from days 1 through 5 post challenge (Gaudreault et al., 2020).

Due to an abundance of case reports, not all case reports reporting serial testing have been included in this table.

Table 3: Studies evaluating the symptomatic infectious period of COVID-19 in humans and animals. (N=107)

Reference	Study Type	-Population & Setting -Time Period	IP determined via: Culture, RT-PCR Serial testing, Epi data, or Model	Key Outcomes
Culture & RT-PCR studies				
(Jeong et al., 2020)	Prospective cohort	-Five COVID-19 patients from Korea and groups of ferrets -February 25 – March 5, 2020	Culture & RT-PCR	Respiratory and fecal swabs -Viable SARS-CoV-2 virus was isolated from three respiratory specimens taken from COVID-19 patients at 11 and 15 days of illness. -Viral loads in urine, saliva, and stool samples were almost equal to or higher than those in naso/oropharyngeal swabs. -To confirm the presence of infectious SARS-CoV-2 in urine and faecal specimens, two urine specimens (from day 11 and 13 of illness) and one faecal specimen (day 15 of illness) were selected for ferret infection experiments. All urine and stool specimen-treated ferrets showed evidence of infection.
(B. E. Young et al., 2020a) *Preprint*	Prospective cohort	-Hospitalized patients (n=100) in Singapore -January 22 – March 6, 2020	Culture & RT-PCR	Respiratory swabs -Viral culture from respiratory samples was positive for 14 of 73 patients. -PCR cycle threshold value ≤30 predicted viral isolation by culture -Average duration of viral RNA shedding was 16.7 days (95% CI 15·2-18·3) and did not differ significantly by disease severity or use of lopinavir-ritonavir.
(Wölfel et al., 2020)	Prospective case series	-Nine hospitalized confirmed patients with mild symptoms in Germany -Cases discovered January 27, 2020	Culture & RT-PCR	Respiratory swab -Live virus was isolated from upper respiratory swabs via viral culture during the first seven days following symptom onset. No isolates were obtained from samples after the eighth day despite the ongoing presence of viral RNA. -Viral RNA shedding was demonstrated in sputum and upper respiratory samples up to 22 and 20 days, respectively. -Viral load peaked on day four post onset at 7.11×10^8 RNA

				copies per throat swab. The average viral RNA load was 6.76 × 10^5 copies per whole swab until day five. Swab samples taken after day five had an average viral load of 3.44 × 10^5 copies per swab and a detection rate of 39.93%. Stool swab -Live virus was not isolated from stool samples despite the presence of on-going viral RNA (detected up to 21 days post symptom onset).
(van Kampen, Jeroen J. A. et al., 2020) *Preprint*	Retrospective cohort	-Hospitalized COVID-19 patients (n=129, 89 intensive care, 40 medium care) in the Netherlands -March 8 – April 8, 2020	Culture & RT-PCR	Upper and lower respiratory swabs -Infectious virus shedding was detected in 62 respiratory samples of 23/129 patients (17.8%). -The median duration of infectious viral shedding was 8 days (5-11 IQR, 0-20 range) and the probability of detecting infectious virus dropped below 5% after 15.2 days (13.4-17.2 95%CI) post symptom onset. -Infectious virus shedding dropped to undetectable levels when viral RNA load threshold was below 7 $\log^{10}$ RNA copies/mL and once serum neutralizing antibodies were present. These associations were significant in uni- and multivariate analysis.
(Folgueira et al., 2020) *Preprint*	Retrospective cohort	-Samples (n=106) from 105 patients in Spain -Timeline not reported	Culture	Respiratory samples -In 49/106 samples (46.2%) a cytopathic effect was detected in culture. -In mild cases, viral viability was maintained up to 10 days post symptom onset. -In severe cases, viral viability was maintained up to 32 days post symptom onset. -Compared to mild cases, severe cases presented infective virus in a significantly higher proportion in samples with moderate or low viral load, ($p < 0.01$).
(La Scola et al., 2020)	Retrospective cohort	-183 samples from 155 patients in France -February 27 – March	Culture & RT-PCR	Nasopharyngeal and sputum swabs -SARS-CoV-2 could not be isolated from samples collected after day eight of symptom onset.

		12, 2020		- Suggest that patients with Ct values ≥34 are no longer infectious and are suitable for discharge.
(Singanayagam et al., 2020)	Retrospective cohort	-324 samples, 81 culture positive in the United Kingdom -January – May, 2020	Culture & RT-PCR	Respiratory swabs -Detection of cultivable virus peaked around the time of symptom onset. Median duration of virus shedding as measured by culture was 4 days (1–8, IQR) from symptom onset. -Ten days after symptom onset, the probability of culturing virus declined to 6.0% (0.9–31.2%, 95%CI) -There was no difference in cycle threshold values between those with asymptomatic, mild-to-moderate, or severe illness. There was no significant difference between age groups.
(Perera et al., 2020)	Retrospective cohort	-Respiratory specimens (n=68) from 35 COVID-19 patients in Hong Kong -Timeline not reported	Culture & RT-PCR	Respiratory swabs -Virus was isolated from 16 patients. -Viable SARS-CoV-2 were rarely detectable beyond 8 days after onset of illness in mild cases. However, viral RNA was detectable for many weeks by reverse transcription PCR.
(Gniazdowski et al., 2020) *Preprint*	Retrospective cohort	-Patients' specimens (n=161) that were positive by molecular testing in the United States -March 11 – May 11, 2020	Culture & RT-PCR	Oropharyngeal swabs -To assess recovery of infectious virus they evaluated a randomly selected subset of 29 patients, many of which had chronic underlying conditions (n=27). - Four patients had viable virus recovered from respiratory specimens collected up to 22 days after the first positive result. -Infectious virus shedding was not associated with a specific outcome as one patient was never admitted, one was hospitalized but mild, and two had severe disease. - Recovery of infectious virus was associated with persistence of symptoms in all but one patient. -Complete viral genome sequencing showed these patients were carrying the same virus over time (no reinfection).
(Bullard et al.,	Retrospective	-RT-PCR SARS-CoV-2	Culture & RT-	Nasopharyngeal and endotracheal swabs

2020)	cross-sectional study of samples submitted to lab	positive samples (N=90) in Canada -Timeline not reported. Samples taken from day of symptom onset (Day 0) up to 21 days post symptom onset	PCR	-Of 90 RT-PCR SARS-CoV-2 positive samples analyzed, SARS-CoV-2 was successfully cultivated from 26 (28.9%). -Positive cultures were only observed up to day 8 post symptom onset. -The probability of obtaining a positive viral culture peaked on day 3 post symptom onset. -Infectivity was significantly reduced when RT-PCR Cycle threshold values were greater than 24.
(Kujawski et al., 2020)	Case series	-First 12 confirmed patients in the United States -January 20 – February 5, 2020	Culture & RT-PCR	Respiratory swab -Viral culture was successful for all 9 patients tested, with positive results from respiratory samples at 9 days post symptom onset. Viral isolation was not attempted on later specimens. -All 12 patients had SARS-CoV-2 RNA detected in respiratory specimens, typically for 2–3 weeks post symptom onset. -SARS-CoV-2 RNA was detected for a max of 36 days post onset, long after symptoms had fully resolved. -Serum and stool specimens also demonstrated positive viral shedding for a maximum of eight and 25 days, respectively.
(Decker et al., 2020)	Case report	-Sixty-two year old male mild COVID-19 patient with a recent heart transplantation in Germany -March 13, 2020 onward	Culture & RT-PCR	Throat swabs -Patient had no clinical symptoms after 20 days since initial presentation, but virus culture of throat swabs on day 18 and 21 confirmed active SARS-CoV-2 viral replication. -Under continued immunosuppression, SARS-CoV-2 viral RNA remained detectable up to day 35 with copy numbers similar to onset of infection.
(W. D. Liu et al., 2020)	Case report	-50 year old woman in Taiwan -Timeline not reported	Culture & RT-PCR	Throat swab and sputum samples -SARS-CoV-2 could be isolated from cultures in throat swab collected upon admission, and all sputum specimens collected within 18 days after symptoms onset. -Viral RNA was detectable via RT-PCR up to 63 days post symptom onset.

(Y. Zhang et al., 2020)	Case report	-One laboratory-confirmed COVID-19 severe case in China -January 16 – February 1, 2020	Culture	Stool swab -SARS-CoV-2 was isolated from a stool specimen of a case who experienced symptom onset on January 16, 2020 and was sampled on February 1, 2020. -The interval between sampling and onset was 15 days.
(F. Xiao et al., 2020)	Case series	-Fatal COVID-19 case and 28 other feces specimens in China -January, 2020	Culture & RT-PCR	Nasopharyngeal, oropharyngeal, and fecal swabs -The viral load was higher in feces than in respiratory samples collected at multiple time points (17–28 days after symptom onset). -Isolation of virus from feces samples collected at later time points was not successful, despite ongoing viral RNA shedding. -Authors also collected feces specimens from 28 patients. 12, including the case mentioned above, were positive for viral RNA. Isolation of SARS-CoV-2 virus was successful for 2 patients.
(Sun et al., 2020)	Case report	-72 year old man in China -January 25 – March 6, 2020	Culture & RT-PCR	Urine -Viral load in urine was low but detectable at day 12 and day 42 post infection, but not at day 30. -In order to prove that the isolated virus was infectious to susceptible cells, RT-PCR positive urine specimens from day 12 post infection was serially diluted in infection media and inoculated onto Vero E6 cells. -Cytopathic effects were clearly observed after 3 days, raising the possibility of fecal/urine-respiratory transmission.
(Mancuso et al., 2020) *Preprint*	Population-based prospective cohort	-COVID-19 cases (n=1162) in Italy -February 26 – April 22, 2020	RT-PCR	Nasopharyngeal swabs -Median time of viral RNA clearance determined via RT-PCR was 36 days (28-45 IQR) from symptom onset. -The time to viral clearance increased with age and hospitalization, although this was not statistically significant.
(K. Wang et al., 2020)	Prospective cohort	-Hospitalized patients (n=68) in China	RT-PCR	Nasopharyngeal and sputum swabs -The median duration of viral RNA shedding from sputum

		-February 10 – March 20, 2020		specimens was significantly longer than from NPS: 34 days (24-40 IQR) vs. 19 days (14-25 IQR), p<0.001. -Elderly age was an independent factor associated with prolonged virus shedding time of SARS-CoV-2 (HR 1.71, 1.01-2.93). - In nine patients, the viral RNA was detected in sputum after NPS had turned negative.
(Yu et al., 2020)	Prospective cohort	-Recovered cases (n=75) in China -March 9 – 14, 2020	RT-PCR	Respiratory samples -Of the 75 cases, 12 took <30 days to yield 2 consecutively negative results from for SARS-CoV-2 RNA, 57 took 31 to 60 days; and 1 recruit took >60 days to fulfil this criterion. -The mean 27.15 days (24.72-29.58 95%CI).
(Shrestha et al., 2020)	Prospective cohort	-Healthcare workers (n=230) in Cleveland, United States -March 16 – April 20, 2020	RT-PCR	Nasopharyngeal swab -Among patients with non-severe COVID-19, viral loads in upper respiratory specimens peaked by two or three days from symptom onset and decrease rapidly thereafter. - In individuals with non-severe illness, transmission potential of COVID-19 is greatly diminished by 7-10 days since the onset of symptoms.
(Y. Xing et al., 2020) *Preprint*	Prospective cohort	-Pediatric cases (n=3) in China -January 17 – February 23, 2020	RT-PCR	Throat swab -Median infectious period from symptom onset to viral clearance was 13.5 days (11-16 range). Fecal swab -Median infectious period from symptom onset to viral clearance was 29 days (24-34 range).
(Yu, Zhang et al., 2020)	Retrospective matched-pair cohort study	-Hospitalized patients with COVID-19 pneumonia, 64 confected with influenza A/B and 64 influenza negative in China	RT-PCR	Throat swabs -The median duration of viral shedding time from admission was longer for patients with influenza coinfection (17.0 days) than for those without influenza coinfection (12.0 days) (P< .001).

		-January 28 – March 17, 2020		
(Spagnuolo et al., 2020) *Preprint*	Retrospective cohort	-Hospitalized patients (n=280) in Italy -February 25 – May 19, 2020	RT-PCR	Nasopharyngeal swabs - Study shows that delayed SARS-CoV-2 clearance in moderate/severe COVID-19 is associated with older age and a more severe disease, but not with early use of corticosteroids.
(X. Zheng et al., 2020)	Retrospective cohort	-Hospitalized patients (n=80) in China, 28 severe, 52 common type -January 17 – March 9, 2020	RT-PCR	Throat and fecal swabs -The longest observed duration of viral shedding for throat-swab and fecal sample in COVID-19 patients was 43 and 46 days after symptom onset, respectively. -There was no correlation between the duration of viral shedding and the severity of COVID-19.
(F. Hu et al., 2020)	Retrospective cohort	-Hospitalized patients (n=190) in China -January 8 – February 9, 2020	RT-PCR	Throat swabs -Time from onset to admission ($P < 0.001$), and administration of corticosteroid ($P = 0.002$), arbidol ($P = 0.008$) and oseltamivir ($P < 0.001$) were independently associated with duration of viral shedding.
(Bahar et al., 2020) *Preprint*	Retrospective cohort	-Pediatric cases (n=6369) that underwent testing in the United States -March 13 – June 21, 2020	RT-PCR	Nasopharyngeal swabs - Median duration of viral shedding (RT-PCR positivity) was 19.5 days and RT-PCR negativity from positivity was 25 days. -Patients aged 6-15 years demonstrated longer durations of viral shedding, compared to patients aged 16-22 years (median=32 vs. 18 days, p=0.015).
(X. Chen et al., 2020)	Retrospective cohort	-Hospitalized patients (n=284) in China -January 20 – March 15, 2020	RT-PCR	Throat swabs -The median duration of viral RNA shedding was 12 days (8–16 IQR) after the symptom onset. -Older age, time lag from illness onset to hospital admission, diarrhea, corticosteroid treatment and lopinavir/ritonavir were significantly and independently associated with prolonged viral RNA shedding.
(Y. Shen et al., 2020)	Retrospective cohort	-Confirmed cases (n=325) in China	RT-PCR	Nasopharyngeal, urine, feces, and blood samples -Median times from onset to negative detection of nucleic acid

		-January 20 – February 29, 2020		by nasopharyngeal swab was 8 days. -Longer duration of viral shedding in blood and feces was detected among patients with mild disease using glucocorticoid. -Median time from illness onset to negative viral detection was longer in severe and critical patients compared with mild patients. -Among 22 mild patients without antiviral treatment, median times from illness onset to negative viral detection in nasopharyngeal swab, urine, feces, and blood samples were 9, 7, 10, and 9.5 days, respectively.
(N. Li et al., 2020)	Retrospective cohort	-Confirmed cases with prolonged viral shedding, >30 days (n=36) in China -February 11 – April 11, 2020	RT-PCR	-Prolonged viral RNA shedding even after symptomatic relief was common, and the median duration of viral RNA shedding was 53.5 days (47.75-60.5 IQR). -The longest duration of viral RNA shedding could be 83 days. -Compared to the late-onset group, the patients with early onset had longer durations of viral shedding and more severe illnesses.
(Korkmaz et al., 2020)	Retrospective cohort	-Hospitalized children (n=81) in Turkey -March 5 – May 5, 2020	RT-PCR	Naso-oropharyngeal swabs -The median time to turn SARS-CoV-2 RNA negative in the RT-PCR test was 5 (3–10) days. - The time to turn negative was significantly longer for those aged five years or younger than others (P=0.037).
(T. Z. Li et al., 2020)	Retrospective cohort	-Hospitalized patients (n=101) in China -January 21 – March 15, 2020	RT-PCR	Throat swab -The median duration of viral RNA shedding from onset was 11 days (8-14.3 IQR). -In univariate analysis, disease severity, corticosteroid use, fever, and time from onset to hospitalization were associated with prolonged viral RNA shedding. -In multivariate analysis, disease severity did not show a significant association.
(X. Du et al.,	Retrospective	-Cases stratified by age,	RT-PCR	Specimen type not reported

2020)	cohort	sex, and severity (n=161) in China -January 20 – March 1, 2020		-Median duration of viral carriage of all cases (n=161) was 20 days (range 6-30). -Median duration of viral carriage in males was 21 days (16.5-29 IQR) in males (n=89) vs. 20 days (16-26.8 IQR) in females (n=72). There was no significant difference between the sexes (p>0.05). -Median duration of viral carriage for cases older or equal to 60 was statistically longer (p<0.01) than cases between 0-59 years old: 28 days (19-33 IQR) vs. 20 days (16-26 QR). -Median duration of viral carriage for cases considered severe (n=37) was statistically longer (p<0.01) than non-severe cases (n=124): 27 days (19-33 IQR) vs. 20 days (16-26 IQR).
(Tang Xiao et al., 2020) *Preprint*	Retrospective cohort	-Cases stratified by age and gender (n=301) in China -January 21 – February 11, 2020	RT-PCR	Upper respiratory swabs (throat and/or nasal swabs) -The median period from symptoms onset to negative RT-PCR test result was 20 days (17–24 IQR, 7–44 range, N=216). -Female patients (n=147) had a shorter median period from positive to negative SARS-CoV-2 RT-PCR test results than male patients (n=154): 19 days (17–24 IQR) vs. 21 days (17–25 IQR). This finding was not statistically significant (p=0.189). -The median period from symptom onset to negative RT-PCR results was significantly longer in older (≥65years, n=110) patients that younger (<65, n=191): 22 days (19–26 IQR) vs. 19 days (IQR, 17–23), p=0.015.
(Voinsky et al., 2020)	Retrospective cohort	-Patients (n=5,769, 3,370 men and 2,399 women) in Israel -April 28, 2020 end date	RT-PCR	Throat swab -Time from first positive to first negative PCR test result was significantly longer (p<0.05) for patients aged >30 years. Recovery periods were: Male<30: 13.84 (±5.67 SD) Male >30: 14.69 (±6.0 SD) Female <30: 13.66 (±5.87 SD) Female >30: 14.24 (±6.16 SD)
(Sharma et al.,	Retrospective	-Hospitalized cases	RT-PCR	Nasopharyngeal swabs

2020) *Preprint*	cohort	(n=234) in India -March 20 – April 30, 2020		-Mean duration of viral RNA detectability was 10.2 days (6.4 SD). -Duration was significantly lower in cases aged less than 40 years old compared to those aged 40-59 and >60 years old: 9.1 days (5.2 SD) vs. 11.3 days (6.1 SD) vs. 16.4 days (13.3 SD), p=0.001.
(G. Wu et al., 2020) *Preprint*	Retrospective cohort	-Confirmed hospitalized patients in China -January 23 – March 8, 2020	RT-PCR	Upper respiratory swab -Mean time of viral RNA shedding from symptom onset to first negative among common patients (n=93) was 15.1 days (± 7.23 SD). -Severe patients (n=41) had a statistically longer (p=0.00) shedding period of 20.56 days (±6.59 SD). Lower respiratory swab -Mean time of viral shedding was 27.45 days (±10.06 SD) for common patients and 29.78 days (±10.11 SD) for severe patients. There was no statistical difference between the groups (p=0.328). Fecal swab -In the digestive tract, the mean time of viral shedding was 22.6 days (±7.69 SD) for common patients and 27.24 days (±7.86 SD) for severe patients, which was statistically longer (P = 0.01).
(F. Xing et al., 2020) *Preprint*	Retrospective cohort	-Hospitalized patients (n=229) in China -January – March, 2020	RT-PCR	Nasopharyngeal swab -The time between diagnosis and first negative test result of common patients was 25.5 days (±11.3 SD) and 37.1 (±14.4 SD) for severe patients. This was statistically significant (p<0.001).
(Zeng et al., 2020)	Retrospective cohort	-Hospitalized COVID-19 patients (n=149) in China -January 20 – March 26, 2020	RT-PCR	Throat swabs -The median duration from illness onset to the second SARS-CoV-2 RNA negative result was 20 days (16-24 IQR). -Patients admitted to the intensive care unit had longer viral shedding period from illness onset than non-ICU patients: 30 days (22-33 IQR) vs. 19 days (15.8-22 IQR), p<0.0001.
(Fu et al., 2020)	Retrospective	-Hospitalized adult	RT-PCR	Throat swab or nasopharyngeal swab

Preprint	cohort	COVID-19 patients (n=3129) in China -January 18 – March 31, 2020		-The viral RNA shedding durations in critically ill patients were significantly longer than non-critically ill patients: 24.0 days (18.9-29.1 95%CI) vs. 18.0 days (16.8-19.1 95%CI). -Non-critically ill patients (n=330) had persistent viral shedding beyond 30 days post-onset. -A lower IgM/IgG antibody titer in 4 weeks after illness onset may be a risk factor of persistent infection.
(P. H. Lee et al., 2020)	Retrospective cohort	-Hospitalized patients (n=201) in Singapore -January 22 – April 5, 2020	RT-PCR	Respiratory swabs -Duration of viral shedding was not significantly associated with sex, age, presence of comorbidities, baseline investigations, prolonged fever, pneumonia, need for supplemental oxygen or use of experimental antiviral agents. - Median duration of viral RNA shedding was significantly longer in patients requiring invasive mechanical ventilation. -Duration of viral RNA shedding was inversely correlated with plasma levels of T-cell cytokines IL-1β and IL-17A at the initial phase of infection.
(Talmy et al., 2020)	Retrospective cohort	-Israel Defense Forces soldiers with mild COVID-19 (n=219) in Israel -March 20 – May 5, 2020	RT-PCR	Oropharyngeal and nasopharyngeal swabs -The median time of viral RNA duration from symptom onset in this group of young and healthy adults was 21 days (15-27 IQR, 4-45 range).
(Corsini Campioli et al., 2020)	Retrospective cohort	-Hospitalized cases (n=251) in the United States -February 1 – May 15, 2020	RT-PCR	Nasopharyngeal swabs -The median time from symptom onset to negative RT-PCR result was 23 days, and did not differ by symptoms.
(T. Y. Yang et al., 2020)	Retrospective cohort	-Hospitalized cases (n=50) in China -February 2 – 13, 2020	RT-PCR	Nasopharyngeal swabs -The duration of viral shedding was significantly longer in cases presenting with gastrointestinal symptoms compared to pulmonary symptoms (10.22 days ± 1.93 vs 8.15 days ± 1.87, P

				< 0.01).
(Jeewandara et al., 2020) *Preprint*	Retrospective cohort	-Severe (n=6), moderate (n=5) and mild/asymptomatic illness (n=13) and also those who had mild illness but with prolonged shedding of the virus (n=21) in Sri Lanka -April, 2020	RT-PCR	Respiratory swabs -The median duration of virus shedding in this whole cohort was 25 days (15-38 IQR) -Ten individuals had shedding longer than 50 days. -Those who had prolonged shedding of the virus, had neutralizing antibodies appearing faster and at higher levels than those who cleared the virus earlier.
(Jiang et al., 2020)	Retrospective cohort	-Hospitalized patients with liver injury (n=76) and without liver injury (n=55) in China -January 19 – February 20, 2020	RT-PCR	Specimen type not reported -Liver injury was related to increased length of viral shedding duration (mean difference: 3.0, 95% CI: 1.0–4.9).
(Carmo et al., 2020)	Retrospective cohort	-Patients (n=210) in Portugal -March 1 – April 30, 2020	RT-PCR	Nasopharyngeal and oropharyngeal swabs -In the group of patients with 2 consecutive negative tests, the first negative RT-PCR test was achieved a mean of 24.8 days (7-46 range) after the first positive test. -In men, the first negative test took 24 days (7-46 range) and in women it took 25 days (9-44 range), p>0.05. -69 patients were discharged home and had mild illness. Mild illness patients maintained viral RNA for a longer period of time. 47 were inpatients who had moderate to severe illness. In the patients discharged home, the number of days until the first negative test was 26.3 days (±8.5 SD) and in the inpatient group it was 22.5 days (±9.3 SD), p=0.027. -The inpatients aged over 65 took longer (23.9 days (± 9.7)) than those aged under 65 days (18.3 (± 9.7 SD)), to reach the first negative test, p=0.026.

(D. Shi et al., 2020) *Preprint*	Retrospective cohort	-Inpatients with laboratory confirmed COVID-19 (n=246) in China -January 27 – March 24, 2020	RT-PCR	Nasopharyngeal or pharyngeal swab -Duration of viral shedding was defined as the duration from illness onset to the date of first negative result of viral shedding. -The median duration of viral shedding was 24 days (6-63 range). -Soluble interleukin-2 receptor >710 U/mL, Lactate dehydrogenase >250 U/L and severe COVID-19 were related to prolongation of viral shedding, p<0.05.
(Qingxian et al., 2020) *Preprint*	Retrospective cohort	-Cases stratified by body mass index in China -January 11 – February 16, 2020	RT-PCR	Nasal Swab -The median time from onset to viral clearance was not significantly different (p=0.14) between different body mass indexes: Normal: 14 days (9-18 IQR), Underweight: 14·5 (10-21 IQR), Overweight: 15 (10-22 IQR), Obese: 14 (9-20 IQR).
(Moriconi et al., 2020)	Retrospective cohort	-Hospitalized cases (n=100) in Italy -March 16 – April 15, 2020	RT-PCR	Pharyngeal and nasal swabs -Patients with obesity showed a longer duration for obtaining a negative oropharyngeal or nasal swab (19 ± 8 vs. 13 ± 7, days, p = 0.002).
(Xiao, Fu, & Yang, 2020) *Preprint*	Retrospective cohort	-Non-severe COVID-19 patients with hypertension (n=24) and without hypertension (n=24) in China -January 23 – February 15, 2020	RT-PCR	Nasopharyngeal swabs -The mean period from symptom onset to negative conversion was 17 days (5.5 SD) and 15 days (3.6 SD) for patients with and without hypertension (p=0.021).
(C. Cao et al., 2020)	Retrospective cohort	-Patients (n=157), 63 (40.1%) with GI symptoms in China -Timeline not reported	RT-PCR	Nasopharyngeal swabs -There was no significant difference in mean viral shedding duration between patients with and without GI symptoms. -Total: 12.4 days (6.4 SD) vs. GI symptoms: 13.0 days (6.1 SD) vs. no-GI symptoms: 12.0 days (6.7 SD), p=0.3509.
(H. Wang et al.,	Retrospective	-Hospitalized patients	RT-PCR	Throat swabs

2020)	cohort	(n=95) in China -January 15 – March 2, 2020		-This study suggests that NCD4LR is a potential and useful biomarker for predicting the virus negative conversion time in COVID-19 patients. -The median negative conversion time (interval between symptom onset and the first of two consecutive negative virus tests) among all patients was 19 days (11–27 IQR). -Patients with high neutrophil to CD4+ lymphocyte ratio showed a relatively longer negative conversion time compared to patients with a lower neutrophil to CD4+ lymphocyte ratio: 24 days (18-33 IQR) vs. 13 days (9-21 IQR) ($p < 0.001$).
(J. Han et al., 2020)	Retrospective cohort	-Hospitalized cases (n=185) in China -January 21 – May 8, 2020	RT-PCR	Respiratory swabs -The median duration of viral RNA shedding was 17 days from illness onset; the longest duration was 51 days, and the shortest duration was 4 days.
(G. Zheng et al., 2020)	Retrospective cohort	-Pediatric cases (n=52) in China -Timeline not reported	RT-PCR	Oropharyngeal swabs -The time from admission to first negative RT-PCR test was 12 days (8.0-16.8 IQR).
(Woodruff et al., 2020)	Retrospective cohort	-First 100 patients in the Mayo Clinic FL Positive COVID Registry in the United States -May 15, 2020 end date	RT-PCR	Nasopharyngeal swabs -The mean time for onset of symptoms to undetectable viral RNA was 21.5 days. -Based on this data, the authors suggest more cautious guidelines for isolation.
(J. Xu et al., 2020)	Retrospective cohort	-Critically ill adult patients (n=239) in China -January 12 – February 3, 2020	RT-PCR	Respiratory and serum samples -The median duration of the negative conversion of SARS-CoV-2 RNA was 30 (range 6-81) days in 49 critically ill survivors that were identified.
(Nakamura et al., 2020) *Preprint*	Retrospective cohort	-Patients with a history of cancer (n=32) in Japan -January 31 – May 25, 2020	RT-PCR	Nasopharyngeal swab - The median period between illness onset and the first effective negative SARS-CoV-2 RNA PCR result was 22 days (interquartile range, 18–25) in survivors. -Viral shedding was detected in one case up to 56 days post

				onset.
(Infante et al., 2020)	Retrospective cohort	-Patients with hematological malignancies (n=26) in Spain -March 8 – April 8, 2020	RT-PCR	Nasal swab -Median duration of viral shedding was 32.7 days (10-70, range).
(Berghoff et al., 2020)	Retrospective cohort	-Patients with cancer (n=4) in Austria -March 21 – May 4, 2020	RT-PCR	Nasal swab -Viral clearance was achieved in three of the four patients 14-56 days after testing positive.
(J. Shi et al., 2020)	Retrospective cohort	-Hospitalized cases (n=99) in China -January 19 – February 17, 2020	RT-PCR	Respiratory and stool samples -One patient tested SARS-CoV-2 negative within 5 days, 9 patients tested negative within 10 days, and 49 tested negative within 20 days from illness onset. A subset of 12 patients had detectable levels of the virus up to 30 days from symptom onset. -The shedding time was significantly increased if fecal SARS-CoV-2 RNA test results was positive. Male sex, immunoglobulin use, APACHE II score, and lymphocyte count were independent factors associated with a prolonged duration of SARS-CoV-2 shedding.
(Ling et al., 2020)	Retrospective cohort	-66 patients that had recovered after treatment (convalescent patients) in China -January 20 – February 10, 2020	RT-PCR	Oropharyngeal swab -The median time from the onset of symptoms to first negative RT-PCR results was 9.5 days (6.0–11.0 IQR). Fecal swab -Stool specimens were negative for SARS-CoV-2 RNA following a median duration of 11.0 days (9.0–16.0 IQR) after symptom onset. -43 (65%) patients had a longer viral RNA duration in stool swabs than for throat swabs, with a median delay of 2.0 days (1.0–4.0 IQR).

				Urine swab -Results for only 4 (6.9%) urine samples were positive for viral nucleic acid out of 58 cases. -Viral RNA was still present in 3 patients' urine specimens after throat swabs were negative. Patients undergoing glucocorticoid treatment had delayed viral clearance compared to those who were not.
(Hua et al., 2020)	Retrospective cohort	-Hospitalized children (n=35) in China -Up to April 20, 2020	RT-PCR	Fecal swab -Fecal SARS-CoV-2 RNA detection was positive in 91.4% (32/35) cases and some children had viral excretion time over 70 days. -Viral clearance time was not different between groups treated with different antiviral regiments.
(J. Huang et al., 2020) *Preprint*	Retrospective cohort	-Hospitalized patients (n=33) in China -January 27 – April 10, 2020	RT-PCR	Throat, sputum, and stool swabs -The median time from symptom onset to undetectable viral RNA in throat swab, sputum, and stool samples was 18.5 days (13.25-22 IQR), 22 days (18.5-27.5 IQR), and 17 days (11.5-32 IQR) days, respectively. -Compared to throat swabs, viral loads in sputum and stool declined significantly slower ($p<0.05$). -3 patients showed a detectable recurrence of viral RNA in sputum when tested 2 weeks after discharge from the hospital.
(P. Liu et al., 2020)	Retrospective cohort	-Hospitalized pediatric COVID-19 cases (n=9) in China -January 19 – April 10, 2020	RT-PCR	Nasopharyngeal swabs -The median duration of viral RNA shedding from the day of illness onset to the last positive was 13 days (6–24 range). Oropharyngeal swabs -3 of 9 patients had oropharyngeal swabs that were SARS-CoV2 RNA-positive for a median duration of 4 days (3–10 range). Stool swabs -8 patients had SARS-CoV-2 shedding in their stools for a median duration of 43 days (28–66 range). All had persistent viral shedding in their stools after discharge, with a median duration from the day of discharge to the day of last positive

				collected stool at follow-up of 22.5 days (4–46 range). -SARS-CoV-2 RNA was not detected in the serum or urine samples.
(N. Zhang et al., 2020)	Retrospective cohort	-Hospitalized patients (n=23) in China -January 20 – February 23, 2020	RT-PCR	Upper respiratory and fecal swabs -A longer virus shedding period was found in fecal samples compared to the upper respiratory samples (22 days vs 10 days), although the viral RNAs in upper respiratory samples were generally detectable earlier. - The viral titers of respiratory swabs peaked at 6–9 days post symptom onset and at 14–18 days for fecal samples. - In one critically ill patient, all samples were negative until 21 days post symptom onset, when the fecal sample was positive.
(Lyu et al., 2020)	Retrospective cohort	-Discharged patients (n=6) in China -January 23 – March 9, 2020	RT-PCR	Throat, sputum, and fecal swabs -Stool samples were positive in 6 discharged patients with negative throat and sputum swabs. -The stool samples were positive up to 52 days from onset.
(Gombar et al., 2020)	Retrospective cohort	-Patients (n=87) and healthcare workers (n=63) with COVID-19 in Stanford, California, United States -March 3 – April 30, 2020	RT-PCR	Respiratory swabs -For patients, the median time from first positive RT-PCR test to first negative test was 25 days. There was no demonstrable difference with healthcare workers who had a median time of 23 days.
(Rivera-Izquierdo et al., 2020)	Case series	-Symptomatic health professionals (n=76) in Spain -March 11 – April 13, 2020	RT-PCR	Specimen type not reported -The median time from start of symptoms to negative PCR was 31 days. -The duration of viral shedding was longer in females compared to males (33 vs. 21 days, p=0.025) and cases aged 55+ years compared to those <55 (33 vs. 28 days, p=0.207).
(Warabi et al., 2020)	Case series	-Hospitalized cases (n=2) in Japan -April 30 – May 14,	RT-PCR	Nasopharyngeal swabs -The average time from the onset of symptoms until the virus was no longer detectable was 31.6 days (11.8 SD, 17-53 range).

		2020		- In two patients who had mental retardation and psychiatric disorders, the viral shedding period continued for 44 days and 53 days, respectively. These two patients did not voluntarily brush their teeth. -The authors propose that tooth brushing and gargling remove viral nucleic acid and improve the accuracy of PCR testing.
(B. E. Young et al., 2020b)	Case series	-First 18 patients diagnosed with SARS-CoV-2 infection in Singapore -January 23 – February 3, 2020	RT-PCR	Nasopharyngeal swabs - Viral shedding was prolonged for 7 days or longer among 15 cases (83%). -The median duration of viral shedding from first to last positive nasopharyngeal swab collected was 12 days (range, 1-24), with decreasing viral loads overtime. - Virus was also detectable in the stool (4/8) and blood (1/12) by PCR but not urine.
(L. Zou et al., 2020)	Case series	-Symptomatic patients (n=17) in China -January 7 – 26, 2020	RT-PCR	Nose and throat swabs -Higher viral loads (inversely related to Ct value) were detected soon after symptom onset, with higher viral loads detected in the nose than in the throat.
(Tepasse et al., 2020)	Case series	-65 and 66 year old males in Germany -Timeline not reported	RT-PCR	Pharyngeal swabs -The virus levels tended to further increase during the disease course and there was no indication of virus clearance at all. -Viremia peaked shortly before death in both patients; furthermore there was no sign of viral clearance at 22 and 30 days after development of first symptoms or rather 22/26 days after first detection of SARS-CoV-2 RNA in pharyngeal swabs.
(Wongsawat et al., 2020)	Case series	-Three pediatric cases in China -Timeline not reported	RT-PCR	Nasopharyngeal and throat swabs -RT-PCR tests for viral RNA turned negative on days 15, 23, and 27 of illness for each child, respectively.
(Navaneethan & LehnerNoguera,	Case report	-43 year old female with past medical history of Crohn's	RT-PCR	Nasopharyngeal swab - Case had a repeat RT-PCR testing for SARS-CoV-2 by nasopharyngeal swab twice and was finally negative after 22

2020)		disease in Florida, United States -Timeline not reported		days of initial presentation.
(Ru et al., 2020) *Preprint*	Case series	-Confirmed cases (n=4) in China -January 17 – April 27, 2020	RT-PCR	Nasopharyngeal, blood, and stool samples -The mean time for RNA shedding was 36.5 days with one case demonstrating shedding up to 68 days post symptom onset. - Viral clearance was observed along with high level of neutralizing antibody in three cases. -In the case of prolonged viral shedding, the authors suggest that neutralizing antibody in was not high enough to clear the virus completely.
(Benotmane et al., 2020) *Preprint*	Case series	-Hospitalized kidney transplant recipients with non-severe (n = 21) and severe (n =19) COVID-19 in France -March 4 – April 7, 2020	RT-PCR	Nasopharyngeal swabs and plasma sample -Ten recipients (25%) displayed persistent viral shedding 30 days after symptom onset.
(Tajima et al., 2020)	Case report	-71 year old man in Japan -February 5 – March 20, 2020	RT-PCR	Nasopharyngeal swabs -Despite becoming asymptomatic after having some mild symptoms of COVID-19, case had SARS-CoV-2 RNA detected in saliva specimens for 37 days after onset.
(De Vriese & Reynders, 2020)	Case series	-Hemodialysis patients (n=7) in Belgium -March 14 – April 7, 2020	RT-PCR	Nasopharyngeal swab - In four survivors, the nucleic acid conversion time, defined as the interval from symptom onset to first negative RT-PCR result, was 34, 37, 37, and 44 days. -Cycle threshold values, an inverse measure of nucleic acid concentration, were lowest in the first week of infection and remained relatively stable thereafter.
(Zhou et al., 2020)	Case series	-Hematological patients concomitant with COVID-19 (n=9) in	RT-PCR	Throat swabs - Positive viral load in 4 survivors lasted longer than 45 days.

		China -February 1 – March 31, 2020		
(Dong et al., 2020)	Case series	-Hospitalized patients with complete data of peripheral blood lymphocyte subsets (n=18) in China -January 30 – February 21, 2020	RT-PCR	Respiratory and stool samples -Cases with viral RNA shedding ≥ 15 days had significantly decreased lymphocytes, T cell and its subsets compared to those who remained positive for less than 15 days.
(Cai et al., 2020)	Case series	-Pediatric cases (n=10) in China -January 19 – February 3, 2020	RT-PCR	Nasopharyngeal/throat swab -Results from all 10 patients were available. The median infectious period from symptom onset to viral clearance was 12 days (8-15 IQR, 6-22 range). Fecal swab -Fecal swabs from 10 patients demonstrated a median infectious period from symptom onset to viral clearance of 24 days (18-30 range).
(Z. Chen et al., 2020)	Case series	-Hospitalized children (n=32) in China -January 15 – March 15, 2020	RT-PCR	Respiratory and fecal samples -The average durations of viral RNA in respiratory samples and gastrointestinal samples were 15.8 days (n=25) and 28.9 days (n=16), respectively. -Viral RNA shedding duration in faeces significantly decreased with age: 39.8 days, 27.5 days and 20.4 days in infants and preschool children, school children, and adolescents respectively.
(Park et al., 2020)	Case series	-Hospitalized patients (n=6) in South Korea -February 14 – March 26, 2020	RT-PCR	Nasopharyngeal/oropharyngeal swabs -Six patients were analyzed. -The median duration of SARS-CoV-2 viral detection after hospitalization was 34 days (22-67 range). -After resolution of symptoms/signs, SARS-CoV-2 RNA was detected for a median of 26 days (9-48 range).

				-One patient had persistent detection until day 67 of hospitalization, which was 30 days after symptom resolution. -This is the longest duration of respiratory SARS-CoV-2 detection reported to date.
(J. Li et al., 2020)	Case report	-71 year old woman in China -January 27 – April 22, 2020	RT-PCR	Oropharyngeal swab -A 71 year old woman experienced viral shedding of SARS-CoV-2 RNA for 60 days post symptom onset. -Viral shedding continued 24 days after complete resolution of symptoms.
(M. C. Yang et al., 2020)	Case series	-Three generation family cluster with 6 infected individuals in Taiwan -February 9 – April 6, 2020	RT-PCR	Throat swabs -Among this cluster, the longest throat swab conversion time for SARS-CoV-2 RNA was 37 days, and the estimated course of disease from symptoms to negative throat swab was 59 days.
(Y. Hu et al., 2020)	Case report	-70 year old man in China -Timeline not reported	RT-PCR	Nasopharyngeal and eye swabs -Reported positive detection of SARS-CoV-2 combined with herpes simplex virus type 1 and human herpesvirus type 6B virus nucleic acid in tear and conjunctival secretions of a non-conjunctivitis COVID-19 patient with obstruction of common lacrimal ducts. -Nasopharyngeal swabs were positive for 22 days but eye swabs were still continuously positive for 2 weeks after nasopharyngeal swabs turned negative.
(Q. Shen et al., 2020)	Case series	-Nine pediatric patients (7 mild & 2 asymptomatic) in China -January 8 – February 19, 2020	RT-PCR	Specimen type not reported -6 children had a family exposure and could provide exact dates of close contact with someone confirmed to have COVID-19.
Epidemiologic studies				
(X. He et al., 2020)	Contact tracing study	-77 infector-infectee pairs in China	Epi data	-Viral dynamics reported by the authors (assuming an incubation period of mean 5.2 days) suggested an infectious

		-December 18, 2019 – March 5, 2020		period that started 12.3 days days prior to symptoms and decline quickly within 7 days from onset. -Authors inferred that infectiousness peaked on or before symptom onset.
(You et al., 2020)	Contact tracing study & SIR Model	-169 cases in China - March 31, 2020 end date	Epi data	-A total of 198 chains of transmission together with dates of symptoms onset and 139 dates of infections were identified among 14,829 confirmed cases. -A total of 169 cases in the collected data were able to identify the dates of infection. -The infectious period had an average of 13.96 days (5.20 SD).
(Cheng et al., 2020)	Contract tracing study	-Cases of confirmed COVID-19 (n=100) and 2761 close contacts in Taiwan -January 15 – April 2, 2020	Epi data	- The overall secondary clinical attack rate was 0.7% with the attack rate being higher among contacts whose exposure to the index case started within 5 days of symptom onset than those who were exposed later.
Modeling studies				
(Lin et al., 2020)	Systematic review of transmission-dynamic models	-Fifty-two articles involving 75 mathematical or statistical models from China -December 1, 2019 – February 21, 2020	Modeled	- The median infectious period was 9.94 days (3.93–13.50 IQR).
(Tang et al., 2020) *Preprint*	SEAIR model	-Cumulative reported COVID-19 infected cases in Ontario, Canada -February 26 – April 21, 2020	Modeled	-Recovery rate parameter estimate of symptomatic infected individuals was 0.1957 (0.0111 SD). -By taking the inverse of this estimate an infectious period of 5.11 (SD 0.31) can be inferred.
(Lourenco et al., 2020)	SIR model	-Death cases in the United Kingdom	Modeled	-Calibrated a susceptible-infected-recovered (SIR) model to data on cumulative reported SARS-CoV-2 associated deaths

Preprint		-January 27 – March 16, 2020		from the United Kingdom (UK). -Median infectious period estimated to be between 3-5 days (posterior model estimate).
(R. Li et al., 2020) *Preprint*	Mathematical model	-Documented cases in China -January 10 – 23, 2020	Modeled	-Applied model-inference framework to the observed outbreak before the travel restrictions imposed on 23 January 2020 -A total of 801 documented cases throughout China. -Median infectious period estimated to be 3.47 days (posterior estimated from model for documented cases).
(Zhu, 2020) *Preprint*	SEIR model	-Confirmed cases in China -April 15, 2020 end date	Modeled	-Mean infectious period estimated to be 12.53 days, SD±11.4. -The parameter was estimated using a Weibull distribution.
(Wan et al., 2020)	SEIR model	-Wuhan outbreak in China -January 22 – February 12, 2020	Modeled	-Analyzed the epidemic dynamics and trend of 2019-nCoV in Wuhan from data collected from the official website of Hubei Provincial Health Committee. -The data showed that the infectious time of the infected person (I) is 14 days.
(Peirlinck, Linka, Sahli Costabal, & Kuhl, 2020)	Integrated global network and SEIR model	-Outbreak in China -January 21 – April 4, 2020	Modeled	-A mean infectious period of 17.82±2.95 days was estimated from model using case data of 30 provinces in China.
(Goyal et al., 2020) *Preprint*	Mathematical model	-Confirmed cases. Location not specified -Timeline not reported	Modeled	-People with SARS-CoV-2 are usually infectious for fewer that two days in agreement with peak viral load several days after infection and that transmission is unlikely below a certain viral load.
Reviews				
(Walsh et al., 2020)	Systematic review	-No restriction on setting -Studies published between December 30 – May 12, 2020	Culture & RT-PCR	-Conclude there is a relatively consistent trajectory of SARS-CoV-2 viral load over the course of COVID-19 from respiratory tract samples, however the duration of infectivity remains uncertain.
(Byrne et al., 2020)	Scoping review and Meta-	-No restriction on setting	RT-PCR	-A meta-analysis of 15 estimates approximated a mean time from symptom onset to 2 negative RT-PCR tests was 13.4 days

Preprint	analysis	-Studies published between December 1 – April 1, 2020.		(95%CI: 10.9-15.8), but was shorter when studies included children or less severe cases (~5.8 days shorter). -Maximum duration of detection ranged from approximately 20-49 days, with the longest duration associated with fecal samples. -A meta-regression approach showed that severe cases tended to have longer duration of viral RNA shedding (estimated to be 4.0 days longer), but the effect was not significant.
(Cevik et al., 2020) *Preprint*	Systematic review and Meta-analysis	-No restriction on setting -Studies published between January 1, 2003 - June 6, 2020	Culture & RT-PCR	Respiratory swabs -Mean SARS-CoV-2 RNA shedding duration in upper respiratory tract (URT), lower respiratory tract (LRT), stool and serum were 17.0, 14.6, 17.2 and 16.6 days, respectively. -Maximum duration of SARS-CoV-2 RNA shedding reported in URT, LRT, stool and serum were 83, 59, 35, 42 and 60 days, respectively. -Pooled mean duration of SARS-CoV-2 RNA shedding was positively associated with age (p=0.002), but not gender (p = 0.277). -Viral load in the URT peaked the first week of illness. -No study to date had cultured live virus beyond day nine of illness despite persistently high viral loads.
(Santos et al., 2020)	Systematic review & meta-analysis	-No restriction on setting -Based on data compiled from 36 pediatric cases from studies published from January 1 – April 19, 2020	RT-PCR	-More children had viral shedding in stools after 14 days of symptoms onset compared to respiratory samples (risk ratio = 3.2, 95% confidence interval 1.2–8.9, I2 = 51%). -Viral RNA shedding was longer in fecal samples with a mean difference of approximately 9 days compared with respiratory samples.
(Jefferson et al., 2020)	Systematic review	-No restriction on setting	RT-PCR	-They identified eight studies that report on the duration of viral shedding as assessed by PCR for SARS-CoV-2 RNA.

Preprint		-Studies published up to August 18, 2020		-The minimum duration of RNA shedding detected by PCR was seven days reported and the maximum duration of shedding was 35 days after symptom onset. Six out of eight studies reported RNA shedding for longer than 14 days.
(C. L. H. Xu et al., 2020)	Systematic review	-No restriction on setting -Based on data compiled from 69 pediatric cases from studies published up to May 8, 2020	RT-PCR	-The duration of viral RNA shedding through the respiratory tract was up to 24 days from symptom onset with a mean of 11.1 ± 5.8 days. -The mean duration of viral shedding through the gastrointestinal tract was 23.6 ± 8.8 days from symptom onset. -In 89% of cases, viral shedding through the gastrointestinal tract persisted up to 4 weeks after nasopharyngeal or throat swabs became negative.
Animal studies				
(Bartlett et al., 2020) *Preprint*	Case series	-Two Malayan tigers, two Amur tigers, and three lions in the Bronx zoo, United States -March, 2020	Culture & RT-PCR	Fecal swabs - The index case shed viral RNA for 14 days, including 5 days beyond the cessation of clinical signs. -In contrast, the asymptomatic tiger shed viral RNA for only 5 days. -The tiger with the longest duration of viral fecal shedding (24 days) was asymptomatic during this time. -Fecal shedding was also prolonged in two lions persisting for more than 30 days. - Virus was isolated from feces of two animals: 5 days after clinical signs ceased and the last day of clinical signs.
(Munster et al., 2020)	Experimental challenge trial	-Adult rhesus macaques inoculated with SARS-CoV-2 in the United States -N/A	Culture & RT-PCR	Bronchoalveolar swab -Infectious virus was isolated from bronchoalveolar lavage fluid collected on one and three days post infection in adult rhesus macaques. Throat swab -Viral loads were high in throat swabs following inoculation. In 1 animal throat swabs were positive on 1 and 10 days post infection but not on any of the sampling dates in between.

				Rectal Swab -One animal showed prolonged shedding of viral RNA in rectal swabs from 7-17 days post infection but infectious virus could not be isolated from these swabs.
(Gaudreault et al., 2020) *Preprint*	Experimental challenge trial	-Male cats (n=10) in the United States -N/A	RT-PCR	Nasal swabs -SARS-CoV-2 RNA was detected in nasal swabs of the principal infected cats at 1 through 10 days post challenge, with maximal quantities observed from 1 through 5 days post challenge

RECURRENCE OF VIRAL SHEDDING IN CONVALESCENT PERIOD

Table 4 lists studies that provide evidence of the intermittent recurrence of viral RNA detection in the convalescent (asymptomatic or post-symptomatic) period of COVID-19 infection. Case reports and follow-up studies have reported on the recurrence of viral RNA detection in patients through post-discharge/recovery quarantine, re-hospitalization, and re-discharge/recovery. To date, only one study has provided evidence of culturable viral shedding during the recurrence of viral RNA detection (Quicke et al., 2020). No evidence of transmission has been reported.

The majority of discharged patients experiencing a recurrence in RT-PCR RNA positivity did so within seven days following consecutive negative test results. Following recurrence, patients remained viral RNA positive for approximately 1-8 days and typically remain asymptomatic (Chen et al., 2020; Lan et al., 2020; McGrath et al., 2020; Quicke et al., 2020; To et al., 2020b; Wong et al., 2020; Wu et al., 2020;Yuan et al., 2020).

Risk factors for recurrence of viral RNA positivity included elevated low-density lipoprotein cholesterol (LDL-C) on admission, the number of pulmonary lobes with infiltration lesions on imaging, CT imaging abnormalities, productive cough, and chest congestion with dyspnea in the convalescent phase (Jin et al., 2020; Yan et al., 2020).

It is unclear whether such recurrence in RT-PCR test results is indicative of prolonged intermittent viral RNA shedding or whether recurrence (virus replication starts again) or reinfection (a new infection occurs) is possible in the convalescent phase. However, recent studies utilizing culture methods have found that redetections of viral RNA are associated with no, or very low levels of infectious virus (Chang et al., 2020; Kang, 2020; Korea CDC, 2020; J. Lu et al., 2020; Quicke et al., 2020).

Table 4: Studies evaluating recurrence of viral shedding in the convalescent period of COVID-19 infection (N=55)

Reference	Study Type	-Population & Setting -Time Period	IP determined via: Culture, RT-	Key Outcomes

			PCR Serial testing, Epi data, or Model	
Culture & RT-PCR studies				
(Korea CDC, 2020)	Prospective cohort	-Re-positive cases (n=285) in South Korea -Up to May 15, 2020	Culture & RT-PCR	Specimen type not specified -Epidemiological investigation and contact investigation was completed for 285 of 447 re-positive cases. -No secondary cases among contacts were reported for re-positive cases. -Viral cell culture testing of 108 re-positive cases all had negative results. -The cycle threshold values in RT-PCR during re-positive period was found to be above 30 in 89.5% of cases.
(Chang et al., 2020)	Prospective cohort	-Discharged cases (n=64) in China -January 28 – April 30, 2020	Culture & RT-PCR	Throat swabs -As part of the regular follow-up, patients that were discharged were followed up every week to obtain their throat swabs. -Four of the patients re-tested positive. -The throat swabs were sent to test for the presence of a live pathogen. The swabs were plated on Vero cells to measure cytopathy and viral replication using qPCR of cell lysates after infection. They failed to detect any cytopathy or presence of viral replication in the infected cells. -Data also showed that patients with persistent viral RNA presence (>16 days) had more severe disease outcomes.
(J. Lu et al., 2020) *Preprint*	Prospective cohort	-Discharged COVID-19 cases (n=619) in China -January 23 – February 25, 2020	Culture & RT-PCR	Respiratory samples -87/619 discharged cases tested re-positive via RT-PCR. -Cases re-tested as SARS-CoV-2 viral RNA positive at a mean of 6.7 days (3-10 range) post-discharge. -77/87 re-positive cases were asymptomatic and ten cases had unproductive cough. -No infective viral strain could be obtained by culture and no full-length viral genomes could be sequenced for re-positive cases.
(Quicke et al., 2020)	Longitudinal surveillance	-454 asymptomatic staff at 5 skilled nursing	Culture (Plaque assay)	Nasopharyngeal swabs -Six individuals had recurrent positive results after 1-2 weeks of

Preprint	study	facilities in Colorado, United States (prevalence varied considerable between facilities) -Timeline not reported	& RT-PCR	undetectable viral RNA. After redetection, viral RNA was detectable for up to one week. -These redetections of viral RNA were associated with no, or very low levels of infectious virus.
(Kang, 2020)	Literature review	-Patients released from quarantine (n=8,922) in South Korea -April 8 – 29, 2020	Culture & RT-PCR	-292 (3.3%) of the 8,922 patients released from quarantine retested positive. -The largest proportion of re-positive cases were between 20-29 years old (24%). -It took an average of 13.5 days (1-35 range) to retest positive after being initially cleared as negative. -Re-positive cases were asymptomatic or only had minor symptoms such as cough, sputum, fever, and sore throat. -Cultivation tests were all negative when researchers tried to confirm if there was any viable virus in the samples of the re-positive cases.
(J. Zheng, Zhou, & Chen, 2020) *Preprint*	Prospective cohort	-Hospitalized patients (n=285) in China -January 20 – March 14, 2020	RT-PCR	Nasopharyngeal swab -27 (9.5%) previously discharged patients tested positive for SARS-CoV-2 in their nasopharyngeal swab. Patients were readmitted after a median duration of seven days (IQR 5-8) since initial discharge. -Age, sex, epidemiological history, clinical symptoms and underlying diseases were similar between patients that experiences reoccurrence and those that did not ($p>0.05$). -Prolonged duration of viral RNA shedding and higher Ct values during the first hospital admission were associated with redetection.
(B. Yuan, Liu, & Yang, 2020) *Preprint*	Prospective cohort	-Recovered and isolated patients that underwent retesting (n=182) in China -Timeline not reported	RT-PCR	Nasopharyngeal swabs and anal swabs -Twenty (10.99 %) patients out of the 182 re-tested had positive results. -Fourteen were positive via nasopharyngeal swabs and 6 were positive via anal swabs; none were found positive for both swabs.

				-More females retested positive than men (13 vs. 7). -No severe patients retested positive. -Most cases turned negative again in subsequent test.
(Abdullah et al., 2020)	Prospective cohort	-Discharged cases (n=138) in Brunei -Timeline not reported	RT-PCR	Nasopharyngeal and throat swabs -Out of 138 discharged patients, 27 (19.6%) re-tested positive after discharge. -On readmission, six (22.2%) patients had mild symptoms which resolved without specific treatment. -Contact tracing carried out after re-testing positive did not detect any new cases linked to these 27 patients. - Time from re-positive to negative was 7.0 ± 5.6 days.
(Yan et al., 2020)	Prospective cohort	-Discharged hospitalized cases (n=337) in China -February 23 – March 14, 2020	RT-PCR	Throat swabs -21/337 (6.2%) COVID-19 patients were SARS-CoV-2 nucleic acid re-positive, and 4 /337(1.2%) patients were suspected positive. -The median day interval between the discharge to nucleic acid re-positivity was 7.5 days (IQR, 6–13), ranging from 6 to 13 days. -Risk factors of nucleic acid re-positivity included the number of pulmonary lobes with infiltration lesions (odds ratio[OR], 1.14; 95% CI, 1.09–1.19), the distribution of pulmonary lesions (OR, 0.16; 95% CI, 0.13–0.19), patchy shadowing accompanied with consolidation in CT imaging (OR, 9.36; 95% CI, 7.84–11.17), respiratory symptoms of cough accompanied with expectoration (OR, 1.39; 95% CI, 1.28–1.52), and chest congestion accompanied by dyspnea (OR, 1.42; 95% CI, 1.28–1.57).
(X. Wei et al., 2020) *Preprint*	Retrospective cohort	-Mild to moderate COVID-19 cases admitted to shelter hospitals (n=231) in China -February 17 – March 7, 2020	RT-PCR	Respiratory swab -The median time of SARS-CoV-2 RNA negative conversion was shorter in the asymptomatic group (n=34) than in the symptomatic group (n=197): 15 days (11.5-17 IQR) vs. 32 days (23-39 IQR), $p<0.05$. -25/221 (11.3%) discharged patients retested positive for SARS-CoV-2 nucleic acids. There was no significant difference in the rate or time of nucleic acid re-positivity between the symptomatic and

				the asymptomatic groups.
(Miyamae et al., 2020)	Retrospective cohort	-Asymptomatic /mild cases (n=23) aboard the Diamond Princess cruise ship -February 18 – 25, 2020	RT-PCR	Oropharyngeal and nasopharyngeal swab -The median duration of SARS-CoV-2 viral RNA shedding was 19 days (6-37 range) from initial viral detection. -Eight cases (35%) had another positive RT-PCR RNA result after testing negative previously.
(Q. Hu et al., 2020) *Preprint*	Retrospective cohort	-Confirmed COVID-19 patients (n=211) in China, among which were 181 mild and moderate cases and 40 severe and critical cases -January 23 – March 3, 2020	RT-PCR	Nasopharyngeal swab -SARS-CoV-2 IgG and IgM antibody concentration and re-detectable positive nucleic acid testing was investigated with antibody testing results of 74 recovered patients within seven days following discharge. -Nasopharyngeal swabs revealed positive SARS-CoV-2 RNA in up to 52.7% of recovered patients after discharge, whose IgG level showed to be significantly lower than that of patients with negative RNA results (P = 0.009). -The protective effect of IgG remains to be investigated.
(J. Chen et al., 2020) *Preprint*	Retrospective cohort	-Discharged hospitalized patients (n=1067) in China -February 24 – March 31, 2020	RT-PCR	Throat swab -Eighty one (7.6%) patients had a repeat positive SARS-CoV-2 RNA result within nine days (3-18 range) following discharge. -For patients with recurrent RT-PCR positivity, the median duration from illness onset to onset of complete RNA negative was33 days (6-82.0 range). -Time from illness onset to recurrence was 50 days (21-95 range).
(Y. Zou et al., 2020)	Retrospective cohort	-Inpatients with confirmed COVID-19 (n=257) in China -January 1 – March 10, 2020	RT-PCR	Throat swabs -Among 257 patients, 53 had a recurrence of positive viral RNA results after have consecutive negative results. -Recurrently positive RT-PCR test results in patients with three consecutive negative results (5.4%) were significantly decreased compared with those in patients with 2 consecutive negative results (20.6%). -Patients reported positive RT-PCR test results within 1-12 days after meeting the discharge criteria.

(W. Zhao et al., 2020)	Retrospective cohort	Children who had been hospitalized for COVID-19 (n=14) in China -Cases discharged between January 21 – April 18, 2020	RT-PCR	Nasopharyngeal swab -Seven (50%) children experienced reactivation, including 2 children who experienced a second reactivation after discharge. -Among those who experienced reactivation of SARS-CoV-2 viral RNA shedding, the median time was 14 days (7-17 range) days from discharge to the first recurrence of a positive SARS-CoV-2 test result.
(B. M. Liu et al., 2020)	Retrospective cohort	-71 confirmed cases of COVID-19 who were discharged from hospital in China. All were hospital employees or their family members. -February 6 – March 26, 2020	RT-PCR	Oropharyngeal swabs -During convalescence, RNA detection results of 35.2% patients (25/71) turned negative to positive. -The longest RNA reversed phase time was 7days.
(To et al., 2020)	Retrospective cohort	-1 patient of a cohort of 23 in Hong Kong -January 22 – February 12, 2020	RT-PCR	Posterior oropharyngeal swab -1 patient showed negative viral RNA tests on days 21 and 22 after symptom onset, with rebound of viral positivity on days 23 and 24, followed by 5 days of undetectable viral load.
(J. Wu et al., 2020) *Preprint*	Retrospective cohort	-Recovered and discharged COVID-19 patients (n=14) in China -January 23 – March 30, 2020	RT-PCR	Nasopharyngeal swab -Of the 14 patients, six (42.86%) were positive for SARS-CoV-2 RNA after discharge. -Cases presented with a mild cough, diarrhea, runny nose, but no fever at readmission. -The time to RT-PCR positive conversion ranged from 3–15 days after the first discharge. -The time to RT-PCR negative conversion ranged from 1-16 days (average 7.5 days) after readmission. -No worsening outcomes or active transmission to close contacts were found for the readmitted contacts.
(Wong et al., 2020)	Retrospective cohort	-Discharged patients (n=106) in Brunei	RT-PCR	Nasopharyngeal -Of 106 patients that had a follow-up swab taken between 11 - 18

Preprint		-April 12, 2020 end date		days post discharge, 21 (19.8%) were found to be re-positive. -Only 1 case reported symptoms post-discharge. -RT-PCR results were negative again in 16 patients within 1-3 days following readmission. -These findings suggest that reinfection is not plausible, but rather prolonged intermittent viral RNA shedding is more likely. -The highest re-positive rate was observed in patients aged 53 and above (38.5%), followed by those with moderate to critical conditions (33.3%) and lopinavir/ritonavir treatment (30.3%).
(L. Wang et al., 2020) *Preprint*	Retrospective cohort	-Discharged patients (n=399) in China -January 19 – March 15, 2020	RT-PCR	Respiratory and anal swabs -35patients (8.8%) showed recurrent positive RT-PCR test results following discharge. -The median interval from the first negative RT-PCR to the recurrent positive RT-PCR was 10 days (7–16 IQR).
(X. Chen, Shui, Li, & Zhang, 2020) *Preprint*	Retrospective cohort	-Discharged patients (n=758) hospitalized in 17 hospitals in China -February 25 – March 15, 2020	RT-PCR	Throat swab -59 patients (7.78%) had recurrent positive RT-PCR test results following discharge. -Time from onset of symptoms to last time of positive results of RT-PCR ranged from 14 to 61 days. -The time from quarantine (discharge) to last time of positive results ranged from 1 to 19 days.
(H. Cao, Ruan, Liu, & Liao, 2020)	Retrospective cohort	-COVID-19 patients (n=108) in China -February 10 – April 13, 2020	RT-PCR	Nasal and throat swabs -8 cases were readmission patients because their PCR test results were positive again following discharge. -On their second admission all cases were symptom free and had normal chest CT. -Two patients were subsequently discharged while six were still hospitalized at time of writing as they had not yet cleared virus. The course of two patients had persisted more than 90 days since first symptom onset.
(S. Chen et al., 2020)	Retrospective cohort	-Discharged patients (n=1282) in China	RT-PCR	Nasopharyngeal and anal swabs -Of 1,282 discharged patients enrolled in this study, 155(12.1%)

Preprint		-January 14 – March 10, 2020		tested positive for SARS-CoV-2 RNA during 14 days' follow-up. -The median time of recurrence of SARS-CoV-2 RNA was 7 days (IQR4-9). -Compared to negative group, the patients from re-positive group were a younger and had a higher proportion of moderate cases. -None of the re-positive patients showed symptoms or blood abnormalities during the second admission to hospital. -The median time of all re-positive patients turned viral RNA negative was 8.0 days (IQR4-14). -None of close contacts (n=202) derived from re-positive patients (n=67) developed to COVID-19 patients.
(Su et al., 2020) *Preprint*	Retrospective cohort	-Discharged patients (n=938) in China -January 18 – May 11, 2020	RT-PCR	Nasal and pharyngeal swab - Of 938 discharged patients, a total of 58 (6.2%) had reappeared positive nucleic acid test results. -Factors associated with re-positive results were coronary artery disease and hypertension.
(L. Chen et al., 2020) *Preprint*	Retrospective cohort	-Confirmed cases (n=15) in China -February 10 – March 31, 2020	RT-PCR	Nasopharyngeal swab -Reviewed the data of 15 recurrent-positive patients and 107 control patients with non-recurrent, moderate COVID-19. - The rate of recurrent-positive disease in the hospital was 1.87%. Recurrent-positive patients were significantly younger than control patients, 43 years (35-54 range) vs. 60 years (43-69) P=0.011. -The length of stay in hospital before recurrence was significantly longer in recurrent-positive patients than in control patients, 36 days (34-45 range) vs 15 days (7-20 range) p=0.001. -The time required for the first conversion of RT-PCR results from positive to negative was significantly longer in recurrent-positive patients than in control patients, 14 days (10-17 range) vs 6 days (3-9 range) p=0.011. -Serum COVID-19 antibody levels were significantly lower in recurrent-positive patients than in control patients.

(Mei et al., 2020)	Retrospective cohort	-Convalescent cases (n=651) in China -January 11 – April 4, 2020	RT-PCR	Nasopharyngeal and oropharyngeal swabs -During follow-up, 23 (3%) of 651 patients tested positive on a retest for SARS-CoV-2 by RT-qPCR. -In this retest-positive group, 12 patients (52%) had moderate, nine (39%) severe, and two (9%) critical conditions during their previous hospitalisation. -The median duration from hospital discharge to a positive retest was 15·0 days (range 4–38, IQR 11·0–16·5; appendix). -Among this retest-positive group, 15 patients (65%) were asymptomatic at the time of the retest whereas eight (35%) had at least one symptom associated with active COVID-19.
(C. Liu et al., 2020)	Retrospective cohort	-Discharged cases (n=51) in China -January 23 – March 28, 2020	RT-PCR	Oropharyngeal swabs -17.6% discharged patients, in which only 33.3% patients complained clinical symptoms.
(Qiao et al., 2020)	Retrospective cohort	-Confirmed severe/critical cases (n=15) in China -January – March, 2020	RT-PCR	Respiratory samples -Most patients showed no clinical symptoms and negative nucleic acid tests during follow-up after discharge. -One patient had an itchy throat, her CT scan showed a light density shadow in the right lower lobe of the lung, and the nucleic acid was re-positive.
(Jin et al., 2020) *Preprint*	Retrospective cohort	-Hospitalized adult COVID-19 patients (n=133) in China -February – April 30, 2020	RT-PCR	Oropharyngeal swab -32.4% of patients were positive for SARS-CoV-2 RNA after initial discharge. The mean recurrence time from the first discharge was 18.22 days. Following readmission, the mean length of stay was 14.2 days. -Univariable and multivariable Cox regression showed that the low-density lipoprotein cholesterol (LDL-C) dyslipidemia on admission was associated with the recurrence of COVID-19 during the follow-up period.
(Habibzadeh et al., 2020)	Retrospective cohort	-Patients (n=35) intending to donate	RT-PCR	Nasopharyngeal swab - Reverse transcription polymerase chain reaction test was positive

		plasma in Iran -March, 2020		in 9 (5 male, 4 female) of 13 recovered patients - a positive rate of almost 70%. - The second RT-PCR test was found positive in these patients after a median of 29 (range 22 to 54) days after initiation of their symptoms/illness and 18 (range 15 to 48) days after complete resolution of their symptoms.
(Bongiovanni et al., 2020)	Retrospective cohort	-Recovered patients (n=1146) in Italy -March 9 – June 30, 2020	RT-PCR	Nasopharyngeal swab -125 (10.9%) had a recurrence of COVID-19 infection. - The mean time to clinical recovery and two negative nasopharyngeal swabs was 27.7 days (95% CI 11-51); after that, the mean time to recurrence was 19.9 days (3-43, 95%CI). - After a mean time of 14.8 days (95% CI 6-36), 102 subjects (81.6%) had two additional negative nasopharyngeal swabs and were considered clinically recovered for the second time. -During follow-up, 11 patients (8.8%) died. Patients who died were older than others (mean age 86.4 years, 95% CI 77-92) and 8 of them (72.7%) had clinical symptoms at the time of recurrence (4 fever and 4 respiratory failure).
(Y. Li et al., 2020b) *Preprint*	Retrospective cohort	-Nasal swabs (n=484) from patients with COVID-19 in China -January – April, 2020	RT-PCR	Nasal swabs -Serum levels of lipoprotein-associated phospholipase A2 were significantly higher in re-positive COVID-19 cases compared to healthy controls and hospitalized COVID-19 patients.
(Peng et al., 2020)	Retrospective cohort	-Hospitalized patients (n=79) in China -January – May, 2020	RT-PCR	Oropharyngeal swab -The median duration of positive nucleic acid test (NAT) results for SARS-CoV-2 was 16.5 (12.0-22.0, IQR) days. -Two weeks after discharge, 5.6% survivors experienced a recurrence of the positive nucleic acid test results.
(Hao et al., 2020)	Case-control study	-Patients with confirmed COVID-19 (n=104), with short and long viral shedding times (cases & controls) in China	RT-PCR	Respiratory swabs -Median viral shedding time from confirmed diagnosis to ≥2 consecutive negative RT-PCR results was 11 days (1-39 range). -Recurrent positive RT-PCR results in respiratory specimens after ≥2 consecutive negative results were observed in 24 patients. The

		-January 19 – March 3, 2020		probabilities of positive RT-PCR results in the next test after 1 or 2 consecutive negative results were 30.5% and 16.4%, respectively. With an increase from 2 to 3 consecutive negative results, the rate of recurrent positive RT-PCR RNA results decreased sharply to 4.8%. -A series of ≥3 consecutive negative results was deemed suitable by authors as a criterion for the end of viral RNA shedding.
(S. Cao et al., 2020) *Preprint*	Citywide screening program	-9,899,828 persons in China -January 23 – April 8, 2020	RT-PCR	Nasopharyngeal and pharyngeal swab - 107 of 34,424 previously recovered patients with a history of COVID-19 diagnosis were re-positive (relapse rate, 0.31%).
(McGrath et al., 2020) *Preprint*	Case series	-4 cases of COVID-19 in healthcare workers in Ireland -March – April, 2020	RT-PCR	Nasopharyngeal and oropharyngeal swabs -All three cases completed 14 day periods of self-isolation with full resolution of symptoms. -Each had distinct episodes of recurrent symptoms following initial resolution and had persistently positive SARS-CoV-2 PCR results, ranging up to 60 days post onset of illness.
(D. Chen et al., 2020)	Case report	-46 year old woman in China -January 17 – February 9, 2020	RT-PCR	Oropharyngeal swab -Reports a confirmed case of COVID-19 whose oropharyngeal swab test of SARS-CoV-2 RNA turned positive in convalescence. -Case developed symptoms on January 17 2020 and on January 24 2020 tested positive for SARS-CoV-2 RNA. -Viral RNA tests were negative on January 28 2020 and January 30 2020, but became positive again on February 2 2020. She was later discharged on February 9 2020.
(H. Zheng, Tan, Ma, & Meng, 2020) *Preprint*	Case report	-37 year old woman in China -January 12 – March 10, 2020	RT-PCR	Oropharyngeal swab -RT-PCR test results were positive during the first menstrual period before admission (February 2 2020). -Case was hospitalized on February 4 2020. -RT-PCR test results turned negative during hospitalization (ten and 12 days after admission) then turned positive again during the second menstrual period (February 24 & 25 2020), which

				occurred after hospital discharge. -The RT-PCR test on March 10 2020 was negative. -Authors suggest sex hormones may play an important role in SARS-CoV-2 infection.
(Lan et al., 2020)	Case series	-One hospitalized patient and 3 patients (all medical personnel) quarantined at home with COVID-19 in China -January 1 – February 15, 2020	RT-PCR	Throat swab -Patients were evaluated with real-time reverse transcriptase–polymerase chain reaction (RT-PCR) tests for COVID-19 nucleic acid to determine if they could return to work. -After discharge or discontinuation of quarantine, the patients were asked to continue the quarantine protocol at home for 5 days. -RT-PCR tests were positive 5-13 days later. Patients had three repeat tests performed over the following 4-5 days and all were positive despite all cases being asymptomatic.
(J. Yuan et al., 2020) *Preprint*	Case series	-Discharged patients with COVID-19 recovery (n=25) in China -January 23 – February 21, 2020	RT-PCR	Respiratory swabs -All cases had previously tested negative on 2 consecutive RT-PCR tests but were re-hospitalized due to the recurrence of viral RNA. -Patients presented with recurring RNA within 3.0 (2-7 range) days after hospital discharge. The median time from their last negative result to turning positive was 6.0 (4-10 range) days. -All patients were asymptomatic at time of recurrence. -Cases were treated with Chinese herbal medicine and within a few days were all negative for viral RNA.
(Z. Zhang et al., 2020) *Preprint*	Case series	-56 COVID-19 patients with symptoms at admission (33 later displayed symptoms) and 19 age-matched symptomatic patients in China -January 23 – April 1, 2020	RT-PCR	Respiratory and anal swab -Among 56 patients without symptoms at admission, 23 remained asymptomatic throughout the follow-up period. -For asymptomatic cases viral RNA reappeared after discharge (Ct value >40) in nasopharyngeal and anal samples 54 and 42 days, respectively, post initial admission. -For pre-symptomatic cases viral RNA reappeared 81 and 40 days post initial admission and in symptomatic cases reappeared 62 and 42 days post initial admission.

(Peng, Wang, Zhang, & Lu, 2020)	Case series	-Seven discharged patients in China -January 22 – March 8, 2020	RT-PCR	Throat and anal swabs -7 cases retested positive for SARS-CoV-2 following discharge. -All 7 patients had shorter hospital stays, lower medical costs, and milder symptoms in their second hospital visit compared to their first hospitalization.
(Loconsole et al., 2020)	Case report	-46 year old woman in China -January 17 – February 17, 2020	RT-PCR	Oropharyngeal swab -Patient had consecutively negative test results on day 12 and 14 following symptom onset. -A recurrence of viral positivity occurred 17 days following symptom onset. -Test results were negative again on days 20, 22, and 32. -Patient was not symptomatic at time of recurrence.
(Pan et al., 2020) *Preprint*	Case series	-Confirmed cases (n=64) in China -January 23 – March 31, 2020	RT-PCR	Stool and pharyngeal swab -There were 64 confirmed patients and 17 patients present re-positive testing after discharge. -The interval between first negative test and first time of re-positive test was 11.82 days (±3.42).
(J. Huang & Zheng et al., 2020) *Preprint*	Case series	-Patients (n=414) in China -January 11 – April 23, 2020	RT-PCR	Nasopharyngeal swabs -16.7% of recovered patients had re-positive PCR results one to three times, despite being in strict quarantine. -Younger patients with mild pulmonary respiratory syndrome had higher risk of PCR positivity recurrence.
(Martinez Alonso, Fábio de O. et al., 2020) *Preprint*	Case report	-26 year old man in Brazil -April 21 – June 18, 2020	RT-PCR	Oropharynx and nasopharynx swabs -On April 21, 2020 the man experienced a headache with no respiratory symptoms. Two days later he tested positive by RT-PCR. -On May 5, 2020 viral RNA was no longer detected. -One month later, the symptoms returned more acutely and included fever, cough, headache, myalgia, arthralgia, anosmia and fatigue, and lasted for almost two weeks. -SARS-CoV-2 RNA detection reversed to positive June 8, 2020. -On June 22, 2020, IgA/IgM and IgG antibodies were detected in

				serum and only N gene was detected by RT-qPCR.
(Tian et al., 2020)	Case series	-Convalescent cases (n=20) in China -May 22, 2020 end date	RT-PCR	Oropharyngeal swab -Of 147 patients, 20 convalescent cases (13.6%) tested re-positive for viral RNA in respiratory specimens 7 to 47 days after discharge. -All cases remained asymptomatic.
(Dou et al., 2020)	Case report	-34 year old man with a history of type 2 diabetes in China -January 27 – April 13, 2020	RT-PCR	Oropharyngeal swab - The patient had a recurrence of positive SARS-CoV-2 ribonucleic acid (RNA) after recovering. - Despite this, he displayed no obvious clinical symptoms and improved chest CT. - Members of his family and other close contacts did not experience any symptoms.
(F. Liu et al., 2020)	Case report	-35 year old man in China -January 30, 2020 onward	RT-PCR	Nasopharyngeal swabs - Case tested re-positive to viral RNA even after apparent recovery (normal CT imaging, no clinical symptoms, negative SARS-CoV-2 on stool sample and negative serum IgM test) from COVID-19. -Viral shedding duration lasted for 65 days and the time from symptom onset to disappearance was up to 95 days.
(F. He et al., 2020)	Case report	-39 year old woman with systemic lupus erythematosus in China -January 21 – April 11, 2020	RT-PCR	Throat swab -On the 8th day of her home isolation (March 5), she reappeared symptoms of dry cough, arthralgia, and headache without fever. -On March 7, her symptoms were relieved. And the retests of SARS-CoV-2 viral RNA for 3 consecutive days were all negative from Mar 7 to Mar 9, and on follow up until April 11.
(González-Calvo, Bores-García, Barba-Martín, & Gallego-Lema, 2020)	Case report	-64 year wold woman in Iran -February 16 – March 22, 2020	RT-PCR	Nasopharyngeal swab -After a few weeks, relapse occurred, as indicated by symptoms of acute meningoencephalitis. Results of COVID-19 RT-PCR testing from her cerebrospinal fluid, nasopharyngeal and tracheal aspiration specimens became positive again, but COVID-19 serum antibodies were negative.
(Alonso et al., 2020)	Case report	-26 year old man in Brazil -April 21 – June 29, 2020	RT-PCR	Respiratory swab -Having a mild infection, the patient remained in isolation for 14

				days at home, recovering after 3 days of symptoms onset. -On 6 June (a month later), symptoms returned more acutely and included fever, cough, headache, myalgia, arthralgia, anosmia, and fatigue, and lasted for 2 weeks. SARS-CoV-2 RNA detection reversed to positive on June 8 and remained positive in another testing on 16 June, although SARS-CoV-2 antibodies remained negative. -On June 22, IgA/IgM and IgG antibodies were detected in serum and only N gene was detected by RT-qPCR and finally, on 29 June, no viral genes were further detected. -Absence of detectable antibodies in the first episode may have allowed for a new infection, rather than a recurrence. However, as the authors did not investigate viral genetics at different times, such a statement is hypothetical.
(Duggan et al., 2020)	Case report	-82 year old male with a history of advanced Parkinson's disease, insulin-dependent diabetes, chronic kidney disease, and hypertension in the United States -April – May, 2020	RT-PCR	Specimen type not reported -Case presented to the emergency department (ED) in early April with one week of fever and shortness of breath. -In early May 2020 two subsequent RT-PCRs for SARS-CoV-2 were negative and he was discharged. - Ten days post-discharge (48 days after first presentation), he re-presented to the emergency department with fever and hypoxia and a positive RT-PCR result. - RT-PCR for SARS-CoV-2 on hospital days 11 and 12 which both resulted as negative.
(Ye et al., 2020)	Case report	-72 year old female in China -January 30, 2020 onward	RT-PCR	Nasopharyngeal swab - The case was admitted to hospital isolation after being infected with COVID-19 as part of a family cluster on January 30, 2020. -The patient recovered and was discharged on February 19. - Because of a low humoral immune response, the chronic lymphocytic leukemia patient could not effectively clear the SARS-Cov-2 infection and suffered from recurrence twice during the 69-day follow-up.

(Alfano et al., 2020)	Case report	-72 year old man with end stage renal disease in Italy -March, 2020	RT-PCR	Nasal/oropharyngeal swab -After 41 days from the primary infection, the clinically recovered patient experienced symptomatic reactivation of SARS-COV-2 infection with immunoglobulin M seroconversion. - He was discharged home on day seven from re-admission with a negative PCR result on the oropharyngeal/nasal swab.

REINFECTION

Table 5 lists studies that provide evidence of reinfection with COVID-19.

Since August 25, 2020, evidence that reinfection can occur has been published. Epidemiological, clinical, serological and genomic analyses provide good evidence of reinfection in a patient from Hong Kong 142 days after initial infection (To, Hung, et al., 2020). There is also strong evidence for a case of re-infection in the United States (Tillet et al., 2020). Additional research is needed to understand the role of immunity in protection against SARS-CoV-2 post initial acute infection, the clinical and epidemiological characteristics of reinfection, and whether recurrent cases can be infectious and the likelihood that they may experience clinical disease.

Table 5: Studies evaluating reinfection with COVID-19 (N=2)

Reference	Study Type	-Population & Setting -Time Period	IP determined via: Culture, RT-PCR Serial testing, Epi data, or Model	Key Outcomes
(To, Hung, et al., 2020)	Case report	-33 year old male in Hong Kong -March – August, 2020	RT-PCR & Whole Genome Sequencing	Respiratory samples -Immunocompetent case tested re-positive for SARS-CoV-2 viral RNA 142 days after the first symptomatic episode. -While re-positive, there was serological evidence of elevated C-reactive protein and SARS-CoV-2 IgG seroconversion. -Viral genomes from first and second episodes belonged to different clades/lineages, confirming reinfection. Epidemiological data, including a recent trip from Spain, supports the virological results.
(Tillet et al., 2020)	Case report	-25 year old case in	RT-PCR & Whole Genome	Nasopharyngeal swabs -Case was positive for the 1st time in mid-April 2020, and after recovering

Preprint		Nevada, United States -April – June, 2020	Sequencing	returned ill at the end of May, 2020. -Nucleic acid sequence analysis showed that the viruses associated with each instance of infection were found to possess a degree of genetic discordance. -The case may have been re-exposed to the virus by an infected parent.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature searches are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The cumulative scan results are maintained in a Refworks database and an excel list that can be searched. The full text of every study that was tagged as Epidemiology, Clinical Data, or Modeling foci by the emerging sciences group were scanned for information relating to the infectious period of COVID-19. Article titles and summaries were scanned for mention of the following key words: "Shedding", "Viral dynamics", "Viral clearance", "Viable", "Culture", "Infectivity", "SARS-CoV-2 detection", "Infectious Period", "Communicability period", "Recurrence", and "Re-positive". This review contains key research articles published up to August 31, 2020. Each potentially relevant reference was examined to confirm it had relevant data and key relevant data was extracted into the review.

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Nouveaux éléments de preuve sur la COVID-19

Revue rapide de la période infectieuse

Introduction

Quelle est la durée de la période infectieuse du SRAS-CoV-2?

La période infectieuse (également appelée période de transmissibilité) est définie comme la période pendant laquelle une personne infectée peut transmettre un agent infectieux à une autre personne. La période infectieuse et sa relation avec la manifestation des symptômes est un paramètre clinique et épidémiologique important à comprendre pour le contrôle de toute maladie infectieuse.

Les estimations de la période infectieuse ont été déterminées à partir d'une combinaison d'investigations épidémiologiques et cliniques qui, ensemble, permettent de savoir quand une personne infectée peut ou est susceptible de transmettre le virus. Pour établir qu'une personne est infectée, la plupart des études font état de l'utilisation de la RT-PCR pour diagnostiquer les cas de COVID-19 et pour surveiller l'excrétion virale au cours du temps. Cependant, la détection de l'ARN viral par test RT-PCR ne fournit pas de preuve d'infectivité et les particules virales sont susceptibles d'être excrétées des tissus infectés pendant un certain temps après que l'infection a été éliminée par le système immunitaire de l'hôte (Jefferson et coll., 2020). Pour déterminer si un virus viable a été isolé dans un échantillon, la réplication virale est établie le plus souvent en culture cellulaire et indique si le virus infectieux est présent. Dans cette revue, peu d'études ont utilisé des méthodes de culture (ou d'inoculation à l'animal), car elles sont lentes, coûteuses et moins sensibles que la RT-PCR. Les résultats des études épidémiologiques, de la RT-PCR, de la qRT-PCR et des cultures fournissent ensemble des éléments de preuve sur le moment où un cas est susceptible d'être infectieux et capable de transmettre le virus.

Cette revue rapide couvre les éléments de preuve de la période infectieuse des cas présymptomatiques, asymptomatiques et symptomatiques de COVID-19 telles qu'elles sont déduites par l'excrétion du virus en culture, la détection de l'ARN viral, les données épidémiologiques et les modèles prédictifs. Les échantillons analysés sont le plus souvent des écouvillons nasopharyngés, mais des écouvillons fécaux/rectaux et des écouvillons oculaires ont également été étudiés pour détecter la présence du SRAS-CoV-2. La transmission respiratoire est considérée comme la plus courante, et il faut davantage d'éléments de preuve pour déterminer l'importance des autres modes de transmission, y compris fécale-orale, fécale-fomite ou fécale-respiratoire, étant donné que des virus SRAS-CoV-2 viables ont été découverts dans les matières fécales.

Il s'agit d'une revue rapide évolutive de la période infectieuse qui contient des études clés saisies par l'analyse quotidienne de la littérature sur la COVID-19 effectuée par le groupe des sciences émergentes de l'ASPC jusqu'au 31 août 2020.

Points clés

Dans l'ensemble, d'après les meilleures données disponibles, on considère que la période infectieuse pour la plupart des cas symptomatiques commence en moyenne 2,5 jours avant l'apparition des symptômes, culmine vers le quatrième jour des symptômes et diminue à de faibles niveaux dans les 8 à 10 jours suivant le début des symptômes, pour un total de 10 à 13 jours. La période infectieuse asymptomatique s'est avérée similaire. Des périodes infectieuses plus longues ont été documentées dans des cas plus graves ou immunodéprimés (de 18 à 32 jours après l'apparition des symptômes).

Période infectieuse présymptomatique, N=25 études

- Le virus viable a été mis en culture' à partir d'échantillons respiratoires de cas présymptomatiques de 1 à 6 jours avant l'apparition des symptômes, comme déterminé par l'observation médicale (tableau 1). Des virus viables ont également été mis en culture'à partir d'échantillons gastro-intestinaux; par exemple, un échantillon rectal a montré des signes de réplication virale active du SRAS-CoV-2 trois jours avant l'apparition des symptômes (Qian et coll., 2020).
- Des études utilisant la RT-PCR pour détecter l'ARN viral à partir d'échantillons respiratoires suggèrent également que l'excrétion se produit en moyenne 2,5 jours (plage de 1 à 7) avant l'apparition des symptômes.

Période infectieuse asymptomatique, N=25 études

- Le virus viable et l'ARN viral détectés dans une cohorte de cas asymptomatiques étaient plus élevés pendant la première semaine de l'infection et ont diminué dans les semaines suivantes (Quicke et coll., 2020). Le virus infectieux n'a pas été détecté avec la technique par plages de lyse dans les écouvillons nasopharyngés des individus ayant moins de 100 000 copies d'ARN/écouvillons.
- Il n'y a que peu de consensus sur la question de savoir si les infections asymptomatiques et légèrement symptomatiques diffèrent en termes de temps d'excrétion du virus (tableau 2). D'après les données actuelles, la période infectieuse totale des cas asymptomatiques semble être similaire ou plus courte que celle des cas légèrement symptomatiques. Dans toutes les études, des charges virales similaires ont été rapportées pour les cas asymptomatiques, présymptomatiques et symptomatiques.

Période infectieuse symptomatique, N=107 études

- Virus viables, résultats des cultures, N=18 études de recherche primaire et 2 revues systématiques :
  - Pour les cas légers, la meilleure estimation de la période infectieuse, mesurée à partir de l'apparition des symptômes autodéclarés à l'aide d'une culture de virus à partir d'échantillons respiratoires, est de 8 à 10 jours avec un pic de charge virale pendant la première semaine de la maladie (tableau 3).
  - Des cas d'excrétion virale viable prolongée (de 18 à 32 jours) ont été répertoriés à l'aide de mis enculture du virus dans le cadre de quelques études. Nombre de ces études sont encore en phase de prépublication et comprennent des cas isolés ou des échantillons de petite taille (tableau 3). Ces

cas sont généralement des personnes atteintes d'une infection grave, qui sont soit immunodéprimées, soit atteintes de plusieurs maladies chroniques sous-jacentes.

- Quelques études ont permis de cultiver le SRAS-CoV-2 à partir d'échantillons fécaux/rectaux d'un cas confirmé (tableau 3). Une étude récente sur des furets inoculés a confirmé la présence du SRAS-CoV-2 infectieux dans des échantillons de fèces et d'urine dès jours 11, 13 et 15 de la maladie (Jeong et coll., 2020).

- Détection de l'ARN viral, résultats de RT-PCR, N=88 études de recherche primaire et 6 revues systématiques :
  - La plupart des études indiquent le temps écoulé entre l'apparition des symptômes ou le diagnostic positif et l'élimination de l'infection virale, déterminée par test RT-PCR. Les résultats positifs de RT-PCR ne constituent pas une preuve d'infectiosité.
  - La présence d'ARN viral varie considérablement selon le type d'échantillon. Les écouvillons respiratoires deviennent généralement négatifs dans les 14 à 20 jours suivant l'apparition des symptômes autodéclarés, tandis que les échantillons de selles restent positifs quelques jours à quatre semaines de plus que les échantillons respiratoires. Des éléments de preuve de la présence de l'ARN du SRAS-CoV-2 ont également été identifiés dans des écouvillons oculaires effectués jusqu'à 22 jours après l'apparition des symptômes signalés.
  - Des périodes prolongées d'excrétion d'ARN viral ont été signalées (jusqu'à 83 jours) dans des échantillons respiratoires, l'excrétion dépassant souvent la durée des symptômes. Cependant, il a été démontré que les concentrations d'ARN viral mesurées dans les échantillons des voies respiratoires supérieures diminuaient après l'apparition des symptômes et il n'y a pas eu de preuve de transmission chez les personnes cliniquement rétablies chez lesquelles l'ARN viral a été détecté de manière persistante, ni de virus viable isolé dans ces cas.
  - Il a été démontré que l'excrétion prolongée d'ARN viral est positivement associée à la gravité de la COVID-19 et à l'âge avancé dans de nombreuses études (tableau 3). Cependant, une récente méta-régression a permis d'identifier que la durée moyenne rapportée d'excrétion de l'ARN viral de quatre jours de plus dans les cas graves n'était pas statistiquement significative (Byrne et coll., 2020). La durée de l'excrétion de l'ARN viral ne diffère pas de manière significative entre le mâle et la femelle.

<u>Récurrence de l'excrétion virale en période de convalescence, N=55 études</u>

- La récurrence de l'excrétion d'ARN viral en période de convalescence après avoir satisfait aux critères de sortie (définis à l'époque comme deux tests RT-PCR consécutifs négatifs) a été signalée dans de multiples rapports de cas et études d'observation (tableau 4). Ces cas ne sont pas considérés comme une réinfection par une nouvelle souche du virus, mais plutôt comme n'ayant pas complètement éliminé l'infection initiale par le SRAS-CoV-2.
  - La récurrence se produit généralement dans les sept jours suivant la sortie.

- Après la récurrence, les patients sont restés positifs à l'ARN viral pendant environ 1 à 8 jours et sont restés généralement asymptomatiques.
- Bien qu'il s'agisse d'un domaine d'étude actif et que de nombreuses nouvelles études aient été publiées, à ce jour, une seule étude a fourni la preuve de la présence d'un virus viable dans un cas de récurrence (Quicke et coll., 2020). Aucune preuve de transmission lors de la récurrence de la détection de l'ARN viral n'a été rapportée.

- Des recherches supplémentaires sont nécessaires pour améliorer notre compréhension des résultats de la RT-PCR et la manière d'interpréter ces résultats en ce qui concerne la période infectieuse et le risque de transmission. En particulier dans les cas où les résultats des tests RT-PCR sont positifs pendant une longue période. En conséquence, le CDC a cessé de recommander deux tests RT-PCR consécutifs négatifs pour déterminer quand mettre fin à l'isolement et aux précautions à prendre pour les cas de COVID.

Réinfection, N=2 études

- Depuis le 25 août 2020, de bonnes preuves qu'une réinfection peut se produire ont été rapportées (tableau 5) :
  - Un patient de Hong Kong a été réinfecté 142 jours après l'infection initiale et cela a été documenté par des preuves épidémiologiques, cliniques et sérologiques convaincantes ainsi que par des analyses génomiques. (Qian et coll., 2020)
  - Il existe également des éléments de preuve solides d'un cas de réinfection aux États-Unis (Tillet et coll., 2020).
- À l'heure actuelle, il existe des lacunes dans les connaissances sur la question de savoir si l'évolution clinique et les caractéristiques épidémiologiques, y compris la période infectieuse des cas de réinfection, sont différentes de l'infection initiale.
- Des recherches supplémentaires sont nécessaires pour comprendre le rôle de l'immunité dans la protection contre le SRAS-CoV-2 après l'infection.

Vue d'ensemble des éléments de preuves

À ce jour, il y a eu de nombreuses publications relatives à la période infectieuse de la COVID-19. La majorité de ces publications sont des rapports de cas et des études d'observation fondées sur la recherche de contacts; ces modèles d'étude présentent un risque élevé de biais et sont donc considérés comme de faible qualité. Nombre d'entre eux sont des prépublications et n'ont pas été soumis à un processus d'examen par les pairs. Les cohortes prospectives présentent un risque de biais plus faible et sont considérées comme des recherches de meilleure qualité, mais peu de ces études contribuent à cette question. Dans l'ensemble, les résultats doivent être interprétés avec prudence, les estimations changent au fur et à mesure que de nouvelles recherches deviennent disponibles et il y a de nombreuses lacunes dans les connaissances; de

nouvelles recherches visant à combler ces lacunes pourraient modifier considérablement notre compréhension de l'infection par le SRAS-CoV-2 chez l'homme.

Les résultats des principales études sont résumés dans les tableaux de données : 1) présymptomatique, 2) asymptomatique, 3) symptomatique, et 4) récurrence de l'excrétion virale. Parmi celles-ci, les informations clés, y compris le type d'étude et les méthodes spécifiques utilisées (par exemple, culture, résultats de RT-PCR en série, données épidémiologiques ou modélisation), sont spécifiées, ainsi que les estimations de la période infectieuse et les facteurs de risque.

L'approche méthodologique utilisée et la façon dont la période infectieuse a été définie varient considérablement d'une étude à l'autre. Les recherches seulement fondées sur les séries de cas et les investigations de recherche de contacts sont considérées comme de très faible qualité. Ces conceptions d'étude souffrent d'une faible taille d'échantillon, d'un biais de sélection et d'un biais de rappel (par exemple, apparition de symptômes autodéclarés). Leurs résultats doivent être interprétés avec prudence, car ils sont susceptibles de changer avec des recherches supplémentaires.

Il existe plusieurs lacunes dans les connaissances sur la période infectieuse. La détection ou la confirmation d'un virus viable plutôt que de l'ARN est étayée par peu d'observations. La relation entre le potentiel de transmission et les résultats des tests RT-PCR n'est pas bien définie. Des recherches supplémentaires sur l'immunité post-infection, la récurrence des tests ARN positifs et la probabilité et les caractéristiques épidémiologiques de la réinfection sont nécessaires pour comprendre si et/ou quand une personne est potentiellement infectieuse après l'infection aiguë initiale. Cette recherche est fondamentale pour comprendre la dynamique de transmission du SRAS-CoV-2.

TABLE DES MATIÈRES

CONTEXTE SUR LA PÉRIODE INFECTIEUSE

La période infectieuse (également appelée période de communicabilité) est définie comme la période pendant laquelle une personne infectée peut transmettre un agent infectieux à une autre personne. La période infectieuse et sa relation avec la manifestation des symptômes sont des paramètres épidémiologiques importants à comprendre pour le contrôle de toute maladie infectieuse. Pour la COVID-19, il existe des éléments de preuve que le SRAS-CoV-2 peut être excrété par une personne infectée avant qu'elle ne présente des symptômes (présymptomatiques) (par exemple, Arons et coll., 2020; Hoehl et coll., 2020; Pan, Zhang, Yang, Poon et Wang., 2020) et par des personnes infectées qui ne développent jamais de symptômes visibles (asymptomatiques) (par exemple, Alshami et coll., 2020; Y. Lu et coll., 2020; Z. Zhang et coll., 2020). Il existe également des études qui suggèrent que l'excrétion virale peut persister pendant la phase de convalescence ou peut réapparaître après que le virus ait été indétectable pendant un certain temps (par exemple, Hoang, Daoet Gautret, 2020; Q. Hu et coll., 2020). Le présent rapport couvre les éléments de preuve pour ces différentes périodes et les études qui tentent d'estimer la période infectieuse complète de la COVID-19. Les études seront divisées en deux parties : les méthodes de détermination de l'excrétion virale et la question de savoir comment la détection de l'ARN viral par test RT-PCR en comparaison à celle de la culture et quelles déductions peuvent être faites pour ces différents résultats.

Les estimations de la période infectieuse ont été déterminées à partir d'une combinaison d'investigations épidémiologiques et cliniques qui, ensemble, permettent de savoir quand une personne infectée peut ou est susceptible de transmettre le virus. Pour déterminer si une personne est infectée, la plupart des études font état de l'utilisation de test RT-PCR pour diagnostiquer les cas de COVID-19 et pour surveiller l'excrétion de l'ARN viral au fil du temps. Cependant, la détection de l'ARN viral par test RT-PCR ne fournit pas de preuve d'infectivité et les particules virales sont susceptibles d'être excrétées des tissus infectés pendant un certain temps après que l'infection a été éliminée par le système immunitaire de l'hôte (Jefferson et coll., 2020). Pour établir si un virus viable a été isolé, la réplication du virus de l'échantillon est établie le plus souvent en culture cellulaire et indique que le virus infectieux est présent. Dans cette revue, peu d'études ont utilisé des méthodes de culture (ou d'inoculation animale), car elles sont lentes, coûteuses et moins sensibles que la RT-PCR. Les résultats des études épidémiologiques, de la RT-PCR, de la qRT-PCR et des cultures fournissent ensemble des éléments de preuve sur le moment où un cas est susceptible d'être infectieux et capable de transmettre le virus.

La variabilité dans la mesure de la période infectieuse est également présente dans les différentes études. La majorité des études mesurent le temps écoulé entre le diagnostic ou l'apparition des symptômes jusqu'à l'élimination de l'ARN viral. Ainsi, il n'y a pas de mesures préalables au diagnostic. La recherche épidémiologique, principalement sous la forme d'investigations sur les grappes de cas et de tests sur les contacts étroits des cas, quel que soit leur statut clinique, a fourni la preuve que l'excrétion du virus peut se produire avant l'apparition des symptômes (Z. Du et coll., 2020; X. He et coll., 2020). L'hétérogénéité des définitions et la manière dont la période infectieuse est déterminée dans chaque étude sont résumées dans les tableaux détaillés des éléments de preuve.

PÉRIODE INFECTIEUSE PRÉSYMPTOMATIQUE

Le tableau 1 énumère vingt-cinq études qui fournissent des estimations de la période infectieuse présymptomatique, identifiée par des séries de cas, des investigations de recherche de contacts et des modélisations. Nombre de ces rapports de cas et études de recherche de contacts proviennent de Chine et montrent des éléments de preuve de la transmission de la COVID-19 par des personnes qui sont en période d'incubation. Le SRAS-CoV-2 a été isolé avec succès des cas présymptomatiques, ce qui prouve une fois de plus qu'une transmission présymptomatique se produit. Cependant, la grande majorité des éléments de preuve est basée sur des rapports de cas et des investigations en grappes qui sont sujets à un biais de rappel, car les cas et leurs contacts sont chargés de fournir des informations sur l'exposition et le moment d'apparition des symptômes. De plus, avec la transmission généralisée de la COVID-19 dans une zone épidémique, il est possible que les infections décrites dans ces études aient été causées par d'autres sources non reconnues.

La période infectieuse présymptomatique dans l'ensemble des études suggère qu'une personne est susceptible d'excréter le SRAS-CoV-2 en moyenne 2,5 jours (fourchette de 1 à 7) avant l'apparition des symptômes d'après les échantillons respiratoires (Hoehl et coll., 2020; Z. Liu et coll., 2020; Nissen et coll., 2020; Pan et coll., 2020; Sakurai et coll., 2020). Les estimations des études de recherche des contacts suggèrent également une période infectieuse présymptomatique moyenne de 2 à 3 jours (fourchette de 1 à 12,3) (X. He et coll., 2020; S. Hu et coll., 2020; R. Huang, Xia, Chen, Shan et Wu, 2020; Kong et coll., 2020; J. Li et coll., 2020; Rothe et coll., 2020; W. E. Wei et coll., 2020). Des éléments de preuve de la réplication active du virus du SRAS-CoV-2 à partir d'un échantillon de rectum trois jours avant l'apparition des symptômes ont également été présentés (Qian et coll., 2020). Une étude menée auprès de résidents d'établissement de soins de longue durée a révélé que le virus viable pouvait être mis en culture jusqu'à six jours avant l'apparition des symptômes et a fait état de valeurs seuils de cycle similaires (c'est-à-dire de la charge virale) pour les cas asymptomatiques, présymptomatiques et symptomatiques (Arons et coll., 2020).

Il existe peu d'études qui prennent des mesures avant le diagnostic/l'apparition des symptômes. D'autres éléments de preuve sont nécessaires pour améliorer la certitude des estimations de la période infectieuse présymptomatique de la COVID-19.

Tableau 1 : Études évaluant la période infectieuse présymptomatique de la COVID-19 (N=25)

Référence	Type d'étude	-Population et environnement -Période de temps	Période infectieuse (PI) déterminée par : Culture, résultats de tests RT-PCR en série, données épidémiologiques ou modèle	Résultats pertinents
Études sur la culture et la RT-PCR				
(Arons et coll., 2020)	Investigation sur l'éclosion	-Résidents d'un établissement de soins infirmiers spécialisés à Washington, États-Unis -3 avril 2020 (date de fin)	Culture et RT-PCR	Écouvillons nasopharyngés et oropharyngés -48 (63 %) des résidents ayant participé aux enquêtes de prévalence ponctuelle ont été testés positifs. -24 étaient présymptomatiques et 2 étaient asymptomatiques selon les évaluations standardisées des symptômes effectuées par les infirmières. -Le virus viable a été isolé à partir de prélèvements collectés six jours avant et neuf jours après l'apparition des symptômes.
(Hoehl et coll., 2020)	Série de cas	-Voyageurs de Wuhan vers l'Allemagne -1er février 2020	Culture et RT-PCR	Écouvillon pharyngé -2 patients étaient asymptomatiques et le test RT-PCR était positif. Un jour plus tard, un des cas présentait une légère éruption cutanée et une pharyngite minime. -Le SRAS-CoV-2 a été isolé avec succès à partir des 2 cas, indiquant une infectiosité potentielle alors qu'ils étaient présymptomatique. -Ces résultats suggèrent que l'infectiosité peut se produire au moins un jour avant l'apparition des symptômes.
(Nissen et coll., 2020) *Prépublication*	Rapport de cas	-Un travailleur de la santé de 36 ans en Suède -Du 2 au 17 avril 2020	Culture et RT-PCR	Écouvillons nasopharyngés et oropharyngés - L'effet cytopathique observé par culture cellulaire, immunofluorescence pour l'ARNdb et la rRT-PCR ont permis de déterminer que le virus SRAS-CoV-2 de deux échantillons (prélevés les 3e et 1er jours avant l'apparition des symptômes) était infectieux dans deux expériences indépendantes.

(Qian et coll., 2020)	Rapport de cas	-Un patient se fait opérer d'un cancer du rectum en Chine -À partir du 16 janvier 2020	Culture et RT-PCR	Écouvillons pour les tissus rectaux et pharyngés -Le 16 janvier 2020, le patient a subi une intervention chirurgicale rectale. Le troisième jour postopératoire, le patient s'est présenté avec de la fièvre et de la toux et on lui a ensuite diagnostiqué la COVID-19 par RT-PCR. En mars, une étude rétrospective a été menée sur les tissus chirurgicalement enlevés du patient. Des sections ultrafines de tissus rectaux ont été préparées et des particules de virus ont été trouvées dans le cytoplasme des cellules épithéliales intestinales. Pour confirmer davantage l'infection spécifique du SRAS-CoV-2 et sa réplication dans le rectum, on a utilisé l'immunohistochimie et l'immunofluorescence à l'aide de l'anticorps NP anti-SRAS-CoV-2 du lapin. -Il s'agit du premier rapport faisant état d'éléments de preuve directs de la réplication active du SRAS-CoV-2 dans le rectum d'un patient pendant la période d'incubation.
(Z. Liu et coll., 2020)	Cohorte prospective	-Transporteurs présymptomatiques en Chine (n=16) -Chronologie non communiquée	RT-PCR	Expectorations et écouvillons pharyngés -La période médiane entre la détection d'ARN positif du SRAS-CoV-2 et l'apparition des symptômes a été calculée comme étant de 2 jours (fourchette de 1 à 5).
(Sakurai et coll., 2020)	Cohorte rétrospective	-Cas asymptomatiques (n=90) et présymptomatiques (n=11) hospitalisés au Japon à bord du navire de croisière Diamond Princess -Du 19 au 26 février 2020	RT-PCR	Type de prélèvements non rapporté -11 patients étaient présymptomatiques et ont développé des symptômes avec une médiane de quatre jours (fourchette de 3 à 7) après le premier test RT-PCR positif. -Les cas asymptomatiques présentent une durée médiane d'excrétion de l'ARN viral du SRAS-CoV-2 de 9 jours (fourchette de 3 à 21) entre le premier test PCR positif et le premier de 2 tests PCR négatifs en série.
Études de données épidémiologiques				
(Pan et coll.,	Étude sur la	-Deux personnes	Données RT-	Écouvillon respiratoire

2020)	recherche des contacts	contacts trouvées en raison de leur exposition à un patient infecté en Chine -Chronologie non communiquée	PCR et données épid.	-Les cas ont été testés en série avant l'apparition des symptômes. -Les cas ont montré des résultats positifs par RT-PCR un jour avant l'apparition des symptômes, ce qui suggère que l'infectiosité peut se produire avant l'apparition des symptômes.
(J. Li et coll., 2020)	Étude sur la recherche des contacts	-Trois grappes de famille en Chine -Du 21 janvier au 9 février 2020	Données épid.	- Les trois cas index ont transmis l'infection à 28 membres de la famille de 2 à 10 jours avant le début de la maladie.
(Kong et coll., 2020)	Étude sur la recherche des contacts	-Dix cas en Chine -Du 8 au 27 janvier 2020	Données épid.	-Les deux dernières générations ont été infectées dans des lieux publics, 3 et 4 jours avant l'apparition de la maladie chez leurs infecteurs.
(R. Huang et coll., 2020)	Étude sur la recherche des contacts	-Grappe familiale d'infection confirmée en Chine -Janvier 2020	Données épid.	-La recherche des cas contacts dans une grappe familiale (n=11) et les dates d'exposition ont montré une période infectieuse présymptomatique médiane de quatre jours (fourchette de 3 à 5).
(Rothe et coll., 2020)	Étude sur la recherche des contacts	-Grappe de cas issus de contacts présymptomatiques en Allemagne -Du 19 au 29 janvier 2020	Données épid.	-La transmission s'est faite d'un cas présymptomatique à 4 contacts. -Les résultats du traçage montrent une période infectieuse présymptomatique médiane de deux jours (fourchette de 1 à 3).
(W. E. Wei et coll., 2020)	Étude sur la recherche des contacts	-Sept grappes à Singapour -Du 23 janvier au 16 mars 2020	Données épid.	-La transmission présymptomatique était évidente dans 4 grappes avec une période infectieuse médiane de deux jours (fourchette de 1 à 3). -L'exposition à la transmission n'a pas été vérifiée pour les trois autres grappes.
(S. Hu et coll., 2020) *Prépublication*	Étude sur la recherche des contacts	-1178 personnes infectées par le SRAS-CoV-2 et leurs 15 648 contacts en Chine -Du 13 janvier au 2 avril	Données épid.	-Quarante-trois événements de transmission présymptomatique ont été enregistrés dans 23 grappes. -On estime que l'infectiosité atteint son maximum 1,8 jour avant l'apparition des symptômes, 95 % des cas de transmission se produisant entre 7,6 jours avant et 7,3 jours

		2020		après la date d'apparition des symptômes. -La proportion de transmission présymptomatique a été estimée à 62,5 %.
(X. He et coll., 2020)	Étude sur la recherche des contacts	-77 paires infecteur-infecté de transmission provenant du Vietnam, de la Malaisie, du Japon, de la Chine, de Taïwan, des États-Unis et de Singapour -Du 18 décembre 2019 au 5 mars 2020	Données épid.	-Les auteurs ont supposé une distribution de la période d'incubation de 5,2 jours en moyenne pour déduire que l'infectiosité commençait à 12,3 jours (de 5,9 à 17, IC de 95 %) avant l'apparition des symptômes et atteignait son maximum à l'apparition des symptômes (de -0,9 à 0,9, IC de 95 %). -Ils ont observé que seulement < 0,1 % de la transmission se produisait avant 7 jours, 1 % de la transmission se produisait avant 5 jours et 9% de la transmission se produisait avant 3 jours avant l'apparition des symptômes. -Une analyse de sensibilité a montré que l'infectiosité atteignait son maximum deux jours avant et un jour après l'apparition des symptômes. -Ils ont estimé que 44 % (de 30 à 57 %, IC de 95 %) des cas secondaires ont été infectés au cours de la phase présymptomatique des cas index.
(Chun, Baek et Kim, 2020) *Prépublication*	Revue documentaire	-72 paires infecteur-infecté de transmission en Corée du Sud -Du 23 janvier au 31 mars 2020	Données épid.	-Les estimations moyennes et médianes étaient respectivement de 1,31 jour (de 0,38 à 2,55, IC de 95 %) et 0,68 jour (de -0,09 à 1,73, IC de 95 %) après l'apparition des symptômes, avec un pic à 0,72 jour avant l'apparition des symptômes. -La proportion de transmission présymptomatique était de 37 % (de 16 à 52 %, IC de 95 %).
(Z. Du et coll., 2020) *Prépublication*	Revue documentaire	-468 paires infecteur-infecté identifiées grâce à la recherche des contacts en Chine -Du 21 janvier au 8 février 2020	Données épid.	-59 des 468 paires infecteur-infecté ont indiqué que la personne infectée avait des symptômes plus tôt que l'infecteur. -Ces intervalles sériels négatifs suggèrent qu'une transmission présymptomatique a pu se produire.
(Casey et coll., 2020)	Revue documentaire	-17 études faisant état de l'intervalle sériel ou du	Données épid.	-Soustraction de la période d'incubation de l'intervalle sériel ou du temps de génération pour déduire la période infectieuse

Prépublication		temps de génération de Hong Kong, Tianjin, données regroupées de Hong Kong et Shenzhen, Singapour, Chine continentale à l'exclusion du Hubei, sources mixtes, Shenzhen, Italie du Nord et Wuhan -Du 1er décembre 2019 au 15 avril 2020		présymptomatique et pour estimer la proportion de transmission présymptomatique. -Le regroupement des estimations de l'intervalle sériel du temps de transmission par rapport à l'apparition des symptômes a donné une période infectieuse présymptomatique moyenne de 0,67 jour (médiane de 0,63 jour). -Le regroupement des estimations basées sur le temps de 5 générations a donné une période infectieuse présymptomatique moyenne de 1,62 jour (médiane de 1,32 jour). -La transmission présymptomatique a été estimée à 56,1 % sur la base des estimations de l'intervalle sériel et à 65,5 % sur la base des estimations du temps de génération.
(Prakash, 2020) *Prépublication*	Revue documentaire	-Personnes signalées dans la littérature (n=1251) -Pas de limite par pays -Aucune chronologie n'a été communiquée	Données épid.	-Le pic d'infectiosité a été atteint deux jours après l'infection. -On estime que 68,4 % (de 67,0 à 69,7 %, IC de 95 %) des infections sont causées par des infecteurs présymptomatiques.
Études de modélisation				
(Nishiura, Linton et Akhmetzhanov, 2020)	Modèle prédictif bayésien	-28 paires infecteur-infecté -Pas de limite par pays -Date de fin : 12 février 2020	Modélisé	-En tenant compte de la troncature à droite et en analysant toutes les paires, les auteurs ont estimé un intervalle sériel de 4,0 jours (de 3,1 à 4,9, IC de 95 %). -Cet intervalle est plus court que les estimations préliminaires de la période d'incubation d'environ 5,0 jours. -Cela suggère que la transmission présymptomatique peut constituer une proportion substantielle de la transmission secondaire.
(Tindale et coll., 2020) *Prépublication*	Modèle statistique	-Cas d'éclosions à Tianjin, en Chine et à Singapour -Du 19 janvier au 27	Modélisé	-La période de transmission présymptomatique a été déduite des estimations de l'intervalle sériel et des périodes d'incubation pour les populations de Tianjin et de Singapour.

		février 2020		-Les périodes infectieuses présymptomatiques moyennes étaient de 2,55 jours (fourchette de 1,2 à 3,3) à Singapour et de 2,89 jours (fourchette de 2,79 à 8,2) à Tianjin.
(Zhu, 2020) *Prépublication*	Modèle SEIR	-Éclosion de Wuhan en Chine -Date de fin : 15 avril 2020	Modélisé	-Les auteurs proposent un nouveau modèle d'épidémie appelé SEIR-HC, avec 2 cercles sociaux différents. En utilisant le modèle avec un algorithme d'optimisation, le processus de propagation de l'éclosion dans la ville de Wuhan est reproduit et les caractéristiques de propagation et les données inconnues sont estimées. -Une période infectieuse présymptomatique de 1,01 jour a été estimée en prenant la différence entre la période de latence et la période d'incubation.
(Siwiak, Szczesny et Siwiak, 2020) *Prépublication*	Modèle de métapopulation SIR	-Pandémie totale (mondiale) -Du 22 janvier au 26 mars 2020	Modélisé	-Construire un mode de transmission modifié SIR de la métapopulation, paramétré analytiquement selon la littérature, et ajuster les paramètres manquants à la dynamique observée de la propagation du virus. -La période infectieuse présymptomatique est estimée à 4,6 jours.
(Peak et coll., 2020) *Prépublication*	Modèle SEIR	-Cas confirmés dans le Massachusetts, États-Unis -Chronologie non précisée	Modélisé	-La période infectieuse présymptomatique a été modélisée en supposant un intervalle sériel de 4,8 -Le délai moyen d'apparition de l'infectiosité était de 0,77 jour avant l'apparition des symptômes (1,98 jour avant, 0,29 jour après, IC de 95 %)
(H. Yuan et coll., 2020) *Prépublication*	Modèle SEIQR à deux niveaux	-Cas locaux importés et confirmés à Hong Kong -Du 18 janvier au 29 février 2020	Modélisé	-Les paramètres épidémiologiques de COVID-19 ont été estimés. -La période de transmission présymptomatique avant l'apparition des symptômes était de 3,49 jours (de 0,48 à 5,80, IC de 95 %).
(S. Zhao, 2020)	Nouveau cadre fondé sur la probabilité	-Cas confirmés -Pays et chronologie non précisés	Modélisé	-Estime que la période de transmission moyenne présymptomatique est de 2,2 jours (IC de 95 % : de 1,3 à 4,7). -Approxime que 32,2 % (de 10,3 à 73,7, IC de 95 %) des

				infections secondaires peuvent être dues à une transmission présymptomatique.

PÉRIODE INFECTIEUSE ASYMPTOMATIQUE

Le tableau 2 énumère vingt-cinq études qui fournissent des estimations de la période infectieuse asymptomatique, identifiée par des séries de cas et des investigations de recherche de contacts. Les cas asymptomatiques peuvent transmettre la COVID-19, mais peu d'études ont été menées sur la période infectieuse des cas asymptomatiques, car ils sont rarement soumis à des tests. En outre, peu d'études de mise en culture ont été menées sur l'excrétion de virus vivants à partir de porteurs asymptomatiques. La majorité des études identifient les cas asymptomatiques grâce à la recherche des contacts et déterminent la durée de l'excrétion de l'ARN viral par RT-PCR du premier jour d'un test RT-PCR positif au premier jour de résultats négatifs consécutifs. La prudence est de mise dans l'interprétation de ces résultats, car la positivité de la RT-PCR n'est pas indicative de l'infectiosité et la durée de détectabilité virale surestime probablement la période infectieuse.

Les meilleurs éléments de preuve disponibles proviennent d'une cohorte de cas asymptomatiques qui a permis de détecter un virus viable et de l'ARN viral par le biais d'une infection. La charge virale était la plus élevée pendant la première semaine d'infection et diminuait les semaines suivantes (Quicke et coll., 2020). De plus, le virus infectieux n'a pas été détecté dans les écouvillons nasopharyngés des individus ayant moins de 100 000 copies d'ARN/écouvillon, ce qui indique que de faibles niveaux d'ARN viral correspondent à de faibles niveaux de virus infectieux.

Certaines études comparant les cas asymptomatiques et symptomatiques montrent que les cas symptomatiques présentent des périodes d'excrétion d'ARN viral plus longues (Alshami et coll., 2020; Y. H. Lee et coll., 2020; S. Lee et coll., 2020; W. Li et coll., 2020; Y. Li et coll., 2020a; Y. Lu et al, 2020; Noh et coll., 2020; Saurabh et coll., 2020; Valente et coll., 2020; X. Wei et coll., 2020; Z. Zhang et coll., 2020), tandis que d'autres études ne montrent aucune différence entre les groupes (Lombardi et coll., 2020; Xiong et coll., 2020) ou font l'association inverse (Long et coll., 2020). Des charges virales similaires ont été rapportées pour des cas asymptomatiques, présymptomatiques et symptomatiques. Ainsi, la période infectieuse totale des cas asymptomatiques est probablement similaire ou plus courte que celle des cas symptomatiques. La durée de l'excrétion de l'ARN viral dans les cas asymptomatiques n'est pas significativement associée à l'âge ou au sexe.

Tableau 2 : Études évaluant la période infectieuse asymptomatique de la COVID-19 (N=25)

Référence	Type d'étude	-Population et environnement -Période de temps	Période infectieuse (PI) déterminée	Résultats pertinents

			par : Culture, Tests RT-PCR en série, données épidémiologique ou modèle	
Études sur la culture et la RT-PCR				
(Quicke et coll., 2020) *Prépublication*	Étude de surveillance longitudinale	-Personnel asymptomatique (n=454) dans 5 établissements de soins infirmiers qualifiés (la prévalence varie considérablement d'un établissement à l'autre) dans le Colorado, aux États-Unis -Chronologie non communiquée	Culture (technique par plages) et RT-PCR	<u>Écouvillons nasopharyngés</u> -Le niveau d'ARN viral N1 a été positivement corrélé avec la quantité de virus infectieux détectée par les techniques par plages. -La durée de l'infection a varié de 1 à 4 semaines, selon la détection de l'ARN viral par qRT-PCR pour le gène du SRAS-CoV-2 N1. -Les niveaux d'ARN viral et de virus infectieux étaient les plus élevés pendant la première semaine de l'infection et ont diminué au cours des semaines suivantes. -Le virus infectieux n'a pas été détecté chez les personnes ayant moins de 100 000 copies/écouvillon d'ARN N1. -Un membre du personnel a eu un résultat faiblement positif détecté par la technique par plages à passage unique trois semaines après le diagnostic initial.
(Lavezzo et coll., 2020)	Cohorte prospective	-Enquête 1 = 2812 résidents et Enquête 2 = 2343 résidents en Italie -Du 21 février au 7 mars 2020	RT-PCR	<u>Écouvillons nasopharyngés</u> -Aucune différence statistiquement significative n'a été constatée dans la charge virale des infections symptomatiques et asymptomatiques. -Il a été constaté que la charge virale a tendance à atteindre son maximum le jour de l'apparition des symptômes et que, pour la plupart des sujets, elle tend à diminuer après l'apparition des symptômes.
(W. Li et coll., 2020)	Cohorte prospective	-Cas asymptomatiques (n=3), présymptomatiques (n=6) et symptomatiques (n=9) en Chine -Du 29 janvier au 5	RT-PCR	<u>Écouvillons respiratoires et anaux</u> - La durée médiane de l'excrétion virale était plus courte chez les patients présymptomatiques (11,5 jours) que chez les cas asymptomatiques (28 jours) et les cas symptomatiques légers (31 jours).

		février 2020		
(Y. H. Lee et coll., 2020)	Cohorte prospective	-Cas asymptomatiques et légers (n=632) en Corée du Sud -Du 2 mars au 12 avril 2020	RT-PCR	Écouvillons buccaux et nasaux -Les patients symptomatiques ont eu une période plus longue entre le diagnostic et les résultats négatifs de la RT-PCR que les patients asymptomatiques : 21,8 jours (ET 7,6) contre 19,1 jours (ET 7,5), p < 0,0001. -Les symptômes respiratoires avaient une corrélation statistiquement significative avec la période d'excrétion de l'ARN (p < 0,0001). Cependant, il n'y avait pas de différences statistiquement significatives liées aux symptômes gastro-intestinaux, aux maux de tête, à la fièvre et à d'autres symptômes. Il n'y avait pas non plus de différences statistiquement significatives en fonction du sexe, de l'âge ou des conditions sous-jacentes.
(Saurabh et coll., 2020)	Cohorte prospective	-Cas asymptomatiques (n=44) et symptomatiques (n=7) en Inde -Du 19 mars au 21 mai 2020	RT-PCR	Écouvillons oropharyngés et nasopharyngés -Les personnes asymptomatiques avaient une durée médiane de persistance du virus de 8,87 jours (IC de 95 % : de 7,65 à 10,27) et une durée de 20,70 jours au 95^{e} centile (IC de 95 % : de 16,08 à 28,20). -Environ un quart des personnes asymptomatiques (10 sur 44) ont démontré une persistance du SRAS-CoV-2 au-delà de 2 semaines. -La durée de persistance du virus chez les personnes symptomatiques était de 10,98 jours (de 8,38 à 14,44, IC de 95 %). Il n'a pas été constaté que cette période était sensiblement plus longue que celle des personnes asymptomatiques (P = 0,222). -L'âge (< 60 ans) ans) et la transmission locale ont été associée de manière significative à une persistance plus longue du virus chez les individus asymptomatiques lors de la régression univariée, mais pas lors de l'analyse multivariée.
(Long et coll., 2020)	Cohorte prospective	-Cas asymptomatiques (n=37) et cas symptomatiques correspondants (n=37) en Chine -Date de fin : 10	RT-PCR	Écouvillons nasopharyngés -La durée médiane de l'excrétion de l'ARN viral dans le groupe asymptomatique était de 19 jours (IQR de 15 à 26). -Le groupe asymptomatique présentait une durée d'excrétion de l'ARN viral nettement plus longue que le groupe symptomatique (log-rang, P = 0,028). -Les données suggèrent que les personnes asymptomatiques ont eu une

		avril 2020		réponse immunitaire plus faible à l'infection par le SRAS-CoV-2.
(Y. Lu et coll., 2020)	Cohorte rétrospective	-Enfants hospitalisés avec des symptômes de COVID-19 légers et ordinaires (n=110) en Chine -Du 30 janvier au 10 mars 2020	RT-PCR	Écouvillon respiratoire -La durée médiane de l'excrétion de l'ARN viral était de 15 jours (de 11 à 20, IQR de 5 à 37). -La durée de l'excrétion virale chez les patients symptomatiques était statistiquement plus longue (p < 0,001) : 17 jours (IQR de 12 à 23) contre 11 jours (IQR de 9 à 13).
(Alshami et coll., 2020) *Prépublication*	Cohorte rétrospective	-Les sujets de COVID-19 confirmés en laboratoire qui ont été mis en quarantaine dans un établissement désigné par le gouvernement suite à un voyage hors du royaume (n=128) en Arabie Saoudite -Du 16 mars au 18 avril 2020	RT-PCR	Écouvillons nasopharyngés et oropharyngés -69 patients (54 %) ne présentaient aucun symptôme. -Pour les patients qui présentaient des symptômes, la durée médiane de résolution était de 5 jours. -La durée médiane avant la clairance virale était significativement plus longue (p=0,011) chez les patients symptomatiques que chez les patients asymptomatiques : 17 jours (de 12,4 à 21,6, IC de 95 %) contre 11 jours (de 8,7 à 13,3, IC de 95 %).
(Noh et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=199) en Corée du Sud, 26,6 % étaient asymptomatiques -Chronologie non communiquée	RT-PCR	Type de prélèvements non rapporté -La durée de l'excrétion virale a été définie comme le temps écoulé entre le diagnostic et le jour précédant la première conversion négative de deux résultats négatifs consécutifs de la RT-PCR. -La durée moyenne de l'excrétion virale était de 24,5 jours (ET ±4,8). -La durée de l'excrétion virale était plus longue chez les patients symptomatiques que chez les patients asymptomatiques : 25,2 jours (ET ±4,9) contre 22,6 jours (ET ±4,0), p < 0,01.

				-Les patients symptomatiques souffrant de douleurs thoraciques ont libéré le virus beaucoup plus longtemps que les autres : 30,0 (ET ±4,7) jours contre 25,0 jours (ET ±4,8), p = 0,01). -Les patients qui se sont plaints d'expectorations ont également connu une excrétion prolongée d'ARN viral : 26,8 jours (ET ±4,8) contre 24,6 jours (ET ±4,8), p = 0,03.
(S. Lee et coll., 2020)	Cohorte rétrospective	-Patients symptomatiques et asymptomatiques (n=303) en Corée -Du 6 au 26 mars 2020	RT-PCR	Nasopharynx, oropharynx, et écouvillon d'expectoration -La durée médiane entre le diagnostic et la première conversion négative de l'ARN viral a été de 17 (erreur type=1,07) jours pour les patients asymptomatiques et de 19,5 (erreur type=0,63) jours pour les patients symptomatiques (y compris présymptomatiques) (p=0,07).
(Xiong et coll., 2020)	Cohorte rétrospective	-Cas pédiatriques hospitalisés (n=244) -Du 21 janvier au 20 mars 2020	RT-PCR	Aspiration nasopharyngée -La durée entre l'aspiration nasopharyngée positive et négative était similaire chez les patients atteints de la COVID-19, qu'ils soient asymptomatiques ou symptomatiques (moyenne de 8,2 jours contre 8,9 jours; P = 0,434), ce qui suggère une durée similaire de l'excrétion virale.
(Lombardi et coll., 2020) *Prépublication*	Cohorte rétrospective	-Travailleurs de la santé en Italie -Du 24 février au 31 mars 2020	RT-PCR	Écouvillon nasopharyngé -Sur les 138 sujets dont le test d'ARN viral était positif, 41 sur 138 (29,7 %) étaient asymptomatiques. -La durée médiane entre le premier test positif et le test négatif ne diffère pas entre les sujets symptomatiques et les cas asymptomatiques, 23 jours (de 18 à 26, IC de 95 %) contre 23 jours (de 19 à 29, IC de 95 %). -La durée médiane de l'excrétion virale n'a pas été statistiquement associée au sexe ou à l'âge.
(Kim et coll., 2020)	Cohorte rétrospective	-Patients affectés par la COVID-19 hospitalisés en Corée du Sud, confirmés par un laboratoire -Du 4 février au 7	RT-PCR	Écouvillon nasopharyngé -10 sur 71 cas confirmés en laboratoire, déterminés par test RT-PCR, étaient asymptomatiques. -La durée médiane avant le premier test RT-PCR négatif après le diagnostic était de 4,5 jours (fourchette de 2,5 à 9). -Les auteurs suggèrent qu'une quarantaine de 14 jours à domicile après le diagnostic peut être suffisante pour les porteurs asymptomatiques.

		avril 2020		
(Y. J. Liu et coll., 2020)	Cohorte rétrospective	-Cas pédiatriques asymptomatiques (n=35) et subcliniques (n=18) en Chine -Chronologie non communiquée	RT-PCR	Écouvillons nasopharyngés -Le temps moyen d'élimination de l'acide nucléique du SRAS-CoV-2 dans les écouvillons nasopharyngés était de 9 ±4 jours.
(M.S. Han et coll., 2020)	Cohorte rétrospective	-Enfants légèrement symptomatiques (n=9) et asymptomatiques (n=3) en Corée du Sud -Du 8 mars au 28 avril 2020	RT-PCR	Écouvillons nasopharyngés, fécaux et de salive -La charge virale d'ARN dans les écouvillons nasopharyngés a atteint un pic au début, à la médiane de 7,56 $\log^{10}$ copies/mL, et a diminué avec le temps (p<0,001 comme tendance). La positivité des échantillons était de 75 % pendant la deuxième semaine et de 55 % pendant la troisième semaine. -En comparaison, la charge fécale initiale médiane d'ARN était de 7,68 $\log^{10}$ copies/mL et est restée constamment élevée (p = 0,148 comme tendance) pendant plus de trois semaines. La positivité fécale est restée supérieure à 80 %. -La charge médiane d'ARN dans les échantillons de selles était significativement plus élevée que celle des échantillons prélevés par écouvillonnage nasopharyngien pendant la deuxième semaine (p = 0,006) et la troisième semaine (p = 0,006). -La charge d'ARN dans la salive a diminué rapidement avec le temps (p = 0,003 comme tendance). La positivité des échantillons de salive était de 80 % la première semaine, mais elle a chuté brusquement à 33 % la deuxième semaine et à 11 % la troisième semaine. -Les enfants symptomatiques avaient une charge initiale d'ARN plus élevée dans les échantillons prélevés par écouvillonnage nasopharyngien que les enfants asymptomatiques (p = 0,048). Il n'y avait pas de différences significatives dans les selles ou la salive et aucune corrélation entre la charge d'ARN et l'âge.
(Shen et coll., 2020)	Cohorte rétrospective	-Patients pédiatriques (sept	RT-PCR	Type de prélèvements non rapporté -6 enfants ont eu une exposition familiale et ont pu fournir les dates

		légers et deux asymptomatiques) en Chine -Du 8 janvier au 26 février 2020		exactes de leur contrat avec une personne dont il a été confirmé qu'elle avait la COVID-19. -Le délai entre l'exposition et des résultats négatifs de test RT-PCR dans les cas asymptomatiques (n=2) était de 10 jours et de 14 jours.
(Z. Zhang et coll., 2020) *Prépublication*	Série de cas	-56 patients atteints de la COVID-19 sans symptômes à l'admission (33 ont présenté des symptômes par la suite) et 19 patients symptomatiques appariés par âge provenant de Chine -Du 23 janvier au 1er avril 2020	RT-PCR	<u>Écouvillons respiratoires et anaux</u> -Parmi les 56 patients ne présentant pas de symptômes à l'admission, 23 sont restés asymptomatiques pendant toute la période de suivi. -Dans cette étude, la période infectieuse a été définie comme la période allant du premier jour de test d'acide nucléique positif au premier jour de test négatif continu pendant l'hospitalisation. -Les auteurs fournissent également des estimations de jours moyens entre l'apparition des symptômes et la conversion négative de l'ARN. -La période infectieuse des patients asymptomatiques (n=19) était statistiquement plus courte que celle des patients présymptomatiques (n=30) : 9,6 jours (ET ±5,3) contre 13,6 (ET ±6,6), p=0,03. -Les patients symptomatiques ont également eu une période infectieuse plus courte, 9,71 jours (ET ±4,3), par rapport aux cas présymptomatiques (p=0,05), mais une durée similaire entre le début de la maladie et la conversion négative, 16,6 (ET ±5,6) et 16,6 (ET ±7,5).
(Mesoraca et coll., 2020)	Série de cas	-Patients asymptomatiques et légers (n=15) en Italie -Du 4 mars au 20 avril 2020	RT-PCR	<u>Écouvillons respiratoires et fécaux</u> -Sur les 10 patients dont l'échantillon fécal était négatif au cours des 10 premiers jours, 6 échantillons sont devenus positifs 2 semaines après leur premier test positif des voies respiratoires. -Dans quatre cas, les échantillons de matières fécales ont montré un ARN viral positif 25 jours de plus que les échantillons de leurs voies respiratoires.
(W. Du et coll., 2020)	Série de cas	-Cas pédiatriques asymptomatiques (n=5) et légers (n=5) en Chine -Du 23 janvier au 9 mars 2020	RT-PCR	<u>Échantillons respiratoires et fécaux</u> -La durée médiane entre l'apparition des résultats négatifs de test RT-PCR dans les échantillons des voies respiratoires et des matières fécales était de 9 jours et 34,43 jours, respectivement.

(Shin et coll., 2020)	Rapport de cas	-Fille asymptomatique de 11 ans originaire de Corée du Sud -Du 12 mars au 13 mai 2020	RT-PCR	Écouvillons nasopharyngés -L'enfant a eu un dépistage positif de l'ARN du SRAS-CoV-2 pendant plus de 62 jours sans aucun symptôme pendant toute la période.
(Mao, Wan, He, Hu et Chen, 2020)	Série de cas	-Cas asymptomatiques (n=2) en Chine -Du 27 janvier au 21 février 2020	RT-PCR	Écouvillon pharyngé -On a découvert qu'après 14 jours d'isolement, 2 cas asymptomatiques étaient toujours porteurs de la COVID-19. -Un cas a produit des résultats positifs aux tests RT-PCR jusqu'à 19 jours après le début de l'isolement.
(Y. Li et coll., 2020a) *Prépublication*	Série de cas	-Cas asymptomatiques (n=38) en Chine -Février et mars 2020	RT-PCR	Écouvillons pharyngés -La durée médiane d'excrétion virale était de 6 jours, avec un minimum de 2 jours et un maximum de 17 jours entre le premier test nucléique positif et le dernier test nucléique positif. - Les auteurs notent que cette période d'excrétion est plus courte que celle constatée dans d'autres études de cas symptomatiques, ce qui suggère une infectiosité plus courte pour les cas asymptomatiques.
(Valente et coll., 2020)	Série de cas	-Patients pédiatriques hospitalisés (n=27) en Italie, 4 étaient asymptomatiques, 15 présentaient des symptômes respiratoires et 8 des symptômes gastro-intestinaux -Du 16 mars au 15 avril 2020	RT-PCR	Écouvillons nasopharyngés et conjonctivaux -Deux cas asymptomatiques sont devenus négatifs trois jours après l'apparition des symptômes, tandis qu'un cas symptomatique s'est révélé négatif au bout de six jours, tout en restant positif sur les écouvillons nasopharyngés. -En outre, l'écouvillon nasopharyngé était négatif en moyenne 8 jours (fourchette de 2 à 17 jours) après l'apparition des symptômes, alors que l'écouvillon conjonctival est devenu négatif chez tous les patients en moyenne en 4 jours (fourchette de 3 à 6 jours).
Études épidémiologiques				
(Z. Hu et coll.,	Tests en série	-Cas d'infection	Données RT-	Écouvillon pharyngé

2020)	et étude de recherche de contacts pour des grappes	asymptomatique (n=24) en Chine -Du 28 janvier au 9 février 2020	PCR et données épid.	-Observation d'une transmission asymptomatique entre membres d'une famille cohabitant, qui a même causé une pneumonie grave due à la COVID-19. -La période médiane de contagion asymptomatique, définie comme l'intervalle entre le premier jour de tests d'acide nucléique positifs et le premier jour de tests négatifs continus, était de 6 jours (IQR de 2 à 12) dans les cas qui ne développaient pas de symptômes, mais présentaient des signes de COVID-19 à la tomodensitométrie (n=19), et de 4 jours (IQR de 2 à 15) dans les cas qui ne développaient pas de symptômes et avaient des résultats de tomodensitométrie normaux.
(Ma et coll., 2020) *Prépublication*	Revue documentaire	-Les cas dont les données permettaient d'estimer au moins un paramètre en Chine, au Japon, à Singapour, en Corée du Sud, au Vietnam, en Allemagne et en Malaisie -Date de fin : 20 février 2020	Données épid.	-Sur 49 cas asymptomatiques, la période infectieuse médiane était de 11,66 jours (fourchette de 9,9 à 13,3) -La période infectieuse a été calculée approximativement comme l'intervalle sériel moins la limite supérieure de la période de latence. Dans ces analyses, la date du diagnostic a été utilisée comme le jour d'apparition de symptômes pour les cas asymptomatiques.

PÉRIODE INFECTIEUSE SYMPTOMATIQUE

Le tableau 3 énumère cent sept études qui évaluent la période infectieuse symptomatique de la COVID-19, identifiée par des revues systématiques/méta-analyses, des séries de cas, des études d'observation et des modélisations. Les études clés font état de preuves solides de l'infectiosité par culture, de l'évaluation des facteurs de risque d'excrétion virale prolongée (par exemple, sexe, âge, gravité), de preuves de différences d'excrétion d'ARN viral entre différents types d'échantillons (fécaux ou respiratoires) et de modèles qui estiment la période infectieuse entière.

Les études qui font état de la culture du virus ne fournissent des mesures qu'à partir de l'apparition des symptômes et risquent de sous-estimer la période infectieuse totale, car elles ne tiennent pas compte de l'infectiosité présymptomatique. Elles sont également fondées sur des échantillons de taille limitée. Pour les cas bénins, les meilleures estimations disponibles pour la période infectieuse mesurée à partir de l'apparition des symptômes sont de 8 à 10 jours déterminées à l'aide d'une culture virale (Arons et coll., 2020; Bullard et coll., 2020; Folgueira et coll., 2020; La Scola et coll., 2020; Perera et coll., 2020; Singanayagam et coll., 2020; van Kampen, Jeroen J. A. et coll., 2020; Wölfel et coll., 2020), avec des charges virales élevées observées dans les cinq premiers jours et un pic viral quatre jours après l'apparition des symptômes (Wölfel et coll., 2020).

Des excrétions virales viables prolongées ont été signalées dans quelques études, principalement encore en prépublication et utilisant des échantillons de petite taille. Les rapports de cas, dont certains détaillent les cas immunodéprimés, démontrent la viabilité du virus jusqu'à 18 à 22 jours après l'apparition des symptômes (Decker et coll., 2020; Gniazdowski et coll., 2020; W. D. Liu et coll., 2020; van Kampen, Jeroen J. A. et coll., 2020). Des durées encore plus longues (jusqu'à 32 jours) ont été signalées dans un petit échantillon de cas graves (Folgueira et coll., 2020). Une étude a confirmé la présence du SRAS-CoV-2 infectieux dans des échantillons d'urine et de fèces dès jours 11, 13 et 15 de maladie grave/critique en démontrant l'infection chez des furets inoculés (Jeong et coll., 2020).

Quelques études ont mis en culture le SRAS-CoV-2 à partir d'échantillons fécaux/rectaux de cas confirmés (Qian et coll., 2020; F. Xiao et coll., 2020; Y. Zhang et coll., 2020). Cependant, il faut davantage d'éléments de preuve pour déterminer la fréquence et la durée probables de l'excrétion d'un virus viable par voie fécale et pour savoir s'il y a transmission fécale-orale, fécale-fomite ou fécale-respiratoire.

La majorité des études sur les tests en série mesurent la période infectieuse par RT-PCR à partir de la date d'apparition des symptômes auto déclarés ou du premier résultat positif par RT-PCR jusqu'au premier de deux résultats négatifs consécutifs par RT-PCR. La prudence est de mise dans l'interprétation de ces résultats, car la positivité de la RT-PCR n'est pas indicative de l'infectiosité et la durée de détectabilité virale surestime probablement la période infectieuse.

Les estimations de la RT-PCR montrent une excrétion prolongée de l'ARN viral, qui dépasse souvent la durée des symptômes. Une récente méta-analyse a estimé que la durée moyenne de la positivité des tests RT-PCR utilisant des échantillons respiratoires, depuis l'apparition des symptômes jusqu'à la guérison ou au décès, était de 13,4 jours (IC de 95 %) : de 10,9 à 15,8) (Byrne et coll., 2020). Les concentrations d'ARN viral mesurées dans les échantillons des voies respiratoires supérieures diminuent après l'apparition des symptômes (Kujawsk et coll., 2020; Lavezzo et coll., 2020; Quicke et coll., 2020; Wölfel et coll., 2020; van Kampen et coll., 2020; B. E. Young et coll., 2020b; L. Zou et coll., 2020). Des auteurs ont également rapporté des périodes prolongées d'excrétion d'ARN viral (jusqu'à 83 jours) dans des échantillons respiratoires (par exemple J. Li, Zhang, Liu et Song, 2020; N. Li, Wang et Lv, 2020; Park et coll., 2020; Shin et coll., 2020).

La présence d'ARN viral a beaucoup varié selon le type d'échantillon. Les échantillons de selles sont initialement positifs par RT-PCR plusieurs jours après l'apparition des symptômes en moyenne et restent positifs plus longtemps que les échantillons respiratoires (Cai et coll., 2020; Z. Chen et coll., 2020; Du et coll., 2020; Hua et coll., 2020; Ling et coll., 2020; Lyu et coll., 2020; Mesoraca et coll., 2020; Santos et coll., 2020; F. Xiao et coll., 2020; Y. Xing et coll., 2020; C. L. H. Xu et coll., 2020; N. Zhang et coll., 2020). Des éléments de preuve de l'excrétion de l'ARN viral du SRAS-CoV-2 ont également été identifiés dans des écouvillons oculaires (Hu et coll., 2020; Valente et coll., 2020; Xia et coll., 2020). Dans une étude, les écouvillons oculaires ont été continuellement positifs pendant deux semaines après que les écouvillons nasopharyngés soient devenus négatifs le 22^{e} jour (Y. Hu et coll., 2020). Alors que dans une autre étude, les écouvillons conjonctifs sont devenus négatifs chez les enfants plus tôt que les écouvillons nasopharyngés (4 jours 'par rapport à 8 jours) (Valente et coll., 2020). Dans une étude portant sur 17 patients atteints de la COVID-19, aucun signe d'excrétion d'ARN viral n'a été trouvé dans les larmes au cours de la maladie (Seah et coll., 2020).

Les caractéristiques des individus ou des maladies qui déterminent la durée de l'excrétion de l'ARN viral ont été étudiées, notamment le cancer, la gravité, l'âge, la symptomatologie. De plus, il a été démontré que la durée de l'excrétion d'ARN viral était inversement corrélée aux niveaux plasmatiques des cytokines IL-1β et IL-17A des cellules T à la phase initiale de l'infection (P. H. Lee et coll., 2020). Il existe également des preuves variables de l'existence d'anticorps neutralisants et de l'association avec la gravité de la COVID-19 et la clairance virale (Jeewandara, et coll., 2020; Ru et coll., 2020).

Trois études portent sur l'excrétion du SRAS-CoV-2 par les animaux. Un essai expérimental de provocation chez le macaque rhésus a permis d'isoler le virus viable jusqu'à trois jours après l'infection, tandis que l'excrétion d'ARN viral s'est poursuivie jusqu'à 17 jours après l'infection (Munster et coll., 2020). Une série de cas de grands félins du zoo du Bronx a rapporté l'isolement d'un virus viable chez deux animaux, cinq jours après que les signes cliniques aient cessé (Bartlett et coll., 2020). Un essai expérimental de provocation sur des chats a montré que les test d'ARN viral dans les écouvillons nasaux étaient positifs du 1er au 10^{e} jour après la provocation, avec des quantités maximales observées du 1er au 5^{e} jour après la provocation (Gaudreault et coll., 2020).

En raison de l'abondance des rapports de cas, tous les rapports de cas faisant état de tests en série n'ont pas été inclus dans ce tableau.

Tableau 3 : Études évaluant la période infectieuse symptomatique de la COVID-19 chez l'homme et l'animal. (N=107)

Référence	Type d'étude	-Population et environnement -Période de temps	Période infectieuse (PI) déterminée par : Culture, Tests RT-PCR en série, données épidémiologique ou modèle	Résultats pertinents
Études sur la culture et la RT-PCR				
(Jeong et coll., 2020)	Cohorte prospective	-Cinq patients atteints de la COVID-19 de Corée et des groupes de furets -Du 25 février au 5 mars 2020	Culture et RT-PCR	Écouvillons respiratoires et fécaux -Le virus SARS-CoV-2 viable a été isolé à partir de trois échantillons respiratoires prélevés sur des patients atteints de la COVID-19 après 11 et 15 jours de maladie. -Les charges virales dans les échantillons d'urine, de salive et de selles étaient presque égales ou supérieures à celles des écouvillons naso-oropharyngés. -Pour confirmer la présence du SRAS-CoV-2 infectieux dans les échantillons d'urine et de matières fécales, deux échantillons d'urine (du 11^{e} et 13^{e} jour de maladie) et un échantillon de matières fécales (15^{e} jour de maladie) ont été sélectionnés pour des expériences d'infection de furets. Tous les furets traités avec des échantillons d'urine et de selles présentaient des signes d'infection.
(B. E. Young et coll., 2020a) *Prépublication*	Cohorte prospective	-Patients hospitalisés (n=100) à Singapour -Du 22 janvier au 6 mars 2020	Culture et RT-PCR	Écouvillons respiratoires -La culture virale à partir d'échantillons respiratoires a été positive pour 14 des 73 patients. -Valeur seuil du cycle PCR ≤ 30 x durée d'isolement viral prévue par culture -La durée moyenne d'excrétion de l'ARN viral était de 16,7 jours (IC de 95 %, de 15,2 à 18,3) et ne différait pas de manière significative en fonction de la gravité de la maladie ou de

				l'utilisation du lopinavir-ritonavir.
(Wölfel et coll., 2020)	Série de cas prospectifs	-Neuf patients confirmés hospitalisés présentant des symptômes légers en Allemagne -Cas découverts le 27 janvier 2020	Culture et RT-PCR	<u>Écouvillon respiratoire</u> -Le virus vivant a été isolé à partir d'écouvillons des voies respiratoires supérieures par culture virale pendant les sept premiers jours suivant l'apparition des symptômes. Aucun isolat n'a été obtenu à partir des échantillons après le huitième jour malgré la présence continue d'ARN viral. -L'excrétion d'ARN viral a été démontrée dans des échantillons d'expectorations et des voies respiratoires supérieures jusqu'à 22^{e} et 20^{e} jours, respectivement. -La charge virale a atteint un pic le quatrième jour après l'apparition du virus, avec $7,11\times10^{8}$ copies d'ARN par écouvillon pharyngé. La charge virale moyenne d'ARN était de $6,76\times10^{5}$ copies par écouvillon entier jusqu'au cinquième jour. Les échantillons prélevés après le cinquième jour avaient une charge virale moyenne de $3,44\times10^{5}$ copies par écouvillon et un taux de détection de 39,93 %. <u>Écouvillon de selles</u> -Le virus vivant n'a pas été isolé dans les échantillons de selles malgré la présence d'ARN viral continu (détecté jusqu'à 21 jours après l'apparition des symptômes).
(van Kampen, Jeroen J. A. et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients atteints de la COVID-19 hospitalisés (n=129, 89 en soins intensifs, 40 en soins moyens) aux Pays-Bas -Du 8 mars au 8 avril 2020	Culture et RT-PCR	<u>Écouvillons respiratoires supérieurs et inférieurs</u> -L'excrétion du virus infectieux a été détectée dans 62 échantillons respiratoires de 23 sur 129 patients (17,8 %). -La durée médiane de l'excrétion virale infectieuse était de 8 jours (de 0 à 20, IQR de 5 à 11) et la probabilité de détecter le virus infectieux est tombée en dessous de 5 % après 15,2 jours (de 13,4 à 17,2, IC de 95 %) après l'apparition des symptômes. -L'excrétion du virus infectieux est tombée à des niveaux indétectables lorsque le seuil de le seuil de la charge d'ARN viral était inférieur à 7 log^{10} copies d'ARN/ml et lorsque des anticorps neutralisants sériques étaient présents. Ces associations étaient significatives dans l'analyse uni- et

				multivariée.
(Folgueira et coll., 2020) *Prépublication*	Cohorte rétrospective	-Échantillons (n=106) provenant de 105 patients en Espagne -Chronologie non communiquée	Culture	<u>Échantillons respiratoires</u> -Dans 49 sur 106 échantillons (46,2 %), un effet cytopathique a été détecté en culture. -Dans les cas bénins, la viabilité virale a été maintenue jusqu'à 10 jours après l'apparition des symptômes. -Dans les cas graves, la viabilité virale a été maintenue jusqu'à 32 jours après l'apparition des symptômes. -Par rapport aux cas bénins, les cas graves présentaient le virus infectieux dans une proportion significativement plus élevée dans les échantillons ayant une charge virale modérée ou faible ($p < 0,01$).
(La Scola et coll., 2020)	Cohorte rétrospective	-183 échantillons provenant de 155 patients en France -Du 27 février au 12 mars 2020	Culture et RT-PCR	<u>Écouvillons nasopharyngés et d'expectoration</u> -Le SRAS-CoV-2 n'a pas pu être isolé à partir des échantillons prélevés après le huitième jour de l'apparition des symptômes. - Suggère que les patients présentant des valeurs Ct ≥ 34 ne sont plus infectieux et qu'ils peuvent sortir de l'hôpital.
(Singanayagam et coll., 2020)	Cohorte rétrospective	-324 échantillons, 81 cultures positives au Royaume-Uni De janvier à mai 2020	Culture et RT-PCR	<u>Écouvillons respiratoires</u> -La détection du virus cultivable a atteint son maximum au moment de l'apparition des symptômes. La durée médiane de l'excrétion du virus, mesurée par culture, était de 4 jours (IQR de 1 à 8) à partir de l'apparition des symptômes. -Dix jours après l'apparition des symptômes, la probabilité de mise en culture du virus est tombée à 6,0 % (de 0,9 à 31,2 %, IC de 95 %) -Il n'y avait pas de différence dans les valeurs seuils du cycle entre les personnes atteintes d'une maladie asymptomatique, bénine à modérée ou grave. Il n'y avait pas de différence significative entre les groupes d'âge.
(Perera et coll., 2020)	Cohorte rétrospective	-Échantillons respiratoires (n=68) de 35 patients atteints de la	Culture et RT-PCR	<u>Écouvillons respiratoires</u> -Le virus a été isolé chez 16 patients. -Le virus SRAS-CoV-2 viable était rarement détectable au-delà

		COVID-19 à Hong Kong -Chronologie non communiquée		de 8 jours après le début de la maladie dans les cas bénins. Cependant, l'ARN viral a été détectable pendant de nombreuses semaines par RT-PCR.
(Gniazdowski et coll., 2020) *Prépublication*	Cohorte rétrospective	-Échantillons de patients (n=161) positifs au test moléculaire aux États-Unis -Du 11 mars au 11 mai 2020	Culture et RT-PCR	<u>Écouvillons oropharyngés</u> -Pour évaluer la récupération du virus infectieux, un sous-ensemble de 29 patients sélectionnés au hasard a été évalué, dont beaucoup présentaient des affections sous-jacentes chroniques (n=27). - Chez quatre patients, des virus viables ont été récupérés à partir d'échantillons respiratoires prélevés jusqu'à 22 jours après le premier résultat positif. -L'excrétion de virus infectieux n'a pas été associée à un résultat spécifique, car un patient n'a jamais été admis, un autre a été hospitalisé, mais sans gravité, et deux ont été gravement malades. - La récupération du virus infectieux a été associée à la persistance des symptômes chez tous les patients sauf un. -Le séquençage complet du génome viral a montré que ces patients étaient porteurs du même virus au fil du temps (pas de réinfection).
(Bullard et coll., 2020)	Étude transversale rétrospective des échantillons soumis au laboratoire	-Test RT-PCR des échantillons positifs pour le SRAS-CoV-2 (N=90) au Canada -Chronologie non communiquée. Échantillons prélevés à partir du jour de l'apparition des symptômes (jour 0) jusqu'à 21 jours après l'apparition des symptômes	Culture et RT-PCR	<u>Écouvillons nasopharyngés et endotrachéaux</u> -Sur les 90 échantillons de SRAS-CoV-2 positifs au test RT-PCR analysés, 26 (28,9 %) ont été cultivés avec succès. -Des cultures positives n'ont été observées que jusqu'au huitième jour suivant l'apparition des symptômes. -La probabilité d'obtenir une culture virale positive a atteint son maximum le troisième jour suivant l'apparition des symptômes. -L'infectivité était significativement réduite lorsque les valeurs seuils du cycle RT-PCR étaient supérieures à 24.

(Kujawski et coll., 2020)	Série de cas	-Les 12 premiers patients confirmés aux États-Unis -Du 20 janvier au 5 février 2020	Culture et RT-PCR	<u>Écouvillon respiratoire</u> -La culture virale a été effectuée avec succès pour les 9 patients testés, avec des résultats positifs des échantillons respiratoires 9 jours après l'apparition des symptômes. Aucun essai d'isolement viral n'a pas été effectué sur les prélèvements ultérieurs. -L'ARN du SRAS-CoV-2 a été détecté dans les échantillons respiratoires des 12 patients, généralement 2 à 3 semaines après l'apparition des symptômes. -L'ARN du SRAS-CoV-2 a été détecté pendant un maximum de 36 jours après l'apparition des symptômes, bien après que ceux-ci aient complètement disparu. -Les échantillons de sérum et de selles ont également montré une excrétion virale positive pendant un maximum de huit et 25 jours, respectivement.
(Decker et coll., 2020)	Rapport de cas	-Homme de 62 ans, patient léger atteint de la COVID-19 avec une récente transplantation cardiaque en Allemagne -À partir du 13 mars 2020	Culture et RT-PCR	<u>Écouvillons pharyngés</u> -Le patient ne présentait aucun symptôme clinique 20 jours après les premiers symptômes, mais la culture du virus sur des écouvillons pharyngés aux jours 18 et 21 a confirmé une réplication active du virus du SRAS-CoV-2. -Sous immunosuppression continue, l'ARN viral du SRAS-CoV-2 est resté détectable jusqu'au 35^{e} jour avec un nombre de copies similaire à celui du début de l'infection.
(W. D. Liu et coll., 2020)	Rapport de cas	-Femme de 50 ans à Taïwan -Chronologie non communiquée	Culture et RT-PCR	<u>Écouvillons pharyngés et échantillons d'expectorations</u> -Le SRAS-CoV-2 a pu être isolé à partir de cultures dans des écouvillons pharyngés prélevés lors de l'admission, et tous les échantillons d'expectorations collectés dans les 18 jours suivant l'apparition des symptômes. -L'ARN viral était détectable par RT-PCR jusqu'à 63 jours après l'apparition des symptômes.
(Y. Zhang et coll., 2020)	Rapport de cas	-Un cas de COVID-19 grave	Culture	<u>Écouvillon de selles</u> -Le SRAS-CoV-2 a été isolé à partir d'un échantillon de selles

		confirmé par laboratoire, en Chine -Du 16 janvier au 1er février 2020		d'un cas dont les symptômes sont apparus le 16 janvier 2020 et a été prélevé le 1er février 2020. -L'intervalle entre le prélèvement et l'apparition des symptômes était de 15 jours.
(F. Xiao et coll., 2020)	Série de cas	-Cas mortel de COVID-19 et 28 autres échantillons de matières fécales en Chine -Janvier 2020	Culture et RT-PCR	<u>Écouvillons nasopharyngés, oropharyngés et fécaux</u> -La charge virale était plus élevée dans les matières fécales que dans les échantillons respiratoires prélevés à plusieurs moments (de 17 à 28 jours après l'apparition des symptômes). -L'isolement du virus à partir d'échantillons d'excréments prélevés à des moments ultérieurs n'a pas n'a pas été un succès, malgré l'excrétion continue d'ARN viral. -Les auteurs ont également recueilli des échantillons d'excréments de 28 patients. 12, y compris le cas mentionné ci-dessus, étaient positifs quant à la détection d'ARN viral. L'isolement du virus du SRAS-CoV-2 a été un succès pour deux patients.
(Sun et coll., 2020)	Rapport de cas	-Un homme de 72 ans en Chine -Du 25 janvier au 6 mars 2020	Culture et RT-PCR	<u>Urine</u> -La charge virale dans les urines était faible, mais détectable au 12e jour et au 42e jour après l'infection, mais pas au 30e jour. -Afin de prouver que le virus isolé était infectieux pour les cellules sensibles, des échantillons d'urine positifs au test RT-PCR du 12e jour après l'infection ont été dilués en série dans des milieux d'infection et inoculés sur des cellules Vero E6. -Des effets cytopathiques ont été clairement observés au bout de 3 jours, ce qui soulève la possibilité d'une transmission fécale/urine-respiratoire.
(Mancuso et coll., 2020) *Prépublication*	Cohorte prospective basée sur la population	-Cas de COVID-19 (n=1162) en Italie -Du 26 février au 22 avril 2020	RT-PCR	<u>Écouvillons nasopharyngés</u> -La durée médiane de clairance de l'ARN viral déterminée par test RT-PCR était de 36 jours (IRQ de 28 à 45) à partir de l'apparition des symptômes. -Le temps nécessaire à la clairance du virus augmente avec l'âge et l'hospitalisation, bien que cela ne soit pas

				statistiquement significatif.
(K. Wang et coll., 2020)	Cohorte prospective	-Patients hospitalisés (n=68) en Chine -Du 10 février au 20 mars 2020	RT-PCR	Écouvillons nasopharyngés et d'expectoration -La durée médiane de l'excrétion de l'ARN viral à partir des échantillons d'expectorations a été significativement plus longue que celle des écouvillons nasopharyngés : 34 jours (IQR de 24 à 40) contre 19 jours (IQR de 14 à 25), p < 0,001. -L'âge avancé était un facteur indépendant associé à la durée prolongée de l'excrétion du virus du SRAS-CoV-2 (HR 1,71, de 1,01 à 2,93). - Chez neuf patients, l'ARN viral a été détecté dans les expectorations après que les écouvillons nasopharyngés soient devenus négatifs.
(Yu et coll., 2020)	Cohorte prospective	-Cas rétablis (n=75) en Chine -Du 9 au 14 mars 2020	RT-PCR	Échantillons respiratoires -Sur les 75 cas, 12 ont pris moins de 30 jours pour obtenir 2 tests de détection de l'ARN du SRAS-CoV-2 négatifs consécutifs, 57 ont pris de 31 à 60 jours; et 1 a pris plus de 60 jours pour remplir ce critère. -La moyenne est de 27,15 jours (de 24,72 à 29,58, IC de 95 %).
(Shrestha et coll., 2020)	Cohorte prospective	-Travailleurs de la santé (n=230) à Cleveland, aux États-Unis -Du 16 mars au 20 avril 2020	RT-PCR	Écouvillon nasopharyngé -Chez les patients atteints de COVID-19 non sévère, les charges virales dans les échantillons des voies respiratoires supérieures ont atteint un pic deux ou trois jours après l'apparition des symptômes et diminuent rapidement par la suite. - Chez les personnes atteintes d'une maladie non grave, le potentiel de transmission de la COVID-19 est fortement diminué de 7 à 10 jours après l'apparition des symptômes.
(Y. Xing et coll., 2020) *Prépublication*	Cohorte prospective	-Cas pédiatriques (n=3) en Chine -Du 17 janvier au 23 février 2020	RT-PCR	Écouvillon pharyngé -La période infectieuse médiane entre l'apparition des symptômes et la clairance du virus était de 13,5 jours (fourchette de 11 à 16 jours). Écouvillon fécal -La période infectieuse médiane entre l'apparition des

				symptômes et la clairance du virus était de 29 jours (fourchette de 24 à 34 jours).
(Yu, Zhang et coll., 2020)	Étude rétrospective de cohorte par paires appariées	-Patients hospitalisés atteints de pneumonie due à la COVID-19, 64 cas souffrant aussi de grippe A/B et 64 cas souffrant aussi de grippe négative en Chine -Du 28 janvier au 17 mars 2020	RT-PCR	Écouvillons pharyngés -La durée médiane de l'excrétion virale à partir de l'admission était plus longue pour les patients présentant une co-infection grippale (17,0 jours) que pour ceux qui n'en présentaient pas (12,0 jours) (P< 0,001).
(Spagnuolo et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients hospitalisés (n=280) en Italie -Du 25 février au 19 mai 2020	RT-PCR	Écouvillons nasopharyngés - Une étude montre qu'un retard dans la clairance du COVID-19 modéré/grave est associé à un âge plus avancé et à une maladie plus grave, mais pas à l'utilisation précoce de corticostéroïdes.
(X. Zheng et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=80) en Chine, 28 de type grave, 52 de type courant -Du 17 janvier au 9 mars 2020	RT-PCR	Écouvillons de gorge et de matières fécales -La plus longue durée observée d'excrétion virale pour les écouvillons de gorge et des matières fécales chez les patients atteints de COVID-19 était respectivement de 43 et 46 jours après l'apparition des symptômes. -Il n'y avait aucune corrélation entre la durée de l'excrétion virale et la gravité de la COVID-19.
(F. Hu et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=190) en Chine -Du 8 janvier au 9 février 2020	RT-PCR	Écouvillons pharyngés -La durée de l'apparition des symptômes à l'admission (P <0,001) et l'administration de corticostéroïdes (P = 0,002), d'arbidol (P = 0,008) et d'oseltamivir (P <0,001) ont été indépendamment associées à la durée de l'excrétion virale.
(Bahar et coll., 2020)	Cohorte rétrospective	-Cas pédiatriques (n=6369) ayant subi des	RT-PCR	Écouvillons nasopharyngés - La durée médiane de l'excrétion virale (test RT-PCR positif)

Prépublication		tests aux États-Unis -Du 13 mars au 21 juin 2020		était de 19,5 jours et du passage de tests RT-PCR positifs à négatifs était de 25 jours. -Les patients âgés de 6 à 15 ans ont présenté une excrétion virale plus longue que les patients âgés de 16 à 22 ans (médiane = 32 contre 18 jours, p = 0,015).
(X. Chen et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=284) en Chine -Du 20 janvier au 15 mars 2020	RT-PCR	Écouvillons pharyngés -La durée médiane de l'excrétion de l'ARN viral était de 12 jours (IQR de 8 à 16) après l'apparition du symptôme. -L'âge avancé, le délai entre le début de la maladie et l'admission à l'hôpital, la diarrhée, le traitement par corticostéroïdes et le lopinavir/ritonavir ont été associés de manière significative et indépendante à une excrétion prolongée d'ARN viral.
(Y. Shen et coll., 2020)	Cohorte rétrospective	-Cas confirmés (n=325) en Chine -Du 20 janvier au 29 février 2020	RT-PCR	Prélèvements nasopharyngés, urinaires, fécaux et sanguins -La durée médiane entre le début et la détection négative de l'acide nucléique par écouvillonnage nasopharyngé était de 8 jours. -Une plus longue durée d'excrétion virale dans le sang et les selles a été détectée chez les patients atteints d'une maladie légère et utilisant des glucocorticoïdes. -La durée médiane entre le début de la maladie et la détection virale négative était plus longue chez les patients graves et critiques que chez les patients légers. -Parmi 22 patients légers sans traitement antiviral, les délais médians entre le début de la maladie et la détection virale négative dans les écouvillons nasopharyngés, les urines, les fèces et les échantillons de sang étaient respectivement de 9, 7, 10 et 9,5 jours.
(N. Li et coll., 2020)	Cohorte rétrospective	-Cas confirmés avec excrétion virale prolongée >30 jours (n=36) en Chine	RT-PCR	-L'excrétion prolongée de l'ARN viral, même après le soulagement des symptômes, était courante, et la durée médiane de l'excrétion de l'ARN viral était de 53,5 jours (IQR de 47,75 à 60,5).

		-Du 11 février au 11 avril 2020		-La plus longue durée d'excrétion de l'ARN viral pourrait être de 83 jours. -Par rapport aux groupes de patients dont les symptômes sont apparus plus tardivement, les patients présentant ses symptômes précoces avaient des durées d'excrétion virale plus longues et souffraient de maladies plus graves.
(Korkmaz et coll., 2020)	Cohorte rétrospective	-Enfants hospitalisés (n=81) en Turquie -Du 5 mars au 5 mai 2020	RT-PCR	Écouvillons naso-oropharyngés -La durée médiane pour que l'ARN du SRAS-CoV-2 devienne négatif au test RT-PCR était de 5 jours (de 3 à 10). -Le délai avant d'avoir un test négatif était significativement plus long pour les patients âgés de cinq ans ou moins que pour les autres (P=0,037).
(T. Z. Li et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=101) en Chine -Du 21 janvier au 15 mars 2020	RT-PCR	Écouvillon pharyngé -La durée médiane de l'excrétion de l'ARN viral à partir de l'apparition des symptômes était de 11 jours (IQR de 8 à 14,3). -Dans l'analyse univariée, la gravité de la maladie, l'utilisation de corticostéroïdes, la fièvre et le temps écoulé entre le début de la maladie et l'hospitalisation ont été associés à une excrétion prolongée d'ARN viral. -Dans l'analyse multivariée, la gravité de la maladie n'a pas montré d'association significative.
(X. Du et coll., 2020)	Cohorte rétrospective	-Cas ventilés par âge, sexe et gravité (n=161) en Chine -Du 20 janvier au 1er mars 2020	RT-PCR	Type de prélèvements non rapporté -La durée médiane du portage viral de tous les cas (n=161) était de 20 jours (fourchette de 6 à 30). -La durée médiane du transport viral chez les hommes était de 21 jours (IQR de 16,5 à 29) chez les hommes (n=89) contre 20 jours (IQR de 16 à 26,8) chez les femmes (n=72). Il n'y avait pas de différence significative entre les sexes (p>0,05). -La durée médiane du portage viral pour les cas âgés de plus de 60 ans était statistiquement plus longue (p<0,01) que les cas âgés de 0 à 59 ans : 28 jours (IQR de 19 à 33) contre 20 jours (IQR de 16 à 26).

				-La durée médiane du portage viral pour les cas considérés comme graves (n=37) était statistiquement plus longue (p<0,01) que pour les cas non graves (n=124) : 27 jours (IQR de 19 à 33) contre 20 jours (IQR de 16 à 26).
(Tang Xiao et coll., 2020) *Prépublication*	Cohorte rétrospective	-Cas ventilés par âge et sexe (n=301) en Chine -Du 21 janvier au 11 février 2020	RT-PCR	<u>Écouvillons des voies respiratoires supérieures (écouvillons pharingés et/ou nasaux)</u> -La période médiane entre l'apparition des symptômes et le résultat négatif du test RT-PCR était de 20 jours (IQR de 17 à 24, de 7 à 44, N=216). -Les femmes (n=147) ont eu une période médiane plus courte entre le résultat positif et négatif du test RT-PCR du SRAS-CoV-2 que les hommes (n=154) : 19 jours (IQR de 17 à 24) contre 21 jours (IQR de 17 à 25). Ce résultat n'est pas statistiquement significatif (p=0,189). -La période médiane entre l'apparition des symptômes et les résultats négatifs au test RT-PCR était significativement plus longue chez les patients plus âgés (≥ 65 ans, n=110) que chez les plus jeunes (< 65 ans, n=191) : 22 jours (IQR de 19 à 26) contre 19 jours (IQR de 17 à 23), p=0,015.
(Voinsky et coll., 2020)	Cohorte rétrospective	-Patients (n=5769, 3370 hommes et 2399 femmes) en Israël -Date de fin : 28 avril 2020	RT-PCR	<u>Écouvillon pharyngé</u> -Le délai entre le premier résultat positif et le premier résultat négatif du test PCR était significativement plus long (p < 0,05) pour les patients de plus de 30 ans. Les périodes de rétablissement étaient : Homme < 30 ans : 13,84 (ET ±5,67) Homme >30 ans : 14,69 (ET ±6,0) Femme < 30 ans : 13,66 (ET ±5,87) Femme > 30 ans : 14,24 (ET ±6,16)
(Sharma et coll., 2020) *Prépublication*	Cohorte rétrospective	-Cas hospitalisés (n=234) en Inde -Du 20 mars au 30 avril 2020	RT-PCR	<u>Écouvillons nasopharyngés</u> -La durée moyenne de détectabilité de l'ARN viral était de 10,2 jours (ET 6,4). -La durée était significativement plus faible dans les cas de

				moins de 40 ans comparés à ceux de 40 à 59 ans et à ceux de plus de 60 ans : 9,1 jours (ET 5,2) contre 11,3 jours (ET 6,1) contre 16,4 jours (ET 13,3), p=0,001.
(G. Wu et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients confirmés hospitalisés en Chine -Du 23 janvier au 8 mars 2020	RT-PCR	Écouvillon des voies respiratoires supérieures -Le temps moyen d'excrétion de l'ARN viral entre l'apparition des symptômes et le premier résultat négatif chez les patients courants (n=93) était de 15,1 jours (ET ±7,23). -Les patients sévères (n=41) ont eu une période d'excrétion statistiquement plus longue (p=0,00) de 20,56 jours (ET ±6,59). Écouvillon des voies respiratoires inférieures -La durée moyenne de l'excrétion virale était de 27,45 jours (ET ±10,06) pour les patients ordinaires et de 29,78 jours (ET ±10,11) pour les patients graves. Il n'y avait pas de différence statistique entre les groupes (p=0,328). Écouvillon fécal -Dans le tube digestif, la durée moyenne de l'excrétion virale était de 22,6 jours (ET ±7,69) pour les patients ordinaires et de 27,24 jours (ET ±7,86) pour les patients graves, ce qui était statistiquement plus long (P = 0,01).
(F. Xing et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients hospitalisés (n=229) en Chine -De janvier à mars 2020	RT-PCR	Écouvillon nasopharyngé -Le délai entre le diagnostic et le premier test négatif chez les patients ordinaires était de 25,5 jours (ET ±11,3) et de 37,1 (ET ±14,4) chez les patients graves. Cela était statistiquement significatif (p < 0,001).
(Zeng et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés pour la COVID-19 (n=149) en Chine -Du 20 janvier au 26 mars 2020	RT-PCR	Écouvillons pharyngés -La durée médiane entre le début de la maladie et le deuxième test négatif d'ARN du SRAS-Cov-2 était de 20 jours (IQR de 16 à 24). -Les patients admis à l'unité de soins intensifs avaient une période d'excrétion virale plus longue à partir du début de la maladie que les patients non hospitalisés : 30 jours (IQR de 22 à 33) contre 19 jours (IQR de 15,8 à 22), p < 0,0001.

(Fu et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients adultes hospitalisés pour la COVID-19 (n=3129) en Chine -Du 18 janvier au 31 mars 2020	RT-PCR	Écouvillon pharyngé ou écouvillon nasopharyngé -La durée d'excrétion de l'ARN viral chez les patients gravement malades était nettement plus longue que chez les patients non gravement malades : 24,0 jours (de 18,9 à 29,1, IC de 95 %) contre 18,0 jours (de 16,8 à 19,1, IC de 95 %). -Les patients non gravement malades (n=330) ont eu une excrétion virale persistante au-delà de 30 jours après l'apparition du virus. -Un titre d'anticorps IgM/IgG plus faible dans les 4 semaines suivant le début de la maladie peut être un facteur de risque d'infection persistante.
(P. H. Lee et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=201) à Singapour -Du 22 janvier au 5 avril 2020	RT-PCR	Écouvillons respiratoires -La durée de l'excrétion virale n'a pas été associée de manière significative au sexe, à l'âge, à la présence de comorbidités, aux investigations de base, à une fièvre prolongée, à une pneumonie, au besoin d'oxygène supplémentaire ou à l'utilisation d'agents antiviraux expérimentaux. -La durée médiane de l'excrétion de l'ARN viral était nettement plus longue chez les patients nécessitant une ventilation mécanique invasive. -La durée de l'excrétion de l'ARN viral était inversement corrélée aux niveaux plasmatiques des cytokines IL-1 β et l'IL-17A des cellules T à la phase initiale de l'infection.
(Talmy et coll., 2020)	Cohorte rétrospective	-Soldats des Forces de défense israéliennes souffrant légèrement du COVID-19 (n=219) en Israël -Du 20 mars au 5 mai 2020	RT-PCR	Écouvillons oropharyngés et nasopharyngés -La durée médiane de l'ARN viral à partir de l'apparition des symptômes dans ce groupe d'adultes jeunes et en bonne santé était de 21 jours (fourchette de 4 à 45, IQR de 15 à 27).
(Corsini Campioli et	Cohorte rétrospective	-Cas hospitalisés (n=251) aux États-Unis	RT-PCR	Écouvillons nasopharyngés -La durée médiane entre l'apparition des symptômes et le

coll., 2020)		-Du 1er février au 15 mai 2020		résultat négatif au test RT-PCR était de 23 jours, et ne différait pas selon les symptômes.
(T. Y. Yang et coll., 2020)	Cohorte rétrospective	-Cas hospitalisés (n=50) en Chine -Du 2 au 13 février 2020	RT-PCR	Écouvillons nasopharyngés -La durée de l'excrétion virale était significativement plus longue dans les cas présentant des symptômes gastro-intestinaux que dans les cas présentant des symptômes pulmonaires (10,22 jours ±1,93 contre 8,15 jours ±1,87, P < 0,01).
(Jeewandara et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients graves (n=6), modérés (n=5) et légers/asymptomatiques (n=13) ainsi que ceux qui étaient légèrement malades, mais avait une excrétion prolongée du virus (n=21), au Sri Lanka -Avril 2020	RT-PCR	Écouvillons respiratoires -La durée médiane de l'excrétion du virus dans l'ensemble de cette cohorte était de 25 jours (IQR de 15 à 38) -Dix personnes ont eu des excrétions du virus pendant plus de 50 jours. -Ceux qui avaient une excrétion prolongée du virus avaient des anticorps neutralisants apparaissant plus rapidement et à des niveaux plus élevés que ceux qui avaient éliminé le virus plus tôt.
(Jiang et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés avec lésions hépatiques (n=76) et sans lésions hépatiques (n=55) en Chine -Du 19 janvier au 20 février 2020	RT-PCR	Type de prélèvements non rapporté -Les lésions hépatiques ont été liées à l'augmentation de la durée de l'excrétion virale (différence moyenne : 3,0, IC de 95 % : de 1,0 à 4,9).
(Carmo et coll., 2020)	Cohorte rétrospective	-Patients (n=210) au Portugal -Du 1er mars au 30 avril 2020	RT-PCR	Écouvillons nasopharyngés et oropharyngés -Dans le groupe de patients ayant subi deux tests négatifs consécutifs, le premier test RT-PCR négatif a été réalisé en moyenne 24,8 jours (fourchette de 7 à 46) après le premier test positif. -Chez les hommes, le premier test négatif a pris 24 jours (fourchette de 7 à 46) et chez les femmes, 25 jours (fourchette

				de 9 à 44), p>0,05. -69 patients ont été renvoyés chez eux et ont été légèrement malades. Les patients légèrement malades ont conservé l'ARN viral pendant une période plus longue. 47 étaient des patients hospitalisés modérément à gravement malades. Chez les patients renvoyés chez eux, le nombre de jours avant le premier test négatif était de 26,3 jours (ET ±8,5) et dans le groupe de patients hospitalisés, il était de 22,5 jours (ET ±9,3), p=0,027. -Les patients hospitalisés âgés de plus de 65 ans ont mis plus de temps (23,9 jours (±9,7)) que ceux de moins de 65 ans (18,3 (ET ±9,7)), pour obtenir le premier test négatif, p=0,026.
(D. Shi et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients hospitalisés dont la COVID-19 (n=246) a été confirmée en laboratoire en Chine -Du 27 janvier au 24 mars 2020	RT-PCR	Écouvillon nasopharyngé ou pharyngé -La durée de l'excrétion virale a été définie comme la durée entre le début de la maladie et la date du premier résultat négatif de l'excrétion virale. -La durée médiane de l'excrétion virale était de 24 jours (fourchette de 6 à 63). -Le récepteur soluble interleukine-2 (>710 U/mL), la lactate déshydrogénase (>250 U/L) et la COVID-19 grave ont été liés à la prolongation de l'excrétion virale, p < 0,05.
(Qingxian et coll., 2020) *Prépublication*	Cohorte rétrospective	-Cas ventilés par indice de masse corporelle en Chine -Du 11 janvier au 16 février 2020	RT-PCR	Écouvillon nasal -La durée médiane entre l'apparition des symptômes et la clairance du virus n'était pas significativement différente (p=0,14) entre les différents indices de masse corporelle : Normal : 14 jours (IQR de 9 à 18), poids insuffisant : 14,5 (IQR de 10 à 21), poids excessif : 15 (IQR de 10 à 22), obèse : 14 (IQR de 9 à 20).
(Moriconi et coll., 2020)	Cohorte rétrospective	-Cas hospitalisés (n=100) en Italie -Du 16 mars au 15 avril 2020	RT-PCR	Écouvillons pharyngés et nasaux -Les patients obèses ont pris plus de temps pour obtenir un écouvillon oropharyngé ou nasal négatif (19 ±8 contre 13 ±7, jours, p = 0,002).

(Xiao, Fu et Yang, 2020) *Prépublication*	Cohorte rétrospective	-Patients avec hypertension (n=24) et sans hypertension (n=24) atteints d'une COVID-19 non grave en Chine -Du 23 janvier au 15 février 2020	RT-PCR	Écouvillons nasopharyngés -La période moyenne entre l'apparition des symptômes et la conversion négative était de 17 jours (ET 5,5) et 15 jours (ET 3,6) pour les patients avec et sans hypertension (p=0,021).
(C. Cao et coll., 2020)	Cohorte rétrospective	-Patients (n=157), 63 (40,1 %) présentant des symptômes gastro-intestinaux en Chine -Chronologie non communiquée	RT-PCR	Écouvillons nasopharyngés -Il n'y a pas eu de différence significative dans la durée moyenne d'excrétion virale entre les patients avec et sans symptômes gastro-intestinaux (GI). -Total : 12,4 jours (ET 6,4) contre avec symptômes GI : 13,0 jours (ET 6,1) contre sans symptômes GI : 12,0 jours (ET 6,7), p=0,3509.
(H. Wang et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=95) en Chine -Du 15 janvier au 2 mars 2020	RT-PCR	Écouvillons pharyngés -Cette étude suggère que la NCD4LR est un biomarqueur potentiel et utile pour prédire le temps de conversion négative du virus chez les patients atteints de la COVID-19. -Le temps de conversion négative médian (intervalle entre l'apparition des symptômes et le premier de deux tests viraux négatifs consécutifs) chez tous les patients était de 19 jours (IQR de 11 à 27). -Les patients présentant un ratio neutrophiles/lymphocytes CD4+ élevé ont montré un temps de conversion négative relativement plus long que les patients présentant un ratio neutrophiles/lymphocytes CD4+ plus faible : 24 jours (IQR de 18 à 33) contre 13 jours (IQR de 9 à 21) (p < 0,001).
(J. Han et coll., 2020)	Cohorte rétrospective	-Cas hospitalisés (n=185) en Chine -Du 21 janvier au 8 mai 2020	RT-PCR	Écouvillons respiratoires -La durée médiane d'excrétion de l'ARN viral était de 17 jours à partir du début de la maladie; la durée la plus longue était de 51 jours, et la plus courte de 4 jours.

(G. Zheng et coll., 2020)	Cohorte rétrospective	-Cas pédiatriques (n=52) en Chine -Chronologie non communiquée	RT-PCR	Écouvillons oropharyngés -Le délai entre l'admission et le premier test RT-PCR négatif était de 12 jours (IQR de 8,0 à 16,8).
(Woodruff et coll., 2020)	Cohorte rétrospective	-Les 100 premiers patients du registre de cas COVID positifs de la clinique Mayo, en Floride, aux États-Unis -Date de fin : 15 mai 2020	RT-PCR	Écouvillons nasopharyngés -Le délai moyen d'apparition des symptômes pour un ARN viral indétectable était de 21,5 jours. -Sur la base de ces données, les auteurs suggèrent d'être plus prudent dans les lignes directives pour l'isolement.
(J. Xu et coll., 2020)	Cohorte rétrospective	-Patients adultes gravement malades (n=239) en Chine -Du 12 janvier au 3 février 2020	RT-PCR	Échantillons respiratoires et de sérum -La durée médiane de la conversion négative de l'ARN du SRAS-CoV-2 était de 30 (fourchette de 6 à 81) jours chez les 49 survivants gravement malades qui ont été identifiés.
(Nakamura et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients ayant des antécédents de cancer (n=32) au Japon -Du 31 janvier au 25 mai 2020	RT-PCR	Écouvillon nasopharyngé - La période médiane entre le début de la maladie et le premier résultat négatif de la PCR de l'ARN du SRAS-CoV-2 était de 22 jours (IQR de 18 à 25) chez les survivants. -L'excrétion virale a été détectée dans un cas jusqu'à 56 jours après le début de l'infection.
(Infante et coll., 2020)	Cohorte rétrospective	-Patients atteints de malignités hématologiques (n=26) en Espagne -Du 8 mars au 8 avril 2020	RT-PCR	Écouvillon nasal -La durée médiane de l'excrétion virale était de 32,7 jours (fourchette de 10 à 70).
(Berghoff et coll., 2020)	Cohorte rétrospective	-Patients atteints d'un cancer (n=4) en Autriche -Du 21 mars au 4 mai 2020	RT-PCR	Écouvillon nasal -La clairance virale a été obtenue chez trois des quatre patients de 14 à 56 jours après le test positif.

(J. Shi et coll., 2020)	Cohorte rétrospective	-Cas hospitalisés (n=99) en Chine -Du 19 janvier au 17 février 2020	RT-PCR	Échantillons respiratoires et de selles -Un patient a été testé négatif pour le SRAS-CoV-2 dans les 5 jours, 9 patients ont été testés négatifs dans les 10 jours, et 49 ont été testés négatifs dans les 20 jours après l'apparition des symptômes. Un sous-ensemble de 12 patients présentait des niveaux détectables du virus jusqu'à 30 jours après l'apparition des symptômes. -Le temps d'excrétion était significativement augmenté si les résultats du test ARN fécal du SRAS-CoV-2 étaient positifs. Le sexe masculin, l'utilisation d'immunoglobulines, le score APACHE II et le nombre de lymphocytes étaient des facteurs indépendants associés à une durée prolongée de l'excrétion du SRAS-CoV-2.
(Ling et coll., 2020)	Cohorte rétrospective	-66 patients rétablis après un traitement (patients convalescents) en Chine -Du 20 janvier au 10 février 2020	RT-PCR	Écouvillon oropharyngé -La durée médiane entre l'apparition des symptômes et les premiers résultats négatifs de la RT-PCR était de 9,5 jours (IQR de 6,0 à 11,0). Écouvillon fécal -Les échantillons de selles avaient des tests d'ARN du SRAS-CoV-2 négatifs après une durée médiane de 11,0 jours (IQR de 9,0 à 16,0) après l'apparition des symptômes. -43 (65 %) patients ont eu une durée d'ARN viral plus longue dans les écouvillons de selles que dans les écouvillons pharingés, avec un délai médian de 2,0 jours (IQR de 1,0 à 4,0). Écouvillon d'urine -Les résultats de seulement 4 (6,9 %) échantillons d'urine testés à l'acide nucléique viral étaient positifs sur 58 cas. -L'ARN viral était toujours présent dans les échantillons d'urine de 3 patients après des tests négatifs des écouvillons pharingés. Les patients sous traitement glucocorticoïde ont eu une clairance virale retardée par rapport à ceux qui n'en avaient pas.
(Hua et coll.,	Cohorte	-Enfants hospitalisés	RT-PCR	Écouvillon fécal

2020)	rétrospective	(n=35) en Chine -Jusqu'au 20 avril 2020		-La détection fécale de l'ARN du SRAS-CoV-2était positive dans 91,4 % (32 sur 35) des cas et certains enfants avaient une durée d'excrétion virale supérieure à 70 jours. -Le temps de clairance virale n'était pas différent entre les groupes traités avec différents régiments d'antiviraux.
(J. Huang et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients hospitalisés (n=33) en Chine -Du 27 janvier au 10 avril 2020	RT-PCR	Écouvillons pharyngés, d'expectorations et de selles -La durée médiane entre l'apparition des symptômes et l'ARN viral indétectable dans les écouvillons pharyngés, les expectorations et les prélèvements de selles était respectivement de 18,5 jours (IQR de 13,25 à 22), 22 jours (IQR de 18,5 à 27,5) et 17 jours (IQR de 11,5 à 32). -Par rapport aux écouvillons pharyngés, les charges virales dans les expectorations et les selles ont diminué beaucoup plus lentement ($p < 0,05$). -3 patients ont montré une récurrence détectable de l'ARN viral dans les expectorations lors d'un test effectué 2 semaines après leur sortie de l'hôpital.
(P. Liu et coll., 2020)	Cohorte rétrospective	-Cas de COVID-19 pédiatriques hospitalisés (n=9) en Chine -Du 19 janvier au 10 avril 2020	RT-PCR	Écouvillons nasopharyngés -La durée médiane de l'excrétion de l'ARN viral entre le jour de l'apparition de la maladie et le dernier résultat positif était de 13 jours (fourchette de 6 à 24). Écouvillons oropharyngés -3 des 9 patients ont eu des écouvillons oropharyngés qui ont eu des tests positifs à l'ARN du SRAS-CoV2 pendant une durée médiane de 4 jours (fourchette de 3 à 10). Écouvillons de selles -8 patients ont présenté une excrétion de SRAS-CoV-2 dans leurs selles pendant une durée médiane de 43 jours (fourchette de 28 à 66). Tous ont eu une excrétion virale persistante dans leurs selles après leur sortie de l'hôpital, avec une durée médiane entre le jour de la sortie et le jour de la dernière selle positive collectée au suivi de 22,5 jours (fourchette de 4 à 46). -L'ARN du SRAS-CoV-2 n'a pas été détecté dans les

				échantillons de sérum ou d'urine.
(N. Zhang et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=23) en Chine -Du 20 janvier au 23 février 2020	RT-PCR	Écouvillons des voies respiratoires supérieures et des selles -Une période d'excrétion du virus plus longue a été constatée dans les échantillons fécaux par rapport aux échantillons des voies respiratoires supérieures (22 jours contre 10 jours), bien que les ARN viraux des échantillons des voies respiratoires supérieures aient été généralement détectables plus tôt. -Les titres viraux des écouvillons respiratoires ont atteint leur maximum 6 à 9 jours après l'apparition des symptômes et 14 à 18 jours pour les échantillons de selles. -Chez un patient gravement malade, tous les échantillons étaient négatifs jusqu'à 21 jours après l'apparition des symptômes, lorsque l'échantillon fécal a alors été testé positif.
(Lyu et coll., 2020)	Cohorte rétrospective	-Patients sortis de l'hôpital (n=6) en Chine -Du 23 janvier au 9 mars 2020	RT-PCR	Écouvillons de gorge, d'expectorations et de selles -Les échantillons de selles ont été testés positifs chez 6 patients sortis de l'hôpital, avec des écouvillons de gorge et d'expectorations testés négatifs. -Les échantillons de selles ont été positifs jusqu'à 52 jours après l'apparition des symptômes.
(Gombar et coll., 2020)	Cohorte rétrospective	-Patients (n=87) et personnel de santé (n=63) atteints de la COVID-19 à Stanford, Californie, États-Unis -Du 3 mars au 30 avril 2020	RT-PCR	Écouvillons respiratoires -Pour les patients, la durée médiane entre le premier test RT-PCR positif et le premier test négatif était de 25 jours. Il n'y avait pas de différence démontrable avec les travailleurs de la santé qui avaient une durée médiane de 23 jours.
(Rivera-Izquierdo et coll., 2020)	Série de cas	-Professionnels de la santé symptomatiques (n=76) en Espagne -Du 11 mars au 13 avril 2020	RT-PCR	Type de prélèvements non rapporté -La durée médiane entre le début des symptômes et la PCR négative était de 31 jours. -La durée de l'excrétion virale était plus longue chez les femmes que chez les hommes (33 contre 21 jours, p=0,025) et les cas âgés de 55 ans et plus par rapport à ceux de moins de

				55 ans (33 c. 28 jours, p = 0,207).
(Warabi et coll., 2020)	Série de cas	-Cas hospitalisés (n=2) au Japon Du 30 avril au 14 mai 2020	RT-PCR	Écouvillons nasopharyngés -Le temps moyen entre l'apparition des symptômes et le moment où le virus n'est plus détectable était de 31,6 jours (fourchette de 17 à 53, ET 11,8). - Chez deux patients souffrant de retard mental et de troubles psychiatriques, la période d'excrétion virale s'est poursuivie pendant 44 jours et 53 jours, respectivement. Ces deux patients ne se sont pas brossé les dents volontairement. -Les auteurs proposent que le brossage des dents et les gargarismes éliminent l'acide nucléique viral et améliorent la précision des tests PCR.
(B. E. Young et coll., 2020b)	Série de cas	-Les 18 premiers patients diagnostiqués comme atteints du SRAS-CoV-2 à Singapour -Du 23 janvier au 3 février 2020	RT-PCR	Écouvillons nasopharyngés -L'excrétion virale a été prolongée de 7 jours ou plus chez 15 cas (83 %). -La durée médiane de l'excrétion virale du premier au dernier écouvillon nasopharyngé positif prélevé était de 12 jours (fourchette de 1 à 24), avec des charges virales décroissantes au fil du temps. - Le virus était également détectable dans les selles (4 sur 8) et le sang (1 sur 12) par PCR, mais pas dans l'urine.
(L. Zou et coll., 2020)	Série de cas	-Patients symptomatiques (n=17) en Chine -Du 7 au 26 janvier 2020	RT-PCR	Écouvillons nasaux et pharyngés -Des charges virales plus élevées (inversement par rapport à la valeur Ct) ont été détectées peu après l'apparition des symptômes, les charges virales étant plus élevées dans le nez que dans la gorge.
(Tepasse et coll., 2020)	Série de cas	-Hommes de 65 et 66 ans en Allemagne -Chronologie non communiquée	RT-PCR	Écouvillons pharyngés -Les niveaux de virus ont eu tendance à augmenter encore au cours de l'évolution de la maladie et il n'y a eu aucune indication de clairance du virus. -La virémie a atteint un pic peu avant la mort des deux patients; en outre, il n'y avait aucun signe de clairance virale à

				22 et 30 jours après l'apparition des premiers symptômes ou plutôt 22 et 26 jours après la première détection de l'ARN du SRAS-CoV-2 dans les écouvillons pharyngés.
(Wongsawat et coll., 2020)	Série de cas	-Trois cas pédiatriques en Chine -Chronologie non communiquée	RT-PCR	Écouvillons nasopharyngés et pharyngés -Les tests RT-PCR de détection de l'ARN viral se sont révélés négatifs aux jours 15, 23 et 27 de la maladie pour chaque enfant, respectivement.
(Navaneethan et LehnerNoguera, 2020)	Rapport de cas	-Femme de 43 ans ayant des antécédents médicaux de maladie de Crohn, Floride, États-Unis -Chronologie non communiquée	RT-PCR	Écouvillon nasopharyngé -Le cas a été soumis à un nouveau test RT-PCR pour détecter le SARS-CoV-2 par écouvillonnage nasopharyngé à deux reprises et s'est finalement révélé négatif, 22 jours après la présentation initiale.
(Ru et coll., 2020) *Prépublication*	Série de cas	-Cas confirmés (n=4) en Chine -Du 17 janvier au 27 avril 2020	RT-PCR	Prélèvements nasopharyngés, sanguins et de selles -La durée moyenne d'excrétion de l'ARN était de 36,5 jours, un cas ayant une excrétion allant jusqu'à 68 jours après l'apparition des symptômes. -Une clairance virale a été observée ainsi qu'un niveau élevé d'anticorps neutralisants dans trois cas. -Dans le cas de l'excrétion virale prolongée, les auteurs suggèrent que l'anticorps neutralisant n'était pas assez élevé pour éliminer complètement le virus.
(Benotmane et coll., 2020) *Prépublication*	Série de cas	-Receveurs de greffes de rein hospitalisés avec une COVID-19 non grave (n = 21) et grave (n =19) en France -Du 4 mars au 7 avril 2020	RT-PCR	Écouvillons nasopharyngés et échantillons de plasma -Dix receveurs (25 %) ont présenté une excrétion virale persistante 30 jours après l'apparition des symptômes.
(Tajima et coll., 2020)	Rapport de cas	-Un homme de 71 ans au Japon	RT-PCR	Écouvillons nasopharyngés -Bien qu'il soit devenu asymptomatique après avoir présenté

		-Du 5 février au 20 mars 2020		quelques symptômes légers de COVID-19, l'ARN du SRAS-CoV-2 a été détecté dans des échantillons de salive pendant 37 jours après l'apparition des symptômes.
(De Vriese et Reynders, 2020)	Série de cas	-Patients sous hémodialyse (n=7) en Belgique -Du 14 mars au 7 avril 2020	RT-PCR	Écouvillon nasopharyngé - Chez quatre survivants, la durée de conversion de l'acide nucléique, défini comme l'intervalle entre l'apparition des symptômes et le premier résultat négatif de RT-PCR, était de 34, 37, 37 et 44 jours. -Les valeurs seuils du cycle (une mesure inverse de la concentration en acides nucléiques) étaient les plus faibles au cours de la première semaine d'infection et sont restées relativement stables par la suite.
(Zhou et coll., 2020)	Série de cas	-Patients hématologiques concomitants à la COVID-19 (n=9) en Chine -Du 1er février au 31 mars 2020	RT-PCR	Écouvillons pharyngés -La charge virale positive chez 4 survivants a duré plus de 45 jours.
(Dong et coll., 2020)	Série de cas	-Patients hospitalisés avec des données complètes sur les sous-ensembles de lymphocytes du sang périphérique (n=18) en Chine -Du 30 janvier au 21 février 2020	RT-PCR	Échantillons respiratoires et de selles -Les cas d'excrétion d'ARN viral ≥ 15 jours ont connu une diminution significative des lymphocytes, des cellules T et de leurs sous-ensembles par rapport à ceux qui sont restés positifs pendant moins de 15 jours.
(Cai et coll., 2020)	Série de cas	-Cas pédiatriques (n=10) en Chine -Du 19 janvier au 3 février 2020	RT-PCR	Écouvillons nasopharyngés/pharyngés -Les résultats des dix patients étaient disponibles. La période infectieuse médiane entre l'apparition des symptômes et la clairance du virus était de 12 jours (fourchette de 6 à 22, IQR de

				8 à 15). Écouvillon fécal -Les écouvillons fécaux de 10 patients ont montré une période infectieuse médiane de 24 jours (de 18 à 30) entre l'apparition des symptômes et la clairance virale.
(Z. Chen et coll., 2020)	Série de cas	-Enfants hospitalisés (n=32) en Chine -Du 15 janvier au 15 mars 2020	RT-PCR	Échantillons respiratoires et fécaux -Les durées moyennes de l'ARN viral dans les échantillons respiratoires et gastro-intestinaux étaient de 15,8 jours (n=25) et 28,9 jours (n=16), respectivement. -La durée de l'excrétion de l'ARN viral dans les selles diminue considérablement avec l'âge : 39,8 jours, 27,5 jours et 20,4 jours chez les nourrissons et les enfants d'âge préscolaire, les écoliers et les adolescents respectivement.
(Park et coll., 2020)	Série de cas	-Patients hospitalisés (n=6) en Corée du Sud -Du 14 février au 26 mars 2020	RT-PCR	Écouvillons nasopharyngés/oropharyngés -Six patients ont été analysés. -La durée médiane de détection du virus du SRAS-CoV-2 après l'hospitalisation était de 34 jours (fourchette de 22 à 67). -Après résolution des symptômes/signaux, l'ARN du SRAS-CoV-2 a été détecté pendant une période médiane de 26 jours (fourchette de 9 à 48). -L'ARN a été détecté de manière persistante chez un patient jusqu'au 67^{e} jour d'hospitalisation, soit 30 jours après la disparition des symptômes. -Il s'agit de la plus longue durée de détection du SRAS-CoV-2 dans les voies respiratoires signalée à ce jour.
(J. Li et coll., 2020)	Rapport de cas	-Femme de 71 ans en Chine -Du 27 janvier au 22 avril 2020	RT-PCR	Écouvillon oropharyngé -Une femme de 71 ans a eu une excrétion virale de l'ARN du SRAS-CoV-2 pendant 60 jours après l'apparition des symptômes. -L'excrétion virale s'est poursuivie 24 jours après la disparition complète des symptômes.
(M. C. Yang et	Série de cas	-Une grappe familiale	RT-PCR	Écouvillons pharyngés

coll., 2020)		de trois générations avec 6 personnes infectées à Taïwan -Du 9 février au 6 avril 2020		-Dans cette grappe, le plus long temps de conversion de l'ARN du frottis de gorge pour le SRAS-CoV-2 était de 37 jours, et l'évolution estimée de la maladie, des symptômes au frottis de gorge négatif, était de 59 jours.
(Y. Hu et coll., 2020)	Rapport de cas	-Un homme de 70 ans en Chine -Chronologie non communiquée	RT-PCR	Écouvillons nasopharyngés et oculaires - Rapport d'un cas de la détection positive du SRAS-CoV-2 associé au virus herpès simplex de type 1 et à l'acide nucléique du virus herpès humain de type 6B dans les sécrétions lacrymales et conjonctivales d'un patient atteint de COVID-19 sans conjonctivite avec obstruction des canaux lacrymaux communs. -Les écouvillons nasopharyngés ont été positifs pendant 22 jours, mais les écouvillons oculaires sont restés positifs en continu pendant 2 semaines après que les écouvillons nasopharyngés soient devenus négatifs.
(Q. Shen et coll., 2020)	Série de cas	-Neuf patients pédiatriques (7 légers et 2 asymptomatiques) en Chine -Du 8 janvier au 19 février 2020	RT-PCR	Type de prélèvements non rapporté -6 enfants ont eu une exposition familiale et ont pu fournir les dates exactes de contact étroit avec une personne dont l'infection du COVID-19 a été confirmée.
Études épidémiologiques				
(X. He et coll., 2020)	Étude sur la recherche des contacts	-77 paires infecteur-infecté en Chine -Du 18 décembre 2019 au 5 mars 2020	Données épid.	-La dynamique virale rapportée par les auteurs (en supposant une période d'incubation de 5,2 jours en moyenne) suggère une période infectieuse qui commence 12,3 jours avant les symptômes et qui décline rapidement dans les 7 jours suivant l'apparition. -Les auteurs en ont déduit que l'infectiosité atteignait son maximum au moment de l'apparition des symptômes ou avant.
(You et coll., 2020)	Étude sur la recherche des	-169 cas en Chine -Date de fin : 31 mars	Données épid.	-Au total, 198 chaînes de transmission ainsi que les dates d'apparition des symptômes et 139 dates d'infection ont été

	contacts et modèle SIR	2020		identifiées parmi 14 829 cas confirmés. -Au total, 169 cas parmi les données collectées ont permis d'identifier les dates d'infection. -La période infectieuse a duré en moyenne 13,96 jours (ET 5,20).
(Cheng et coll., 2020)	Étude de recherche de contacts	-Cas de COVID-19 confirmés (n=100) et 2761 contacts étroits à Taiwan -Du 15 janvier au 2 avril 2020	Données épid.	-Le taux global d'attaque clinique secondaire était de 0,7 %, le taux d'attaque étant plus élevé chez les contacts dont l'exposition au cas index a commencé dans les 5 jours suivant l'apparition des symptômes que chez ceux qui ont été exposés plus tard.
Études de modélisation				
(Lin et coll., 2020)	Revue systématique des modèles dynamiques de transmission	-Cinquante-deux articles portant sur 75 modèles mathématiques ou statistiques de Chine -Du 1er décembre 2019 au 21 février 2020	Modélisé	-La période infectieuse médiane était de 9,94 jours (IQR de 3,93 à 13,50).
(Tang et coll., 2020) *Prépublication*	Modèle SEAIR	-Cumul des cas d'infection par la COVID-19 signalés en Ontario, Canada -Du 26 février au 21 avril 2020	Modélisé	-L'estimation du paramètre du taux de guérison des personnes infectées symptomatiques était de 0,1957 (ET 0,0111). -En prenant l'inverse de cette estimation, on peut déduire une période infectieuse de 5,11 jours (ET 0,31).
(Lourenco et coll., 2020) *Prépublication*	Modèle SIR	-Cas de décès au Royaume-Uni -Du 27 janvier au 16 mars 2020	Modélisé	-Étalonnage d'un modèle susceptible-infecté-rétabli (SIR) aux données sur les décès cumulés associés au SRAS-CoV-2 signalés au Royaume-Uni (UK). -La période infectieuse médiane est estimée à 3 à 5 jours (estimation postérieure du modèle).
(R. Li et coll., 2020) *Prépublication*	Modèle mathématique	-Cas documentés en Chine -Du 10 au 23 janvier	Modélisé	-Application du cadre d'interférence modèle à l'éclosion observée avant les restrictions de voyage imposées le 23 janvier 2020 – Un total de 801 cas documentés dans toute la

		2020		Chine. -La période infectieuse médiane est estimée à 3,47 jours (estimation postérieure du modèle pour les cas documentés).
(Zhu, 2020) *Prépublication*	Modèle SEIR	-Cas confirmés en Chine -Date de fin : 15 avril 2020	Modélisé	-La période infectieuse moyenne est estimée à 12,53 jours (ET±11,4). -Le paramètre a été estimé à l'aide d'une distribution de Weibull.
(Wan et coll., 2020)	Modèle SEIR	-Éclosion de Wuhan en Chine -Du 22 janvier au 12 février 2020	Modélisé	-A analysé la dynamique et la tendance de l'épidémie de nCoV-2019 à Wuhan à partir de données recueillies sur le site officiel du Comité de santé de la province d'Hubei. -Les données ont montré que la période infectieuse de la personne infectée (I) est de 14 jours.
(Peirlinck, Linka, Sahli Costabal et Kuhl, 2020)	Réseau mondial intégré et modèle SEIR	-Épidémie en Chine -Du 21 janvier au 4 avril 2020	Modélisé	-Une période infectieuse moyenne de 17,82 ±2,95 jours a été estimée à partir d'un modèle utilisant les données de cas de 30 provinces en Chine.
(Goyal et coll., 2020) *Prépublication*	Modèle mathématique	-Cas confirmés. Lieu non précisé -Chronologie non communiquée	Modélisé	-Les personnes atteintes du SRAS-CoV-2 sont généralement contagieuses pendant moins de deux jours en accord avec la charge virale maximale plusieurs jours après l'infection et cette transmission est peu probable en dessous d'une certaine charge virale.
Revues				
(Walsh et coll., 2020)	Revue systématique	-Aucune restriction sur le cadre -Études publiées entre le 30 décembre et le 12 mai 2020	Culture et RT-PCR	- Il a été conclu qu'il qu'il existe une trajectoire relativement cohérente de la charge virale du SRAS-CoV-2 durant la COVID-19 à partir d'échantillons des voies respiratoires, mais la durée de l'infectiosité reste incertaine.
(Byrne et coll., 2020) *Prépublication*	Revue de la portée et méta-analyse	-Aucune restriction sur le cadre -Études publiées entre le 1er décembre et le 1er avril 2020.	RT-PCR	-Une méta-analyse de 15 estimations a montré que la durée moyenne entre l'apparition des symptômes et 2 tests RT-PCR négatifs était de 13,4 jours (IC de 95 % : de 10,9 à 15,8), mais elle était plus courte lorsque les études portaient sur des enfants ou des cas moins graves (environ 5,8 jours de moins). -La durée maximale de détection est d'environ 20 à 49 jours, la

				durée la plus longue étant associée aux échantillons de matières fécales. -Une approche de méta-régression a montré que les cas graves avaient tendance à présenter une excrétion d'ARN viral de plus longue durée (estimée à 4,0 jours de plus), mais l'effet n'était pas significatif.
(Cevik et coll., 2020) *Prépublication*	Revue systématique et méta-analyse	-Aucune restriction sur le cadre -Études publiées entre le 1er janvier 2003 et le 6 juin 2020	Culture et RT-PCR	<u>Écouvillons respiratoires</u> -La durée moyenne d'excrétion de l'ARN du SRAS-CoV-2 dans les voies respiratoires supérieures (VRS), les voies respiratoires inférieures (VRI), les selles et le sérum était respectivement de 17,0, 14,6, 17,2 et 16,6 jours. -La durée maximale de l'excrétion de l'ARN du SRAS-CoV-2 signalée dans les VRS, VRI, les selles et le sérum était de 83, 59, 35, 42 et 60 jours, respectivement. -La durée moyenne combinée de l'excrétion de l'ARN du SRAS-CoV-2 a été positivement associée à l'âge (p=0,002), mais pas au sexe (p = 0,277). -La charge virale dans les VRS a atteint son maximum la première semaine de la maladie. -Aucune étude à ce jour n'avait mis en culture un virus actif/vivant au-delà du neuvième jour de la maladie malgré des charges virales toujours élevées.
(Santos et coll., 2020)	Revue systématique et méta-analyse	-Aucune restriction sur le cadre -Basé sur des données compilées à partir de 36 cas pédiatriques provenant d'études publiées entre le 1er janvier et le 19 avril 2020	RT-PCR	-Les enfants ont été plus nombreux à présenter une excrétion virale dans les selles après 14 jours d'apparition des symptômes que dans les échantillons respiratoires (rapport de risque = 3,2, intervalle de confiance de 95 % de 1,2 à 8,9, I2 = 51 %). -L'excrétion de l'ARN viral était plus longue dans les échantillons fécaux, avec une différence moyenne d'environ 9 jours par rapport aux échantillons respiratoires.
(Jefferson et	Revue	-Aucune restriction sur	RT-PCR	-Les auteurs ont identifié huit études qui rendent compte de la

coll., 2020) *Prépublication*	systématique	le cadre -Études publiées jusqu'au 18 août 2020		durée de l'excrétion virale telle qu'elle est évaluée par PCR de l'ARN du SRAS-CoV-2. -La durée minimale de l'excrétion de l'ARN détectée par PCR était de sept jours et la durée maximale de l'excrétion était de 35 jours après l'apparition des symptômes. Six des huit études ont fait état d'une excrétion d'ARN de plus de 14 jours.
(C. L. H. Xu et coll., 2020)	Revue systématique	-Aucune restriction sur le cadre -Basée sur les données compilées à partir de 69 cas pédiatriques provenant d'études publiées jusqu'au 8 mai 2020	RT-PCR	-La durée d'excrétion de l'ARN viral par les voies respiratoires a atteint 24 jours à partir de l'apparition des symptômes, avec une moyenne de 11,1 ± 5,8 jours. -La durée moyenne de l'excrétion virale par le tractus gastro-intestinal était de 23,6 ± 8,8 jours après l'apparition des symptômes. -Dans 89 % des cas, l'excrétion virale dans le tractus gastro-intestinal a persisté jusqu'à 4 semaines après que les écouvillons nasopharyngés ou pharyngés sont devenus négatifs.
Études sur les animaux				
(Bartlett et coll., 2020) *Prépublication*	Série de cas	-Deux tigres malaisiens, deux tigres de l'Amour et trois lions dans le zoo du Bronx, États-Unis -Mars 2020	Culture et RT-PCR	<u>Écouvillons fécaux</u> -Le cas index a libéré de l'ARN viral pendant 14 jours, dont 5 jours après la cessation des signes cliniques. -En revanche, le tigre asymptomatique ne perd son ARN viral que pendant 5 jours. -Le tigre ayant la plus longue durée d'excrétion virale (24 jours) était asymptomatique pendant cette période. -L'excrétion fécale a également été prolongée chez deux lions persistant plus de 30 jours. -Le virus a été isolé à partir des excréments de deux animaux : 5 jours après l'arrêt des signes cliniques et le dernier jour des signes cliniques.
(Munster et coll., 2020)	Essai expérimental de provocation	-Macaques rhésus adultes inoculés avec le SRAS-CoV-2 aux États-	Culture et RT-PCR	<u>Écouvillon broncho-alvéolaire</u> -Le virus infectieux a été isolé à partir du liquide de lavage bronchoalvéolaire recueilli un et trois jours après l'infection

		Unis -S.O.		chez des macaques rhésus adultes. <u>Écouvillon pharyngé</u> -Les charges virales étaient élevées dans les écouvillons pharyngés après l'inoculation. Dans un cas, les écouvillons pharyngés d'un animal se sont révélés positifs 1 et 10 jours après l'infection, mais aucun des écouvillons effectués entre ces deux dates n'a été positif. <u>Écouvillon rectal</u> -Un animal a présenté une excrétion prolongée d'ARN viral dans des écouvillons rectaux de 7 à 17 jours après l'infection, mais le virus infectieux n'a pas pu être isolé à partir de ces écouvillons.
(Gaudreault et coll., 2020) *Prépublication*	Essai expérimental de provocation	-Chats mâles (n=10) aux États-Unis -S.O.	RT-PCR	<u>Écouvillons nasaux</u> -L'ARN du SRAS-CoV-2 a été détecté dans des écouvillons nasaux des principaux chats infectés entre le 1er et le 10e jour suivant la provocation, les quantités maximales étant observées entre le 1er et le 5e jour suivant la provocation

RÉCURRENCE DE L'EXCRÉTION VIRALE EN PÉRIODE DE CONVALESCENCE

Le tableau 4 énumère les études qui fournissent des éléments de preuve de la récurrence intermittente de la détection de l'ARN viral pendant la période de convalescence (asymptomatique ou post-symptomatique) de l'infection par la COVID-19. Des rapports de cas et des études de suivi ont fait état de la récurrence de la détection de l'ARN viral chez les patients durant leur quarantaine de rétablissement après leur sortie de l'hôpital, leur ré-hospitalisation et leur nouvelle sortie de l'hôpital/rétablissement. À ce jour, une seule étude a fourni des éléments de preuve d'excrétion virale pouvant être mise en culture lors de la récurrence de la détection d'ARN viral (Quicke et coll., 2020). Aucune preuve de transmission n'a été rapportée.

La majorité des patients sortis de l'hôpital et présentant une récurrence de la positivité de l'ARN au test RT-PCR l'ont fait dans les sept jours suivant les résultats négatifs consécutifs des tests. Après une récurrence, les patients sont restés positifs à l'ARN viral pendant environ 1 à 8 jours et sont restés généralement asymptomatiques (Chen et coll., 2020; Lan et coll., 2020; McGrath et coll., 2020; Quicke et coll., 2020; To et coll., 2020b; Wong et coll., 2020; Wu et coll., 2020;Yuan et coll., 2020).

Les facteurs de risque de récurrence de la positivité de l'ARN viral comprenaient un taux élevé de cholestérol des lipoprotéines de basse densité (C-LDL) à l'admission, le nombre de lobes pulmonaires présentant des lésions d'infiltration à l'imagerie, des anomalies de l'imagerie par tomodensitométrie, la toux productive et la congestion thoracique avec dyspnée en phase de convalescence (Jin et coll., 2020; Yan et coll., 2020).

Il n'est pas clair si cette récurrence dans les résultats des tests RT-PCR indique une excrétion intermittente et prolongée de l'ARN viral ou si une récurrence (la réplication du virus recommence) ou une réinfection (une nouvelle infection se produit) est possible pendant la phase de convalescence. Cependant, des études récentes utilisant des méthodes de culture ont montré que les nouvelles détections de l'ARN viral sont associées à des niveaux de virus infectieux nuls ou très faibles (Chang et coll., 2020; Kang, 2020; Korea CDC, 2020; J. Lu et coll., 2020; Quicke et coll., 2020).

Tableau 4 : Études évaluant la récurrence de l'excrétion virale pendant la période de convalescence de l'infection par la COVID-19 (N=55)

Référence	Type d'étude	-Population et environnement -Période de temps	Période infectieuse (PI) déterminée par : Culture, Tests RT-PCR en série, données épidémiologique ou modèle	Résultats pertinents
Études sur la culture et la RT-PCR				
(Corée CDC, 2020)	Cohorte prospective	-Cas positifs à nouveau (n=285) en Corée du Sud -Jusqu'au 15 mai 2020	Culture et RT-PCR	Type de prélèvements non indiqué -Une investigation épidémiologique et une investigation sur les contacts ont été menées à bien pour 285 des 447 cas positifs. -Aucun cas secondaire parmi les contacts n'a été signalé pour les cas positifs. -Les tests de culture de cellules virales effectués sur 108 cas positifs ont tous donné des résultats négatifs. -Les valeurs seuils de cycle dans la RT-PCR pendant la période de nouvelle positivité se sont avérées supérieures à 30 dans 89,5 % des cas.
(Chang et	Cohorte	-Patients sortis d'hôpital	Culture et RT-	Écouvillons pharyngés

coll., 2020)	prospective	(n=64) en Chine -Du 28 janvier au 30 avril 2020	PCR	-Dans le cadre du suivi régulier, les patients qui sont sortis d'hôpital ont été suivis chaque semaine pour obtenir leur écouvillon pharyngé. -Quatre des patients ont été à nouveau testés positifs. -Les écouvillons pharyngés ont été envoyés pour tester la présence d'un agent pathogène vivant. Les écouvillons ont été ensemencées sur des cellules Vero pour mesurer la cytopathie et la réplication virale en utilisant la qPCR des lysats cellulaires après l'infection. Ils n'ont détecté aucune cytopathie ou présence de réplication virale dans les cellules infectées. -Les données ont également montré que les patients avec une présence persistante d'ARN viral (>16 jours) avaient des conséquences plus graves.
(J. Lu et coll., 2020) *Prépublication*	Cohorte prospective	-Patients atteints de la COVID-19 (n=619) sortis d'hôpital en Chine -Du 23 janvier au 25 février 2020	Culture et RT-PCR	<u>Échantillons respiratoires</u> -87 sur 619 cas sortis d'hôpital ont un nouveau test RT-PCR positif. -Les cas ont été testés à nouveau comme étant positifs à l'ARN viral du SRAS-CoV-2 en moyenne 6,7 jours (fourchette de 3 à 10) après leur sortie de l'hôpital. -77 sur 87 cas positifs étaient asymptomatiques et dix cas présentaient une toux sèche. -Aucune souche virale infectieuse n'a pu être obtenue par culture et aucun génome viral complet n'a pu être séquencé pour les cas à nouveau positifs.
(Quicke et coll., 2020) *Prépublication*	Étude de surveillance longitudinale	-454 personnes asymptomatiques dans 5 centres de soins infirmiers qualifiés du Colorado, aux États-Unis (la prévalence varie considérablement d'un centre à l'autre) -Chronologie non	Culture (technique par plages) et RT-PCR	<u>Écouvillons nasopharyngés</u> -Six personnes ont eu des résultats positifs récurrents après une à deux semaines d'ARN viral indétectable. Après la redétection, l'ARN viral était détectable pendant une semaine au maximum. -Ces redétections d'ARN viral ont été associées à des niveaux de virus infectieux nuls ou très faibles.

		communiquée		
(Kang, 2020)	Revue documentaire	-Patients sortis de quarantaine (n=8 922) en Corée du Sud -Du 1er au 29 avril 2020	Culture et RT-PCR	-292 (3,3 %) des 8922 patients sortis de quarantaine ont à nouveau été testés positifs. -La plus grande proportion de cas positifs se situe entre 20 et 29 ans (24 %). -Il a fallu en moyenne 13,5 jours (fourchette de 1 à 35 jours) pour avoir un test positif à nouveau après avoir été initialement déclaré négatif. -Les cas à nouveau positifs étaient asymptomatiques ou ne présentaient que des symptômes mineurs tels que toux, expectorations, fièvre et mal de gorge. -Les tests de culture étaient tous négatifs lorsque les chercheurs ont essayé de confirmer s'il y avait un virus viable dans les échantillons des cas à nouveau positifs.
(J. Zheng, Zhou et Chen, 2020) *Prépublication*	Cohorte prospective	-Patients hospitalisés (n=285) en Chine -Du 20 janvier au 14 mars 2020	RT-PCR	<u>Écouvillon nasopharyngé</u> -27 (9,5 %) des patients précédemment sortis d'hôpital ont eu un test de SRAS-CoV-2 utilisant leur écouvillon nasopharyngé positif. Les patients ont été réadmis après une durée médiane de sept jours (IQR de 5 à 8) après leur sortie initiale. -L'âge, le sexe, les antécédents épidémiologiques, les symptômes cliniques et les maladies sous-jacentes étaient similaires entre les patients qui ont connu une récurrence et ceux qui n'en ont pas connu (p>0,05). -La durée prolongée de l'excrétion de l'ARN viral et des valeurs C_t plus élevées lors de la première admission à l'hôpital ont été associées à la redétection.
(B. Yuan, Liu et Yang, 2020) *Prépublication*	Cohorte prospective	-Patients rétablis et isolés qui ont subi de nouveaux tests (n=182) en Chine -Chronologie non communiquée	RT-PCR	<u>Écouvillons nasopharyngés et anaux</u> -Vingt (10,99 %) des 182 patients ayant subi un nouveau test ont obtenu des résultats positifs. -Quatorze d'entre eux étaient positifs par écouvillonnage nasopharyngé et six par écouvillonnage anal; aucun n'était positif pour les deux écouvillonnages.

				-Les femmes sont plus nombreuses que les hommes à avoir eu un test positif (13 contre 7). -Aucun patient sévère n'a eu de test positif. -La plupart des cas ont eu des tests négatifs ultérieurement.
(Abdullah et coll., 2020)	Cohorte prospective	-Patients sortis d'hôpital (n=138) au Brunei -Chronologie non communiquée	RT-PCR	<u>Écouvillons nasopharyngés et pharyngés</u> -Sur les 138 patients sortis, 27 (19,6 %) ont eu un test positif après leur sortie. -Lors de leur réadmission, six (22,2 %) patients présentaient des symptômes légers qui se sont résolus sans traitement spécifique. -La recherche des contacts effectuée après un nouveau test positif n'a pas permis de détecter de nouveaux cas liés à ces 27 patients. - Le délai entre le résultat positif et le résultat négatif était de 7,0 ± 5,6 jours.
(Yan et coll., 2020)	Cohorte prospective	-Patients sortis de l'hôpital (n=337) en Chine -Du 23 février au 14 mars 2020	RT-PCR	<u>Écouvillons pharyngés</u> -21 sur 337 (6,2 %) des patients atteints de la COVID-19 ont eu à nouveau un test d'acide nucléique du SRAS-CoV-2 positif, et 4 sur 337 (1,2 %) patients étaient soupçonnés d'être positifs. -L'intervalle médian entre leur sortie de l'hôpital et la réactivité des acides nucléiques était de 7,5 jours (fourchette de 6 à 13 jours, IQR de 6 à 13). -Les facteurs de risque de la nouvelle réactivité des acides nucléiques comprenaient le nombre de lobes pulmonaires présentant des lésions d'infiltration (rapport de la cote [RC] 1,14; IC de 95 %, de 1,09 à 1,19), la distribution des lésions pulmonaires (RC, 0,16; IC de 95 %, de 0,13 à 0,19), des ombres irrégulières accompagnées d'une consolidation en imagerie par tomodensitométrie (RC, 9,36; IC de 95 %, de 7,84 à 11,17), des symptômes respiratoires de toux accompagnés d'expectorations (RC, 1,39; IC de 95 %, de 1,28 à 1,52) et une congestion thoracique accompagnée d'une dyspnée (RC, 1,42; IC de 95 %, de 1,28 à 1,57).
(X. Wei et	Cohorte	-Cas légers à modérés de	RT-PCR	<u>Écouvillon respiratoire</u>

coll., 2020) *Prépublication*	rétrospective	COVID-19 admis dans les hôpitaux de refuge (n=231) en Chine -Du 17 février au 7 mars 2020		-La durée médiane de conversion négative de l'ARN du SRAS-CoV-2 était plus courte dans le groupe asymptomatique (n=34) que dans le groupe symptomatique (n=197) : 15 jours (IQR de 11,5 à 17) contre 32 jours (IQR de 23 à 39), p < 0,05. -25 sur 221 (11,3 %) patients sortis de l'hôpital ont été testés à nouveau positifs pour les acides nucléiques du SRAS-CoV-2. Il n'y a pas eu de différence significative dans le taux de nouvelle réactivité des acides nucléiques ou durée de conversion négative entre le groupe symptomatique et le groupe asymptomatique.
(Miyamae et coll., 2020)	Cohorte rétrospective	-Cas asymptomatiques /mineurs (n=23) à bord du navire de croisière Diamond Princess -Du 18 au 25 février 2020	RT-PCR	Écouvillons oropharyngés et nasopharyngés -La durée médiane de l'excrétion de l'ARN viral du SRAS-CoV-2 était de 19 jours (fourchette de 6 à 37) à partir de la détection initiale du virus. -Huit cas (35 %) ont eu un autre résultat positif au test de l'ARN par RT-PCR après avoir été testés négatifs auparavant.
(Q. Hu et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients atteints de la COVID-19 confirmés (n=211) en Chine, dont 181 cas légers et modérés et 40 cas graves et critiques -Du 23 janvier au 3 mars 2020	RT-PCR	Écouvillon nasopharyngé -La concentration d'anticorps IgG et IgM du SRAS-CoV-2 et les tests d'acide nucléique positifs redétectables ont été étudiés avec les résultats des tests d'anticorps de 74 patients rétablis dans les sept jours suivant leur sortie d'hôpital. -Les écouvillons nasopharyngés ont révélé un test d'ARN du SRAS-CoV-2 positif chez jusqu'à 52,7 % des patients guéris après leur sortie de l'hôpital, et ceux-ci avaient un taux d'IgG significativement inférieur à celui des patients dont le test d'ARN était négatif (P = 0,009). -L'effet protecteur des IgG reste à étudier.
(J. Chen et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients sortis de l'hôpital (n=1067) en Chine -Du 24 février au 31 mars 2020	RT-PCR	Écouvillon pharyngé -Quatre-vingt-un (7,6 %) patients ont eu un test d'ARN du SRAS-CoV-2 positif répété dans les neuf jours (fourchette de 3 à 18) suivant leur sortie. -Pour les patients présentant une positivité récurrente à la RT-PCR, la durée médiane entre le début de la maladie et l'apparition

				d'un ARN négatif complet était de 33 jours (fourchette de 6 à 82,0). -Le délai entre le début de la maladie et sa réapparition était de 50 jours (fourchette de 21 à 95).
(Y. Zou et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés atteints de la COVID-19 (n=257) en Chine -Du 1er janvier au 10 mars 2020	RT-PCR	<u>Écouvillons pharyngés</u> -Sur 257 patients, 53 ont eu une récurrence de résultats de détections d'ARN viral positifs après avoir eu des résultats négatifs consécutifs. -Les résultats positifs récurrents des tests RT-PCR chez les patients ayant obtenu trois résultats négatifs consécutifs (5,4 %) ont diminué de manière significative par rapport à ceux des patients ayant obtenu deux résultats négatifs consécutifs (20,6 %). -Les patients ont fait état de résultats positifs au test RT-PCR dans les 1 à 12 jours suivant la date à laquelle ils ont rempli les critères de sortie d'hôpital.
(W. Zhao et coll., 2020)	Cohorte rétrospective	Enfants ayant été hospitalisés pour la COVID-19 (n=14) en Chine -Patients sortis de l'hôpital entre le 21 janvier et le 18 avril 2020	RT-PCR	<u>Écouvillon nasopharyngé</u> -Sept (50 %) enfants ont fait l'expérience d'une réactivation de l'excrétion d'ARN, dont deux ont en fait l'expérience deux fois après leur sortie. -Parmi ceux qui ont subi une réactivation de l'excrétion de l'ARN viral du SRAS-CoV-2, la durée médiane était de 14 jours (de 7 à 17 jours) entre la sortie et la première récurrence d'un test positif de dépistage du SRAS-CoV-2.
(B. M. Liu et coll., 2020)	Cohorte rétrospective	-71 cas confirmés de COVID-19 qui sont sortis de l'hôpital en Chine. Tous étaient des employés de l'hôpital ou des membres de leur famille. -Du 6 février au 26 mars 2020	RT-PCR	<u>Écouvillons oropharyngés</u> -Pendant la convalescence, les résultats de la détection de l'ARN chez 35,2 % des patients (25 sur 71) sont passés de négatifs à positifs. -La plus longue période de phase inversée de l'ARN était de 7 jours.

(To et coll., 2020)	Cohorte rétrospective	-1 patient d'une cohorte de 23 personnes à Hong Kong -Du 22 janvier au 12 février 2020	RT-PCR	Écouvillon oropharyngé postérieur -Un patient a eu des tests d'ARN viral négatifs les jours 21 et 22 après l'apparition des symptômes, avec un rebond de la positivité virale les jours 23 et 24, suivi de 5 jours de charge virale indétectable.
(J. Wu et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients atteints de la COVID 19, rétablis et ayant quitté l'hôpital (n=14) en Chine -Du 23 janvier au 30 mars 2020	RT-PCR	Écouvillon nasopharyngé -Sur les 14 patients, six (42,86 %) ont eu un test d'ARN du SRAS-CoV-2 positif après leur sortie. -Les cas présentaient une légère toux, de la diarrhée, un écoulement nasal, mais pas de fièvre à la réadmission. -Le délai de conversion positive du test RT-PCR était de 3 à 15 jours après la première sortie d'hôpital. -Le délai de conversion négative du test RT-PCR était de 1 à 16 jours (7,5 jours en moyenne) après la réadmission. -Aucune aggravation des résultats ni aucune transmission active à des contacts proches n'ont été constatées pour les contacts réadmis.
(Wong et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients sortis d'hôpital (n=106) au Brunei -Date de fin : 12 avril 2020	RT-PCR	Nasopharyngien -Sur les 106 patients qui ont subi un écouvillon de suivi entre 11 et 18 jours après leur sortie, 21 (19,8 %) se sont révélés positifs. -Un seul cas a fait état de symptômes après la sortie de l'hôpital. -Les résultats des tests RT-PCR se sont à nouveau révélés négatifs chez 16 patients dans les 1 à 3 jours suivant la réadmission. -Ces résultats suggèrent que la réinfection n'est pas plausible, mais qu'une excrétion intermittente et prolongée de l'ARN viral est plus probable. -Le taux de nouvelle positivité le plus élevé a été observé chez les patients âgés de 53 ans et plus (38,5 %), suivis de ceux présentant des conditions modérées à critiques (33,3 %) et ayant reçu un traitement au lopinavir/ritonavir (30,3 %).
(L. Wang et coll., 2020)	Cohorte rétrospective	-Patients sortis de l'hôpital (n=399) en	RT-PCR	Écouvillons respiratoires et anaux -35 patients (8,8 %) ont présenté des résultats positifs récurrents

Prépublication		Chine -Du 19 janvier au 15 mars 2020		au test RT-PCR après leur sortie. -L'intervalle médian entre le premier test RT-PCR négatif et le test RT-PCR positif récurrent était de 10 jours (IQR de 7 à 16).
(X. Chen, Shui, Li et Zhang, 2020) *Prépublication*	Cohorte rétrospective	-Patients (n=758) sortis de 17 hôpitaux en Chine -Du 25 février au 15 mars 2020	RT-PCR	Écouvillon pharyngé -59 patients (7,78 %) ont eu des résultats positifs récurrents au test RT-PCR après leur sortie. -Le délai entre l'apparition des symptômes et le dernier test positif de RT-PCR varie de 14 à 61 jours. -Le délai entre la mise en quarantaine (sortie) et les derniers résultats positifs varie de 1 à 19 jours.
(H. Cao, Ruan, Liu et Liao, 2020)	Cohorte rétrospective	-Patients atteints de la COVID-19 (n=108) en Chine -Du 10 février au 13 avril 2020	RT-PCR	Écouvillons nasaux et pharyngés -8 cas étaient des patients réadmis parce que les résultats de leur test PCR étaient à nouveau positifs après leur sortie. -Lors de leur deuxième admission, tous les cas ne présentaient aucun symptôme et avaient un scanner thoracique normal. -Deux patients sont ensuite sortis alors que six étaient encore hospitalisés au moment de la rédaction du présent rapport, car ils avaient toujours le virus. La maladie chez les deux patients avait persisté plus de 90 jours depuis l'apparition des premiers symptômes.
(S. Chen et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients sortis de l'hôpital (n=1282) en Chine -Du 14 janvier au 10 mars 2020	RT-PCR	Écouvillons nasopharyngés et anaux -Sur les 1282 patients sortis de l'hôpital qui ont participé à cette étude, 155 (12,1 %) ont été testés positifs à l'ARN du SRAS-CoV-2 pendant les 14 jours de suivi. -La durée médiane de récurrence de l'ARN du SRAS-CoV-2 était de 7 jours (IQR de 4 à 9). -Comparés au groupe négatif, les patients du groupe positif étaient plus jeunes et présentaient une proportion plus élevée de cas modérés. -Aucun des patients à nouveau positifs n'a présenté de symptômes ou d'anomalies sanguines lors de la deuxième admission à l'hôpital.

				-La durée médiane pendant laquelle tous les patients à nouveau positifs sont redevenus négatifs à l'ARN viral était de 8,0 jours (IQR de 4 à 14). -Aucun des contacts étroits (n=202) issus de patients à nouveau positifs (n=67) n'a été infecté par la COVID-19.
(Su et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients sortis de l'hôpital (n=938) en Chine -Du 18 janvier au 11 mai 2020	RT-PCR	Écouvillons nasaux et pharyngés - Sur les 938 patients ayant obtenu leur congé, 58 (6,2 %) ont retrouvé des résultats positifs au test d'acide nucléique. -Les facteurs associés aux résultats positifs étaient la coronaropathie et l'hypertension.
(L. Chen et coll., 2020) *Prépublication*	Cohorte rétrospective	-Cas confirmés (n=15) en Chine -Du 10 février au 31 mars 2020	RT-PCR	Écouvillon nasopharyngé -A examiné les données de 15 patients positifs récurrents et de 107 patients témoins atteints d'une COVID-19 modérée et non récurrente. - Le taux de récurrence des maladies positives à l'hôpital était de 1,87 %. Les patients positifs récurrents étaient significativement plus jeunes que les patients témoins, 43 ans (de 35 à 54 ans) contre 60 ans (de 43 à 69 ans) P=0,011. -La durée du séjour à l'hôpital avant la récurrence était significativement plus longue chez les patients récurrents positifs que chez les patients témoins, 36 jours (fourchette de 34 à 45) contre 15 jours (fourchette de 7 à 20) p=0,001. -Le temps nécessaire pour la première conversion des résultats de RT-PCR de positifs à négatifs était significativement plus long chez les patients récurrents positifs que chez les patients témoins, 14 jours (fourchette de 10 à 17) contre 6 jours (fourchette de 3 à 9) p=0,011. -Les taux d'anticorps sériques contre la COVID-19 étaient significativement plus faibles chez les patients récurrents positifs que chez les patients témoins.
(Mei et coll., 2020)	Cohorte rétrospective	-Patients convalescents (n=651) en Chine	RT-PCR	Écouvillons nasopharyngés et oropharyngés -Au cours du suivi, 23 (3 %) des 651 patients ont été testés positifs

		-Du 11 janvier au 4 avril 2020		lors d'un nouveau test de dépistage du SRAS-CoV-2 par RT-qPCR. -Dans ce groupe de patients testés à nouveau positifs, 12 patients (52 %) ont eu des problèmes de santé modérés, neuf (39 %) graves et deux (9 %) critiques lors de leur précédente hospitalisation. -La durée médiane entre la sortie de l'hôpital et un nouveau test positif était de 15,0 jours (fourchette de 4 à 38, IQR de 11,0 à 16,5; annexe). -Parmi ce groupe de patients testés à nouveau positifs, 15 (65 %) étaient asymptomatiques au moment du nouveau test alors que huit (35 %) présentaient au moins un symptôme associé à une COVID-19 active.
(C. Liu et coll., 2020)	Cohorte rétrospective	-Patients sortis d'hôpital (n=51) en Chine -Du 23 janvier au 28 mars 2020	RT-PCR	<u>Écouvillons oropharyngés</u> -17,6 % des patients sont sortis de l'hôpital, et seulement 33,3 % d'entre eux se sont plaints de symptômes cliniques.
(Qiao et coll., 2020)	Cohorte rétrospective	-Cas graves/critiques confirmés (n=15) en Chine -De janvier à mars 2020	RT-PCR	<u>Échantillons respiratoires</u> -La plupart des patients ne présentaient aucun symptôme clinique et les tests d'acide nucléique étaient négatifs lors du suivi après la sortie de l'hôpital. -Une patiente avait la gorge qui démangeait, son scanner a montré une ombre de densité lumineuse dans le lobe inférieur droit du poumon, et l'acide nucléique était à nouveau positif.
(Jin et coll., 2020) *Prépublication*	Cohorte rétrospective	-Patients adultes hospitalisés pour la COVID-19 (n=133) en Chine -De février au 30 avril 2020	RT-PCR	<u>Écouvillon oropharyngé</u> -32,4 % des patients étaient positifs à l'ARN du SRAS-CoV-2 après leur sortie initiale. La durée moyenne de récurrence à partir de la première sortie d'hôpital était de 18,22 jours. Après la réadmission, la durée moyenne du séjour était de 14,2 jours. -Une régression de Cox univariable et multivariable a montré que la dyslipidémie du cholestérol des lipoprotéines de basse densité (C-LDL) à l'admission était associée à la récurrence de la COVID-19 pendant la période de suivi.

(Habibzadeh et coll., 2020)	Cohorte rétrospective	-Patients (n=35) ayant l'intention de donner du plasma en Iran -Mars 2020	RT-PCR	Écouvillon nasopharyngé -Le test de réaction en chaîne de la polymérase par transcription inverse était positif chez 9 (5 hommes, 4 femmes) des 13 patients rétablis – un taux positif de près de 70 %. -Le deuxième test RT-PCR s'est révélé positif chez ces patients après une période médiane de 29 (entre 22 et 54) jours après le début de leurs symptômes/maladie et de 18 (entre 15 et 48) jours après la disparition complète de leurs symptômes.
(Bongiovanni et coll., 2020)	Cohorte rétrospective	-Patients rétablis (n=1146) en Italie -Du 9 mars au 30 juin 2020	RT-PCR	Écouvillon nasopharyngé -125 (10,9 %) ont eu une récurrence de l'infection par la COVID-19. -Le délai moyen de guérison clinique et de deux écouvillons nasopharyngés négatifs était de 27,7 jours (IC de 95 %, de 11 à 51); après cela, le délai moyen de récurrence était de 19,9 jours (de 3 à 43, IC de 95 %). -Après une période moyenne de 14,8 jours (IC de 95 %, de 6 à 36), 102 sujets (81,6 %) ont eu deux écouvillons nasopharyngés négatifs supplémentaires et ont été considérés comme cliniquement rétablis pour la deuxième fois. -Au cours du suivi, 11 patients (8,8 %) sont décédés. Les patients décédés étaient plus âgés que les autres (âge moyen 86,4 ans, IC de 95 %, de 77 à 92) et 8 d'entre eux (72,7 %) présentaient des symptômes cliniques au moment de la récurrence (4 de fièvre et 4 d'insuffisance respiratoire).
(Y. Li et coll., 2020b) *Prépublication*	Cohorte rétrospective	-Écouvillons nasaux (n=484) de patients atteints de COVID-19 en Chine -De janvier à avril 2020	RT-PCR	Écouvillons nasaux -Les taux sériques de phospholipase A2 associée aux lipoprotéines étaient significativement plus élevés chez les cas de COVID-19 à nouveau positifs que chez les patients témoins sains et les patients atteints de la COVID-19 et hospitalisés.
(Peng et coll., 2020)	Cohorte rétrospective	-Patients hospitalisés (n=79) en Chine De janvier à mai 2020	RT-PCR	Écouvillon oropharyngé -La durée médiane des résultats positifs du test d'acide nucléique (TAN) pour le SARS-CoV-2 était de 16,5 (IQR de 12,0 à 22,0) jours.

				-Deux semaines après la sortie de l'hôpital, 5,6 % des survivants ont connu une récurrence des résultats positifs du test d'acide nucléique.
(Hao et coll., 2020)	Étude cas-témoin	-Patients atteints de la COVID-19 (n=104) confirmés, avec des durées d'excrétion virale courtes et longues (cas et patients témoins) en Chine -Du 19 janvier au 3 mars 2020	RT-PCR	Écouvillons respiratoires -La durée médiane d'excrétion virale entre le diagnostic confirmé et 2 (ou plus) résultats négatifs consécutifs de test RT-PCR était de 11 jours (fourchette de 1 à 39). -Des résultats positifs récurrents de test RT-PCR dans les échantillons respiratoires après 2 (ou plus) résultats négatifs consécutifs ont été observés chez 24 patients. Les probabilités de résultats positifs de test RT-PCR lors du test suivant après un ou deux résultats négatifs consécutifs étaient de 30,5 % et 16,4 %, respectivement. Avec une augmentation de 2 à 3 résultats négatifs consécutifs, le taux de résultats positifs récurrents d'ARN par test RT-PCR a fortement diminué pour atteindre 4,8 %. -Une série de résultats négatifs consécutifs (3 ou plus) a été jugée appropriée par les auteurs comme critère pour la fin de l'excrétion de l'ARN viral.
(S. Cao et coll., 2020) *Prépublication*	Programme de dépistage dans toute la ville	-9 899 828 personnes en Chine -Du 23 janvier au 8 avril 2020	RT-PCR	Écouvillons nasopharyngés et pharyngés -107 des 34 424 patients déjà guéris ayant des antécédents de diagnostic de COVID-19 étaient de nouveau positifs (taux de rechute, 0,31 %).
(McGrath et coll., 2020) *Prépublication*	Série de cas	-4 cas de COVID-19 chez des travailleurs de la santé en Irlande -De mars à avril 2020	RT-PCR	Écouvillons nasopharyngés et oropharyngés -Ces trois cas ont tous trois connu des périodes d'auto-isolement de 14 jours avec une résolution complète des symptômes. -Chacun d'entre eux a connu des épisodes distincts de symptômes récurrents après la résolution initiale et a obtenu des résultats positifs persistants au test PCR du SRAS-CoV-2, allant jusqu'à 60 jours après le début de la maladie.
(D. Chen et coll., 2020)	Rapport de cas	-Une femme de 46 ans en Chine -Du 17 janvier au 9	RT-PCR	Écouvillon oropharyngé -Rapport d'un cas confirmé de COVID-19 dont le test de l'écouvillon oropharyngé de l'ARN du SRAS-CoV-2 s'est révélé

		février 2020		positif en convalescence. -Le 17 janvier 2020, la patiente a développé des symptômes et le 24 janvier 2020, elle a été testée positive à l'ARN du SRAS-CoV-2. -Les tests d'ARN viral ont été négatifs le 28 janvier 2020 et le 30 janvier 2020, mais sont redevenus positifs le 2 février 2020. Elle est ensuite sortie de l'hôpital le 9 février 2020.
(H. Zheng, Tan, Ma et Meng, 2020) *Prépublication*	Rapport de cas	-Femme de 37 ans en Chine -Du 12 janvier au 10 mars 2020	RT-PCR	<u>Écouvillon oropharyngé</u> -Les résultats du test RT-PCR ont été positifs pendant la première période menstruelle avant l'admission (2 février 2020). -La patiente a été hospitalisée le 4 février 2020. -Les résultats du test RT-PCR sont devenus négatifs pendant l'hospitalisation (dix et douze jours après l'admission) puis sont redevenus positifs pendant la deuxième période menstruelle (24 et 25 février 2020), qui a eu lieu après la sortie de l'hôpital. -Le test RT-PCR du 10 mars 2020 était négatif. -Les auteurs suggèrent que les hormones sexuelles pourraient jouer un rôle important dans l'infection par le SRAS-CoV-2.
(Lan et coll., 2020)	Série de cas	-Un patient hospitalisé et 3 patients (tout le personnel médical) mis en quarantaine à domicile, atteints de COVID-19 en Chine -Du 1er janvier au 15 février 2020	RT-PCR	<u>Écouvillon pharyngé</u> -Les patients ont été évalués à l'aide de tests de réaction d'amplification en chaîne par polymérase par transcription inverse en temps réel (RT-PCR) pour détecter l'acide nucléique de la COVID-19 afin de déterminer s'ils pouvaient reprendre le travail. -Après leur sortie de l'hôpital ou l'arrêt de la quarantaine, les patients ont été invités à poursuivre le protocole de quarantaine à domicile pendant 5 jours. -Les tests RT-PCR se sont révélés positifs 5 à 13 jours plus tard. Les patients ont subi trois tests répétés au cours des 4 à 5 jours suivants et tous ont été positifs bien que tous les cas soient asymptomatiques.
(J. Yuan et coll., 2020) *Prépublication*	Série de cas	-Patients sortis d'hôpital rétablis de la COVID-19 (n=25) en Chine	RT-PCR	<u>Écouvillons respiratoires</u> -Tous les cas avaient auparavant obtenu des résultats négatifs à deux tests RT-PCR consécutifs, mais ont été réhospitalisés en

		-Du 23 janvier au 21 février 2020		raison de la récurrence de l'ARN viral. -Les patients se sont présentés avec un ARN récurrent dans les 3,0 (fourchette de 2 à 7) jours suivant leur sortie de l'hôpital. La durée médiane entre leur dernier résultat négatif et leur résultat positif était de 6,0 (fourchette de 4 à 10) jours. -Tous les patients étaient asymptomatiques au moment de la récurrence. -Les cas ont été traités avec des plantes médicinales chinoises et en quelques jours, tous étaient négatifs au test d'ARN viral.
(Z. Zhang et coll., 2020) *Prépublication*	Série de cas	-56 patients atteints de la COVID-19 et présentant des symptômes à l'admission (33 ont présenté des symptômes plus tard) et 19 patients symptomatiques appariés par âge en Chine -Du 23 janvier au 1er avril 2020	RT-PCR	<u>Écouvillons respiratoires et anaux</u> -Parmi les 56 patients ne présentant pas de symptômes à l'admission, 23 sont restés asymptomatiques pendant toute la période de suivi. -Pour les cas asymptomatiques, l'ARN viral est réapparu après leur sortie (valeur C_t > 40) dans des échantillons nasopharyngés et anaux, respectivement 54 et 42 jours après l'admission initiale. -Dans les cas présymptomatiques, l'ARN viral est réapparu 81 et 40 jours après l'admission initiale et dans les cas symptomatiques, 62 et 42 jours après l'admission initiale.
(Peng, Wang, Zhang et Lu, 2020)	Série de cas	-Sept patients sortis de l'hôpital en Chine -Du 22 janvier au 8 mars 2020	RT-PCR	<u>Écouvillons de gorge et d'anus</u> -7 cas ont été testés à nouveau positifs au SRAS-CoV-2 après leur sortie. -Les 7 patients ont tous eu des séjours hospitaliers plus courts, des frais médicaux moins élevés et des symptômes plus légers lors de leur deuxième visite à l'hôpital par rapport à leur première hospitalisation.
(Loconsole et coll., 2020)	Rapport de cas	-Une femme de 46 ans en Chine -Du 17 janvier au 17 février 2020	RT-PCR	<u>Écouvillon oropharyngé</u> -Le patient a eu des résultats négatifs consécutifs aux tests les 12e et 14e jours suivant l'apparition des symptômes. -Une récurrence de la positivité virale est survenue 17 jours après l'apparition des symptômes.

				-Les résultats des tests ont de nouveau été négatifs aux jours 20, 22 et 32. -Le patient n'était pas symptomatique au moment de la récidive.
(Pan et coll., 2020) *Prépublication*	Série de cas	-Cas confirmés (n=64) en Chine -Du 23 janvier au 31 mars 2020	RT-PCR	Écouvillon pharyngé et selles -Il y a eu 64 patients confirmés et 17 patients présentent un test positif après leur sortie. -L'intervalle entre le premier test négatif et le premier test positif était de 11,82 jours (±3,42).
(J. Huang & Zheng et coll., 2020) *Prépublication*	Série de cas	-Patients (n=414) en Chine -Du 11 janvier au 23 avril 2020	RT-PCR	Écouvillons nasopharyngés -16,7 % des patients guéris ont eu des résultats PCR positifs une à trois fois, malgré une quarantaine stricte. -Les jeunes patients atteints d'un syndrome respiratoire pulmonaire léger présentaient un risque plus élevé de récidive de la positivité de la PCR.
(Martinez Alonso, Fábio de O. et coll., 2020) *Prépublication*	Rapport de cas	-Un homme de 26 ans au Brésil Du 21 avril au 18 juin 2020	RT-PCR	Écouvillons oropharyngés et nasopharyngés -Le 21 avril 2020, l'homme a eu un mal de tête sans aucun symptôme respiratoire. Deux jours plus tard, il a eu un test RT-PCR positif. -Le 5 mai 2020, l'ARN viral n'a plus été détecté. -Un mois plus tard, les symptômes sont réapparus de façon plus aiguë et comprenaient fièvre, toux, maux de tête, myalgie, arthralgie, anosmie et fatigue, et ont duré près de deux semaines. -La détection de l'ARN du SRAS-CoV-2 est devenue positive le 8 juin 2020. -Le 22 juin 2020, des anticorps IgA/IgM et IgG ont été détectés dans le sérum et seul le gène N a été détecté par RT-qPCR.
(Tian et coll., 2020)	Série de cas	-Patients convalescents (n=20) en Chine -Date de fin : 22 mai 2020	RT-PCR	Écouvillon oropharyngé -Sur 147 patients, 20 cas de convalescence (13,6 %) ont eu des tests d'ARN viral positifs dans des échantillons respiratoires 7 à 47 jours après la sortie de l'hôpital. -Tous les cas sont restés asymptomatiques.
(Dou et coll.,	Rapport de	-Un homme de 34 ans	RT-PCR	Écouvillon oropharyngé

2020)	cas	avec des antécédents de diabète de type 2 en Chine -Du 27 janvier au 13 avril 2020		-Le patient a eu une récurrence de l'acide ribonucléique (ARN) positif du SRAS-CoV-2 après sa guérison. -Malgré cela, il ne présentait aucun symptôme clinique évident et son scanner thoracique s'est amélioré. -Les membres de sa famille et d'autres contacts proches n'ont ressenti aucun symptôme.
(F. Liu et coll., 2020)	Rapport de cas	-Un homme de 35 ans en Chine -À partir du 30 janvier 2020	RT-PCR	Écouvillons nasopharyngés -Cas testé positif à l'ARN viral même après une guérison apparente (imagerie par tomodensitométrie normale, pas de symptômes cliniques, test SRAS-CoV-2 négatif sur l'échantillon des selles et test IgM sérique négatif) de la COVID-19. -L'excrétion virale a duré 65 jours et le délai entre l'apparition des symptômes et la disparition a atteint 95 jours.
(F. He et coll., 2020)	Rapport de cas	-Une femme de 39 ans atteinte de lupus érythémateux systémique en Chine -Du 21 janvier au 11 avril 2020	RT-PCR	Écouvillon pharyngé -Le 8e jour de son isolement à domicile (5 mars), des symptômes de toux sèche, d'arthralgie et de maux de tête sans fièvre sont réapparus. -Le 7 mars, ses symptômes ont disparu. Les nouveaux tests de l'ARN viral du SRAS-CoV-2 pendant 3 jours consécutifs ont tous été négatifs du 7 au 9 mars, et plus tard jusqu'au 11 avril.
(González-Calvo, Bores-García, Barba-Martín et Gallego-Lema, 2020)	Rapport de cas	-Une femme de 64 ans en Iran -Du 16 février au 22 mars 2020	RT-PCR	Écouvillon nasopharyngé -Après quelques semaines, la femme a fait une rechute, comme l'indiquent les symptômes de la méningo-encéphalite aiguë. Les résultats du test RT-PCR pour la COVID-19 de ses échantillons de liquide céphalorachidien, d'aspiration nasopharyngée et trachéale sont redevenus positifs, mais les anticorps sériques contre la COVID-19 étaient négatifs.
(Alonso et coll., 2020)	Rapport de cas	-Un homme de 26 ans au Brésil Du 21 avril au 29 juin 2020	RT-PCR	Écouvillon respiratoire -Ayant une infection légère, le patient est resté en isolement pendant 14 jours à la maison, se rétablissant 3 jours après l'apparition des symptômes. -Le 6 juin (un mois plus tard), les symptômes sont réapparus de

				manière plus aiguë et comprenaient fièvre, toux, maux de tête, myalgie, arthralgie, anosmie et fatigue, et ont duré deux semaines. La détection de l'ARN du SRAS-CoV-2 est redevenue positive le 8 juin et est restée positive lors d'un autre test le 16 juin, bien que le test des anticorps contre le SRAS-CoV-2 soit resté négatif. -Le 22 juin, des anticorps IgA/IgM et IgG ont été détectés dans le sérum et seul le gène N a été détecté par RT-qPCR et enfin, le 29 juin, plus aucun gène viral n'a été détecté. -L'absence d'anticorps détectables lors du premier épisode peut avoir permis une nouvelle infection, plutôt qu'une récurrence. Cependant, comme les auteurs n'ont pas étudié la génétique virale à différentes époques, une telle affirmation est hypothétique.
(Duggan et coll., 2020)	Rapport de cas	-Un homme de 82 ans ayant des antécédents de maladie de Parkinson avancée, de diabète insulinodépendant, de maladie rénale chronique et d'hypertension aux États-Unis -D'avril à mai 2020	RT-PCR	Type de prélèvements non rapporté -Cas présenté au service des urgences début avril avec une semaine de fièvre et d'essoufflement. -Début mai 2020, deux tests RT-PCR ultérieurs du SRAS-CoV-2 ont été négatifs et il est sorti d'hôpital. -Dix jours après sa sortie (48 jours après sa première arrivée à l'hôpital), il s'est présenté à nouveau aux urgences avec de la fièvre et de l'hypoxie et un résultat positif au test RT-PCR. -Les tests RT-PCR du SRAS-CoV-2 les 11^{e} et 12^{e} jours d'hospitalisation ont tous deux été négatifs.
(Ye et coll., 2020)	Rapport de cas	-Femme de 72 ans en Chine -À partir du 30 janvier 2020	RT-PCR	Écouvillon nasopharyngé -Le cas a été admis en isolement à l'hôpital après avoir été infecté par la COVID-19 dans le cadre d'une grappe familiale le 30 janvier 2020. -Le patient s'est rétabli et est sorti de l'hôpital le 19 février. - En raison d'une faible réponse immunitaire humorale, le patient atteint de leucémie lymphocytaire chronique n'a pas pu éliminer efficacement l'infection par le SRAS-Cov-2 et a souffert de deux récurrences au cours du suivi de 69 jours.

(Alfano et coll., 2020)	Rapport de cas	-Un homme de 72 ans atteint d'une maladie rénale en phase terminale en Italie -Mars 2020	RT-PCR	Écouvillon nasal/oropharyngé -Après 41 ans jours depuis l'infection primaire, le patient cliniquement rétabli a connu une réactivation symptomatique du SRAS-CoV-2 avec séroconversion de l'immunoglobuline M. - Il a été renvoyé chez lui le septième jour après sa réadmission avec un résultat de test PCR négatif sur l'écouvillon oropharyngé/nasal.

RÉINFECTION

Le tableau 5 énumère les études qui fournissent des éléments de preuve de réinfection par la COVID-19.

Depuis le 25 août 2020, des éléments de preuve qu'une réinfection peut se produire ont été publiés. Les analyses épidémiologiques, cliniques, sérologiques et génomiques fournissent de bonnes preuves de la réinfection chez un patient de Hong Kong 142 jours après l'infection initiale (To, Hung, et coll., 2020). Il existe également des éléments de preuve solides d'un cas de réinfection aux États-Unis (Tillet et coll., 2020). Des recherches supplémentaires sont nécessaires pour comprendre le rôle de l'immunité dans la protection contre le SRAS-CoV-2 après l'infection aiguë initiale, les caractéristiques cliniques et épidémiologiques de la réinfection, et pour savoir si les cas récurrents peuvent être infectieux et la probabilité qu'ils soient atteints d'une maladie clinique.

Tableau 5 : Études évaluant la réinfection par la COVID-19 (N=2)

Référence	**Type d'étude**	**-Population et environnement -Période de temps**	**Période infectieuse (PI) déterminée par :** **Culture, Tests RT-PCR en série, données épidémiologique ou modèle**	**Résultats pertinents**
(To, Hung et coll., 2020)	Rapport de cas	-Un homme de 33 ans à Hong Kong -De mars à août 2020	RT-PCR et séquençage du génome entier	Échantillons respiratoires -Le cas immunocompétent a eu un test positif de l'ARN viral du SRAS-CoV-2 142 jours après le premier épisode symptomatique. -Bien qu'à nouveau positif, il y avait des éléments de preuve sérologiques de l'élévation de la protéine C-réactive et de la séroconversion des IgG du SRAS-CoV-2.

				-Les génomes viraux des premier et deuxième épisodes appartenaient à des clades/lignes différentes, ce qui confirme la réinfection. Les données épidémiologiques, dont un récent voyage en Espagne, confirment les résultats virologiques.
(Tillet et coll., 2020) *Prépublication*	Rapport de cas	-Un patient de 25 ans dans le Nevada, aux États-Unis -D'avril à juin 2020	RT-PCR et séquençage du génome entier	Écouvillons nasopharyngés -Le cas a été positif pour la première fois à la mi-avril 2020, et après s'être rétabli, il est retombé malade à la fin du mois de mai 2020. -L'analyse des séquences d'acides nucléiques a montré que les virus associés à chaque cas d'infection présentaient un certain degré de discordance génétique. -Le cas peut avoir été réexposé au virus par un parent infecté.

Méthodologies :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches pour trouver la littérature sur la COVID-19 pertinente sont menées par Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et sont recoupées avec la littérature de la liste de littérature sur la COVID de l'OMS, et les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Les résultats cumulatifs de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. Le texte intégral de chaque étude qui a été étiquetée comme étant Épidémiologie, Données cliniques ou Modélisation FOCI par le groupe des sciences émergentes a été analysé pour obtenir des informations relatives à la période infectieuse de la COVID-19. Les titres et les résumés des articles ont été scannés afin de trouver les mots clés suivants : « Excrétion », « Dynamique virale », « Clairance virale », « Viable », « Culture », « Infectivité », « Détection du SRAS-CoV-2 », « Période infectieuse », « Période de transmissibilité », « Récidive » et « À nouveau positif». Cette revue contient les articles de recherche clés publiés jusqu'au 31 août 2020. Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes et les données pertinentes ont été extraites pour être incluses dans la revue.

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Emerging Evidence on COVID-19

Living Summary of SARS-CoV-2 Variants of Concern: The B.1.1.7 (Alpha) Variant Profile

Highlights up to July 1, 2021

Introduction

SARS-CoV-2 **variants of concern** (VOCs) are circulating variants that have been flagged by national or global public health organizations. VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or diagnostic detection failures (1-3). Canada has established a national definition (2). In May 2021, the World Health Organization (WHO) released a naming system for VOCs and variants of interest (VOIs) using Greek letters to improve the ease of communication on variants and potential stigma related to places where variants were first identified, which has been adopted in this report (1).

TABLE 1: CURRENT VARIANTS OF CONCERN (VOCs)*

WHO name (05-21)	Pango lineage	Nextstrain clade	GISAID clade	Alternate name	First detected in	Earliest samples	Characteristic spike mutations
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	United Kingdom	Sep 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Beta	B.1.351	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	South Africa	May 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, P.1.1. P.1.2	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brazil and Japan	Nov 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G H655Y, T1027I, V1176F
Delta	B.1.617.2 AY.1 AY.2 AY.3	21A	G/478K.V1		India	Oct 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R,

							del157/158, T478K, D950N)

* A VOC/VOI lexicon and other resources are available in the appendix.

The goal of this living summary on the SARS-CoV-2 VOC literature is to highlight new data on the B.1.1.7 (Alpha) variant, its epidemiology and how the attributes of the VOC may impact the management of the pandemic. This living evidence profile on Alpha is part of a larger project that summarizes the data on each VOC as well as captures data on variants of interest (VOIs). The focus will be on changes to epidemiological parameters (e.g., transmission rates, clinical outcomes of severity and mortality, shifts in age groups affected or asymptomatic proportions), impacts on diagnostic tests, immune evasion/vaccine effectiveness and impacts on other public health measures. The full dataset in Excel can be accessed here and filtered by the VOCs and VOIs of interest. The recent living evidence reviews on other VOCs (Beta, Gamma and Delta) and a high level contrasting table of VOC evidence can be requested here.

In this summary, "original variant" refers to any variant that was not designated as a VOC or VOI.

What's New

This update includes literature up to July 1, 2021. A total of 200 new studies on B.1.1.7 (Alpha) were identified since the last update on June 1, 2021 and are included in the dataset.

- In Canada, the national proportion of Alpha cases have continued to decline and was surpassed by Delta the week of June 13th, 2021 (37% vs 41%) (4). Studies in the UK, India, USA and Japan have also reported that Delta has replaced Alpha cases and become the dominant variant (5-15).

Key Points

As of July 1, 2021 there were 543 studies that reported on the Alpha variant. This summary considered 293 studies for inclusion that focused on transmission efficiency (n=57), clinical severity (n=54), immune escape (n=30), diagnostic performance (n=46), variant spread (n=153), and other epidemiological research (n=4). Studies not summarized in the evidence profiles (n=250): case reports or case series (n=21), point prevalence estimates (n=2), animal studies (n=40), zoonotic investigations (n=3), predictive models in which the time period has already passed (n=4), and cell infectivity, binding affinity, or genomic characterization studies (n=62), and *in vitro* studies looking at neutralization by convalescent and/or vaccinated sera (n=83), and therapeutic products (n=48).

However, details for all 543 studies can be found in the Excel dataset accessed here.

Transmissibility:

- Ninety-one percent of studies that assessed transmissibility, reported increased transmissibility of the Alpha variant (Table 2) compared to the original variant (34-118%) with large variation that can be attributed to stringency of restrictive public health measures, increasing vaccination coverage as well as the local epidemiology and other VOCs in circulation.

- In Canada, general population surveillance data reported 34% between December 2020 and March 2021 (16) and 63% between March and April 2021increased transmissibility for Alpha compared to the original variants (17). Canadian household transmission studies reported 31% higher secondary attack rates (SAR) for Alpha compared to non-VOCs in February 2021 (18) and higher SAR for Alpha compared to the original variant (24.3% vs 20.2%)between March and April 2021 (19).

Variant Spread:

- Surveillance data from the UK and the US reported that following an increase from December 2020 to March 2021, Alpha infections plateaued in April 2021 and dropped rapidly by June with the rise of the Delta variant (10, 14). A predictive model forecasting variants in North America, reported Alpha cases are expected to reach close to 0% by October 2021 and remain stable (20).

Clinical Severity:

- There was conflicting evidence on the odds of being admitted to hospital and ICU admissions with Alpha compared to the original variant. Risk of mechanical ventilation or higher severity score in the ICU was not associated with Alpha compared to the original variant. However, these data are based on a limited number of retrospective studies that analysed surveillance and hospital data.
- Indicators of changes in severity with the Alpha variant were not consistent, some reported age-stratified risk of hospitalization and increased odds in adult age groups between 20-59 years old compared to the original variant, while others reported no associations**.**
- Associations with mortality were conflicting across studies for Alpha infections.
- Ninety-six percent of studies that assessed viral load, reported that it was consistently 2-10 fold higher for Alpha compared to the original variant.
- A longer infectious period for Alpha compared to the original variant has been reported in three studies although the magnitude of the increase is highly variable across studies ranging from 0.86 days to 5.1 days (21-23). Further evidence is needed to improve confidence in this result. One small retrospective cohort in Japan that included Alpha cases (n=30) from March 2020 to March 2021 reported the mean incubation period of Alpha was shorter compared to the original variant (3.53 vs 5.71 days) (24). As well, surveillance in the UK estimated the median incubation period for Alpha was 4 days in March-June 2021 (25). Further evidence is needed to improve confidence in this result.

Immune Escape:

- Three reinfection studies from the UK and the US reported low reinfection rates of 0.7% for Alpha and is comparable to the original variant (26-28).
- Most vaccine effectiveness studies comparing the Alpha variant with the original variant have reported reduced protection after the first dose of mRNA (BNT162b2 (Pfizer) and mRNA-1273 (Moderna)) and ChAdOx1 (AstraZeneca) vaccines, but equivalent protection after the second dose of vaccine.

- An Alpha outbreak study at a long-term care facility in Germany 7 days post two doses of BNT162b2 (Pfizer), reported that the infectious period of those with COVID-19 was significantly shorter for fully vaccinated patients than in unvaccinated patients (7.5 vs 31 days) and viral load was lower in vaccinated patients, but not statistically significant (6.45 vs. 8.15 log10 copies/mL) (29).

Other Categories:

- Additional categories related to diagnostic performance and epidemiological research on spread and impact of public health measures are summarized in Table 2.
    - No studies evaluating diagnostic or detection tests for SARS-CoV-2 described failure or performance issues for detecting the VOCs, besides the well characterized S-gene drop out for Alpha.
    - Several predictive models studies reported on public health measures (e.g. restrictions to gatherings, closures, masking and lockdowns, and vaccinations) and conclude that higher stringency, more closures and restrictions, and higher vaccine coverage were needed to control Alpha due to higher transmissibility.
    - Studies on VOC introduction and spread in a geographic region as well as risk factors for spread were also reported.

Overview of the Evidence

Study designs included in this summary ranged from low risk of bias double blinded RCTs to a number of different observational study designs with varying levels of evidence. The observational studies offer low to moderate evidence depending on the specific study design and consistency across studies. Descriptive studies included in this report such as case series and case reports, predictive models, ecological studies, animal models and *in vitro* studies are low to very low evidence and generally can only be used to generate hypotheses that need to be further examined with a different study design. Given this very wide variation, an indication in the level of confidence of the evidence is provided for a particular outcome. Study designs are provided, but no formal risk of bias assessment has been conducted.

There are several knowledge gaps or areas where there is very little research noted in the key points table and additional research is needed to improve confidence in summary results and to fill in current knowledge gaps regarding the Alpha variant.

CONTENTS

ALPHA

The detailed evidence profile developed for the Alpha variant is reported below (Table 2). It covers data on transmission efficiency, clinical severity, immune escape, testing and diagnostics, and other epidemiological studies including VOC spread. The excel dataset includes summaries of all the individual studies on the Alpha variant and can be accessed here.

Categories of evidence in the tables below include the following if reported:

Transmissibility includes changes in transmissibility, secondary attack rates, and estimates of selective advantage.

Clinical Severity includes proportion of infections that are symptomatic, proportion of severe disease and mortality as well as risk factors for severe disease or mortality, viral load, infectious period, incubation period. Note risk factors for severe disease would include special populations e.g. persons who are pregnant if they are reported.

Immune Escape includes changes to vaccine efficacy, risk of re-infection in humans, animal models, *in vitro* or *in silico* experiments as well as impacts on therapeutics if reported.

Diagnostic / Detection Test Failure is captured in the individual sections, and will only be included in Table 2 if there is a concern about test performance.

Other Epidemiology includes all studies that document the emergence and spread of VOCs in a geographic area, ecological studies that examine VOC spread and risk factors for hot spots, and studies on effective public health interventions against VOCs, genomic epidemiology as subcategories.

Table 2: Evidence Profile of Alpha VOC (n=293)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency (n=57)		
Transmissibility Compared to Original Variant	Across studies, estimates of the increased relative transmissibility of Alpha (1-$R_{voc}/R_{original\ variant}$) were 34-118% higher: • Canada: 34% (95%CI: 31-38) (16), 63% (95%CI 28%-108%) (17). • UK: 50-100% (30), 75% (95% CrI 70–80%) (31), 52% (95% CI 46 – 58%) (32), 43-90% (CrI range: 38-130%) (33), 44-55% (95%CI 38-61%) (34), 50% (35), 83-118% (71-140%) across the UK (36), 13.4-41.3% across UK regions in Dec 2020 (37), higher transmissibility 62% (95%CI 59%-65%) to 45% (95%CI 43%-48%) (6) and a 0.3 unit higher reproduction number compared to other lineages (38).	This section is informed by 46 observational studies including analysis of surveillance data, cross sectional, outbreak investigations, retrospective cohort, ecological studies, and predictive models. There is agreement that Alpha is more transmissible and there is a fair amount of overlap in

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• Europe: France 41% (95%CI 38-44) (39) and 52% (95%CrI 54-66%) (40), Denmark 55% (CrI 45–66%) (33) and 58% (95%CI 56-60%) (41), Switzerland 74% (CrI 66–82%) (33) and 54% (95%CI 49-65%) (42) and 37% (95%CI: 25–63%) (23), Norway 24% (95%CI 0-52%) (43), Italy 55-57% (95%CI 45-66%) (44), Wales and the USA 65-72% (46-104%) (36). • USA: 59% (CrI 56–63%) (33), 35-46% (45). • Israel: 45% (95%CI 20-60) (46). • Japan: estimated a 60% increase in relative transmissibility of VOCs (not specified) (47) and 45% for Alpha in another study (15). Some studies did not provide enough data to calculate transmission efficiency, but indicated that it was higher (26, 48, 49). Other studies indicated transmissibility decreased over time (30, 49, 50) or remain unaffected (51), which may be associated with lockdown stringency or increasing vaccinations (23, 51, 52). Estimates from the UK were higher than other countries (36). In studies with multiple VOCs in circulation, Alpha had higher transmissibility than Beta or Gamma (49), except in one study from France that reported a transmission advantage of Beta over Alpha (53).	the estimates of magnitude. Transmissibility estimates may be impacted by the stringency of restrictive public health measures and increasing vaccination coverage as well as the local epidemiology and other VOCs in circulation. These studies are at risk of selection, information and confounding biases that have been inconsistently adjusted for across studies. Low level of evidence.
Selective Advantage Compared to Original Variant	• A model of selective advantage found Alpha was estimated to have a selective advantage of 0.337 (0.336-0.339) over original variants in the UK (54).	One predictive model. Low level of evidence.
Secondary Attack Rate Compared to Original Variant	• Canadian household transmission studies reported Alpha had a secondary attack rate (SAR) that was RR=1.31(95%CI 1.14-1.49) times higher than non VOCs and the risk of transmission was accentuated for asymptomatic index cases (RR=1.91, 95% CI 0.96-3.80) and presymptomatic cases (RR=3.41, 95%CI 1.13-10.26) (18). In a another study the SAR was 20% higher for household transmission from Alpha cases compared to the original variant (24.3% vs 20.2%) (17). • SAR in households was 60% (20%-114%) more transmissible in Norway (43), 50-70% higher transmission in Denmark (55), 37% (95%CI 28-47) in Germany and was similar for child 32% and adult 39% index cases (56), 88% (95%CI 67-108) in the UK (57).	Seven studies of household transmission including an outbreak in a kindergarten classes. The ratio of secondary attack rates was also provided as a measure of higher transmissibility for Alpha in some studies based on contact tracing studies. The results were conflicting across the studies summarized. These studies include four surveillance data analysis,

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	In Israel transmission in households due to Alpha was increased by 60% (95%CI 20-110) for adults and 150% (95%CI 60-300) for children compared to spring 2020 original variant SARs (58).	two outbreak investigations, and one retrospective study. Low level of evidence.
Public Health Measures Compared to Original Variant	Stringency: • UK: December 2020 had the highest values of Rt (~1.8) in areas with the least restrictions, lowest values in areas with the highest restrictions and lockdowns effectively reduced Rt by ~0.9 by March 2021 (6). • Canada: A predictive model of the Alpha variant conducted in January 2021 examined various levels of restrictions and school closures. It assumed transmission rates were 50% higher in children and 70% higher in adults compared with the original variant. Compared to restrictive lockdown, cases were estimated to be 3 times greater in Toronto with schools closed and community opened under moderate restrictions, 7 times higher if schools were closed, and 7.5 times higher if schools are open and the community was under light restrictions (59). • Portugal: A predictive model that assumed 50% increased transmission with Alpha and does not include Delta, reported that the scenario with partial lifting of measures and on-going vaccinations reduces R to less than 1 by June 2021 and does not lead to significant rise in hospitalization between April 2021 and January 2022, whereas other scenarios that involve faster lifting of PHMs resulted in higher cases and hospitalizations (60). • A Susceptible-Exposed-Infectious-Recovered (SEIR) model based on the situation in France described the inability of non-pharmaceutical interventions such as curfew and physical distancing measures to reduce the Ro of Alpha under 1, when the same interventions were successful against original variants (61). • An age-stratified regionally structured transmission model to control the transmission of Alpha estimated that adherence to short stricter lockdowns would result in decreased hospital admissions and a moderate lockdown would reduce distress and improve sustainability (62).	14 studies reported public health measures. The majority of studies were predictive models, with 1 ecological study, and 3 surveillance data analyses. Predictive models are excellent tools to compare options, but caution should be exercised when extrapolating results beyond comparing model scenarios. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	Quarantine: • A model examining quarantine and test scenarios to control importations of SARS-CoV-2 in the EU reported Alpha did not change how effective quarantine and test strategies are (63). Personal Protective Measures: • US: A predictive model explores the impact of mask use for both source control and user protection using transmission data for the original variant and alpha. The model finds that the basic Ro of 2.5 could be decreased to Re<1.0 and Ro of 4 decreased to Re~1.6 for the original variant and Alpha respectively, suggesting masks are an effective PHM (64). • Germany: A predictive disease transmission model that estimated work place transmission risk found that the transmission rate of Alpha was 0.014 per proximity contact which is 3 times higher than the original variant. With mask use the risk is still 2 times larger than the original variant (65). Vaccination: • Vaccine strategies were examined considering the higher transmissibility of Alpha and predicted that even with 100% of the population fully vaccinated with ChadOx1 vaccine (AstraZeneca), R value would only reduce to 1.33 with 100% of the population vaccinated and could increase to 1.98 if 79% is vaccinated. The BNT162b2 (Pfizer) vaccine would require 81.9% of the population to be vaccinated to reduce the value of R to 1 (52). • A predictive model showed decreased transmission of Alpha with increased vaccination coverage had the greatest effect once transmission was already decreasing through public health mitigation strategies (66). • A predictive model in the US forecasted data from June 2021 to May 2022 which assumed 59% increased transmissibility of Alpha, 88.5% vaccine effectiveness with ≥1 dose, and included the impact of the Delta variant. This model reported that restoring social activity to pre-pandemic levels with increasing vaccination coverage (60% to 70%) would still result in epidemic control measured by decreased infections and deaths (67).	

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Infection, Prevention, and Control Measures	• One study reported Alpha was susceptible to heat, from 45°C TCID50/mL after 60 min and titres decreased from 8.5 to 1.5 and at 60 °C and after 10 minutes and titres decreased from 8.5 to 0.5 (68), and another study reported decrease in viral titres within 30 minutes of exposure to heat at 56°C (69). • Two studies assessed susceptibility of Alpha to irradiation: Alpha was highly susceptible to UV-C irradiation, decreasing from 8.5 to 0.5 log10 TCID50n/mL after 30 min of exposure (68), and another study reported infectious titer reduction rate for Alpha was 96.3% after exposure to continuous deep-ultraviolet light-emitting diode irradiation for 1 second and the rate increased to 99.9% after irradiation for 5 seconds (70). • Alpha was efficiently inactivated by treatment with at least 30 % (v/v) ethanol for 30 seconds or after exposure to soap for 1 - 5 minutes (69). • Another study reported Alpha was susceptible to heat and UV irradiation at increasing temperatures and durations (68).	Four in vitro studies of infection, prevention and control measures. Low level of evidence.
Clinical Severity (n=54)		
Virulence / Severity or Duration of Disease Compared to Original Variant	• Conflicting evidence on whether Alpha results in more asymptomatic infections: Prevalence of symptomatic disease was the same in an Italian study (71). Symptomatic proportion: Alpha cases, 72.6% (5,365/7,390) vs. original variant cases (81.4%; 547/672; p < 0.001) (72). Majority of studies reported higher hospitalizations rates with Alpha infection: • Higher hospitalizations with Alpha (11% vs. 7.5% p<0.001) (72); (5.8% vs 4.1% p=0.04) (27). Higher hospital admission 2.39% during the Alpha wave vs. 1.55% in the initial wave in Spain (73). • Higher odds of Alpha cases being admitted to hospital compared to original variant (aOR 1.7, 95%CI 1.0-2.9) (72); OR 1.64 (95%CI 1.32-2.04) (74); OR 1.25 (95%CI 1.22 - 1.28) (74); (OR 1.36 95%CI 1.16-1.60, p=0.0002) (75); OR 2.25 (95% CI 2.10-2.40) (76). The hazard ratio for hospitalization due to Alpha vs. original variant (aHR 1.34, 95%CI 1.07-1.66) and length of stay was similar in both groups p=0.07 (77).	25 studies on severity, these included surveillance data analysis, outbreak investigations, ecological studies, prospective cohorts, retrospective cohorts, and cross sectional studies, most of which have been conducted in the UK. Moderate level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• A study in Czech Republic reported no change in hospitalizations (78). Higher ICU admissions with Alpha infection was reported in most studies: • ICU admission was 1.4% for Alpha vs original variant 0.6% p=0.002, or a higher odds of ICU admission for Alpha of aOR 2.3 (95%CI 1.4-3.5) (72). • OR 3.31 (95%CI 2.84-3.86) (76); aHR: 2.15 (95%CI 1.75 - 2.65) (79). • Among hospitalized cases there was higher odds of ICU admission (OR 2.56) (76). • One study reported no association in intensive care admission with Alpha HR 1.01 (95% CI 0.75-1.37, P=0.94), thus the risk was the same as the original variant (80). • Among hospitalized cases there was no association between severe disease and death among Alpha vs. original variants, adjusted PR 1·02 (95%CI: 0·76–1·38) (81); ICU scores or mechanical ventilation requirements (82); or mechanical ventilation support (oxygen therapy, mechanical ventilation) (p=0.265) (83). Symptoms: • Two studies reported higher rates of hypoxia (70.0% vs 62.5%, p=0.029) and respiration (p=0.001) in patients with the Alpha variant (84, 85). • One study found fever over 38°C was significantly higher among hospital patients infected with the Alpha variant vs. the original variant (46% vs 22%, p=0.015) (86). • One study found that a sore throat was more frequent: OR 1.6 (95% CI: 1.0–2.6), and anosmia or ageusia were less frequent OR 0.5 (95% CI: 0.3–0.9) (87) in those with the Alpha variant. • Another study reported longer (≥7 days) symptom duration (p=0.02) in Alpha cases compared to the original variant (87).	
Severity Risk Factors Compared to Original Variant	There was no agreement across studies on whether ethnicity or gender were risk factors for Alpha infection severity, however several studies identify higher risk in certain age groups (with a lot of variability) and that individuals infected with Alpha were less likely to have comorbidities:	14 studies on severity risk factors. These included surveillance data analysis, prospective cohorts, retrospective cohorts, and cross sectional studies,

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• Two studies reported no significant difference in patient age, gender and median length of hospital stay (75, 82). • Three studies showed a small but significant age difference (37 vs. 39 years) (88), (37 vs 38 years) (76), and (58 vs 64 years) (78). • Another study found increased risk of hospitalization with age: HR of 0.93-1.21 in patients younger than 20, HR 1.29 aged 20-29 and HR 1.45-1.65 in those over 30 years (74). • In the age-stratified models, Alpha cases in the age groups 20–39 and 40–59 years had, respectively, 3.0 and 2.3 times higher odds of hospitalisation when compared with original variant cases (72). Pre-existing conditions were lower with Alpha, vs original variant, (44.8% vs. 89% p<0.001) (72). • A prospective cohort study in hospital patients identified a statistically significant difference in the age of those infected with the Alpha variant (39 years, IQR: 30.50 - 62.50) compared to those infected with the B.1.470 non-variant (31 years, IQR: 27.50 - 41.00) (P = 0.014) (86). • A hospital cohort between Dec 2020 - Jan 2021 in France describes younger patients (63% >65 years dropped to 50%) with a mean age of 59.2 down from 70.7, patients without comorbidities increased from 16% to 42% (p=0.007) (85). • A study of hospitalized COVID-19 cases reported a higher proportion of females with Alpha (48.0% vs 41.8%, p=0.01), fewer frail patients (14.5% vs 22.4% p=0.001) and higher proportions of obese cases (30.2% v 24.8%, p=0.048), but no difference by age or ethnicity (84). • For intensive care admission, there were no significant associations between Alpha and ethnic group (p = 0.09), lower risk in pregnant women HR 0.13 (95% CI 0.02 to 0.98, P=0.048), higher risk with male sex HR 1.33 (1.05-1.68; P=0.02), strongly associated with higher age, and higher with one or more comorbidities: HR: R 1.25 (0.92-1.71) for one comorbidity, 1.24 (0.89-1.74) for two and 0.79 (0.54-1.15) for ≥three vs none; P=0.03) (80). • A Canadian study on VOCs (predominately Alpha during the study period) reported hospitalized cases were	most of which have been conducted in the UK. Moderate level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	younger (59 vs 64 years) and were more likely to be male (57% vs. 52%) (76). Compared to females, male VOC cases had a larger increase in the odds of hospitalization (OR 3.11, 2.83-3.41 vs OR 1.63, 1.49-1.79) and ICU admission (OR 7.35, 5.68-9.52 vs OR 1.86, 1.51-2.30) (76).	
Mortality Compared to Original Variant	There is conflicting evidence on the association of mortality and Alpha infection: • Seven studies reported no significant difference in mortality overall: Italy (2.1 vs. 4.1%) (71), USA (27, 75), UK 1.01 (95% CI: 0.79-1.28, p=0.94) (80), and no association with 28 day mortality in UK (OR: 0.90, 95%CI 0.57-1.41, p=0.64) (77), no significant difference in 28-day mortality in UK (32.1% vs 20.7%, p=0.326) (83), or 60-day mortality in the UK (89), or case fatality (OR= 1.37; CI: 0.5808-3.215, p = 0.52) (78). • Two studies report Alpha had a lower odds of mortality compared to original variant in the multivariable analysis (aOR 0.5, 95%CI 0.3-0.9) (72), lower risk of mortality in care home residents HR 0.52 (95% CI: 0.27-1.02) (80). • Eleven studies reported higher risk of mortality: higher odds of mortality OR 1.75 (95% CI 1.47-2.09) (76), higher among hospitalized cases OR 1.62 (95% CI 1.23-2.15) (76), higher 28-day hazard of death (55%, 95% CI: 39-72%) (90), aHR 1.65 (95%CI 1.36-2.01) (79), aHR 1.67 (95%CI 1.34 – 2.09; P <0.0001) (81), aHR 1.59 (1.44 to 1.74) (74). HR 1.64 (95%CI 1.32 - 2.04, p <0.001) (91), which equates to an increase of 2.5 to 4.1 deaths per 1000 detected cases (73, 92, 93). The meta-analysis of these four studies had a pooled mortality risk of HR=1.45 (95%CI 1.18-1.78) (94). An ecological studies from the UK estimates that Alpha is 33% more lethal (95).	19 studies reported on mortality these included surveillance data analysis, ecological studies, prospective cohorts, retrospective cohorts, and cross sectional studies, most of which have been conducted in the UK. Moderate level of evidence.
Mortality Risk Factors Compared to Original Variant	There was no agreement across studies on whether any risk factors were associated with Alpha mortality risk including age, and sex, and ethnicity, but one study did report that Alpha infections with more comorbidities were at higher risk. • One study found mortality was higher in younger age groups than older age groups (59.0% in 1-34 year olds vs 55.4% in those 85 or older) and was higher among Blacks (69.6%), mixed or unknown ethnicity (64.8%), White (58.0%) and Asian (57.6%) (90).	Two studies which include surveillance data analysis, a retrospective cohort. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• No significant associations between Alpha and sex (p = 0.35), ethnic group (p = 0.75) or age group (p = 0.30) (79). • Male sex was a risk factor HR 1.46 (95% CI: 1.22-1.75, p<0.001, age was strongly associated, higher risk with one or more comorbidities: HR: 1.78 (95% CI: 1.26-2.52) for one comorbidity, HR: 2.03 (95% CI: 1.43-2.88) for two comorbidities, and HR: 2.89 (95% CI: 2.04-4.08) for three comorbidities; p < 0.001), and ethnicity was not associated (p=0.36) (80).	
Viral Load Compared to Original Variant	• Several studies measured viral load as Ct or estimated copies/mL for different target proteins (usually N and ORF1ab). They consistently indicate that Alpha samples are more likely to have lower Ct values or higher estimated viral loads. The median order of magnitude higher varies across studies and target protein from 2 to 10-fold differences (21, 23, 38, 39, 71, 75, 78, 86-88, 96-99, 99-103). • One study reported no significant difference in Ct values between Alpha and the original variant (median 20.2 vs. 20.1; OR = 0.1, 95% CI: −0.9 to 1.6) (87).	28 studies that were mainly surveillance data analyses, cohort or cross sectional studies that analysed the PCR Ct values across Alpha samples and original variant samples. This measure is indirect and all study designs are observational, however the conclusion that Alpha cases have lower Ct values (indicative of higher viral loads) was consistent across the majority of studies. Low to moderate level of evidence.
Animal Model of Viral Load Compared to Original Variant and Other VOCs/VOIs	• Studies in hamsters, ferrets, and rhesus macaques identified higher viral loads of genomic RNA in the nasal mucosa of Alpha infected animals compared to those infected with the original variant, or Beta variant (104-107). • A mouse model identified viral load was significantly lower for the Alpha virus in the lungs of infected mice compared to Beta and Gamma viruses in both C57BL/6 and BALB/c lungs, with no infectious virus detected in the BALB/c lungs (108). Studies in hamsters and rhesus	Seven animal model studies in agreement offer consistent evidence of decreased viral load in lungs and increased viral loads in nasal mucosa. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	macaques identified viral antigens in lung tissues were lower compared to the original variant (105, 106)	
Infectious Period	Alpha cases had a longer infectious period compared to other variants. • A small prospective study in the USA that included Alpha cases (n=7) between November 2020 and January 2021, reported average infections last 13.3 days compared with 8.2 days for other variants (21). • A surveillance study that included data from Niger, Brazil, USA, France, and Japan between February until April 2021, reported Alpha had a longer infectious period with a median increase in the duration of the decline phase of the virus load of 0.86 days (HR 0.81, 95%CI: [0.75-0.88]) (22). • A surveillance study that included data from Switzerland and South Africa between October 2020 and March 2021, reported 51% (95% CI: 32–80%) increase of the infectious duration (23).	One small prospective cohort, one large longitudinal study, and one surveillance data analysis. This outcome needs further evaluation with a larger sample size and range of cases. Low level of evidence.
Incubation Period	• A retrospective cohort that included Alpha cases (n=30) between March 2020 and March 2021 reported the mean (median) incubation period of Alpha was shorter compared to the original variant (3.53 (3.0) days vs 5.71 (5.0) days. The incubation period for Alpha in close-contact environments was 0.62 times shorter than other strains (95% CI: 0.47, 0.82) after adjusting for age and sex (24).	One small retrospective cohort. This outcome needs further evaluation with a larger sample size and range of cases. Very low level of evidence.
Immune Escape - Re-infection and Impact on Vaccine Efficacy (n=30)		
Re-infection from Infection Compared to Original Variant	Three studies estimate the rate of re-infection. A study in the UK identified re-infection of 0.7% (95%CI: 0.6-0.8) (26) and in the USA previous seropositivity rate for persons with Alpha was 0.7% compared to original variant infections at 0.9% (27). A prospective study in the UK HCWs reported there was no evidence that Alpha changed the extent of protection from any PCR positive infection in those who were seropositive (aIRR 0.40, 95%CI 0.10-1.64, p=0.20) (28).	Three re-infection studies have included analysis on Alpha and are in agreement that Alpha does not evade natural immunity. These include surveillance data analysis, cohort and ecological studies. Moderate level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Animal Model of Re-infection Compared to Original Variant	Hamsters infected with original SARS-CoV-2 and recovered were all protected from re-infection with Alpha (106, 109).	Two animal models reported consistent findings and support the evidence documented in human and *in vitro* studies. Low level of evidence.
***In vitro* studies Convalescent Sera** Compared to Original Variant	The majority of *in vitro* studies consistently showed minimal or small reductions in neutralization of Alpha compared to an original variant. Studies can be found in the dataset. There is consistency in the findings, the evidence is obtained from low quality studies.	There are many *in vitro* studies and this list is not complete at this time. Low level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness (VE) Compared to Original Variant	Breakthrough: • Prospective and surveillance studies also report breakthrough infections were not more common 1.29 fold (95%CI 0.75-2.20, p=0.468) with Alpha cases in the USA after mRNA-1273 (Moderna) or BNT162b2 (Pfizer) (110), higher aOR 2.4 (95%CI 1.2-5.1) between first dose and up to 14 days after the second dose of BNT162b2 (Pfizer) in Israel (111), and fewer following the first dose of ChAdOx1 (AstraZeneca) aHR 0·32 (0·15-0·66) and of BNT162b2 (Pfizer) aHR 0·35 (0·17, 0·71) vaccines at 35-48 days in the UK (112) compared to unvaccinated individuals. Vaccination 1 dose: Vaccine effectiveness (VE) studies have reported protection against symptomatic and asymptomatic Alpha infection and reduced risk of hospitalization after the first dose of vaccines for Alpha infection compared to unvaccinated individuals • In a prospective UK HCW study, there was no evidence that Alpha changed the extent of protection afforded against symptomatic or asymptomatic infection by the first vaccine dose of ChAdOx-1 (AstraZeneca) or BNT162b2 (Pfizer) VE 64-67%, compared to the original variant (aIRR=1.84, 95%CI 0.75-4.49, p=0.18) (28). • In a prospective study in the UK after the first dose of ChAdOx-1 (AstraZeneca) or BNT162b2 (Pfizer), VE was 62% (23-81%) at 35-48 days (112).	27 studies reported on breakthrough infection after vaccination or VE. The generalizability depends on the representativeness of the evidence to the general population. Consistent findings across studies improves the certainty in the results. These studies include RCTs, prospective cohorts, retrospective cohorts, outbreak investigations, predictive models, case-control studies, longitudinal studies, and surveillance data analysis. High level of evidence for RCTs cohort studies, moderate evidence for prospective cohort studies and low level of evidence for all other study designs. Overall, moderate to high level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• In the UK, VE after the first dose of BNT162b2 (Pfizer) in adults aged 70 +, VE was 60% at 28-34 days (113), adjusted VE was 71.4% (95%CI 46.5-90.6) in adults 80+ after 14 days (114). • In the UK, adjusted VE after the first dose of ChAdOx-1 (AstraZeneca) was 80.4% (95%CI 36.4-94.5) in adults 80+ after 14 days (114). • After the first dose of BNT162b2 (Pfizer) or ChAdOx-1 (AstraZeneca) the reduced risk of emergency hospital admission was estimated to be 43% (33% to 52%) and 37% (3% to 59%) respectively and a 51% (37% to 62%) reduced risk of death in adults aged 70 years and older in England (115). • Scotland, among Alpha cases, vaccination with ChAdOx-1 (AstraZeneca) or BNT162b2 (Pfizer) (>28 days post first dose (majority of cases) or second dose) was associated with a reduced risk of hospitalization compared to unvaccinated HR= 0.28 (95% CI 0.18–0.43) (116). • A prospective UK cohort study reported significantly lower viral load (mean Ct 31·3, p<0·001) in vaccinated individuals with first dose of BNT162b2 (Pfizer) or ChAdOx-1 (AstraZeneca) vs unvaccinated individuals (mean Ct 26.6) (112). Vaccination 2 doses: Across studies VE for Alpha >7 days after being fully vaccinated was similar to the original variant: • In Canada, two doses of the mRNA-1273 (Moderna) or BNT162b2 (Pfizer) vaccine had comparable adjusted VE (≥ 88%) against symptomatic Alpha, Beta, and Gamma variant infections, ≥7 days after receiving the second dose (117). • ChAdOx1 (AstraZeneca) vaccine efficacy in a UK RCT was 70.4% (95%CI 43.6- 84.5) against symptomatic COVID-19 caused by Alpha and 81.5% (95%CI 67.9-89.4) against symptomatic COVID-19 caused by original variants (118). For asymptomatic or unknown symptom infection, vaccine efficacy for non-Alpha infections (69.7%, 95%CI 33.0-86.3) were not statistically different then the uncertain estimate for Alpha (28.9%, 95%CI –77.1-71.4) (118). In Scotland the VE was 73% (95%CI 66-78) for Alpha (116).	

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• ChAdOx1 (AstraZeneca) and BNT162b2 (Pfizer) combined VE in asymptomatic and symptomatic cases was 80% (95%CI 74–84%; P < 0.001) (119). • BNT162b2 (Pfizer) VE against symptomatic infection was >96% 14 days after the second dose in Israel (120, 121), 90% in 70+ in UK (113), 79.3% (95%CI 47.0-92.5) in 80+ in the UK (114), 92% (95%CI 90–93) in Scotland (116), 89.8% (95%CI 85.9-92.3) in Qatar and against severe disease was 100% (95% CI: 81.7-100) (122, 123). • NVX-CoV2373 (Novavax) vaccine efficacy in a UK RCT against Alpha 86.3% (95%CI 71.3-93.5) and original variant 96.4% (95%CI 73.8-99.5) was not statistically different (124). • A meta-analysis of VE for Alpha against symptomatic illness estimates across trials of BNT162b2 (Pfizer) reported VE after dose 1:51% (95%CI: 47-55%), after dose 2: 93% (95%CI: 90-96%) and ChAdOx1 (AstraZeneca) VE after dose 1: 49% (95%CI: 43-55%) after dose 2: 66% (95%CI: 54-75%) (125). • In the UK, VE against hospitalizations was 86% (95%CI 53-96) for ChAdOx1 (AstraZeneca) and 95% (95%CI 78-99) BNT162b2 (Pfizer) in the UK and was similar to Delta (126). • Germany, In an Alpha outbreak at a long-term care facility in Germany 7 days post two doses of BNT162b2 (Pfizer), those vaccinated with BNT162b2 (Pfizer), had less hospitalizations (12.5% vs 100%), fewer required oxygen therapy (6.3% vs 75%), and fewer required oxygen therapy after discharge (6.3% vs 25%) compared to unvaccinated cases (29). The infectious period was shorter for vaccinated patients 7.5 days (95%CI 7–17.3) than unvaccinated patients 31 days (95%CI 21.5–34.5; p=0.003) and viral load was lower in fully vaccinated patients, but not statistically significant (6.45 vs. 8.15 log10 copies/mL; p = 0.10) (29). • In Greece there was no difference in viral load (measured by CT value) (p=0.70) or the presence of symptoms (p=0.76) between fully vaccinated BNT162b2 (Pfizer) HCWs and unvaccinated cases during an outbreak of Alpha (127).	

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Animal Model of Vaccination Compared to Original Variant	• Hamsters vaccinated with ChAdOx1 (AstraZeneca) and then challenged with Alpha resulted in no weight loss, no lung pathology and no virus detected in tissue samples compared to controls who had extensive pulmonary pathology (128). Another study reported vaccinated hamsters with ChAdOx1 (AstraZeneca) vaccine and challenged with Alpha continued to gain weight while control animals had weight loss and extensive pulmonary pathology caused by Alpha in the control animals was observed, but not in the vaccinated animals (129). • Animals vaccinated with other vaccine candidates including spike RBD proteins (130-133) and SARS-CoV-2 infected human plasma, DNA vaccines (134), and circRNA vaccines (135) all had neutralization activities against Alpha.	18 studies in animals were inconsistent in weight loss but consistent with pathology findings which are in agreement with human studies and *in vitro* studies. Low level of evidence.
***In vitro* study of Vaccinated Sera** Compared to Original Variant	• There are many *in vitro* studies that are available in the dataset. The *in vitro* studies consistently showed minimal or small reductions in neutralization of Alpha compared to an original variant. They have not been summarized in the evidence profile.	There are many *in vitro* studies and this list is not complete at this time. Low level of evidence.
Animal Model of Therapeutics Compared to Original Variant	• A number of monoclonal antibodies tested protected mice and hamsters against Alpha (136, 137). • Locked nucleic acid antisense oligonucleotides (138) and 4'-fluorouridine, a ribonucleoside analog (139) efficiently suppressed viral replication in hamsters and ferrets, respectively. • Convalescent plasma treatment resulted in decreased viral copy number in the lungs of mice infected with either the wild-type or Alpha variant. Convalescent plasma treatment did not reduce viral copy number in brain tissue of mice infected with Alpha compared to wild-type (132). • LY-CoV555 monotherapy protected against the Alpha infections whereas AbbVie 2B04/47D11 showed a partial loss of activity against Alpha (140).	Five animal models. Low level of evidence.
Therapeutics	• A case-control study that included Alpha cases (n=30) found that compared to non-Alpha patients, Alpha patients more often received dexamethasone (72% vs 42%, P=0.049), remdesivir (14% vs 5%, P=0.547), and tocilizumab (4% vs 0% P=1.000) (83).	One small case-control study. This outcome needs further evaluation with a

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
		larger sample size and range of cases. Very low level of evidence.
Testing and Diagnostics (n=46)		
Testing and Detection	• PCR is effective at detecting and distinguishing the variant (141-148). • Detection of Alpha in wastewater at proportions as low as 0.1% of SARS-CoV-2 (149) and PCR approaches are effective in detecting Alpha in wastewater (150). • Multiple studies report reliable assays for rapid detection of variants including detection in wastewater samples (143, 149, 151-153).	46 studies, 40 diagnostic test accuracy studies, 6 surveillance data analyses that also described a new test or set of primers. As these are all describing different tests the studies are considered to be individual and cannot be summarized together. Low level of evidence.
Spread Epidemiology (n=153)		
VOC Emergence Over Time	Studies were captured from many countries around the world, most describe the first detection of Alpha in mid to late December followed by a rapid increase in the variant over 3.5 to 10 weeks. It was noted to have become the dominant strain in several studies (38, 78). Alpha infections plateaued in April, have continued to decrease and was surpassed by the Delta variant in mid-June (10, 14). A predictive model forecasting variants in North America estimates Alpha will reach close to 0% by October 2021 (20). • Canadian studies conducted between December 2020 and March 2021: Two Canadian studies detail that Alpha cases were initially clustered in two regions and quickly spread (154, 155). Similarly, two studies from Ontario have documented the rapid increase in Alpha (16, 156).	147 studies report on the emergence and spread of Alpha in a country or region over time. Most of these studies are based on surveillance data, prospective cohorts often of HCWs, retrospective cohorts of hospital records, longitudinal studies, and ecological studies. Point prevalence or case reports of infected travellers were excluded from this summary. Low to moderate level of evidence.
Attribution to Alpha	In a model fit to data in the UK, an increase of 0.1 in the proportion of Alpha, considering the pre-peak period, was found to be associated with 35.8% increase in the height of the second wave peak. During the period from 1 January to	One model used to estimate the additional burden of COVID-19 due to Alpha.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	25 February 2021, an increase of 0.1 in the proportion of Alpha was related with a 15.3% increase in the cumulative number of deaths during that period (157).	Low level evidence.
Risk Factors for Spread	• An ecological study conducted in Toronto and Peel regions in Ontario showed that Alpha growth rate (11.3%, 19.8%, and 30.8%), overall cases (19.0%, 32.7%, and 48.3%) and VOC cases (18.4%, 30.8% and 50.8%) were positively correlated with the proportion of essential workers (30.4%, 47.9% and 63.2%) and median income ($33k, $45k and $60k CAD) of the community, respectively (158). • Surveillance data from France found the Alpha variant infections were more common among older individuals compared to Beta or B.1.525. In hospital settings, there was an under-representation of Alpha compared to Beta. In specific regions of France, the odds of being infected by the original variant or a B.1.525 virus were either identical or lower than being infected by Alpha (53). • Three studies report a shift towards younger individuals being infected with Alpha in France, Germany and Japan, however the cause of this shift in demographics is not explained and may be due to a combination of factors such as increased contacts in younger age groups, and vaccine coverage in older groups rather than a biological explanation (24, 87, 159, 160)	Five studies assessed risk factors. These include ecological studies, prospective cohorts, predictive models, and surveillance data analysis. Moderate level of evidence for prospective cohort studies. Low level of evidence for all other study designs.
Genomic Analysis of Spread	• Results do not suggest that the canonical mutations of VOC Alpha evolved independently in different locations and points to an origin in and spread of the VOC Alpha from the UK (161-163).	Four studies of genomic surveillance data. Low level of evidence.

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio, aHR = adjusted Hazard Ratio, aPR= adjusted Prevalence Ratio, HCW= Healthcare worker

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and

an excel list that can be searched. One of the foci is to identify studies as variants of concern or under investigation. Studies identified under this foci are further characterized in our VOC/VOI database and VOC results are extracted into this review. A cross check for relevant articles is also conducted within the databases using targeted keyword searching (B.1.1.7 OR Alpha OR 202012/02 OR 501Y.V1).

This review contains research published up to July 1, 2021.

Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX

a) VOC AND VOI LEXICON

WHO label (2021-05-27)	**Pango lineage**	**GISAID clade/lineage**	**Nextstrain clade**	**Earliest documented samples**	**Date of designation**
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I/S:501Y.V1	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2 AY.3	G/452R.V3	21A/S:478K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR	20B/S.484K	Brazil, Apr-2020	17-Mar-2021
Eta	B.1.525	G/484K.V3	20A/S484K	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR	20B/S:265C	Philippines, Jan-2021	24-Mar-2021
Iota	B.1.526	GH	20C/S:484K	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	India, Oct-2020	4-Apr-2021

b) VACCINE BRAND AND GENERIC NAMES

Brand Name	**Generic Name**
AstraZeneca/ Covishield	ChAdOx1-S (AZD1222)
Pfizer-BioNTech	BNT162b2
Janssen (Johnson & Johnson)	Ad26.COV2.S
Moderna	mRNA-1273
Novavax	NVX-CoV2373
Sinopharm	CoronaVac

Sinopharm	BBIBP-CorV
Bharat Biotech	Covaxin (BBV152)
Russian vaccine- produced by 14 companies via partnership (Aug-21)	Sputnik V (Gam-COVID-Vac)

c) OTHER RESOURCES

Reference	Description
Living Evidence Review on SARS-CoV-2 variants Australia On-going, last examined March 10.	This is table highlights recent relevant evidence under the different categories of study similar to what has been laid out in the profiles in this review.
CDC VOC page	Summary of each VOC is available.
WHO situation reports	Summary includes a VOC section.
Review	
Transmission characteristics of SARS-CoV-2 variants of concern (MAR 2021) Curran, et al Data up to Feb 21, 2021	Rapid scoping review done as part of the COVID-END network.
Grey lit	
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 13. 2021 May	This report has been published to continue to share detailed surveillance of VOC-21APR02 (B.1.617.2) and information on a new variant under investigation VUI-21MAY-02 (C.36.3).
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 12. 2021 May	This report has been published to continue to share detailed surveillance of VOC-21APR02 (B.1.617.2) and information on a new variant under investigation VUI-21MAY-02 (C.36.3).
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. 2020 Dec to present	Technical reports compile information from various studies and surveillance across the UK on the VOC and VOIs that are circulating. There is a lot of overlap from these reports and research publications.
Public Health England. Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01 [Internet]. 2020 Dec	The VOC (Alpha) has grown rapidly in the UK and has been assessed as having substantially increased transmissibility
Public Health England. Analysis of transmissibility based on genomics [Internet]. 2020 Dec	Indication that Alpha grows 71% (95% CI: 67%-75%) faster per generation (6.5 days), yet consistent frequency does not indicate a constant selective advantage of Alpha
NERVTAG. NERVTAG meeting on SARS-CoV-2 variant under investigation VUI-202012/01 [Internet]. 2020 Dec	Moderate confidence that Alpha demonstrates a substantial increase in transmissibility compared to other variants.

NERVTAG. Update note on B.1.1.7 severity [Internet]. 2021 Feb	It is likely that infection with VOC Alpha is associated with an increased risk of hospitalization and death compared to infection with original variant viruses

Emerging Evidence on COVID-19

Living Summary of SARS-CoV-2 Alpha, Beta and Gamma Variants of Concern

Highlights up to June 1, 2021

Introduction

SARS-CoV-2 **variants of concern** (VOCs) are circulating variants that have been flagged by national or global public health organizations. VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or diagnostic detection failures (1, 2). Canada has established a national definition (2). The goal of this living summary on the SARS-CoV-2 VOC literature is to highlight new data on the B.1.1.7 (Alpha), B.1.351 (Beta) and P.1 (Gamma) VOCs, their epidemiology and how the attributes of the VOCs may impact the management of the pandemic. The focus will be on changes to epidemiological parameters (e.g., transmission rates, clinical outcomes of severity and mortality, shifts in age groups affected or asymptomatic proportions), impacts on diagnostic tests, immune evasion/vaccine effectiveness and impacts on other public health measures. In May 2021, the World Health Organization (WHO) released naming system for VOCs and variants of interest (VOIs) using Greek letters to improve the ease of communication on variants and potential stigma related to places where variants were first identified, which has been adopted in this report (1). Literature on the Delta VOC is highlighted in a separate living summary.

TABLE 1: CURRENT VARIANTS OF CONCERN (VOCS)

WHO name (05-21)	Pango lineage	Nextstrain clade	GISAID clade	Alternate name	First detected in	Earliest samples	Characteristic spike mutations
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	United Kingdom	Sep 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Beta	B.1.351	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	South Africa	Aug 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, B.1.1.28.1	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brazil and Japan	Dec 2020	L18F, T20N, P26S, D138Y, R190S,

							K417T, E484K, N501Y, D614G H655Y, T1027I, V1176F
Delta	B.1.617.2[1]		G/452R.V3		India	Oct 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R, del157/158, T478K, D950N)

[1] B.1.617.2 (Delta) was added to the VOC list May 11, 2021 and is summarized in a separate evidence profile.

Variants of interest (VOIs), also referred to as variants under investigation (VUI), is a designation used to flag a variant that has the potential to be a VOC, but requires further investigation or evidence. Indicators for a VOI designation include; phenotypic change or acquisition of mutations with established phenotypic implication AND has been the cause of community transmission/clusters or is detected in multiple countries OR is assessed to be a VOI by an authority such as WHO (1, 2). In Canada, the Canadian SARS-CoV-2 Variant Surveillance Group (CSVSG) has established the VOI definition, and are responsible for the evaluation and designation of potential VOIs (2). Data on VOIs is collected, but is not highlighted in this summary. The full dataset in excel can be accessed here and filtered by the VOIs of interest.

This living evidence review profiles the key evidence on Alpha, Beta and Gamma VOCs, including changes in epidemiology, immune evasion/vaccine effectiveness, impacts on diagnostic testing, and public health measures.

What's New

This update includes literature up to June 1, 2021. A total of 345 new studies on B.1.1.7 (Alpha, n=200 studies), B.1.351 (Beta, n=163) or P.1 (Gamma, n=91) since the last update on April 28, 2021 are included in the dataset.

Key Points

As of June 1, 2021 there were 548 studies that report on a VOC or VOI. 501 studies identified report on B.1.1.7 (Alpha), B.1.351 (Beta) and P.1 (Gamma) and were considered for the summaries below. Studies on VOIs (n=47 studies), case reports and point prevalence estimates (n=35), and cell infectivity, binding affinity, or genomic characterization studies (n=77) were not summarized in the evidence profiles. Overall summaries can be found in the key points (Table 2) with more detailed summaries of each VOC in the corresponding review sections. Individual study details can be found in the Excel dataset accessed here. Overall, the predominance of available evidence was on Alpha (n=342) compared with Beta (n=229) and Gamma (n=125).

Transmissibility:

- All studies showed increased transmissibility for Alpha (Table 5), Beta (Table 4), and Gamma (Table 3) compared to the original variant although the extent ranged greatly. For Alpha, two Canadian studies

using general population surveillance data and household transmission data reported 34% increased transmissibility and 31% higher secondary attack rates, respectively. Alpha had higher transmission efficiency than Beta and Gamma variants.

Clinical Severity:

- For Alpha there was conflicting evidence on odds of being admitted to hospital, whereas a small number of studies reported higher odds of hospitalization for both Beta and Gamma. Conflicting associations were reported for ICU admissions with Beta and Alpha and higher odds for Gamma. Risk of mechanical ventilation or higher severity score in the ICU was not associated with Alpha, Beta, compared to the original variant. However, these data are based on a limited number of studies that retrospectively analysed surveillance and hospital data
- For severity indicators,
    - A few studies on Alpha, Beta and Gamma reported age-stratified risk of hospitalization and increased odds in adult age groups between 20-59 years old, while others reported no associations**.**
    - Several studies also reported a lower proportion of pre-existing conditions among VOC cases with the exception of obesity.
- Associations with mortality were conflicting across studies for Alpha, Beta and Gamma. Increased ICU mortality for Beta was reported in one study. Risk of mortality was reported to have increased in some adult age groups for Alpha and Gamma variants.
- Compared to the original variant, viral load was consistently 2-10 fold higher for Alpha. It was also higher for Gamma and Beta than the original variant, but lower than that of Alpha.
- There were no studies assessing infectious period for Gamma and Beta. One small study, 7 people with Alpha, found that average infection, cultured virus, with Alpha lasted for 13.3 days compared with 8.2 days for other variants. Additional research is needed to improve confidence in this result.
- There were no studies on incubation period for any of the VOCs.

Immune Escape:

- There is no evidence that the reinfection rate for Alpha has changed compared to the original variant, no data for Beta. Two studies from Brazil that suggest there may be substantial reinfections from Gamma, however this is based on ecological analyses and needs further study.
- Data from vaccine effectiveness studies has reported reduced protection after the first dose of vaccines, but equivalent protection after the second dose in most studies for Alpha and Gamma, whereas the studies for Beta have had variable results.

Other Categories:

- Additional categories related to diagnostic performance and epidemiological research on spread and impact of non-pharmaceutical interventions are summarized in the in-depth VOC sections.
    - No studies evaluating diagnostic or detection tests for SARS-CoV-2 described failure or performance issues for detecting the VOCs, besides the well characterized S-gene drop out for Alpha.
    - Several predictive models studies reported on non-pharmaceutical interventions (e.g.restrictions to gatherings, closures, masking and lockdowns). Although higher stringency, more closures and restrictions, was needed to control the VOCs due to higher transmissibility, no changes to individual interventions were needed.

- Studies on VOC introduction and spread in a geographic region were not included in the table below, but summaries are available within the profiles for the individual VOCs, as were summaries of animal models and in vitro studies on re-infection, vaccine efficacy and potential impact of VOCs on therapeutics.

Categories of evidence in the tables below include the following if reported:

Transmissibility includes changes in transmissibility, secondary attack rates, and estimates of selective advantage.

Clinical severity includes proportion of infections that are symptomatic, proportion of severe disease and mortality as well as risk factors for severe disease or mortality, viral load, infectious period, incubation period. Note risk factors for severe disease would include special populations e.g. persons who are pregnant if they are reported.

Immune Escape includes changes to vaccine efficacy, risk of re-infection in humans, animal models, *in vitro* or *in silico* experiments as well as impacts on therapeutics if reported.

Diagnostic / Detection Test Failure is captured in the individual sections, and will only be included in Table 2 if there is a concern about test performance.

Other Epidemiology includes all studies that document the emergence and spread of VOCs in a geographic area, ecological studies that examine VOC spread and risk factors for hot spots, and studies on effective public health interventions against VOCs, genomic epidemiology as subcategories.

TABLE 2: SUMMARY OF KEY EVIDENCE OF P.1 (GAMMA) VOC (N=125), B.1.351 (BETA) VOC (N=229) AND B.1.1.7 (ALPHA) VOC (N=342)

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
TRANSMISSION EFFICACY			
Transmissibility Compared to Original Variant or to Alpha	3 surveillance data analyses, 1 cross-sectional study, and 1 predictive model: • 27% higher in France (combined Gamma / Beta) (3) • 160% - 100% higher in Brazil (4, 5) • A model studying Gamma in Italy reported 12% - 39% higher transmissibility depending on whether Gamma exhibits any immune evasion (6).Other studies place Gamma transmissibility between the original variant and Alpha (7) Low level of evidence.	5 reports of surveillance data: • 27% higher in France (combined Gamma / Beta) (3) vs. the original variant. • 55% (8, 9) and 20-100% higher in South Africa (10) vs. the original variant. • 15.8%-17.1% transmission advantage compared to Alpha, in some regions of France from April to May 2021 (11). Low level of evidence.	34 surveillance and observational studies: • Alpha increased relative transmissibility (1-$R_{voc}/R_{original\ variant}$) estimates varied between 34-118% higher across studies, some of the variation by time (12) and country (higher in UK) (9): o Canada 34% (95% CI: 31-38) (13), USA 35-59% (14, 15). o UK: Ranged from 43-118% (9, 12, 14, 16-18), 13.4% - 41.3% across UK regions in Dec 2020 (19). o Europe: France 41 -52% (3, 20), Denmark 55%, Switzerland 54-74% (14), (21), Norway 24% (22), Italy 55-57% (23), Wales and the USA 65-72% (9). o Israel 45% (24). o Japan estimated a 60% increase in relative transmissibility of VOCs (not specified) (25). o Alpha had higher transmission efficiency than Beta and Gamma variants (7) • Similarly ratios of secondary attack rates among household transmission studies was 30-70% higher in Canada (26), Norway (22) and Denmark (27). Low to moderate level of evidence.

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
		CLINICAL SEVERITY	
Virulence / Severity or Duration of Disease Compared to Original Variant or to Alpha	2 surveillance studies: • A higher proportion of cases were hospitalized (p<0.001) (28). • Higher odds of being admitted to hospital (aOR 2.6, 95%CI 1.4-4.8) (28). • Higher odds of being admitted to ICU (aOR 2.2, 95%CI 1.8-2.9) (28). • Exponential growth of hospitalized cases was reported in Rio Grande do Sul and Porto Alegre (29). Low level of evidence.	4 studies including surveillance and observational studies: • Higher odds of hospitalization due to Beta vs. the original variant (aOR 3.6, 95% CI: 2.1-6.2) (28) or Alpha (OR 1.56) in several European countries (11). Conflicting evidence on Beta related ICU admissions, with a higher odds (aOR 3.3, 95% CI: 1.9-5.7) reported in European countries (30), and a lower proportion (35% vs. 48.5%, p=0.03) reported in South Africa (31), compared to the original variant. Low level of evidence.	17 surveillance and observational studies: • Conflicting evidence on prevalence of symptomatic disease found no difference in one study and fewer symptomatic cases (p<0.001) in another (28, 32). • 7 studies found higher odds of being admitted to hospital (aOR 1.36 – 1.7 and aHR 1.34) (28, 33-38) and one report no difference (39). • Two studies found higher odds of ICU admission (aOR 2.3, aHR 1.99) (28, 40). • In one study, there was no association of Alpha and severe disease and death (aPR 1·02) among hospitalized cases (41). • There was no significant difference in ICU scores or mechanical ventilation requirement between Alpha, Beta, and the original variant (42). • Higher rates of hypoxia on admission to hospital were reported in two studies (43, 44). Moderate level of evidence.
Severity Risk Factors Compared to Original Variant or to Alpha	1 European surveillance study: • Gamma cases had a 3.0 - 13.1 times higher odds of hospitalization in the age groups 20–79 years (28).	3 studies including surveillance and observational studies: • Beta cases had higher odds of hospitalization among adults aged 40-59 and 60-79 (OR 3.5-3.6) in several European countries (28), and hospitalized cases were significantly	10 observational studies: • One study of hospitalized COVID-19 cases reported a higher proportion of females (48.0% vs 41.8%, p=0.01), fewer frail patients (14.5% vs 22.4% p=0.001) and a higher proportion of obese cases (30.2% vs 24.8%,

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
	• Admission to ICU was 2.9–13.9 times higher in ≥ 40 age groups (28). • Pre-existing conditions were lower 27.8% in Gamma vs 89% original variant, p<0.001 (28). Low level of evidence. 3 other observational studies were conducted in which whole genome sequencing was not performed (very low level of evidence).	older (57 vs. 54 years, p=0.03) in South Africa (31) compared to original variant cases. • Conflicting evidence on the age of Beta ICU admissions, with a higher odds for adults aged 40-59 (aOR 8, 95% CI: 3.7-17.3) in several European countries (28) and no significant difference in age (63 vs. 67 years, p=0.15) in France (42), compared to the original variant. • Beta cases were less likely to have comorbidities compared to original variant cases in Europe and South Africa (28, 31). Low level of evidence.	p=0.048), but no difference by age or ethnicity (43). • Studies reported no significant difference in patient age, gender and median length of hospital stay (35, 42). Age difference was statistically significant in another study (37 vs. 39 years) (45). • One study reported a 3.0 higher odds ratio of hospitalization in 20–39 year olds and a 2.3 times higher odds ratio in 40–59 years and that pre-existing conditions were lower (44.8% vs. 89% p<0.001) (28). • A hospital study from France noted mean age was 59.2, down from 70.7 and patients without comorbidities increased 16% to 42% (p=0.007) (44). Low to moderate level of evidence.
Mortality Compared to Original Variant or to Alpha	2 observational studies and 1 predictive model: • Gamma had lower odds of mortality overall (aOR 0.6, 95%CI 0.3-1.0) (28). • Higher hospital mortality rates in adults aged 18-50 (46). • Predictive model estimated mean mortality 1.5 (50%CrI	3 studies including surveillance and observational studies: • Conflicting evidence from studies in different countries/contexts on Beta mortality, with South Africa reporting an increased proportion of mortality (36.4% vs. 32.6%, p=0.26) (31), and several European countries reporting no difference in the odds of death (aOR 1.1, 95% CI: 0.4-3.4) (28) compared to the original variant.	16 surveillance and observational studies: • Five studies reported no significant difference in mortality overall (2.1 vs. 4.1%) (32, 35, 38, 39), or after 28 days (OR: 0.90, 95%CI 0.57-1.41, p=0.64) (36). • One study reported lower odds of mortality (aOR 0.5, 95%CI 0.3-0.9) (28). • Eight studies reported higher risk of mortality: higher 28 day hazard of death (55%, 95% CI: 39-72%) (47), aHR 1.59 (95%CI 1.25-2.03) (40), aHR 1.67 (95%CI 1.34 – 2.09;

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
	1.2–1.9) times higher after emergence of Gamma (5). Low level of evidence.	• Higher proportion of Beta ICU mortality (74.4% vs. 57.1%, p=0.002) compared to the original variant in South Africa (31), and a higher odds of ICU death (OR 5.67, 95% CI: 1.04-30.81, P=0.04) compared to Alpha in France (42). Low level of evidence.	P <0.0001) (41). HR 1.64 (95%CI 1.32 - 2.04, p <0.001) (48), which equates to an increase of 2.5 to 4.1 deaths per 1000 detected cases (37, 49, 50). An ecological study estimated that Alpha was 33% more lethal in the UK (51). • Among ICU patients in France, Beta cases had higher odds of dying within 60 days after ICU admission compared to Alpha cases (OR 5.67, 95% CI 1.04-30.81) (42). Moderate level of evidence.
Mortality Risk Factors Compared to Original Variant	1 surveillance study from Brazil: • Mortality in COVID-19 cases <60 years old increased from 18% in Nov 2020 to 28% in Feb 2021 (52). • Mortality among people with no pre-existing conditions was higher after Gamma emerged for women 20-39 years old (RR 5.65, 95%CI 2.9-11.03; p <0.0001) and 40-59 years old (RR 7.7, 95%CI 5.01-11.83; p <0.0001) (52). Low level of evidence.	No studies	2 surveillance and retrospective cohort studies: • One study found mortality was higher in younger age groups than older age groups (59.0% in 1-34 year olds vs 55.4% in those 85 or older) and was higher among Blacks (69.6%), mixed or unknown ethnicity (64.8%), White (58.0%) and Asian (57.6%) (47). • Another study found no increased mortality by sex (p = 0.90), ethnic group (p = 0.64) or age group (p = 0.15) (40). Low level of evidence.
Viral Load Compared to Original Variant	2 surveillance studies: • Viral load from Gamma cases were ~ 10-fold higher than	No studies	22 observational studies and surveillance analyses:

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
	non- Gamma (original variants) cases (53). • Viral load was higher than original variant but lower than Alpha (3). Low level of evidence.		• Consistently found lower Ct values or higher estimated viral loads. The median order of magnitude higher varies across studies and target protein from 2 to 10 fold differences (3, 32, 35, 45, 54-59, 59-61). Low to moderate level of evidence.
Infectious Period Compared to Original Variant	No studies	No studies	One small study (n=7 Alpha cases) conducted in the USA calculated average infections last 13.3 days compared with 8.2 days for other variants (57). Very low level of evidence.
Incubation Period	No studies	3 studies including surveillance and observational studies: • Beta cases had higher odds of hospitalization among adults aged 40-59 and 60-79 (OR 3.5-3.6) in several European countries (28), and hospitalized cases were significantly older (57 vs. 54 years, p=0.03) in South Africa (31) compared to original variant cases. • Conflicting evidence on the age of Beta ICU admissions, with a higher odds for adults aged 40-59 (aOR 8, 95% CI: 3.7-17.3) in several European countries (28) and no significant difference in age (63 vs. 67 years, p=0.15) in France (42), compared to the original variant.	No studies.

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
		• Beta cases were less likely to have comorbidities compared to original variant cases in Europe and South Africa (28, 31). Low level of evidence.	
IMMUNE ESCAPE - Potential Impact on Vaccine Efficacy/Effectiveness, Possibility of Re-infection			
Re-infection from Infection Compared to Original Variant	2 surveillance studies: • Assuming 78% of population was previously infected, 28% of the cases in Manaus from Nov 2020 to Jan 2021 estimated to be re-infections (4). • 16.9% of P.1 cases (95% CI 9.48-28.5) in Manaus from Jan 2021 to Mar 2021 estimated to be re-infections (81). Low level of evidence.	3 studies including case reports and observational studies: • Three cases of re-infection with Beta have been reported (62-64). Very low level of evidence.	3 studies found Alpha does not evade natural immunity: • One estimated re-infection rate of 0.7% (95%CI: 0.6-0.8) (65). • In a USA study, previous seropositivity rate for persons with Alpha was 0.7% compared to non- VOC infections at 0.9% (38). • A UK study found no evidence that Alpha changed the extent of protection from any-PCR positive infection in those who were seropositive (aIRR 0.40, 95%CI 0.10-1.64, p=0.20) (66). Moderate level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness Compared to Original Variant	2 case-control studies: Vaccination 1 dose: • Vaccination with at least one CoronaVac dose was associated with a 0.50-fold reduction (adjusted VE, 49.6%; 95% CI 11.3 - 71.4) in the odds of symptomatic	7 studies including RCTs, and observational studies: Breakthroughs: • No breakthrough infections were identified >14 days post second dose (mainly Pfizer) in Israel case control study (67).	13 studies that included RCTs, cohorts and surveillance studies: Breakthroughs: • An outbreak investigation in HCWs reported two fully Pfizer-BioNTech vaccinated physicians became infected with Alpha, with the second dose given 1 month before symptom onset (73).

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
	SARS-CoV-2 infection 14 days after first dose (82). Vaccination 2 doses: • Moderna or Pfizer vaccine 7 or more days after the second dose had an adjusted VE against symptomatic P.1 infection of 88% (95%CI 61-96) versus symptomatic wild-type infection (93%, 95%CI 87-96). Adjusted VE for one dose against P.1 was 43% (95%CI 22-59) versus wild-type (61%, 95% CI 53-67) (72). Low level of evidence.	• 50% (13/26) of nursing home residents and 5.2% (1/19) of staff who received the Pfizer-BioNTech vaccine experienced breakthrough Beta infections (64). Vaccinated 2 doses: • AstraZeneca (ChAdOx1-S): 10.4% efficacy for prevention of symptomatic disease (68). • Johnson and Johnson: VE was 52% and 64% for moderate and 73% and 82% for severe disease at 14 days and 28 days respectively (69). • Novavax (NVX-CoV2373: 51.0% (95% CI: -0.6 – 76.2) VE against symptomatic disease in HIV-negative individuals (70). • Pfizer-BioNTech (BNT162b2): 75.0% (95% CI: 70.5% – 78.9%) VE against Beta infection ≥ 2 weeks after the second dose in Qatar (71). A VE of 50% (95% CI: 34%-73%) among nursing home residents (median age: 87.0±8.2 years) for two doses spaced 19 days apart (64). • Moderna/Pfizer-BioNTech: Comparable VE of ≥ 88% against symptomatic Beta infection, ≥ 7 days after receiving the second dose (72).	• In the USA, breakthrough cases of Alpha were not more common than the original variant (1.29 fold, 95%CI 0.75-2.20, p=0.468) (74). Vaccination 1 dose: • Pfizer-BioNTech (BNT162b2) in Israel where 94% of cases were Alpha, vaccine effectiveness against symptomatic infection between the first dose and up to 14 days after the second dose (aOR 2.4 (95%CI: 1.2 to 5.1) (67). • Pfizer-BioNTech (BNT162b2) or AstraZeneca (ChAdOx1-S) first dose of vaccine reduced risk of emergency hospital admission in adults aged 70 years and older by 43% (33% to 52%) and 37% (3% to 59%) in England, respectively (75). • Risk of death was reduced by 51% (37% to 62%) in adults aged 70 years and older in England who had received one dose of Pfizer-BioNTech (75). • A UK study found no difference in protection for Alpha compared to other variants following a first vaccine dose (aIRR=1.84, 95%CI 0.75-4.49, p=0.18) (66). Vaccination 2 doses: • AstraZeneca/ COVISHIELD (ChAdOx1) vaccine effectiveness was 70.4% (95%CI 43.6-

Category	P.1 (Gamma)	B.1.351 (Beta)	B.1.1.7 (Alpha)
			84.5) vs 81.5% (67.9 - 89.4) in original variants in a UK RCT (76). • Novavax (NVX-CoV2373) vaccine efficacy against Alpha 86.3% (71.3 to 93.5) vs the original variant 96.4% (73.8 to 99.5) in a UK RCT (77). • Pfizer-BioNTech (BNT162b2) in Israel where 94% of cases were Alpha, vaccine effectiveness was >96% 14 days after the second dose (78) and >90% in 70+ year olds (79) • In Canada, two doses of the Moderna (mRNA-1273) or Pfizer-BioNTech vaccine had comparable adjusted vaccine effectiveness (≥ 88%) against symptomatic Alpha, Beta, and Gamma variant infections, ≥ 7 days after receiving the second dose (72). Variable levels of evidence from RCT (moderate to high) to case reports (very low).
		Low to moderate level of evidence.	

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio, aHR = adjusted Hazard Ratio, aPR= adjusted Prevalence Ratio

Overview of the Evidence

Study designs included in this summary ranged from low risk of bias double blinded RCTs to a number of different observational study designs with varying levels of evidence. The observational studies offer low to moderate evidence depending on the specific study design and consistency across studies. Descriptive studies included in this report such as case series and case reports, predictive models, ecological studies, animal models and *in vitro* studies are low to very low evidence and generally can only be used to generate hypotheses that need to be further examined with a different study design. Given this very wide variation, an indication in the level of confidence of the evidence is provided for a particular outcome. Study designs are provided, but no formal risk of bias assessment has been conducted.

There are several knowledge gaps or areas where there is very little research noted in the key points table and additional research is needed to improve confidence in summary results particularly for Beta and Gamma.

CONTENTS

P.1 (GAMMA)

The excel dataset includes summaries of individual studies and can be accessed here. Below is the detailed evidence profile developed for Gamma and covers data on changes in transmission efficiency, changes in clinical severity, immune escape, testing and diagnostics, and other epidemiological studies mainly on VOC spread.

Table 3: Evidence Profile of P.1 (Gamma) VOC (n=125)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency		
Transmissibility Compared to Original Variant	Increased transmissibility above the original variant: • 27% higher in France for combined Gamma and Beta (3). • 2.6 (95% CI: 2.4-2.8) times higher (4) and 2.0 (50%CrI 1.7-2.4) times more transmissible with median cross immunity	Five studies provided estimates of Gamma transmissibility including: 3 surveillance data analyses from Brazil (2) / global (1), 1 cross-sectional study from France, and 1 predictive model from Italy. Across studies there is little

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	estimated at 68% (50%CrI 54-79) in Brazil (5). • 1.12 (95%CI 1.03-1.23) times more transmissible with complete immune evasion to 1.39 (95%CI 1.26-1.56) with complete cross protection in Italy (6). • Other studies place Gamma transmissibility between the original variant and Alpha (Alpha) and show the transmissibility of Gamma has slightly decreased over time from Jan 2021 to April 2021 worldwide (7).	consistency. Heterogeneity in increased transmissibility estimates may be due to factors such as geographic location and time points in which estimates were taken. Low level of evidence.
Non-Pharmaceutical Interventions Compared to Original Variant	• Gamma emerged in Manaus Brazil in late Nov 2020 and showed a high effective reproductive number (Re) of 2.6 (95% Highest Posterior Density [HPD]: 1.5-4.5) during Dec 2020. After increased social distancing restrictions, the Re was estimated to have decreased to 1.2 (95% HPD: 0.9-1.6) in late Dec 2020 and January 2021 (53). In comparison, a previous variant also had a Re of 2.6 (HPD 1.6-3.8) in Mar 2020 that decreased to 1.0 (HPD 0.8-1.2) in Apr 2020 after social distancing increased by more than 50% in Manaus (due to implementation of NPIs).	1 surveillance data analyses from Brazil. Low level of evidence.
Clinical Severity		
Virulence / Severity or Duration of Disease Compared to Original Variant	• A higher proportion of hospitalized Gamma cases were reported compared to the original variant (20% vs. 7.5% p<0.001) (28). • One study reported a higher adjusted odds ratio (aOR 2.6, 95%CI 1.4-4.8) of Gamma cases being admitted to hospital or to ICU (aOR 2.2, 95%CI 1.8-2.9) compared to original variant (28). • Hospitalized cases exhibited exponential growth in Rio Grande do Sul, with an average doubling time of 13.4 days and a daily growth rate of 5.3% from Feb 2021-Mar 2021 (29). • Similar exponential growth (doubling time 13.3 days, daily growth rate 5.4%) for	2 surveillance data analyses from Europe and Brazil. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	hospitalizations was reported in the city of Porto Alegre (29).	
Severity Risk Factors Compared to Original Variant	• In age-stratified analysis Gamma cases had 3.0-13.1 times higher odds of hospitalization in the age groups 20–39, 40–59 and 60–79 (28). • Odds of admission to ICU were 2.9–13.9 times higher in 40–59, 60–79 and ≥ 80 age groups (28). • Pre-existing conditions were lower in Gamma cases (27.8%) vs original variant (89%), p<0.001 (28). In three studies, cases were not whole genome sequenced so the lineage was not determined (very low level of evidence): • Among severe cases, people under 60 years of age increased from 39% in the first wave (Nov-Dec 2020) to 47% in the second wave (Feb 2021) when Gamma was predominant (52). • There was no increase in the proportion hospitalized in any age group before (Feb-Oct 2020) and after (Oct 2020-Feb 2021) when Gamma emerged in Brazil (46). • There was no significant difference in the mean age of infected hospitalized patients before and after Mar 2021 when Gamma became dominant in Sao Paulo, Brazil (80).	2 surveillance data analyses from European countries and Brazil, 1 ecological study in Brazil, and 1 retrospective cohort study in Brazil. Low level of evidence.
Mortality Compared to Original Variant	• Lower odds of mortality due to Gamma compared to original variant in multivariable analysis (aOR 0.6, 95%CI 0.3-1.0) (28). • A differentiated increase in COVID-19 mortality among adults aged 18-50 after Gamma emerged in Brazil suggests the possibility of greater severity of Gamma in this population. Young adults had high hospital mortality rates >10% (46). • Predictive model estimated Gamma infections in Manaus are median 1.5 (50%CrI 1.2–1.9) times more likely to result in mortality in the period following the emergence of Gamma in	1 surveillance data analysis from European countries, and 1 ecological study and 1 predictive model from Brazil.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	Nov 2020, compared to before (5). However, it cannot be determined whether the estimated increase in relative mortality risk is due to Gamma infection, stresses on the Manaus healthcare system, or both.	Low level of evidence.
Mortality Risk Factors Compared to Original Variant	1 study in which cases were not whole genome sequenced so the lineage was not determined (very low level of evidence): • Mortality in COVID-19 cases <60 years old increased from 18% in November 2020 to 28% in February 2021 when Gamma was predominant (52). • The case fatality ratio increased the most in 20 -59 year olds and among patients without pre-existing risk conditions. Among severe cases, the proportion of patients without pre-existing risk conditions was higher in February 2021 (33% vs. 25% in Nov 2020) (52). • Compared with Nov/Dec 2020, females 20-39 years old, with no pre-existing risk conditions, were at 5.65 (95%CI 2.9-11.03; p <0.0001) times higher risk of death in Feb 2021 and 40-59 year olds were at 7.7 (95%CI 5.01-11.83; p <0.0001) times higher (52).	1 surveillance data analysis from Brazil. Low level of evidence.
Viral Load Compared to Original Variant	• Viral load (measured by Ct values) in Gamma samples was lower than Alpha samples and higher compared to original variants (3). • The viral load (measured by Ct values) in Gamma infections was approximately 10-fold higher compared to non- Gamma infections (53). • Viral load for Gamma infections was significantly lower than non-Gamma infections in adult (18-59 years) men (P=0.0005), adult women (P<0.0001), and elderly (>59 years) women (P=0.0149), but not significantly different in elderly men (P=0.4624) (53). 1 study in which cases were not whole genome sequenced so the lineage was not determined (very low level of evidence):	2 surveillance data analyses from France and Brazil, and 1 retrospective cohort study in Brazil.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• There was no significant difference in mean Ct values among infected hospitalized patients and healthcare workers before and after March 2021 when Gamma became dominant in Brazil (80).	Low level of evidence.
Infectious Period	No studies	
Incubation Period	No studies	
Immune Escape - Potential Impact on Vaccine Efficacy, Possibility of Re-infection		
Re-infection from Infection Compared to Original Variant	• 28% of the cases in Manaus Brazil from Nov 2020 to Jan 2021 were estimated to be re-infections considering 78% of the population was previously infected (4). • 16.9% of Gamma cases (95%CI 9.48-28.5) in Manaus from Jan 2021 to Mar 2021 were estimated to be re-infections. If probable reinfections are also included, then 25.8% were reinfections (95%CI 16.7-37.4). If possible reinfections are also included, then 31.0% were reinfections (95%CI 21.4-42.5) (81).	2 surveillance data analyses from Brazil. Low level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness Compared to Original Variant	• In Manaus Brazil where >75% of the cases were Gamma during the study period, vaccination with at least one CoronaVac dose was associated with a 0.50-fold reduction (adjusted VE, 49.6%; 95% CI, 11.3 - 71.4) in the odds of symptomatic SARS-CoV-2 infection during the period 14 days or more after receiving the first dose. Female sex (OR, 0.50; 95% CI, 0.38 - 0.81) and a positive SARS-CoV-2 RT-PCR or antigen test in the prestudy period (OR, 0.38; 95% CI, 0.17 - 0.87) were associated with a reduced odds of symptomatic SARS-CoV-2 infection (82). • Moderna or Pfizer vaccine 7 or more days after the second dose had an adjusted VE against symptomatic Gamma infection of 88% (95%CI 61-96) versus symptomatic wild-type infection (93%, 95%CI 87-96). Adjusted VE against symptomatic Gamma infection for one dose was 43% (95%CI 22-59) versus symptomatic wild-type infection (61%, 95% CI 53-67) (72).	2 case-control studies from Brazil and Canada. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
In Vitro Study of Therapeutics Compared to Original Variant	• Multiple therapeutics have been shown to have reduced effectiveness against Gamma compared to the original variant, including Casirivimab (83-85), Bamlanivimab (85), Etsevimab and Imdevimab (83). • The combination of Imdevimab and Casirivimab was shown to efficiently inhibit Gamma (85).	*In vitro* studies are a low level of evidence that offer preliminary insights into what we may expect in vivo.
***In vitro* Studies of Convalescent and Vaccinated Sera** Compared to Original Variant	Most studies have shown that convalescent sera and vaccinated sera (Pfizer, CoronaVac, Sinopharm, Moderna) have reduced neutralizing activity for Gamma compared to the original variant (86-89). *Note: Many in vitro studies have been identified, please see the excel dataset for details on each study.*	Very low level of evidence. The immune response is complex, and lack of or reduced neutralizing antibodies does not mean a lack of immune protection. Further research is needed (see the PHAC Emerging Science review on protective immunity).
Testing and Diagnostics		
Testing and Detection Compared to Original Variant	• No testing failures have been reported for Gamma PCR, antigen tests, or serological assays (90).	One diagnostic test accuracy study evaluated the performance of these tests. Low level of evidence.
Spread Epidemiology		
VOC Emergence Over Time	• Many studies use whole genome sequencing to report the point or period prevalence of Gamma in a specific area, which have not been summarized (11, 91). • The prevalence of Gamma grew from 0% in Nov 2020 to 73.8% in Amazonas, Brazil (53) and almost 30% in Amazonas, Columbia by Jan 2021 (92). • The prevalence of Gamma in Italy remained relatively stable from Feb 2021 (5.0%, 95%CI 3.9-6.4) to Mar 2021 (4.8%, 95%CI 3.9-5.9) compared to Alpha, which grew from 53.1% (95%CI 50.3-55.9) to 85.7% (95%CI 84.1-87.3) (23).	3 surveillance data analyses from Brazil (2) and Italy (1). Low level of evidence.
Predictions of Spread	• If a full return to pre-pandemic levels of contact is attempted after 50% of the USA population is vaccinated in July 2021, Gamma is predicted to outcompete Alpha and Beta	2 predictive models. A limitation is that these models do not take into account B.1.617 (Delta), and only compare the predicted

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	and become the dominant strain in 2-3 months. The model assumes Gamma has 68% vaccine or wild-type immune efficacy (93). • If Gamma and Beta become established in the New York City population simultaneously, Gamma is predicted to outcompete Alpha and become co-dominant with Beta by August 2021. However, if Gamma becomes established in the population before Beta, Gamma would suppress Beta and become dominant. The model assumes Gamma has the same VE as wild-type (94).	spread of Gamma with Alpha and Beta. Low level of evidence.

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio

B.1.351 (BETA)

The excel dataset includes summaries of individual studies and can be accessed here. Below is the detailed evidence profile developed for Beta and covers data on changes in transmission efficiency, changes in clinical severity, immune escape, testing and diagnostics, and other epidemiological studies mainly on VOC spread.

Table 4: Evidence Profile of B.1.351 (Beta) VOC (n=229)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency		
Transmissibility Compared to Original Variant or Alpha	• Increased transmissibility above the original variant: 27% in France for combined Beta and Gamma (3), 55% (8, 9) and 20-100% (as high as 175%) in South Africa (10). • Increased transmission advantage compared to the Alpha variant in Ile-de-France (15.8%, 95% CI: 15.1%-16.1%) and Hauts-de-France (17.1%, 95% CI: 16.1% - 18.8%) between April to May 2021 (11).	These have been estimated from 5 surveillance data analyses. Across studies there is little consistency. Heterogeneity in increased transmissibility estimates may be due to many factors including the point in the pandemic estimates are taken. Low level of evidence.
Secondary Attack Rates Compared to Original Variant	• SAR=76.9% which was equivalent to (R_{eff}=4) in this investigation(95)	1 outbreak investigation. Low level of evidence.
Clinical Severity		
Virulence / Severity or Duration of Disease Compared to Original Variant or Alpha	• Symptomatic proportion: Beta cases (90.3%; 28/31) vs. original variant cases (81.4%; 547/672, p = 0.2) in multiple European countries (28). Increased hospitalization and ICU admission: • Higher odds of hospitalization with Beta (19.3%) vs. original variant (7.5%) p<0.001 in a multivariable analysis (aOR = 3.6, 95% CI: 2.1-6.2) in several European countries (28). • Increased proportion of Beta cases in the ICU (2.3%) vs. original variant (0.6%) p=0.001, and higher odds of ICU admission among Beta cases compared to original variant cases (aOR = 3.3, 95% CI: 1.9-5.7), in several European countries (28). • Beta cases were more likely to be hospitalized (OR = 1.56, p < 0.0001) compared to Alpha cases in France (11).	4 studies on severity, including 2 surveillance studies and 2 retrospective cohort studies from France and South Africa. The cohort studies are single-centered, therefore have limited external validity and are at risk of confounding bias. Low confidence in the increased/decreased severity of the Beta variant. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	Decreased ICU admission: • In hospitalized cases there were lower ICU admissions (35% vs. 48.5%, p = 0.03) and mechanical ventilation (8.9% vs. 15.5%, p = 0.009) during the Beta wave compared to the original variant wave in South Africa (31). No difference: • No significant difference in ICU scores and mechanical ventilation requirements between Beta, original variant or Alpha cases in a hospital in France (42).	
Severity Risk Factors Compared to Original Variant or Alpha	Age: • In an age-stratified analysis Beta cases had 3.5–3.6 times higher odds of hospitalization for age groups 40–59 and 60–79 years compared to original variant cases of the same age, in several European countries (28). • Admission to the ICU was significantly more likely for Beta cases (aOR 8, 95% CI 3.7–17.3) aged 40–59 years (28). • Hospitalized cases during the Beta wave were significantly older (median age 57 vs. 54 years, p = 0.03) compared to cases during the original variant wave in South Africa (31). • No significant difference in the age (63 years vs. 67 years, p = 0.15) or sex of ICU admissions among Beta cases compared to original variant or Alpha cases in France (42). Comorbidities: • Pre-existing conditions were lower in all 3 VOC (79.6% Beta vs. 89% original variant, p<0.001) (28). • More cases during the Beta wave had no comorbidities (47% vs. 36.9%, p = 0.008) and less hypertension (32.2% vs. 45.2%, p < 0.001) compared to the original variant wave in South Africa (31). • No difference in diabetes mellitus, chronic respiratory disease, cerebrovascular disease, and HIV positivity (31).	3 studies on severity risk factors, including 1 surveillance study of European countries and 2 retrospective cohort studies from France and South Africa. The cohort studies are single-centered, therefore have limited external validity and are at risk of confounding bias. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Mortality Compared to Original Variant or Alpha	Increased mortality: • Increased overall mortality (36.4% vs. 32.6%, p = 0.26) and significantly higher ICU mortality (74.4% vs. 57.1%, p = 0.002) during the Beta wave compared to the original variant wave in South Africa (31). • Hospital admission during the Beta wave (p=0.006) was independently associated with mortality, in a multivariate analysis (31). • Higher odds of death within 60 days of ICU admission (OR = 5.67, 95% CI: 1.04-30.81, p = 0.04) for Beta cases compared to Alpha cases in France (42). No difference: • No difference in the odds of death for Beta cases compared to original variant cases in the multivariable analysis (aOR 1.1, 95%CI 0.4-3.4) (28).	3 studies on mortality, including 1 surveillance study of European countries and 2 retrospective cohort studies from South Africa and France. The cohort studies are single-centered, therefore have limited external validity and are at risk of confounding bias. Low level of evidence.
Mortality Risk Factors Compared to Original Variant	No studies	
Viral Load Compared to Original Variant	• Viral load (measured by CT values) in Beta samples was lower than Alpha samples and higher compared to original variants (3, 54).	2 studies, secondary outcomes. Very low level of evidence.
Infectious Period	No studies	
Incubation Period	No studies	
Immune Escape - Potential Impact on Vaccine Efficacy, Possibility of Re-infection		
Re-infection from Infection Compared to Original Variant	• Three cases of re-infection with Beta have been reported (62-64).	3 studies report re-infection, including 2 case reports and 1 prospective cohort study. These studies have a very low level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness	Vaccine Efficacy/Effectiveness: • AstraZeneca: 10.4% efficacy for prevention of symptomatic disease (68). • Johnson and Johnson: Estimates of efficacy in South Africa were lower than other countries.	7 studies on breakthrough infections and vaccine efficacy/effectiveness, including 3 RCTs, 1 prospective cohort study, and 3 case control studies. These studies have a low to moderate

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Compared to Original Variant	VE for Beta was 52% and 64% for moderate and 73% and 82% for severe disease at 14 days and 28 days respectively (69). • Novavax: 51.0% (95% CI: -0.6 – 76.2) VE against symptomatic disease in HIV-negative individuals (70). • Pfizer-BioNTech: 75.0% (95% CI: 70.5% – 78.9%) VE against Beta infection ≥ 2 weeks after the second dose, and 97.4% (95% CI: 92.2%-99.5%) VE against severe, critical, or fatal outcomes for any SARS-CoV-2 variant in Qatar (71). A VE of 50% (95% CI: 34%-73%) among nursing home residents (median age: 87.0±8.2 years) for two doses spaced 19 days apart (64). • Moderna/Pfizer-BioNTech: Comparable VE of ≥ 88% against symptomatic Beta infection ≥ 7 days after receiving the second dose (72). Breakthrough Infection after Vaccination: • No breakthrough infections of Beta were identified >14 days post second dose (mainly Pfizer) in an Israel case control study (67). • 50% (13/26) of nursing home residents and 5.2% (1/19) of staff who received the Pfizer-BioNTech vaccine experienced breakthrough Beta infections. Residents were infected 24 to 41 days after receiving the second dose (15.4% were asymptomatic, 69.2% had mild to moderate symptoms and 15.4% developed acute respiratory distress syndrome) (64).	level of evidence. There were single studies per vaccine from RCT's, therefore additional trials are needed to improve confidence in these estimates.
Therapeutics Compared to Original Variant	• Casirivimab and Etesevimab showed reduced neutralization (83, 85, 96), Bamlanivimab showed no neutralization (85), and there was conflicting evidence on the neutralization of Imdevimab (83, 96) against Beta.	3 in vitro studies on therapeutics. Very low level of evidence.
Animal Models of convalescent or vaccinated protection	• Animal models challenged with Beta concluded that previously infected or vaccinated hamsters have shown protection from clinical disease (97, 98).	2 animal models. Very low level of evidence.
In vitro Studies	• Most vaccine and convalescent sera have shown reduced neutralizing activity for Beta	Very low level of evidence. The immune response is complex,

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	compared to the original variant or Alpha. In most studies Beta has more reduced neutralization than Gamma. The neutralization experiments are not summarized, but can be found in the dataset.	and lack of or reduced neutralizing antibodies does not mean a lack of immune protection. Further research is needed (see the PHAC Emerging Science Group review on protective immunity).
Testing and Diagnostics		
Testing and Detection Compared to Original Variant or Alpha	• PCR, antigen tests, serological assays and sequencing methods are effective at detecting and/or distinguishing Beta (90, 99-108). • The TRF-ELISA S1-based antigen assay detected Beta with a 2 to 3-fold reduced sensitivity compared to the original and Alpha variant (109).	12 studies on testing and detection, including 10 diagnostic test accuracy studies and 2 in vitro studies. As these are all describing different tests, the studies are considered to be individual and cannot be summarized together. Low level of evidence.
Spread Epidemiology		
VOC Emergence Over Time	• Studies that report the point or period prevalence of Beta have not been summarized. • Two studies show the growth of Beta in different areas of South Africa and British Columbia, Canada (110, 111). • In South Africa, Beta emerged around August 2020, and was first detected in October 2020. By March 2021, it became the dominant variant representing approximately 20% (1769/8746) of genomes (112). • Studies from countries outside of South Africa, report the first detection of Beta since December 2020 (113-115).	16 studies on the emergence and spread of Beta, including 12 surveillance studies, 1 outbreak investigation, 1 predictive model, and 2 retrospective cohort studies. Low level of evidence.

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio, aHR = adjusted Hazard Ratio, aPR= adjusted Prevalence Ratio

B.1.1.7 (ALPHA)

The excel dataset includes summaries of individual studies and can be accessed here. Below is the detailed evidence profile developed for Alpha and covers data on changes in transmission efficiency, changes in

clinical severity, immune escape, testing and diagnostics, and other epidemiological studies on mainly on VOC spread.

Table 5: Evidence Profile of B.1.1.7 (Alpha) VOC (n=342)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency		
Transmissibility Compared to Original Variant	Alpha increased relative transmissibility (1-$R_{voc}/R_{original\ variant}$) estimates varied between 34-118% higher across studies, some of the variation is due to when in the Alpha emergence the data was drawn. One study notes variation over time (12) and most of the estimates from the UK are higher than other countries (9): • Canada: 34% (95% CI: 31-38) (13). • UK: 50-100% (12), 75% (95% CrI 70–80%) (16), 52% (95% CI 46 – 58%) (17), 43-90% (CrI range: 38-130%) (14), 44-55% (95%CI 38-61%) (18), 83-118% (71-140%) across the UK (9), 13.4-41.3% across UK regions in Dec 2020 (19), higher transmissibility 62% (95%CI 59%-65%) to 45% (95%CI 43%-48%) (116), 0.3 unit higher reproduction number compared to other lineages (117). • Europe: France 41% (95%CI 38-44) (3) and 52% (95%CrI 54-66%) (20), Denmark 55% (CrI 45–66%), Switzerland 74% (CrI 66–82%) (14) and 54% (95%CI 49-65%) (21), Norway 24% (95%CI 0-52%)(22), Italy 55-57% (95%CI 45-66%) (23), Wales and the USA 65-72% (46- 104%) (9). • USA: 59% (CrI 56–63%) (14), 35-46% (15). • Israel: 45% (95%CI 20-60) (24). • Japan estimated a 60% increase in relative transmissibility of VOCs (not specified) compared to original variants (25). • Alpha has higher transmissibility than Beta or Gamma in one study that did not report estimates (7). • In some areas of France (April-May) where Beta was increasing beta was estimated to have a transmission advantage of 15.8% (95%CI 15.1-16.1) in Île de France and 17.1% (95%CI 16.1-	This section is informed by 35 observational studies including analysis of surveillance data, cross sectional, retrospective cohort, ecological studies, and predictive models. There is agreement that Alpha is more transmissible and there is a fair amount of overlap in the estimates of magnitude. Transmissibility may be impacted by restrictive public health measures and increasing vaccinations. These studies are at risk of selection, information and confounding biases that have been inconsistently adjusted for across studies. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	18.8) in Hauts de France compared to Alpha (11). • A predictive model explored the impact of increased speed of transmission and transmissibility on the epidemiology of Alpha (118). Some studies do not provide enough data to calculate increased transmission efficiency, but indicated that it was higher (7, 65, 119). Other studies indicated transmissibility decreased over time (7, 120) or remain unaffected (121), which may be associated with lockdown stringency or increasing vaccinations (121, 122). A scoping review on transmissibility included studies up to Feb 21, 2021 (8).	
Selective Advantage Compared to Original Variant	• A model of selective advantage found Alpha was estimated to have a selective advantage of 0.337(0.336-0.339) over original variants in the UK (123).	One predictive model. Low level of evidence.
Secondary Attack Rate Compared to Original Variant	• In a Canadian study of household transmission Alpha had a secondary attack rate (SAR) that was RR=1.31(95%CI 1.14-1.49) times higher than non VOCs and the risk was accentuated for asymptomatic index cases (RR=1.91, 95% CI 0.96-3.80) and presymptomatic cases (RR=3.41, 95%CI 1.13-10.26) (26). • Within households in Norway alpha was 60% (20%-114%) more transmissible compared to original variants and overall the SAR was 0.13 for original variant and 0.15 for Alpha, which equates to 16% (-6% - 43%) more infectious (ratio of SARs) even when adjusting for age (22). • A study from Denmark reported 50-70% higher transmission among Alpha households compared to the original variants. Age specific transmissibility followed a U shaped pattern with the lowest transmission from primary cases in the 10 to 30 years age range, higher from younger children, and highest from elderly cases (27).	Five studies of household transmission including an outbreak in a kindergarten classes. The ratio of secondary attack rates was also provided as a measure of higher transmissibility for Alpha in some studies based on contact tracing studies. The results were conflicting across the studies summarized. These studies include three surveillance data analysis and one retrospective study. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• A German study reported household SAR in children and adults was 37% (95%CI 28-47) and was similar for child 32% vs adults 39& (124). Among daycare contacts the SAR for children 23% was similar to adults 30% (124). • In the UK, Alpha cases were almost twice as likely to lead to household clusters compared to the original variant (adjusted OR = 1.88, 95% CI 1.67 to 2.08, p<0.001) (125).	
Non-Pharmaceutical Interventions Compared to Original Variant	Stringency: • In the UK a Bayesian hierarchical model was used to show Tier 1 (light restrictions) had negligible effect on cases while Tiers 2 (moderate restrictions) and 3 (strong restrictions) reduced transmission by 6% (5%-7%) and 23% (21%-25%), respectively (120). Another analysis highlights that during December 2020 in the UK the highest values of Rt (~1.8) were recorded in areas with the least restrictions, lowest values in areas with the highest restrictions and Lockdowns effectively reduced Rt by ~0.9 by March 2021 (116). • A predictive model based in Canada parameterized Alpha (50% increased transmission in children and 70% in adults). Compared to restrictive lockdown, cases were estimated to be 3 times greater in Toronto with schools closed and community opened under moderate restrictions, 7 times higher if schools are closed/ 7.5 if they are open and the community is under light restrictions (126). • An SEIR model based on the situation in France describes the inability of non-pharmaceutical interventions such as curfew and physical distancing measures to reduce the Ro of Alpha under 1, when the same interventions were successful against original variants (127). • An age-stratified regionally structured transmission model to control the transmission of Alpha estimate that adherence to short stricter lockdowns would result in decreased	Seven predictive models and 1 ecological study, 1 surveillance data analysis. Predictive models are excellent tools to compare options, but caution should be exercised when extrapolating results beyond comparing model scenarios. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	hospital admissions and a moderate lockdown would reduce distress and improve sustainability (128). Quarantine: • A model to examine quarantine and test scenarios to control importations of SARS-CoV-2 in the EU reports Alpha does not change how effective quarantine and test strategies are (129). Personal Protective Measures: • This model is based on the US data and explores the impact of mask use for both source control and user protection using transmission data for the original variant and alpha the basic Ro of 2.5 could be decreased to Re<1.0 and Ro of 4 decreased to Re~1.6 respectively, thus better and more stringent mask use would be needed (130). • This disease transmission model estimated work place transmission risk for Alpha (0.041 transmission/contact vs. 0.014 for the original variant), with mask use the risk is still 2 times larger than the the original variant (131). Vaccination: • Vaccine strategies were given the higher transmissibility of Alpha were examined and predicted that even with 100% of the population vaccinated with AstraZeneca, R value would only reduce to 1.33 with 100% of the population vaccinated and could increase to 1.98 if 79% is vaccinated. The Pfizer-BioNTech vaccine would require 81.9% of the population to be vaccinated to reduce the value of R to 1 (122). • A predictive model showed decreased transmission of Alpha with vaccination had the greatest effect once transmission was already decreasing through public health mitigation strategies (132).	
Clinical Severity		

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Virulence / Severity or Duration of Disease Compared to Original Variant	More Alpha cases were hospitalized in 5 studies and admitted to the ICU in 2 studies of the general population. • Conflicting evidence on whether Alpha results in more asymptomatic infections: Prevalence of symptomatic disease was the same in an Italian study (32). Symptomatic proportion: Alpha cases, 72.6% (5,365/7,390) vs. original variant cases (81.4%; 547/672; p < 0.001) (28). • Majority of studies reported higher hospitalizations with Alpha infection: • Higher hospitalizations with Alpha vs original variant (11% vs. 7.5% p<0.001) (28); (5.8% vs 4.1% p=0.04) (38). Higher hospital admission 2.39% during the alpha wave vs. 1.55% in the initial wave in Spain (37). • Higher odds of Alpha cases being admitted to hospital compared to original variant (aOR 1.7, 95%CI 1.0-2.9) (28); OR 1.64 (95%CI 1.32-2.04) (33); OR 1.58 (95%CI 1.50 - 1.67) (34); (OR 1.36 95%CI 1.16-1.60, p=0.0002) (35). The hazard ratio for hospitalization due to Alpha vs. original variant (aHR 1.34, 95%CI 1.07-1.66) and length of stay was similar in both groups p=0.07 (36). • A study in Czech Republic reported no change in hospitalizations (39). • Higher ICU admissions with Alpha infection was reported in several studies: • ICU admission was 1.4% for Alpha vs original variant 0.6% p=0.002, which was a higher odds of ICU admission for Alpha aOR 2.3(95%CI 1.4-3.5) (28). ICU admission for Alpha aHR: 1.99 95%CI 1.59 - 2.49 compared to original variant (40). • Among hospitalized cases there was no association between severe disease and death among Alpha vs. original variants, adjusted PR 1·02 (95%CI: 0·76–1·38) (41); ICU scores or mechanical ventilation requirements (42). Symptoms:	14 studies on severity, these included surveillance data analysis, prospective cohorts, retrospective cohorts, and cross sectional studies, most of which have been conducted in the UK. Moderate level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	• Hypoxia (70.0% vs 62.5%, p=0.029) and higher respiratory rates (p=0.001) were reported among Alpha admissions in two studies (43, 44). • Fever over 38°C was significantly higher among hospital patients infected with the Alpha vs. the original variant (46% vs 22, p=0.015) (133)	
Severity Risk Factors Compared to Original Variant	There was no agreement across studies on whether any risk factors were associated with Alpha severity including age, and gender, but several studies did report that Alpha infections were less likely to have comorbidities: • A study from the USA reported no significant difference in patient age, gender, median length of hospital stay (35). • In another study age difference was statistically significant (37 vs. 39 years) (45). A study from Czech Republic reported significantly younger patients were hospitalized with the Alpha (median difference 58 vs 64 years of age) compared to the original variant (39). • In the age-stratified models, Alpha cases in the age groups 20–39 and 40–59 years had, respectively, 3.0 and 2.3 times higher odds of hospitalisation when compared with original variant cases (28). • A prospective cohort study in hospital patients identified a statistically significant difference in the age of those infected with the Alpha variant (39 years, IQR: 30.50 - 62.50) compared to those infected with the B.1.470 non-variant (31 years, IQR: 27.50 - 41.00) (P = 0.014) (133). • Among ICU patients in France, no significant difference in age or sex between Alpha and the original variant or Beta was documented (42). • A hospital cohort between Dec 2020 - Jan 2021 in France describes younger patients (63% >65 years dropped to 50%) with a mean age of 59.2 down from 70.7, patients without comorbidities increased 16% to 42% (p=0.007) (44). Pre-	9 studies on severity risk factors. These included surveillance data analysis, prospective cohorts, retrospective cohorts, and cross sectional studies, most of which have been conducted in the UK. Moderate level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	existing conditions were lower with Alpha, vs original variant, (44.8% vs. 89% p<0.001) (28). • A study of hospitalized COVID-19 cases reported a higher proportion of females with Alpha (48.0% vs 41.8%, p=0.01), fewer frail patients (14.5% vs 22.4% p=0.001) and higher proportions of obese cases (30.2% v 24.8%, p=0.048), but no difference by age or ethnicity (43).	
Mortality Compared to Original Variant	There is conflicting evidence on the association of mortality and Alpha infection: • Five studies reported no significant difference in mortality overall: Italy (2.1 vs. 4.1%) (32), USA (35, 38) and no association with 28 day mortality in UK (OR: 0.90, 95%CI 0.57-1.41, p=0.64) (36) or case fatality (OR= 1.37; CI: 0.5808-3.215, p = 0.52) (39). • One study estimated Alpha had a lower odds of mortality compared to original variant in the multivariable analysis (aOR 0.5, 95%CI 0.3-0.9) (28). • Four studies reported higher risk of mortality: higher 28 day hazard of death (55%, 95% CI: 39-72%) (47), aHR 1.59 (95%CI 1.25-2.03) (40), aHR 1.67 (95%CI 1.34 – 2.09; P <0.0001) (41). HR 1.64 (95%CI 1.32 - 2.04, p <0.001) which equates to an increase of 2.5 to 4.1 deaths per 1000 detected cases (48). The meta-analysis of these four studies had a pooled mortality risk of HR=1.45 (95%CI 1.18-1.78) (134). • Ecological studies from the UK estimates that Alpha is 33% more lethal (51) and has higher mortality (49).	13 studies reported on mortality these included surveillance data analysis, ecological studies, prospective cohorts, retrospective cohorts, and cross sectional studies, most of which have been conducted in the UK. Moderate level of evidence.
Mortality Risk Factors Compared to Original Variant	• Demographics of Alpha mortalities were similar in males and females, but was more prevalent in younger age groups than older age groups (59.0% in 1-34 year olds vs 55.4% in those 85 or older) (47). There was also variation by ethnicity: Black (69.6%), mixed or unknown ethnicity (64.8%), White (58.0%) and Asian (57.6%) and	Two studies which include surveillance data analysis, a retrospective cohort. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	was lowest in the most deprived quintile of the index of multiple deprivation (53.9%) (47). • No evidence of a significant associations between Alpha and sex (p = 0.90), ethnic group (p = 0.64) or age group (p = 0.15) (40).	
Viral Load Compared to Original Variant	• Several studies (n=14) measured viral load as Ct or estimated copies/mL for different target proteins (usually N and ORF1ab). They consistently indicate that Alpha samples are more likely to have lower Ct values or higher estimated viral loads. The median order of magnitude higher varies across studies and target protein from 2 to 10 fold differences (3, 32, 35, 39, 45, 54-59, 59-61, 117, 133, 135, 136).	22 studies that were mainly surveillance data analyses, cohort or cross sectional studies that analysed the PCR Ct values across Alpha samples and original variant samples. This measure is indirect and all study designs are observational, however the conclusion that Alpha cases have lower Ct values was consistent across studies Low to moderate level of evidence.
Animal Model of Viral Load Compared to Original Variant and Other VOCs/VOIs	• An animal study in rhesus macaques identified higher viral loads of genomic RNA in the nasal mucosa of Alpha infected animals compared to those infected with the wild-type and Beta variant and lower viral antigens in lung tissues compared to the wild-type (137). • Another study documented Alpha infected hamsters demonstrated high viral RNA shedding through nasal secretions during the first weeks of infection (138). • A mouse model identified viral load was significantly lower for the Alpha virus in the lungs of infected mice compared to Beta and Gamma viruses in both C57BL/6 and BALB/c lungs, with no infectious virus detected in the BALB/c lungs (139).	Three animal model studies in agreement offer consistent evidence of decreased viral load in lungs and increased viral loads in nasal mucosa. Low level of evidence.
Infectious Period	A prospective study that included Alpha cases (n=7) reported average infections last 13.3 days compared with 8.2 days for other variants (57).	One small prospective cohort. This outcome needs further evaluation

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
		with a larger sample size and range of cases. Very low level of evidence.
Incubation Period	*No studies*	
Immune Escape - Potential Impact on Vaccine Efficacy, Possibility of Re-infection		
Re-infection from Infection Compared to Original Variant	Three studies estimate the rate of re-infection. A study in the UK identified re-infection of 0.7% (95%CI: 0.6-0.8) (65) and in the USA previous seropositivity rate for persons with Alpha was 0.7% compared to original variant infections at 0.9% (38). A prospective study in the UK HCWs reported there was no evidence that Alpha changed the extent of protection from any PCR positive infection in those who were seropositive (aIRR 0.40, 95%CI 0.10-1.64, p=0.20) (66).	Three re-infection studies have included analysis on Alpha and are in agreement that Alpha does not evade natural immunity. These include surveillance data analysis, cohort and ecological studies. Moderate level of evidence.
Animal Model of Re-infection Compared to Original Variant	Hamsters infected with original SARS-CoV-2 and recovered were all protected from re-infection with Alpha (97, 140).	Two animal models reported consistent findings and support the evidence documented in human and *in vitro* studies. Low level of evidence.
***In vitro* studies Convalescent Sera** Compared to Original Variant	The majority of *in vitro* studies consistently showed minimal or small reductions in neutralization of Alpha compared to an original variant. Studies can be found in the dataset. There is consistency in the findings, the evidence is obtained from low quality studies.	There are many *in vitro* studies and this list is not complete at this time. Low level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness Compared to Original Variant	Breakthrough: • Case reports and case series report asymptomatic break through infections with Alpha in adults (73, 74, 141, 142) and elderly (143), HCWs in Brazil after Sinopharm (144), and HCW in India after Covishield vaccine (AZD1222) (145). • Alpha was 1.29 fold (95% CI [0.75, 2.20], p=0.468) more common in vaccine	20 studies reported on breakthrough infection after vaccination or vaccine effectiveness. The generalizability depends on the representativeness of the evidence to the general population. Consistent findings across studies improves the certainty in the results.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	breakthrough cases compared to the original variant cases (74). • In New York, among SARS-CoV-2 positive fully vaccinated persons, 22% were infected with Alpha compared to 44% had non-VOC infections (38). • A disproportionate number of Pfizer-BioNTech (BNT162b2) breakthrough infections between first dose and up to 14 days after the second dose in Israel resulted in an adjusted higher odds of being PCR positive with Alpha (aOR 2.4 (95%CI: 1.2 to 5.1) (67). • Real world studies in the UK have reported no difference in vaccine effectiveness (combined data with AstraZeneca and Pfizer-BioNTech) with Alpha variant (146). • After Pfizer-BioNTech vaccination the adjusted odds of inadequate neutralisation activity against the Alpha variant in the older (>80) age group compared to adult HCWs was aOR 4.4 (1.5-12.6, p<0.007) (147). Vaccination 1 dose: • In a prospective UK HCW study, there was no evidence that Alpha changed the extent of protection afforded by the first vaccine dose compared to the original variant (aIRR=1.84, 95%CI 0.75-4.49, p=0.18) (66). • After the first dose of Pfizer-BioNTech or AstraZeneca the reduced risk of emergency hospital admission was estimated to be 43% (33% to 52%) and 37% (3% to 59%) respectively and a 51% (37% to 62%) reduced risk of death in adults aged 70 years and older in England (75). Vaccination 2 doses: • After two doses of the Moderna or Pfizer-BioNTech vaccine a comparable adjusted vaccine effectiveness (≥ 88%) against symptomatic Alpha, Beta and Gamma variant	These studies include RCTs, prospective cohorts, case-control studies, longitudinal studies, and surveillance data analysis. High level of evidence for RCTs cohort studies, moderate evidence for prospective cohort studies and low level of evidence for all other study designs. Overall, moderate to high level of evidence. Case series and reports are very low levels of evidence but can be used to inform hypotheses for future research.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	infections ≥ 7 days after receiving the second dose were observed (72). • AstraZeneca (ChAdOx1-S) vaccine efficacy in a UK RCT of was 70.4% (95%CI 43.6- 84.5) against symptomatic COVID-19 caused by the Alpha and 81.5% (67.9 - 89.4) against symptomatic COVID-19 caused by original variants (76). For asymptomatic or unknown symptom infection, vaccine efficacy was higher for non-Alpha infections (69.7%, 33.0-86.3) than for Alpha (28.9%, –77.1-71.4) (76). • Novavax (NVX-CoV2373) vaccine efficacy in a UK RCT against Alpha and original variant was 86.3% (71.3 to 93.5) vs 96.4% (73.8 to 99.5), respectively (77). • Pfizer-BioNTech (BNT162b2) in Israel where 94% of cases were Alpha demonstrated vaccine effectiveness was >96% 14 days after the second dose (78, 148), this was 90% in adults 70+ in the UK (79). • A meta-analysis of vaccine efficacy trials of Pfizer-BioNTech VE after dose 1 51% (95%CI: 47-55%), after dose 2 93% (95%CI: 90-96%) and AstraZeneca VE after dose 1 49% (95%CI: 43-55%) after dose 2 66% (95%CI: 54-75%) (149).	
Animal Model of Vaccination Compared to Original Variant	• Hamsters vaccinated with AstraZeneca and then challenged with Alpha resulted in no weight loss, no lung pathology and no virus detected in tissue samples compared to controls who had extensive pulmonary pathology (98). Another study reported vaccinated hamsters with AstraZeneca vaccine and challenged with Alpha continued to gain weight while control animals had weight loss and extensive pulmonary pathology caused by Alpha in the control animals was observed, but not in the vaccinated animals (150). • Animals vaccinated with other vaccine candidates including spike RBD proteins (151-154) and SARS-CoV-2 infected human plasma,	Nine studies in animals were inconsistent in weight loss but consistent with pathology findings which are in agreement with human studies and *in vitro* studies. Low level of evidence.

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	DNA vaccines (155), and circRNA vaccines (156) all had neutralization activities against Alpha.	
***In vitro* study of Vaccinated Sera** Compared to Original Variant	There are many *in vitro* studies that are available in the dataset. The *in vitro* studies consistently showed minimal or small reductions in neutralization of Alpha compared to an original variant. They have not been summarized in the evidence profile.	There are many *in vitro* studies and this list is not complete at this time. Low level of evidence.
Animal Model of Therapeutics Compared to Original Variant	• A number of monoclonal antibodies tested protected mice and hamsters against Alpha (157). • Locked nucleic acid antisense oligonucleotides (158) and 4'-fluorouridine, a ribonucleoside analog (159) efficiently suppressed viral replication in hamsters and ferrets, respectively. • Convalescent plasma treatment resulted in decreased viral copy number in the lungs of mice infected with either the wild-type or Alpha variant. Convalescent plasma treatment did not reduce viral copy number in brain tissue of mice infected with Alpha compared to wild-type (153).	Four animal models. Low level of evidence
***In vitro* study of Therapeutics** Compared to Original Variant	Minimal loss of activity: several monoclonal antibodies (157, 160-162), polyclonal CP or purified hCoV-2-IG antibody preparations (163).	*In vitro* studies offer preliminary insights into what we may expect in vivo. Low level of evidence.
***In vitro* study of Infectivity** Compared to Original Variant	Pseudovirus carrying the UK-N501Y mutation to transduce its target cells compared to the original variant was significantly increased, up to 9-fold (164).	*In vitro* studies offer preliminary insights into what we may expect in vivo. Low level of evidence.
Testing and Diagnostics		
Testing and Detection	PCR is effective at detecting and distinguishing the variant (90, 165-171). Detection of Alpha in wastewater at proportions as low as 0.1% of SARS-CoV-2 (172). Multiple studies report reliable assays for rapid detection of variants including detection in wastewater samples (90, 100, 101, 172, 173).	32 studies, 28 diagnostic test accuracy studies, 3 surveillance data analyses that also described a new test or set of primers, and one *in silico* study designing primers. As

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
		these are all describing different tests the studies are considered to be individual and cannot be summarized together. Low level of evidence.
Spread Epidemiology		
VOC Emergence Over Time	• Two Canadian studies detail that Alpha cases were initially clustered in two regions and quickly increased (111, 174). Similarly, two studies from Ontario have documented the rapid increase in Alpha (13, 175). Studies were captured from many countries around the world, most describe the first detection of Alpha in mid to late December followed by a rapid increase in the variant over 3.5 to 10 weeks. It was noted to have become the dominant strain in several studies (39, 117). • One study from Israel documented a plateau and decline in the >60 years age group as >50% of the population had been vaccinated (1 dose Pfizer-BioNTech> 14 days) (24). The USA documented several introductions of Alpha around the country (15). One study from the USA documented daily SARS-CoV-2 positive tests from Alpha increased from 0.25% to 0.5% from October to December 2020 (176). Several studies document detection of Alpha in wastewater (172, 177-179).	116 studies report on the emergence and spread of Alpha in a country or region over time. Most of these studies are based on surveillance data, prospective cohorts often of HCWs, retrospective cohorts of hospital records, longitudinal studies, and ecological studies. Point prevalence or case reports of infected travellers were excluded from this summary.Low to moderate level of evidence.
Attribution to Alpha	An increase of 0.1 in the proportion of Alpha, considering the pre-peak period, was found to be associated with 35·8% increase in the height of the second wave peak. During the period from 1 January to 25 February 2021, an increase of 0.1 in the proportion of Alpha was related with a 15.3% increase in the cumulative number of deaths during that period (180).	One model used to estimate the additional burden of COVID-19 due to Alpha. Low level evidence.
Risk factors for spread	• An ecological study conducted in Toronto and Peel regions in Ontario showed that Alpha growth rate (11.3%, 19.8%, and 30.8%), overall	Five studies assessed risk factors. These include ecological studies,

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
	cases (19.0%, 32.7%, and 48.3%) and VOC cases (18.4%, 30.8% and 50.8%) were positively correlated with the proportion of essential workers (30.4%, 47.9% and 63.2%) and median income ($33k, $45k and $60k CAD) of the community, respectively (181). • Surveillance data from France found the Alpha variant infections were more common among older individuals compared to Beta or B.1.525. In hospital settings, there was an under-representation of Alpha compared to Beta. In specific regions of France, the odds of being infected by the original variant or a B.1.525 virus were either identical or lower than being infected by Alpha (11).	prospective cohorts, predictive models, and surveillance data analysis. Moderate level of evidence for prospective cohort studies. Low level of evidence for all other study designs.
Genomic Analysis of Spread	Results do not suggest that the canonical mutations of VOC Alpha evolved independently in different locations and points to an origin in and spread of the VOC Alpha from the UK (182).	One study of genomic surveillance data. Low level of evidence.

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio, aHR = adjusted Hazard Ratio, aPR= adjusted Prevalence Ratio

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. One of the foci is to identify studies as variants of concern or under investigation. Studies identified under this foci are further characterized in our VOC/VOI database and VOC results are extracted into this review. A cross check for relevant articles is also conducted within the databases using targeted keyword searching. This table is evolving as the evidence evolves.

Variant of Concern	Search terms
Alpha, B.1.1.7, 202012/01, 501Y.V1, Kent variant (Mutations: Δ69/70, Δ144Y, (E484K*), (S494P*), N501Y, A570D, D614G, P681H) * new variants with * mutations have been reported and are categorized as B.1.1.7 + E484K	B.1.1.7 OR 202012/02 OR 501Y.V1 OR Alpha

Beta, B.1.351, 501Y.V2, 20H/501.V2, South African variant (mutations: K417N, E484K, N501Y, D614G)	B.1.351 OR 501Y.V2 OR Beta
Gamma, P.1, B.1.1.28.1, 501Y.V3, 20J/501Y.V3, Brazil variant (mutations: K417N/T, E484K, N501Y, D614G)	P.1 OR B.1.1.28 OR 501Y.V3 OR Gamma
Delta, UK new VOC: 202102/02, B.1.1.7 with E484K mutation (name?)	See B.1.1.7 OR Delta
Variant Under Investigation	
USA: Epsilon, B.1.429 and B.1.427, 20C/S:452R, (mutations: L452R, D614G and S13I, W152C in 429 only)	B.1.429 and B.1.427, 20C/S:452R, CAL.20C, L452R OR Epsilon
Zeta P.2, B.1.1.28.2, in Brazil B.1.1.33	P.2 OR B.1.1.28 OR B.1.1.33 OR Zeta
UK: A.28.1	A.28.1
UK, Mexico, Nigeria: Eta, B.1.525	B.1.525 OR Eta
UK: B.1.318	B.1.318
Russia: B.1.317	B.1.317
New York: Iota B.1.526	B.1.526 OR Iota
USA others: B.1.426, recombinant B.1.1.7 + B.1.429	B.1.426 others captured with string for B.1.429
Theta, P.3, VUI-21MAR-02 named in Philippines (and has mutations E484, N501Y, P681H, LGV141-143)	P.3 OR Theta
B.1.617 India, sub-lineages: Kappa/ B.1.617.1 Delta/B.1.617.2 B.1.617.3 (double mutant E484Q and L452R)	B.1.617 or Delta or Kappa
B.1.618 India (triple mutant)	B.1.618

This review contains research published up to June 1, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX

a) VOC AND VOI LEXICON

WHO label (2021-05-27)	**Pango lineage**	**GISAID clade/lineage**	**Nextstrain clade**	**Earliest documented samples**	**Date of designation**
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I/S:501Y.V1	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/452R.V3	21A/S:478K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR	20B/S.484K	Brazil, Apr-2020	17-Mar-2021
Eta	B.1.525	G/484K.V3	20A/S484K	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR	20B/S:265C	Philippines, Jan-2021	24-Mar-2021
Iota	B.1.526	GH	20C/S:484K	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	India, Oct-2020	4-Apr-2021

b) VACCINE BRAND AND GENERIC NAMES

Brand Name	**Generic Name**
AstraZeneca	ChAdOx1-S
Covishield	AZD1222
Pfizer-BioNTech	BNT162b2
Janssen (Johnson & Johnson)	Ad26.COV2.S
Moderna	mRNA-1273
Novavax	NVX-CoV2373
Sinopharm	CoronaVac

c) OTHER RESOURCES

Reference	Description
Living Evidence Review on SARS-CoV-2 variants Australia On-going, last examined March 10.	This is table highlights recent relevant evidence under the different categories of study similar to what has been laid out in the profiles in this review.
CDC VOC page	Summary of each VOC is available.
WHO situation reports includes a VOC section.	
Review	
Transmission characteristics of SARS-CoV-2 variants of concern (MAR 2021) Curran, et al	Rapid scoping review done as part of the COVID-END network.

Data up to Feb 21, 2021	
Grey lit	
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 13. 2021 May	This report has been published to continue to share detailed surveillance of VOC-21APR02 (B.1.617.2) and information on a new variant under investigation VUI-21MAY-02 (C.36.3).
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 12. 2021 May	This report has been published to continue to share detailed surveillance of VOC-21APR02 (B.1.617.2) and information on a new variant under investigation VUI-21MAY-02 (C.36.3).
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. 2020 Dec to present	Technical reports compile information from various studies and surveillance across the UK on the VOC and VOIs that are circulating. There is a lot of overlap from these reports and research publications.
Public Health England. Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01 [Internet]. 2020 Dec	The VOC (Alpha) has grown rapidly in the UK and has been assessed as having substantially increased transmissibility
Public Health England. Analysis of transmissibility based on genomics [Internet]. 2020 Dec	Indication that Alpha grows 71% (95% CI: 67%-75%) faster per generation (6.5 days), yet consistent frequency does not indicate a constant selective advantage of Alpha
NERVTAG. NERVTAG meeting on SARS-CoV-2 variant under investigation VUI-202012/01 [Internet]. 2020 Dec	Moderate confidence that Alpha demonstrates a substantial increase in transmissibility compared to other variants.
NERVTAG. Update note on B.1.1.7 severity [Internet]. 2021 Feb	It is likely that infection with VOC Alpha is associated with an increased risk of hospitalization and death compared to infection with original variant viruses

Nouveaux éléments de preuve sur la COVID-19

Résumé évolutif à propos des variants préoccupants Alpha, Bêta et Gamma du SRAS-CoV-2

Faits saillants jusqu'au 1er juin 2021

Introduction

Les **variants préoccupants** (VP) du SRAS-CoV-2 sont des variants en circulation qui ont été signalés par les organisations nationales ou mondiales de santé publique. Ces variants deviennent préoccupants lorsqu'on les compare aux variants originaux du SRAS-CoV-2, puisque la complémentation de leurs mutations crée une transmissibilité et une virulence accrues (morbidité ou mortalité), des changements dans la présentation clinique de la maladie, de l'évasion immunitaire, une diminution de l'efficacité des vaccins, des thérapies ou des mesures de santé publique disponibles ou des échecs dans la détection aux fins de diagnostic (1, 2). Le Canada a créé sa propre définition nationale (2). Ce résumé évolutif axé sur la littérature sur les variants préoccupants du SRAS-CoV-2, soit B.1.1.7 (Alpha), B.1.351 (Bêta) et P.1 (Gamma), vise à présenter de nouvelles données sur les VP, leur épidémiologie et la façon dont leurs attributs peuvent influer sur la gestion de la pandémie. Ce résumé porte sur les changements dans les paramètres épidémiologiques (p. ex., taux de transmission, résultats cliniques en ce qui concerne la gravité et la mortalité, changements dans les groupes d'âge touchés ou proportions de personnes asymptomatiques), les répercussions sur les tests de diagnostic, l'évasion immunitaire ou et l'efficacité des vaccins, ainsi que les répercussions des VP sur d'autres mesures de santé publique. En mai 2021, l'Organisation mondiale de la Santé (OMS) a publié un système de nomenclature des variants préoccupants (VP) et des variants d'intérêt (VI) utilisant des lettres grecques afin de simplifier la communication à propos des variants et d'éliminer la stigmatisation potentielle découlant des endroits où les variants ont été identifiés la première fois et cette nomenclature est celle qui a été utilisée dans le présent résumé (1). La documentation sur le VP Delta est présentée dans un résumé évolutif distinct.

TABLEAU 1 : VARIANTS PRÉOCCUPANTS ACTUELS (VP)

Dénomination de l'OMS (mai 2021)	Lignée Pango	Clade Nextstrain	Clade GISAID	Autre nom	Premier cas détecté	Premiers échantillons	Mutations du spicule caractéristiques
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	Royaume-Uni	Septembre 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Bêta	B.1.351	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	Afrique du Sud	Août 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, B.1.1.28.1	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brésil et Japon	Décembre 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G H655Y, T1027I, V1176F
Delta	B.1.617.2[1]		G/452R.V3		Inde	Octobre 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R, del157/158, T478K, D950N)

[1] B.1.617.2 (Delta) a été ajouté à la liste des variants préoccupants le 11 mai 2021 et est présenté dans un résumé évolutif distinct.

La désignation **variants d'intérêt** (VI) ou variants à suivre est utilisée pour signaler un variant qui a le potentiel d'être un VP, mais pour lequel une enquête ou des preuves plus poussées sont requises. Les indicateurs de la désignation de VI incluent des changements phénotypiques ou l'acquisition de mutations ayant des implications phénotypiques établies EN PLUS du fait que ce variant doit avoir été à l'origine de la transmission dans la communauté, de plusieurs cas ou de concentration de cas de COVID-19 ou doit avoir été détecté dans plusieurs pays OU est par ailleurs vu comme un variant d'intérêt (VI) par un organisme comme l'OMS (1, 2). Au Canada, le groupe de surveillance des variants du SRAS-CoV-2 a établi la définition des VI et est responsable de l'évaluation et de la désignation des VI potentiels (2). Les données sur les VI ont été recueillies, mais ne sont pas mises en évidence dans le présent résumé. Le jeu complet de données en Excel est accessible ici et peut être filtré par variant d'intérêt.

Cet examen évolutif des éléments de preuve présente les éléments de preuve clé sur les variants Alpha, Bêta et Gamma, y compris les changements dans l'épidémiologie, l'échappement immunitaire et l'efficacité des vaccins, les répercussions sur les tests de diagnostic et les mesures de santé publique.

Quoi de neuf

Cette mise à jour comprend la littérature disponible jusqu'au 1er juin 2021. Au total, 345 nouvelles études sur le variant B.1.1.7 (Alpha, n = 200 études), B.1.351 (Bêta, n = 163) ou P.1 (Gamma, n = 91) depuis la dernière mise à jour du 28 avril 2021 sont incluses dans le jeu de données.

Points clés

En date du 1er juin 2021, 548 études faisaient état des VP ou des VI. 501 études portaient sur les variants B.1.1.7 (Alpha), B.1.351 (Bêta) et P.1 (Gamma) et ont été prises en compte dans les résumés présentés ci-dessous. Les études sur les VI (n = 47 études), les rapports de cas et les estimations ponctuelles de la prévalence (n = 35), ainsi que les études sur l'infectivité cellulaire, l'affinité de liaison ou la caractérisation génomique (n = 77) n'ont pas été résumées dans les profils des éléments de preuve. Des résumés généraux sont présentés dans le tableau des points clés (tableau 2) alors que des résumés plus détaillés de chacun des VP figurent dans les sections correspondantes du résumé. Les détails de chacune des études figurent dans le jeu de données en Excel accessible ici. Dans l'ensemble, les éléments de preuve portaient surtout sur le variant Alpha (n = 342) comparativement au Bêta (n = 229) et au Gamma (n = 125).

Transmissibilité :

- Toutes les études ont montré une augmentation de la transmissibilité pour les variants Alpha (tableau 5), Bêta (tableau 4) et Gamma (tableau 3) comparativement au variant original, bien que la portée soit très variable. En ce qui concerne le variant Alpha, deux études canadiennes utilisant des données de surveillance sur la population générale et des données sur la transmission intrafamiliale ont indiqué une augmentation de 34 % de la transmissibilité et de 31 % des taux d'attaque secondaires, respectivement. Le variant Alpha avait une plus grande efficacité de transmission que les variants Bêta et Gamma.

Gravité clinique :

- En ce qui concerne le variant Alpha, les différentes études ont présenté des preuves contradictoires à propos des probabilités d'admission à l'hôpital, alors qu'un petit nombre d'études ont signalé des probabilités plus élevées d'hospitalisation pour les variants Bêta et Gamma. Des associations conflictuelles ont été signalées pour les admissions aux soins intensifs avec les variants Bêta et Alpha, alors que les probabilités étaient plus élevées en ce qui concerne le variant Gamma. Par rapport au variant original, les variants Alpha et Bêta n'ont pas été associés au risque de devoir être mis sous ventilation mécanique ou d'avoir un score de sévérité plus élevé pendant le séjour à l'USI. Toutefois, ces données sont fondées sur un nombre limité d'études ayant analysé rétrospectivement la surveillance et les données sur les hospitalisations.
- En ce qui concerne les indicateurs de sévérité
    - Quelques études sur les variants Alpha, Bêta et Gamma ont fait état d'un risque d'hospitalisation stratifié selon l'âge et d'une augmentation des probabilités chez les adultes de 20 à 59 ans, tandis que d'autres n'ont signalé aucune association.
    - Plusieurs études ont également rapporté une proportion plus faible de conditions préexistantes, à l'exception de l'obésité, parmi les cas associés aux VP.
- Les associations avec la mortalité étaient conflictuelles entre les études portant sur les variants Alpha, Bêta et Gamma. Une étude a fait état d'une augmentation de la mortalité à l'USI pour le variant Bêta. Le

risque de mortalité aurait également augmenté dans certains groupes d'âge adulte pour les variants Alpha et Gamma.

- Comparativement au variant original, la charge virale était toujours de 2 à 10 fois plus élevée pour le variant Alpha. Elle était également plus élevée pour les variants Gamma et Bêta que le variant original, mais inférieur à celui du variant Alpha.
- Aucune étude n'a évalué la période infectieuse pour les variants Gamma et Bêta. Une petite étude, portant sur 7 personnes ayant été infectées par le variant Alpha, a révélé que l'infection moyenne, un virus cultivé, a duré 13,3 jours avec le variant Alpha comparativement à 8,2 jours pour les autres variants. Des recherches supplémentaires sont nécessaires pour augmenter la confiance dans ce résultat.
- Aucune étude n'a cependant été effectuée sur la période d'incubation des VP.

Échappement immunitaire :

- Rien n'indique que le taux de réinfection pour le variant Alpha a changé par rapport au variant original, aucune donnée n'est disponible pour le variant Bêta. Deux études effectuées au Brésil indiquent qu'il pourrait y avoir d'importantes réinfections associées au variant Gamma, mais ces études sont fondées sur des analyses écologiques et études plus poussées à ce sujet seront donc requises.
- Les données tirées des études sur l'efficacité des vaccins indiquent un niveau de protection réduit après la première dose du vaccin, mais une protection équivalente après la deuxième dose dans la plupart des études portant sur les variants Alpha et Gamma, alors que les études sur le variant Bêta ont donné des résultats variables.

Autres catégories :

- D'autres catégories liées à la performance diagnostique et à la recherche épidémiologique sur la diffusion et l'incidence des interventions non pharmaceutiques sont résumées dans les sections approfondies sur les VP.
    - Aucune étude évaluant les tests de diagnostic ou de détection du SRAS-CoV-2 n'a décrit de problèmes d'échec ou de performance pour la détection des VP, à l'exception de la perte bien caractérisée du gène S pour le variant Alpha.
    - Plusieurs études de modélisation prédictives ont mentionné les interventions non pharmaceutiques (p. ex., limitation des rassemblements, fermetures, port du couvre-visage et confinement). Bien qu'une plus grande rigueur, un plus grand nombre de fermetures et de restrictions, ait été nécessaire pour contrôler les VP en raison d'une transmissibilité plus élevée, aucune modification des interventions individuelles n'a cependant été nécessaire.
    - Les études sur l'introduction et la propagation des VP dans une région géographique n'ont pas été incluses dans le tableau ci-dessous, mais des résumés à ce sujet sont disponibles dans les profils des VP individuels, tout comme les résumés portant sur les modèles animaux et les études in vitro sur la réinfection, l'efficacité des vaccins et l'incidence potentielle des VP sur les traitements.

Les catégories de preuve indiquées dans les tableaux ci-dessous comprennent les preuves suivantes, lorsqu'elles sont déclarées :

La **transmissibilité** comprend les changements dans la transmissibilité, les taux d'attaque secondaires et les estimations de l'avantage sélectif.

La **gravité clinique** comprend la proportion des infections qui sont symptomatiques, la proportion d'atteinte grave et de mortalité, ainsi que les facteurs de risque pour les atteintes graves ou la mortalité, la charge virale,

la période infectieuse et la période d'incubation. Il faut cependant noter que les facteurs de risque d'une atteinte grave incluraient les populations spéciales, p. ex., les femmes enceintes, si elles sont déclarées.

L'**échappement immunitaire** comprend les changements dans l'efficacité du vaccin, le risque de réinfection chez les humains, les modèles animaux, les expériences *in vitro* ou *in silico*, ainsi que les répercussions sur les thérapies si elles sont déclarées.

Les **échecs des tests de diagnostic/détection** sont saisis dans les sections individuelles, et ne seront inclus dans le tableau 2 que si la performance du test est préoccupante.

La mention **Autres épidémiologies** inclut toutes les études qui documentent l'émergence et la propagation des VP dans une région géographique, les études écologiques qui examinent la propagation des VP et les facteurs de risque pour les points chauds, ainsi que les études sur les interventions en santé publique efficaces contre les VP et l'épidémiologie génomique comme sous-catégories.

TABLEAU 2 : RÉSUMÉ DES PREUVES CLÉS DU VP P.1 (GAMMA) (N = 125), DU VP B.1.351 (BÊTA) (N = 229) ET DU VP B.1.1.7 (ALPHA) (N = 342)

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
EFFICACITÉ DE LA TRANSMISSION			
Transmissibilité Comparativement au variant original ou au variant Alpha	Trois analyses de données de surveillance, une étude transversale et un modèle prédictif : • 27 % de plus en France (variants Gamma et Bêta combinés) (3) • 160 % à 100 % plus élevé au Brésil (4, 5) • Un modèle qui a examiné le variant Gamma en Italie a signalé une transmissibilité de 12 à 39 % plus élevée selon que ce variant présentait ou non un échappement immunitaire (6). D'autres études placent la transmissibilité du variant Gamma entre celle du variant original et celle du variant Alpha (7).	Cinq rapports de données de surveillance : • 27 % de plus en France (variants Gamma et Bêta combinés) (3) par rapport au variant original. • 55 % (8, 9) et entre 20 et 100 % plus élevé en Afrique du Sud (10) par rapport au variant original. • Avantage de transmission de 15,8 % à 17,1 % par rapport au variant Alpha dans certaines régions de la France entre avril et mai 2021 (11). Faible niveau de preuve.	34 études de surveillance et d'observation : • Les estimations de l'augmentation de la transmissibilité relative du variant Alpha (1-$R_{VP}/R_{Variant\ original}$) variaient entre 34 et 118 % entre les différentes études, une partie de cette variation étant due à l'époque (12) et au pays (plus élevée au Royaume-Uni) (9) : ○ Canada : 34 % (IC à 95 %, 31 à 38) (13), É.-U. : 35 à 59 % (14, 15). ○ Royaume-Uni : de 43 à 118 % (9, 12, 14, 16 à 18), de 13,4 à 41,3 % dans les régions du Royaume-Uni en décembre 2020 (19). ○ Europe : France 41 à 52 % (3, 20), Danemark 55 %, Suisse 54 à 74 % (14), (21), Norvège 24 % (22), Italie 55 à 57 % (23), Pays de Galles et É.-U. 65 à 72 % (9). ○ Israël 45 % (24). ○ Le Japon a estimé une augmentation de 60 % de la transmissibilité relative des VP (aucune précision indiquée) (25). ○ Le variant Alpha avait une plus grande efficacité de transmission que les variants Bêta et Gamma (7).

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
	Faible niveau de preuve.		• De même, les ratios des taux d'attaque secondaire parmi les études sur la transmission intrafamiliale étaient de 30 à 70 % plus élevés au Canada (26), en Norvège (22) et au Danemark (27). Niveau de preuve faible à modéré.
SÉVÉRITÉ CLINIQUE			
Virulence/gravité ou durée de la maladie Comparativement au variant original ou au variant Alpha	Deux études de surveillance : • Une proportion plus élevée de cas qui ont été hospitalisés (p < 0,001) (28). • Une plus grande probabilité d'être admis à l'hôpital (RCa 2,6, IC à 95 %, 1,4 à 4,8) (28). • Une plus grande probabilité d'être admis aux soins intensifs (RCa 2,2, IC à 95 %, 1,8 à 2,9) (28). • Une croissance exponentielle du nombre d'hospitalisations a été signalée à Rio Grande do Sul et à Porto Alegre (29).	Quatre (4) études, incluant des études de surveillance et d'observation : • Une plus grande probabilité d'hospitalisation en raison du variant Bêta comparativement au variant original (RCa 3,6, IC à 95 %, 2,1 à 6,2) (28) ou au variant Alpha (RC 1,56) dans plusieurs pays européens (11). Données contradictoires sur les admissions aux soins intensifs associées au variant Bêta, avec des probabilités plus élevées (RCa 3,3, IC à 95 %, 1,9 à 5,7) dans les pays européens (30) et une proportion plus faible (35 % contre 48,5 %, p = 0,03) en Afrique du Sud (31) comparativement au variant original.	17 études de surveillance et d'observation : • Des données contradictoires sur la prévalence de la maladie symptomatique n'ont révélé aucune différence dans une étude et moins de cas symptomatiques (p < 0,001) dans une autre (28, 32). • Sept études ont révélé une probabilité plus élevée d'admission à l'hôpital (RCa 1,36 à 1,7 et RRa 1,34) (28, 33 à 39) alors qu'une autre n'a indiqué aucune différence (39). • Deux études ont révélé une probabilité plus élevée d'admission aux soins intensifs (RCa 2,3, RRa 1,99) (28, 40). • Une étude n'a indiqué aucune association entre le variant Alpha et la forme grave de la maladie (RPa 1 02) parmi les cas ayant été hospitalisés (41). • Il n'y avait aucune différence significative entre les scores de l'unité de soins intensifs ou les exigences associées à la ventilation mécanique entre les variants Alpha, Bêta et le variant original (42).

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
	Faible niveau de preuve.	Faible niveau de preuve.	• Des taux plus élevés d'hypoxie à l'admission à l'hôpital ont été signalés dans deux études (43, 44). Niveau de preuve modéré.
Facteurs de risque sur la gravité Comparativement au variant original ou au variant Alpha	Une étude de surveillance européenne : • Les cas associés au variant Gamma avaient une probabilité d'hospitalisation de 3,0 à 13,1 fois plus élevée dans les groupes d'âge 20 à 79 ans (28). • L'admission à l'USI était 2,9 à 13,9 fois plus élevée dans les groupes d'âge ≥ 40 ans (28). • Les conditions préexistantes étaient moins nombreuses, soit 27,8 % pour le variant Gamma contre 89 % pour le variant original, p < 0,001 (28). Faible niveau de preuve. Trois autres études d'observation ont été effectuées	Trois études comprenant des études de surveillance et d'observation : • La probabilité d'hospitalisation était plus élevée dans plusieurs pays européens (28) chez les adultes de 40 à 59 ans et de 60 à 79 ans (RC 3,5 à 3,6) infectés par le variant Bêta alors qu'en Afrique du Sud, les patients qui ont été hospitalisés après avoir été infectés par ce variant étaient beaucoup plus âgés (57 contre 54 ans, p = 0,03) (31) que ceux qui ont été infectés par le variant original. • Les preuves sont contradictoires en ce qui concerne l'âge de l'admission à l'unité des soins intensifs en raison du variant Bêta puisqu'on a vu une probabilité plus élevée chez les adultes âgés de 40 à 59 ans (RCa 8, IC à 95 %, 3,7 à 17,3) dans plusieurs pays européens (28), mais aucune différence significative d'âge (63 contre 67 ans, p = 0,15) en France (42), par rapport au variant original.	Dix études d'observation : • Une étude sur les cas de patients atteints de COVID-19 et hospitalisés a indiqué une plus grande proportion de femmes (48,0 % contre 41,8 %, p = 0,01), un plus petit nombre de patients fragiles (14,5 % contre 22,4 %, p = 0,001) et une plus grande proportion de personnes atteintes d'obésité (30,2 % contre 24,8 %, p = 0,048), mais aucune différence en ce qui concerne l'âge ou l'ethnie (43). • Les études n'ont signalé aucune différence significative en ce qui concerne l'âge et le sexe des patients, ainsi que la durée médiane du séjour à l'hôpital (35, 42). La différence d'âge était cependant statistiquement significative dans une autre étude (37 et 39 ans) (45). • Une étude a indiqué un ratio de probabilité d'hospitalisation 3,0 fois plus élevé chez les 20 à 39 ans et 2,3 fois plus élevé chez les 40 à 59 ans alors que les conditions préexistantes étaient moins nombreuses (44,8 % contre 89 % p < 0,001) (28). • Une étude réalisée dans les hôpitaux en France a révélé que l'âge moyen était de

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
	sans séquençage du génome entier (très faible niveau de preuve).	• Les cas infectés par le variant Bêta étaient moins susceptibles d'avoir des comorbidités comparativement aux cas infectés par le variant original en Europe et en Afrique du Sud (28, 31). Faible niveau de preuve.	59,2 ans, en baisse par rapport à 70,7 ans, et que le nombre de patients sans comorbidité avait augmenté de 16 % à 42 % (p = 0,007) (44). Niveau de preuve faible à modéré.
Mortalité Comparativement au variant original ou au variant Alpha	Deux études observationnelles et un modèle prédictif : • Le variant Gamma présentait une probabilité de mortalité globale plus faible (RCa 0,6, IC à 95 %, 0,3 à 1,0) (28). • Taux de mortalité à l'hôpital plus élevé chez les jeunes adultes de 18 à 50 ans (46). • Le modèle prédictif a estimé que la mortalité moyenne était 1,5 fois (50 %, intervalle de crédibilité 1,2 à 1,9) plus élevée après l'émergence du variant Gamma (5).	Trois études comprenant des études de surveillance et d'observation : • Des études effectuées dans différents pays et contextes à propos de la mortalité liée au variant Bêta ont donné des données contradictoires. Ainsi, l'Afrique du Sud a indiqué une proportion accrue de mortalité (36,4 % contre 32,6 %, p = 0,26) (31) alors que plusieurs pays européens n'ont signalé aucune différence dans les probabilités de décès (RCa 1,1, IC à 95 %, 0,4 à 3,4) (28) par rapport au variant original. • Une proportion plus élevée de mortalité liée au variant Bêta à l'USI (74,4 % contre 57,1 %, p = 0,002) comparativement au variant original en Afrique du Sud (31) et probabilité de décès à l'USI plus élevée (RC 5,67, IC à 95 %, 1,04 à 30,81, P = 0,04)	16 études de surveillance et d'observation : • Cinq études n'ont signalé aucune différence significative en matière de mortalité globale (2,1 contre 4,1 %) (32, 35, 38, 39) ou après 28 jours (RC : 0,90, IC à 95 %, 0,57 à 1,41, p = 0,64) (36). • Une étude a fait état de probabilités de mortalité plus faibles (RCa 0,5, IC à 95 %, 0,3 à 0,9) (28). • Huit études ont fait état d'un risque de mortalité plus élevé : risque plus élevé de décès après 28 jours (55 %, IC à 95 %, 39 à 72 %) (47), RRa 1,59 (IC à 95 %, 1,25 à 2,03) (40), RRa 1,67 (IC à 95 %, 1,34 à 2,09; P < 0,0001) (41). RR 1,64 (IC à 95 %, 1,32 à 2,04, p < 0,001) (48), ce qui équivaut à une augmentation de 2,5 à 4,1 décès par 1 000 cas détectés (37, 49, 50). Une étude écologique a estimé qu'au Royaume-Uni, le variant Alpha était 33 % plus meurtrier (51).

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
	Faible niveau de preuve.	comparativement aux données enregistrées en France avec le variant Alpha (42). Faible niveau de preuve.	• Parmi les patients qui se trouvaient dans l'USI en France, les cas associés au variant Bêta présentaient des probabilités plus élevées de mourir dans les 60 jours suivant l'admission à l'USI comparativement aux cas infectés par le variant Alpha (RC 5,67, IC à 95 %, 1,04 à 30,81) (42). Niveau de preuve modéré.
Facteurs de risque de mortalité comparativement au variant original	Une étude de surveillance au Brésil : • La mortalité chez les personnes atteintes de la COVID-19 et âgées de moins de 60 ans est passée de 18 % en novembre 2020 à 28 % en février 2021 (52). • La mortalité chez les personnes ne présentant aucune condition préexistante était plus élevée chez les femmes (RR 5,65, IC à 95 %, 2,9 à 11,03; p < 0,0001) et chez les personnes âgées de 40 à 59 ans (RR 7,7, IC à 95 %, 5,01 à 11,83; p < 0,0001) après l'émergence du variant Gamma (52). Faible niveau de preuve.	Aucune étude	Deux études de surveillance et de cohorte rétrospective : • Une étude a révélé que la mortalité était plus élevée dans les groupes d'âge plus jeunes que dans les groupes plus âgés (59,0 % chez les 1 à 34 ans contre 55,4 % chez les 85 ans ou plus) et qu'elle était plus élevée chez les Noirs (69,6 %), les personnes d'origine ethnique mixte ou inconnue (64,8 %), les Blancs (58,0 %) et les Asiatiques (57,6 %) (47). • Une autre étude n'a trouvé aucune augmentation de la mortalité en fonction du sexe (p = 0,90), du groupe ethnique (p = 0,64) ou du groupe d'âge (p = 0,15) (40). Faible niveau de preuve.

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
Charge virale Comparativement au variant original	Deux études de surveillance : • La charge virale des cas associés au variant Gamma était environ 10 fois plus élevée que celle des cas non associés à ce variant (variants originaux) (53). • La charge virale était plus élevée que celle associée au variant original, mais était inférieure à celle associée au variant Alpha (3). Faible niveau de preuve.	Aucune étude	Vingt-deux études d'observation et analyses de surveillance : • On a toujours trouvé des valeurs de Ct plus faibles ou des charges virales estimées plus élevées. L'ordre de grandeur médian supérieur varie selon les études et la protéine cible de 2 à 10 fois la différence (3, 32, 35, 45, 54 à 59, 59 à 61). Niveau de preuve faible à modéré.
Période infectieuse par rapport au variant original	Aucune étude	Aucune étude	Une petite étude (n = 7 cas infectés par le variant Alpha) effectuée aux É.-U. a calculé que les infections durent en moyenne 13,3 jours comparativement à 8,2 jours pour les autres variants (57). Très faible niveau de preuve.
Période d'incubation	Aucune étude	Trois études comprenant des études de surveillance et d'observation : • La probabilité d'hospitalisation était plus élevée dans plusieurs pays européens (28) chez les adultes de 40 à 59 ans et de 60 à 79 ans (RC 3,5 à 3,6) infectés par le variant Bêta alors qu'en Afrique du Sud, les patients qui ont été hospitalisés après avoir été infectés par ce variant étaient beaucoup plus âgés	Aucune étude.

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
		(57 contre 54 ans, p = 0,03) (31) que ceux qui ont été infectés par le variant original. • Les preuves sont contradictoires en ce qui concerne l'âge de l'admission à l'unité des soins intensifs en raison du variant Bêta puisqu'on a vu une probabilité plus élevée chez les adultes âgés de 40 à 59 ans (RCa 8, IC à 95 %, 3,7 à 17,3) dans plusieurs pays européens (28), mais aucune différence significative d'âge (63 contre 67 ans, p = 0,15) en France (42), par rapport au variant original. • Les cas infectés par le variant Bêta étaient moins susceptibles d'avoir des comorbidités comparativement aux cas infectés par le variant original en Europe et en Afrique du Sud (28, 31). Faible niveau de preuve.	
ÉCHAPPEMENT IMMUNITAIRE – Incidence potentielle sur l'efficacité du vaccin, possibilité de réinfection			
Réinfection par infection naturelle comparativement au variant original	Deux études de surveillance : • En supposant que 78 % de la population était déjà infectée, on estime que 28 % des cas à Manaus signalés entre novembre 2020 et janvier 2021 étaient des réinfections (4).	Trois études, incluant des exposés de cas et des études d'observation : • Trois cas de réinfection par le variant Bêta ont été signalés (62 à 64).	Trois études ont montré que le variant Alpha n'échappait pas à l'immunité naturelle : • un taux de réinfection estimé à 0,7 % (IC 95 % : 0,6 à 0,8) (65). • Dans une étude menée aux États-Unis, le taux de séropositivité antérieur chez les personnes atteintes du variant Alpha était

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
	• On estime que 16,9 % des cas associés au P.1 (IC à 95 %, 9,48 à 28,5) à Manaus signalés entre janvier 2021 et mars 2021 étaient des réinfections (81). Faible niveau de preuve.	Très faible niveau de preuve.	de 0,7 % comparativement aux infections sans VP qui était de 0,9 % (38). • Une étude britannique n'a trouvé aucune preuve que le variant Alpha modifiait l'étendue de la protection positive à l'infection par PCR chez les personnes séropositives (RTIa 0,40, IC à 95 %, 0,10 à 1,64, p = 0,20) (66). Niveau de preuve modéré.
Infection sporadique après la vaccination, efficacité réelle ou prévue du vaccin comparativement au variant original	Deux études cas-témoins : Une dose du vaccin : • La vaccination avec au moins une dose de CoronaVac a été associée à une réduction d'un facteur de 0,50 (EV ajustée, 49,6 %; IC à 95 %, 11,3 à 71,4) des probabilités d'infection symptomatique par le SRAS-CoV-2 14 jours après administration de la première dose (82). Deux doses du vaccin : • Sept jours ou plus après la deuxième dose, le vaccin Moderna ou Pfizer avait une EV ajustée de 88 % (IC à 95 %, 61 à 96) contre une infection symptomatique au variant P.1 comparativement	Sept études, incluant des essais cliniques randomisés (ECR) et des études d'observation : Infection ayant percé après la vaccination : • Aucune infection ayant percé n'a été identifiée plus de 14 jours après l'administration de la deuxième dose (principalement Pfizer) dans une étude cas/témoins menée en Israël (67) • 50 % (13 sur 26) des résidents des maisons de soins infirmiers et 5,2 % (1 sur 19) des membres du personnel qui ont reçu le vaccin Pfizer-BioNTech ont été atteints par des infections ayant percé associées au variant Bêta (64). Deux doses du vaccin :	Treize études comprenant des ECR, des cohortes et des études de surveillance : Infection ayant percé après la vaccination : • Une enquête sur une éclosion chez des travailleurs de la santé a révélé que deux médecins pleinement vaccinés par Pfizer-BioNTech ont été infectés par le variant Alpha. Ils ont reçu la deuxième dose un mois avant l'apparition des symptômes (73). • Aux États-Unis, les cas d'infection ayant percé associée au variant Alpha n'étaient pas plus courants que ceux associés au variant original (1,29 fois, IC à 95 %, 0,75 à 2,20, p = 0,468) (74). Une dose du vaccin : • Pfizer-BioNTech (BNT162b2) en Israël, où 94 % des cas étaient associés au variant Alpha, efficacité du vaccin contre l'infection symptomatique entre la première dose et

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
	à une infection par la souche sauvage (93 %, IC à 95 %, 87 à 96). L'EV ajustée pour une dose contre le variant P.1 était de 43 % (IC à 95 %, 22 à 59) par rapport à la souche sauvage (61 %, IC à 95 %, 53 à 67) (72). Faible niveau de preuve.	• AstraZeneca (ChAdOx1-S) : 10,4 % d'efficacité pour la prévention de la maladie symptomatique (68). • Johnson et Johnson : EV de 52 % et de 64 % pour la forme modérée de la maladie et de 73 % et de 82 % pour la forme grave après 14 jours et 28 jours respectivement (69). • Novavax (NVX-CoV2373) : EV de 51,0 % (IC à 95 %, -0,6 à 76,2) contre la maladie symptomatique chez les personnes séronégatives (70). • Pfizer-BioNTech (BNT162b2) :Au Qatar, EV de 75,0 % (IC à 95 %, 70,5 % à 78,9 %) contre l'infection par le variant Bêta 2 semaines après la deuxième dose (71). Une EV de 50 % (IC à 95 %, 34 % à 73 %) chez les résidents des maisons de soins infirmiers (âge médian : 87,0 ±8,2 ans) avec deux doses espacées de 19 jours (64). • Moderna/Pfizer-BioNTech : EV comparable de 88 % contre l'infection symptomatique associée au variant Bêta 7 jours après avoir reçu la deuxième dose (72).	jusqu'à 14 jours après la deuxième dose (RCa 2,4 (IC à 95 %, 1,2 à 5,1) (67). • Pfizer-BioNTech (BNT162b2) ou AstraZeneca (ChAdOx1-S) La première dose du vaccin a réduit le risque d'hospitalisation d'urgence chez les adultes de 70 ans et plus de 43 % (33 % à 52 %) et de 37 % (3 % à 59 %) en Angleterre, respectivement (75). • Le risque de décès a été réduit de 51 % (37 % à 62 %) chez les adultes de 70 ans et plus en Angleterre qui avaient reçu une dose de Pfizer-BioNTech (75). • Une étude menée au Royaume-Uni n'a révélé aucune différence dans la protection contre le variant Alpha par rapport aux autres variants après une première dose de vaccin (RTIa = 1,84, IC à 95 %, 0,75 à 4,49, p = 0,18) (66). Deux doses du vaccin : • Dans un ECR effectué au Royaume-Uni, l'efficacité du vaccin AstraZeneca/ COVISHIELD (ChAdOx1) était de 70,4 % (IC à 95 %, 43,6-84,5) comparativement à 81,5 % (67,9 à 89,4) pour les variants originaux (76). • Dans un ECR effectué au Royaume-Uni, l'efficacité du vaccin Novavax (NVX-CoV2373) contre le variant Alpha était de 86,3 % (71,3 à 93,5) alors qu'elle était de

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7 (Alpha)
			96,4 % (73,8 à 99,5) pour le variant original (77). • Pfizer-BioNTech (BNT162b2) En Israël, où 94 % des cas étaient associés au variant Alpha, l'efficacité du vaccin était supérieure à 96 % 14 jours après la deuxième dose (78) et supérieure à 90 % chez les 70 ans et plus (79). • Au Canada, deux doses du vaccin Moderna (ARNm-1273) ou Pfizer-BioNTech avaient une efficacité comparable ajustée (≥88 %) contre les infections symptomatiques associées aux variants Alpha, Bêta et Gamma, ≥7 jours après l'administration de la deuxième dose (72).
		Niveau de preuve faible à modéré.	Niveaux de preuve variables, allant des ECR (modérés à élevés) aux observations cliniques (très faibles).

IC = intervalle de confiance, Ct = seuil du cycle, USI = unité de soins intensifs, RC = rapport des cotes, PCR = réaction en chaîne par polymérase, EV = efficacité du vaccin, RCa = rapport de cotes ajusté, RRa = rapport de risque ajusté, RPa = rapport de prévalence ajusté

Vue d'ensemble des éléments de preuve

Les modèles d'étude inclus dans ce résumé vont des essais cliniques randomisés en double aveugle à faible risque de biais à un certain nombre de modèles d'étude par observation différents ayant différents niveaux de preuves. Les études d'observation permettent d'obtenir des éléments de preuve de qualité faible à modérée selon la méthodologie particulière utilisée et de la cohérence entre les études. Les études descriptives incluses dans le présent examen, ce qui inclut les séries de cas et rapports de cas, les modèles prédictifs, les études écologiques, les modèles animaux et les études *in vitro*, présentent de faibles à très faibles éléments de preuve et ne peuvent généralement pas être utilisés pour générer des hypothèses, car celles-ci devront être examinées plus à fond avec une méthodologie distincte. Compte tenu de la très grande variation observée, une indication du niveau de confiance des éléments de preuve est donc requise pour s'assurer d'obtenir un résultat particulier. Les méthodologies sont indiquées, mais aucune évaluation officielle du risque de biais n'a été effectuée.

Il y a plusieurs lacunes dans les connaissances ou des domaines où très peu de recherche figure dans le tableau des points clés, et des recherches supplémentaires sont nécessaires pour améliorer la confiance dans les résultats sommaires, en particulier pour les variants Bêta et Gamma.

TABLE DES MATIÈRES

P.1 (GAMMA)

Le jeu de données en Excel comprend des résumés de chacune des études et est accessible ici. Vous trouverez ci-dessous le profil détaillé des éléments de preuve élaboré pour le variant Gamma. Il porte notamment sur les données sur les changements dans l'efficacité de la transmission, les changements dans la gravité clinique, l'échappement immunitaire, les tests et diagnostics, ainsi que d'autres études épidémiologiques portant principalement sur la propagation des VP.

Tableau 3 : Profil fondé sur les éléments de preuve pour le VP P.1 (Gamma) (n = 125)

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
Efficacité de transmission		
Transmissibilité comparativement au variant original	Une transmissibilité accrue par rapport au variant original : • 27 % de plus en France pour les variants Gamma et Bêta combinés (3). • 2,6 (IC à 95 % : 2,4 à 2,8) fois plus élevé (4) et 2,0 (50 % intervalle de crédibilité 1,7 à 2,4) fois plus transmissible avec une immunité croisée médiane estimée à 68 % (50 % intervalle de crédibilité 54 à 79) au Brésil (5). • 1,12 (IC à 95 %, 1,03 à 1,23) fois plus transmissible avec un échappement immunitaire complet à 1,39 (IC à 95 %, 1,26 à 1,56) et protection complète en Italie (6). • D'autres études placent la transmissibilité du variant Gamma entre celle du variant original et celle du variant Alpha et montrent que la transmissibilité du variant Gamma a légèrement diminué au fil du temps entre janvier 2021 et avril 2021 partout dans le monde (7).	Cinq études ont fourni des estimations de la transmissibilité du variant Gamma, notamment : trois analyses de données de surveillance portant sur le Brésil (2) et à l'échelle mondiale (1), une étude transversale provenant de la France et un modèle prédictif établi en Italie. Il y a peu de cohérence entre les études. L'hétérogénéité des estimations de la transmissibilité accrue peut être due à des facteurs tels que l'emplacement géographique et les moments où les estimations ont été faites. Faible niveau de preuve.
Interventions non pharmaceutiques comparativement au variant original	• Gamma est apparu à Manaus, au Brésil, à la fin de novembre 2020, et a montré un taux de reproduction effectif (Rt) élevé de 2,6 (densité postérieure la plus élevée (DPÉ) de 95 % : 1,5 à 4,5) en décembre 2020. Après un renforcement des restrictions en ce qui concerne la distanciation sociale, on a estimé que le Rt avait diminué à 1,2 (DPÉ de 95 % : 0,9 à 1,6) à	Une analyse de données de surveillance au Brésil.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	la fin de décembre 2020 et en janvier 2021 (53). En comparaison, un variant précédent avait également un Rt de 2,6 (DPÉ 1,6 à 3,8) en mars 2020 qui a ensuite diminué pour atteindre 1,0 (DPÉ 0,8 à 1,2) en avril 2020, une fois que la distanciation sociale a été augmentée de plus de 50 % à Manaus (en raison de la mise en œuvre des interventions non pharmaceutiques (INP)).	Faible niveau de preuve.
Gravité clinique		
Virulence / gravité ou durée de la maladie comparativement au variant original	• Une proportion plus élevée de cas associés au variant Gamma ayant été hospitalisés a été signalée par rapport au nombre d'hospitalisations pour le variant original (20 % contre 7,5 % p<0,001) (28). • Une étude a signalé un rapport de cotes ajusté (RCa 2,6, IC à 95 % 1,4 à 4,8) plus élevé pour les cas associés au variant Gamma ayant été admis à l'hôpital ou à l'USI (RCa 2,2, IC à 95 % 1,8 à 2,9) par rapport au variant original (28). • Il y a eu croissance exponentielle des hospitalisations dans le Rio Grande do Sul, avec un temps de doublement moyen de 13,4 jours et un taux de croissance quotidien de 5,3 % entre février 2021 et mars 2021 (29). • Une croissance exponentielle similaire (temps de doublement de 13,3 jours, taux de croissance quotidien de 5,4 %) pour les hospitalisations a été signalée dans la ville de Porto Alegre (29).	Deux analyses de données de surveillance effectuées en Europe et au Brésil. Faible niveau de preuve.
Facteurs de risque de la gravité comparativement au variant original	• Dans l'analyse stratifiée par âge, les cas associés au variant Gamma avaient une probabilité d'hospitalisation 3,0 à 13,1 fois plus élevée dans les groupes d'âge de 20 à 39 ans, de 40 à 59 ans et de 60 à 79 ans (28). • Les probabilités d'admission à l'USI étaient 2,9 à 13,9 fois plus élevées dans les groupes d'âge	Deux analyses de données de surveillance provenant de pays européens et du Brésil, une étude écologique effectuée au Brésil et une étude de cohorte rétrospective menée au Brésil.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	de 40 à 59 ans, de 60 à 79 ans et chez les personnes âgées de 80 ans et plus (28). • Les conditions préexistantes étaient moins nombreuses pour les cas associés au variant Gamma (27,8 %) que pour les cas associés au variant original (89 %), p < 0,001 (28). Dans trois études, comme le génome entier n'a pas été séquencé pour tous les cas, la lignée n'a donc pas été déterminée (très faible niveau de preuve) : • parmi les cas graves, le nombre de personnes de moins de 60 ans est passé de 39 % dans la première vague (novembre et décembre 2020) à 47 % dans la deuxième vague (février 2021) alors que le variant Gamma était prédominant (52). • Il n'y a pas eu d'augmentation de la proportion d'hospitalisations dans aucun des groupes d'âge avant (février à octobre 2020) et après (octobre 2020 à février 2021) l'apparition du variant Gamma au Brésil (46). • Il n'y avait pas de différence significative dans l'âge moyen des patients hospitalisés infectés avant et après mars 2021 au moment où le variant Gamma est devenu dominant à Sao Paulo, au Brésil (80).	Faible niveau de preuve.
Mortalité comparativement au variant original	• Diminution du risque de mortalité dû au variant Gamma comparativement au variant original dans l'analyse multivariable (RCa 0,6, IC à 95 % 0,3 à 1,0) (28). • Une augmentation différenciée de la mortalité associée à la COVID-19 chez les adultes âgés de 18 à 50 ans après l'apparition du variant Gamma au Brésil suggère la possibilité que le variant Gamma ait des répercussions plus sévères dans cette population. Les jeunes adultes présentaient des taux de mortalité à l'hôpital supérieurs à 10 % (46). • Le modèle prédictif a estimé que le risque médian de mortalité des suites des infections	Une analyse de données de surveillance provenant de pays européens, et une étude écologique et un modèle prédictif effectués au Brésil.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	associées au variant Gamma à Manaus était 1,5 (50 % intervalle de crédibilité 1,2 à 1,9) plus élevé après qu'avant l'émergence du variant Gamma en novembre 2020 (5). Il n'est cependant pas possible de déterminer si l'augmentation estimée du risque de mortalité relatif est due à une infection associée au variant Gamma, aux pressions exercées sur le système de santé de Manaus, ou aux deux.	Faible niveau de preuve.
Facteurs de risque de mortalité comparativement au variant original	Une étude dans laquelle le génome entier n'a pas été séquencé pour tous les cas, ce qui veut dire que la lignée n'a pas été déterminée (très faible niveau de preuve) : • La mortalité dans les cas de COVID-19 chez les personnes de moins de 60 ans est passée de 18 % en novembre 2020 à 28 % en février 2021 alors que le variant Gamma était prédominant (52). • La plus forte augmentation du taux de létalité s'est produite chez les personnes âgées de 20 à 59 ans et chez les patients sans condition à risque préexistante. Parmi les cas graves, la proportion de patients qui n'avaient aucun problème de santé préexistant était plus élevée en février 2021 (33 % comparativement à 25 % en novembre 2020) (52).	Une analyse de données de surveillance au Brésil.
	• Comparativement à novembre et à décembre 2020, les femmes âgées de 20 à 39 ans, sans condition de risque préexistante, étaient 5,65 (IC à 95 %, 2,9 à 11,03; $p < 0,0001$) fois plus à risque de décéder en février 2021 alors que les personnes de 40 à 59 ans étaient 7,7 (IC à 95 %, 5,01 à 11,83; $p < 0,0001$) fois plus à risque de subir le même sort (52).	Faible niveau de preuve.
Charge virale comparativement au variant original	• La charge virale (mesurée à l'aide des valeurs Ct) des échantillons du variant Gamma était inférieure à celle des échantillons du variant Alpha et supérieure à celle des variants originaux (3).	Deux analyses de données de surveillance provenant de la France et du Brésil, une étude de cohorte rétrospective menée au Brésil.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	• La charge virale (mesurée à l'aide des valeurs Ct) des infections associées au variant Gamma était environ 10 fois plus élevée que dans les infections non associées au variant Gamma (53). • La charge virale liée aux infections associées au variant Gamma était considérablement inférieure à celle des infections non associées au variant Gamma chez les hommes (18 à 59 ans) (P = 0,0005), les femmes adultes (P<0,0001) et les femmes âgées (plus de 59 ans) (P = 0,0149), mais pas significativement différente chez les hommes âgés (P = 0,4624) (53). Une étude dans laquelle le génome entier n'a pas été séquencé pour tous les cas, ce qui veut dire que la lignée n'a pas été déterminée (très faible niveau de preuve) : • Il n'y avait pas de différence significative dans les valeurs Ct moyennes chez les patients hospitalisés infectés et chez les travailleurs de la santé avant et après mars 2021, au moment où le variant Gamma est devenu dominant au Brésil (80).	Faible niveau de preuve.
Période infectieuse	Aucune étude	
Période d'incubation	Aucune étude	
Échappement immunitaire - incidence potentielle sur l'efficacité du vaccin, possibilité de réinfection		
Réinfection par infection naturelle comparativement au variant original	• On a estimé que 28 % des cas à Manaus au Brésil signalés entre novembre 2020 et janvier 2021 étaient des réinfections, étant donné que 78 % de la population avait déjà été infectée (4). • On estime que 16,9 % des cas associés au variant Gamma (IC à 95 %, 9,48 à 28,5) à Manaus déclarés entre janvier 2021 et mars 2021 étaient des réinfections. Si les réinfections probables sont également	Deux analyses de données de surveillance du Brésil.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	incluses, le total passe alors à 25,8 % de réinfections (IC à 95 %, 16,7 à 37,4). Si les réinfections possibles sont aussi incluses, alors 31,0 % de ces cas étaient des réinfections (IC à 95 %, 21,4 à 42,5) (81).	Faible niveau de preuve.
Infection sporadique après la vaccination, efficacité réelle ou prévue du vaccin comparativement au variant original	• À Manaus, au Brésil, où plus de 75 % des cas étaient des cas associés au variant Gamma pendant la période à l'étude, la vaccination avec au moins une dose de CoronaVac a été associée à une réduction de 0,50 fois (EV ajustée, 49,6 %; IC à 95 %, 11,3 à 71,4) des probabilités d'infection symptomatique par le SRAS-CoV-2 pendant la période de 14 jours ou plus après avoir reçu la première dose. Le sexe féminin (RC 0,50; IC à 95 %, 0,38 à 0,81) et un résultat positif au test RT-PCR ou à l'antigène du SRAS-CoV-2 au cours de la période précédant l'étude (RC 0,38; IC à 95 %, 0,17 à 0,87) ont été associés à une probabilité réduite d'infection symptomatique par le SRAS-CoV-2 (82). • Sept jours ou plus après la deuxième dose du vaccin Moderna ou Pfizer, on a obtenu une EV ajustée de 88 % (IC à 95 %, 61 à 96) pour une infection symptomatique au variant Gamma comparativement à une infection par la souche sauvage (93 %, IC à 95 %, 87 à 96). L'EV ajustée pour l'infection symptomatique au variant Gamma pour une dose était de 43 % (IC à 95 %, 22 à 59) comparativement à la souche symptomatique sauvage (61 %, IC à 95 %, 53 à 67) (72).	Deux études cas-témoins en provenance du Brésil et du Canada. Faible niveau de preuve.
Études in vitro sur les traitements Comparativement au variant original	• Il a été démontré que les traitements multiples sont moins efficaces contre le variant Gamma que contre le variant original, ce qui inclut le casirivimab (83-85), le bamlanivimab (85), l'etsevimab et l'imdevimab (83). • Il a aussi été démontré que la combinaison d'imdevimab et de casirivimab inhibe efficacement le variant Gamma (85).	Les études *in vitro* constituent des preuves de bas niveau qui donnent un aperçu préliminaire des résultats que l'on s'attend à obtenir avec les études *in vivo*.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
Études *in vitro* effectuées avec du sérum de phase convalescente et du sérum provenant de personnes vaccinées Comparativement au variant original	La plupart des études ont montré que les sérums de phase convalescente et provenant de personnes vaccinées (Pfizer, Coronavac, Sinopharm, Moderna) ont réduit l'activité neutralisante du variant Gamma comparativement au variant original (86 à 89). *Remarque : De nombreuses études in vitro ont été relevées. Veuillez consulter le jeu de données Excel pour plus de détails sur chacune des études.*	Très faible niveau de preuve. La réponse immunitaire est complexe, et l'absence d'anticorps neutralisants ou le manque de ces derniers ne signifie pas un manque de protection immunitaire. D'autres recherches sont nécessaires (voir la revue effectuée par le Groupe des sciences émergentes de l'ASPC sur l'immunité protectrice).
Tests et diagnostics		
Test et détection comparativement au variant original	• Aucun échec dans les tests n'a été déclaré pour le PCR du variant Gamma, les tests d'antigènes ou les tests sérologiques (90).	Une étude visant à évaluer la fiabilité des tests de diagnostic a examiné la performance de ces tests. Faible niveau de preuve.
Épidémiologie de la propagation		
Émergence des VP **Au fil du temps**	• De nombreuses études utilisent le séquençage du génome entier pour déclarer la prévalence ponctuelle ou à un moment donné du variant Gamma dans une région spécifique, élément qui n'a pas été résumé ici (11, 91). • La prévalence du variant Gamma est passée de 0 % en novembre 2020 à 73,8 % à Amazonas, au Brésil (53) et à près de 30 % à Amazonas, en Colombie, en janvier 2021 (92). • La prévalence du variant Gamma en Italie est demeurée relativement stable de février 2021 (5,0 %, IC à 95 %, 3,9 à 6,4) à mars 2021 (4,8 %, IC à 95 %, 3,9 à 5,9), comparativement à celle du variant Alpha, qui est passée de 53,1 % (IC à 95 %, 50,3 à 55,9) à 85,7 % (IC à 95 %, 84,1 à 87,3) (23).	Trois analyses de données de surveillance au Brésil (2) et en Italie (1). Faible niveau de preuve.
Prédictions en ce qui concerne la propagation	• Si l'on tente de revenir au niveau des contacts prépandémiques une fois que 50 % de la population des États-Unis aura été vaccinée en juillet 2021, on prévoit que le variant Gamma surpassera alors les souches Alpha et Bêta et deviendra la souche dominante dans 2 à	Deux modèles prédictifs. L'une des limites associées à ces modèles est le fait qu'ils ne tiennent pas compte du B.1.617 (delta) et qu'ils ne comparent que la propagation prévue du variant

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	3 mois. Le modèle suppose que le variant Gamma possède une efficacité immunitaire de 68 % en réponse au vaccin ou à la souche sauvage (93). • Si les variants Gamma et Bêta s'établissent simultanément dans la population de New York, on prévoit que le variant Gamma sera supplantera le variant Alpha et deviendra co-dominant avec le variant Bêta d'ici août 2021. Si, toutefois, le variant Gamma s'établit dans la population avant le variant Bêta, le variant Gamma éliminerait le variant Bêta et deviendrait alors dominant. Le modèle suppose que le variant Gamma a la même EV que la souche sauvage (94).	Gamma avec les valeurs pour les variant Alpha et variant Bêta. Faible niveau de preuve.

IC = intervalle de confiance, Ct = seuil du cycle, USI = unité des soins intensifs, RC = rapport de cotes, PCR = réaction en chaîne de la polymérase, EV = efficacité du vaccin, RC = rapport de cotes, RCa = rapport de cotes ajusté

B.1.351 (BÊTA)

Le jeu de données en Excel comprend des résumés de chacune des études et est accessible ici. Vous trouverez ci-dessous le profil détaillé des éléments de preuve élaboré pour le variant Bêta. Il porte notamment sur les données sur les changements dans l'efficacité de la transmission, les changements dans la gravité clinique, l'échappement immunitaire, les tests et diagnostics, ainsi que d'autres études épidémiologiques portant principalement sur la propagation des VP.

Tableau 4 : Profil fondé sur les éléments de preuve pour le VP B.1.351 (Bêta) (n = 229)

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
Efficacité de transmission		
Transmissibilité comparativement au variant original ou au variant Alpha	• Une transmissibilité accrue par rapport au variant original : 27 % en France pour les variants Bêta et Gamma combinés (3), 55 % (8, 9) et 20 à 100 % (jusqu'à 175 %) en Afrique du Sud (10) • Augmentation de l'avantage de transmission par rapport au variant Alpha en Île-de-France (15,8 %, IC à 95 % : 15,1 % à 16,1 %) et dans la région Hauts-de-France (17,1 %, IC à 95 % : 16,1 % à 18,8 %) en avril et en mai 2021 (11).	Ces chiffres ont été estimés à partir de cinq analyses de données de surveillance. Il y a peu de cohérence entre les études. L'hétérogénéité des estimations de la transmissibilité accrue peut être due à de nombreux facteurs, notamment le moment où sont effectuées les estimations de la pandémie. Faible niveau de preuve.
Taux d'attaque secondaire comparativement au variant original	• TAS = 76,9 %, ce qui équivaut à (R_{eff} = 4) dans la présente enquête (95).	Une enquête épidémiologique. Faible niveau de preuve.
Gravité clinique		
Virulence / gravité ou durée de la maladie comparativement au variant original	• Proportion des cas symptomatiques : les cas associés au variant Bêta (90,3 %; 28 sur 31) par rapport aux cas associés au variant original (81,4 %; 547 sur 672, p = 0,2) (28) dans plusieurs pays européens (28). Augmentation des hospitalisations et des admissions à l'USI : • Une plus grande probabilité d'hospitalisation en raison du variant Bêta (19,3 %) comparativement au variant original (7,5 %) p<0,001 dans une analyse multivariable (RCa = 3,6, IC à 95 % : 2,1 à 6,2) dans plusieurs pays européens (28).	Quatre études sur la gravité, dont deux études de surveillance et deux études de cohortes rétrospectives menées en France et en Afrique du Sud. Les études de cohorte sont centrées sur un seul centre et ont donc une validité externe limitée et risquent d'être faussées. Faible niveau de confiance en ce qui concerne l'augmentation ou la diminution de la gravité de la maladie associée au variant Bêta.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	• Augmentation de la proportion de cas associés au variant Bêta dans l'USI (2,3 %) comparativement au variant original (0,6 %) p = 0,001, et plus grande probabilité d'être admis à l'USI pour les cas associés au variant Bêta comparativement à ceux qui sont associés au variant original (RCa = 3,3, IC à 95 % : 1,9 à 5,7) dans plusieurs pays européens (28). • En France, les cas associés au variant Bêta étaient plus susceptibles d'être hospitalisés (RC = 1,56, p < 0,0001) que ceux qui sont liés au variant Alpha (11). Diminution des admissions à l'USI : • En Afrique du Sud, parmi les patients hospitalisés, il y a eu moins d'admissions à l'USI (35 % contre 48,5 %, p = 0,03) et moins de recours à la ventilation mécanique (8,9 % contre 15,5 %, p = 0,009) pendant la vague associée au variant Bêta comparativement aux vagues associées au variant original (31). Aucune différence : • Dans un hôpital en France, on n'a vu aucune différence significative dans les scores des soins intensifs et les exigences de ventilation mécanique pour ce qui est des cas associés au variant Bêta, au variant original ou au variant Alpha (42).	Faible niveau de preuve.
Facteurs de risque de la gravité comparativement au variant original	Âge : • Dans une analyse stratifiée par âge, les cas associés au variant Bêta présentaient une probabilité d'hospitalisation 3,5 à 3,6 fois plus élevée pour les groupes d'âge de 40 à 59 ans et de 60 à 79 ans par rapport aux cas associés au variant original dans les mêmes groupes d'âge dans plusieurs pays européens (28). • L'admission à l'USI était significativement plus probable pour les cas associés au variant Bêta (RCa 8, IC à 95 % : 3,7 à 17,3) âgés de 40 à 59 ans (28).	Trois études sur les facteurs de risque de gravité, y compris une étude de surveillance établie dans certains pays d'Europe et deux études de cohortes rétrospectives menées en France et en Afrique du Sud. Les études de cohorte sont centrées sur un seul centre et ont donc une validité externe limitée et risquent d'être faussées. Faible niveau de preuve.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	• En Afrique du Sud, les cas hospitalisés pendant la vague associée au variant Bêta étaient beaucoup plus âgés (âge médian de 57 ans comparativement à 54 ans, p = 0,03) comparativement aux cas vus pendant la vague associée au variant original (31). • En France, on n'a vu aucune différence significative entre l'âge (63 ans contre 67 ans, p = 0,15) ou le sexe des personnes admises à l'USI parmi les cas associés au variant Bêta comparativement aux cas associés au variant original ou au variant Alpha (42). Comorbidités : • Les conditions préexistantes étaient moins nombreuses pour les trois VP (79,6 % pour le variant Bêta contre 89 % pour le variant original, p<0,001) (28). • Un plus grand nombre de cas vus pendant la vague liée au variant Bêta n'avaient aucune comorbidité (47 % contre 36,9 %, p = 0,008) et moins d'hypertension (32,2 % contre 45,2 %, p < 0,001) comparativement aux personnes touchées dans la vague liée au variant original en Afrique du Sud (31). • Il n'y avait pas non plus de différence entre les personnes atteintes de diabète sucré, de maladies respiratoires chroniques, de maladies cérébrovasculaires et séropositives (31).	
Mortalité comparativement au variant original ou au variant Alpha	Augmentation de la mortalité : • Augmentation de la mortalité globale (36,4 % contre 32,6 %, p = 0,26) et augmentation significative de la mortalité dans l'USI (74,4 % contre 57,1 %, p = 0,002) pendant la vague associée au variant Bêta comparativement à la vague associée au variant original en Afrique du Sud (31). • L'admission à l'hôpital pendant la vague associée au variant Bêta (p = 0,006) a été indépendamment associée à la mortalité, dans une analyse multivariée (31).	Trois études sur la mortalité, dont une étude de surveillance réalisée dans les pays européens et deux études de cohortes rétrospectives menées en France et en Afrique du Sud. Les études de cohorte sont centrées sur un seul centre et ont donc une validité externe limitée et risquent d'être faussées. Faible niveau de preuve.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	• Plus grande probabilité de décès dans les 60 jours suivant l'admission à l'USI (RC = 5,67, IC à 95 % : 1,04 à 30,81, p = 0,04) pour les cas associés au variant Bêta comparativement aux cas liés au variant Alpha en France (42). Aucune différence : • Aucune différence dans les probabilités de décès pour les cas associés au variant Bêta comparativement à ceux qui sont liés au variant original dans l'analyse multivariable (RCa 1,1, IC à 95 % 0,4 à 3,4) (28).	
Facteurs de risque de mortalité Comparativement au variant original	Aucune étude	
Charge virale comparativement au variant original	• La charge virale (mesurée à l'aide des valeurs Ct) des échantillons du variant Bêta était inférieure à celle des échantillons du variant Alpha et supérieure à celle des variants originaux (3, 54).	Deux études, résultats secondaires. Très faible niveau de preuve.
Période infectieuse	Aucune étude	
Période d'incubation	Aucune étude	
Échappement immunitaire - incidence potentielle sur l'efficacité du vaccin, possibilité de réinfection		
Réinfection par infection naturelle comparativement au variant original	• Trois cas de réinfection par le variant Bêta ont été signalés (62 à 64).	Trois études déclarent une réinfection, y compris deux exposés de cas et une étude de cohorte prospective. Ces études présentent un niveau de preuve très faible.
Infection sporadique après la vaccination, efficacité réelle ou prévue du vaccin comparativement au variant original	Efficacité et efficacité du vaccin : • AstraZeneca : 10,4 % d'efficacité pour la prévention de la maladie symptomatique (68). • Johnson et Johnson : Les estimations d'efficacité étaient plus faibles en Afrique du Sud que dans les autres pays. L'efficacité du vaccin (EV) contre le variant Bêta était de 52 % et de 64 % pour la forme modérée de la	Sept études sur les infections ayant percé et l'efficacité des vaccins, dont trois ECR, une étude de cohorte prospective et trois études de cas/témoins. Ces études présentent un niveau de preuve faible à modéré. Il n'y a eu qu'une seule étude par vaccin

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	maladie et de 73 % et de 82 % pour la forme grave après 14 jours et 28 jours respectivement (69). • Novavax : EV de 51,0 % (IC à 95 %, -0,6 à 76,2) contre la maladie symptomatique chez les personnes séronégatives (70). • Pfizer-BioNTech : EV de 75,0 % (IC à 95 %, 70,5 % à 78,9 %) contre l'infection par le variant Bêta ≥2 semaines après la deuxième dose et de 97,4 % (IC à 95 % : 92,2 % à 99,5 %) contre les formes graves, critiques ou mortelles des variants du SRAS-CoV-2 au Qatar (71). Une EV de 50 % (IC à 95 %, 34 % à 73 %) chez les résidents des maisons de soins infirmiers (âge médian : 87,0 ±8,2 ans) avec deux doses espacées de 19 jours (64). • Moderna/Pfizer-BioNTech : EV comparable de ≥88 % contre l'infection symptomatique associée au variant Bêta ≥7 jours après avoir reçu la deuxième dose (72). Infection ayant percé après la vaccination : • Aucune infection ayant percé associée au variant Bêta n'a été identifiée plus de 14 jours après la deuxième dose (principalement Pfizer) dans une étude cas-témoins menée en Israël (67). • 50 % (13 sur 26) des résidents des maisons de soins infirmiers et 5,2 % (1 sur 19) des membres du personnel qui ont reçu le vaccin Pfizer-BioNTech ont été atteints par des infections ayant percé associées au variant Bêta. Les résidents ont été infectés de 24 à 41 jours après avoir reçu la deuxième dose (15,4 % étaient asymptomatiques, 69,2 % ont présenté des symptômes légers à modérés et 15,4 % présentaient un syndrome de détresse respiratoire aiguë) (64).	provenant d'essais cliniques aléatoires, de sorte que des essais supplémentaires sont nécessaires pour améliorer la confiance dans ces estimations.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
Traitements Comparativement au variant original	• Le casirivimab et l'etesevimab ont montré une réduction de la neutralisation (83, 85, 96), le bamlanivimab n'a montré aucune neutralisation (85), et il y avait des preuves contradictoires sur la neutralisation associée à l'imdevimab (83, 96) contre le variant Bêta.	Trois études *in vitro* sur les traitements. Très faible niveau de preuve.
Modèles animaux pour la protection convalescente ou la vaccination	• Dans des modèles animaux soumis à l'épreuve du variant Bêta, des hamsters préalablement infectés ou vaccinés ont montré une protection contre la maladie clinique (97, 98).	Deux modèles animaux. Très faible niveau de preuve.
Études *in vitro*	• La plupart des sérums vaccinaux et de phase convalescente ont montré une activité neutralisante réduite pour le variant Bêta par rapport au variant original ou au variant Alpha. Dans la plupart des études, le variant Bêta avait une neutralisation plus réduite que le variant Gamma. Les expériences de neutralisation ne sont pas résumées, mais on peut les trouver dans le jeu de données.	Très faible niveau de preuve. La réponse immunitaire est complexe, et l'absence d'anticorps neutralisants ou le manque de ces derniers ne signifie pas un manque de protection immunitaire. D'autres recherches sont nécessaires (voir la revue effectuée par le Groupe des sciences émergentes de l'ASPC sur l'immunité protectrice).
Tests et diagnostics		
Test et détection comparativement au variant original	• La PCR, les tests de détection des antigènes, les tests sérologiques et les méthodes de séquençage sont efficaces pour détecter ou distinguer le variant Bêta (90, 99 à 108). • Le test antigénique TRF-ELISA basé sur S1 a détecté le variant Bêta avec une sensibilité réduite de 2 à 3 fois comparativement au résultat obtenu avec le variant original et le variant Alpha (109).	Douze études sur les tests et la détection, dont dix études sur la précision des tests de diagnostic et deux études in vitro. Comme elles décrivent toutes des tests différents, les études sont considérées comme individuelles et ne peuvent être résumées ensemble. Faible niveau de preuve.
Épidémiologie de la propagation		
Émergence des VP au fil du temps	• Les études qui font état de la prévalence ponctuelle ou à un moment donné du variant Bêta n'ont pas été résumées. • Deux études montrent la croissance du variant Bêta dans différentes régions d'Afrique du Sud et de Colombie-Britannique au Canada (110, 111).	Seize études sur l'émergence et la propagation du variant Bêta, dont douze études de surveillance, une enquête sur l'éclosion, un modèle prédictif et deux études de cohorte rétrospectives.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	• En Afrique du Sud, le variant Bêta a émergé vers août 2020 et été détecté pour la première fois en octobre 2020. En mars 2021, le variant Bêta est devenu le variant dominant et représentait environ 20 % (1 769 sur 8 746) des génomes (112). • Des études effectuées dans des pays autres que l'Afrique du Sud ont indiqué que le variant Bêta avait été déclaré la première fois en décembre 2020 (113 à 115).	Faible niveau de preuve.

IC = intervalle de confiance, Ct = seuil du cycle, USI = unité de soins intensifs, RC = rapport des cotes, PCR = réaction en chaîne par polymérase, EV = efficacité du vaccin, RCa = rapport de cotes ajusté, RRa = rapport de risque ajusté, RPa = rapport de prévalence ajusté

B.1.1.7 (ALPHA)

Le jeu de données en Excel comprend des résumés de chacune des études et est accessible ici. Vous trouverez ci-dessous le profil détaillé des éléments de preuve élaboré pour le variant Alpha. Il porte notamment sur les données sur les changements dans l'efficacité de la transmission, les changements dans la gravité clinique, l'échappement immunitaire, les tests et diagnostics, ainsi que d'autres études épidémiologiques portant sur principalement sur la propagation des VP.

Tableau 5 : Profil fondé sur les éléments de preuve pour le VP B.1.1.7 (Alpha) (n = 342)

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
Efficacité de transmission		
Transmissibilité comparativement au variant original	Les estimations de l'augmentation de la transmissibilité relative du variant Alpha (1-$R_{VP}/R_{Variant\ original}$) variaient entre 34 et 118 % entre les différentes études, une partie de cette variation étant due au moment où les données ont été obtenues en ce qui concerne l'émergence du variant Alpha. Une étude note une variation dans le temps (12) et la plupart des estimations du Royaume-Uni sont plus élevées que celles des autres pays (9) : • Canada : 34 % (IC à 95 % : 31 à 38) (13). • Royaume-Uni : 50 à 100 % (12), 75 % (IC à 95 %, 70 à 80 %) (16), 52 % (IC 46 à 58 %) (17), 43 à 90 % (fourchette de l'intervalle de crédibilité : 38 à 130 %) (14), 44 à 55 % (IC 38 à 61 %) (18), 83 à 118 % (71 à 140 %) au Royaume-Uni (9), 13,4 à 41,3 % dans les régions du Royaume-Uni en décembre 2020 (19), transmissibilité supérieure de 62 % (IC à 95 %, 59 à 65 %) à 45 % (IC 43 à 48 %) (116), taux de reproduction de 0,3 unité supérieur à celui des autres lignées (117). • Europe : France 41 % (IC à 95 % 38 à 44) (3) et 52 % (IC à 95 % 54 à 66 %) (20), Danemark 55 % (intervalle de crédibilité 45 à 66 %), Suisse 74 % (intervalle de crédibilité 66 à 82 %) (14) et 54 % (IC à 95 % 49 à 65 %) (21), Norvège 24 % (IC à 95 % 0 à 52 %) (22), Italie 55 à 57 % (IC à 95 % 45 à 66 %) (23), Pays de Galles et États-Unis 65 à 72 % (46 à 104 %) (9).	Cette section s'appuie sur 35 études par observation, y compris des analyses des données de surveillance, des études transversales, des études de cohorte rétrospectives, des études écologiques et des modèles prédictifs. On s'accorde pour dire que le variant Alpha est plus transmissible et il y a un chevauchement assez important dans les estimations de l'ampleur. La transmissibilité peut être influencée par des mesures de santé publique restrictives et par l'augmentation de la vaccination. Ces études risquent de présenter un biais de sélection, d'information et de confusion qui n'a pas été pris en compte de manière cohérente dans toutes les études. Faible niveau de preuve.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	• États-Unis : 59 % (intervalle de crédibilité 56 à 63 %) (14), 35 à 46 % (15). • Israël : 45 % (IC à 95 %, 20 à 60) (24). • Le Japon a estimé une augmentation de 60 % de la transmissibilité relative des VP (non spécifiés) par rapport aux variants originaux (25). • Une étude qui n'a pas donné d'estimations indique que la transmissibilité du variant Alpha est plus élevée que celle du variant Bêta ou du variant Gamma (7). • Dans certaines régions de la France (avril et mai) où le variant Bêta augmentait, on a estimé que l'avantage de transmission était de 15,8 % (IC à 95 %, 15,1 à 16,1) à l'île de France et de 17,1 % (IC à 95 %, 16,1 à 18,8) dans les Hauts de France comparativement au variant Alpha (11). • Un modèle prédictif a examiné l'incidence de l'augmentation de la vitesse de transmission et de la transmissibilité sur l'épidémiologie du variant Alpha (118). Certaines études ne fournissent pas suffisamment de données pour calculer l'efficacité accrue de la transmission, mais indiquent qu'elle était plus élevée (119). D'autres études ont indiqué que la transmissibilité diminuait au fil du temps (7, 120) ou ne changeait pas (121), ce qui peut être associé à la rigueur du confinement ou à l'augmentation de la vaccination (121, 122). Un examen systématique de la transmissibilité a inclus des études disponibles jusqu'au 21 février 2021 (8).	
Avantage sélectif Comparativement au variant original	• Selon un modèle d'avantage sélectif, on a estimé que le variant Alpha présentait un avantage sélectif de 0,337 (0,336 à 0,339) par rapport aux variants originaux au Royaume-Uni (123).	Un modèle prédictif. Faible niveau de preuve.
Taux d'attaque secondaire comparativement au variant original	• Dans une étude canadienne sur la transmission intrafamiliale, le taux d'attaque secondaire (TAS) du variant Alpha était plus élevé (RR = 1,31 (IC à 95 %, 1,14 à 1,49) que celui des autres VP, et le risque était accentué pour les cas index	Cinq études sur la transmission intrafamiliale, y compris une éclosion dans des classes de maternelle.

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	asymptomatiques (RR = 1,91, IC à 95 %, 0,96 à 3,80) et les cas présymptomatiques (RR = 3,41, IC à 95 %, 1,13 à 10,26) (26). • Dans les ménages norvégiens, le variant Alpha était 60 % (20 % à 114 %) plus transmissible que les variants originaux et, dans l'ensemble, le TAS était de 0,13 pour le variant original et de 0,15 pour le variant Alpha, ce qui veut dire qu'il est 16 % (-6 % à 43 %) plus infectieux (ratio du TAS), même en tenant compte de l'âge (22). • Une étude réalisée au Danemark a révélé une transmission de 50 à 70 % plus élevée parmi les ménages infectés par le variant Alpha comparativement aux variants originaux. La transmissibilité selon l'âge suivait un modèle en forme de U avec la transmission la plus faible provenant des cas primaires dans la tranche d'âge des 10 à 30 ans, une transmission plus élevée chez les enfants plus jeunes et encore plus élevée chez les personnes âgées (27). • Une étude allemande a révélé que le TAS des enfants et des adultes des ménages s'établissait à 37 % (IC de 95 %, 28 à 47) et était semblable chez les enfants (32 %) par rapport aux adultes (39 %) (124). Parmi les gens qui ont été en contact dans les services de garde, le TAS pour les enfants (23 %) était semblable à celui des adultes (30 %) (124). • Au Royaume-Uni, les cas associés au variant Alpha étaient presque deux fois plus susceptibles de créer des grappes de ménages que le variant original (RC ajusté = 1,88, IC à 95 %, 1,67 à 2,08, p<0,001) (125).	Le ratio des taux d'attaque secondaire a également été fourni comme mesure d'une transmissibilité plus élevée pour le variant Alpha dans certaines études basées sur des études de recherche de contacts. Les résultats étaient contradictoires d'une étude à l'autre. Ces études comprennent trois analyses de données de surveillance et une étude rétrospective. Faible niveau de preuve.
Interventions non pharmaceutiques comparativement au variant original	Rigueur : • Au Royaume-Uni, un modèle bayésien hiérarchique a été utilisé pour montrer que le niveau 1 de mesures restrictives (restrictions légères) avait un effet négligeable sur les cas, tandis que les niveaux 2 (restrictions modérées) et 3 (restrictions sévères) avaient permis de réduire la transmission 6 % (5 % à 7 %) et de	Sept modèles prédictifs, une étude écologique et une analyse des données de surveillance. Les modèles prédictifs sont d'excellents outils pour comparer les options, mais il convient de faire preuve

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	23 % (21 % à 25 %), respectivement (120). Une autre analyse souligne qu'en décembre 2020, au Royaume-Uni, les valeurs les plus élevées de Rt (environ 1,8) ont été enregistrées dans les régions ayant mis en œuvre le plus bas niveau de mesures restrictives. Malgré le fait que ces valeurs étaient les plus faibles, lorsque ces régions les ont combinées avec des mesures restrictives plus rigoureuses et des mesures de confinement, cela a effectivement permis de réduire le Rt qui a ainsi pu atteindre environ 0,9 en mars 2021 (116). • Un modèle prédictif basé sur le variant Alpha paramétré au Canada (augmentation de 50 % de la transmission chez les enfants et de 70 % chez les adultes) a également été utilisé. Si l'on compare ces données à celles obtenues avec les mesures de confinement restrictives, on peut voir que le nombre de cas estimatif était trois fois plus élevé à Toronto lorsque les écoles étaient fermées et que les entreprises restaient ouvertes, mais devaient se conformer à des restrictions modérées, qu'il était sept fois plus élevé si les écoles étaient fermées et qu'il était 7,5 fois plus élevé si les écoles étaient ouvertes et que les entreprises étaient soumises à des mesures restrictives légères (126). • Un modèle SEIR basé sur la situation en France décrit l'incapacité des interventions non pharmaceutiques telles que le couvre-feu et les mesures de distanciation physique à réduire le Ro du variant Alpha à un niveau inférieur à 1, alors que ces mêmes interventions, lorsqu'utilisées contre les variants originaux, ont permis de réduire ce Ro (127). • Un modèle de transmission structuré par région et stratifié selon l'âge afin de contrôler la transmission du variant Alpha estime que le respect de mesures de confinement plus restrictives à court terme entraînerait une diminution du nombre d'admissions à l'hôpital alors qu'un confinement modéré réduirait la	de prudence lors de l'extrapolation des résultats au-delà des scénarios de comparaison des modèles. Faible niveau de preuve.

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	détresse et améliorerait la viabilité de cette mesure (128). Quarantaine : • Un modèle permettant d'examiner les scénarios de quarantaine et de test pour contrôler les importations de SRAS-CoV-2 aux États-Unis indique que le variant Alpha ne modifie pas l'efficacité des stratégies de quarantaine et de test (129). Mesures de protection individuelle : • Ce modèle est basé sur les données américaines et examine l'incidence de l'utilisation du couvre-visage pour le contrôle à la source et la protection de l'utilisateur grâce à des données sur la transmission du variant original et du variant Alpha. Ainsi, le Ro de base de 2,5 pourrait diminuer jusqu'à obtenir un Rt inférieur à 1,0 alors que le Ro de 4 pourrait permettre d'obtenir un Rt d'environ 1,6 respectivement si les règles en ce qui concerne le port du couvre-visage étaient plus strictes et plus rigoureuses (130). • Ce modèle de transmission de la maladie a estimé le risque de transmission en milieu de travail pour le variant Alpha (0,041 transmission ou contact contre 0,014 pour le variant original). Malgré le port du couvre-visage, le risque était toujours deux fois plus important qu'avec le variant original (131). Vaccination : • On a examiné les stratégies de vaccination avec une plus grande transmissibilité du variant Alpha et prédit que même si 100 % de la population avait reçu le vaccin AstraZeneca, la valeur R ne diminuerait que pour atteindre 1,33 % de la population vaccinée et pourrait atteindre 1,98 si 79 % de la population était vaccinée. Le vaccin Pfizer-BioNTech nécessiterait la vaccination de 81,9 % de la population pour réduire à 1 la valeur de R (122).	

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	• Un modèle prédictif a montré que la diminution de la transmission du variant Alpha par la vaccination avait l'effet le plus important une fois que la transmission avait déjà commencé à diminuer grâce à des stratégies d'atténuation en matière de santé publique (132).	
Gravité clinique		
Virulence / gravité ou durée de la maladie comparativement au variant original	Cinq études montrent qu'il y a eu plus de cas d'hospitalisations liés au variant Alpha alors que deux études effectuées sur la population en général montrent qu'il y a eu plus d'admissions à l'USI. • Les preuves sont contradictoires quant à savoir si le variant Alpha entraîne davantage d'infections asymptomatiques : La prévalence de la maladie symptomatique était la même dans une étude italienne (32). Proportion des cas symptomatiques : 72,6 % cas associés au variant Alpha (5 365 sur 7 390) comparativement aux cas liés aux variants originaux (81,4 %; 547 sur 672; p < 0.001) (28). • La majorité des études ont signalé un nombre plus élevé d'hospitalisations avec une infection causée par le variant Alpha : • Plus grand nombre d'hospitalisations avec le variant Alpha comparativement au variant original (11 % contre 7,5 % p<0,001) (28) ; (5,8 % contre 4,1 % p = 0,04) (38). Nombre d'hospitalisations plus élevé, soit 2,39 % pendant la vague liée au variant Alpha, alors qu'il a atteint 1,55 % pendant la vague initiale en Espagne (37). • Plus grande probabilité d'hospitalisation des cas associés au variant Alpha comparativement à la probabilité recensée avec le variant original (RCa 1,7, IC à 95 % 1,0 à 2,9) (28); RC 1,64 (IC à 95 % 1,32 à 2,04) (33); RC 1,58 (IC à 95 % 1,50 à 1,67) (34); (RC 1,36 IC à 95 % 1,16 à 1,60, p = 0,0002) (35). Le rapport de risque pour l'hospitalisation associée au variant Alpha comparativement au variant original (RRa 1,34, IC à 95 % 1,07 à 1,66). La durée du séjour était	Quatorze études sur la sévérité, incluant des analyses de données de surveillance, des cohortes prospectives, des cohortes rétrospectives et des études transversales, dont la plupart ont été menées au Royaume-Uni. Niveau de preuve modéré.

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	cependant similaire dans les deux groupes p = 0,07 (36). • Une étude menée en République tchèque n'a révélé aucun changement dans le nombre d'hospitalisations (39). • Plusieurs études ont fait état d'un nombre plus élevé d'admissions à l'USI en raison des infections associées au variant Alpha : • Le taux d'admission à l'USI était de 1,4 % pour le variant Alpha alors qu'il était de 0,6 % pour le variant original, p = 0,002, ce qui représente une probabilité plus élevée d'admission à l'USI pour le variant Alpha RCa 2,3 (IC 95 % 1,4 à 3,5) (28). Admission à l'USI pour le variant Alpha : RRa 1,99 IC à 95 % 1,59 à 2,49 comparativement au variant original (40). • Parmi les cas hospitalisés, il n'y avait pas d'association entre la forme grave de la maladie, le décès, le variant Alpha et les variants originaux, RPa 1,02 (IC à 95 % : 0,76 à 1,38) (41); scores aux soins intensifs ou besoin d'une ventilation mécanique (42). Symptômes : • L'hypoxie (70,0 % contre 62,5 %, p = 0,029) et des taux respiratoires plus élevés (p = 0,001) ont été signalés parmi les cas associés au variant Alpha inclus dans deux études (43, 44). • Une fièvre de plus de 38 °C était beaucoup plus commune chez les patients hospitalisés infectés par le variant Alpha que chez ceux qui avaient contracté le variant original (46 % contre 22, p = 0,015) (133)	
Facteurs de risque de la gravité comparativement au variant original	Il n'y avait pas de cohérence entre les études pour savoir si des facteurs de risque étaient associés à la gravité du variant Alpha, y compris l'âge et le sexe, mais plusieurs études ont rapporté que les personnes infectées par le variant Alpha étaient moins susceptibles d'avoir des comorbidités : • Une étude réalisée aux États-Unis n'a pas signalé de différence significative en ce qui	Neuf études sur les facteurs de risque de gravité. Il s'agit notamment d'analyses de données de surveillance, de cohortes prospectives, de cohortes rétrospectives et d'études transversales,

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	concerne l'âge et le sexe des patients ni en ce qui concerne la durée médiane du séjour à l'hôpital (35). • Dans une autre étude, la différence d'âge était statistiquement significative (37 contre 39 ans) (39). Une étude menée en République tchèque a révélé que des patients beaucoup plus jeunes ont été hospitalisés en raison du variant Alpha (différence médiane de 58 ans par rapport à 64 ans) comparativement au variant original (39). • Dans les modèles stratifiés par âge, les cas associés au variant Alpha dans les groupes d'âge de 20 à 39 ans et de 40 à 59 ans avaient, respectivement, une probabilité d'hospitalisation 3,0 et 2,3 fois plus élevée que les cas associés au variant original (28). • Une étude de cohorte prospective menée auprès de patients hospitalisés a révélé une différence statistiquement significative entre l'âge des personnes infectées par le variant Alpha (39 ans, EI : 30,50 à 62,50) et celui des personnes infectées par la souche B.1.470 (qui n'est pas un variant) (31 ans, EI : 27,50 à 41,00) (P = 0,014) (133). • Parmi les patients aux soins intensifs en France, aucune différence significative pour l'âge ou le sexe entre le variant Alpha et le variant original ou le variant Bêta n'a été documentée (42). • Une cohorte hospitalière entre décembre 2020 et janvier 2021 en France décrit des patients plus jeunes (63 % de personnes ayant moins de 65 ans, contre 50 %) avec un âge moyen de 59,2 ans contre 70,7 ans; les patients sans comorbidité ont augmenté de 16 % à 42 % (p = 0,007) (44). Les conditions préexistantes étaient plus faibles avec le variant Alpha comparativement au variant original (44,8 % contre 89 % p<0,001) (28). • Une étude sur les cas de COVID-19 ayant été hospitalisés a rapporté une plus grande	dont la plupart ont été menées au Royaume-Uni. Niveau de preuve modéré.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
	proportion de femmes atteintes du variant Alpha (48,0 % contre 41,8 %, p = 0,01), moins de patients fragiles (14,5 % contre 22,4 %, p = 0,001) et une plus grande proportion de personnes souffrant d'obésité (30,2 % contre 24,8 %, p = 0,048), mais aucune différence en fonction de l'âge ou de l'ethnie (43).	
Mortalité comparativement au variant original	Il existe des preuves contradictoires sur l'association entre la mortalité et l'infection causée par le variant Alpha : • Cinq études n'ont rapporté aucune différence significative dans la mortalité globale : Italie (2,1 % contre 4,1 %) (32), États-Unis (35, 38) et aucun lien avec la mortalité après 28 jours au Royaume-Uni (RC : 0,90, IC à 95 %, 0,57 à 1,41, p = 0,64) (36) ou la légalité (RC = 1,37; IC : 0,5808 à 3,215, p = 0,52) (39). • Une étude a estimé que le variant Alpha présentait une probabilité de mortalité plus faible que le variant original dans l'analyse multivariable (RCa 0,5, IC à 95 % 0,3 à 0,9) (28). • Quatre études ont fait état d'un risque de mortalité plus élevé : risque plus élevé de décès après 28 jours (55 %, IC à 95 %, 39 à 72 %) (47), RRa 1,59 (IC à 95 %, 1,25 à 2,03) (40), RRa 1,67 (IC à 95 %, 1,34 à 2,09; P < 0,0001) (41). HR 1,64 (IC 95 % 1,32 à 2,04, p < 0,001), ce qui équivaut à une augmentation de 2,5 à 4,1 décès par 1 000 cas détectés (48). La méta-analyse de ces quatre études indiquait un risque de mortalité combiné avec RR = 1,45 (IC à 95 %, 1,18 à 1,78) (134). • Des études écologiques effectuées au Royaume-Uni estiment que le variant Alpha est 33 % plus mortel (51) et que son taux de mortalité est plus élevée (49).	Treize études ont fait état de la mortalité; il s'agissait d'analyses de données de surveillance, d'études écologiques, de cohortes prospectives, de cohortes rétrospectives et d'études transversales, dont la plupart ont été menées au Royaume-Uni. Niveau de preuve modéré.

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVE
Facteurs de risque de mortalité comparativement au variant original	• Les données démographiques sur les décès liés au variant Alpha étaient similaires chez les hommes et les femmes, mais la prévalence était plus élevée dans les groupes d'âge plus jeune que dans les groupes d'âge plus âgés (59,0 % chez les 1 à 34 ans contre 55,4 % chez les 85 ans ou plus) (47). Il y avait également des variations selon l'origine ethnique : noire (69,6 %), mixte ou d'origine ethnique inconnue (64,8 %), blanche (58,0 %) et asiatique (57,6 %). La variation était la plus faible dans le quintile le plus défavorisé de l'indice de privation multiple (53,9 %) (47). • Il n'y avait aucune preuve d'une association significative entre le variant Alpha et le sexe (p = 0,90), le groupe ethnique (p = 0,64) ou le groupe d'âge (p = 0,15) (40).	Deux études, y compris une analyse des données de surveillance et une cohorte rétrospective. Faible niveau de preuve.
Charge virale comparativement au variant original	• Plusieurs études (n = 14) ont mesuré la charge virale en tant que Ct ou copies estimées/ml pour différentes protéines cibles (généralement N et ORF1ab). Elles indiquent systématiquement que les échantillons de variant Alpha sont plus susceptibles de présenter des valeurs Ct plus faibles ou des charges virales estimées plus élevées. L'ordre de grandeur médian supérieur varie de 2 à 10 fois selon les études et la protéine cible (3, 32, 35, 39, 45, 54 à 59, 59 à 61, 117, 133, 135, 136).	22 études qui étaient principalement des analyses de données de surveillance, des études de cohorte ou transversales qui ont analysé les valeurs Ct de la PCR entre les échantillons de variant Alpha et les échantillons du variant original. Cette mesure est indirecte et toutes les études sont conçues sur la base d'observations. La conclusion selon laquelle les cas associés au variant Alpha ont des valeurs Ct plus basses était cohérente entre les études. Niveau de preuve faible à modéré.

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Modèle animal pour la charge virale Comparativement au variant original et à d'autres VP/VI	• Une étude sur les animaux effectuée chez les macaques rhésus a révélé une charge virale plus élevée d'ARN génomique dans la muqueuse nasale des animaux infectés par le variant Alpha comparativement à ceux qui étaient infectés par la souche sauvage et le variant Bêta et des antigènes viraux plus faibles dans les tissus pulmonaires comparativement à la souche sauvage (137). • Une autre étude a démontré que les hamsters infectés par le variant Alpha présentaient un taux élevé d'excrétion d'ARN viral par les sécrétions nasales pendant les premières semaines d'infection (138). • Un modèle avec souris a révélé que la charge virale était beaucoup plus faible pour le variant Alpha dans les poumons des souris infectées que pour les variant Bêta et variant Gamma dans les poumons C57BL/6 et BALB/c, et qu'aucun virus infectieux n'avait été détecté dans les poumons BALB/c (139).	Trois études sur des modèles animaux démontrent toutes une diminution de la charge virale dans les poumons et une augmentation de la charge virale dans la muqueuse nasale. Faible niveau de preuve.
Période infectieuse	Une étude prospective portant sur des cas associés au variant Alpha (n = 7) a révélé que les infections duraient en moyenne 13,3 jours comparativement à 8,2 jours pour d'autres variants (57).	Une petite cohorte prospective. Ce résultat nécessite une évaluation plus approfondie avec un échantillon plus grand et une gamme de cas plus étendue. Très faible niveau de preuve.
Période d'incubation	*Aucune étude*	
Échappement immunitaire - incidence potentielle sur l'efficacité du vaccin, possibilité de réinfection		
Réinfection par infection naturelle comparativement au variant original	Trois études ont estimé le taux de réinfection. Une étude menée au Royaume-Uni a révélé un taux de réinfection de 0,7 % (IC à 95 % : 0,6 à 0,8) (65) alors qu'aux États-Unis, le taux de séropositivité antérieur chez les personnes atteintes du variant Alpha était de 0,7 % comparativement aux infections associées aux variants originaux dont le taux était de 0,9 % (38). Une étude prospective menée auprès des travailleurs de la santé du Royaume-Uni a révélé	Trois études de réinfection ont inclus une analyse du variant Alpha et conviennent que ce variant n'échappe pas à l'immunité naturelle. Ces études incluent notamment une analyse des données de

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	qu'il n'y avait aucune preuve indiquant que variant Alpha avait modifié l'étendue de la protection contre une infection par PCR positive chez les personnes séropositives (RTI 0,40, IC à 95 %, 0,10 à 1,64, p = 0,20) (66).	surveillance, ainsi que des études de cohorte et des études écologiques. Niveau de preuve modéré.
Modèle animal de réinfection comparativement au variant original	Les hamsters infectés par le SRAS-CoV-2 original et guéris ont tous été protégés contre une réinfection par le variant Alpha (97, 140).	Deux modèles animaux ont donné des résultats cohérents qui appuient les données probantes documentées dans des études sur les humains et *in vitro*. Faible niveau de preuve.
Études *in vitro* avec sérums de phase convalescente comparativement au variant original	La majorité des études *in vitro* ont systématiquement montré des réductions minimes ou faibles de la neutralisation du variant Alpha par rapport au variant original. Les études sont présentées dans le jeu de données. On voit des résultats cohérents, mais les éléments de preuve proviennent d'études de faible qualité.	Il existe de nombreuses études *in vitro* et la liste n'est pas exhaustive à ce jour. Faible niveau de preuve.
Infection sporadique après la vaccination, efficacité réelle ou prévue du vaccin comparativement au variant original	Infection ayant percé après la vaccination : • Les exposés de cas et les rapports sur les séries de cas indiquent une rupture asymptomatique des infections associées au variant Alpha ayant percé chez les adultes (73, 74, 141, 142) et les personnes âgées (143), les travailleurs de la santé au Brésil après la vaccination avec Sinopharm (144) et les travailleurs de la santé en Inde après la vaccination avec Covishield (AZD1222) (145). • Comparativement au taux de cas associé au variant original, le taux associé au variant Alpha était 1,29 fois plus élevé (IC à 95 % [0,75, 2,20], p = 0,468) dans les cas d'infection ayant percé après la vaccination (74). • À New York, parmi les personnes pleinement vaccinées contre le SRAS-CoV-2, 22 % ont été infectées par le variant Alpha comparativement à 44 % dont les infections n'étaient pas liées aux VP (38).	Vingt études ont fait état d'une infection ayant percé après la vaccination ou ont porté sur l'efficacité du vaccin. Le caractère généralisable dépend de la représentativité de la preuve pour la population générale. Des conclusions cohérentes entre les études améliorent la certitude des résultats. Ces études comprennent les ECR, les cohortes prospectives, les études cas-témoins, les études longitudinales et l'analyse des données de surveillance. Niveau de preuve élevé pour les études de cohorte

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	• Un nombre disproportionné d'infections ayant percé entre la première dose et jusqu'à 14 jours après la deuxième dose du vaccin Pfizer-BioNTech (BNT162b2) en Israël a entraîné une probabilité plus élevée ajustée d'être positif à la PCR avec le variant Alpha (RCa 2,4 (IC à 95 % : 1,2 à 5,1) (67). • Des études en situation réelle au Royaume-Uni n'ont signalé aucune différence dans l'efficacité du vaccin (données combinées avec AstraZeneca et Pfizer-BioNTech) avec le variant Alpha (146). • Après l'administration du vaccin Pfizer-BioNTech, la probabilité ajustée d'une activité de neutralisation inadéquate contre le variant Alpha dans le groupe d'âge le plus élevé (plus de 80 ans) par rapport aux travailleurs de la santé adultes était de RCa 4,4 (1,5 à 12,6, p<0,007) (147). Une dose du vaccin : • Dans une étude prospective britannique sur les travailleurs de la santé, rien n'indiquait que le variant Alpha avait modifié l'étendue de la protection offerte par la première dose du vaccin comparativement au variant original (RTIa = 1,84, IC à 95 %, 0,75 à 4,49, p = 0,18) (66). • Après la première dose de Pfizer-BioNTech ou d'AstraZeneca, la réduction de la probabilité d'être admis à l'urgence a été estimée à 43 % (33 % à 52 %) et à 37 % (3 % à 59 %), respectivement, sans oublier une réduction de 51 % (37 % à 62 %) du risque de décès chez les adultes de 70 ans et plus en Angleterre (75). Deux doses du vaccin : • On a pu voir une efficacité comparable ajustée (≥88 %) contre les infections symptomatiques associées aux variants Alpha, Bêta et Gamma ≥7 jours après l'administration de la deuxième	avec ECR, niveau modéré pour les études de cohorte prospectives et faible niveau pour tous les autres plans d'étude. Dans l'ensemble, le niveau de preuve varie de modéré à élevé. Les séries de cas et les rapports constituent des niveaux de preuve très faibles, mais peuvent être utilisés pour formuler des hypothèses en vue de recherches ultérieures.

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	dose des vaccins Moderna ou Pfizer-BioNTech (72). • L'efficacité du vaccin AstraZeneca (ChAdOx1-S) dans un ECR du Royaume-Uni était de 70,4 % (IC à 95 %, 43,6 à 84,5) contre la COVID-19 symptomatique causée par le variant Alpha et de 81,5 % (67,9 à 89,4) contre la COVID-19 symptomatique causée par les variants originaux (76). Dans le cas d'une infection asymptomatique ou à symptôme inconnu, l'efficacité du vaccin était plus élevée pour les infections non liées au variant Alpha (69,7 %, 33,0 à 86,3) que pour les infections associées au variant Alpha (28,9 %, -77,1 à 71,4) (76). • L'efficacité du vaccin Novavax (NVX-CoV2373) dans un ECR au Royaume-Uni était de 86,3 % (71,3 à 93,5) comparativement à 96,4 % (73,8 à 99,5) pour le variant original (77). • En Israël, où 94 % des cas étaient associés au variant Alpha, on a pu voir que l'efficacité du vaccin Pfizer-BioNTech (BNT162b2) était supérieure à 96 % 14 jours après la deuxième dose (78) et supérieure à 90 % chez les 70 ans et plus (79). • Une méta-analyse des essais d'efficacité du vaccin Pfizer-BioNTech VE a indiqué une efficacité de 51 % (IC à 95 % : 47 à 55 %) après la première dose, de 93 % (IC à 95 % : 90 à 96 %) après la deuxième dose alors que le vaccin AstraZeneca VE a obtenu une efficacité de 49 % (IC à 95 % : 43 à 55 %) après une première dose et de 66 % (IC à 95 % : 54 à 75 %) après une deuxième dose (149).	
Modèle animal de vaccination comparativement au variant original	• Les hamsters vaccinés avec l'AstraZeneca, puis exposés au B.1.1.7 n'ont pas perdu de poids, n'ont pas présenté de pathologie pulmonaire, et aucun virus n'a été détecté dans les échantillons de tissus, alors que les témoins présentaient une pathologie pulmonaire étendue (98) Une autre étude a signalé que des hamsters ayant reçu l'AstraZeneca et infectés par le variant Alpha ont	Neuf études effectuées des animaux différaient en ce qui concerne la perte de poids, mais avaient des résultats pathologiques qui concordaient avec les études effectuées sur des

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	continué de prendre du poids alors que les animaux témoins perdaient du poids et avaient une importante pathologie pulmonaire causée par le variant Alpha (150). • On a pu voir chez les animaux ayant reçu d'autres candidats vaccins, y compris le RBD de la protéine spicule (151 à 154) et le plasma humain infecté par le SRAS-CoV-2, les vaccins à l'ADN (155) et les vaccins circulaires d'ARNc (156), une activité de neutralisation contre le variant Alpha.	humains et les études *in vitro*. Faible niveau de preuve.
Étude *in vitro* des sérums provenant de personnes vaccinées comparativement au variant original	De nombreuses études *in vitro* sont disponibles dans le jeu de données. Ces études ont systématiquement indiqué des réductions minimes ou faibles de la neutralisation du variant Alpha comparativement au variant original. Elles n'ont pas été résumées dans le profil des éléments de preuve.	Il existe de nombreuses études *in vitro* et la liste n'est pas exhaustive à ce jour. Faible niveau de preuve.
Modèle animal de traitement comparativement au variant original	• Un certain nombre d'anticorps monoclonaux testés ont protégé les souris et les hamsters contre le variant Alpha (157). • Les oligonucléotide antisens de l'acide nucléique verrouillé (158) et la 4'-fluorouridine, un ribonucléoside analogue (159) ont efficacement supprimé la réplication virale chez les hamsters et les furets, respectivement. • Le traitement au sérum en phase convalescente a entraîné une diminution du nombre de copies virales dans les poumons des souris infectées par la souche sauvage ou le variant Alpha. Comparativement aux résultats obtenus avec la souche sauvage, le traitement n'a cependant pas réduit le nombre de copies virales dans les tissus cérébraux des souris infectées par le variant Alpha.	Quatre modèles animaux. Faible niveau de preuve.
Étude *in vitro* du traitement comparativement au variant original	Perte minime d'activité : plusieurs anticorps monoclonaux (160 à 162), antigènes polyclonaux de la CP ou préparations d'anticorps hCoV-2-IG purifiés (163).	Les études *in vitro* donnent un aperçu préliminaire des résultats que l'on s'attend à obtenir avec les études *in vivo*. Faible niveau de preuve.

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Étude *in vitro* de l'infectivité comparativement au variant original	La capacité du pseudovirus porteur de la mutation UK-N501Y à transduire ses cellules cibles par rapport au variant original a été considérablement augmentée, jusqu'à neuf fois (164).	Les études *in vitro* donnent un aperçu préliminaire des résultats que l'on s'attend à obtenir avec les études *in vivo*. Faible niveau de preuve.
Tests et diagnostics		
Test et détection	La PCR est efficace pour détecter et distinguer le variant (90, 165 à 171). Détection du variant Alpha dans les eaux usées à dans des proportions aussi faibles que 0,1 % de SRAS-CoV-2 (172). Plusieurs études font état de tests fiables pour la détection rapide des variants, y compris la détection dans des échantillons d'eaux usées (90, 100, 101, 172, 173).	32 études, 28 études sur l'exactitude des tests de diagnostic, trois analyses de données de surveillance qui décrivaient également un nouveau test ou un ensemble d'amorces, et une étude *in silico* sur les amorces. Comme elles décrivent toutes des tests différents, les études sont considérées comme individuelles et ne peuvent être résumées ensemble. Faible niveau de preuve.
Épidémiologie de la propagation		
Émergence des VP au fil du temps	• Trois études canadiennes précisent que les cas associés au variant Alpha initialement regroupés dans deux régions ont rapidement augmenté (174). De même, deux études réalisées en Ontario ont documenté l'augmentation rapide du variant Alpha (13, 175). Les études provenaient de nombreux pays du monde dont la plupart décrivaient la première détection du variant Alpha à la mi-décembre ou à la fin de ce mois, suivie d'une augmentation rapide du nombre de cas associés au variant dans les 3,5 à 10 semaines suivantes. On a alors constaté que ce variant était devenu la souche dominante dans plusieurs études. • Une étude israélienne a documenté un plateau et un déclin dans le groupe d'âge des plus de	116 études rendent compte de l'émergence et de la propagation du variant Alpha dans un pays ou une région au fil du temps. La plupart de ces études sont basées sur des données de surveillance, des cohortes prospectives souvent constituées de travailleurs de santé, des cohortes rétrospectives de dossiers hospitaliers, des études longitudinales et des études écologiques. Les rapports de prévalence ponctuelle ou de cas de

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	60 ans, alors que plus de 50 % de la population avait été vaccinée (première dose de Pfizer > 14 jours) (24). Les États-Unis ont documenté plusieurs introductions du variant Alpha dans l'ensemble du pays (15). Une étude menée aux États-Unis a indiqué que les résultats positifs quotidiens aux tests de dépistage du variant Alpha du SARS-CoV-2 sont passés de 0,25 % à 0,5 % entre octobre et décembre 2020 (176). Plusieurs études documentent la détection du variant Alpha dans les eaux usées (172, 177 à 179).	voyageurs infectés ont été exclus de ce résumé. Niveau de preuve faible à modéré.
Attribution au variant Alpha	On a constaté qu'une augmentation de 0,1 dans la proportion du variant Alpha, lorsqu'on tient compte de la période préalable au sommet, était associée à une augmentation de 35,8 % de la hauteur du sommet de la deuxième vague. Au cours de la période du 1er janvier au 25 février 2021, une augmentation de 0,1 de la proportion du variant Alpha a été liée à une augmentation de 15,3 % du nombre cumulé de décès au cours de cette période (180).	Un modèle a été utilisé pour estimer le fardeau supplémentaire associé à la COVID-19 en raison du variant Alpha. Preuve de faible niveau.
Facteurs de risque de propagation	• Une étude écologique menée dans les régions de Toronto et de Peel, en Ontario, a montré que le taux de croissance du variant Alpha (11,3 %, 19,8 % et 30,8 %), l'ensemble des cas (19,0 %, 32,7 % et 48,3 %) et les cas associés aux VP (18,4 %, 30,8 % et 50,8 %) étaient positivement corrélés avec la proportion de travailleurs essentiels (30,4 %, 47,9 % et 63,2 %) et le revenu médian (33 000 $, 45 000 $ et 60 000 $ CAN) de la communauté, respectivement (181). • Les données de surveillance de la France ont révélé que comparativement au variant Bêta ou au B.1.525, les infections associées au variant Alpha étaient plus fréquentes chez les personnes âgées. Dans les milieux hospitaliers, il y avait une sous-représentation du variant Alpha par rapport au variant Bêta. Dans certaines régions de la France, la probabilité d'être infecté par le variant original ou par le B.1.525 était	Cinq études ont évalué les facteurs de risque. Il s'agit notamment d'études écologiques, de cohortes prospectives, de modèles prédictifs et d'analyses de données de surveillance. Niveau de preuve modéré pour les études de cohorte prospectives. Faible niveau de preuve pour tous les autres plans d'étude.

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	identique ou inférieure à celle d'être infecté par le variant Alpha (11).	
Analyse génomique de la propagation	Les résultats ne suggèrent pas que les mutations canoniques du variant Alpha ont évolué indépendamment dans différents endroits, et indiquent une origine et une propagation du variant Alpha à partir du Royaume-Uni (182).	Une étude des données de la surveillance génomique. Faible niveau de preuve.

IC = intervalle de confiance, Ct = seuil du cycle, USI = unité de soins intensifs, RC = rapport des cotes, PCR = réaction en chaîne par polymérase, EV = efficacité du vaccin, RCa = rapport de cotes ajusté, RRa = rapport de risque ajusté, RPa = rapport de prévalence ajusté

Méthodologies :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. L'un des objectifs vise à déterminer si les études portent sur des variants préoccupants ou des variants d'intérêt. Les études correspondantes sont présentées plus en détail dans notre base de données sur les VP et VI alors que les résultats associés aux VP figurent dans le présent résumé. Une contre-vérification afin de trouver des articles pertinents a également été effectuée dans les bases de données en utilisant pour ce faire des recherches ciblées par mot clé. Ce tableau évolue au fur et à mesure que les preuves évoluent.

Variant préoccupant	**Termes de recherche**
Alpha, B.1.1.7, 202012/01, 501Y.V1, variant Kent (Mutations : Δ69/70, Δ144Y, (E484K*), (S494P*), N501Y, A570D, D614G, P681H) * de nouveaux variants avec des mutations ont été signalés et sont classés dans la catégorie B.1.1.7 + E484K	B.1.1.7 OU 202012/02 OU 501Y.V1 OU Alpha
Bêta, B.1.351, 501Y.V2, 20H/501.V2, Variant sud-africain (mutations : K417N, E484K, N501Y, D614G)	B.1.351 OU 501Y.V2 OU Bêta
Gamma, P.1, B.1.1.28.1, 501Y.V3, 20J/501Y.V3, variant du Brésil (mutations : K417N/T, E484K, N501Y, D614G)	P.1 OU B.1.1.28 OU 501Y.V3 OU Gamma
Delta, nouveau VP au Royaume-Uni : 202102/02, B.1.1.7 avec mutation E484K (nom?)	Voir B.1.1.7 OU Delta
Variants à l'étude	
États-Unis : Epsilon, B.1.429 et B.1.427, 20C/S:452R, (mutations : L452R, D614G et S13I, W152C en 429 uniquement)	B.1.429 et B.1.427, 20C/S:452R, CAL.20C, L452R OU Epsilon
Zeta P.2, B.1.1.28.2, au Brésil B.1.1.33	P.2 OU B.1.1.28 OU B.1.1.33 OU Zeta
Royaume-Uni : A.28.1	A.28.1
Royaume-Uni, Mexique, Nigeria : Êta, B.1.525	B.1.525 OU Êta
Royaume-Uni : B.1.318	B.1.318
Russie : B.1.317	B.1.317
New York : Iota B.1.526	B.1.526 OU Iota
Autres aux États-Unis : B.1.426, recombinant B.1.1.7 + B.1.429	B.1.426 et autres capturés avec la chaîne du B.1.429

Thêta, P.3, VUI-21MAR-02 nommé aux Philippines (et inclut les mutations E484, N501Y, P681H, LGV141-143)	P.3 OU Theta
B.1.617 Inde, sous-lignées : Kappa/B.1.617.1 Delta/B.1.617.2 B.1.617.3 (double mutant E484Q et L452R)	B.1.617 OU Delta OU Kappa
B.1.618 Inde (triple mutant)	B.1.618

La présente revue contient des recherches publiées jusqu'au 1er juin 2021.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

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ANNEXE

a) LEXIQUE SUR LES VP ET LES VI

Dénomination de l'OMS (27 mai 2021)	**Lignée Pango**	**Clade/lignée GISAID**	**Clade Nextstrain**	**Premiers échantillons**	**Date de la désignation**
Alpha	B.1.1.7	GRY (auparavant GR/501Y.V1)	20I/S:501Y.V1	Royaume-Uni, septembre 2020	2020-12-18
Bêta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	Afrique du Sud, mai 2020	2020-12-18
Gamma	P.1	GR/501Y.V3	20J/S:501Y.V3	Brésil, novembre 2020	2021-01-11
Delta	B.1.617.2	G/452R.V3	21A/S:478K	Inde, octobre 2020	VI : 4 avril 2021 VP : 2021-05-11
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	États-Unis, mars 2020	2021-03-05
Zeta	P.2	GR	20B/S.484K	Brésil, avril 2020	2021-03-17
Êta	B.1.525	G/484K.V3	20A/S484K	Plusieurs pays, décembre 2020	2021-03-17
Thêta	P.3	GR	20B/S:265C	Philippines, janvier 2021	24 mars 2021
Iota	B.1.526	GH	20C/S:484K	États-Unis, novembre 2020	24 mars 2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	Inde, octobre 2020	2021-04-04

b) NOMS DE MARQUE ET NOM GÉNÉRIQUE DES VACCINS

Nom de marque	**Nom générique**
AstraZeneca	ChAdOx1-S
Covishield	AZD1222
Pfizer-BioNTech	BNT162b2
Janssen (Johnson & Johnson)	Ad26.COV2.S
Moderna	aRNm-1273
Novavax	NVX-CoV2373
Sinopharm	CoronaVac

c) AUTRES RESSOURCES

Référence	Description
Living Evidence Review on SARS-CoV-2 variants Australie En cours, dernière consultation le 10 mars.	Ce tableau présente des éléments de preuve pertinents récents en ce qui concerne les différentes catégories d'études semblables à ce qui a été présenté dans le profil présenté dans le cadre de la présente revue.
Page sur les VP du CDC	Un résumé sur chacun des VP est disponible.
Rapports de situation de l'OMS; comprennent une section sur les VP.	
Consultation	
Transmission characteristics of SARS-CoV-2 variants of concern (Mars 2021) Curran, et coll. Données disponibles jusqu'au 21 février 2021	Revue rapide du champ d'application effectuée dans le cadre du réseau COVID-END.
Littérature grise	
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 13. Mai 2021	Ce rapport a été publié pour continuer à partager les données de surveillance détaillée du VOC-21APR02 (B.1.617.2) et les renseignements sur un nouveau variant VUI-21MAY-02 (C.36.3) en cours d'investigation. (C.36.3).
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 12. Mai 2021	Ce rapport a été publié pour continuer à partager les données de surveillance détaillée du VOC-21APR02 (B.1.617.2) et les renseignements sur un nouveau variant en cours d'investigation VUI-21MAY-02 (C.36.3).
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. Décembre 2020 à aujourd'hui	Les rapports techniques compilent les différentes informations provenant de diverses études et de la surveillance de l'ensemble du Royaume-Uni en ce qui concerne les VP et les VI en circulation. Ces rapports et publications de recherche se recoupent largement.
Public Health England. Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01 [Internet]. Décembre 2020	Le variant Alpha s'est répandu rapidement au Royaume-Uni et a été évalué comme ayant une transmissibilité considérablement accrue.
Public Health England. Analysis of transmissibility based on genomics [Internet]. Décembre 2020	Indique que le variant Alpha se répand 71% (IC à 95 %, 67 % à 75 %) plus rapidement par génération (6,5 jours), bien qu'une fréquence constante n'indique pas un avantage sélectif constant du variant Alpha.

NERVTAG. NERVTAG meeting on SARS-CoV-2 variant under investigation VUI-202012/01 [Internet]. Décembre 2020	Confiance modérée dans le fait que le variant Alpha démontre une augmentation substantielle de la transmissibilité par rapport aux autres variants.
NERVTAG. Update note on B.1.1.7 severity [Internet]. Février 2021	Il est probable que l'infection causée par le VP Alpha soit associée à un risque accru d'hospitalisation et de décès par rapport à l'infection découlant des virus du variant original.

Emerging Evidence on COVID-19

Living Summary of SARS-CoV-2 Variants of Concern: The Beta Variant (B.1.351) profile

Highlights up to July 1, 2021

Introduction

SARS-CoV-2 **variants of concern** (VOCs) are circulating variants that have been flagged by national or global public health organizations. VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or are associated with diagnostic detection failures (1-3). Canada has established a national definition (2). In May 2021, the World Health Organization (WHO) released a naming system for VOCs and variants of interest (VOIs) using Greek letters to improve the ease of communication on variants and potential stigma related to places where variants were first identified, which has been adopted in this report (1).

TABLE 1: CURRENT VARIANTS OF CONCERN (VOCs)*

WHO name (05-21)	Pango lineage	Nextstrain clade	GISAID clade	Alternate name	First detected in	Earliest samples	Characteristic spike mutations
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	United Kingdom	Sep 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Beta	B.1.351 B.1.351.2 B.1.351.3	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	South Africa	May 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, P.1.1 P.1.2	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brazil and Japan	Nov 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G H655Y, T1027I, V1176F
Delta	B.1.617.2 AY.1 AY.2	21A	G/478K.V1		India	Oct 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R,

	AY.3						del157/158, T478K, D950N)

* A VOC/VOI lexicon and other resources are available in the appendix.

The goal of this living summary on the SARS-CoV-2 VOC literature is to highlight new data on the VOC B.1.351 (Beta), its epidemiology, and how the attributes of this variant may impact the management of the pandemic. This living evidence profile on Beta is part of a larger project that summarizes the data on each VOC as well as captures data on VOIs. The focus will be on changes to epidemiological parameters (e.g., transmission rates, clinical outcomes of severity and mortality, shifts in age groups affected or asymptomatic proportions), impacts on diagnostic tests, immune evasion/vaccine effectiveness and impacts on other public health measures. The full dataset in Excel can be accessed here and filtered by the VOCs and VOIs of interest. The recent living evidence reviews on other VOCs (Alpha, Gamma and Delta) and a high level contrasting table of VOC evidence can be requested here.

In this summary, "original variant" refers to any variant that was not designated as a VOC or VOI.

Key Points

As of July 1, 2021, there were 341 studies that report on the Beta variant of concern. 65 studies were summarized in the profile including studies describing transmission efficiency (n=8), clinical severity (n=7), immune escape (n=24), testing and diagnostics (n=21), and epidemiology including spread (n=8). Some studies reported outcomes for more than one category. 276 studies were not summarized in the profile, including: studies on case reports or case series (n=5), point or period prevalence estimates (n=25), studies reporting the detection of Beta or phylogenetic analysis (n=12), cell infectivity, binding affinity, or genomic characterization studies (n=29), *in vitro studies* with no extractable outcomes and neutralization experiments on convalescent or vaccinated sera (n=154), predictive models with no extractable outcomes or in which the time for projections has already passed (n=8), animal models with no extractable outcomes or neutralization experiments on convalescent or vaccinated protection (n=23), studies of non-commercialized therapeutics (n=9), diagnostic test accuracy studies evaluating a new test/method to detect VOCs (n=10), and vaccine breakthrough data with no control group to compare the VOC proportion of breakthrough cases vs. VOC proportion of all COVID-19 cases (n=1).

However, details for all 341 studies that report on Beta can be found in the Excel dataset accessed here.

Transmissibility:

- Studies from multiple countries demonstrate the increased transmissibility of Beta compared to the original variant and Alpha, although the extent ranged greatly; 20%-175% above the original variant across multiple countries and 9.12%-17.21% above Alpha in France (4-7). One Canadian surveillance study

on household transmission reported that Beta has 58% increased transmissibility and a 31% higher secondary attack rate compared to the original variant (8).

Clinical Severity:

- Studies from several European countries reported higher odds of hospitalization for Beta compared to the original variant and Alpha (10, 11). There are conflicting findings regarding ICU admissions due to Beta compared to the original variant. A surveillance study of European countries reported an increased proportion (2.3% for Beta vs. 0.6% for the original variant) and odds (aOR 3.3, 95% CI 1.9-5.7) of ICU admission among Beta cases compared to original variant cases, while a retrospective cohort study from South Africa reported a lower proportion of ICU admissions (35% for Beta vs. 48.5% for the original variant) (10, 12).
- For severity indicators, there is conflicting evidence on the age of hospital and ICU admission due to Beta infection. A surveillance study of several European countries reported an increased odds of hospitalization and ICU admission in adults aged 40-59 due to Beta infection (10). Two studies reported a lower proportion of pre-existing conditions among Beta cases compared to original variant cases (10, 12).
- Two retrospective cohort studies from South Africa and France reported increased overall mortality and higher ICU mortality among Beta cases compared to original variant and Alpha cases (12, 13).
- A cross-sectional study and a surveillance study using data from France reported that Beta has a higher viral load compared to the original variant (4, 14), and a surveillance study from France reported that the viral load of Beta was lower compared to Alpha (5).
- One surveillance study using data from France reported no significant difference in the infectious period for combined Beta and Gamma case data compared to the original variant (HR 95% CI 0.79-1.06) (4).
- There were no studies on incubation period for Beta.

Immune Escape:

- Single dose vaccination: The vaccine effectiveness (VE) against severe disease or mortality due to Beta was 56.5% for BNT162b2 (Pfizer-BioNTech) 15 to 21 days following the first dose in Qatar (15, 16). VE against moderate and severe disease caused by Beta was 52%-64% and 73-82%, respectively, for the Ad26.COV2.5 (Janssen) vaccine in South Africa (22).
- Two dose vaccination: The VE against Beta infection was 50%-93.48% for BNT162b2 (Pfizer-BioNTech) in Qatar, France, and Canada, where the lower estimate was for long term care residents (median age=87 years) (15-18). The VE against symptomatic infection was ≥ 88% for BNT162b2 (Pfizer) or mRNA-1273 (Moderna) in Ontario, Canada (19), 10.4% for ChAdOx1 (AstraZeneca) in South Africa (20), and 51% for NVX-CoV2373 (Novavax) in South Africa (21). VE against severe disease or mortality due to Beta was 97.4%-100%, greater than 14 days following the second dose of the BNT162b2 (Pfizer-BioNTech) vaccine in Qatar (15, 16) (22).

Testing and Diagnostics:

- Several diagnostic test accuracy studies report effectively detecting and/or distinguishing Beta (41-60).
- One study describes the failed detection of a Beta sample carrying the R246I mutation (58).

Spread Epidemiology:

- In South Africa, Beta was first detected in October 2020, and became the dominant variant by March 2021 (64).
- The prevalence of Beta is expected to outgrow Alpha in regions where the seroprevalence of the original variant exceeds 20%-40% (9).

Overview of the Evidence

Study designs on VOC research range widely from observational studies with a high risk of bias to double blind randomized controlled trials (RCTs) with a lower risk of bias. The highest level of evidence was from double-blind randomized controlled trials that were done to evaluate vaccine efficacy. The observational studies, including surveillance data analyses, retrospective cohorts and case control studies, are generally considered low levels of evidence, but may be upgraded for a given outcome when multiple studies are in agreement and when they have a prospective design. Other studies including predictive models, ecological studies, animal models, *in vitro* studies and *in silico* studies are low to very low evidence**.** Generally these types of studies are used to generate hypotheses that are then tested with a more rigorous study design. For this profile, study designs were identified, but no formal risk of bias assessment was conducted for each study. A summary indication of the level of confidence of the evidence was given for each category of study.

The greatest amount of evidence was on the transmissibility and spread of Beta over time. There were gaps in knowledge regarding epidemiological parameters including infectious period and incubation period, impact on public health measures, and vaccine effectiveness. There are several knowledge gaps or areas where there is very little research noted in the key points table, and additional research is needed to improve confidence in summary results, and to fill in current knowledge gaps regarding the Beta variant.

CONTENTS

BETA

The excel dataset includes summaries of individual studies and can be accessed here. Below is the detailed evidence profile developed for Beta.

Categories of evidence in the tables below include the following if reported:

Transmissibility includes changes in transmissibility, secondary attack rates, and estimates of selective advantage.

Clinical Severity includes proportion of infections that are symptomatic, proportion of severe disease and mortality as well as risk factors for severe disease or mortality, viral load, infectious period, incubation period. Note risk factors for severe disease would include special populations e.g. persons who are pregnant (when reported).

Immune Escape includes changes to vaccine efficacy, risk of re-infection in humans, animal models, *in vitro* or *in silico* experiments as well as impacts on therapeutics if reported.

Diagnostic / Detection Test Failure is captured in the individual sections, and will only be included in Table 2 if there is a concern about test performance.

Other Epidemiology includes all studies that document the emergence and spread of VOCs in a geographic area, ecological studies that examine VOC spread and risk factors for hot spots, and studies on effective public health interventions against VOCs, genomic epidemiology as subcategories when reported.

Table 2: Evidence Profile of B.1.351 (Beta) VOC (n=341)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency		
Transmissibility Compared to Original Variant or B.1.1.7 (Alpha)	Beta vs. Original Variant: • Increased transmissibility above the original variant: 58% (95%CI -7%-167%) in Ontario, Canada (8), 55% in multiple countries (6), 20-100% (as high as 175%) in South Africa (7), and 26%-27% in Niger and France that combined Beta and Gamma case data (4, 5) Beta vs. Alpha: • France: Between April to May 2021, Beta had a significant transmission advantage over Alpha in Ile-de-France (15.8%, 95%CI 15.1%-16.1%) and Hauts-de-France (17.1%, 95%CI 16.1% - 18.8%) compared to January to March 2021(11). • France: Between May to June 2021, combined Beta, Gamma and Eta data indicated a significant transmission advantage over Alpha in Ile-de-France (17.2%, 95%CI 15.6%-18.9%), Hauts-de- France (16.1%, 95%CI 4.63%-28.5%), and Normandie (9.12%, 95%CI 7.34%-10.9%) (23).	7 studies on transmissibility, including 6 surveillance data analyses from France (n=3), Canada (n=1), Niger (n=1), multiple countries (n=1), and 1 predictive model from South Africa. Across studies there is little consistency. Heterogeneity in increased transmissibility estimates may be due to many factors including the point in the pandemic estimates are taken and public health measures in place. Low level of evidence.
Secondary Attack Rates	• Canada: An Ontario household transmission investigation reported that Beta had a 31%	2 studies including 1 surveillance data analysis from Canada, and 1

Compared to Original Variant	higher secondary attack rate (SAR) (26.4%) compared to the original variant (20.2%) from March to April 2021 (8). • France: In an outbreak investigation of Beta, involving 20 secondary cases among 31 confirmed/probable cases, the SAR was 76.9%, equivalent to an R_{eff} of 4 (24).	outbreak investigation from France. Low level of evidence.
Clinical Severity		
Virulence / Severity or Duration of Disease Compared to Original Variant or B.1.1.7 (Alpha)	• European countries: There was no difference in the symptomatic proportion among Beta cases (90.3%; 28/31) vs. original variant cases (81.4%; 547/672, p = 0.2) (10). Increased hospitalization: • European countries: A higher odds of hospitalization with Beta (19.3%) vs. the original variant (7.5%) p<0.001.0, in a multivariable analysis (aOR = 3.6, 95% CI: 2.1-6.2) (10). • France: Beta cases were more likely to be hospitalized (OR=1.56, p<0.0001) compared to Alpha cases (11). Conflicting evidence on ICU admission: • European countries: Increased proportion of Beta cases in the ICU (2.3%) vs. the original variant (0.6%) p=0.001, and higher odds of ICU admission among Beta cases compared to original variant cases (aOR = 3.3, 95%CI 1.9-5.7) (10). • South Africa: In hospitalized cases, there were lower ICU admissions (35% vs. 48.5%, p=0.03) and mechanical ventilation (8.9% vs. 15.5%, p=0.009) during the Beta wave compared to the original variant wave. Although patients were of older age, they had less comorbidities during the Beta wave. The shortage of ICU beds was not a factor influencing this finding (12). France: No significant difference in ICU scores and mechanical ventilation requirements between Beta, original variant or Alpha cases in a hospital (13).	4 studies on severity, including 2 surveillance studies from multiple European countries and France, and 2 retrospective cohort studies from France and South Africa. The cohort studies are single-centered, therefore have limited external validity and are at risk of confounding bias. Low confidence in the increased/decreased severity of the Beta variant. Low level of evidence.
Severity Risk Factors	Age:	3 studies on severity risk factors, including 1 surveillance study of

Compared to Original Variant or B.1.1.7 (Alpha)	• European countries: In an age-stratified analysis, Beta cases had 3.5–3.6 times higher odds of hospitalization for age groups 40–59 and 60–79 years compared to original variant cases of the same age (10). • European countries: Admission to the ICU was significantly more likely for Beta cases (aOR 8, 95%CI 3.7–17.3) aged 40–59 years (10). • South Africa: Hospitalized cases during the second wave, Oct 2020- Jan 2021, where Beta was dominant, were significantly older (median age 57 vs. 54 years, p = 0.03) compared to cases during the original variant wave (12). • France: No significant difference in the age (63 years vs. 67 years, p = 0.15) or sex of ICU admissions among Beta cases compared to original variant or Alpha cases (13). Comorbidities: • European countries: Pre-existing conditions were lower in Beta cases (79.6%) vs. original variant cases (89%), p<0.001 (10). • South Africa: More cases during the Beta wave had no comorbidities (47% vs. 36.9%, p=0.008) and less hypertension (32.2% vs. 45.2%, p<0.001) compared to the original variant wave, and there was no difference in diabetes mellitus, chronic respiratory disease, cerebrovascular disease, and HIV positivity (12).	European countries and 2 retrospective cohort studies from France and South Africa. The cohort studies are single-centered, therefore have limited external validity and are at risk of confounding bias. Low level of evidence.
Mortality Compared to Original Variant or B.1.1.7 (Alpha)	Increased mortality: • South Africa: During the Beta wave, hospital admission was independently associated with mortality (p=0.006), there was increased overall mortality (36.4% vs. 32.6%, p=0.26), and significantly higher ICU mortality (74.4% vs. 57.1%, p=0.002) compared to the original variant wave. Lack of ICU capacity may have contributed to increased mortality (12). • France: Higher odds of death within 60 days of ICU admission (OR=5.67, 95% CI: 1.04-30.81,	3 studies on mortality, including 1 surveillance study of European countries and 2 retrospective cohort studies from South Africa and France. The cohort studies are single-centered, therefore have limited external validity and are at risk of confounding bias. Low level of evidence.

	p=0.04) for Beta cases compared to Alpha cases (13). No difference: • European countries: No difference in the odds of death for Beta cases compared to original variant cases in a multivariable analysis (aOR 1.1, 95% CI: 0.4-3.4) (10).	
Mortality Risk Factors Compared to Original Variant	No studies	
Viral Load Compared to Original Variant or B.1.1.7 (Alpha)	Beta vs. Original Variant: • France: The viral load of Beta was 2 times higher than the original variant (14), and Beta had a CT value difference of 0.754 (p<0.0072) lower (indicating higher viral load) compared to the original variant (4). Beta vs. Alpha: • France: Viral load (measured by CT values) in Beta samples was lower than Alpha samples (CT values: 22.2 for Beta vs. 21.9 for Alpha) (5).	3 studies including 2 surveillance data analysis using data from France, and 1 cross sectional study from France. Viral load is reported as a secondary outcome in these studies. Very low level of evidence.
Infectious Period Compared to Original Variant	• No significant difference in the infectious period duration of decline in viral load of combined Beta/Gamma data compared to the original variant (95% CI of the HR: 0.79-1.06) (4).	1 surveillance data analysis from multiple countries. Low level of evidence.
Incubation Period	No studies	
Immune Escape - Potential Impact on Vaccine Efficacy, Possibility of Re-infection		
Re-infection from Infection Compared to Original Variant	• Only case reports have been reported and are not summarized.	
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness Compared to Original Variant	Vaccine Efficacy/Effectiveness: BNT162b2 (Pfizer-BioNTech): • Qatar: 75.0% (95% CI: 70.5% – 78.9%) VE against any Beta infection ≥ 2 weeks after the second dose. 56.5% (95% CI: 0.0% – 82.8%) VE 15 to 21 days following the first dose and 97.4% (95% CI: 92.2%-99.5%)/100.0% (95% CI: 73.7% - 100.0%) VE ≥14 days following the	10 studies on breakthrough infections and vaccine efficacy/effectiveness, including 3 RCTs from South Africa, 1 prospective cohort study from France, 1 retrospective cohort study from Israel, 3 case control studies from Qatar (n=2) and Canada (n=1), 1 surveillance data

	second dose against severe, critical, or fatal outcomes due to Beta infection (15, 16). • France: A VE against infection of 50% (95% CI: 34%-73%) among nursing home residents (median age: 87.0±8.2 years) for two doses spaced 19 days apart was observed in an outbreak investigation (17). • Canada: In Ontario, fully vaccinated long-term care residents had a VE of 93.48% against Beta infection (18). • Canada: A study from Ontario reported BNT162b2 (Pfizer)/mRNA-1273 (Moderna), had a VE of ≥ 88% against symptomatic Beta infection ≥ 7 days after receiving the second dose (19). ChAdOx1 (AstraZeneca): • South Africa: 10.4% (95%CI: -76.8%-54.8%) VE for prevention of symptomatic disease > 14 days following the second dose (20). Ad26.COV2.S (Johnson and Johnson): • In South Africa, where Beta is the dominant variant, the reported VE was 52% and 64% for moderate disease and 73% and 82% for severe disease at 14 days and 28 days, respectively, following a single dose (22). NVX-CoV2373 (Novavax): • South Africa: 51.0% (95%CI -0.6 – 76.2) VE against symptomatic disease in HIV-negative individuals (21). Breakthrough Infection after Vaccination: • Studies from France and Canada describe Beta breakthrough infections among fully vaccinated long term care (LTC) residents and fully/partially vaccinated LTC staff, however there is no indication that the Beta breakthrough rate is higher than expected compared to its representation in all COVID-19 cases in the community (17, 18). • USA: In an underpowered study (n=20 breakthrough cases), Beta was overrepresented among breakthrough infections (5%, 1/20) compared to its	analysis from the USA, and 1 outbreak investigation from Canada. Most VE estimates for each vaccine are only based on one study, therefore additional trials are needed to improve confidence in these estimates. These studies have a low to moderate level of evidence.

	representation in COVID-19 cases (1%) from February to April 2021 in Washington State (25). Israel: There was a significantly higher proportion of Beta breakthrough infections among cases who received the second dose of the Pfizer-BioNTech vaccine vs. unvaccinated controls (OR=8:1, p=0.02), of which 7/8 cases were identified 7 to 13 days after the second dose and 1/8 cases were identified14 days after the second dose (26).	
Studies of Therapeutics Compared to Original Variant	• In *in vitro* experiments, Casirivimab and Etesevimab showed reduced neutralization (27-30), Bamlanivimab showed no neutralization and failed to inhibit binding of the Beta spike to ACE2 (29-32), and there was conflicting evidence on the neutralization of Imdevimab (27, 28) against Beta. • In mice and hamster models, combination monoclonal antibody treatment involving Casirivimab and Imdevimab showed protection against Beta infection, and higher doses (35 mg kg^{-1}) could compensate for the loss in neutralization potency (30).	6 studies on therapeutics including 5 *in vitro* studies and 1 animal model. Very low level of evidence.
Animal Models of convalescent or vaccinated protection	• Animal models challenged with Beta concluded that previously infected or vaccinated hamsters and mice have shown protection from clinical disease (33-40).	8 animal models. Very low level of evidence.
***In vitro* Studies** Compared to Original Variant or B.1.1.7 (Alpha)	• Most vaccine and convalescent sera have shown reduced neutralizing activity for Beta compared to the original variant or Alpha. In most studies Beta has more reduced neutralization than Gamma. The neutralization experiments are not summarized, but can be found in the dataset.	95 *in vitro* experiments have been identified with results specific to Beta neutralization. Very low level of evidence. The immune response is complex, and lack of or reduced neutralizing antibodies does not mean a lack of immune protection. Further research is needed (see the PHAC Emerging Science Group review on protective immunity).
Testing and Diagnostics		

Testing and Detection Compared to Original Variant or B.1.1.7 (Alpha)	• PCR, antigen tests, serological assays and sequencing methods are effective at detecting and/or distinguishing Beta, including detection in wastewater samples (41-60). • The TRF-ELISA S1-based antigen assay detected Beta with a 2 to 3-fold reduced sensitivity compared to the original variant and Alpha (61). • The ADESSO assay, which uses specific high-sensitivity enzymatic reporter unlocking, failed to detect one Beta sample carrying the R246I mutation among 13 Alpha/Beta samples (58).	21 studies on testing and detection, including 20 diagnostic test accuracy studies and 1 *in silico* study. As these are all describing different tests, the studies are considered to be individual and cannot be summarized together. Low level of evidence.
Spread Epidemiology		
VOC Emergence Over Time	• Two studies show the growth of Beta in different areas of South Africa from October to November 2020 and British Columbia, Canada from January to February 2021 (62, 63). • In South Africa, Beta emerged around August 2020, and was first detected in October 2020. By March 2021, it became the dominant variant representing approximately 20% (1769/8746) of genomes (64). • Studies from countries outside of South Africa, report the first detection of Beta since December 2020. Beta emerged in North America in January 2021 (65-68).	7 studies including 6 surveillance data analysis from South Africa (n=1), Canada (n=1), Comoros Islands (n=1), Bangladesh (n=1), multiple countries (n=2), and 1 predictive model from multiple North American countries. Low level of evidence.
Predictions of Spread	• Based on predictive models, the frequency of Beta will remain stable (<5%) from July 2021 onwards in North America, assuming that vaccination will not affect the proportion of variants and there will be equal and sustained rates of infectivity. The frequency of Beta will gradually increase to 5% by March 2022 in North America, assuming that herd immunity will be reached in July 2021 with 75% of the population being vaccinated (68). • Due to the assumed immune evasion of Beta (25% to 75%), it is predicted to outgrow Alpha (no immune evasion assumed for Alpha) in regions where the seroprevalence of the original variant exceeds 20% to 40% (9).	2 predictive models from multiple North American countries and South Africa. Low level of evidence.

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, , PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds, HR=Hazard Ratio, ratio, aHR = adjusted Hazard Ratio, aPR= adjusted Prevalence Ratio

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. One of the foci is to identify studies as variants of concern or under investigation. Studies identified under this foci are further characterized in our VOC/VOI database and Beta results were extracted into this review. A cross check for relevant articles is also conducted within the databases using targeted keyword searching (B.1.351 OR Beta). This table is evolving as the evidence evolves.

This review contains research published up to July 1, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Peer-review
This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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APPENDIX

a) VOC AND VOI LEXICON

WHO label (2021-05-27)	**Pango lineage**	**GISAID clade/lineage**	**Nextstrain clade**	**Earliest documented samples**	**Date of designation**
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I/S:501Y.V1	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov-2020	11-Jan-2021

	P.1.2				
Delta	B.1.617.2 AY.1 AY.2 AY.3	G/452R.V3	21A/S:478K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR	20B/S.484K	Brazil, Apr-2020	17-Mar-2021
Eta	B.1.525	G/484K.V3	20A/S484K	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR	20B/S:265C	Philippines, Jan-2021	24-Mar-2021
Iota	B.1.526	GH	20C/S:484K	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021

b) VACCINE BRAND AND GENERIC NAMES

Brand Name	**Generic Name**
AstraZeneca/ Covishield	ChAdOx1-S (AZD1222)
Pfizer-BioNTech	BNT162b2
Janssen (Johnson & Johnson)	Ad26.COV2.S
Moderna	mRNA-1273
Novavax	NVX-CoV2373
Sinopharm	CoronaVac
Sinopharm	BBIBP-CorV
Bharat Biotech	Covaxin (BBV152)
Russian vaccine- produced by 14 companies via partnership (Aug-21)	Sputnik V (Gam-COVID-Vac)

c) OTHER RESOURCES

Reference	Description
Living Evidence Review on SARS-CoV-2 variants Australia	This table highlights recent relevant evidence under the different categories of study similar to what has been laid out in the profiles in this review.

On-going, last examined March 10.	
CDC VOC page	Summary of each VOC is available.
WHO situation reports	Summaries include a VOC section.
Review	
Transmission characteristics of SARS-CoV-2 variants of concern (MAR 2021) Curran, et al Data up to Feb 21, 2021	Rapid scoping review done as part of the COVID-END network.
Grey lit	
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 13. 2021 May	This report has been published to share detailed surveillance of VOC-21APR02 (B.1.617.2) and information on a new variant under investigation VUI-21MAY-02 (C.36.3).
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 12. 2021 May	This report has been published to continue to share detailed surveillance of VOC-21APR02 (B.1.617.2) and information on a new variant under investigation VUI-21MAY-02 (C.36.3).
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. 2020 Dec to present	Technical reports compile information from various studies and surveillance across the UK on the VOC and VOIs that are circulating. There is a lot of overlap from these reports and research publications.
Public Health England. Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01 [Internet]. 2020 Dec	The VOC (Alpha) has grown rapidly in the UK and has been assessed as having substantially increased transmissibility
Public Health England. Analysis of transmissibility based on genomics [Internet]. 2020 Dec	Indication that Alpha grows 71% (95% CI: 67%-75%) faster per generation (6.5 days), yet consistent frequency does not indicate a constant selective advantage of Alpha
NERVTAG. NERVTAG meeting on SARS-CoV-2 variant under investigation VUI-202012/01 [Internet]. 2020 Dec	Moderate confidence that Alpha demonstrates a substantial increase in transmissibility compared to other variants.
NERVTAG. Update note on B.1.1.7 severity [Internet]. 2021 Feb	It is likely that infection with VOC Alpha is associated with an increased risk of hospitalization and death compared to infection with original variant viruses

Nouveaux éléments de preuve sur la COVID-19

Résumé évolutif à propos des variants préoccupants du SRAS-CoV-2 : Le profil du variant Delta (B.1.617.2)

Faits saillants jusqu'au 30 juin 2021

Introduction

Les variants préoccupants (VP) du SRAS-CoV-2 sont des variants en circulation qui ont été signalés par les organisations nationales ou mondiales de santé publique. Ces variants deviennent préoccupants lorsqu'on les compare aux variants originaux du SRAS-CoV-2, puisque la complémentation de leurs mutations crée une transmissibilité et une virulence accrues (morbidité ou mortalité), des changements dans la présentation clinique de la maladie, de l'évasion immunitaire, une diminution de l'efficacité des vaccins, des thérapies ou des mesures de santé publique disponibles ou des échecs dans la détection aux fins de diagnostic (1, 2). Ce résumé évolutif axé sur la littérature sur les VP du SRAS-CoV-2 vise à présenter de nouvelles données sur le VP B.1.617.2 (Delta), leur épidémiologie et la façon dont leurs attributs peuvent influer sur la gestion de la pandémie. Ce résumé porte sur les changements dans les paramètres épidémiologiques (p. ex., taux de transmission, résultats cliniques en ce qui concerne la gravité et la mortalité, changements dans les groupes d'âge touchés ou proportions de personnes asymptomatiques), les répercussions sur les tests de diagnostic, l'évasion immunitaire ou et l'efficacité des vaccins, ainsi que les répercussions des VP sur d'autres mesures de santé publique. En mai 2021, l'OMS a publié un système de nomenclature des variants préoccupants (VP) et des variants d'intérêt (VI) utilisant des lettres grecques afin de simplifier la communication à propos des variants et d'éliminer la stigmatisation potentielle découlant des endroits où les variants ont été identifiés la première fois, système qui a été adopté dans ce rapport (3).

TABLEAU 1 : VARIANTS ACTUELS PRÉOCCUPANTS (VP)

Dénomination de l'OMS (05-2021)	Lignée Pango	Clade Nextstrain	Clade GISAID	Nom alternatif	Détecté initialement dans	Premiers échantillons	Mutations caractéristiques du spicule
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VP 202012/01	Royaume-Uni	Sept. 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Bêta	B.1.351	20H/501Y.V2	GH/501Y.V2	VP 202012/02	Afrique du Sud	Août 2020	D80A, D215G, 241/243del, K417N,

							E484K, N501Y, D614G, A701V
Gamma	P.1, B.1.1.28.1	20J/501Y.V3	GR/501Y.V3	VP 202101/02	Brésil et Japon	Déc. 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G H655Y, T1027I, V1176F
Delta	B.1.617.2		G/452R.V3		Inde	Oct. 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R, del157/158, T478K, D950N)

Cette revue évolutive des éléments de preuve présente les éléments de preuve clés sur le variant Delta et fait partie d'un projet plus vaste qui résume les données sur chacun des VP et enregistre les données sur les VI, ce qui inclut les changements dans l'épidémiologie, dans l'évasion immunitaire et dans l'efficacité des vaccins, ainsi que les répercussions sur les tests diagnostiques et les mesures de santé publique. L'ensemble complet de données en Excel est accessible ici et peut être filtré par les variants préoccupants ou les variants d'intérêt. La récente revue des preuves vivantes sur les autres VP (Alpha, Beta, Gamma) peut être demandée ici.

Points clés

Au 30 juin 2021, quarante-sept études font état du variant préoccupant Delta (dont 30 ont été ajoutées depuis la dernière mise à jour du 7 juin 2021). Treize d'entre elles ne sont pas incluses dans cette revue, car l'une d'entre elles était un rapport de cas, deux étaient des études *in silico* et dix ne spécifiaient pas la lignée étudiée (c'est-à-dire qu'elles étaient rapportées B.1.617). En outre, quatre rapports de littérature grise pertinents du Royaume-Uni ont été inclus, car ils fournissent des données sur le variant Delta qui n'ont pas encore été rapportées dans la littérature. Les détails individuels de toutes les études pour la lignée B.1.617 (n=51) se trouvent dans l'ensemble de données Excel accessible ici.

- Les données de surveillance du Royaume-Uni et de l'Inde sur l'introduction et le taux de croissance du variant Delta entre février et juin 2021 indiquent que le variant Delta représente désormais 91 à 96 % des cas (4 à 9). Des études menées aux États-Unis et au Japon ont révélé que le variant Delta est en train de remplacer B.1.1.7 (Alpha) comme variant dominant (10, 11). La prévalence du variant Delta devrait dépasser Alpha au Japon vers le 12 juillet 2021, avant le début des Jeux olympiques de Tokyo (11). Les projections de modèles visant à examiner l'impact potentiel du variant Delta en Inde au cours des six prochains mois montrent qu'alors que le pays entre dans la saison de la mousson à partir de juin, les infections pourraient ressurgir si les mesures d'intervention sont levées prématurément (12).

- Public Health England a signalé qu'un petit nombre de séquences Delta ont été détectées qui ont acquis la mutation K417N de la protéine du spicule qui a été associée à l'échappement immunitaire dans le variant B.1.351 (Bêta) où elle a été identifiée pour la première fois) (13, 14). Au 22 juin 2021, 161 génomes de cette nouvelle sous-lignée Delta, désignée comme B.1.617.2.1, Delta+ ou AY.1, ont été classés sur GISAID en provenance du Canada (1), de l'Inde (8), du Japon (15), du Népal (3), de la Pologne (9), du Portugal (22), de la Russie (1), de la Suisse (18), de la Turquie (1), ainsi que des États-Unis (83) et de l'Angleterre (41). B.1.617.2.1 est inclus dans la classification du VP Delta par l'Organisation mondiale de la santé (15).
- En Ontario, au Canada, le profil de mutation N501Y-/E484K- (qui représente le variant Delta ou le variant original) est passé d'un déficit de transmission de 29 % par rapport à Alpha le 1er avril à un avantage de transmission de 50 % le 12 juin. Le séquençage du génome entier des cas N501Y-/E484K a confirmé que cette augmentation de la transmissibilité coïncidait avec le remplacement du variant original par le variant Delta (16).
- D'après deux études de surveillance menées au Royaume-Uni et en Inde, le variant Delta a augmenté la transmissibilité par rapport au variant Alpha de 43 à 115 % (7, 17). Une étude japonaise rapporte une transmissibilité 1,2 fois plus élevée pour le variant Delta par rapport au variant Alpha (11). Les données de recherche des contacts recueillies au Royaume-Uni ont permis d'estimer que le taux de transmission secondaire parmi les contacts non liés à un voyage était supérieur de 35 % à celui du variant Alpha (14).
- Trois études utilisant la valeur Ct (seuil de cycle) comme indicateur de la charge virale ont signalé que les charges virales de Delta pouvaient être plus élevées que celles du variant Alpha et du variant original (7, 18, 19). Un rapport de surveillance britannique suggère qu'il pourrait y avoir un risque plus élevé d'hospitalisation avec Delta par rapport au variant Alpha (13, 20). En outre, un rapport de surveillance de Singapour a montré que l'infection par Delta était associée à un risque plus élevé de besoin d'oxygène supplémentaire, d'admission en unité de soins intensifs ou de décès (RCa 4,90, IC à 95 % de 1,43 à 30,78) par rapport à l'infection par le variant original de type sauvage (18). Une surveillance et des recherches supplémentaires sont nécessaires pour confirmer ces résultats dans d'autres contextes.
- La 12e ronde de l'étude REACT-1 au Royaume-Uni a noté une croissance exponentielle du variant Delta en mai-juin 2021, ce dernier étant devenu dominant, et l'analyse montre que la plupart des infections se produisaient dans des groupes plus jeunes qui n'étaient pas non plus vaccinés (9).
- Les données sur l'évasion immunitaire montrent qu'il peut y avoir une réduction modérée de la neutralisation de Delta par rapport aux variants Alpha et original (19, 21 à 25) et les modèles prédictifs ont estimé que Delta est capable d'échapper à environ 20 à 55 % de la protection immunitaire fournie par une infection antérieure avec des lignées non Delta (12, 19). Une étude de cohorte prospective à long terme a fait état d'une légère augmentation des taux de réinfection en juin au Royaume-Uni, où la plupart des cas de SRAS-CoV-2 en circulation sont des cas Delta. Malgré cette légère hausse, les

réinfections restent à un niveau très bas (14). Une étude sur l'efficacité d'un vaccin dans le monde réel, réalisée au Royaume-Uni à l'aide d'un modèle de témoins ayant obtenu un résultat de test négatif pour étudier l'efficacité des vaccins BNT162b2 (Pfizer) et ChAdOx1 (AstraZeneca), a révélé que l'efficacité était nettement inférieure contre le variant Delta après une dose de l'un ou l'autre des vaccins par rapport au variant Alpha; toutefois, après deux doses de l'un ou l'autre des vaccins, il n'y avait pas de différence significative dans l'efficacité du vaccin avec les cas du variant Delta (20, 26).

Vue d'ensemble des éléments de preuves

La conception des études sur les VP est très variée, allant des études d'observation avec un risque élevé de biais aux essais contrôlés randomisés (ECR) à double insu avec un risque plus faible de biais. Aucun essai clinique n'a été identifié pour cette revue sur le variant Delta. Il y avait des études d'observation, y compris des analyses de données de surveillance et des études de cas-témoins qui sont considérées comme des niveaux de preuve faibles. La certitude des preuves fournies par ces études d'observation peut être améliorée pour un résultat donné lorsque plusieurs études concordent et sont de conception prospective. Cette revue ne comportait qu'une seule étude prospective. Les autres études identifiées étaient des expériences *in vitro* qui sont considérées comme ayant un niveau de preuve faible à très faible. En général, ces types d'études sont utilisés pour générer des hypothèses qui sont ensuite testées avec un plan d'étude plus rigoureux. Pour cette revue, les modèles d'étude ont été identifiés, mais aucune évaluation formelle du risque de biais n'a été réalisée pour chaque étude. Une indication sommaire du niveau de confiance des preuves a été donnée pour chaque catégorie d'étude. Le plus grand nombre de preuves concernait la transmissibilité, la propagation de Delta dans certaines zones géographiques, les résultats cliniques de la gravité et l'échappement immunitaire. Dans les données publiées actuellement, il y avait des lacunes dans les connaissances sur les paramètres épidémiologiques, notamment la période infectieuse et la période d'incubation, les impacts sur la précision des tests de diagnostic, les impacts sur la thérapeutique et les impacts sur d'autres mesures de santé publique.

Dans l'ensemble, le niveau de preuve concernant le variant Delta est faible et il existe des lacunes dans la base de données bibliographiques existante. Des études supplémentaires sont donc nécessaires pour améliorer la confiance dans les résultats sommaires et pour combler les lacunes dans les connaissances actuelles concernant le variant Delta.

TABLE DES MATIÈRES

DELTA

L'ensemble de données en Excel comprend des résumés de chacune des études et est accessible ici. Vous trouverez ci-dessous le profil détaillé des preuves élaboré pour Delta.

Les catégories de preuve indiquées dans le tableau ci-dessous comprennent les données suivantes :

La **transmissibilité** comprend les changements dans la transmissibilité, les taux d'attaque secondaire, l'intervalle sériel (intervalle de temps entre l'apparition des symptômes dans le cas primaire et secondaire) et les estimations de l'avantage sélectif.

La **gravité clinique** comprend la proportion d'infections qui sont symptomatiques, la proportion de maladies graves et de mortalité ainsi que les facteurs de risque de maladie grave ou de mortalité, la charge virale (la valeur Ct est souvent utilisée comme indicateur de la charge virale, une valeur Ct plus faible indiquant une charge virale plus élevée), la période infectieuse, la période d'incubation. Veuillez noter que les facteurs de risque d'une atteinte grave incluraient les populations spéciales, p. ex., les femmes enceintes (lorsqu'elles sont déclarées).

L'**échappement immunitaire** comprend les changements dans l'efficacité du vaccin, le risque de réinfection chez les humains, les modèles animaux, les expériences *in vitro* ou *in silico*, ainsi que les répercussions sur les thérapies lorsqu'elles sont déclarées.

L'**échec du test de diagnostic ou de la détection** est indiqué dans le tableau.

La mention **Autre épidémiologie** inclut toutes les études qui documentent l'émergence et la propagation des VP dans une région géographique, les études écologiques qui examinent la propagation des VP et les facteurs de risque pour les points chauds, ainsi que les études sur les interventions en santé publique efficaces contre les VP, avec l'épidémiologie génomique comme sous-catégories, lorsqu'elle est déclarée.

Tableau 2 : Profil fondé sur les éléments de preuve pour le VP Delta (n = 38)

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	VUE D'ENSEMBLE DES ÉLÉMENTS DE PREUVES
Efficacité de transmission		
Transmissibilité par rapport au variant B.1.1.7 (Alpha)	• En Ontario (Canada), le profil de mutation N501Y-/E484K- (qui représente Delta ou le variant original de type sauvage) est passé d'un déficit de transmission de 29 % par rapport à Alpha (Re relatif = 0,71, IC à 95 % de 0,64 à 0,77) le 1er avril à un avantage de transmission de 50 % le 12 juin (Re relatif = 1,50, IC à 95 % de 1,31 à 1,71). Le séquençage du génome entier des cas N501Y-/E484K a confirmé que cette augmentation de la transmissibilité coïncide	5 analyses de données de surveillance et un modèle prédictif, tous prépubliés. Faible niveau de preuve.

	avec le remplacement du type sauvage par le variant Delta (16). • Une étude britannique estime que Delta était de 43 à 115 % plus transmissible qu'Alpha sur des périodes hebdomadaires (du 3 avril au 22 mai) (17). • Des études menées en Inde estiment que la transmissibilité de Delta était 1,1 à 1,4 fois plus élevée que celle des lignées circulant précédemment à Mumbai en janvier 2021 (19), 50 % plus élevée que celle d'Alpha (7) et 60 % plus infectieuse que celle des variants originaux (12). • L'étude japonaise estime que Delta est 94,8 % et Alpha 43,7 % plus transmissible que les variants non préoccupants. Cela se traduit par une transmissibilité 1,4 fois plus élevée pour Delta par rapport à Alpha (11).	
Taux d'attaque secondaire par rapport au variant B.1.1.7 (Alpha)	• TAS 35 % supérieur : 10,7 % (IC à 95 % de 10,5 % à 10,9 %) pour B.1.617.2 (Delta) comparativement à 7,9 (de 7,7 % à 8,0 %) pour B.1.1.7 (Alpha) en ce qui concerne les cas sans lien avec les voyages (14). • TAS 39,5 % supérieur : 12,0 % (de 11,7 % à 12,2 %) des contacts à domicile sans lien avec les voyages pour Delta comparativement à 8,6 % (8,4 % à 8,8 %) (14). • L'augmentation de la transmission par contact à domicile pour Delta par rapport à Alpha était un RCa 1,64 (IC à 95 % de 1,26 à 2,13, p<0,001) (27)	1 rapport résumant l'analyse des données de la surveillance provenant de plusieurs études (du 29 mars au 7 juin). 1 étude nationale de cas-témoins. Faible niveau de preuve.
Intervalle de série par rapport au variant original	• Une étude de Singapour et un rapport d'Angleterre indiquent que l'intervalle de série n'a pas changé (données d'avril à mai) par rapport aux intervalles de série antérieurs au VP (13, 28). • Médiane de 3 jours (IQR de 2 à 4) (28) • La médiane de 4 jours pour les contacts à domicile et hors domicile (13) est la même que celle d'Alpha.	1 analyse des données de surveillance et 1 rapport résumant l'analyse des données de surveillance de plusieurs études. Faible niveau de preuve.

Études *in vitro* de l'infectiosité par rapport au variant original	• On pense que l'augmentation de la transmissibilité est au moins partiellement due à une mutation du gène P618R dans la protéine S qui améliore la capacité de la furine à dissocier le peptide (29).	2 études *in vitro*. Très faible niveau de preuve.
Gravité clinique		
Virulence, gravité ou durée de la maladie par rapport au B.1.1.7 (Alpha) ou au variant original	• L'analyse effectuée en Angleterre indique une augmentation significative du risque d'hospitalisation dans les 14 jours suivant la date de prélèvement du spécimen (TR 2,26, IC à 95 % de 1,32 à 3,89, p < 0,001), et de la demande de soins d'urgence ou d'hospitalisation dans les 14 jours (TR 1,45, IC à 95 % de 1,08 à 1,95, p < 0,001) pour les cas de personnes infectées par Delta comparativement à Alpha après ajustement pour les variables confondantes (âge, sexe, origine ethnique, région de résidence, indice de privation multiple, semaine du diagnostic et état de vaccination) (13). • Une étude effectuée en Écosse rapportant le délai d'admission à l'hôpital a révélé que les cas Delta étaient associés à un risque accru d'admission à l'hôpital en raison de la COVID-19 : taux de risque (TR) 1,85 (IC à 95 % de 1,39 à 2,47) par rapport au variant B.1.1.7 (Alpha), après ajustement pour l'âge, le sexe, la privation, la tendance temporelle et les comorbidités rapportées (20). • Singapour, l'infection par Delta a été associée à une probabilité plus élevée de gravité de la maladie qui incluait les cas nécessitant une oxygénation supplémentaire, une admission en unité de soins intensifs ou le décès (rapport de cotes ajusté (RCa) 4,90, IC à 95 % de 1,43 à 30,78) (18). Le RCa pour la pneumonie était 1,88 fois plus élevé (IC à 95 % de 0,95 à 3,76) pour les personnes infectées par Delta par rapport à l'infection par le variant original, bien que non significatif (18).	1 rapport résumant l'analyse des données de surveillance de plusieurs études et 2 analyses de données de surveillance. Faible niveau de preuve.

Facteurs de risque de la gravité par rapport au variant original	• L'analyse préliminaire de l'étude EAVE II en Écosse a suggéré que les cas Delta étaient plus jeunes et appartenaient à des groupes sociodémographiques plus élevés que les autres cas, mais il n'est pas clair si ces observations sont basées sur des analyses contrôlant les facteurs confondant, notamment la vaccination. Des recherches supplémentaires sont nécessaires pour tirer la moindre conclusion (20).	1 analyse des données de surveillance. Très faible niveau de preuve.
Mortalité par rapport au variant original	• Aucune étude	
Facteurs de risque de mortalité par rapport au variant original	• Aucune étude	
Charge virale par rapport au B.1.1.7 (Alpha) ou au variant original	• La charge virale peut être plus élevée chez Delta que chez Alpha. Par rapport à la base de référence créée entre décembre 2020 et février 2021 en Inde, les valeurs Ct ont chuté en mars lorsque Alpha est devenu dominant avant de diminuer encore davantage en avril lorsque B.1.617 a pris la relève (il s'agissait principalement de la souche Delta) (7). La variation des valeurs Ct (-6) correspond à une augmentation de 50 fois la charge virale (7). • Parmi les travailleurs de la santé vaccinés dans trois hôpitaux de Delhi et testés positifs pour le SRAS-CoV-2, la valeur médiane de Ct des infections par le variant Delta était de 16,5 contre 19 pour les variants non Delta ($p<0,05$), ce qui indique une charge virale plus élevée (19). • À Singapour, le variant Delta a été associé à des valeurs Ct significativement plus faibles et à une durée plus longue de maintien de faibles valeurs Ct (≤30) (durée médiane de 18 jours) par rapport aux lignées de variants non préoccupants du SRAS-CoV-2 (13 jours) (18).	2 analyses de données de surveillance et 1 étude d'enquête sur les éclosions utilisant les valeurs Ct comme indicateur de la charge virale. Faible niveau de preuve.
Période infectieuse	• Aucune étude	
Période d'incubation	• Aucune étude	

Échappement immunitaire – incidence potentielle sur l'efficacité du vaccin, possibilité de réinfection		
Réinfection après infection par rapport au variant original	• La cohorte SIREN a signalé une légère augmentation des réinfections au cours du mois de juin après des chiffres très bas de mars à mai, mais le nombre de cas de réinfection reste faible (14). • Deux modèles prédictifs estiment que Delta est capable d'échapper à environ 20 à 55 % de la protection immunitaire fournie par une infection antérieure avec des lignées non Delta (12, 19).	1 étude de cohorte prospective et 2 modèles prédictifs. Faible niveau de preuve.
Infection percée après la vaccination / efficacité ou efficience du vaccin par rapport au B.1.1.7 (Alpha), B.1.617.1 (Kappa) ou au variant original	Infections parmi les vaccinés : • Dans une étude menée en Inde entre novembre 2020 et mai 2021, 19 sur 27 cas infectés après vaccination étaient des Delta. Ce chiffre est plus élevé que ce à quoi on pourrait s'attendre compte tenu des variants en circulation et correspond à un risque d'infection après vaccination plus élevé pour Delta que pour Alpha (7). L'analyse des infections après vaccination chez plus de 100 travailleurs de la santé dans trois centres en Inde a conclu qu'il y avait un risque plus élevé d'infection chez les travailleurs de la santé ayant reçu en grande partie le vaccin ChadOx-1 (Covishield) par rapport à Alpha ou B.1.617.1 (Kappa) (p=0,02) (19). • Au Royaume-Uni, les cas séquentiels détectés après une ou deux doses de vaccin présentaient un risque plus élevé d'infection au variant B.1.617.2 (Delta) que les cas non vaccinés (RC 1,40; IC à 95 % de 1,13 à 1,75) (26). • En Écosse, la vaccination (> 28 jours après la première dose) a été associée à une diminution du risque d'hospitalisation pour les cas Delta TR= 0,38 (IC à 95 % de 0,24 à 0,58), légèrement diminuée par rapport à Alpha (20), et le taux de risque chez les patients Delta vaccinés était TR 0,37 (IC à 95 % de 0,22 à 0,63) après une dose et TR 0,29 (IC à 95 % de 0,11 à 0,72) après deux	4 analyses de données de surveillance, 1 étude d'investigation d'épidémie et 2 études de contrôle de cas négatifs. Faible niveau de preuve.

	doses de n'importe quel vaccin par rapport aux non-vaccinés (30). • Aux États-Unis, une infection Delta (après la vaccination avec JNJ-78436735 (J&J)) a été signalée parmi 2 551 tests d'amplification de l'acide nucléique effectués sur des personnes entièrement vaccinées sur un campus universitaire (31). Efficacité après une dose de vaccin : • Royaume-Uni : Après une dose, on a constaté une réduction absolue de 14 % de l'efficacité du vaccin (EV) contre la maladie symptomatique due au Delta par rapport à Alpha (14). • Royaume-Uni : L'EV de BNT162b2 (Pfizer) ou de ChAdOx1 (AstraZeneca) contre la maladie symptomatique était d'environ 33,5 % (IC à 95 % de 20,6 à 44,3), une réduction de 15 à 20 % par rapport au variant B.1.1.7 (Alpha). • Royaume-Uni : L'EV de ChAdOx1 (AstraZeneca) contre l'hospitalisation était de 92 % (IC à 95 % de 75 à 97) après 1 dose (30). • Royaume-Uni : L'EV de BNT162b2 (Pfizer) contre l'hospitalisation était de 94 % (IC à 95 % de 46 à 99) après 1 dose (30). Efficacité du vaccin après deux doses : • Royaume-Uni : L'EV de ChAdOx1 (AstraZeneca) contre la maladie symptomatique était de 59,8 % (IC à 95 % de 28,9 à 77,3) (26). L'efficacité contre l'hospitalisation était de 92 % (IC à 95 % de 75 à 97) (30); Écosse : L'EV de prévention de l'infection confirmée >14 jours après la vaccination était de 60 % (IC à 95 % de 53 à 66) (20). • Royaume-Uni : L'EV de BNT162b2 (Pfizer) contre la maladie symptomatique était de 87,9 % (IC à 95 % de 78,2 à 93,2) (26). L'efficacité contre l'hospitalisation était de 96 % (IC à 95 % de 86 à 99) (30); Écosse :	

	L'EV de prévention de l'infection confirmée >14 jours après la vaccination était de 79 % (IC à 95 % de 75 à 82) (20). • Les résultats d'EV après 2 doses étaient similaires à ceux d'Alpha (26) avec une réduction de 10 % pour la maladie symptomatique causée par Delta par rapport à Alpha dans un autre rapport (14).	
Études *in vitro* du sérum de phase convalescente par rapport au B.1.1.7 (Alpha) ou au variant original	• Les sérums de phase convalescente prélevés chez des cas présentaient une neutralisation réduite de 1,2 à 6 fois pour Delta par rapport à Alpha ou au variant original selon les études (19, 21 à 25).	6 études *in vitro*. Très faible niveau de preuve.
Études *in vitro* du sérum des personnes vaccinées par rapport au B.1.1.7 (Alpha) ou au variant original	• Après la vaccination, la neutralisation des sérums était 5 à 8 fois plus faible pour Delta que pour le variant original; la perte de neutralisation contre Delta était 4 à 6 fois plus élevée pour ChAdOx-1 (Astrazeneca) et 3 à 11 fois plus élevée pour BNT162b2 (Pfizer) (19, 32). Une autre étude a montré qu'après deux doses de ChAdOx-1 (Astrazeneca), la neutralisation contre Delta était réduite de 2,5 fois (IC à 95 % de 1,4 à 2,7) par rapport à BNT162b2 (Pfizer) (33). Deux autres études n'ont révélé qu'une faible réduction de la neutralisation pour les sérums provenant de personnes vaccinées, 2 à 4 semaines après la seconde dose du vaccin BNT162b2 (Pfizer) (24, 34). La neutralisation était 2,7 fois plus faible que celle des variants originaux contre les sérums de personnes vaccinées au BBV152 (Covaxin) (22). • La neutralisation des sérums (8 semaines après la vaccination par BNT162b2 (Pfizer)) était 3 fois plus faible pour Delta que pour Alpha (21). La plupart des sérums provenant de personnes vaccinées avec BNT162b2 (Pfizer) ont neutralisé Delta (94 %); en revanche, seuls 8 % des sérums provenant de personnes vaccinées avec ChAdOx-1	7 études *in vitro*. Très faible niveau de preuve.

	(Astrazeneca) ont été capables de neutraliser Delta (21).	
Études *in vitro* sur les thérapies par rapport au variant original	• Le bamlanivimab a perdu son activité antivirale contre Delta, ce qui démontre que L452R est une mutation d'échappement pour cet anticorps monoclonal (mAb) (21, 24, 35). • L'etesivimab, le casirivimab et l'imdevimab sont demeurés actifs contre le variant Delta (21). • Une combinaison de meplazumab et de l'anticorps C anti-CD147 a inhibé efficacement le pseudovirus Delta *in vitro* (36).	4 études *in vitro*. Très faible niveau de preuve.
Échec du test de diagnostic/détection		
Test et détection par rapport au variant original	• Il n'y a pas eu d'indication de problèmes de test (c'est-à-dire de changements de sensibilité/spécificité) avec Delta. Cependant, une étude a identifié 16 mutations de sites d'amorces dans des spécimens de la lignée B.1.617 qui ont un impact sur les sites d'amorces qui perturbent le séquençage du génome entier par deux protocoles de laboratoire largement utilisés (3 affectent le protocole de Freed et col. et 13 affectent le protocole ARTIC, version 3) (37). • L'amorce cible P681R a été introduite dans le test PCR de génotypage de Public Health England pour détecter le variant B.1.617 qui est principalement le variant Delta (13). • Un document propose des amorces PCR conçues pour identifier les VP, incluant Delta (38).	2 études sur la précision des tests de diagnostic et 1 rapport. Faible niveau de preuve.
Autre épidémiologie		
Mesures/interventions de santé publique	• Les projections de modèles visant à examiner l'impact potentiel du variant Delta en Inde au cours des six prochains mois montrent qu'alors que le pays entre dans la saison de la mousson à partir de juin, les infections pourraient ressurgir si les mesures	1 modèle prédictif. Faible niveau de preuve.

	d'intervention sont levées prématurément (12). Les projections indiquent qu'une accélération du déploiement de la vaccination de masse (jusqu'à 4 fois le rythme actuel) pourrait réduire le pic de charge, mais n'empêcherait probablement pas la résurgence. La combinaison d'un délai de 4 semaines avec un déploiement de la vaccination beaucoup plus rapide (par exemple, 4 fois le rythme actuel) et une couverture vaccinale très élevée pourrait permettre de maintenir les taux d'infection à des niveaux similaires à ceux observés fin mai 2021. Toutefois, sans une diffusion plus rapide de la vaccination, un report de la réouverture de 8 semaines pourrait être nécessaire pour empêcher la résurgence des taux d'infection.	
Émergence des VP au fil du temps	• Selon le GISAID (consulté le 10/06/2021), un total de 31 997 séquences (Europe = 24 606, Asie = 4 974, Amérique du Nord = 2 210, Océanie = 163, Afrique = 36, Amérique du Sud = 8) ont été assignées à la lignée B.1.617.2 (Delta) (32). • Le séquençage du génome à l'échelle de l'Ontario des échantillons N501Y-/E484K– (qui représente le variant Delta ou le variant original de type sauvage) a démontré le remplacement du type sauvage par le variant Delta (la proportion est passée de 2,2 % début avril à 83 % fin mai) (16). • Un rapport britannique indique qu'au 14 juin 2021, la proportion de cas Delta était de 98,2 % de tous les cas séquencés et génotypés au Royaume-Uni (14). • De nouvelles données datant de la fin du mois de juin indiquent que les temps de doublement Delta ont atteint un plateau ou ont commencé à diminuer dans toute l'Angleterre (14). Delta a été introduit à plusieurs reprises et a augmenté rapidement via la transmission	14 études de surveillance et deux rapports. Faible niveau de preuve.

	communautaire d'avril à la mi-mai 2021. Le taux de croissance a été estimé à environ 37 % (IC à 95 % de 26 à 49) au-dessus d'Alpha et le temps de doublement estimé à 5 à 14 jours, mais pouvant atteindre 21 jours dans certaines communautés (5, 9, 39, 40). L'indice de reproduction de mai/juin 2021 était de 1,44 en Angleterre (9). • L'étude REACT-1 menée en Angleterre a permis de détecter le variant Delta pour la première fois (2 sur 115) dans la ronde 11 de l'étude (15 avril au 3 mai) (6). Depuis lors, on a assisté à un remplacement rapide du variant Alpha par le variant Delta (9). Au cours de la ronde 12 (entre le 20 mai et le 7 juin), la proportion d'échantillons positifs qui étaient Delta est passée d'environ 60 % à environ 90 %. • En Inde, les lignées du B.1.617 sont passées de 5 % en février 2021 à 10 % en mars et à 60 % en avril. Delta est passé de moins de 10 % à 80 % des cas de B.1.617 (7, 12, 19, 41) et l'analyse phylogénétique a montré la propagation du B.1.617 et l'émergence de sous-lignées (8). • Une étude effectuée au Texas (É. -U.) entre janvier et avril 2021 a montré que 7 sur 2 543 échantillons étaient associés au variant B.1.617 (sous-lignée non confirmée) (42). • Aux États-Unis, P.1 (Gamma) et Delta étaient les principaux variants remplaçant Alpha. Ils ont représenté au moins 16 % et 14 % des cas pour la semaine du 9 au 15 juin, respectivement. Le taux de croissance de Delta était plus rapide que celui de Gamma (k = 0,61 contre 0,22), en particulier dans les comtés où les taux de vaccination sont plus faibles (10). • Au Japon, la fréquence de Delta devrait prendre le relais d'Alpha vers le 12 juillet 2021 (IC à 95 % du 8 au 16 juillet 2021) et	

	avant le début officiel des Jeux olympiques de Tokyo le 23 juillet 2021(11). • Public Health England a signalé qu'un petit nombre de séquences Delta ont été détectées qui ont acquis la mutation K417N de la protéine du spicule (13, 14). Au 22 juin 2021, 161 génomes de ce variant, désigné comme B.1.617.2.1, Delta-AY.1 ou Delta+, ont été identifiés dans GISAID : Canada (1), Inde (8), Japon (15), Népal (3), Pologne (9), Portugal (22), Russie (1), Suisse (18), Turquie (1), États-Unis (83) et Angleterre (41).	

TL = taux de létalité, IC = intervalle de confiance, Ct = seuil du cycle, USI = unité des soins intensifs, RC = rapport de cotes, PCR = réaction en chaîne de la polymérase, EV = efficacité du vaccin, RCa = rapport de cotes ajusté, GISAID = Global Initiative on Sharing Avian Influenza Data (Initiative mondiale sur le partage des données sur l'influenza aviaire)

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le groupe des sciences émergentes de l'ASPC. L'analyse a permis de compiler la littérature sur la COVID-19 depuis le début de l'épidémie et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données Refworks et une liste Excel consultable. L'un des objectifs vise à déterminer si les études portent sur des variants préoccupants ou des variants d'intérêt. Les études correspondantes ont été présentées plus en détail dans notre base de données sur les VP et VI alors que les résultats associés aux VP ont été inclus dans le présent résumé. Une contre-vérification afin de trouver des articles pertinents a également été effectuée dans les bases de données en utilisant pour ce faire des recherches ciblées par mot clé (B.1.617 OU Delta).
Cette revue contient des recherches publiées jusqu'au 30 juin 2021.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

Revue

Le Bureau de la Conseillère scientifique en chef a facilité la revue de ce document, qui comprenait des suggestions d'un rédacteur scientifique, un examen par les pairs d'un expert en la matière et la contribution d'un conseiller principal en politiques ayant une perspective de la science à la politique.

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APPENDICE

a) LEXIQUE SUR LES VP/VI

Étiquette de l'OMS (2021-05-27)	**Lignée de Pango**	**Clade/lignée des GISAID**	**Clade de Nexstrain**	**Plus anciens échantillons documentés**	**Date de la désignation**
Alpha	B.1.1.7	GRY (anciennement GR/501Y.V1)	20I/501Y.V1	Royaume-Uni, Sept 2020	18 déc. 2020
Bêta	B.1.351	GH/501Y.V2	20H/501Y.V2	Afrique du Sud, Mai 2020	18 déc. 2020
Gamma	P.1	GR/501Y.V3	20J/S:501Y.V3	Brésil, Nov 2020	11 janv. 2021
Delta	B.1.617.2	G/452R.V3	21A/S:478K	Inde, Oct. 2020	VI : 4 avril 2021 VP : 11 mai 2021
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	États-Unis d'Amérique, Mars 2020	5 mars 2021
Zêta	P.2	GR	20B/S.484K	Brésil, Avril 2020	17 mars 2021
Êta	B.1.525	G/484K.V3	20A/S484K	Plusieurs pays, Déc. 2020	17 mars 2021
Thêta	P.3	GR	20B/S:265C	Philippines, Janv. 2021	24 mars 2021
Iota	B.1.526	GH	20C/S:484K	États-Unis d'Amérique, Nov. 2020	24 mars 2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	Inde, Oct. 2020	4 avr. 2021
Lambda	C.37	GR/452Q.V1	20D	Pérou, Août-2020	14 juin 2021

b) AUTRES RESSOURCES

Référence	Description
Revue des preuves évolutives sur les variants du SRAS-CoV-2 Australie	Ce tableau présente des éléments de preuve pertinents récents en ce qui concerne les différentes catégories d'études semblables à ce qui a été présenté dans le profil présenté dans le cadre de la présente revue.

En cours, dernière consultation le 10 mars.	
Page des VP du CDC	Un résumé de chaque VP est disponible.
Les rapports de situation de l'OMS contiennent une section sur les VP.	
Littérature grise	
SAGE communications	La page sur les vaccins et les variants contient des rapports et des résumés sur les VP.
ALL Public Health England. Research and analysis reports on Investigation of SRAS-CoV-2 variants of concern technical briefings. De déc. 2020 à aujourd'hui	Les rapports techniques compilent les différentes informations provenant de diverses études et de la surveillance de l'ensemble du Royaume-Uni en ce qui concerne les VP et les VI en circulation. Ces rapports et publications de recherche se recoupent largement.

Emerging Evidence on COVID-19

Living Summary of SARS-CoV-2 Variants of Concern: The Delta variant (B.1.617.2) profile

Highlights up to July 29, 2021

Introduction

SARS-CoV-2 **variants of concern** (VOCs) are circulating variants that have been flagged by national or global public health organizations. VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or diagnostic detection failures (1-3). In May 2021 WHO released a naming system for VOCs and variants of interest (VOIs) using Greek letters to improve the ease of communication on variants and reduce potential stigma related to places where variants were first identified, which has been adopted in this report (4).

TABLE 1: CURRENT VARIANTS OF CONCERN (VOCs)*

WHO name (05-21)	Pango lineage	Nextstrain clade	GISAID clade	Alternate name	First detected in	Earliest samples	Characteristic spike mutations
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	United Kingdom	Sep 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Beta	B.1.351 B.1.351.2 B.1.351.3	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	South Africa	May 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, P.1.1 P.1.2	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brazil and Japan	Nov 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G H655Y, T1027I, V1176F
Delta	B.1.617.2 AY.1 AY.2 AY.3	21A	G/478K.V1		India	Oct 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R,

							del157/158, T478K, D950N)

* A VOC/VOI lexicon and other resources are available in the appendix.

The goal of this living summary on the SARS-CoV-2 VOC literature is to highlight new data on the VOC B.1.617.2 (Delta), its epidemiology and how the attributes of this variant may impact the management of the pandemic. This living evidence profile on Delta is part of a larger project that summarizes the data on each VOC as well as captures data on VOIs. The focus will be on changes to epidemiological parameters (e.g., transmission rates, clinical outcomes of severity and mortality, shifts in age groups affected or asymptomatic proportions), impacts on diagnostic tests, immune evasion/vaccine effectiveness and impacts on other public health measures. The full dataset in Excel can be accessed here and filtered by the VOCs and VOIs of interest. The recent living evidence review on other VOCs (Alpha, Beta, Gamma) can be requested here.

In this summary, "original variant" refers to any variant that was not designated as a VOC or VOI.

What's New in July 2021

- A UK report indicates that Delta accounted for approximately 99% of sequenced and 96% genotyped cases from 27 June to 10 July 2021 (5, 6).
- A study including data on VOCs in Canada reported that Delta accounted for 0.82% of the cumulative VOC cases sequenced in Canada up to June 15th, 2021 with the highest prevalence in Alberta and British Columbia (7). The overall proportion of Delta cases for the week of June 13th was 37% and Delta was at the point of overtaking Alpha (41%) (8). Since late June, Delta has been the dominant VOC in Canada (8).
- A global surveillance study showed increased transmissibility of Delta compared to the original variant, Alpha, Beta, and Gamma was 97% (95%CI: 76-117), 55% (43-68), 60% (48-73), and 34% (26-43), respectively (9).
- Three new modelling studies investigated the level of public health interventions, including vaccination, restrictive measures and masking, that are needed to prevent or reduce resurgence in the context of Delta variant in France, Germany, and Australia (10-12) and a fourth model cautions lifting restrictive public health measures and masking for fully vaccinated people in Europe (13).
- A study from China reported a shorter time interval between exposure and first PCR positive test in quarantined cases involved in an outbreak of Delta across the province of Guangdong (n=34) compared to cases caused by 19A/19B genetic strains during the early 2020 epidemic (n=29): 4 days (IQR 3-5) vs. 6 days (IQR 5-8) (14). This finding is based on a small sample size and lacks statistical significance; additional research is needed to confirm this finding.
- A retrospective cohort study from Canada reported higher risk of hospitalization 120% (95%CI 93-153%), ICU admission 287% (198-399%), and death 137% (50-230%) associated with Delta compared to non-VOCs (15).

- In Canada, protection against symptomatic Delta infection after two doses of BNT162b2 (Pfizer) (87%; 95% CI, 64–95%) was comparable to that of Alpha and a combined Beta and Gamma VE (analysed together due to low sample size) (16). After one dose, vaccine effectiveness (VE) against symptomatic infection with Delta tended to be lower compared to Alpha for BNT162b2 (Pfizer) (56% vs. 66%) and mRNA-1273 (Moderna) (72% vs. 83%) but similar for ChAdOx1 (AstraZeneca) (67% vs. 64%) (16). In India, ChAdOx1 (AstraZeneca) demonstrated 63.1% (95%CI 51.5-72.1) vaccine effectiveness against infection with the Delta variant, with 81.5% (95%CI: 9.9, 99.0) protection against moderate/severe infection (17).

Key Points

As of July 29, 2021 there were 87 studies and 7 grey literature reports (6 from UK and 1 from Canada) that report on the Delta variant of concern (45 of which have been added/updated since the last update of this summary on June 30, 2021) and were considered for inclusion. The included grey literature reports provide data on Delta not yet reported in the primary literature. In total, 67 studies/reports were summarized in this profile, including studies describing transmission efficiency (n=19), clinical severity (n=8), immune escape (n=32), testing and diagnostics (n=5), and spread epidemiology (n=24). Twenty-seven are not included in this summary as two were case reports/case series, three were an animal model, three were *in silico* studies, seven were deemed irrelevant (e.g., presented outdated models), and twelve did not specify the lineage studied (i.e., reported B.1.617). Individual study details of all studies for B.1.617 lineage (n=99) can be found in the Excel dataset accessed here.

Delta Spread

- Surveillance data from the UK and India on the introduction and growth rate of Delta from February to July 2021 indicate Delta now represents 91-99% of cases (5, 6, 18-24). Studies from the USA and Japan found that the Delta variant is replacing B.1.1.7 (Alpha) as the dominant variant (25, 26). As of June 15th, 2021, Delta accounted for 0.82% of the cumulative VOC cases sequenced in Canada (7). The overall proportion of Delta cases for the week of June 13th was 37% and Delta was at the point of overtaking Alpha (41%) (8). Since late June, Delta has been the dominant variant in Canada.
- Included within the Delta VOC classification by the World Health Organization are sub-lineages AY.1, AY.2 and AY.3 that have acquired additional mutations (3, 27). Many countries have reported a relatively small number of Delta sequences with the additional mutations of these sub-lineages (5, 6, 28, 29).

Transmissibility

- In Ontario, Canada, the N501Y-/E484K- mutation profile (which represents Delta or the original variant) went from having a 29% transmission deficit relative to Alpha on April 1st to having a 50% transmission advantage on June 12th. Whole genome sequencing of N501Y-/E484K-cases confirmed that this increase in transmissibility coincided with the replacement of the original variant with the Delta variant (30).

- Three studies from the UK, India, and Japan, as well as a global surveillance analysis, have shown that Delta has increased transmissibility over Alpha by 43-120% (9, 21, 26, 31).
- Four studies using Ct (cycle threshold) value as a proxy for viral load reported that Delta viral loads may be higher than Alpha and original variant (14, 21, 32, 33) while one found no significant difference between Delta and non-Delta infections among vaccinated healthcare workers (most of whom were fully vaccinated) (34).
- Public Health England estimated incubation period at median 4 days (28) and a study from China reported a shorter time interval between exposure and first PCR positive test in quarantined cases involved in an outbreak of Delta across the province of Guangdong compared to cases caused by the original variant during the early 2020 epidemic (4 days, IQR 3-5 vs. 6 days, IQR 5-8) (14).

Public Health Measures

- Four predictive models explored the impact of public health measures in India, France, Germany, and Australia to control the epidemic in the context of Delta. Higher risk of resurgence was shown when interventions such as masking and restrictive policies that limit contact rates were lifted prematurely or when vaccine rollout slowed down or did not speed up depending on the country (10-12, 35). The fifth model caution against allowing fully vaccinated people to stop adhering to public health measures in Europe (13).

Clinical Outcomes

- Four studies, including one from Canada, report a higher risk of severe outcomes such as hospitalization, ICU admission, and death associated with Delta compared to non-VOCs or Alpha (15, 28, 32, 36). Additional surveillance and research are needed to confirm these findings.

Immune Escape

- Immune escape from vaccination or previous *in vitro* neutralization data shows there may be a small to moderate reduction (1.2 – 6 fold) in neutralization of Delta compared to Alpha, Beta, Gamma and the original variants (17, 34, 37-42). Predictive models have estimated that Delta is able to evade approximately 16 to 55% of the immune protection provided by prior infection with non-Delta lineages (34, 35). An ongoing prospective cohort initiated June 2020 reported that reinfection rates in the UK are increasing and a national surveillance analysis found an increased risk of reinfection with Delta compared to Alpha (adjusted odds ratio 1.46, 95%CI 1.03-2.05) (6).
- Four studies on vaccine effectiveness report a reduction in protection against Delta infection (n=2) and symptomatic disease (n=2) compared to Alpha after the first dose, but comparable protection after the second (16, 17, 36, 43).

Overview of the Evidence

Study designs on VOC research range widely from observational studies with a high risk of bias to double blind randomized controlled trials (RCTs) with a lower risk of bias. One clinical trial was identified for this review on the Delta variant. There were observational studies, including analyses of surveillance data and case control studies that are considered low levels of evidence. Certainty in the evidence from these observational studies may be upgraded for a given outcome when multiple studies are in agreement and have prospective designs. There was only one prospective study in this review. Other studies identified were *in vitro* experiments that are considered a low to very low level of evidence. Generally these types of studies are used to generate hypotheses that are then tested with a more rigorous study design. For this review, study designs were identified, but no formal risk of bias assessment was conducted for each study. A summary indication of the level of confidence of the evidence was given for each category of study. The greatest amount of evidence was on transmissibility, the spread of Delta in some geographic areas, clinical outcomes of severity, and immune escape. In the current published evidence, there were gaps in knowledge on epidemiological parameters including infectious period, incubation period, impacts on the accuracy of diagnostic tests, and impacts on therapeutics.

Overall, the level of evidence on the Delta variant is low and there are knowledge gaps in the existing and evolving literature base. Thus additional studies are needed to improve confidence in the summary results, and to fill in current knowledge gaps regarding the Delta variant.

CONTENTS

DELTA

The excel dataset includes summaries of individual studies and can be accessed here. Below is the detailed evidence profile developed for Delta.

Categories of evidence in the table below include the following:

Transmissibility includes changes in transmissibility, secondary attack rates, serial interval (time interval between the onset of symptoms in the primary and secondary case), and estimates of selective advantage.

Clinical Severity includes proportion of infections that are symptomatic, proportion of severe disease and mortality as well as risk factors for severe disease or mortality, viral load (Ct value is often used as a proxy for viral load with lower Ct value indicative of higher viral load), infectious period, incubation period. Note risk factors for severe disease would include special populations, e.g., persons who are pregnant (when reported).

Immune Escape includes changes to vaccine efficacy/effectiveness, risk of re-infection in humans, animal models, *in vitro* or *in silico* experiments as well as impacts on therapeutics when reported.

Diagnostic / Detection Test Failure is captured in the table.

Other Epidemiology includes all studies that document the emergence and spread of VOCs in a geographic area, ecological studies that examine VOC spread and risk factors for hot spots, and studies on effective public health measures/interventions against VOCs, with genomic epidemiology as subcategories when reported.

Table 2: Evidence Profile of Delta VOC (n=67)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency		
Transmissibility Compared to original variant and other VOCs	• A global surveillance study showed a 97% (95%CI: 76-117), 55% (43-68), 60% (48-73), and 34% (26-43) increase in the pooled mean effective reproduction number (transmissibility) for Delta compared to the original variant, Alpha, Beta, and Gamma, respectively (9). • In Ontario, Canada, the N501Y-/E484K- mutation profile (which represents Delta or the original wild-type variant) went from having a 29% transmission deficit relative to Alpha (relative Re = 0.71, 95%CI 0.64-0.77) on April 1st to having a 50% transmission advantage on June 12th (relative Re = 1.50, 95% CI: 1.31, 1.71). Whole genome sequencing of N501Y-/E484K-cases confirmed that this increase in transmissibility coincided with the replacement of wild-type with the Delta variant (30). • UK study estimates Delta was 43-115% more transmissible than Alpha across weekly time periods (April 3- May 22) (31). • Studies from India estimate that the transmissibility of Delta was 1.1-1.4 fold more transmissible than previously circulating lineages in Mumbai during Jan 2021 (34), 50% more transmissible than Alpha (21), and 60% more infectious than original variants (35). Another study also found significantly higher transmissibility for Delta compared to original variants and Kappa (Rt: 1.1 vs. ~1.0, p<0.001) (44). • Japan study estimates that Delta is 94.8% and Alpha is 43.7% more transmissible than the non-VOC variants.	7 surveillance data analysis and 2 predictive models, all preprints. Low level of evidence.

	This translates to a 1.4 times higher transmissibility for Delta compared to Alpha (26). • Based on a logistic growth model of three regions in France from May 31-Jun 21, 2021, Delta had a median transmission advantage over Alpha greater than 70% (10).	
Secondary Attack Rate Compared to B.1.1.7 (Alpha)	• 5.8% (95%CI 5.6% - 5.9%) for Delta vs. 5.6 (5.5% - 5.8%) for Alpha for non-travel related cases (6). • 11.0% (10.9%-11.1%) of non-travel related household contacts for Delta vs. 10.2% (10.1%-10.3%) (6). • Increased household transmission for Delta vs. Alpha was adjusted odds ratio (aOR 1.64 (95%CI 1.26-2.13, p<0.001) (45)	1 report summarizing surveillance data analysis from several studies (Mar 29- Jul 21). 1 national case-control study. Low level of evidence.
Serial Interval Compared to Original Variant	• A study from Singapore indicates the serial interval has not changed (Apr-May data) compared to pre-VOC serial intervals: Median 3 days (IQR 2-4) (46). •	1 surveillance data analysis. Low level of evidence.
***In vitro* studies of infectivity** Compared to Original Variant	• Increased transmissibility is thought to be at least partially due to a P618R mutation in the S protein that enhances the ability of furin to cleave the peptide (39, 47).	2 *in vitro* studies. Very low level of evidence.
Public health measures / interventions	• Model projections to examine the potential impact of Delta in India over the next 6 months demonstrate that as the country enters its monsoon season starting in June, infections could resurge if intervention measures are lifted prematurely (35). Projections indicate that accelerating the rollout of mass-vaccination (up to 4 times the current rate) could reduce the peak burden but likely would not prevent resurgence. Combining a delay of 4 weeks with a much faster vaccination rollout (e.g., 4x the current rate) and very high vaccination coverage could help to keep infection rates at levels similar to those observed during late May 2021. However, without a faster vaccination rollout, a delay of reopening by 8 weeks may be needed to keep infection rates from resurging. • Model projections from France find that the Delta variant has the potential to initiate an epidemic rebound by the	5 predictive models. Low level of evidence.

	end of the summer that can be amplified by a slowdown in vaccine rollout (60% fully vaccinated) and an increase in infectious contact rate in September (e.g. back to school) (10). • In Germany, models show that timely implementation of non-pharmaceutical interventions in combination with masks and testing would considerably reduce the chance of a further surge in infections (12). • In Australia, a high level of compliance with physical distancing (80%) is required to reduce new cases below 10 per day approximately a month after a peak in incidence peak (11). • A SIR (susceptible, infected, and recovered) model investigating Vaccine Passports (VP) in Europe found that while VP holders could initially allow more freedom, the incomplete protection afforded by vaccines against the highly transmissible Delta variant will likely lead to a resurgence in cases (13). The resurgence can be avoided in the short/long-term only when the restrictions are kept high for the rest of the population, and the reduction in restrictions for the VP holders is moderate or small.	
Clinical Severity		
Virulence / Severity or Duration of Disease Compared to B.1.1.7 (Alpha) or Original Variant	• Canada, analysis of over 200,000 COVID-19 cases showed the risk of hospitalization and ICU admission associated with Delta compared to non-VOCs increased by 120% (95%CI 93-153%) and 287% (198-399%), and compared to N501Y-positive VOCs (i.e., Alpha, Beta, and Gamma) increased by 55% (45-63%) and 101% (79-124%), respectively (15). • England, analysis indicates significantly increased risk of hospitalisation within 14 days of specimen date (HR 2.26, 95%CI 1.32-3.89, p<0.001), and emergency care attendance or hospitalisation within 14 days (HR 1.45, 95%CI 1.08-1.95, p<0.001), for Delta cases compared to Alpha cases after adjustment for confounders (age, sex, ethnicity, area of residence, index of multiple deprivation, week of diagnosis and vaccination status) (28). • Scotland, Delta cases were associated with an increased risk of COVID-19 hospital admission: hazard ratio (HR) 1.85 (95%CI 1.39–2.47) when compared to Alpha, after adjusting for age, sex, deprivation, temporal trend, and comorbidities reported (36).	4 surveillance data analyses, 1 retrospective cohort study. Low level of evidence.

	• Singapore, infection with Delta was associated with higher odds of disease severity that included cases who required supplemental oxygen, intensive care unit admission, or death (aOR 4.90, 95%CI 1.43-30.78) (32). The aOR for pneumonia was 1.88 times higher (95%CI 0.95-3.76) for those infected with Delta compared to infection from original variant although not significant (32). • A surveillance study conducted in Houston, Texas, reported no significant difference in admission rate, disease severity or hospital length of stay for Delta cases compared to all other COVID-19 patients diagnosed in the city health system (33).	
Severity Risk Factors Compared to Original Variant	• Preliminary analysis from the EAVE II study in Scotland suggested that Delta cases were younger and from higher sociodemographic groups than other cases, however it is unclear if these observations are based on analyses controlling for confounding factors including vaccination. Further research is needed to draw any conclusions (36).	1 surveillance data analysis. Very low level of evidence.
Mortality Compared to Original Variant	• Canada, analysis of over 200,000 COVID-19 cases showed the risk of death associated with Delta compared to non-VOCs increased 137% (95%CI 50-230%) and 59% (39-85%) higher than N501Y-positive VOC (15).	1 retrospective cohort study. Low level of evidence.
Mortality Risk Factors Compared to Original Variant	• No studies	
Viral Load Compared to B.1.1.7 (Alpha) or Original Variant	• India, viral load may be higher for Delta than for Alpha based on analysis of Ct values (a proxy for viral load), which were stable at baseline from Dec 2020 to Feb 2021, dropped in March when Alpha was dominant and fell further in April when B.1.617 took over (mainly Delta) (21). The change in Ct values (-6) corresponds to a 50-fold increase in viral load. A study of vaccinated healthcare workers at three Delhi hospitals that tested positive for SARS-CoV-2, the median Ct value of Delta infections was not significantly different than non-Delta infections (34). • Singapore, the Delta variant was associated with significantly lower Ct values and a longer duration of sustained low Ct values (≤30) (median duration of 18	3 surveillance data analyses and 2 outbreak investigation study using Ct values as a proxy for viral load. Low level of evidence.

	days) compared to non-VOC lineages of SARS-CoV-2 (13 days) (32). • Houston, TX, Delta cases had significantly lower PCR cycle threshold (Ct) values on initial diagnosis than other cases (~21 vs. 26) (33). • In a Chinese sample, the viral loads in the Delta infections (n=62) were ~1000 times higher than those in the earlier 19A/19B strain infections (n=63) when they first tested positive by PCR during quarantine (Ct 24 vs. 34) (14).	
Infectious Period	• No studies	
Incubation / Latent Period	• Public Health England reports the incubation period to be a median of 4 days for both household and non-household contacts and was the same as Alpha (28). • A study from China reported a shorter time interval between exposure and first PCR positive test in quarantined cases involved in an outbreak of Delta across the province of Guangdong (n=34) compared to cases caused by 19A/19B genetic strains during the early 2020 epidemic (n=29): 4 days (IQR 3-5) vs. 6 days (IQR 5-8) (14).	1 outbreak report and 1 surveillance data analysis Low level of evidence.
Immune Escape - Re-infection and Impact on Vaccine Efficacy		
Re-infection after Infection Compared to Original Variant	• The SIREN cohort study is reporting an increase in the rate of PCR positive cases from 0.1/1000 (April/May) to 5.4/1000 (June); reinfections have increased from 7 cases (April/May) to 44 cases (June/July) (6). • Preliminary analysis of surveillance data from the UK found an increased risk of reinfection with Delta compared to Alpha (adjusted odds ratio 1.46, 95%CI 1.03-2.05), particularly when the primary infection was ≥180 days earlier (aOR 2.37, 95%CI 1.43-3.93) (6). • Two predictive models estimate that Delta is able to evade approximately 16 to 55% of the immune protection provided by prior infection with non-Delta lineages (34, 35).	1 prospective cohort study and 2 predictive models. Low level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness Compared to B.1.1.7 (Alpha),	Breakthrough Infections: • In a study from India conducted between Nov 2020 and May 2021, 19/27 vaccine breakthrough cases were Delta. This is higher than would be expected given the variants in circulation and consistent with a higher vaccination breakthrough risk of Delta compared to Alpha (21). Analysis of ChadOx1 vaccine (AstraZeneca) vaccine	5 surveillance data analyses, 1 outbreak investigation study, 1 randomized controlled trial, and 3 test negative case control studies.

B.1.617.1 (Kappa) or Original Variant	breakthrough infections in over 100 healthcare workers in India concluded that there was a higher risk of Delta breakthrough infections as compared to Alpha or B.1.617.1 (Kappa) (Odds Ratio: 5.14, 95%CI 1.32-20.0, p=0.018), after adjusting for age, sex, and hospital (34). • UK, sequenced cases detected after 1 or 2 doses of vaccination had higher odds of infection with Delta compared to unvaccinated cases (OR 1.33, 95%CI 1.17-1.53) (43). • In Houston, Texas, Delta variants caused a significantly higher rate of vaccine breakthrough cases (19.7% compared to 5.8% for all other variants) (33). Vaccine effectiveness one dose: • BNT162b2 (Pfizer): A Canadian study reported a 56% vaccine effectiveness (VE) against symptomatic disease caused by Delta (VE was higher against Alpha at 66%) (16), and a UK study reported a VE of 94% (95%CI 46-99) against hospitalisation after one dose (48). • mRNA-1273 (Moderna): A Canadian study reported a VE of 72% against symptomatic disease caused by Delta (VE was higher against Alpha at 83%) following one dose (16). • ChAdOx1 (AstraZeneca): A Canadian study reported a VE of 67% against symptomatic disease caused by Delta, similar to that of Alpha (64%) (16). An Indian study reported a VE of 46.2% (95%CI 31.6-57.7) against infection, and 79.2% (95%CI 46.1-94.0) in preventing moderate-severe COVID-19 (17), and a UK study reported a VE of 92% (95%CI 75-97) against hospitalisation after 1 dose (48). General Vaccination: In the UK, BNT162b2 (Pfizer) or ChAdOx1 (AstraZeneca) VE against symptomatic disease was ~30.7% (95%CI: 25.2 35.7%) effective, an 18% reduction compared to Alpha (43). Another study found that, after one dose there was a 14% absolute reduction in VE against symptomatic disease with Delta compared to Alpha (29). In Scotland, vaccination (>28d post first dose) was associated with a decreased risk of hospitalization for Delta cases HR= 0.38 (95% CI 0·24–0·58), but was slightly diminished compared to Alpha (36) and the hazard ratio among vaccinated Delta patients was HR 0.37 (95%CI 0.22-0.63) after one dose and HR 0.29 (95%CI 0.11-0.72) after two doses of any vaccine compared to unvaccinated (48).	Low level of evidence.

	Vaccine effectiveness two doses: • BNT162b2 (Pfizer): In Scotland, VE in preventing confirmed infection was 79% (95%CI: 75–82) (36). Canadian and UK studies found that protection against symptomatic Delta infection was ~88%, which was comparable to that of Alpha and Beta/Gamma (16, 43). Protection against hospitalization/death was higher (96%, 95%CI 86-99) (16, 48). • ChAdOx1 (AstraZeneca): Studies from the UK and India found that VE against infection, symptomatic disease, moderate/severe disease, and hospitalization was 63% (95%CI 51-72) (17)/ 60% (95%CI: 53–66) (36), 67% (95%CI 61-72) (43), 81.5% (95%CI 10-99)(17) and 92% (95%CI 75-97) (48), respectively. • BBV152 (Covaxin, Bharat Biotech): In India, VE against Delta infection was 65.2% (95% CI: 33·1–83·0) (49). This vaccine was effective in preventing severe disease and mortality caused by the Delta variant in completely vaccinated hospitalized patients in India (50). • General Vaccination: In the UK, VE following 2 doses of BNT162b2 (Pfizer) or ChAdOx1 (AstraZeneca) was 7.5-10% lower for Delta compared to Alpha (29, 43).	
***In vitro* studies Convalescent Sera** Compared to other VOCs or Original Variant	• Convalescent sera from cases had a reduced neutralization of 1.2-6.8 fold for Delta compared to other VOCs or the original variant across studies (17, 34, 37-41, 41, 42). However, T-cell responses have been shown to be preserved against the recombinant mutant receptor binding domain antigens suggesting cell-mediated immune protection (17).	8 *in vitro* studies. Very low level of evidence.
***In vitro* studies Vaccinated Sera** Compared to B.1.1.7 (Alpha) or Original Variant	• There was a 1.4-11.3-fold reduction of neutralization of the Delta variant by BNT162b2 (Pfizer) relative to the original variant (34, 40, 41, 41, 51-55) and 3-fold reduction relative to Alpha (37). • Studies evaluating ChAdOx-1 (AstraZeneca) report a 3-6-fold reduction of the Delta variant compared to original variant (34, 41, 41, 54, 56). • After two doses of ChAdOx-1 (AstraZeneca), neutralization against Delta was reduced by 2.5-fold (95%CI 1.4-2.7) relative to BNT162b2 (Pfizer) (57). • A single dose of BNT162b2 (Pfizer) or ChAdOx-1 (AstraZeneca) was either poorly or not at all efficient against Delta variant (37), while two doses of either	16 *in vitro* studies. Very low level of evidence.

	vaccine generated a sufficient neutralizing response in most individuals (37, 41). • A study evaluating BBV152 (Covaxin) reported a 2.7-fold reduction of Delta compared to the original variant (38). • A study evaluating Ad26.COV2.S (Janssen) reported a 1.6-fold reduction of Delta compared to the original variant (58). • A study evaluating mRNA-1273 (Moderna) reported a 2.1-fold reduction of Delta compared to the original variant (59). • A study evaluating ZF2001 vaccine reported a non-significant 1.2-fold reduction of Delta compared to the original variant (60). • Convalescent cases following the first dose of vaccine had significantly higher neutralizing antibody (Nab) titers compared to COVID-19 negative people post first dose, (56).	
***In vitro* studies Therapeutics** Compared to Original Variant	• Bamlanivimab lost antiviral activity against Delta, demonstrating that L452R is an escape mutation for this monoclonal antibody (mAb) (34, 37, 40, 61). • Etesivimab, Casirivimab and Imdevimab remained active against Delta (37). • A combination of Meplazumab and anti-CD147 antibody C effectively inhibited Delta pseudovirus *in vitro* (62). • Remdseivir and B12 compounds were effective at inhibiting replication of Delta *in vitro* (63). • mAbs being developed for clinical use, including those by AstraZeneca, Regeneron, Lilly, and Adagio, generally demonstrated potent neutralizing activity against Delta, with small (up to 5-fold) reductions in neutralization for some antibodies (41). The exception was LY-CoV555, which was severely reduced for Delta.	7 *in vitro* studies. Very low level of evidence.
Diagnostic / Detection Test Failure		
Testing and Detection Compared to Original Variant	• There has been no indication of test issues (i.e. changes in sensitivity/specificity) with Delta. However, one study identified 16 primer site mutations in B.1.617 lineage specimens that impact the primer sites which disrupt whole genome sequencing by two widely used laboratory protocols (3 affect the Freed et al. protocol and 13 affect the ARTIC version 3 protocol) (64).	4 diagnostic test accuracy studies and 1 report. Low level of evidence.

	• The P681R target primer was introduced to Public Health England's genotyping PCR test to detect B.1.617 which are mainly Delta (28). • One paper proposes PCR primers designed to identify the VOCs including Delta (65). • A deep learning model for genetic sequencing demonstrated test accuracy scores for Delta (B.1.617.2) of 75.75% (66). • A sensitive RT-qPCR assay for the direct detection of Delta in wastewater samples has also been proposed (67).	
Other Epidemiology		
VOC Emergence Over Time	• According to GISAID (accessed on 10/06/2021), a total of 31,997 sequences (Europe = 24,606, Asia = 4,974, North America = 2,210, Oceania = 163, Africa = 36, South America = 8) have been assigned to lineage B.1.617.2 (Delta) (54). • Ontario-wide genome sequencing of N501Y-/E484K- samples (which represents Delta or the original wild-type variant) demonstrated the replacement of wild-type with Delta variant (proportion increased from 2.2% in early April, to 83% in late May) (30). A study including data on VOCs in Canada reported that Delta accounted for 0.82% of the cumulative VOC cases sequenced in Canada up to June 15th, 2021 (7). The variant specific prevalence of Delta was highest in Alberta, British Columbia, Manitoba, Ontario and Saskatchewan at 73 per 1 million population and lowest in the eastern provinces at 2 per 1 million population (7). The overall proportion of Delta cases for the week of June 13th in Canada was 37% and Delta was at the point of overtaking Alpha (41%) (8). Since late June, Delta has been the dominant variant in Canada. • A UK report indicates that the Delta variant accounted for approximately 99% of sequenced and ~96% genotyped cases from 27 June to 10 July 2021 (5). New data from the end of June indicate that Delta doubling times have plateaued or started to decline across England (29). Delta was repeatedly introduced and rapidly increased via community transmission from April to mid-May 2021. The growth rate was estimated to be around 37% (95%CI 26-49) above Alpha and doubling	18 surveillance studies and six reports. Low level of evidence.

	time estimated to be 5-14 days but as long as 21 days in some communities (19, 23, 68, 69).The May/Jun 2021 reproduction number was 1.44 in England (23). • REACT-1 study in England detected Delta for the first time (2/115) in round 11 (Apr 15-May 3) (20). Since then, there was rapid replacement of the Alpha variant with the Delta variant (23). During round 12 (between May 20-Jun 7), the proportion of positive samples that were Delta rose from ~60% to ~90%. Within round 13 (Jun 24-Jul 5, 2021), prevalence amongst those reporting they were unvaccinated was over three-fold higher at 1.15% (95%CI: 0.92%, 1.43%) compared with those reporting two doses of vaccine at 0.35% (0.26%, 0.45%) (70). • In India, B.1.617 lineages increased from 5% in Feb 2021 to 10% in March and 60% in April. Delta rose from less than 10% to >80% of B.1.617 cases (21, 24, 34, 35, 71) and phylogenetic analysis showed the spread of B.1.617 and the emergence of sub-lineages (22). • USA, P.1 (Gamma) and Delta were the main variants replacing Alpha. They represented at least 16% and 14% of the cases for the week of June 9 to June 15, respectively. The growth rate of Delta was faster than Gamma (k = 0.61 vs. 0.22), particularly in counties with lower vaccination rates (25). Between March 15 to July 3, 2021, Delta variants increased to cause 58% of all COVID-19 cases and spread throughout the metropolitan Houston area (33). • In Japan, the frequency of Delta is expected to take over Alpha around July 12, 2021 (95%CI from July 8 to July 16, 2021) and before the Tokyo Olympic Games official start on July 23, 2021(26). • VOCs including Delta have been increasing in Australia. Out of 17,694 SARS-CoV-2 sequences in Australia from Jan 23, 2020 to May 23, 2021, 122 (0.7%) were Delta (72). • Public Health England reported that a small number of Delta sequences have been detected which have acquired the spike protein mutation K417N (5, 6, 28, 29). As of July 16, 2021, 873 genomes of this variant, designated as B.1.617.2.1, Delta-AY.1, or Delta+, have been identified in GISAID: US (n=592), Portugal (56), Japan (47), England (45), Switzerland (41), Poland (27), India (23), France (11), Nepal (11), Germany (3), Netherlands (2), Spain (2), Qatar (2), Australia (2), Mexico	

	(2), Canada (1), Kuwait (1), Ecuador (1), Romania (1), Russia (1), Denmark (1), and Czech Republic (1)(6).	

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio, GISAID = global initiative on sharing avian influenza data

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. One of the foci is to identify studies as variants of concern or under investigation. Studies identified under this foci were further characterized in our VOC/VOI database and Delta results were extracted into this review. A cross check for relevant articles was also conducted within the databases using targeted keyword searching (B.1.617 OR Delta).
This review contains research published up to July 29, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Review
The Office of the Chief Science Officer facilitated the review of this document, which included suggestions from a scientific editor, peer-review by a subject matter expert, and input from a senior policy advisor with a science-to-policy perspective.

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APPENDIX

a) VOC/VOI LEXICON

WHO label (2021-05-27)	**Pango lineage**	**GISAID clade/lineage**	**Nextstrain clade**	**Earliest documented samples**	**Date of designation**
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I/S:501Y.V1	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2 AY.3	G/452R.V3	21A/S:478K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR	20B/S.484K	Brazil, Apr-2020	17-Mar-2021

Eta	B.1.525	G/484K.V3	20A/S484K	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR	20B/S:265C	Philippines, Jan-2021	24-Mar-2021
Iota	B.1.526	GH	20C/S:484K	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	20D	Peru, Aug-2020	14-Jun-2021

b) OTHER RESOURCES

Reference	Description
Living Evidence Review on SARS-CoV-2 variants Australia On-going, last examined March 10.	This table highlights recent relevant evidence under the different categories of study similar to what has been laid out in the profiles in this review.
CDC VOC page	Summary of each VOC is available.
WHO situation reports	Summary Includes a VOC section.
Grey lit	
SAGE communications	The vaccines and variants page has reports and summaries on VOCs.
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. 2020 Dec to present	Technical reports compile information from various studies and surveillance across the UK on the VOC and VOIs that are circulating. There is a lot of overlap from these reports and research publications.

Emerging Evidence on COVID-19

Living Summary of SARS-CoV-2 Variants of Concern: The Gamma variant (P.1) profile

Highlights up to July 1, 2021

Introduction

SARS-CoV-2 **variants of concern** (VOCs) are circulating variants that have been flagged by national or global public health organizations. VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or diagnostic detection failures (1-3). Canada has established a national definition (2). In May 2021 WHO released naming system for VOCs and variants of interest (VOIs) using Greek letters to improve the ease of communication on variants and potential stigma related to places where variants were first identified, which has been adopted in this report (1, 4).

TABLE 1: CURRENT VARIANTS OF CONCERN (VOCS)*

WHO name (05-21)	Pango lineage	Nextstrain clade	GISAID clade	Alternate name	First detected in	Earliest samples	Characteristic spike mutations
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	United Kingdom	Sep 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Beta	B.1.351 B.1.351.2 B.1.351.3	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	South Africa	May 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, P.1.1 P.1.2	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brazil and Japan	Nov 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G H655Y, T1027I, V1176F
Delta	B.1.617.2 AY.1 AY.2 AY.3	21A	G/478K.V1		India	Oct 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R, del157/158, T478K, D950N)

* A VOC/VOI lexicon and other resources are available in the appendix.

The goal of this living summary on the SARS-CoV-2 VOC literature is to highlight new data on the VOC P.1 (Gamma), its epidemiology and how the attributes of this variant may impact the management of the

pandemic. This living evidence profile on Gamma is part of a larger project that summarizes the data on each VOC as well as captures data on VOIs. The focus will be on changes to epidemiological parameters (e.g., transmission rates, clinical outcomes of severity and mortality, shifts in age groups affected or asymptomatic proportions), impacts on diagnostic tests, immune evasion/vaccine effectiveness and impacts on other public health measures. The full dataset in Excel can be accessed here and filtered by the VOCs and VOIs of interest. The recent living evidence review on other VOCs (Alpha, Beta, Delta) and a high level contrasting table of VOC evidence can be requested here.

In this summary, "original variant" refers to any variant that was not designated as a VOC or VOI.

Key Points

As of July 1, 2021 there were 187 studies that report on the Gamma variant of concern. 39 studies were summarized in the profile, including studies describing transmission efficiency (n=9), clinical severity (n=16), immune escape (n=16), testing and diagnostics (n=5), and spread epidemiology (n=10).

148 studies were not summarized in the profile, including: case reports and case series (n=10); point prevalence or period prevalence estimates (n=25); studies reporting detection of Gamma or phylogenetic analysis only (n=9); studies reporting outcomes related to cell infectivity, binding affinity, or genomic characterization and no outcomes related to therapeutics (n=30); studies on therapeutics that are not commercialized, e.g., individual monoclonal antibodies (n=17); predictive models in which the time period for projections has already passed (n=4); *in vitro* studies with no relevant extractable outcomes and neutralization experiments on convalescent or vaccinated sera (n=35); diagnostic test accuracy studies evaluating a new test/method (not commercially available) to detect VOCs (n=15); vaccine breakthrough data with no control group to compare the VOC proportion of breakthrough cases vs. VOC proportion of all COVID-19 cases (n=3).

However, details for all 187 studies that report on Gamma can be found in the Excel dataset accessed here.

Transmissibility:

- Studies from several countries showed increased transmissibility for Gamma compared to the original variant, although the magnitude of increased transmissibility ranged widely (12%-160%). One Canadian study of household transmission reported Gamma had 62% increased transmissibility and 8% higher secondary attack rates compared to the original variant (5).

Clinical Severity:

- One European study reported a higher proportion of hospitalized cases for Gamma compared to the original variant (20% vs. 7.5%), and higher odds of Gamma cases being admitted to hospital or ICU (6). For severity indicators, this study also reported:
    - Higher odds of hospitalization in the 20-79 age group and admission to ICU in the 40-80 age group compared to the original variant.
    - A significantly lower proportion of pre-existing conditions among Gamma cases compared to the original variant (27.8% vs. 89%).
- There was conflicting evidence on mortality risk for Gamma compared to the original variant, with most studies indicating higher mortality risk for Gamma.

- Three studies using Ct values as a proxy for viral load reported that Gamma viral load was higher compared to the original variant. One study reported Gamma viral load was lower than Alpha (7).
- One study using data from France reported no significant difference in the infectious period for combined Gamma and Beta case data compared to original variant (95% CI of the HR: 0.79-1.06) (8).
- There were no studies on incubation period for Gamma.

Immune Escape:

- Two studies from Brazil suggest there may be substantial reinfections with Gamma, however this is based on ecological analyses and needs further study.
- One Canadian vaccine effectiveness (VE) study reported the BNT162b2 (Pfizer) and mRNA-1273 (Moderna) vaccines have reduced protection against symptomatic infection with Gamma compared to the original variant after the first (VE = 43% vs. 61%) and second dose (VE= 88% vs. 93%), although the confidence intervals overlap in both comparisons (9).

Testing and Diagnostics:

- No studies evaluating diagnostic tests for SARS-CoV-2 described failure or performance issues for detecting Gamma.
- One study found that mutations in Gamma disrupted genomic sequencing in the Freed *et al.* primer scheme (10).

Spread Epidemiology:

- Three studies from Brazil reported on the rapid spread of Gamma over time. Gamma first emerged in November 2020 and became the dominant lineage in Brazil by February 2021 (11).

Overview of the Evidence

Study designs on VOC research range widely from observational studies with a high risk of bias to double blind randomized controlled trials (RCTs) with a lower risk of bias. No clinical trials were identified for this review on the Gamma variant. There were observational studies, including surveillance data analyses, retrospective cohort studies, and case-control studies, which are considered low levels of evidence. Certainty in the evidence from these observational studies may be upgraded for a given outcome when multiple studies are in agreement and have prospective designs. Other studies identified in this profile were predictive models, ecological studies, animal models and *in vitro* studies, which are considered a low to very low level of evidence. Generally these types of studies are used to generate hypotheses that are then tested with a more rigorous study design. For this profile, study designs were identified, but no formal risk of bias assessment was conducted for each study. A summary indication of the level of confidence of the evidence was given for each category of study. The greatest amount of evidence was on transmissibility and the spread of Gamma over time. There were gaps in knowledge on epidemiological parameters including infectious period and incubation period, impact of public health measures, and vaccine effectiveness.

Overall, the level of evidence on the Gamma variant is low and there are several knowledge gaps. Thus additional research is needed to improve confidence in the summary results, and to fill in current knowledge gaps regarding the Gamma variant.

CONTENTS

GAMMA

The excel dataset includes summaries of individual studies and can be accessed here. Below is the detailed evidence profile developed for Gamma.
Categories of evidence in the tables below include the following:

Transmissibility includes changes in transmissibility, secondary attack rates, and estimates of selective advantage.

Clinical Severity includes proportion of infections that are symptomatic, proportion of severe disease and mortality as well as risk factors for severe disease or mortality, viral load, infectious period, incubation period. Note risk factors for severe disease would include special populations e.g., persons who are pregnant (when reported).

Immune Escape includes changes to vaccine efficacy, risk of re-infection in humans, animal models, *in vitro* or *in silico* experiments as well as impacts on therapeutics when reported.

Diagnostic / Detection Test Failure is captured in the table.

Other Epidemiology includes all studies that document the emergence and spread of VOCs in a geographic area, ecological studies that examine VOC spread and risk factors for hot spots, and studies on effective public health interventions against VOCs, with genomic epidemiology as subcategories when reported.

Table 2: Evidence Profile of Gamma VOC (n=187)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency		
Transmissibility Compared to Original Variant	Increased transmissibility above the original variant: • Brazil: 2.6 (95%CI 2.4-2.8) (12) and 2.0 (50%CrI 1.7-2.4) times more transmissible than the original variant with median cross-immunity estimated at 68% (50%CrI 54-79) (13). • Italy: 1.12 (95%CI 1.03-1.23) times more transmissible assuming complete immune evasion to	Seven studies provided estimates of Gamma transmissibility including: 6 surveillance data analyses from Brazil (2) / France (2) / global (2), and 1 cross-sectional study from Italy.

	1.39 (95%CI 1.26-1.56) assuming complete cross protection (14). • Global: Combined Gamma and Beta case data showed a higher transmission advantage over the original variants ranging between 18-26% in Japan, France, Brazil, USA and Niger (8). • France: 27% higher transmissibility for combined Gamma and Beta (7). Between May-Jun 2021, the transmission advantage of combined Gamma, Beta, and Eta over Alpha was 17.2% (95% CI 15.6-18.9) in Ile-de-France, 16.1% (95% CI 4.63-28.5) in Hauts-de-France, and 9.12% (95% CI 7.34-10.9) in Normandie (15). • Other studies place Gamma transmissibility between that of the original variant and Alpha and show the transmissibility of Gamma has slightly decreased over time from Jan 2021 to Apr 2021 worldwide (16).	Across studies there is little consistency. Heterogeneity in increased transmissibility estimates may be due to factors such as geographic location and time points in which estimates were taken. Low level of evidence.
Secondary Attack Rate Compared to Original Variant	• In a Canadian study of household transmission, the secondary attack rate for Gamma index cases was 28.2%, which was higher than the rate for the original variant cases at 20.2%. This equated to Gamma index cases had higher odds of transmitting infection to household members, compared to wild-type cases (aOR 1.62, 95% CI 1.21-2.16) (5).	1 surveillance data analysis from Canada. Low level of evidence.
Public Health Measures/ Interventions Compared to Original Variant	• Gamma emerged in Manaus Brazil in late Nov 2020 and showed a high effective reproductive number (Re) of 2.6 (95% Highest Posterior Density [HPD]: 1.5-4.5) during Dec 2020. After increased social distancing restrictions, the Re was estimated to have decreased to 1.2 (95% HPD: 0.9-1.6) in late Dec 2020 and Jan 2021 In comparison, a previous variant also had a Re of 2.6 (HPD 1.6-3.8) in Mar 2020 that decreased to 1.0 (HPD 0.8-1.2) in Apr 2020 after social distancing increased by more than 50% in Manaus (due to implementation of non-pharmaceutical interventions) (17).	1 surveillance data analysis from Brazil. Low level of evidence.
Clinical Severity		
Virulence / Severity or Duration of Disease Compared to Original Variant	• Europe: A higher proportion of hospitalized Gamma cases were reported compared to the original variant (20% vs. 7.5% p<0.001) (6). o Higher adjusted odds ratio (aOR 2.6, 95%CI 1.4-4.8) of Gamma cases being admitted to hospital	2 surveillance data analyses from Europe and Brazil. Low level of evidence.

	or to ICU (aOR 2.2, 95%CI 1.8-2.9) compared to original variant (6). • Brazil: From Feb 2021-Mar 2021, hospitalized cases in one state exhibited exponential growth, with an average doubling time of 13.4 days and a daily growth rate of 5.3% (18). ○ Similar exponential growth (doubling time 13.3 days, daily growth rate 5.4%) for hospitalizations was reported in one city (18).	
Severity Risk Factors Compared to Original Variant	• Europe: In an age-stratified analysis, Gamma cases had 3.0-13.1 times higher odds of hospitalization in the age groups 20–39, 40–59 and 60–79 (6). • Odds of admission to ICU were 2.9–13.9 times higher in 40–59, 60–79 and ≥ 80 age groups (6). • Pre-existing conditions were lower in Gamma cases (27.8%) vs original variant (89%), p<0.001 (6). No whole genome sequencing: • Brazil: Among severe cases, people under 60 years old increased from 39% in the first wave (Nov-Dec 2020) to 47% in the second wave (Feb 2021) when Gamma was predominant (19). • Brazil: There was no increase in the proportion hospitalized in any age group before (Feb-Oct 2020) and after (Oct 2020-Feb 2021) Gamma emerged (20). • In Sao Paulo, Brazil, there was no significant difference in the mean age of infected hospitalized patients before and after Mar 2021 when Gamma became dominant (21).	2 surveillance data analyses from European countries and Brazil, 1 ecological study in Brazil, and 1 retrospective cohort study in Brazil. In three studies, whole genome sequencing was not conducted so the lineage was not determined. Low level of evidence.
Mortality Compared to Original Variant	• Brazil: the risk ratio of Gamma case fatality risk (CFR) vs. non-Gamma variant CFR is 1.54 (95% CI: 1.13-2.02), which indicates increased mortality risk for Gamma (11). • Brazil: A differentiated increase in COVID-19 mortality among adults aged 18-50 after Gamma emerged suggests the possibility of greater severity of Gamma in this population. Young adults had high hospital mortality rates >10% (20). • Predictive model estimated Gamma infections in Manaus Brazil are a median 1.5 (50%CrI 1.2–1.9) times more likely to result in mortality in the period following the emergence of Gamma in Nov 2020, compared to before (13). However, it cannot be	1 surveillance data analysis from European countries, and 2 ecological studies and 1 predictive model from Brazil. Low level of evidence.

	determined whether the estimated increase in relative mortality risk is due to Gamma infection, stresses on the Manaus healthcare system, or both. • Europe: Lower odds of mortality due to Gamma compared to original variant in multivariable analysis (aOR 0.6, 95%CI 0.3-1.0) (6). This result conflicts with the other three studies reporting a higher mortality risk for Gamma, which may be due to the fact that this analysis used data from European countries and is based on a few observations while the other studies were from Brazil, where Gamma first emerged and has had a large impact.	
Mortality Risk Factors Compared to Original Variant	• Brazil: mortality in COVID-19 cases <60 years old increased from 18% in Nov 2020 to 28% in Feb 2021 when Gamma was predominant (19). • The case fatality ratio increased the most in 20-59 year olds and among patients without pre-existing risk conditions. Among severe cases, the proportion of patients without pre-existing risk conditions was higher in Feb 2021 (33% vs. 25% in Nov 2020) (19). • Compared with Nov/Dec 2020, females 20-39 years old, with no pre-existing risk conditions, were at 5.65 (95%CI 2.9-11.03; p <0.0001) times higher risk of death in Feb 2021 and 40-59 year olds were at 7.7 (95%CI 5.01-11.83; p <0.0001) times higher risk of death (19).	1 surveillance data analysis from Brazil. Whole genome sequencing was not conducted so the lineage was not determined. Very low level of evidence.
Viral Load Compared to Original Variant	• France: Viral load (measured by Ct values) of Gamma samples was lower than Alpha samples and higher than original variant samples (7). Similarly, Ct values for combined Gamma and Beta were significantly lower compared to the original variant, Ct difference was 0.754 (p=0.0072), which indicates higher viral load for combined Gamma and Beta (8). • Brazil: Approximately 10-fold higher viral load in Gamma infections compared to non-Gamma infections (other variants circulating in Brazil up to Jan 2021). Regression analysis found Gamma infections were significantly higher than non-Gamma infections in adult (18-59 years) men (P=0.0005), adult women (P<0.0001), and elderly (>59 years) women (P=0.0149), but not significantly different in elderly men (P=0.4624) (17). No whole genome sequencing:	3 surveillance data analyses from France / Brazil / global, and 1 retrospective cohort study in Brazil. In one study, whole genome sequencing was not conducted so the lineage was not determined. Low level of evidence.

	• Brazil: There was no significant difference in mean Ct values among infected hospitalized patients and healthcare workers before and after Mar 2021 when Gamma became dominant (21).	
Infectious Period	• France: There was no indication that the infectious period (data in graphs only) was significantly different for combined Gamma and Beta compared to the original variant (95% CI of the HR: 0.79-1.06), measured by the duration of decline in viral load (8).	1 surveillance data analysis using data from France. Low level of evidence.
Incubation Period	No studies	
Immune Escape - Re-infection and Impact on Vaccine Efficacy		
Re-infection After Infection Compared to Original Variant	• 28% of the cases in Manaus Brazil from Nov 2020 to Jan 2021 were estimated to be re-infections considering 78% of the population was previously infected in an ecological analysis of syndromic surveillance data (12). • 16.9% of Gamma cases (95%CI 9.48-28.5) in Manaus from Jan 2021 to Mar 2021 were estimated to be re-infections in an analysis of blood donor data. If probable reinfections are also included, then 25.8% were reinfections (95%CI 16.7-37.4). If possible reinfections are also included, then 31.0% were reinfections (95%CI 21.4-42.5) (22).	2 surveillance data analyses from Brazil. Low level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness Compared to Original Variant	• In Manaus Brazil where >75% of the cases were Gamma during the study period, vaccination with at least one CoronaVac (Sinopharm) dose was associated with a 0.50-fold reduction (adjusted VE 49.6%, 95% CI 11.3-71.4) in the odds of symptomatic SARS-CoV-2 infection during the period 14 days or more after receiving the first dose. Female sex (OR 0.50, 95% CI 0.38-0.81) and a positive SARS-CoV-2 RT-PCR or antigen test in the prestudy period (OR 0.38, 95% CI 0.17-0.87) were associated with a reduced odds of symptomatic SARS-CoV-2 infection (23). • In Sao Paulo state Brazil where >75% of the cases were Gamma during the study period, CoronaVac (Sinopharm) 14 or more days after the second dose among individuals ≥70 years old had an adjusted VE against symptomatic SARS-CoV-2 infection of 41.6% (95% CI 26.9-53.3), against hospitalization 59.0% (95% CI 44.2-69.8), and against deaths 71.4% (95% CI 53.7-82.3) (24).	3 case-control studies from Brazil (2) and Canada (1), and 1 surveillance data analysis from USA. Low level of evidence.

	• Canada: mRNA-1273 (Moderna) or BNT162b2 (Pfizer) vaccine >7 days after the second dose had an adjusted VE against symptomatic Gamma infection of 88% (95%CI 61-96) versus symptomatic original variant infection of 93%, (95%CI 87-96). Adjusted VE against symptomatic Gamma infection for one dose was 43% (95%CI 22-59) versus symptomatic wild-type infection (61%, 95% CI 53-67) (9). • In an underpowered study (n=20 breakthrough cases) from Washington State USA, Gamma was not over represented in breakthrough infections compared to its representation in COVID-19 cases during Feb-Apr 2021 (25).	
***In Vitro* Studies of Therapeutics** Compared to Original Variant	• Multiple therapeutics have been shown to have reduced effectiveness against Gamma, including Casirivimab (26-29), Bamlanivimab (28, 30), Etsevimab and Imdevimab (26). • The combination of Imdevimab and Casirivimab was shown to efficiently inhibit Gamma (28).	5 *in vitro* experiments have been identified with results specific to commercialized therapeutics against Gamma. *In vitro* studies are a low level of evidence that offer preliminary insights into what we may expect *in vivo*.
***In Vitro* Studies of Convalescent and Vaccinated Sera** Compared to Original Variant	• Most studies have shown that convalescent sera and fully vaccinated sera (BNT162b2 (Pfizer), CoronaVac (Sinopharm), mRNA-1273 (Moderna), Ad26.COV2.S (Janssen)) have reduced neutralizing activity for Gamma. *Note: Many in vitro studies have been identified, please see the Excel dataset for details on each study.*	31 *in vitro* experiments have been identified with results specific to Gamma neutralization. Very low level of evidence. The immune response is complex, and lack of or reduced neutralizing antibodies does not mean a lack of immune protection. Further research is needed (see the PHAC Emerging Science review on protective immunity.)
Testing and Diagnostics		
Testing and Detection	• No testing failures have been reported for Gamma PCR, antigen tests, or serological assays (31, 32).	4 diagnostic test accuracy studies and 1 surveillance data analysis that described

Compared to Original Variant	• Mutations in Gamma were shown to disrupt genomic sequencing of Gamma clinical specimens in the Freed *et al.* primer scheme, resulting in significantly reduced depth of coverage at three primer sites compared to non-Gamma specimens (p-values <0.00001) (10). • Studies report reliable sequencing methods for detection of Gamma from wastewater samples (33, 34). In Missouri USA, the daily wastewater load of Gamma (in genome copies/day) was significantly correlated with clinical case counts of Gamma during the same time period (R^2=0.89) (34).	a new method for analyzing sequencing data from wastewater. Low level of evidence.
Spread Epidemiology		
VOC Emergence Over Time	• The prevalence of Gamma grew from 0% in Nov 2020 to 73.8% in Amazonas, Brazil (17) and almost 30% in Amazonas, Columbia by Jan 2021 (35). • Brazil: The weekly prevalence of Gamma increased rapidly since Dec 2020 and reached more than 50% in Feb 2021 (11). • Brazil: The frequency of Gamma among asymptomatic and mild symptomatic cases at a university was 9.1% on Jan. 21, 2021, and increased to 42.9% two weeks later. By the start of Apr 2021, 100% of cases were Gamma, completely displacing P.2 and original variants (36). • Italy: The prevalence of Gamma remained relatively stable from Feb 2021 (5.0%, 95%CI 3.9-6.4) to Mar 2021 (4.8%, 95%CI 3.9-5.9) compared to Alpha, which grew from 53.1% (95%CI 50.3-55.9) to 85.7% (95%CI 84.1-87.3) (14). • USA: From Apr-Jun 2021, the main variants replacing Alpha were Delta and Gamma. Delta was shown to have a faster growth rate than Gamma (k=0.66 vs. 0.34) (37).	4 surveillance data analyses from Brazil (2) / Colombia (1) / USA (1), 1 cross-sectional study from Italy, and 1 ecological study from Brazil. Low level of evidence.
Predictions of Spread	Two scenarios were explored in a model of VOCs in North America based on data collected until the end of April 2021: • If vaccination does not affect the proportion of VOCs, the frequency of Gamma is predicted to be at just over 15% by Mar 2022. Meanwhile, Alpha would be dominant at more than 60%, Beta would be at just under 5%, and Delta would be at 20% (38).	3 predictive models from North America. Low level of evidence.

	• If 75% of the population in North America is fully vaccinated in Jul 2021, the frequency of Gamma is predicted to be at 5% by Mar 2022. Meanwhile, Alpha would be at 0%, and Beta and Delta would each be at 5%. The model assumes 100% vaccine efficacy (38). Two predictive models that do not take Delta into account: • Based on data from March 2021, an SIR (susceptible-infected-recovered) model was developed to evaluate the impact of a full return to pre-pandemic levels of contacts once 50% of the USA population is vaccinated in Jul 2021. Gamma was predicted to outcompete Alpha and Beta and become the dominant strain in 2-3 months The model assumes Gamma reduces the protection from vaccine or previous infection immunity by 32% (39). • In a simulation of May 2021-Aug 2021 where Gamma and Beta become established in the New York City population simultaneously, Gamma is predicted to outcompete Alpha and become co-dominant with Beta by Aug 2021. However, if Gamma becomes established in the population before Beta, Gamma would suppress Beta and become dominant. The model assumes Gamma has the same VE for symptomatic infection and hospitalizations as the original variant (40).	
Evolution of Variant	• The most recent common ancestor of Gamma emerged in mid-Aug 2020 in the state of Amazonas, Brazil. Gamma then emerged around late Nov 2020 (41). • Analysis of Gamma sequences in Brazil suggests that lineage-defining mutations of Gamma did not accumulate within one infected individual over a period of time, but were sequentially added during transmission between hosts (41).	1 surveillance data analysis from Brazil. Low level of evidence.

CFR = case fatality rate, CI = confidence interval, CrI = Credible Interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. One of the foci is to identify studies as variants of concern or under investigation. Studies identified under this foci were further characterized in our VOC/VOI database and Gamma results were extracted into this review. A cross check for relevant articles was also conducted within the databases using targeted keyword searching (P.1 OR B.1.1.28 OR 501Y.V3 OR Gamma).
This review contains research published up to July 1, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Review

The Office of the Chief Science Officer facilitated the review of this document, which included suggestions from a scientific editor, peer-review by a subject matter expert, and input from a senior policy advisor with a science-to-policy perspective.

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APPENDIX

a) VOC AND VOI LEXICON

WHO label (2021-05-27)	**Pango lineage**	**GISAID clade/lineage**	**Nextstrain clade**	**Earliest documented samples**	**Date of designation**
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I/S:501Y.V1	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2 AY.3	G/452R.V3	21A/S:478K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR	20B/S.484K	Brazil, Apr-2020	17-Mar-2021
Eta	B.1.525	G/484K.V3	20A/S484K	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR	20B/S:265C	Philippines, Jan-2021	24-Mar-2021

Iota	B.1.526	GH	20C/S:484K	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021

b) OTHER RESOURCES

Reference	Description
Living Evidence Review on SARS-CoV-2 variants Australia On-going, last examined March 10.	This table highlights recent relevant evidence under the different categories of study similar to what has been laid out in the profiles in this review.
CDC VOC page	Summary of each VOC is available.
WHO situation reports	Summary includes a VOC section.
Grey lit	
SAGE communications	The vaccines and variants page has reports and summaries on VOCs.
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. 2020 Dec to present	Technical reports compile information from various studies and surveillance across the UK on the VOC and VOIs that are circulating. There is a lot of overlap from these reports and research publications.

Emerging Evidence on COVID-19

Living Summary of SARS-CoV-2 Variants of Interest: The C.37 (Lambda) Variant Profile

Highlights up to August 10, 2021

Introduction

SARS-CoV-2 **variants of concern** (VOCs) are circulating variants that have been flagged by national or global public health organizations. VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or diagnostic detection failures (1-3). Canada has established a national VOC definition (2). **Variant of interest** (VOI), also referred to as variant under investigation (VUI), is a designation used to flag a variant that has the potential to be a VOC, but requires further investigation or evidence. Indicators for a VOI designation include; phenotypic change or acquisition of mutations with established phenotypic implication AND has been the cause of community transmission/clusters or is detected in multiple countries OR is assessed to be a VOI by an authority such as WHO (1, 2). Canada, has established a national VOI definition (2). In May 2021 WHO released a naming system for VOCs and VOIs using Greek letters to improve the ease of communication on variants and reduce potential stigma related to places where variants were first identified, which has been adopted in this report (4).

TABLE 1: CURRENT VARIANTS OF CONCERN (VOCS) AND VARIANTS OF INTEREST (VOIS)

WHO name (05-21) VOC	Pango lineage	Nextstrain clade	GISAID clade	Alternate name	First detected in	Earliest samples	Characteristic spike mutations
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	United Kingdom	Sep 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Beta	B.1.351 B.1.351.2 B.1.351.3	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	South Africa	Aug 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, P.1.1 P.1.2	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brazil and Japan	Dec 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y,

							D614G H655Y, T1027I, V1176F
Delta	B.1.617.2 AY.1 AY.2 AY.3	21A	G/478K.V1		India	Oct 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R, del157/158, T478K, D950N)
VOI							
Epsilon	B.1.427/ B.1.429	20C/S.452R	GH/452R.V1	VOC 202012/02	United States of America	Mar 2020	S13I, W152C, L452R, D614G
Zeta	P.2	20B/S.484K	GR	VOC 202101/02	Brazil	Apr 2020	E484K, D614G, V1176F
Eta	B.1.525	20A/S484K	G/484K.V3		Multiple countries	Dec 2020	Q52R, A67V, Δ69-70, Δ144, E484K, D614G, Q677H, F888L
Theta	P.3	20B/S:265C	GR		Philippines	Jan 2021	Δ141-143, E484K, N501Y, D614G, P681H, E1092K, H1101Y, V1176F
Iota	B.1.526	20C/S:484K	GH		United States of America	Nov 2020	L5F, (D80G*), T95I, (Y144-*), (F157S*), D253G, (L452R*), (S477N*), E484K, D614G, A701V, (T859N*), (D950H*), (Q957R*)
Kappa	B.1.617.1	21A/S:154K	G/452R.V3		India	Oct 2020	T95I, G142D, E154K, L452R, E484Q, D614G, P681R, Q1071H
Lambda	C.37	20D	GR/452Q.V1		Peru	Aug 2020	G75V, T76I, L452Q, F490S, D614G, T859N, RSYLTPGD246-253N

On June 14, 2021, the C.37 variant was assigned a global VOI by WHO and was given the label “Lambda” (14). Lambda was subsequently identified as a VOI in Canada on July 20, 2021 (2). The goal of this living summary on the SARS-CoV-2 VOC and VOI literature is to highlight the existing data on the VOI C.37 (Lambda), its epidemiology and how the attributes of this variant may impact the management of the pandemic. This living

evidence profile on Lambda is part of a larger project that summarizes the data on each VOC, captures data on VOIs and develops summaries for the VOIs as needed. The focus will be on changes to epidemiological parameters (e.g., transmission rates, clinical outcomes of severity and mortality, shifts in age groups affected or asymptomatic proportions), impacts on diagnostic tests, immune evasion/vaccine effectiveness and impacts on other public health measures. The full dataset in Excel can be accessed here and filtered by the VOCs and VOIs of interest. The recent living evidence review on VOCs (Alpha, Beta, Gamma, Delta) can be requested here.

In this summary, "original variant" refers to any variant that was not designated as a VOC or VOI.

Key Points

As of August 10, 2021 there were 9 studies that report on the Lambda VOI. No studies were excluded due to the limited evidence available on the Lambda variant. Individual study details of all studies for the C.37 lineage (n=9) can be found in the Excel dataset accessed here.

Currently in Canada, the larger provinces, British Columbia, Alberta, Ontario, and Quebec have reported cases of the Lambda variant (2).

Lambda Spread/ Epidemiology

- The earliest record of Lambda on the Global Initiative on Sharing Avian Influenza Data (GISAID) is from Argentina on November 8, 2020 (5, 6), however Bayesian tip-dating analysis estimates its emergence in July 2020 (January-October 2020) (6).
- Analysis of Lambda sequences revealed that it emerged in July 2020 and the earliest sequenced sample was from August 2020 in Peru and November 2020 in Argentina. Despite sequence analyses revealing emergence and sample sequencing as early as July 2020, Lambda was first officially reported in Lima, Peru in December 2020 and was present in 1/192 (0.5%) of genomes (5, 6, 14). It expanded to 20.5%, 36.4%, 79.2%, and 96.6% of genomes in January, February, March, and April 2021, respectively (5).
- Across South America the percentage of the Lambda sequence was increasing in Peru, Chile, and Argentina starting as early as November 2020 until June 2021, by which time the variant was also identified globally (5-10). By the end of June 2021, there were 1,908 Lambda sequences identified from 26 countries where sequencing could detect Lambda (6).

Lambda Mutations

- The spike protein of the consensus sequence of the Lambda variant bears six substitution mutations (G75V, T76I, L452Q, F490S, D614G and T859N) which are relatively highly (> 90%) conserved and a 7-amino-acid deletion in the N-Terminal Domain (NTD) (RSYLTPGD246-253N), which is also highly

conserved (15% do not harbour the mutation), the latter mutation is reported to be responsible for the infection spread in South America (6).

Transmissibility

- A pseudotyped virus (a virus consisting of a surrogate viral core that is surrounded by an envelope of surface glycoproteins of another virus of interest) carrying the Lambda spike was found to have significantly increased infectivity by up to 2-fold compared to Alpha, Gamma, and original variants (6, 8, 11). The T76I and L452Q mutations were found to be responsible for the higher infectivity of the Lambda variant, while insertion of the RSYLTPGD246-253N mutation was not found to affect viral infectivity (6).

Clinical severity and risk factors

- There have been no studies to date documenting its virulence, severity, duration of the disease or severity risk factors.

Immune Escape

- *In vitro* studies showed a reduction (1.5 – 6.1 fold) in neutralization of Lambda with convalescent and vaccinated sera compared to the original variants (6, 8, 11-13).
- Resistance of the Lambda variant to BNT162b2 (Pfizer) and mRNA-1273 (Moderna) vaccines was attributed to both the L452Q and F490S mutations. (6, 12). Further, the RSYLTPGD246-253N mutant exhibited a significant resistance to the vaccine-induced neutralization and the G75V, T76I, GT75-76VI and T852N mutations did not affect the vaccine-induced neutralization (6).
- Lambda had 3.6-fold increased resistance to neutralization by monoclonal antibody REGN10987 (Imdevimab) compared to the original variant (11), but Lambda was neutralized by REGN10933 (Casirivimab) alone and by a REGN10933 (Casirivimab) and REGN10987 (Imdevimab) cocktail with no significant decrease in neutralizing titers (11, 12).

Overview of the Evidence

Study designs on VOC/VOI research range widely from observational studies with a high risk of bias to double blind randomized controlled trials (RCTs) with a lower risk of bias. All studies included in the review of the Lambda variant were considered a very low level of evidence. While certainty in the evidence from observational studies may be upgraded for a given outcome when multiple studies are in agreement and have prospective designs, there were only two retrospective analyses of surveillance data available. Two case reports are also included (despite the fact that they are considered to be a very low level of evidence) due to the limited evidence currently available on the Lambda variant. Lastly, five *in vitro* experiments were identified. These experiments are generally used to generate hypotheses that are then tested with more rigorous study design. For this review, study designs were identified, but no formal risk of bias assessment was conducted for each study. A summary indication of the level of confidence of the evidence was given for each category of study. The greatest amount of evidence was available on infectivity, *in vitro* resistance to

vaccination, and VOI emergence over time. Given the currently very limited published evidence base, there are substantial gaps in knowledge for transmissibility, secondary attack rate, serial interval, public health measures/interventions, clinical severity parameters, and immune escape parameters re-infection after infection and breakthrough infection after vaccination/vaccine efficacy or effectiveness. Thus, additional studies are needed to improve confidence in the current summary results, and to fill in existing knowledge gaps regarding the Lambda variant.

CONTENTS

LAMBDA

The excel dataset includes summaries of individual studies and can be accessed here. Below is the detailed evidence profile developed for Lambda.

Categories of evidence in the table below include the following:

Transmissibility includes changes in transmissibility, secondary attack rates, serial interval (time interval between the onset of symptoms in the primary and secondary case), and estimates of selective advantage.

Clinical Severity includes proportion of infections that are symptomatic, proportion of severe disease and mortality as well as risk factors for severe disease or mortality, viral load (Ct value is often used as a proxy for viral load with lower Ct value indicative of higher viral load), infectious period, incubation period. Note risk factors for severe disease would include special populations, e.g., persons who are pregnant (when reported).

Immune Escape includes changes to vaccine efficacy/effectiveness, risk of re-infection in humans, animal models, *in vitro* or *in silico* experiments as well as impacts on therapeutics when reported.

Diagnostic / Detection Test Failure is captured in the table.

Other Epidemiology includes all studies that document the emergence and spread of VOCs in a geographic area, ecological studies that examine VOC spread and risk factors for hot spots, and studies on effective public health measures/interventions against VOCs, with genomic epidemiology as subcategories when reported.

Table 2: Evidence Profile of Lambda VOI (n=9)

CATEGORY	KEY SUMMARY OUTCOMES	OVERVIEW OF THE EVIDENCE
Transmission Efficiency		
Transmissibility	No studies	
Secondary Attack Rate	No studies	
Serial Interval	No studies	
***In vitro* studies of infectivity** Compared to VOCs and original variant	• A pseudotyped virus carrying the Lambda spike was found to have significantly increased infectivity compared to pseudotyped viruses carrying the D614G mutation, Alpha, and Gamma spikes(6, 8). • A pseudotyped virus carrying the Lambda spike had significantly increased infectivity by 2-fold compared to wild-type due to a L452Q mutation (11). • Lambda spikes had a 3-fold increase in soluble ACE2 binding compared to wild-type (11, 12). • T76I and L452Q mutations are responsible for the higher infectivity of Lambda, while insertion of the RSYLTPGD246-253N mutation was not found to affect viral infectivity (6).	4 *in vitro* studies. Very low level of evidence.
Public health measures / interventions	No studies	
Clinical Severity		
Virulence / Severity or Duration of Disease	No studies	
Severity Risk Factors	No studies	
Mortality	No studies	
Mortality Risk Factors	No studies	
Viral Load	No studies	

Infectious Period	No studies	
Incubation / Latent Period	No studies	
Immune Escape - Potential Impact on Vaccine Efficacy/Effectiveness, Possibility of Re-infection		
Re-infection after Infection	No studies	
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness	No studies	
***In vitro* studies Convalescent Sera** Compared to original variant	• Lambda had 3.3-fold higher resistance to neutralization by convalescent sera compared to the wild-type (11). • Neutralizing titers from individuals infected prior to the emergence of Lambda were decreased 3.2-fold relative to D614G (12).	2 *in vitro* studies. Very low level of evidence.
***In vitro* studies Vaccinated Sera** Compared to Original Variant	• Lambda had 3.0-fold higher resistance to neutralization by sera from BNT162b2 (Pfizer)-vaccinated individuals compared to wild-type (P≤0.001) (11). Lambda was 1.5-fold, on average (2.63-fold at a maximum), more resistant to neutralization by BNT162b2-induced antisera than the parental D614G S antisera (6). Antibodies from fully vaccinated BNT162b2 (Pfizer) sera cross-reacted on Lambda with a 3.2 fold decreased titer compared to D614G (12). At 90-days post injection with BNT162b2 (Pfizer), the neutralizing titer against Lambda was decreased 4.2-fold (12). • Lambda had 2.3-fold higher resistance to neutralization by sera from mRNA-1273 (Moderna)-vaccinated individuals compared to wild-type (P≤0.05) (11). Antibodies from sera collected 7-days post second injection with mRNA-1273 (Moderna) cross-reacted on Lambda with a 2.6 fold decrease in titer. At 80-days post injection, the neutralizing titer against Lambda was decreased 3.6-fold (12). • Resistance of the Lambda variant to BNT162b2 (Pfizer) and mRNA-1273 (Moderna) vaccines was attributed to both the L452Q and F490S mutations (6, 12). Further, the RSYLTPGD246-253N (7-amino-acid deletion in the NTD) mutant exhibited a significant resistance to the BNT162b2 (Pfizer) vaccine-induced neutralization) and	5 *in vitro* studies. Very low level of evidence.

	the G75V, T76I, GT75-76VI and T852N mutations did not affect the BNT162b2 (Pfizer) vaccine-induced neutralization (6). • At 82 days post injection with Ad26.COV2.S (Janssen), compared to D614G, the neutralizing titer against Lambda was decreased 6.1-fold (12). • A study evaluating plasma samples from CoronaVac-vaccinated individuals showed that the ID50 neutralization titer decreased by a factor of 3.05 (95% CI: 2.57 – 3.61) for Lambda compared to the wild-type (8). • The geometric mean titer (GMT) of neutralization of Lambda was reduced by 4.6 fold compared to WA1 by sera from mRNA-vaccinated participants (13).	
***In vitro* studies Therapeutics** Compared to Original Variant	• Lambda had 3.6-fold increased resistance to neutralization by monoclonal antibody REGN10987 (Imdevimab) compared to wild-type (11). • Lambda was neutralized by REGN10933 (Casirivimab) with no decrease in neutralizing titers compared to wild-type (11). • Lambda was neutralized by a Regeneron monoclonal antibody therapeutic consisting of both REGN10933 and REGN10987 with no significant decrease in neutralizing titers compared to wild-type (11, 12).	2 *in vitro* studies. Very low level of evidence.
Diagnostic / Detection Test Failure		
Testing and Detection	No studies	
Other Epidemiology		
VOC Emergence Over Time	• Analysis of Lambda sequences revealed that it emerged on July 12, 2020 and the earliest sequenced sample was from August 2020 in Peru and then Argentina November 2020 (5, 6, 14). The percentage of the Lambda sequence was increasing in South American countries including Peru, Chile, and Argentina from November 2020 until June 2021. By the end of June 2021 there were 1,908 Lambda sequences identified from more than 26 countries including Chile, USA, Peru, Argentina, Germany, Mexico, Spain, and Ecuador (5, 6, 14). The RSYLTPGD246-253N (7-amino-acid deletion in the NTD) mutant of the Lambda variant is shown to have emerged and quickly became the dominant version at the beginning of 2021 while Lambda cases were rapidly increasing (6).	2 surveillance studies, 2 *in vitro* studies and 2 case reports. Very low level of evidence.

	○ Lambda was first officially reported in Lima, Peru in December 2020 and was present in 1/192 (0.5%) of genomes. It expanded to 20.5%, 36.4%, 79.2%, and 96.6% of genomes in January, February, March, and April 2021, respectively (5). ○ Lambda has expanded rapidly in Chile and Argentina, reaching 33% and 12% of all sequenced genomes on GISAID by April 2021, respectively (5). • Molecular surveillance from Argentina revealed that the Lambda variant showed a continuous increase since epidemiological week 20 of 2021 (EW 20/2021) in the city of Buenos Aires (CABA) and Great Buenos Aires (GBA), reaching frequencies of 48.4% (95% CI = 36.6-60.4) in the EW 20/2021. The proportion of cases associated with Alpha, Gamma, and Lambda among individuals with no travel history or contact with travelers in CABA and GBA surpassed 98% of the total samples in EW 20/2021. Between EW 9/2021 and EW 20/2021, north GBA presented 9/39 cases of Lambda (23.1%), west GBA presented Lambda in 58/176 cases (33.0%), CABA presented Lambda in 150/508 cases (29.5%), south GBA presented a predominance of Lambda (127/253 cases, 50.2%) (7). • In Chile, up to June 24, 2021 there was a dominance of Gamma and Lambda variants, together accounting for 79% of 3695 sequences analyzed (8). • A surveillance study reported two cases of possible coinfection between Alpha and Lambda in the city of Buenos Aires (CABA) and these cases will be further analyzed (7). • The spread of the Lambda variant to Brazil and Italy are documented in case reports. One described the first case of the Lambda variant in southern Brazil, who had travelled to Argentina (9). The second described a 53-year old female Peruvian immigrant who entered Italy on June 2, 2021 after an indirect flight Lima-Madrid-Milan, who initially tested negative leaving Peru on June 1, but tested positive on follow-up in Italy on June 11. She was confirmed to be infected with the Lambda variant (10). • The S protein of the consensus sequence of the Lambda variant bears six substitution mutations (G75V, T76I, L452Q, F490S, D614G and T859N) which are relatively highly (> 90%) conserved and a 7-amino-acid deletion in	

	the NTD (RSYLTPGD246-253N), which is also highly conserved (15% do not harbour the mutation). The data suggest that there are at least two virological features on the Lambda variant: increasing viral infectivity (by the T76I and L452Q mutations) and exhibiting resistance to antiviral immunity (by the RSYLTPGD246-253N, L452Q and F490S mutations) (6).	

CFR = case fatality rate, CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, VE = vaccine effectiveness, OR= odds ratio, aOR= adjusted odds ratio, GISAID = global initiative on sharing avian influenza data

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a Refworks database and an Excel list that can be searched. One of the foci is to identify studies as variants of concern or under investigation. Studies identified under this foci were further characterized in our VOC/VOI database and Lambda results were extracted into this review. A cross check for relevant articles was also conducted within the databases using targeted keyword searching (C.37 OR Lambda).
This review contains research published up to July 29, 2021.
Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Review
The Office of the Chief Science Officer facilitated the review of this document, which included suggestions from a scientific editor, peer-review by a subject matter expert, and input from a senior policy advisor with a science-to-policy perspective.

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APPENDIX

a) OTHER RESOURCES

Reference	Description
Living Evidence Review on SARS-CoV-2 variants Australia On-going, last examined August 16.	This table highlights recent relevant evidence under the different categories of study similar to what has been laid out in the profiles in this review.
CDC VOC page	Summary of each VOC is available.
WHO situation reports	Summary includes a VOC section.
Grey lit	
SAGE communications	The vaccines and variants page has reports and summaries on VOCs.
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. 2020 Dec to present	Technical reports compile information from various studies and surveillance across the UK on the VOC and VOIs that are circulating. There is a lot of overlap from these reports and research publications.

VOC Comparison Table of Alpha, Beta, Gamma, and Delta

Context

SARS-CoV-2 **variants of concern** (VOCs) are circulating variants that have been flagged by national or global public health organizations. VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures and/or diagnostic detection failures (1-3). Canada has established a national definition (2). This summary table highlights the key data from individual VOC risk profiles (available upon request) on B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma) and B.1.617.2 (Delta).

Overview of the Risk Profiles

A total of 543 Alpha, 341 Beta, 187 Gamma and 94 Delta studies were identified and the full dataset can be accessed here. Data were summarized on 293 Alpha, 65 Beta, 39 Gamma up to July 1 and 67 Delta up to July 29, 2021 studies on the following key categories of evidence and were compared to the original variants (non-VOC variants) in circulation at the time of the study unless otherwise stated:

Transmissibility includes changes in transmissibility, secondary attack rates, and estimates of selective advantage.

Clinical Severity includes proportion of infections that are symptomatic, proportion of severe disease and mortality as well as risk factors for severe disease or mortality, viral load, infectious period, incubation period. Note risk factors for severe disease would include special populations e.g., persons who are pregnant if they are reported.

Immune Escape includes changes to vaccine efficacy, risk of re-infection in humans, animal models, *in vitro* or *in silico* experiments as well as impacts on therapeutics if reported.

Other Epidemiology includes all studies that document the emergence and spread of VOCs in a geographic area, ecological studies that examine VOC spread and risk factors for hot spots, and studies on effective public health interventions against VOCs, genomic epidemiology as subcategories.

Studies not summarized in the evidence profiles include case reports or case series, point prevalence estimates, animal studies, zoonotic investigations, predictive models in which the time period has already passed, cell infectivity, binding affinity, or genomic characterization studies, and most *in vitro* studies looking at neutralization by convalescent and/or vaccinated sera, and therapeutic products. An excel dataset with summaries of all the studies on the Alpha, Beta, Gamma, Delta VOCs as well as all variants of interest can be accessed here. Overall, the level of evidence was low to moderate.

Reference: Emerging Science Group of the Public Health Agency of Canada. Living Summary of SARS-CoV-2 Variants of Concern for Alpha, Beta, Gamma and Delta. July 2021. Full report available from: ocsoevidence-bcscdonneesprobantes@phac-aspc.gc.ca

TABLE 1: SUMMARY OF KEY EVIDENCE FROM THE ALPHA (N=543), BETA (N=341), GAMMA (N=187) AND DELTA (N=94) RISK PROFILES.

CATEGORY	P.1 (GAMMA) UPDATED JUL 1, 2021	B.1.351 (Beta) UPDATED JUL 1, 2021	B.1.1.7 (ALPHA) UPDATED JUL 1, 2021	B.1.617.2 (DELTA) UPDATED JUL 29, 2021
TRANSMISSION EFFICACY				
Transmissibility Compared to Original Variant unless otherwise stated	6 surveillance data analyses and 1 cross-sectional study: • Increased transmission ranging from 12%-160% has been reported in countries from South America, North America, Europe and Africa. • One Canadian study of household transmission reported Gamma had 62% increased transmissibility and 8% higher secondary attack rates. Low level of evidence.	6 surveillance studies and 1 predictive model: • Studies from multiple countries report an increased transmissibility of 20% to 175%. • One Canadian study of household transmission reported Beta has 58% increased transmissibility and a 31% higher secondary attack rate. Low level of evidence.	54 surveillance and observational studies: • 91% of studies reported increased relative transmissibility of Alpha (1-$R_{voc}/R_{original\ variant}$) ranging between 34-118% higher across studies from North America, Europe, Middle East, and Asia. • Canadian studies (n=3) reported higher transmissibility of 34%-63% and a 20%-31% higher secondary attack rate for Alpha. • Other secondary attack rates among household transmission studies were 30-88% higher in Norway, Denmark, Germany, Israel, and UK. Low to moderate level of evidence.	13 surveillance and observational studies: • Delta's estimated higher transmissibility over Alpha ranges from 43-120% in North America, Europe and Asia. • A global study estimated higher transmissibility of 97% (95%CI: 76-117), 55% (43-68), 60% (48-73), and 34% (26-43) compared to original variant, Alpha, Beta, and Gamma, respectively. • Recently revised surveillance data from the UK reported 3.5-8% higher secondary attack rates for Delta vs. Alpha, however a UK case control study estimated this to be 64%. Low level of evidence.
CLINICAL SEVERITY				
Virulence / Severity or Duration of Disease	2 surveillance data analyses: • In Europe, a higher proportion of cases were	2 surveillance studies and 2 observational studies: • Studies from several European countries	25 surveillance and observational studies: • Conflicting evidence on whether there are fewer	5 surveillance and observational studies: • Three studies reported a higher risk of

CATEGORY	P.1 (GAMMA) UPDATED JUL 1, 2021	B.1.351 (Beta) UPDATED JUL 1, 2021	B.1.1.7 (ALPHA) UPDATED JUL 1, 2021	B.1.617.2 (DELTA) UPDATED JUL 29, 2021
Compared to Original Variant unless otherwise stated	hospitalized vs. original variant (20% vs. 7.5%: aOR 2.6, 95%CI 1.4-4.8). • In Europe, higher odds of being admitted to ICU (aOR 2.2, 95%CI 1.8-2.9). • Exponential growth of hospitalized cases was reported in Brazil during predominance of Gamma. Low level of evidence.	reported higher odds of hospitalization for Beta compared to the original variant (OR=3.6) and Alpha (OR= 1.6). • Conflicting evidence for ICU admissions due to Beta has been reported across different settings, including increased odds (OR=3.3) across several European countries, and a lower risk in South Africa and no association in France. Low level of evidence.	symptomatic cases among Alpha infections. • Six studies found higher odds of hospitalization (OR 1.25–2.25) and one reported no difference. • Four studies found higher odds of ICU admission (OR 2.15-3.31) and one study reported no difference. • Two studies reported Alpha cases had higher rates of hypoxia on admission to hospital. • Longer symptom duration (≥7 days), fewer loss of smell and taste symptoms, and more sore throat symptoms occurred in Alpha cases in two studies. Moderate level of evidence.	hospitalization; OR= 2.2 Canada compared to original variant and OR=1.5, aHR= 1.45-2.26 England, HR= 1.85 Scotland compared to Alpha, while no difference was reported in Houston, Texas. • Two studies reported a higher risk of ICU admission; OR= 3.9 Canada and aOR 4.9 Singapore compared to original variant and OR=2.01 Canada compared to Alpha. Low level of evidence.
Severity Risk Factors Compared to Original Variant unless otherwise stated	1 surveillance data analysis from Europe: • Odds of hospitalization in 20-79 age groups were 3.0 - 13.1 times higher.	1 surveillance study and 2 observational studies: • Odds of hospitalization among adults aged 40-79 were 3.5-3.6 times higher in several European countries and hospitalized Beta cases in	13 observational studies: • Indicators of changes in severity with the Alpha variant were not consistent, some reported age-stratified risk of hospitalization and increased odds in adult age groups between 20-59 years old, while	1 surveillance study: • Analysis suggested there may be higher risk of severe outcomes in some younger age groups. More data is needed.

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	• Odds of ICU admission for ≥40 year olds was 2.9–13.9 times higher. • Pre-existing conditions were lower in Gamma cases vs. original variant cases (27.8% vs 89%, p<0.001). Low level of evidence.	South Africa were significantly older (57 vs. 54 years, p=0.03). • Odds of ICU admission for adults aged 40-59 years were 8 times higher in several European countries, but not different in a study from France. • Beta cases were less likely to have comorbidities in studies from Europe and South Africa. Low level of evidence.	others reported no associations. Higher risk in males and those with comorbidities were also reported. • ICU admission due to Alpha was associated with being male, higher age, and comorbidities in two studies. Low to moderate level of evidence.	Very low level of evidence.
Mortality Compared to Original Variant unless otherwise stated	1 surveillance data analysis, 1 ecological study, and 1 predictive model: • There was conflicting evidence on mortality risk for Gamma in studies from Brazil indicating a higher mortality risk (RR = 1.5) and a study from Europe reporting a borderline lower risk (RR=0.6).	1 surveillance study and 2 observational studies: • Beta cases were not associated with a change in mortality in one surveillance study in European countries. • Two retrospective cohort studies from South Africa and France reported increased ICU mortality among Beta cases	19 surveillance and observational studies: • Associations with mortality were conflicting across studies (11 indicated increased mortality, 7 found no change, 2 lower mortality) for Alpha infections.	1 retrospective cohort: • In this Canadian study Delta mortality risk was increased by 137% over the original variants and 59% over other VOCs.

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	Low level of evidence.	compared to original variant and Alpha cases. Low level of evidence.	Moderate level of evidence.	Low level of evidence.
Mortality Risk Factors Compared to Original Variant unless otherwise stated	1 surveillance data analysis: • Brazil data not confirmed by whole genome sequencing, reported an increase in mortality for cases<60 years (from 18% to 28%) and higher risk of mortality among women aged 20-59 with no pre-existing conditions (RR 5.6-7.7). Very low level of evidence.	No studies. No evidence.	2 surveillance data analyses and 1 retrospective cohort study: There was no agreement across studies on whether any risk factors were associated with Alpha mortality risk including age, and sex, and ethnicity, but one study did report that Alpha infections with comorbidities were higher risk. Low level of evidence.	No studies. No evidence.
Viral Load Compared to Original Variant unless otherwise stated Ct (cycle threshold) value was used as a	3 surveillance data analyses: • Viral load from Gamma cases were lower than Alpha but higher than the original variant. • Viral load from Gamma cases was ~10-fold	2 surveillance studies and 1 cross sectional study: • Studies from France report a higher viral load of Beta compared to the original variant, but is lower compared to Alpha.	28 observational studies and surveillance analyses: • With the exception of one study, most reported lower Ct values or higher estimated viral loads. The median order of magnitude higher varies across studies and target	5 surveillance and observational studies: • Four studies reported that Delta viral loads may be higher than Alpha and the original variant. • One study reported no significant difference in viral loads for Delta

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proxy for viral load (where lower Ct values indicate higher viral load).	higher than original variants in Brazil. Low level of evidence.	 Low level of evidence.	protein from 2 to 10 fold differences. Low to moderate level of evidence.	compared to non-Delta infections among vaccinated healthcare workers (most of whom were fully vaccinated). Low level of evidence.
Infectious Period Compared to Original Variant unless otherwise stated	1 surveillance study from European countries: • No significant difference in infectious period for combined Gamma and Beta data vs. original variant (95% CI of the HR: 0.79-1.06), measured by the duration of decline in viral load. Low level of evidence.	1 surveillance study from European countries: • No significant difference in infectious period for combined Gamma and Beta data vs. original variant (95% CI of the HR: 0.79-1.06), measured by the duration of decline in viral load. Low level of evidence.	1 prospective study , 1 longitudinal study and 1 surveillance analysis: • Alpha was reported to have a longer infectious period in all studies, although the magnitude of the increase was highly variable across studies ranging from 0.86 days to 5.1 days. Low level of evidence.	No studies. No evidence.
Incubation Period Compared to Original Variant unless otherwise stated	No studies.	No studies.	1 retrospective cohort and 1 surveillance report: • Mean incubation period was 3.53 vs. 5.71 for original variant in a small study (n=60). • Public Health England also estimated incubation period at median 4 days.	1 contact tracing study and 1 surveillance report: • Small study from China reported a shorter time interval between exposure and first PCR positive test in quarantined cases was reported for Delta (4 days,

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				IQR 3-5) compared to cases from the early 2020 epidemic (6 days, IQR 5-8). • Public Health England also estimated incubation period at median 4 days. Very low level of evidence.
	No evidence.	No evidence.	Very low level of evidence.	
IMMUNE ESCAPE – Re-infection and Impact on Vaccine Efficacy				
Re-infection after Infection Compared to Original Variant unless otherwise stated	2 surveillance data analyses: • Two studies from Brazil suggest there may be substantial reinfections with Gamma, however this is based on ecological analyses and needs further study. Very low level of evidence.	• Only case reports have been reported and are not summarized. Very low level of evidence.	3 surveillance, cohort and ecological studies: • There is no change in the re-infection rate (0.7-0.9%) with Alpha based on data from the UK and USA. Low-moderate level of evidence.	1 prospective cohort study and 2 predictive models: • In the UK there have been more reinfections with Delta (aOR 1.46) compared to Alpha • Predictive models estimate Delta can evade 16-55% of immune protection from prior infections. Low level of evidence.
Breakthrough Infection After Vaccination / Vaccine Efficacy or Effectiveness Compared to Original Variant	3 case-control studies and 1 surveillance data analysis: Among vaccinated: • One Canadian vaccine effectiveness (VE) study reported the BNT162b2 (Pfizer) and mRNA-1273 (Moderna) vaccines have	10 studies including RCTs, cohorts, case-control studies, a surveillance study, and an outbreak investigation: Among fully vaccinated: • VE against Beta infection was 50%-93.48% for	27 studies that included RCTs, cohorts and surveillance studies: • Most VE studies comparing the Alpha variant with the original variants have reported reduced protection after the first dose of mRNA (BNT162b2 (Pfizer), mRNA-1273 (Moderna)) and ChAdOx1 (AstraZeneca)	5 surveillance data analyses, 1 outbreak investigation, 1 RCT, and 3 test negative case control studies: • Four studies on VE report a reduction in protection against Delta infection (n=2) and symptomatic disease (n=2) compared to

CATEGORY	P.1 (GAMMA) UPDATED JUL 1, 2021	B.1.351 (Beta) UPDATED JUL 1, 2021	B.1.1.7 (ALPHA) UPDATED JUL 1, 2021	B.1.617.2 (DELTA) UPDATED JUL 29, 2021
unless otherwise stated	reduced protection against symptomatic infection with Gamma after the first (VE = 43% vs. 61%) and second dose (VE= 88% vs. 93%), although the confidence intervals overlap in both comparisons. • Two studies on CoronaVac (Sinopharm) reported VEs 42-50% against infection, 59% hospitalizations and 71% mortality. • One underpowered study (n=20) indicated Gamma was not over represented in breakthrough infections. Low level of evidence.	BNT162b2 (Pfizer-BioNTech). • VE against symptomatic infection was ≥ 88% for BNT162b2 (Pfizer) or mRNA-1273 (Moderna), 10.4% for ChAdOx1 (AstraZeneca), and 51% for NVX-CoV2373 (Novavax). • VE against moderate disease caused by Beta was 52%-64% after Ad26.COV2.5 (Janssen) vaccine. • VE against severe disease or mortality due to Beta was 97.4%-100% after second dose of BNT162b2 (Pfizer) and 73-82% for Ad26.COV2.5 (Janssen). • Breakthrough infections in long-term care facilities in France and Canada show no indication that the Beta breakthrough rate is higher than expected, however one underpowered study (n=20) in the USA indicated	vaccines, but equivalent protection after the second dose of vaccine. • Many studies report breakthrough infections of Alpha, however there is conflicting evidence on whether they are more common among Alpha VOCs than would be expected. • Breakthrough Alpha infections compared to unvaccinated Alpha cases had a shorter infectious (7.1 vs. 31 days) period and viral load (6.45 vs. 8.15 log10 copies/mL) in one study and no difference in viral load in another, and less severe outcomes were reported in vaccinated cases. Low to moderate level of evidence.	Alpha after the first dose (e.g., 56% Delta vs. 66% Alpha for BNT162b2/ 72% vs. 83% for mRNA-1273 and 67% vs. 64% for ChAdOx1). • Protection following two doses reported a 7.5-10% reduction in protection in one study and comparable protection after the second (>88% for BNT162b2 and mRNA-1273 and 63% for ChAdOx1) in another compared to Alpha. • Four studies on breakthrough infections from UK, USA and India indicated a higher than expected rate of Delta breakthrough cases was observed. Low to moderate level of evidence.

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		Beta was overrepresented in breakthrough infections. Low to moderate level of evidence.		
VARIANT SPREAD AND PUBLIC HEALTH MEASURES				
Spread of the Variant Globally compared to Original Variant unless otherwise specified.	4 surveillance analyses 1 cross-sectional, 1 ecological study and 1 predictive model in Brazil (3) / Colombia (1) / USA (1)/ Italy (1)/ North America (1): • Rapid spread of Gamma in Brazil and Columbia is reported in 4 studies from Nov 2020 onward. • In countries e.g., USA and Italy, Gamma cases remained stable while Alpha was dominant and growing and a similar trend is reported in a predictive model that included Delta where Gamma is predicted to remain at 5% by Mar 2022 assuming 75% vaccine coverage in North America.	6 surveillance analyses and 2 predictive models from South Africa (2) / Canada (1) / Comoros Islands (1) / Bangladesh (1) / multiple countries (2)/ North America (1): • Beta emerged in South Africa around Aug 2020 and was first detected in Oct 2020. First detection of Beta in other countries started in Dec 2020. • A predictive model of North America that included Delta predicts Beta remains stable (<5%) of cases from July 2021 gradually increasing to 5% in Mar 2022 assuming 75% of the population is vaccinated in July 2021. • In a predictive model, Beta outgrows Alpha in regions	147 studies report on emergence and spread of Alpha: • Many countries including Canada are reporting that the proportion of new cases attributed to Alpha has declined and was surpassed by Delta in June/July 2021. • A predictive model forecasting variants in North America estimates Alpha will reach close to 0% of the cases by Oct 2021.	18 surveillance studies and 6 reports: • Delta has become the dominant variant in Canada overtaking Alpha in late June. • Surveillance data from the UK and India on the introduction and growth rate of Delta from February to July 2021 indicate Delta now represents 91-99% of cases. • Studies from the USA and Japan found that the Delta variant is replacing Alpha as the dominant variant. • The Delta VOC classification includes sub-lineages AY.1, AY.2 and AY.3 for which small numbers of cases for these sub-lineages have

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	Low level of evidence.	with a high seroprevalence (20-40%) because of assumed 25-75% immune evasion by Beta. Low level of evidence.	Moderate level of evidence.	been reported in several countries. Low level of evidence.
Changes in Public Health Measures (PHMs) or the stringency of PHMs to control the VOC compared to Original Variant unless otherwise specified.	1 surveillance study: • Evidence of the impact of social distancing mandates in Brazil show a large reduction in Re values, but in Apr 2020 the Re of original variant was reduced from 2.6 to below 1.0 and in Jan 2021 the Re of Gamma was only reduced from 2.6 to 1.2, however there could be many confounding factors besides Gamma that impact Re.	No studies.	14 studies; 10 predictive models, 1 ecological study and 3 surveillance studies: • Studies on stringency of restrictive measures show the impact of higher stringency (more than in other waves or outbreaks) on reducing Rt or the number of cases given the circulation of Alpha in the UK, Canada, Portugal, France. • No change to quarantine and test strategies were needed in a model based on the EU. • Personal protective measures such as masks and physical distancing were explored in two models of the US and a workplace, where personal protective measures were less	5 predictive models: • Four predictive models explored the impact of public health measures in India, France, Germany, and Australia to control the epidemic in the context of Delta. Higher risk of resurgence was shown when interventions such as masking and restrictive policies that limit contact rates were lifted prematurely or when vaccine rollout slowed down or did not speed up depending on the country. • The fifth model cautions against allowing fully vaccinated people to stop

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	Very low level of evidence.	No evidence.	effective with Alpha in circulation. • Three models explored vaccination strategies and the need to vaccinate more of the population to reduce Ro below 1 with Alpha circulating. Very low level of evidence.	adhering to public health measures in Europe. Very low level of evidence.

CI = confidence interval, Ct = cycle threshold, ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, OR= odds ratio, aOR= adjusted odds ratio, aHR = adjusted Hazard Ratio, aPR= adjusted Prevalence Ratio, RCT= Randomized Controlled Trial, VE= vaccine effectiveness.

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Rapid Review on Protective Immunity

Context

Understanding the extent and limits of protective immunity has important implications for the COVID-19 pandemic. An evidence review was conducted to address whether antibodies to SARS-CoV-2 confer immunity against reinfection; to determine if protective immunity lasts more than 6 months; and to identify if past infection with wild-type SARS-CoV-2 protects against variants of concern (VOC).

Key Findings

There were 49 studies identified:15 cohort studies on risk of reinfection, 21 studies on antibody kinetics and other immunity markers >6 months post initial infection, 10 studies on immunity and the new VOCs and three systematic reviews. The appendix summarizes 21 case reports of confirmed reinfection.

Documented cases of confirmed reinfection of COVID-19, based on genomic data, are rare. In most cohort studies, reinfection was based on serology, documented proof of a non-infected phase between infections and PCR evidence of reinfection.

- Cohort studies on reinfection that targeted the general population or healthcare workers indicate a low risk of reinfection (0% - 3.4%) compared to the COVID-19 susceptible population (1.3 – 27.7%). Data on time to reinfection was highly variable, with a median of 52-172 days across studies and a range of 13-250 days.
- Older age, duration of symptoms, and number of symptoms were correlated with higher IgG antibody levels after primary infection. Higher and prolonged serum IgG antibody levels were correlated with milder symptoms and a lower risk of reinfection.

Protective immunity lasts at least 6 months:

- Immunity following an infection arises from both B-cell and T-cell responses. Memory B-cell and T-cell activity was elevated and expanded beyond 6 months post infection in 8 studies, which may be better measures of long term protective immunity than circulating antibodies. CD4+ T-cell activity continued to be detected in 92% of individuals between 6-8 months following infection.
- Twenty studies reported on circulating antibodies, 11 of which reported >86% of people remained positive for SARS-CoV-2 specific neutralizing antibodies (NAbs) ≥6 months after infection.

There is preliminary evidence that the extent of cross-protection of the original wild type SARS-CoV-2 for VOCs depends on the variant, with better cross-protection for B.1.1.7 than B.1.351.

Considerations

Greater access to sequencing data is needed to confirm reinfection and the extent of cross-protection between the original wild-type virus and VOCs.

Source: Emerging Science Group of the Public Health Agency of Canada. Emerging Evidence on COVID-19: Rapid Review on Protective Immunity. Full report available from: phac.evidence-donnees.probantes.aspc@canada.ca

Aperçu des éléments de preuve :

Revue rapide de l'immunité protectrice, mise à jour 1

Contexte

Comprendre la portée et les limites de l'immunité protectrice a d'importantes répercussions sur la pandémie de COVID-19. Une revue rapide a été effectuée afin de résumer les éléments de preuve récents sur la question de savoir si les anticorps provenant d'une infection naturelle ou d'une vaccination contre le SRAS-CoV-2 peuvent protéger contre les infections et si l'immunité contre le SRAS-CoV-2 peut durer plus de six mois, ainsi que de déterminer si les preuves actuelles indiquent que la protection peut différer en ce qui concerne les variants préoccupants (VP).

Principales constatations

Cette revue comprend 30 études sur la réinfection après une infection naturelle, 7 études avec série complète sur l'infection sporadique après la vaccination, 36 études et 4 revues sur la cinétique des anticorps et les marqueurs immunitaires cellulaires plus de six mois après l'infection ou la vaccination disponibles, toutes disponibles au 9 avril 2021.

Risque de réinfection et infections sporadiques après la vaccination :

- Les cas documentés de réinfection confirmée à la COVID-19 fondée sur des données génomiques sont rares. Bon nombre des cohortes ont plutôt utilisé des données longitudinales associées au PCR et à la sérologie combinées à des données épidémiologiques pour identifier les infections initiales et de réinfection ou les infections sporadiques.
- On a pu voir que l'infection qui avait entraîné la présence d'anticorps détectables avait également assuré une protection de 96 à 99 % contre la réinfection pendant un maximum de 8 mois pour les cas initiaux confirmés et de 83 à 96 % pour les cas dont l'infection était soupçonnée. Même si le risque de réinfection était semblable, tant pour la souche originale que pour le variant B.1.1.7, une étude a indiqué que la réinfection ne protégeait pas contre le variant B.1.351.
- Un petit nombre d'infections sporadiques qui se sont produites plus de 14 jours après la vaccination complète ont cependant été signalées. L'incidence était plus faible de plus de 90 % après l'administration des vaccins PfizerBioNTech, Moderna ou Oxford-AstraZeneca alors qu'elle était de 85 % après l'infection naturelle.
- Les données préliminaires présentées dans une des études indiquent cependant que la protection contre les infections sporadiques était la même pour le variant B.1.1.7 (VP) que pour la souche originale.

Réactions immunitaires qui se sont produites plus de six mois après l'infection ou la vaccination :

- Onze des études ont indiqué qu'après six mois, les marqueurs immunitaires cellulaires et l'activité des cellules B et T étaient élevés et avaient même augmenté après l'infection, en plus d'être détectables même chez les personnes dont les anticorps circulants étaient devenus indétectables.
- Trente-cinq études ont fait état d'anticorps circulants spécifiques au SRAS-CoV-2 après l'infection naturelle (6 à 12 mois) alors qu'une seule étude a indiqué la même chose après la

vaccination (6 mois). Des anticorps neutralisants, des protéines de spicule ou des anticorps IgG contre le domaine de liaison du récepteur (RBD) ont été détectés chez 70 % à 99 % des personnes six mois après l'infection ou la vaccination.

Facteurs dont il faut tenir compte

On voit une grande variabilité dans les études incluses. Il faut un meilleur accès aux données de séquençage pour confirmer la réinfection et l'étendue de la protection croisée avec les variants du SRAS-CoV-2, ainsi qu'une meilleure compréhension de la corrélation entre les marqueurs immunitaires et l'immunité protectrice.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Preuve émergente sur la COVID-19 : Revue rapide de l'immunité protectrice, mise à jour 1. Rapport complet disponible auprès de : p**phac.evidence-donnees.probantes.aspc@canada.ca**

Emerging Evidence on COVID-19

Evidence Brief on SARS-CoV-2 antibodies in patients that retest RT-PCR positive

Introduction

Do hospitalized SARS-CoV-2 patients that successfully recover with no subsequently positive RT-PCR tests present with SARS-CoV-2 antibody levels or seropositivity rates that differ from those that do retest positive?

Confirmed cases of recovered COVID-19 patients retesting positive after discharge raise concerns of potential reinfection or reactivation of the virus. Research comparing immune response indicators from hospitalized patients that successfully recovered from SARS-CoV-2 with no subsequent positive RT-PCR test compared to those who retested RT-PCR positive were identified to investigate possible relationships between viral RNA test positive and immune response. This report summarizes the COVID-19 literature published up to September 9, 2020, on the differences in the immune response between patients that retest positive and those who do not, as well as SARS-CoV-2 antibody dynamics in relation to the possibility for virus reinfection or reactivation.

In this review, nine studies were identified as fitting the inclusion criteria (please see the Methods section). All nine studies occurred in China. As such, all patients that were discharged from hospital had at least two consecutive negative RT-PCR tests at least 24 hours apart. After discharge, all patients were moved to separate facilities for a mandatory 14 days monitored quarantine. It should be noted that patients that retest positive after discharge are referred to as 'RP patients', however, studies use slightly different terms - retest positive, re-detectable positive, re-positive, or recurrent positive. Patients that do not retest positive are referred to as NRP.

Key Points

- The rate of retesting positive (prevalence of RP) varied from 1.87% of discharged patients (Chen et al., 2020) to 52.7% (Hu et al., 2020) for an average of 16.5% from all studies (397/2412 patients). No study found a difference in sex distribution, but four of the nine studies found RP patients to be significantly younger than NRP patients. A wider review would be needed to explore this further (Chen et al., 2020, Lu et al., 2020, Huang et al., 2020, Yang et al., 2020).
- Of six studies that reported on the positivity rate of patients for IgG or IgM antibodies, RP patients exhibited positivity rates that did not differ from the positivity rates of NRP patients. This indicates that the presence of IgG or IgM antibodies is unlikely to be predictive of retesting positive (Yang et al., 2020, Liu et al., 2020., Yuan et al., 2020, Zou et al., 2020, Huang et al., 2020, Zhu et al., 2020).
- Of the four studies that reported on the level of IgG or IgM antibodies in serum, the results are mixed. One study found that the levels of IgM and IgG antibodies were significantly lower in RP patients than

NRP patients (Chen et al., 2020). A second found no difference (Liu et al., 2020). The third found IgG to be significantly lower in RP patients but no difference in IgM levels (Hu et al., 2020). The fourth found no difference in IgG, but that IgM levels varied over time – initially RP patients had higher IgM titers (week 3 post discharge), but the levels of IgM antibodies eventually became significantly lower for RP patients compared to NRP patients (week 6-8 post discharge) (Yang et al., 2020). This suggests that lower antibody levels might play a role in retesting positive after discharge, but the evidence is not conclusive at this point.

- It is still unclear why patients retest positive. All nine studies took place in China, which enforced a mandatory 14-day quarantine following hospital discharge at separate facilities with individual rooms. Three studies that only followed patients during this period found up to 52.7% of patients retested positive (Chen et al., 2020, Hu et al., 2020, Yuan et al., 2020). One plausible explanation for retesting positive within the two-week quarantine period is a 'reactivation' of the initial infection, following incomplete clearing of the virus. It is also possible that concentration of viral RNA in samples fluctuate during clearance of the virus resulting in two false negative results leading to discharge. In Zou et al., 2020, patients retested positive less often when required to have three negative PCR tests prior to hospital discharge, instead of the usual two.
- One study demonstrated that some patients will retest positive more than once. Upon retesting positive, patients were re-hospitalized until discharged again following two consecutive negative RT-PCR tests, only to retest positive a second, third and even fourth time (Yang et al., 2020).
- Another study found that requiring three consecutive negative tests prior to discharge significantly reduced the chance of retesting positive (Zou et al., 2020). This indicates that false-negatives may play a role in retesting positive after discharge, although an additional review would need to uncover any additional literature on this topic.

Overview of the Evidence

Nine papers were identified, eight of which were cohort studies and one of which was a case control study, scored using the Newcastle-Ottawa Scale Risk of Bias Tool. The maximum score is four for selection criteria, two for comparability between groups, and three for exposure or outcome criteria. Adequate follow-up was cut off at four weeks of follow-up.

- Three prospective cohort studies
  - Clinical, immunological and virological characterization of COVID-19 patients that test re-positive for SARS-CoV-2 by RT-PCR (Lu et al., 2020), score: 4, 0, 3.
  - Recurrence of positive SARS-CoV-2 viral RNA in recovered COVID-19 patients during medical isolation observation (Yuan et al., 2020), score: 4, 0, 1.
  - Viral RNA level, serum antibody responses, and transmission risk in discharged COVID-19 patients with recurrent positive SARS-CoV-2 RNA test results: a population-based observational cohort study (Yang et al., 2020), score: 4, 0, 2.

  - Three retrospective cohort studies
    - The production of antibodies for SARS-CoV-2 and its clinical implication (Hu et al., 2020), score: 4, 0, 1.
    - Clinical features of COVID-19 convalescent patients with re-positive nucleic acid detection (Zhu et al., 2020), score: 4, 0, 2.
    - The issue of recurrently positive patients who recovered from COVID-19 according to the current discharge criteria: investigation of patients from multiple medical institutions in Wuhan, China (Zou et al., 2020), score: 3, 0, 1.
  - Two cohort studies (unclear if prospective or retrospective)
    - Recurrent positive SARS-CoV-2 - immune certificate may not be valid (Liu et al., 2020), score: 4, 0, 1.
    - Kinetics of SARS-CoV-2 Positivity of Infected and Recovered Patients: A Single Center COVID-19 Experience and Potential Implications (Huang et al., 2020), score: 4, 0, 2.
  - One case-control study
    - Clinical Characteristics of Recurrent-positive Coronavirus Disease 2019 after Curative Discharge: a retrospective analysis of 15 cases in Wuhan China (Chen et al., 2020), score: 2, 0, 3.

- Limitations
  - All nine studies occurred in China, with no other jurisdictions producing similar studies.
  - The sample size in some of the studies was small; two studies had fewer than 100 patients (Hu et al., 2020, Zhu et al., 2020) and three studies had fewer than 200 patients (Chen et al., 2020, Liu et al., 2020, Yuan et al., 2020).
  - The duration of follow-up varied greatly. Many studies only followed patients during the mandatory, centralized two-week quarantine that follows discharge from hospital in China, while others followed patients for many weeks afterward. There were also a wide range of RT-PCR testing intervals, spanning from a single test near the end of the 14-day quarantine period, to testing every three to five days. In combination, these limitations casts some doubt on the prevalence of retesting positive and average time to retest positive following discharge.
- Data Gaps
  - All studies that met the inclusion criteria were from China where all cases were hospitalized, caution in extrapolation of these results to other settings is recommended.
  - This review does not consider other factors that may be predictive or contribute to retesting positive following hospital discharge, including immune cell counts, comorbidities, severity of disease upon initial hospitalization, and more. These are topics for potential future reviews.
  - In this series of studies, 'reactivation' or a series of false negatives are both plausible reasons for patients retesting PCR positive shortly after discharge. A separate review and more research is needed to explore the reason and mechanism by which patients are retesting positive.

TABLE 1: SEROLOGICAL CHARACTERISTICS OF DISCHARGED HOSPITALIZED COVID-19 CASES WHO RETESTED RT-PCR POSITIVE COMPARED TO THOSE THAT DID NOT

Reference	Report Details	Key Findings
Lu et al., 2020 Prospective cohort study Guangdong, China. Jan 23 - Feb 19, 2020	This followed 619 discharged patients and serology was the main outcome of this study. 288 patients had serological testing a median of 35 days post symptom onset (range = 23 to 47 days). Patients were followed for up to 66 days.	- Neutralizing antibody titers for RP and NRP patients were not significantly different 14 days post hospital discharge. - This study had the largest cohort that was followed for the longest period of time, recording a RP incidence rate of 14% (87/619 patients). - RP patients in this study were significantly younger than NRP patients. Sex distribution did not differ between groups. - Patients were followed for 66 days post discharge, and experience reactivation on day 10 on average (tested on day 7 and 14 only).
Yang et al., 2020 (Preprint) Prospective cohort study Shenzhen, China Feb 1 – May 5, 2020	This study followed 479 discharged patients. Serology is main outcome of this study, with serum specimens collected on the 1st, 3rd, 7th, and 14th days of each of the post-discharge 14-day quarantine period. Patients were followed up to 90 days.	- RP and NRP patients did not differ in rates of testing positive for IgG antibodies (99% and 98%, respectively). Serum levels of IgG antibodies also did not differ between groups at any point after disease onset. -RP and NRP patients did not differ in rates of testing positive for IgM antibodies (37% and 50%, respectively). Serum levels of IgM antibodies differed between groups at different points post-disease onset: In week 3, RP patients had significantly higher levels of IgM, while in weeks 6 through 8, RP patients had significantly lower IgM levels. -The incident rate of RP in this study was 19% (93/479 patients). In addition, 45 (9%) experience multiple RP events: two (n=32, 7%), three (n=9, 2%), or four (n=4, 1%) RP events. - RP patients in this study were significantly younger than NRP patients (34 years compared to 45 years). Sex distribution did not differ between groups. - Patients were followed for 90 days post discharge, and experience reactivation on day 8 on average. An average of 46 days elapsed between disease onset and the final RP event for each patient.

Yuan et al., 2020 Prospective cohort study Shenzhen, China Before Apr 21, 2020	This prospective cohort study followed 182 discharged patients. Serology is one of the main outcomes of this study, with 147 patients submitting for serological testing at some point after discharge. Patients were followed for 14 days.	- RP and NRP patients did not differ in rates of testing positive for IgG antibodies (100% and 99.2%, respectively). - RP and NRP patients did not differ in rates of testing positive for IgM antibodies (71.4% for both). -The incident rate of RP in this study was 11% (20/182 patients). However, only a subset had serology results (14 RP patients and 133 NRP patients). - RP patients were not significantly younger in this study, however, patients under 18 years of age were overrepresented in the RP group. Sex distribution did not differ between groups. - Patients were followed during the mandatory 14-day quarantine following hospital discharge, and retested on day 7 and 14 of quarantine.
Zhu et al., 2020 Retrospective cohort study Zhejiang, China Before Apr 2, 2020	This retrospective cohort study followed 98 discharged patients. Serology was part of a wide range of factors examined, with testing measuring temporal changes in antibody levels. The exact timing of tests is not stated. The follow-up period is at least 17 days.	- In this study, 35.5% of RP patients tested positive for both IgG and IgM antibodies, compared to 8.6% of NRP patients. 58.8% of RP patients tested positive for IgG and negative for IgM antibodies, compared to 44.4% of NRP patients. Two RP and one NRP patients tested negative for both IgG and IgM antibodies. The groups were not determined to be significantly different. - The incident rate of RP in this study was 17% (17/98 patients). - Neither age nor sex was found to differ between RP and NRP patients. - Patients were followed for at least 17 days following discharge, with the average time to RP being 7 days.
Hu et al., 2020 (Preprint) Retrospective cohort study Chongquin, China Jan 23 - Mar 3, 2020	This study followed 221 hospitalized patients. Serology was the main outcome, with serum samples taken every 3 days post-symptom onset. Only 74 patients were discharged and followed for	- Patients that experienced RP had post-discharge IgG levels of 8.94 on average, compared to 20.19 in NRP patients, which is significantly different. Levels are expressed as a ratio of the chemiluminescence signal to the cutoff value (S/CO). - RP and NRP patients did not have significantly different post-discharge IgM levels (0.90 compared to 1.39, respectively). - Reports the highest RP incidence rate of the ten studies (39/74, or 52.7%). No average time to reactivation was stated. - No age/sex differences between RP and NRP patients. - Patients were followed for up for 14 days.

	the 14-day quarantine period.	
Zou et al., 2020 Retrospective cohort study Wuhan, China Jan 1 – Mar 10, 2020	This study followed 257 hospitalized patients. Serology was not main outcome of the study. It is unclear how long patients were followed for or when they underwent serological testing.	- RP and NRP patients did not differ in rates of testing positive for IgG antibodies (94.4% and 85.1%, respectively). - RP and NRP patients did not differ in rates of testing positive for IgM antibodies (52.8% and 58.8%, respectively). - The incident rate of RP in this study was 20.6% (53/257 patients). However, only a subset had serology results (36 RP patients and 114 NRP patients). - Neither age nor sex was found to differ between RP and NRP patients. - It is unclear how long patients were followed for, but were said to retest positive an average of 4.6 days post-discharge. - The goal of this study was to compare RP rates for patients with two subsequent negative PCR tests compared to three subsequent negatives to qualify for discharge. 20.6% of patients with two negative tests experience RP, compared to only 5.4% of patients with three negative tests.
Huang et al., 2020 (Preprint) Cohort study - unclear if prospective or retrospective Shenzhen, China Jan 11 - Apr 23, 2020	This study followed 414 hospitalized patients. Serology was part of a wide range of factors examined. 154 patients had serological testing at discharge from hospital. Patients were followed for four weeks.	- RP and NRP patients did not differ in rates of testing positive for IgG antibodies (100% and 99.1%, respectively). - RP and NRP patients did not differ in rates of testing positive for IgM antibodies (75.0% and 48.2%, respectively). - The incident rate of RP in this study was 16.7% (69/414 patients). - RP patients in this study were significantly younger than NRP patients. Sex distribution did not differ between groups. - Patients were followed for four weeks following discharge. Reactivation occurred on the day 10 on average, with RT-PCR testing done every 3-5 days.
Liu et al., 2020 Cohort study- unclear if prospective or retrospective Wuhan, China Mar 1 - 13, 2020	This study followed 150 discharged patients. Serology was main outcome measure, but neither timing of serology nor the duration of follow-up was noted.	- RP and NRP patients did not differ in rates of testing positive for IgG antibodies (100% and 90.6%, respectively). Serum levels of IgG antibodies also did not differ between groups (243 AU/mL and 185 AU/mL, respectively). -RP and NRP patients did not differ in rates of testing positive for IgM antibodies (45.5% and 47.5%, respectively). Serum levels of IgM antibodies also did not differ between groups (9.6 AU/mL and 8.9 AU/mL, respectively). - The incident rate of RP in this study was 7.3% (11/150 patients). - Neither age nor sex was found to differ between RP and NRP patients. - Testing at different points following discharge may have affected the results.

Chen et al., 2020 Case-control study Wuhan, China Feb 10 - Mar 31, 2020	This study examined the serology of 15 RP cases and 107 controls admitted to a single hospital. Serology was part of a wide range of factors examined. The timing of the serological testing is not clear.	- Patients experiencing RP had IgG levels of 78.53 AU/mL on average, compared to 147.85 AU/mL in NRP patients, which is significantly different. - Patients experiencing RP had IgM levels of 13.69 AU/mL on average, compared to 68.10 AU/mL in NRP patients, which is significantly different. - Reports the lowest RP incidence rate of the ten studies (2/107, or 1.9%) from the cohort in a single hospital. 15 cases from multiple sites were compared to 107 controls. - Age and sex were not matched between cases and controls. RP patients were found to be significantly younger than NRP patients (43 years compared to 60 years). There was no significant difference in sex of RP versus NRP patients. - Patients were followed up for 14 days. Reactivation occurred at day 12 post-discharge on average. However, patients were only tested near the end of the 14-day quarantine.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Sciences Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: Reactivation, reinfection, reoccurrence, recurrent, in conjunction with hospitalization, discharge, antibody and immunity (including terms with similar endings and alternative spelling).

This review contains research published up to September 9, 2020.

Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

All studies included in this review focus on characteristics of hospitalized patients who retested positive (RP) compared to those who did not retest positive (NRP) after discharge, and also included serology data for both RP and NRP groups. Papers included in this review were either case-control or cohort studies. Review articles were excluded to avoid double counting. Case-series or case reports were also excluded as they do not present a comparison between patients that retested positive versus those that did not.

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Nouveaux éléments de preuve sur la COVID-19

Synthèse en bref sur la présence des anticorps dirigés contre le SRAS-CoV-2 chez les patients ayant obtenu un nouveau résultat positif au test RT-PCR

Introduction

Une fois rétablis, est-ce que les patients hospitalisés en raison du SRAS-CoV-2 qui n'ont pas obtenu de résultat positif subséquent au test RT-PCR présentent des niveaux d'anticorps contre le SRAS-CoV-2ou des taux de séropositivité différents de ceux qui ont reçu un résultat positif à un nouveau test?

Les cas confirmés de patients qui ont eu la COVID-19 et ont reçu un nouveau résultat positif après avoir obtenu leur congé de l'hôpital soulèvent des préoccupations quant à une possible réinfection ou réactivation du virus. Les recherches visant à comparer les indicateurs de réponse immunitaire des patients rétablis après avoir été hospitalisés en raison du SRAS-CoV-2 et qui n'ont pas reçu de résultat positif lors d'un test RT-PCR subséquent à ceux des patients qui ont obtenu un résultat positif au test RT-PCR test ont été sélectionnées afin d'étudier les liens possibles entre les résultats positifs au test d'ARN viral et la réponse immunitaire. Cette revue résume la documentation sur la COVID-19 publiée jusqu'au 9 septembre 2020 portant sur les différences entre les réponses immunitaires des patients qui ont obtenu un résultat positif à un nouveau test et ceux qui ont obtenu un résultat négatif. Elle porte également sur le lien entre la dynamique des anticorps du SRAS-CoV-2 et la possibilité de réinfection ou de réactivation du virus.

Cette synthèse comprend neuf études qui correspondaient aux critères d'inclusion (veuillez consulter la section Méthodologies pour plus de détails). Ces neuf études ont toutes été réalisées en Chine. Dans le cadre de ces études, tous les patients qui ont obtenu leur congé de l'hôpital avaient reçu au moins deux résultats négatifs consécutifs à des tests RT-PCR effectués à au moins 24 heures d'intervalle. Après leur congé, tous les patients ont été transférés dans des établissements distincts pour une quarantaine obligatoire surveillée d'une durée de 14 jours. Il est à noter que les es patients qui ont reçu un nouveau résultat positif après avoir obtenu leur congé sont généralement appelés « patients RP », mais certaines études utilisent des termes légèrement différents, par ex., nouveau résultat positif, positif de nouveau détectable, positif à nouveau ou positif récurrent. Les patients dont le résultat n'était pas positif sont, quant à eux, appelés patients NRP.

Points clés

- Le taux de résultat positif (prévalence de résultats positifs (RP)) variait de 1,87 % chez les patients ayant reçu leur congé (Chen et coll., 2020) à 52,7 % (Hu et coll., 2020) avec une moyenne de 16,5 % pour l'ensemble des études (397 patients sur 2 412). Aucune étude n'a relevé de différence dans la répartition selon le sexe, mais quatre des neuf études ont mentionné que les patients RP étaient

beaucoup plus jeunes que les patients NRP. Un plus vaste examen serait cependant nécessaire pour explorer cette question en profondeur (Chen et coll., 2020, Lu et coll., 2020, Huang et coll., 2020, Yang et coll., 2020).

- Parmi les six études ayant indiqué une proportion de cas positifs pour les anticorps IgG ou IgM chez les patients, aucune n'a mentionné de différence quelconque entre les taux des patients RP et ceux des patients NRP. Il est donc peu probable que la présence d'anticorps IgG ou IgM permette de prédire le résultat positif d'un nouveau test (Yang et coll., 2020, Liu et coll., 2020, Yuan et coll., 2020, Zou et coll., 2020, Huang et coll., 2020, Zhu et coll., 2020).
- Les résultats des quatre études qui ont mentionné la concentration d'anticorps IgG ou IgM dans le sérum sont cependant mitigés. Ainsi, la première étude a révélé que les taux d'anticorps IgM et IgG étaient beaucoup plus faibles chez les patients RP que chez les patients NRP (Chen et coll., 2020). La seconde n'a trouvé aucune différence à cet égard (Liu et coll., 2020). La troisième a, quant à elle, indiqué que le taux d'anticorps IgG était significativement plus faible chez les patients RP, mais qu'aucune différence n'avait été observée pour le taux d'anticorps IgM (Hu et coll., 2020). La quatrième n'a relevé aucune différence entre les taux d'anticorps IgG, mais a cependant indiqué que les niveaux d'IgM variaient avec le temps. Ainsi, au départ, les patients RP avaient des titres d'IgM plus élevés (troisième semaine après le congé), mais ces niveaux sont finalement devenus beaucoup plus faibles chez les patients RP que chez les patients NRP (entre six et huit semaines après le congé; Yang et coll., 2020). Ces observations suggèrent que des niveaux d'anticorps plus faibles pourraient jouer un rôle dans le nouveau résultat positif obtenu après le congé. Les preuves à cet égard ne sont cependant pas concluantes pour le moment.
- On ne sait toujours pas précisément pourquoi les patients ont de nouveau reçu un résultat positif. Comme cela a été indiqué ci-dessus, les neuf études ont été réalisées en Chine qui imposait une quarantaine obligatoire de 14 jours après tout congé d'hôpital. Cette quarantaine a été effectuée dans des établissements distincts avec des chambres individuelles. Trois études qui n'ont suivi les patients que pendant cette période ont révélé qu'un maximum de 52,7 % des patients avait reçu un nouveau résultat positif (Chen et coll., 2020, Hu et coll., 2020, Yuan et coll., 2020). Une « réactivation » de l'infection initiale en raison de l'élimination incomplète du virus pourrait expliquer de façon plausible pourquoi ces patients ont reçu un résultat positif au test effectué pendant la période de quarantaine de deux semaines. Il est également possible que la concentration d'ARN viral dans les échantillons ait fluctué pendant l'élimination du virus, ce qui a entraîné deux faux négatifs qui ont permis au patient d'obtenir son congé. L'étude réalisée par Zou et coll., 2020 indique que les patients ont reçu des résultats positifs moins souvent lorsqu'ils devaient obtenir trois résultats négatifs au test PCR plutôt que les deux tests habituels avant d'obtenir leur congé de l'hôpital.
- Une étude a démontré que certains patients obtenaient des résultats positifs à plus d'une reprise. Lorsque les patients ont reçu un nouveau résultat positif au test, ils ont alors été hospitalisés de nouveau et ne se sont vus accorder de congé que lorsqu'ils ont eu deux résultats négatifs à deux tests

RT-PCR consécutifs, pour finalement subir d'autres tests et recevoir un résultat positif au deuxième, au troisième et même au quatrième test (Yang et coll., 2020).

- Une autre étude a révélé que le fait d'exiger trois résultats négatifs consécutifs avant d'accorder un congé aux patients réduisait significativement le risque de nouveaux résultats positifs (Zou et coll., 2020), ce qui indique que les faux négatifs peuvent jouer un rôle dans l'obtention d'un nouveau résultat positif chez un patient ayant obtenu son congé. Un examen supplémentaire sera cependant requis pour obtenir plus de précisions à cet égard.

Vue d'ensemble des éléments de preuve

Neuf documents ont été recensés, dont huit étaient des études de cohorte et un, une étude cas-témoins. Tous ont été évalués à l'aide de l'outil de mesure du risque de partialité dans l'échelle Newcastle-Ottawa (NOS). Pour les critères de sélection, le score maximal est de quatre, alors qu'il est de deux pour la comparabilité entre les groupes et de trois pour les critères d'exposition ou de résultat. Le suivi approprié a cependant été interrompu après quatre semaines de suivi.

- Trois études de cohorte prospectives
  - Clinical, immunological and virological characterization of COVID-19 patients that test re-positive for SARS-CoV-2 by RT-PCR (Lu et coll., 2020), score : 4, 0, 3.
  - Recurrence of positive SARS-CoV-2 viral RNA in recovered COVID-19 patients during medical isolation observation (Yuan et coll., 2020), score : 4, 0, 1.
  - Viral RNA level, serum antibody responses, and transmission risk in discharged COVID-19 patients with recurrent positive SARS-CoV-2 RNA test results: a population-based observational cohort study (Yang et coll., 2020), score : 4, 0, 2.
- Trois études de cohortes rétrospectives
  - The production of antibodies for SARS-CoV-2 and its clinical implication (Hu et coll., 2020), score : 4, 0, 1.
  - Clinical features of COVID-19 convalescent patients with re-positive nucleic acid detection (Zhu et coll., 2020), score : 4, 0, 2.
  - The issue of recurrently positive patients who recovered from COVID-19 according to the current discharge criteria: investigation of patients from multiple medical institutions in Wuhan, China (Zou et coll., 2020), score : 3, 0, 1.
- Deux études de cohorte (aucune indication à savoir si elles étaient prospectives ou rétrospectives)
  - Recurrent positive SARS-CoV-2 - immune certificate may not be valid (Liu et coll., 2020), score : 4, 0, 1.

        - Kinetics of SARS-CoV-2 Positivity of Infected and Recovered Patients: A Single Center COVID-19 Experience and Potential Implications (Huang et coll., 2020), score : 4, 0, 2.
    - Une étude cas/témoins
        - Clinical Characteristics of Recurrent-positive Coronavirus Disease 2019 after Curative Discharge: a retrospective analysis of 15 cases in Wuhan China (Chen et coll., 2020), score : 2, 0, 3.
    - Limites Les neuf études ont été réalisées en Chine, et aucune autre administration n'a produit d'études semblables.
    - La taille de l'échantillon dans certaines études était petite. Ainsi, deux études comptaient moins de 100 patients (Hu et coll., 2020, Zhu et coll., 2020) alors que trois autres comptaient moins de 200 patients (Chen et coll., 2020, Liu et coll., 2020, Yuan et coll., 2020).
    - La durée du suivi variait considérablement. De nombreuses études n'ont suivi les patients que pendant les deux semaines de quarantaine obligatoire et centralisée qui a suivi l'obtention du congé de l'hôpital, tandis que d'autres ont plutôt suivi les patients pendant de nombreuses semaines par la suite. L'éventail était également assez large en ce qui concerne l'intervalle des tests RT-PCR puisqu'il variait d'un seul test vers la fin de la quarantaine de 14 jours à des tests effectués tous les trois à cinq jours. Cumulativement, ces limites, laissent planer un doute sur la prévalence des résultats positifs répétés et sur le temps moyen requis pour qu'ils soient de nouveau positifs après qu'un patient ait obtenu son congé.
- Lacunes dans les données
    - Toutes les études qui répondaient aux critères d'inclusion provenaient de la Chine où tous les cas ont été hospitalisés. Il faut donc faire preuve de prudence au moment d'extrapoler ces résultats à d'autres contextes.
    - Cette synthèse ne tient pas compte d'autres facteurs pouvant être prédictifs ou contribuer à un nouveau diagnostic positif une fois qu'un patient a reçu son congé de l'hôpital, ce qui inclut la numération des cellules immunitaires, les comorbidités, la gravité de la maladie au moment de l'hospitalisation initiale, et plus encore. Ces sujets pourraient faire l'objet de synthèses à venir.
    - Dans cette série d'études, la « réactivation » ou une série de faux négatifs sont deux raisons plausibles pour lesquelles les patients obtiennent un nouveau résultat positif au test PCR peu de temps après avoir obtenu leur congé. Une synthèse distincte et des recherches supplémentaires sont nécessaires pour examiner la raison et le mécanisme par lequel les patients reçoivent de nouveaux résultats positifs aux tests.

TABLEAU 1 : CARACTÉRISTIQUES SÉROLOGIQUES DES PATIENTS AYANT OBTENU LEUR CONGÉ APRÈS UNE HOSPITALISATION EN RAISON DE LA COVID-19 ET DONT LE RÉSULTAT DU TEST RT-PCR EST POSITIF, COMPARATIVEMENT À CEUX DONT LE RÉSULTAT EST NÉGATIF

Référence	Détails du rapport	Principales conclusions
Lu et coll., 2020 Étude de cohorte prospective Guangdong, en Chine. Du 23 janvier au 19 février 2020	Cette étude, qui a suivi 619 patients ayant reçu leur congé, a permis d'en établir la sérologie. Ainsi, 288 patients ont subi des tests sérologiques pendant une période médiane de 35 jours après l'apparition des symptômes (intervalle variant entre 23 et 47 jours). Ils ont ensuite été suivis pendant une période pouvant aller jusqu'à 66 jours.	- Les titres des anticorps neutralisants pour les patients RP et NRP ne différaient pas significativement 14 jours après qu'ils aient reçu leur congé de l'hôpital. - Cette étude comportait la plus grosse cohorte suivie pendant la plus longue période de temps avec un taux d'incidence de RP de 14 % (87 patients sur 619). - Dans cette étude, les patients RP étaient beaucoup plus jeunes que les patients NRP. La répartition selon le sexe ne différait cependant pas entre les groupes. - Les patients ont été suivis pendant une période de 66 jours après qu'ils aient obtenu leur congé et la réactivation s'est produite en moyenne le jour 10 (tests effectués les jours 7 et 14 seulement).
Yang et coll., 2020 (prépublication) Étude de cohorte prospective Shenzhen, en Chine Du 1er février au 5 mai 2020	Cette étude a suivi 479 patients ayant reçu leur congé. Elle portait principalement sur la sérologie, puisque des spécimens de sérum ont été prélevés les 1er, 3e, 7e et 14e jours de chacune des périodes de quarantaine de 14 jours, après le congé de l'hôpital. Les patients ont ensuite été suivis	- Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgG des patients RP et NRP (99 % et 98 %, respectivement). Quant aux niveaux sériques des anticorps IgG, ils ne différaient pas non plus d'un groupe à l'autre en tout temps après l'apparition de la maladie. - Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgM pour les patients RP et NRP (37 % et 50 %, respectivement). Les niveaux sériques des anticorps IgG variaient entre les groupes à différents moments après l'apparition de la maladie : ainsi, pendant la troisième semaine, les patients RP présentaient des taux d'IgM beaucoup plus élevés, alors que les taux d'IgM étaient beaucoup plus faibles pendant les semaines 6 à 8 chez les patients RP. -Le taux d'incidence des résultats positifs (PR) dans cette étude était de 19 % (93 patients sur 479). De plus, 45 (9 %) d'entre eux ont été associés à plusieurs événements de résultat positif

	pendant une période pouvant aller jusqu'à 90 jours.	connexes, soit deux (n=32,7 %), trois (n=9,2 %) ou quatre (n=4,1 %) événements. - Dans cette étude, les patients RP étaient beaucoup plus jeunes que les patients NRP (34 ans comparativement à 45 ans). La répartition selon le sexe ne différait cependant pas entre les groupes. - Les patients ont été suivis pendant une période de 90 jours après qu'ils aient obtenu leur congé et la réactivation s'est produite en moyenne le jour 8. Il s'est donc écoulé en moyenne 46 jours entre l'apparition de la maladie et l'événement RP final pour chaque patient.
Yuan et coll., 2020 Étude de cohorte prospective Shenzhen, en Chine Avant le 21 avril 2020	Cette étude de cohorte prospective a suivi 182 patients ayant reçu leur congé. Elle portait principalement sur la sérologie avec 147 patients qui ont été soumis à des tests sérologiques à un moment donné après avoir obtenu leur congé. Ils ont ensuite été suivis pendant 14 jours.	- Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgG des patients RP et NRP (100 % et 99,2 %, respectivement). - Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgM des patients RP et NRP (71,4 % pour les deux). - Le taux d'incidence des RP dans cette étude atteignait 11 % (20 patients sur 182), mais des résultats de sérologie n'ont été obtenus que pour un seul sous-ensemble (14 patients RP et 133 patients NRP). - Bien que, dans cette étude, les patients RP n'étaient pas beaucoup plus jeunes, les patients de moins de 18 ans étaient cependant surreprésentés dans le groupe RP. La répartition selon le sexe ne différait cependant pas entre les groupes. - Les patients ont été suivis pendant leur quarantaine obligatoire de 14 jours qui a suivi l'obtention du congé de l'hôpital, avant d'être soumis à un nouveau test les jours 7 et 14 de la quarantaine.
Zhu et coll., 2020 Étude de cohorte rétrospective Zhejiang, en Chine Avant le 2 avril 2020	Cette étude de cohorte rétrospective a suivi 98 patients ayant reçu leur congé. La sérologie faisait partie d'une vaste gamme de facteurs examinés, puisque les tests ont mesuré les changements dans les niveaux d'anticorps en fonction du temps.	- Dans le cadre de cette étude, 35,5 % des patients RP ont reçu un résultat positif pour les anticorps IgG et IgM, comparativement à 8,6 % des patients NRP alors que 58,8 % des patients RP ont reçu un résultat positif pour l'IgG et un résultat négatif pour les anticorps IgM, comparativement à 44,4 % des patients NRP. Deux patients RP et un patient NRP ont obtenu des résultats négatifs pour les anticorps IgG et IgM. Il n'a pas été jugé que ces groupes sont significativement différents. - Le taux d'incidence des RP dans cette étude était de 17 % (17 patients sur 98). - Il a été jugé que ni l'âge ni le sexe ne différaient entre les patients RP et NRP. - Les patients ont été suivis pendant au moins 17 jours après avoir reçu leur congé, avec une durée moyenne de 7 jours pour les patients RP.

	Les dates exactes des tests ne sont pas précisées, mais le suivi a duré au moins 17 jours.	
Hu et coll., 2020 (prépublication) Étude de cohorte rétrospective Chongquin, en Chine Du 23 janvier au 3 mars 2020	Cette étude a suivi 221 patients hospitalisés. Elle portait principalement sur la sérologie puisque des échantillons de sérum ont été prélevés tous les trois jours après l'apparition des symptômes. Seuls 74 patients ont reçu leur congé et ont été suivis pendant la période de quarantaine de 14 jours.	- Les patients RP présentaient des taux d'IgG après leur congé de 8,94 en moyenne alors que les patients NRP ont obtenu des résultats significativement différents avec un taux de 20,19. Les niveaux sont exprimés sous forme de rapport entre le signal de chimiluminescence et la valeur seuil. - Les niveaux d'IgM des patients RP et NRP n'étaient pas significativement différents après leur congé (0,90 comparativement rapport à 1,39, respectivement). - Cette étude est celle qui comporte le taux d'incidence de RP le plus élevé parmi les dix études (39 sur 74 ou 52,7 %). Aucune durée moyenne de réactivation n'a été indiquée. - Aucune différence d'âge ou de sexe entre les patients RP et NRP n'a été mentionnée. - Les patients ont été suivis pendant une période pouvant aller jusqu'à 14 jours.
Zou et coll., 2020 Étude de cohorte rétrospective Wuhan, en Chine Du 1er janvier au 10 mars 2020	Cette étude a suivi 257 patients hospitalisés. L'étude ne portait pas principalement sur la sérologie. Ni la durée du suivi des patients ni la date à laquelle ils ont subi des tests sérologiques n'ont été indiquées.	- Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgG des patients RP et NRP (94,4 % et 85,1 %, respectivement). - Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgM des patients RP et NRP (52,8 % et 58,8 %, respectivement). - Le taux d'incidence des RP dans cette étude était de 20,6 % (53 patients sur 257). Cependant, un seul sous-ensemble incluait des résultats sérologiques (36 patients RP et 114 patients NRP). - Il a été jugé que ni l'âge ni le sexe ne différaient entre les patients RP et NRP. - L'étude n'indique pas précisément la durée du suivi, mais précise que le nouveau résultat positif au test s'est produit en moyenne 4,6 jours après que les patients aient obtenu leur congé. - Cette étude visait à comparer les taux de RP chez les patients qui ont reçu deux résultats négatifs subséquents à des tests PCR comparativement à trois résultats négatifs subséquents avant de pouvoir obtenir leur congé. Ainsi, 20,6 % des patients qui ont obtenu deux tests négatifs ont ensuite obtenu un RP

		comparativement à seulement 5,4 % des patients qui ont obtenu trois résultats négatifs.
Huang et coll., 2020 (prépublication) Étude de cohorte - aucune indication à savoir si elle était prospective ou rétrospective Shenzhen, en Chine Du 11 janvier au 23 avril 2020	Cette étude a suivi 414 patients hospitalisés. La sérologie faisait partie d'un large éventail de facteurs examinés. Dans cette étude, 154 patients ont passé des tests sérologiques avant d'obtenir leur congé de l'hôpital. Ces patients ont été suivis pendant quatre semaines.	- Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgG des patients RP et NRP (100 % et 99,1 %, respectivement). - Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgM des patients RP et NRP (75,0 % et 48,2 %, respectivement). - Le taux d'incidence des RP dans cette étude était de 16,7 % (69 patients sur 414). - Dans cette étude, les patients RP étaient beaucoup plus jeunes que les patients NRP. La répartition selon le sexe ne différait cependant pas entre les groupes. - Les patients ont été suivis pendant quatre semaines après avoir obtenu leur congé. La réactivation s'est produite en moyenne le dixième jour, avec des tests RT-PCR effectués tous les 3 à 5 jours.
Liu et coll., 2020 Étude de cohorte - aucune indication à savoir si elle était prospective ou rétrospective Wuhan, en Chine Du 1er mars au 13 avril 2020	Cette étude a suivi 150 patients ayant reçu leur congé. La sérologie était la principale mesure visée, mais ni la date à laquelle elle a eu lieu ni la durée du suivi n'ont été indiquées.	- Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgG des patients RP et NRP (100 % et 90,6 %, respectivement). Les concentrations sériques d'anticorps IgG ne différaient pas non plus entre les groupes (243 AU/ml et 185 AU/ml, respectivement). - Aucune différence n'a été observée en ce qui concerne les taux de résultats positifs aux tests d'anticorps IgM des patients RP et NRP (45,5 % et 47,5 %, respectivement). Les concentrations sériques d'anticorps IgM ne différaient pas non plus d'un groupe à l'autre (9,6 AU/ml et 8,9 AU/ml, respectivement). - Le taux d'incidence des résultats positifs dans cette étude était de 7,3 % (11 patients sur 150). - Il a été jugé que ni l'âge ni le sexe ne différaient entre les patients RP et NRP. - Les tests effectués à différents moments après l'attribution du congé peuvent avoir eu une incidence sur les résultats.

Chen et coll., 2020 Étude cas/témoins Wuhan, en Chine Du 10 février au 31 mars 2020	Cette étude a examiné la sérologie de 15 patients RP et de 107 témoins admis dans un seul hôpital. La sérologie faisait partie d'un large éventail de facteurs examinés. La date à laquelle les tests sérologiques ont été effectués n'est pas indiquée de façon précise.	- Les patients RP avaient des taux moyens d'IgG de 78,53 AU/ml comparativement à 147,85 AU/ml chez les patients NRP, ce qui est significativement différent. - Les patients RP présentaient également des taux moyens d'IgM de 13,69 AU/ml comparativement à 68,10 AU/ml chez les patients NRP, ce qui est aussi significativement différent. - Cette étude a le taux d'incidence de RP le plus faible parmi les dix études évaluées (2 sur 107, ou 1,9 %) et ce taux provient d'une cohorte prise dans un seul hôpital. Elle a comparé 15 patients provenant de sites multiples à 107 cas témoins. - L'âge et le sexe ne correspondaient pas entre les patients et les témoins. L'étude a indiqué que les patients RP étaient beaucoup plus jeunes que les patients NRP (43 ans comparativement à 60 ans). Il n'y avait aucune différence significative entre le sexe des patients RP et celui des patients NRP. - Les patients ont été suivis pendant 14 jours. La réactivation s'est produite en moyenne au 12^{e} jour après qu'ils aient reçu leur congé. Toutefois, les patients n'ont été testés qu'à la fin de la quarantaine de 14 jours.

Méthodologies :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient : Réactivation, réinfection, récurrence, récidive, en liaison avec l'hospitalisation, le congé de l'hôpital, les anticorps et l'immunité (y compris les termes ayant une terminaison similaire et une orthographe différente).

La présente revue contient des recherches publiées jusqu'au 9 septembre 2020.

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

Toutes les études incluses dans cette revue portent sur les caractéristiques de patients hospitalisés qui ont reçu un nouveau résultat positif (RP) par rapport à ceux qui n'ont pas eu de résultat positif (NRP) après leur congé de l'hôpital, et comprennent également des données sérologiques pour les groupes RP et NRP. Les articles inclus dans cette revue étaient soit des études cas-témoins, soit des études de cohorte. Les articles de synthèse ont été exclus pour éviter tout double comptage. Les séries de cas ou les rapports de cas ont également été exclus, car ils ne présentent aucune comparaison entre les patients dont les résultats de test sont positifs comparativement à ceux dont le résultat est négatif.

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Nouveaux éléments de preuve sur la COVID-19

Résumé des éléments de preuve sur les procédures pouvant générer des aérosols dans le milieu des soins dentaires

Introduction

Quelles sont les preuves existantes de la transmission du SRAS-CoV-2 en milieu dentaire et de la transmission de l'infection dans le cadre de procédures pouvant générer des aérosols (PGA) utilisées dans les soins dentaires?

Les PGA peuvent augmenter le risque de transmission de l'infection d'un patient infecté à un travailleur de la santé en raison de la proximité et de la production de forts volumes d'aérosols. Le présent résumé des éléments de preuve résume la littérature et les conseils disponibles sur les procédures pouvant générer des aérosols (PGA) dans le milieu des soins dentaires en ce qui concerne la transmission du SRAS-CoV-2 et peut être utilisée avec le résumé des éléments de preuve sur l'analyse aérodynamique du SRAS-CoV-2 datée du 28 mai 2020, qui résume les preuves sur l'aérosolisation du SRAS-CoV-2, qui est disponible par l'intermédiaire du Secrétariat des sciences émergentes de l'ASPC.

Points clés

- Aucun rapport publié sur la transmission de la COVID-19, les grappes ou les éclosions dans le milieu des soins dentaires n'a pu être recensé.
- Aérosolisation du SRAS-CoV-2 :
    - Des échantillons d'air prélevés dans le milieu des soins hospitaliers traitant des cas de COVID-19 ont démontré une contamination par l'ARN du SRAS-CoV-2, probablement par des aérosols et de petites gouttelettes respiratoires (Guo *et al.*, 2020; Liu *et al.*, 2020; Santarpia *et al.*, 2020). On a constaté que le SRAS-CoV-2 restait viable sous forme d'aérosol pendant une période pouvant aller jusqu'à 4 heures, mais ni le caractère infectieux ni la dose infectieuse de ces particules n'ont été établis (van Doremalen *et al.*, 2020).
    - Les procédures dentaires peuvent induire des réflexes nauséeux entraînant une augmentation de la sécrétion de salive et de la toux chez les patients. Les instruments dentaires à grande vitesse peuvent créer de grands volumes d'aérosols contenant de l'eau, de la salive, du sang, des micro-organismes et d'autres débris (Ather, Patel, Ruparel, Diogenes, et Hargreaves, 2020; Jamal *et al.*, 2020; Sales, Sales et Da Hora Sales, 2020).

- Une publication récente de Workman *et al.* fait état de simulations à l'aide de cadavres au cours desquelles les risques d'aérosolisation liés aux procédures endonasales ont été évalués (Workman *et al.*, 2020). L'étude conclut que les procédures de forage chirurgical à grande vitesse ont entraîné une contamination substantielle par des aérosols dans toutes les conditions testées. Ces résultats peuvent être étendus aux forages et aux procédures dentaires, qui sont considérés comme des procédures générant des aérosols.

- Documents d'orientation :
  - Les directives publiées indiquent que les patients chez qui la COVID-19 est confirmée ou suspectée ne doivent PAS être traités dans un environnement de soins dentaires de routine et ne doivent être pris en charge que dans des chambres d'isolement des infections aéroportées (CIIA) (Ather *et al.*, 2020; Jamal *et al.*, 2020).
  - L'examen de plusieurs documents d'orientation sur les soins dentaires et la COVID-19 révèle que certaines procédures et certains équipements utilisés sont associés à un risque accru de production d'aérosols et devraient être soit évités soit modifiés pendant la pandémie de COVID-19 (tableau 1). Les orientations spécifiques liées aux procédures et aux instruments qui génèrent des aérosols tirées de ces publications sont résumées ci-dessous.
    - Les radiographies intra-orales doivent être évitées et remplacées par l'imagerie extra-orale telle que la radiographie panoramique ou la tomographie assistée par ordinateur à faisceau conique lorsque l'imagerie intra-orale est inévitable (Ather *et al.*, 2020; Jamal *et al.*, 2020; Meng, Hua et Bian, 2020).
    - L'utilisation d'une digue en caoutchouc pour minimiser la génération d'éclaboussures est la norme de soins pour les traitements endodontiques non chirurgicaux. Les recommandations suggèrent qu'il peut être avantageux de placer la digue en caoutchouc de manière à ce qu'elle couvre le nez (Ather *et al.*, 2020; Jamal *et al.*, 2020; Sales, Sales et Da Hora Sales, 2020). En outre, lorsque la digue en caoutchouc est utilisée, il est recommandé d'aspirer à très haut volume les aérosols et les éclaboussures, en plus de l'aspiration régulière (Peng *et al.*, 2020).
    - Il a été établi que les instruments à ultrasons tels que les seringues à triples voies, les fraises dentaires à haute vitesse, les détartreurs à ultrasons, les dispositifs d'abrasion à l'air et les sableuses intra-orales sont associés à un risque accru d'aérosolisation qu'il convient d'éviter ou de réduire au minimum (Ather *et al.*, 2020; Jamal *et al.*, 2020; Meng *et al.*, 2020; Sales *et al.*, 220). Si l'utilisation d'un tel équipement est inévitable, l'application de pompes à salive à grand volume est recommandée en plus des instruments applicables (Ather *et al.*, 2020; Jamal *et al.*, 2020; Meng *et al.*, 2020).
    - Pour réduire au minimum le risque d'aérosols dentaires, il est recommandé d'utiliser, dans la mesure du possible, des instruments à main, des fraises dentaires à faible vitesse, des

instruments sans jet d'eau et des instruments à main équipés d'une valve anti-retrait ou d'une autre technologie anti-reflux (Ather *et al.*, 2020; Jamal *et al.*, 2020).

- Peng *et al.* suggèrent que l'utilisation d'instruments à main dentaires sans fonction anti-retrait devrait être interdite durant l'épidémie de COVID-19. Un instrument à main dentaire doté de valves anti-retrait spécialement conçues ou d'autres conceptions anti-reflux sont fortement recommandés comme mesure préventive supplémentaire des infections croisées. Il est important de noter que ces recommandations sont basées sur des preuves antérieures de la transmission de l'hépatite B dans le milieu des soins dentaires (Peng *et al.*, 2020).

Vue d'ensemble des éléments de preuve

Actuellement, il n'existe aucun rapport publié sur les grappes ou les éclosions de COVID-19 liées aux soins dentaires. Aucune étude de simulation publiée n'a évalué spécifiquement la dispersion des gouttelettes ou la génération d'aérosols associées aux procédures dentaires depuis l'apparition de la COVID-19. La désignation de PGA en milieu dentaire est largement fondée sur des preuves issues de simulations d'interventions médicales ou sur les conseils de diverses associations dentaires à l'échelle nationale. Les éléments de preuve disponibles établis à la lumière d'interventions médicales sont peu nombreux, largement théoriques, et ne prennent pas explicitement en compte l'infectiosité des aérosols du SRAS-CoV-2; toutefois, ils ne semblent pas être de mauvaise qualité.

Les procédures pouvant générer des aérosols (PGA) et la transmission de la COVID-19 dans les soins dentaires sont des sujets peu étudiés qui présentent des lacunes importantes en matière de connaissances. Ces domaines pourraient tirer des avantages de recherches et de rapports supplémentaires axés sur les expériences en dentisterie pendant la pandémie de COVID-19.

TABLE DES MATIÈRES

DIRECTIVES SUR LA COVID-19 POUR LE MILIEU DES SOINS DENTAIRES

Tableau 1 : Cinq examens décrivent les procédures dentaires générant des aérosols, les données probantes sous-jacentes et les conseils disponibles pour réduire les aérosols générés au cours des procédures dentaires.

Référence	Principales caractéristiques
(Ather *et al.*, 2020)	Fournit un aperçu de l'épidémiologie, des symptômes et des voies de transmission de la COVID-19, ainsi que des recommandations spécifiques pour la pratique dentaire pendant la pandémie actuelle. Ces recommandations s'appuient sur les nouvelles données probantes concernant le SRAS-CoV-2 et sur les expériences de transmission passées du SRAS-CoV-2 dans les établissements de santé.
(Jamal *et al.*, 2020)	Examine et résume les directives sur la COVID-19 publiées par plusieurs associations dentaires nationales, notamment les directives de l'American Dental Association, du Scottish Dental Clinical Effectiveness Programme, de la déclaration conjointe de la New Zealand Dental Association et de l'International federation of Endodontic Association - Indian Endodontic Society et de l'American Association of Endodontics.
(Meng *et al.*, 2020)	Décrit les procédures et les techniques générant des aérosols qui ont été évitées dans un hôpital de stomatologie à Wuhan, en Chine, lors de l'émergence de la pandémie COVID-19 au début de l'année 2020.
(Peng *et al.*, 2020)	Fournit un aperçu des données probantes disponibles sur les voies de transmission de l'infection par la COVID-19 et décrit les mesures de prévention de l'infection par la COVID-19 et les conseils pour les milieux dentaires. Les auteurs plaident fortement pour l'interdiction de l'utilisation d'instruments à main dentaires sans fonction anti-retrait pendant la pandémie. Les preuves contre l'utilisation d'instruments à main sans fonction anti-retrait proviennent d'études sur le risque d'infection croisée par le virus de l'hépatite B (qui n'est pas un virus respiratoire).

(Sales *et al.*, 2020)	Examine la documentation disponible et fournit des recommandations pour les soins dentaires à la lumière de la pandémie de COVID-19. Recommande d'éviter les instruments à grande vitesse et d'utiliser des barrages en caoutchouc pour atténuer les risques liés aux aérosols.

Méthodologies

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des science émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé est effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2. Les termes de recherche utilisés comprenaient les suivants : aérosol, dentaire

La présente revue contient des recherches publiées jusqu'au 9 juin 2020.

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue.

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Emerging Evidence on COVID-19

Rapid Review on SARS-CoV-2 Aerosol Transmission, Update 2

Introduction

What is the emerging cluster/outbreak, experimental and biological evidence implicating aerosol transmission of SARS-CoV-2?

The scientific evidence and understanding of SARS-CoV-2 modes of transmission has rapidly evolved over the past year. Expelled respiratory particles containing infectious pathogens can occur in a continuum of sizes, and smaller respiratory particles (often termed aerosols) can remain suspended in air and disperse further distances than large respiratory droplets. Other pathogens that are known to primarily transmit through large droplets (e.g., Influenza, SARS-CoV-1, streptococcus pneumonia, and *Legionella*) can also spread by aerosols in some settings and conditions (1-6). As such, a range of evidence has been produced to describe the characteristics and relative importance of aerosols in SARS-CoV-2 transmission in different settings and conditions.

This evidence brief summarizes the scientific literature providing evidence on SARS-CoV-2 aerosol transmission published up to March 12, 2021 and is organized into the follow evidence sections:

1) SARS-CoV-2 cluster or outbreak investigations that have implicated aerosol transmission;
2) Experiments on indirect transmission of SARS-CoV-2 virus using animal models;
3) Experimental evidence on SARS-CoV-2 virus stability and viability in aerosols;
4) Biological monitoring studies on SARS-CoV-2 RNA in exhaled breath; and
5) Biological monitoring studies on SARS-CoV-2 RNA and viability in environmental air samples in patient care and in community (i.e., non-hospital/patient care) settings.

The evidence section on fluid dynamic simulations and *in-silico* analyses has been omitted from this update given the increasing amount of empirical evidence supporting the potential for SARS-CoV-2 aerosol transmission.

What's New

- This update identified 46 new studies, pre-published and published, between November 6, 2020 (the last update date) and March 12, 2021 on SARS-CoV-2 aerosol transmission potential. These studies are summarized below and identified as *new* throughout the evidence tables.
- The update includes twelve new reports of SARS-CoV-2 outbreaks/cluster investigations in real-world settings (Table 1). These aerosol implicated transmission events were reported to have occurred inside a post-travel quarantine hotel, nursing home, hospital hematology unit,

passenger bus, a restaurant, fitness facilities, department store, and apartments arranged in a vertical line in an apartment building (7-16). In these reports, most reported mask use was infrequent or improper at the time of assumed aerosol transmission, and index cases were reported to be at pre-symptomatic or early symptomatic stages of infection.

- Two new animal model-based experiments reported on multiple modes of SARS-CoV-2 transmission, including aerosols, between infected and susceptible hamster pairs (17, 18). One study suggested aerosol exposure led to earlier virus replication, shedding in respiratory tissue, and more acute disease manifestation in hamsters, when compared to fomite and intranasal exposures (17). The other study found aerosols from naïve infected hamsters can infect previously infected hamsters, which suggests recovery from a primary SARS-CoV-2 infection does not eliminate subsequent infection risk by aerosols (18).
- A newly included experimental study investigating the viability and decay rates of SARS-CoV-2 virus in aerosols reported the infectiousness of virus in aerosols to be highly dependent on environmental conditions in the following order of influence: simulated sunlight exposure levels (midday summer, spring midday, indoor/night tested) >temperature (10-40 °C tested)> humidity (20-70% tested) (19). A 90% reduction in infectious virus was estimated to take 4.8 minutes (at 40^0C, 20% relative humidity) with midday summer sunlight exposure, with similar reductions estimated to take more than 2 hours (at 40^0C, 20% relative humidity) under no sunlight exposure conditions (i.e., indoors or at night). Sunlight had the largest influence on decay rate, however higher decay was also noted at 30°C with high (70%) humidity or at 40°C regardless of humidity.
- One new biological monitoring study on exhaled breath samples from five patients found viral RNA to only be detected in exhaled air samples of COVID-19 patients with positive oropharyngeal, nasopharyngeal, and/or salivary swabs at the time of sampling (20).
- Twenty-eight new biological monitoring studies that investigated SARS-CoV-2 virus contamination in environmental air samples in patient care (includes hospitals and long-term care studies) and in community (i.e., non- patient care) settings are included in this update.
    - Two Canadian studies suggested viral RNA contamination in environmental air samples from a hospital (~ 3 meters from COVID-19 patients) and on no touch surfaces from long-term care home settings (21, 22) to indicate SARS-CoV-2 can spread through aerosols.
    - A new study confirmed the presence of viable virus in air samples collected from a car driven by a mildly symptomatic individual (23). This highlights SARS-CoV-2 virus can be expelled in to the surrounding air, even by a mild case over a short period of time (23).
    - Another study compares environmental air samples collected from inpatient hospital rooms and quarantine households with active cases (24). The household environmental air samples were estimated to be approximately eight times (OR 8.75 [95% CI 1.21-63.43; p=0.058]) more likely to be contaminated with viral RNA than hospital air samples. Based on these study findings the investigators suggest differences in air exchanges and

ventilation to be a key difference that is more important than disease acuity, with respect to environmental air contamination.

Key Points

- In total, 84 studies on the potential for aerosol transmission have now been identified in the published and pre-published literature. Multiple outbreak and cluster investigations suggest aerosol transmission of SARS-CoV-2 may have occurred in some settings. Emerging experimental evidence in separated animals indicates infection can spread from aerosol exposure, and infectious virus can remain stable and viable within suspended aerosols. Biological monitoring studies confirm the presence of viral RNA in exhaled breath and environmental air samples. Clinical evidence informed systematic review and meta-analysis estimates of viable respiratory virus emission of SARS-CoV-2.
- Twenty-six investigations of twenty different COVID-19 outbreaks/clusters in different real-world settings (e.g., nursing home, hospital hematology unit, post-travel quarantine hotel/facility, meat processing plants, indoor choir practice, restaurant, cruise ship, passenger bus, fitness facilities, high-rise apartment building and shopping mall), have implicated aerosol transmission among cases (Table 1). The outbreak investigations suggest aerosol transmission is amplified and/or more likely to occur in some settings and under some conditions such as poorly ventilated or crowded indoor spaces, presence of early symptomatic or pre-symptomatic cases, or when individuals are engaged in physically exertive activities (e.g., singing, fitness classes).
- A systematic review and meta-analysis of clinical estimates found the likelihood of viable virus in respiratory aerosols expelled by an individual at peak viral load to be 61.1% (95% CI: 51.8-70.4%), and the likelihood estimates to be substantially lower at ≤ 0.69% (95% CI: 0.43-0.95%) for an individual with a mean viral load Peak viral load was estimated to happen between 1 day before symptom onset to 5 days post symptom onset (Table 7). This is consistent with the findings across outbreaks where the index case was usually pre-symptomatic or very early in their symptomatic illness when transmission occurred.
- Animal studies provide evidence on infection by aerosols, and infection transmission even when infected and susceptible animals are separated by cage setup or barriers. This indirect infection transmission is at least partially attributed to aerosols and air flow by the study investigators (Table 2).
- Three studies report on aerosol virus stability and viability, as well as the influence of environmental factors (e.g., temperature, humidity and sunlight exposure) on virus persistence in aerosols (Table 3). Experimental evidence has demonstrated prolonged viability of SARS-CoV-2 virus within laboratory aerosols for up to several hours (range 2 to 16 hours).
- Biomonitoring studies measure viral RNA in exhaled breath samples of infected individuals (Table 4) and environmental air from patient care and community settings (Table 5 and Table 6). The increasing number of studies that confirm the presence of SARS-CoV-2 in environmental air provide

additional evidence to support aerosol transmission in community settings. The few studies that confirmed virus viability in cell culture reported collecting environmental air samples near (<2 meters) infected individuals (Table 5 and Table 6).

Overview of the Evidence

The available body of evidence on the potential transmission of SARS-CoV-2 by aerosols in the published and pre-published literature is rapidly evolving. This review includes studies (n=84) accessed up to March 12, 2021 and deemed relevant by a single reviewer. The overall quality of the evidence reviewed is broadly described below for each section of presented evidence based on study design, quantity, and consistency of the presented data. Briefly, the hierarchy of evidence and general quality ratings consider well-conducted randomized controlled trials to be high quality due to their low risk of bias. Other experimental designs may be considered moderate quality, but may also be downgraded due to power or conduct issues. Experiments using animal models are considered low quality evidence. Observational studies are generally considered to be at high risk of bias and thus low quality, however some large, well-conducted, prospective cohort studies may be assessed to be of moderate or low risk of bias, and thus may be considered moderate to high quality.

There are 26 outbreak/cluster investigation studies focusing on 20 different human outbreaks that suggest aerosol transmission of SARS-CoV-2 (Table 1). These are retrospective observational studies that are at risk of numerous biases. The retrospective nature of these investigations and the lack of genotyping data on the majority of identified cases mean that inferences about aerosol transmission are limited to epidemiological linkages. Multiple cluster investigations include both a description of the investigation as well as *in silico* simulations that explore the potential for aerosol transmission in real world settings.

Animal models provide experimental evidence on infection by aerosol exposure, by assessing indirect transmission from infected to susceptible animals by either passive or directed air flow, when separated using a variety of cage and barrier setups (Table 2). These studies did not provide sufficient details about the symptoms and behaviors of the infected animals (e.g., sneezing and respiratory fluid transfer by sniffing/licking barriers) or the experimental setup to rule out infection transmission by contact with respiratory and oral fluids in most experiments. Overall, animal models of transmission offer the lowest quality of evidence for aerosol transmission.

Three experimental studies provide evidence confirming the stability and viability of infectious virus in artificially generated and suspended aerosols (Table 3). Although these studies provide robust evidence that supports the longevity of infectious virus in laboratory environments for as much as 16 hours, the extension of these findings to real-world settings by biological monitoring studies remains largely unestablished.

The majority of identified biological monitoring studies looked for SARS-CoV-2 viral RNA in exhaled breath (Table 4) and environmental air samples in different settings (Table 5 and Table 6). These provide moderate quality evidence that viral RNA can either travel or linger in air at some distance from an

infected individual in some settings and conditions. There is limited reporting of information on virus concentration in positive samples, sampling distance from infected individuals, and whether or not there was virus viability documented by cell culture. The lack of these details limit the generalizability of biological monitoring evidence to all indoor settings and all infected individuals, and hinder the identification of settings and conditions that lead to increased concentration of viable virus from exhaled breath and aerosolized particles in the air. Furthermore, it is likely the large range of sample collection settings (e.g., patient care vs. community settings) and techniques (e.g., exhaled breath vs. exhaled breath condensate) may have influenced the sensitivity of viral RNA quantification and viable virus detection tests, applied in biological monitoring samples. Additional research is needed to confirm the infectiousness and viability of SARS-CoV-2 within air samples to know where and when the risk of aerosol transmission of SARS-CoV-2 becomes more likely.

This review summarizes the evidence on aerosol transmission of SARS-CoV-2 and characterizes the settings and/or conditions that have been studied. Additional evidence is needed to address knowledge gaps on aerosol transmission of SARS-CoV-2:

1) Quantifying the infectious dose of SARS-CoV-2;

2) The case attributes and environmental conditions under which viable virus is likely to be present in exhaled breath, remain suspended and be circulated in environmental air;

3) Genomic data from cluster and outbreak investigations suggesting indirect SARS-CoV-2 infection transmission in humans;

4) Confirmation of the relatedness of cases by genotyping data, and better quality data supporting aerosol transmission in the implicated outbreaks/clusters; and

5) Formal review of fluid dynamic literature from experts in this field that best outline the environmental conditions and behavioral activities that increase (or decrease) respiratory aerosol release and infection transmission, as well as quantify aerosol transmission risk estimates.

CONTENTS

CLUSTER/OUTBREAK INVESTIGATIONS

This section provides a summary of twenty six studies describing twenty different COVID-19 cluster/outbreaks in real-world settings that epidemiologically support infection transmission by aerosols (Table 1). In a number of studies the same COVID-19 cluster/outbreaks were investigated by separate groups of investigators who all concluded aerosols or the long-range indirect transmission of virus to have played a role in infection spread among cases. These outbreaks have been organized according to the setting in which infection transmission was assumed to have occurred by the study investigators. The settings included a hematology unit at a hospital, a travel quarantine hotel, passenger buses, fitness classes and facilities, a meat processing plant, dine-in restaurants, a choir practice, a cruise ship, department stores, and different high-rise apartment buildings. The evidence includes epidemiological investigations, computational fluid dynamic analyses/simulations, video surveillance footage, or spatial analysis of cases during the transmission event.

Interestingly, multiple COVID-19 cluster/outbreaks were described to have occurred in settings similar to one another, which suggests these settings may be more favorable to aerosol transmission. Common attributes were closed spaces with minimal ventilation (i.e. few or no windows, insufficient ventilation and air circulation), presence of pre-symptomatic, early symptomatic index case(s), and the spread of virions beyond 2 meters enhanced by artificial air flow, ventilation systems, air ducts, drainage pipes or inefficient ventilation. Additionally, in some situations the infector and infectees were engaged in activities that typically increase exhalation rates (e.g., physical exercise, singing), or were in crowded spaces during the transmission events.

It is worth noting other than for one of the summarized studies, none reported on the genetic sequences of virus isolated from outbreak/cluster cases, and many studies do not describe mask use during the exposure events. These are important gaps within the existing evidence because genotyping data would confirm the relatedness of cases while mask use data would provide insights regarding the effectiveness of this prevention measure. The lack of this information within the summarized outbreak/cluster investigations is a key limitation of this evidence.

Table 1: SARS-CoV-2 cluster or outbreak investigations that have implicated aerosol transmission (n=26)

STUDY	METHOD	KEY OUTCOMES
Hospital hematology setting		
Saidel-Odes (2021) (25) Cluster Investigation Israel Sep – Oct 2020	Investigation of a COVID-19 outbreak linked to an index patient who was immunocompromised with multiple myeloma and underwent stem cell	Seven healthcare staff in the transplant unit housing the index patient were diagnosed with the infection; attack rate of 19% (n=7/37). The infected staff included 2 doctors, 4 nurses, and 1 housekeeping worker. Two of the positive staff did not report any direct contact with the index

new	transplant. Patient was treated in an AIIR following COVID-19 diagnosis, and healthcare staff donned appropriate PPE (i.e., N95, face shield, gown and gloves) prior to entering the patient's isolation room. All staff in the unit wore gowns, gloves and masks.	patient. The outbreak investigation and univariate analysis found infected healthcare workers were more likely to have reported spending time in the unit's corridor or nurses' station ([RR], R = 7.2; 95% CI, 1.22–42.49; *P* = .018), but not in the index patient's room. The investigators suggest aerosol transmission to be the only plausible explanation for this outbreak.
Hotel quarantine and airplane setting		
Eichler (2021) (14) Cluster Investigation New Zealand Sep 2020 *new*	Investigation of a COVID-19 outbreak that occurred during repatriation, at a mandatory isolation and quarantine facility (hotel) and among household contacts in the community. Cases who were returning from other countries were required to complete a mandatory quarantine and isolation at a facility for 14 days after landing at their destination.	Based on the application of video surveillance data and viral genomic analysis of cluster cases, the investigators suggest multiple transmission chains. The suspected sites of transmission were international and domestic flights, the quarantine facility, and households. While aerosol transmission may have been the mode in each transmission event, but an in-depth investigation concluded aerosol transmission was the primary mode of infection transmission at the hotel quarantine facility The case exposures/transmissions in the outbreak are assumed to be as follows: - 2 index cases infected around the time of repatriation travel from India to Christchurch, NZ. 1 exposed on the flight to Christchurch, 2 exposed in hallway at the quarantine facility (by aerosols see below), 1 exposed on the flight from Christchurch to Auckland (transmission from the 2 aerosol exposed cases who tested negative on day 12 of quarantine), with additional cases among household contacts of the last three cases. Based on computer footage the investigators concluded aerosol transmission to have taken place at the doorway of two different hotel rooms

		that housed individuals in quarantine by suspended aerosols. Transmission was assumed to have occurred during a 50-second window between closing the door to the room of one case and opening the door to the room of other cases. Note: A review of the hotel's ventilation system found the rooms in question had a net positive pressure compared with the corridor so air flow into the corridor when the door was open was likely.
Nursing home setting		
de Man (2020) (15) LTE Cluster Investigation Netherlands Jun –Jul 2020 *new*	Investigation of a COVID-19 outbreak in a single ward of a 7 ward Dutch nursing home.	A total of 17/21 residents in the ward and 13/34 healthcare workers from the ward, and an additional 4 laboratory workers were confirmed cases linked to the cluster; attack rate among residents was 81% and among healthcare workers was 50%. All 106 healthcare workers and 95 residents of other wards remained negative for COVID-19. Healthcare workers wore facemasks during patient care and worked in designated wards to limit contacts. The outbreak was limited to a single ward (out of 7 wards in the facility) with a ventilation system that recirculated unfiltered air. The ventilation system was new and monitored CO2 concentrations to determine when to refresh the air with outside air. Viral RNA was detected in the ventilation system (air conditioners and ventilation cabinet dust filters). The investigators state transmission was likely the result of aerosol transmission in an inadequately ventilated setting/ward given the simultaneous detection of a large number of cases limited to one ward, and occurred during a time of low community transmission.
Transportation bus setting		
Luo (2020) (7)	Investigation of a COVID-19 outbreak linked to	A total of 12 cases were identified following the investigation of 243 individuals who were

Cluster Investigation China Jan 2020 *new*	multiple bus trips by the index case, in Hunan China.	epidemiologically linked to multiple bus trips taken by the index case, attack rate of 7.0%. The seated distance of the infected individuals during bus rides ranged from 1-4.5 meters from the index case. The 2.5 hour coach ride resulted in 8 cases and not all cases were clustered close to each other during the trip. Infection was also identified in an individual who sat (approximately) on the same seat as the index case, after the index case had existed the bus. 2 cases were identified from the 1 hour minibus trip. 2 cases were tertiary cases to one of those infected on the bus. None of the identified cases reported wearing face masks during bus rides. The investigators suggest aerosols traveling beyond 2 meters and air flow to have influenced infection transmission in the crowded and closed environment of these transportation buses.
Shen (2020) (26) Cluster Investigation China Jan 2020	A COVID-19 outbreak among 128 people driven to a worship event in Eastern China on two separate buses. Round trip was 100 minutes on the bus. Attack rates were measured for Bus 1 vs. Bus 2 that had the index case. Air conditioning systems of both buses were on recirculation mode. Spatial analysis of passenger seating was estimated.	None of the passengers on Bus 1 were infected, 24 of the 68 passengers on Bus 2 developed COVID-19. Passengers riding Bus 2 with the index case had an attack rate of 34.3% (95% CI, 24.1%-46.3%), compared to passengers on bus 1. Although sitting near bus windows and doors appeared to have had a protective effect on infection transmission, the authors conclude, the lack of a significant increase in infection risk between individuals sitting in high risk zones (i.e. closer to the index case) and low risk zones, and elevated attack rates among bus passengers riding with the index case, to be partially explained by aerosol transmission of infection.
Meat processing plant setting		
Guenther (2020) (27) *preprint*	Investigation of a super-spreader event among	The analysis of index cases (flatmates) and 18 co-worker cases suggest working the early morning

Cluster Investigation Germany Spring 2020*	meat processing plant workers that included: possible routes of transmission, spatial relationship between workers, climate/ventilation conditions, sharing of living quarters and transportation, and genetic typing of oropharyngeal swab samples.	shift (140 early shift workers) to be the common source of infection. Statistically significant infection rates were observed for workers working within an 8-meter radius of the suspect index case. Authors conclude indoor confined settings, demanding physical work, and the facility's environmental conditions (i.e. air being constantly re-circulated and cooled to 10°C, with low air exchange rates) all created conditions for aerosol transmission. Note: quantitative risk estimates were not provided.
Restaurant setting		
Kwon (2020) (8) Cluster Investigation Korea Jun 2020 *new*	Investigation of a cluster among 3 patrons at a restaurant. The investigation considered epidemiological data, television images, air flow patterns and cell phone location information.	The investigators concluded infection transmission occurred from an infected customer to two individuals at the restaurant venue, attack rate of 15.4% (2/13). Source and time of exposure was assumed to be one day prior to symptom onset in the index case. The assumed mode of transmission was aerosols that travelled greater than 6.5 meters via air conditioner air flow current inside the restaurant venue. The exposure time between the infector and the infected is reported to be approximately 5 minutes. Mask use is reported to have been improper among staff and patrons.
Lu (2020) (28) Cluster Investigation China Jan-Feb 2020	Investigation of a COVID-19 cluster among restaurant patrons. The investigation included a spatial analysis of restaurant table arrangement and where cases were seated.	An outbreak among 91 individuals at a restaurant, 83 had dined at 15 tables, and the remaining 8 individuals were staff. A single asymptomatic case led to 9 COVID-19 infections among diners from three families. None of the families had met previously and did not have any close contact during lunch. No additional cases were identified during the 14 days quarantine of the remaining diners.

		Spatial analysis of case tables during lunch (i.e., exposure event reveal) found the affected tables had been arranged in line with airflow from an air conditioning unit. Authors suggest infection transmission could not be explained by droplets alone, and aerosols travelling with air flow may have contributed to infection transmission.
Li (2020) (29) *In silico* study China Feb 2020 Note: Same outbreak described by Lu (2020).	An investigation and analysis of a COVID-19 cluster among 3 families who ate at the same restaurant. The analysis included: epidemiological data, spatial analysis of restaurant table arrangement, video surveillance data, and computer fluid dynamic and tracer gas simulations of event's fine droplet spread.	10 people from three different families seated at different tables were found to have been infected with SARS-CoV-2 following a Chinese New Year's Eve (January 24, 2020) lunch. None of the waiters or patrons at the remaining tables became infected. Ventilation rate was estimated to be 0.9L/s (0.75-1.04 L/s) per person. No close contact or fomite contact was observed among cases, aside from back-to-back sitting by some patrons. Using computer simulations the authors demonstrate infection distribution to be consistent with the spread pattern of exhaled virus aerosols. These results highlight transmission occurring in a crowded and poorly ventilated indoor situation.
Choir practice setting		
Charlotte (2020) (16) Cluster Investigation France Mar 2020 *new*	The investigation of a COVID-19 outbreak linked to a choir practice, in Whir au Val, France.	Twenty-seven participants (25 singers, 1 conductor and 1 accompanist) attended the indoor choir practice that took place in a non ventilated space of 45 m^2. No attendees reported being symptomatic in the 14 days prior to the practice date. 19/27 attendees developed COVID-19 infections at 1 to 12 days post practice date (median of 5.1 days). The secondary attack rate was 70% among all attendees. The investigators assume infection transmission occurred by aerosols from presymptomatic or

		asymptomatic individual(s) who attended the choir practice as the index case was not definitively identified.
Hamner (2020) (30) Cluster Investigation USA Mar 2020 Note: Same outbreak described by Miller (2020).	The investigation of a COVID-19 outbreak linked to a choir practice, in Skagit County, Washington. The practice lasted for 2.5h. During practice people were singing and seated 6-10 inches apart, socializing with communal snacks, and stacking chairs. None of the attendees reported physical contact.	Among the 61 choir members attending the practice, at least one singer was known to be a symptomatic COVID-19 case. The epidemiological investigation reported 53 cases (33 confirmed, 20 probable cases). Secondary attack rates were 53.3% among confirmed cases and 86.7% among all cases. The odds of infection were 125.7 (95% CI: 31.7-498.9) times greater among members who attended the March 10 practice (assumed exposure event). The investigators introduce the potential for aerosol emission and COVID-19 transmission during singing in the COVID-19 literature.
Miller (2020) (31) *In silico* study USA Mar 2020 Note: Same outbreak described by Hamner (2020).	Monte Carlo simulations and mathematical modeling were used to estimate aerosol emission rates in the outbreak linked to a choir practice, in Skagit County. The applied model assumes infection transmission during the outbreak was dominated by inhalation of respiratory aerosols in a well mixed indoor environment (i.e. the aerosols were evenly distributed in the air). The viral load emitted was expressed as quanta emission rate (quanta per hour^{-1}) where a quantum	*In silico* analysis supported aerosol transmission from respiratory aerosols based on assumption that high emission rates occurred given the high attack rate (53-87%), which was higher than would be expected if the transmission was due to fomites or large respiratory droplets. The model estimates the mean respiratory aerosol emission rate for a single infected case at the exposure event to be 970 [IQR 680-1190] quanta per hour^{-1}.

	was defined as the dose of aerosol droplet nuclei required to cause infection in 63% of susceptible persons.	
Multiple outbreaks		
Buonanno (2020) (32) *In silico* study China and US (sites of applied outbreaks) Feb-Mar 2020 Note: A different analysis of restaurant and choir practice outbreaks described above	This is an emission and exposure model that used a step-wise approach to quantify individual infection risk among susceptible subjects exposed to an asymptomatic/ mildly symptomatic case in choir practice and dine-in restaurant. Also used Monte Carlo method; individual infection risks were calculated as a function of quanta emission characteristics.	The model illustrated individual infection risk increased based on ventilation rates, activities and amount of virus exhaled. For instance, sedentary activities for 1 hour may have an infection risk of 2.1%, which can increase to 27% with higher emission rates. Based on risk assessment approach and available data, quanta emission rates were estimated to be 61 quanta/hour for the restaurant and 341 quanta/hour for the Skagit Valley choir practice. In both of the examples, varying the ventilation would not have achieved an individual risk <0.1. The authors concluded aerosol transmission represents the main route of transmission for both outbreaks.
Kriegel (2020) (33) *In silico* study Germany, China, USA, (sites of applied outbreaks) Feb-Mar 2020 Note: Included the following clusters: Meat Processing plant- Guenther (2020), Choir Practice- Hamner	An extension of the Wells-Riley equation was used to estimate predicted infection risk via aerosols in twelve published and unpublished COVID-19 outbreaks. Predicted infection risks were compared to observed attack rates in each event. To estimate a "credible interval" for model predicted infection risks, the quanta emission rate,	In nine out of the twelve outbreaks the observed attack rates were in range with the predicted infection risk via aerosols and the corresponding ranges (with the variation of the boundary conditions). Predicted Infection Risk via Aerosols (PIRA)/attack rate (AR) Meat processing plant: 25% (17-35)/ 26% Choir: 97% (88-99)/ 87% Restaurant: 40% (35-56)/ 45% Bus tour: 35% (19-58)/ 34%

(2020), Bus Passengers – Shen (2020), and Restaurant – Lu (2020)	the respiratory rate as well as the air volume flows were varied. The analysis assumes long range aerosol transmission in an ideally mixed environment.	The attack rates from all these outbreaks are reported to be in-line with estimated infection risk via aerosols.
Cruise ship settings		
Azimi (2021) (34) *In silico* study Cruise ship Jan-Feb 2020 Note: Same outbreak described by Almilaji (2020) and Xu (2020)	Analysis of case data from the Diamond Princess cruise ship outbreak. Applied a framework based on stochastic Markov chain and negative exponential dose-response modeling with empirical data, to inform a modified version of the Reed-Frost epidemic model, to predict case count rates. Assumed infected individuals could be infectious upto 1 day post incubation period, effective incubation periods were estimated to be 5-11/13 days, and considered different modes of transmission. Note: Case data from early 2020 were included in the analysis.	712 COVID-19 cases were identified in 3711 passengers and crew members, yielding an attack rate of 19%. Key estimates derived from the model included - short-range droplets and aerosols (35%), long-range aerosols (35%), and fomite (30%) as modes of infection transmission - large respiratory droplets (41%) and small respiratory aerosols (59%) as source of infectious virus - Case transmission proportions prior to and after the passenger quarantine was 58% (±5% SD) and 42% (±5% SD), respectively. T - Effective reproduction number before and after the quarantine period was 3.8 (±0.9 SD) and 0.1 (±0.2 SD). Based on the modeled estimates the authors concludes smaller respiratory aerosols contributed to a greater proportion to infection transmission aboard the cruise ship, on average, across all time periods (i.e., both before and after passenger quarantine). It was estimated that aerosol transmission was the dominant mode of transmission (>70% of cases) despite the high ventilation rates (9-12 air changes per hour) with no air recirculation in the cruise ship.
Almilaji (2020) (35)	Analysis of clinical and case count data from	Infection rates among passengers in cabins without previously confirmed cases was 1.2%,

Cluster Investigation Cruise ship Jan-Feb 2020 Note: Same outbreak described by Azimi (2020) and Xu (2020)	Diamond Princess cruise ship outbreak. Post quarantine symptomatic infection onset rates (SIRR) among lab confirmed cases were examined and the design of the cruise ship's air conditioning system was considered. Note: Case data up to February 20, 2020 were included in the analysis, and a median 5 day incubation period was assumed.	which was higher than rates among passengers in cabins with previously confirmed cases 0.8%. Based on this difference, the authors suggest airborne transmission of SARS-CoV-2 through the cruise ship's ventilation system may have contributed to the outbreak, and explain the higher infection rates in cabins without previously confirmed cases.
Xu (2020) (36) *preprint* Cluster Investigation Cruise ship Jan-Feb 2020 Note: Same outbreaks described by Azimi (2020) and Almilaji (2020).	Analysis of COVID-19 case data from the Diamond Princess cruise ship outbreak was analyzed based on individual risk factors, stateroom occupancy and the air conditioning (i.e. HVAC) system of the ship to explore the most plausible modes of transmission. Case data from January 20 to February 18, 2020 were included in this analysis.	Daily infection rates for passenger cases (n=146) were predicted based on close contact vs. non-close contact status, and pre- and post-quarantine data (February 5 was the start of quarantine). The investigators concluded most passenger cases were likely exposed before the passengers were quarantined and the cruise ship's air conditioning system did not play a role in long-range aerosol transmission of COVID-19.
Fitness/sports facility settings		
Groves (2021) (9) Cluster Investigation US Jun 2020	Investigation of a COVID-19 outbreak associated with multiple exposure events in Hawaii between a stationary cycling class instructor, a kick	20 cases were linked to two pre-symptomatic fitness instructors, at different fitness classes. The kick boxing/personal training instructor was a secondary case of the stationary cycling class instructor.

new	boxing/personal training instructor and their clients. Note: The average community transmission rate at the time of the outbreak was 2–3 cases per 100,000 persons per day, which suggests alternative exposures were unlikely.	The index instructor wore a face mask during the stationary bike class but the participants did not. The instructor was > 6 feet away and facing participants during the class. The room windows and doors were closed and floor fans (for cooling) directed air at participants. The transmission events with the second instructor are assumed to have occurred during small group kick boxing and personal training sessions when the instructor did not wear a mask and mask use was minimal among participants. Both instructors taught classes prior to symptom onset and the following aggregate attack rates for were calculated: - <1 day pre symptom onset (attack rate 95%) - 1 to <2 days pre symptom onset (attack rate 13%) - ≥2 days pre symptom onset (attack rate 0%) The outbreak investigators suggest infection transmission to have been facilitated by the lack of face mask use, extended close contact, poor room ventilation, and aerosol emission during physical activity and loud speech.
Lendacki (2021) (10) Cluster Investigation US Aug-Sep 2020 *new*	Investigation of a COVID-19 outbreak associated with indoor fitness classes that were conducted at ≤25% capacity (i.e., 10–15 persons) with participants ≥6 ft apart. Note: the building was not originally designed for exercise classes and the	55 COVID-19 cases (49 confirmed and 6 probable cases) were identified among 81 individuals who participated in indoor high-intensity exercise classes, attack rate of 68%. Mask use during the exercise sessions was reported to have been infrequent and approximately 75%. Outbreak was attributed to 2 index cases who attended multiple exercise classes when symptomatic and potentially infectious. Both attendees reported mask use ≤60% of the time in class (infrequent mask use). The odds of infrequent mask use compared to consistent mask use during classes was more

	buildings ventilation system was not assessed.	common among attendees with COVID-19 than attendees not diagnosed with COVID-19 (odds ratio [OR] = 3.5; 95% CI = 0.9–15.1). Attendees diagnosed with COVID-19 also reported attending more exercise classes (median of 5 vs. 3 classes) The authors suggest infrequent mask use, increased respiratory exertion during exercise, aerosol transmission, and sub-optimal ventilation may have contributed to infection transmission in this outbreak.
Jang (2020) (37) Cluster Investigation South Korea Feb-Mar 2020	Investigation of a COVID-19 outbreak associated with Zumba classes at 12 different fitness sports facility locations following an instructor workshop in Cheonan, South Korea.	The initial transmission event is assumed to have occurred among instructors at a 4-hour workshop where 8 of the 27 attendees tested positive for SARS-CoV-2. In the following weeks case counts associated with infected instructors grew to 112 cases across multiple fitness facilities. The workshop attack rate was 26.3% (95% CI 20.9%–32.5%) and the secondary attack rate from 8 instructors was 4.10% (95% CI 2.95%–5.67%, 830 close contacts). The investigators state approximately half of identified cases (50.9%) were due to transmission from instructors to fitness class participants; 38 cases (33.9%) were in-family transmission from instructors and students; and 17 cases (15.2%) were from transmission during meetings with coworkers or acquaintances. No secondary cases were observed among Pilates and yoga class students, led by an infected instructor. Authors state intense physical activity, large number of participants in a fitness class (i.e. crowded space), and the moist warm atmosphere of the sports facility may have contributed to high rates of infection in the outbreak.

Brlek (2020) (38) Cluster Investigation Slovenia Feb-Mar 2020	Investigation of a COVID-19 cluster linked to a squash court in a fitness facility.	The cluster involved 6 cases assumed to be linked through indirect transmission of infection. Epidemiological investigation indicated the index case developed symptoms during the game of squash, and four confirmed and one suspect case were linked to the same squash hall and potentially the same change rooms. None of the cases shared sports equipment or had contact with the facility staff. No additional cases were identified. Authors suggest the infection transmission within the cluster likely occurred due to aerosolization of virus in the indoor setting including small confined space, inadequate ventilation and strenuous physical activity.
Apartment building settings		
Hwang (2021) (11) Cluster Investigation South Korea Aug 2020 *new*	Investigated the role of aerosol transmission in a COVID-19 outbreak associated with an apartment building in Seoul.	10 COVID-19 cases in 7 households were identified along two vertical lines of apartments in a building, each line of apartments were connected through a single air duct in the bathroom for natural ventilation. Attack rate of 2% among the apartment building residents (n=10/437). None of the tested surfaces, including household ventilation grills and drains were positive for viral RNA. Transmission through droplets when occupying the same common space (e.g., an elevator) was assumed to have been unlikely due to the spatial arrangement of case apartments. The outbreak investigators assume vertical air flow through a single air duct in the bathroom (consistent with air flow in a vertical shaft) to have spread the infection to upstairs and downstairs apartment residents in the building.

Lin (2021) (12) Cluster Investigation China Jan – Feb 2020 *new* Note: A different analysis of the cluster described by Kang (2020).	Investigation of a COVID-19 cluster linked to families living in three vertically aligned units of the same apartment building. The index family reported possible travel related exposure in Wuhan, but the two other families with subsequent cases did not. Tracer gas was used to simulate air flow among units.	10 COVID-19 cases were identified in 3 households, phylogenetic analysis confirmed all cases were infected by the same strain. Video surveillance footage did not identify exposures between the index household members and other cases. Investigators conclude infection transmission to have likely occurred through drain pipes connected to the toilet which were connected to sewer pipes and flood drains, a system that was shared by the vertically aligned apartments.
Kang 2020 (39) Cluster Investigation China Jan – Feb 2020 *new* Note: A different analysis of the cluster described by Lin (2021).	Investigate infection transmission among three families living in the same apartment building. The index family reported possible travel related exposure in Wuhan, but the two other families with subsequent cases did not. Investigators used Ethane tracer gas as a surrogate for gas in the buildings drainage system and computational fluid dynamics to investigate possible sources of infection and transmission among families.	10 COVID-19 cases among three families who lived in vertically aligned apartments connected by drainage pipes in the master bathrooms. Attack rate of 4% among apartment building residents and staff (n=10/217) No exposure from the building's elevators were identified, and viral RNA was not detected on elevator buttons or air vent surfaces. The surfaces most frequently contaminated with viral RNA were in the master bathrooms, suggesting these areas to be probable infection transmission sites. Based on the epidemiological and *in-silico* analyses the investigators conclude infection transmission from the index family to the other two families likely occurred through fecal aerosols traveling within vertical drainage stacks of the apartment building. Note: none of the collected air samples from this setting were positive for viral RNA.
Shopping malls/stores		
Jiang (2020) (13) Cluster Investigation	Investigation of 43 SARS-CoV-2 cases linked to a cluster at a department store in Baodi, China.	43 COVID-19 cases linked to the outbreak at a department store: 6 salespersons, 18 customers, and 19 of their close contacts. The close contact

China Jan – Feb 2020 *new*	Epidemiological data, video surveillance footage, store layout and ventilation conditions were considered in the investigation.	cases were determined to have been secondary cases without exposure to the department store. The investigators conclude aerosols to have been a significant mode of transmission among 11 cases of the outbreak. The index case was not identified but it was assumed to have been one of the infected salespersons.
Cai 2020 (40) Cluster Investigation China Jan 2020	Investigation of a SARS-CoV-2 cluster linked to a shopping mall. Clinical, epidemiological and laboratory (RT-PCR) data of cases was analyzed to assess possible modes of infection transmission.	Two shopping mall co-workers were the index cases: this was associated with 7 infections among co-workers on the same floor, 7 mall staff from other floors, 10 mall shoppers, and 2 close case contacts outside of the mall. Shoppers and co-workers from other floors denied close contact with the index cases. Based on the available data the authors suggest infection spread could have resulted from spread via fomites or virus aerosolization in a confined public space (e.g. restrooms or elevators).

LTE= letter to the editor

ANIMAL EXPERIMENTS ON AEROSOL EXPOSURE AND TRANSMISSION OF SARS-COV-2

This section summarizes the six identified animal model studies that provided experimental evidence supporting aerosol transmission of SARS-CoV-2 (Table 2). The animal models used in the studies were non-human primates, ferrets and hamsters, all of which have been established as suitable animal models for the study of SARS-CoV-2 transmission in humans (41, 42)

Two experiments involved the controlled exposure of non-human primates and hamsters to artificially generated infectious aerosols at different virus concentrations to determine if infection can occur and to follow the clinical course of the infected host animals (17, 43). These studies provide evidence that SARS-CoV-2 infection can occur from exposure to infectious aerosols in a controlled setting. One of the studies in hamsters, that compared multiple modes of transmission (i.e., aerosol, fomite and intranasal) reported virus replication and shedding in the animals to be linked to the type of exposure. The authors observed earlier viral replication, higher viral loads, acute manifestation of respiratory symptoms, and different viral shedding patterns in the respiratory tissue of animals infected through aerosols compared to animals infected by intranasal and fomites mode of exposure (17).

Five experiments investigated SARS-CoV-2 transmission between infected and susceptible host animals (i.e., transmission pairs) that were physically separated by different barriers and cage setups (17, 18, 44-46). In most experiments, transmission pairs were separated by barriers that prevented direct contact but allowed for air flow. This led to 25-100% of the susceptible animals becoming infected after some duration of exposure. These experiments provide evidence supporting aerosol transmission among host animals in experimental settings.

Additional evidence from two experiments demonstrate how air flow and ventilation can impact indirect transmission of infection (17, 45). In one of these experiments transmission pairs of ferrets were housed in physically separated cages but shared air through connected air ducts, which led to 50% of the susceptible animals becoming infected (45). In another experiment the influence of air flow direction on likelihood of infection transmission was investigated, and results show infection only occurred in the susceptible hamster housed downwind from the infected hamster (17).

The small sample sizes, animals not being separated by large distances, the lack of details on animal behavior during the experiment (e.g., coughing or sneezing symptoms in infected animals), and at times the lack of detail regarding the permeability of separation barriers to respiratory and oral fluids, fecal and food particle movement, limit this evidence from completely supporting aerosol transmission.

Table 2: Animal experiments on aerosol exposure and indirect transmission of SARS-CoV-2 (n=6)

STUDY	METHOD	KEY OUTCOMES
Edwards (2020) (43) *In Vivo Study* USA Oct 2020*	Eight non-human primates Macaca mulatta (rhesus macaque) and Chlorocebus aethiops (African green monkey)) were infected with aerosols (≈2 µm) containing SARS-CoV-2 (~2.5x10^3 TCID50) using a laboratory inhalation system	Mucosal sampling by nasal swabs showed viral RNA detected as early as +1 day post infectious aerosol exposure with viral titers reaching peak levels at +7 days post infection, and clear decline of RNA by day +14 days post infection, and undetectable by +28 days post infection. These findings confirm SARS-CoV-2 infection by infectious aerosols can occur. Mucosal sampling by nasal swabs showed viral RNA detected as early as +1 day post infectious aerosol exposure. Exhaled breath particle production started 3 days post infection rose to day 7 and decreased to baseline by day 14 in primates. Exhaled breath particle production was temporally consistent with viral replication in nasal swab samples.

		There was a significant association between exhaled breath particles and viral load in most primates and correlated with viral kinetics. Viral RNA was undetectable in nasal swab samples of infected primates by day 28 post-infection.
Port (2020) (17) *Preprint* *In Vivo Study* USA Dec 2020* *new*	Three groups of female *Mesocricetus auratus* (Syrian hamsters) (n=36) were infected with SARS-Cov-2 virus aerosols and other types of exposures (i.e., fomites and intranasal). Infected animals were compared to unexposed controls (n=12). Exposure by SARS-CoV-2 aerosols ($1.5x10^3$ TCID50) was by a 3 jet collision nebular; particle size ranged from 1-5 um. Viral shedding and replication patterns measured in respiratory tissue and by fecal and oropharyngeal swabs. During separate airborne transmission experiments two transmission pairs (n=4) were co-housed in cages separated by a perforated plastic divider that prevented direct contact. The susceptible animals were placed in the direction or against the air flow from infected animals; four transmission pairs (n=8). Infection	The authors found mode of SARS-CoV-2 infection transmission played a factor in disease severity, viral load, and virus shedding in the animal model. Early virus replication (1 day post infection), peak respiratory shedding of virus at 2 days from exposure, and higher early viral loads in lung and tracheal tissue (p = <0.0001), was observed among aerosol exposed animals when compared to other exposure types. Viral titers in lung tissue showed a positive relationship with upper and lower respiratory tract pathology and weight loss, which lead the authors to suggest early respiratory shedding (as observed among animals infected by aerosols) may predict acute disease manifestation. In the indirect contact experiments assessing airflow based transmission no symptoms linked to infection were observed in the susceptible animals but 25% (n=1/4) seroconverted. This seroconversion (i.e., virus exposure) was linked to directional airflow from the infected to host animals. Of note, it was observed fomite transmission was linked to delayed disease manifestation with longer duration of time between exposure and viral replication in respiratory tissue, which led to reduced disease severity.

	detected based on serum seroconversion.	
Zhang (2021) (18) *Preprint* *In Vivo Study* USA Jan 2021* *new*	Investigated the risk of SARS-CoV-2 infection transmission from aerosol exposure, and risk of re-infection at re-challenge between naïve infected and previously infected transmission pairs of *Mesocricetus auratus* (Syrian hamsters). In the aerosol transmission experiments infected and donor hamsters (n=6) were housed in transmission cages with wire mesh partitions that prevent indirect and direct contact between animals, but permitted airflow. Live virus levels in respiratory tissue over the post exposure period was measured to confirm re-infection.	Experiments found SARS-CoV-2 was efficiently transmitted from infected naïve hamsters to previously infected hamsters by airborne transmission, among all transmission pairs. Based on viral RNA levels in respiratory tissue, the investigators conclude prior infection to have provided provide some good protective immunity but not complete immunity against re-infection at re-challenge; replicating live virus was present in the re-infected animals.
Sia (2020) (44) *In Vivo* Study Hong Kong* May 2020*	Experimental study that investigated SARS-CoV-2 infection transmission via aerosols in Mesocricetus auratus (Syrian hamsters). Infected and susceptible animals were housed in adjacent wire cages placed 1.8 cm away from one another (3 different pairs)	Efficient indirect transmission of infection to susceptible hamsters occurred in all three pairs within experimental settings. Peak viral load in aerosol exposed hamster was at 3 days post contact.

	were exposed to one another for 8 hours.	
Kutter (2020) (45) *Preprint* *In Vivo Study* Netherlands* Oct 2020*	An experimental set-up where infected and susceptible pairs (i.e. transmission pairs) of individually housed *Mustela putorius furo* (ferret) (n=8) were connected through a hard 15 cm air duct opening with multiple 90^0 turns. Airflow was directed upwards from the donor to indirect recipient animals. Air travelled an average of 118 cm (approx. 3 ft.) through the tube systems. Note: transmission of SARS-CoV-2 and SARS-CoV was investigated.	Indirect transmission of SARS-CoV-2 between two ferrets more than 1 meter away was confirmed in 50% separately housed transmission pairs. Infection in susceptible animals were confirmed through the detection of viral RNA in throat and nose swabs.
Kim (2020) (46) *In Vivo Study* South Korea* May 2020*	An experimental study of SARS-CoV-2 transmission between *Mustela putorius furo* (ferret) separated by a partition (n=6). Indirect contact of ferrets was maintained by a permeable partition between cages to separate susceptible and infected ferrets.	The authors found 33% of indirect contact ferrets were positive for viral RNA in nasal washes and fecal specimens. Authors suggest aerosol transmission to have occurred among indirect contact ferrets.

*Estimated based on author affiliations and publication date.

SARS-COV-2 VIABILITY IN AEROSOLS

Three studies measured the half-life of viral particles suspended in artificial aerosols within experimental settings studies and confirmed the viability of virus in artificial aerosols by plaque assays and cell culture (19, 47, 48). These studies found SARS-CoV-2 virus titers remained stable in artificially created aerosols up to timeframes that ranged from 2 to 16 hours (19, 47, 48). The stability and infectiousness of virus in artificial aerosols appear to be dependent on environmental factors such as temperature, humidity and simulated sunlight levels, as previously suggested in some computer generated analysis. One experimental study demonstrated simulated sunlight had the largest impact on decay rate, high temperatures (only 10-40°C were tested) had a moderate impact and a significant interaction with sunlight whereas relative humidity had the least influence on decay overall and only at high (70%) relative humidity (19).

Table 3: Experimental evidence confirming SARS-CoV-2 virus stability in aerosols (n=3)

STUDY	METHOD	KEY OUTCOMES
Dabisch (2020) (19) Simulation experiments USA* Aug 2020* *new*	Measured the viability and persistence of SARS-CoV-2 in artificially generated aerosols within a drum aerosol chamber across a range of temperatures (10 °C, 20 °C, 30 °C and 40°C), relative humidity (20%, 45% and 70%), and simulated sunlight levels of zero integrated UVB irradiance (i.e., indoor/night/darkness), 0.9 W/m2 UVB irradiance and 1.9 W/m2 integrated UVB irradiance (i.e., summer midday sunlight). Viral concentration was held at mean value of 2.3 ± 0.4 $\log_{10}$ $TCID_{50}$/L-air during the experiment. Infectiousness of virus within aerosols was measure using micro titration assay and Vero cells. Experiment results informed a regression model predicting	The time needed for a 90% decrease in infectious virus at 400C, 20% relative humidity increased from 4.8 min with sunlight representative of noon on a clear summer day outdoors, to more than 2 hours under conditions representative of indoors or at night. Across other temperature and humidity levels the decay per minute in midday sun simulations ranged from 38.1% ± 8.9% per minute at 40 °C and 20% relative humidity, to 18.9 ± 4.8% per minute at 10 °C and 20% relative humidity. For moderate sunlight representing spring and fall intensity at 40 °C, decay rates ranged from18.0 ± 6.2% per minute at 30 °C and 45% relative humidity, to 11.1 ± 4.6% per minute at 10 °C and 20% relative humidity. In the absence of sunlight <2% decay (mean) per minute rate was estimated, for

	aerosolized SARS-CoV-2 decay under variable conditions.	most tested temperature and humidity levels. Exceptions were in the higher temperature and/or humidity ranges: - Decay rate at 30 °C with 70% relative humidity was 6.3 ± 2.6% per minute. - Decay rate at 40 °C with 20% relative humidity was 3.9 ± 0.4%. In the regression analysis sunlight had the largest influence on decay followed by temperature and a sunlight x temperature interaction. Humidity (relative or absolute) had the lowest influence on the decay constant. Thus, more intense sunlight and high temperatures >30°C had faster decay rates.
Fears (2020) (47) Simulation experiments USA* Sep 2020*	The long-term persistence of artificially generated viral aerosol suspensions of SARS-CoV-2 was measured at different time intervals. Viral contents were quantified by RT-PCR, and infectiousness of virus was measured by plague assay. Samples were qualitatively assessed by electron microscopy.	Infectious SARS-CoV-2 was detected at 10 minutes, 30 minutes, 2, 4, and 16 hours during the aerosol suspension stability experiment. A minimal reduction in viral genome copies in aerosol samples (as measured by RT-PCR) was noted for the measured time points. A minor but constant fraction of the SARS-CoV-2 virus in aerosols maintained replication-competence at all measured time points, including at 16 hours. Qualitative assessment of virion integrity revealed virions were either ovoid or spherical in shape, and maintained the expected morphologies up to 16 hours in aerosol suspension.
Van Doremalen (2020) (48) *LTE* Simulation experiment	In this experiment SARS-CoV-2 and SARS-CoV-1 virus titer stability and decay was measured from artificially generated aerosols, in Vero 6	SARS-CoV-2 virus remained viable in experimentally generated aerosols up to 3 hours (duration of the experiment), with a reduction in infectious titer from $10^{3.5}$ to $10^{2.7}$ $TCID_{50}$ per liter of air

USA* Spring 2020*	cell culture. Analysis used a Bayesian regression model.	In aerosols the half life of SARS-CoV-2 virus was estimated to be 1.1-1.2 with a 95% credible interval of 0.64-2.64.

*Estimated based on author affiliations and publication date.
LTE= letter to the editor

SARS-COV-2 RNA IN EXHALED BREATH

Six studies investigated the presence of viral RNA in exhaled air samples or exhaled breath condensate samples of SARS-CoV-2 from human cases (20, 50-53).

Two different exhaled breath sampling techniques were identified across the studies: some studies collected exhaled breath condensate while others collected exhaled air samples from infected individuals. Exhaled breath condensate techniques collect 1-2 ml of condensate by the cooling and condensation of exhaled air during quiet breathing. Some investigators have suggested the exhaled breath condensate technique is better suited for identifying biomarkers expelled from the lower respiratory tract, and results in reduced false negative results by RT-PCR (50, 54).

Five of the included studies reported at least one exhaled air sample positive for viral RNA. Among the identified studies that confirmed the presence of viral RNA in some exhaled samples, four applied the exhaled breath condensate technique while two were based on exhaled air sampling. Sample positivity ranged from 16%-93.5% in exhaled breath condensate sampling studies to 40% in the single exhaled breath sampling study with positive results. One study reported no positive samples, for both exhaled breath condensate and exhaled air collection techniques (53). The variability in viral RNA positivity across exhaled breath samples may be linked to the infectious course of sampled individuals. However, the lack of clinical information on exposure and symptom onset dates, symptoms, as well as viral loads and viral replication in respiratory tissue, at the time of sample collection limit inferences between viral exhalation and infection course. Based on evidence that peak viral load occurs between one day before and up to five days post symptom onset, hospitalized or symptomatic individuals several days into their infection may not be an appropriate sample for measuring viral RNA within exhaled breath (43, 55). Hospitalized individuals may no longer be infectious at the time of sample collection, which should not be interpreted as a lack of evidence supporting infection emission by exhaled breath during the early infection period.

Table 4: Biological monitoring studies on SARS-CoV-2 RNA in exhaled breath (n=6)

STUDY	METHOD	KEY OUTCOMES
Reporting SARS-CoV-2 in samples		
Ryan (2020) (50)	Exhaled breath condensate samples were collected	93.5% (29/31) of the collected exhaled breath samples from SARS-CoV-2 patients (clinically

Exhaled breath condensate monitoring study Ireland Apr - May 2020 *new*	from COVID-19 patients using RTUBE condensers. The sample included nasopharyngeal swab positive (n=16) and nasopharyngeal swab negative with clinical diagnosis of COVID (n=15) patients. Additional samples from pre-SARS-CoV-2 were included as controls (n=14). Virus in samples was detected by RT-PCR using different viral gene assays. Note: Clinical diagnoses of COVID-19 were based on clinical expertise and imaging results.	confirmed and/or positive nasopharyngeal swab results) were positive by RT-PCR targeting all four genes (E, S, N, ORF1ab). All pre-pandemic control samples were negative. In this study exhaled breath was shown to be a sensitive and non-invasive sample type. Positivity of samples varied by RT-PCR assay target sequence among nasopharyngeal swab negative patients (n=15): - 66% (10/15) positivity for viral envelope (E)/ spike (S) proteins gene assays (used for the nasopharyngeal swab). - 73% (11/15) positivity for viral nucleocapsid (N)/open reading frame (ORF1ab) gene assays. The combined results equated to 14/15 clinically diagnosed cases positive on at least one assay.
Zhou (2021) (49) Exhaled breath condensate monitoring study China Feb - Mar 2020 *new* Note: Additional results on viral RNA in air samples are summarized in Table 5.	COVID-19 patients (n=10) about to be discharged from hospital (as per negative throat and nasal swabs) were recruited from multiple hospital sites. Exhaled breath condensate was sampled using using a BioScreen II device. SARS-CoV-2 RNA in breath samples was quantified using RT-PCR.	22.2% of 9 COVID-19 patients about to be discharged from hospital had SARS-CoV-2 in their exhaled breath samples at a concentration of ~10^5 RNA copies/m^3. Both patients were over the age of 70. It was estimated that some COVID-19 patients in the sample were exhaling the virus at a rate of ~1400 RNA copies per minute into the air at discharge.
Ma (2020) (51) *Preprint*	Exhaled breath condensate samples were collected from COVID-19 patients	The study confirms the emission of SARS-CoV-2 virus RNA into the air from exhaled breath condensate of infected individuals (16.7% n=5/30). The positive samples were detected either <3 days from symptom onset

Exhaled breath condensate monitoring study China Spring 2020* Note: Additional results on viral RNA in environmental air samples are summarized in Table 5.	(n=30) using a BioScreen device.	(n=3) or within 7-14 days from symptom onset (n=2). SARS-CoV-2 levels in exhaled breath were estimated to reach 10^5-10^7 copies/m^3 if an average breathing rate of 12 L/min is assumed and is highest during early stages of infection.
Di Carlo (2021) (20) Exhaled air monitoring study Italy Apr - Jun 2020 Note: Additional results on viral RNA in environmental air samples are summarized in Table 5 *new*	Tests the release of SARS-CoV-2 RNA into the air during normal breathing – without coughing, sneezing or talking among infected cases (n=5). These cases were all in hospital patients admitted to hospital for non-COVID symptoms who later developed COVID symptoms during hospital stay. Sampled individuals were housed in airborne infection isolation rooms (AIIR) and exhaled breath samples were collected using Sartorius AirPort sampler. Patient oropharyngeal, nasopharyngeal and salivary swabs samples were also collected at the time of breath samples.	The days since symptom onset to sample collection varied from 7- 56 days in the patient sample. Oropharyngeal and nasopharyngeal swabs of 4 patients were positive at the time of sampling. Viral RNA was detected at 1 cm distance from patients' mouths in two patients (40% n=2/5). Both had positive oropharyngeal, nasopharyngeal and salivary swabs. Salivary swabs were negative in the patients with negative exhaled air samples who were reported to be infected based on consecutive positive swab samples. In one of these patients, wearing a surgical mask effectively blocked viral RNA detection at 1 cm (masked samples were not collected from the other patient with positive exhaled air samples). Air samples at 1 cm from RT-PCR negative patients were negative for viral RNA.
Feng (2020) (52)	Sampled exhaled breath and environmental air of COVID-19 patients using a NIOSH bio-aerosol sampler.	SARS-CoV-2 RNA was not detected in any of the patients' expired breath samples (n=0/9). Viral RNA was isolated in exhaled breath

Exhaled air & exhaled breath condensate monitoring study China Feb - Mar 2020 Note: Additional results on viral RNA in environmental air samples are summarized in Table 5.	Exhaled breath condensate was sampled using a sterile laboratory-made collection system. Air samples were segregated by aerosol size. Samples were collected from COVID-19 patients in the later stages of infection in hospital settings.	condensate (25%; n=2/8), and bedside environmental air samples (8%; n=1/12). The authors attributed minimal contamination of viral RNA in study samples to reduced respiratory viral shedding among patients in later stages of infection.
Reporting NO SARS-CoV-2 in samples		
Ding (2020) (53) *Preprint* Exhaled air and exhaled breath condensate monitoring study Hong Kong Feb 2020 Note: Additional results on viral RNA in environmental air samples are summarized in Table 5.	Exhaled breath condensate samples (n=2) and expired air samples (n=2) were collected from COVID-19 patients housed in airborne infection isolation rooms (AIIR). Multiple devices were used for air sample collection (n=27), which was conducted on different days. Note: sample collection distances from patient(s) are not reported.	All collected exhaled condensate samples and expired air samples were negative for SARS-CoV-2 RNA.

*Estimated based on author affiliations and publication date.

SARS-COV-2 RNA IN ENVIRONMENTAL AIR

Forty-nine biological monitoring studies that investigated SARS-CoV-2 in air samples collected from patient care settings, such as airborne infection isolation rooms (AIIR), ICU, emergency wards, hospital wards, nursing homes, diagnostic areas (e.g., CT scan) and outpatient clinics, were identified (Table 5). All of these studies report the presence of confirmed case(s) in the proximity of sample collection. The majority of studies (n=29/40) reported the isolation of viral RNA from at least one collected air sample by RT-PCR. Three studies successfully cultured virus particles isolated from a very small number of positive air samples in cell culture, thus providing evidence to support virus viability in air (56-58). All of these air

samples with viable virus were collected close (<2 meters) to confirmed cases. Furthermore, air samples taken at 1-4.8 m from confirmed cases consistently identified SARS-COV-2 RNA, with higher concentrations of viral RNA when the collection apparatus was positioned closer to the case (21, 56-61, 64, 65, 93)

A single study in a patient care setting demonstrated opening the windows in the COVID-19 patient's room to be beneficial and reduced the viral concentration in the air sample from 10^5/ml to less than 10^4 (61). Another study compares environmental air samples collected from inpatient hospital rooms and quarantine households with active cases (24). The household environmental air samples were estimated to be approximately eight times (OR 8.75 [95% CI 1.21-63.43; p=0.058]) more likely to be contaminated with viral RNA than hospital air samples. The investigators suggested variability in air exchanges and ventilation between patient care and community settings to be the main difference that influenced air contamination between the two settings, as such room ventilation was suggested to be a more important factor than disease acuity with respect to environmental air contamination.

Nine biological monitoring studies of SARS-CoV-2 in air samples from community settings (i.e., a car driven by an infected case, shopping mall, concert hall, hotel quarantine rooms and households, mink farm, public buses and subway trains) were identified (Table 6). The majority of these studies (n=5/9) confirm the presence of viral RNA by RT-PCR and in one study, air samples from a car with a COVID-19 case isolated virus in cell culture (23). The study in the car highlights that significant quantities of viable SARS-CoV-2 can be expelled from even mild cases over short periods of time (23). A study on a mink farm with an ongoing outbreak highlights high levels of virus within the farm, which is a risk for the workers, however there was low risk outside of the farm to the surrounding community (66). The identification of positive air samples from quarantine households and hotel rooms with active cases was variable and requires further investigation, as some studies identified positive samples while others did not (24, 67, 68). Two environmental sampling studies of public venues, including a concert hall, a shopping mall, and public buses and subway trains also confirm the presence of viral RNA in air samples (61, 69). Interestingly, these studies do not confirm the presence of cases in the proximity of air sample collection but indicated high levels of community transmission in sampled settings (61, 69).

A range of air sampling methods were used across the included biological monitoring studies. Some studies used different air sampler models while others used fluid filled petri dishes, gelatin filters, agar plates and novel COVID-19 traps to sample environmental air. The variability in sampling methodologies may have contributed to the observed differences in viral RNA detection and confirmation of virus viability and infectiousness in environmental air samples. Only a small number of studies confirmed the viability of virus in cell culture and all samples were very close (<2 meters) to infected individuals.

The authors who reported no virus contamination in air samples collected from patient care settings often suggested effective disinfection, high efficiency air ventilation and filtration systems fitted to AIIR as possible reasons for negative results. This rationale is further supported by one biological monitoring study which was unable to detect viral RNA in collected samples when the air sampler inlet was covered with a HEPA filter (56).

Among the identified studies, viral RNA concentration within contaminated samples, isolated aerosol particle sizes and fractions, sampling distance from COVID-19 cases, air sample volume, and any attempts to culture isolated virus particles were not consistently reported. Moreover, the majority of studies did not provide clinical information, such as symptom onset data or presence of respiratory symptoms, on the cases present during air sample collection, nor ventilation and air flow in the sampled setting. These data gaps make it difficult to determine the conditions upon which infectious virus in environmental air samples becomes more frequent.

Table 5: Biological monitoring studies investigating SARS-CoV-2 within air in patient care settings (n=40)

STUDY	METHOD	KEY OUTCOMES
SARS-CoV-2 in cell culture samples		
Lednicky (2020) (56) Biological monitoring study USA* Nov 2020*	Air samples were collected in triplicate from hospital rooms of COVID-19 patients in the absence of aerosol generating procedures. Air samples were collected using a VIVAS air sampler at 2 to 4.8 meters away from patients, with and without a HEPA filter on the air sampler inlet tube. Virus in isolated air samples was measured using RT-PCR, and infectiousness was measured based on cytopathic effects in cell culture (LLC-MK2 and Vero-E6). The genomes of isolated virus was sequenced.	Viable (infectious) SARS-CoV-2 was found to be present in aerosols sampled from hospital patient rooms by RT-PCR and cell culture (via cytopathic effects) All air samples collected without a HEPA filter was positive for viral RNA. A single nearly complete virus sequence was isolated from the air samplers that collected environmental air. This genetic sequence matched the virus strain isolated from nasopharyngeal sample of one of the two patients who occupied the room during sampling. The matched person was diagnosed with acute infection at the time of air sampling.
Santarpia (2020) (57) *Preprint* Biological monitoring study USA Apr 2020	Patient generated aerosols in hospital air samples were collected using a NIOSH BC251 aerosol sampler at the foot of COVID-19 patient beds. Aerosol sizes and concentration was concurrently measured during sample collection using an	RNA was detected in all six patient rooms, and included all aerosol particle size fractions (defined as >4.1 µm, 1-4 µm, and <1 µm). Replicating virus in cell culture was observed in most <1 µm aerosol samples, two of the 1-4 µm size aerosol

	Aerodynamic Particle Sizer Spectrometer. Aerosols were distinguished by the proportion of different sizes (>4.1 µm, 1-4 µm, and <1 µm) among samples. Presence of the virus in isolated aerosols (<5µm) was measured using RT-PCR, western blot, and transmission electron microscopy and infectiousness of isolated viral particles was examined using cell culture (Vero-E6). Note: The study does not specify if the patients were housed in regular wards or AIIR.	samples and two of the >4.1µm samples. Western blot and TEM analysis of these samples also showed evidence of viral proteins and intact virions. The authors conclude the infectious nature of the aerosols collected in this study suggests that aerosol transmission of COVID-19 is possible.
Santarpia (2020) (58) Biological monitoring study USA Mar 2020	Air samples from negative pressure isolation spaces and wards housing COVID-19 cases were collected using a Sartorius Airport MD8 air sampler and tested for SARS-CoV-2 viral RNA by RT-PCR. A subset of positive samples were examined for viral propagation in Vero E6 cells. Several indicators were utilized to determine viral replication including cytopathic effect, immunofluorescent staining, time course PCR of cell culture supernatant, and electron microscopy.	63.2% of in-room air samples were positive by RT-PCR (mean concentration 2.42 copies/L of air). Two samples placed at different proximity to a patient, including a sample from <2 meters away the patient, were positive. Viral concentration was higher in the air sample collected closer to the patient (4.07 vs. 2.48 copies/L of air). 58.3% of air samples collected from hallways were positive (mean concentration of 2.51 copies/L of air). Some viral replication was observed in a single positive sample collected from a hallway.
SARS-CoV-2 RNA in samples		
Munoz-Price (2021) (24) Biological monitoring study US Spring 2021*	Air samples (n=16) collected from hospital ICU inpatient rooms occupied by confirmed COVID-19 cases. Air samples were collected using the Sartorius MD8 airscan sampler, positioned at 0.3 -1.8	12.5% (n=2/16) of hospital air samples were only positive for viral RNA. These samples where collected at 0.3 meters from confirmed cases. The patients had mild severity of illness and were not on

new Note: Additional results on viral RNA in environmental air from household settings are summarized in Table 6.	meters from patients' head. Viral RNA in samples was measured by RT-PCR.	supplemental oxygen at the time of sample collection.
Razzini (2020) (70) Biological monitoring study Italy Apr 2020* *new*	Air samples (n=5) collected from hospital areas with COVID-19 cases using a MD8 Airport Portable Air Sampler with gelatin membrane filters. Samples were collected from three zones, contaminated (corridor for patients and ICU), semi-contaminated (undressing room) and clean areas (medical staff dressing and locker areas). Viral RNA in samples was measured by RT-PCR.	All the air samples collected from COVID-19 cases' ICU and corridor were positive for viral RNA; samples from other areas were negative. Viral concentration in (mean Ct) across ICU air samples was 22.6, and 31.1 for corridor air samples.
Ge (2020) (71) Biological monitoring study China Jun 2020* *new*	Air samples (n=33) were collected using the NIOSH bioaerosol sampler BC251. Sampled settings were ICU, hemodialysis clinics, fever clinics, and respiratory wards. Viral RNA in samples was measured by RT-PCR.	All air samples (n=3) from the ICU setting were positive for viral RNA. Viral concentrations in samples ranged from Ct 36.5 - 37.8.
Hu (2020) (72) Biological monitoring study Feb – Mar 2020 China *new*	Air (aerosol) samples were collected from multiple hospital sites using a centrifugal aerosol-to-hydrosol sampler (n=123). Viral RNA in samples was measured by RT-PCR and viability by Vero-E6 cell culture.	Eight air samples (21%) from ICU environments and one same from (16%) from the CT (computerized tomography) room were positive for viral RNA. The range of virus concentrations in the positive air (aerosol) samples was 1.11×10^3 to 1.12

		× 10^4 RNA copies m^{-3}. The virus could not be cultured from positive samples.
Seyyed (2020) (73) Biological monitoring study Iran May 2020* *new*	Air samples (n=10) were collected from COVID-19 patient ICU wards using a sampling pump with a porous midget impeller. Viral RNA in samples was measured by RT-PCR.	60% of air samples were positive for viral RNA. The highest RNA concentrations were measured in samples from between patient beds (3913 copies per ml). These were air samples collected at 1.5 to 2 meters from patient beds.
Moore (2020) (59) Biological monitoring study England Mar –May 2020 *new*	Air samples (n=55) were collected from COVID-19 patients with and without respiratory symptoms, from eight different hospitals. Sampled settings included AIIR, general COVID-19 wards and non-COVID-19 wards. Samples were collected using a Coriolis µ air sampler and/or Sartorius MD8 air sampler. Viral RNA in samples was measured by RT-PCR, and viability by Vero-E6 cell culture.	7% (n=4) of air samples were positive for viral RNA, at low concentrations from <10 to 460 genomic copies/m^3 air. The virus could not be cultured from positive samples. All positive samples were collected at 1 meter distance from patients, and days since symptom onset among the patients ranged from 8-10 days.
Hernández López (2021) (60) Biological monitoring study Jan 2021* Mexico *new*	Air samples (n=15) from emergency, internal medicine and COVID-19 patient rooms and multiple bed patient care rooms in two hospitals were collected using a Millipore sampler. Viral RNA in samples was measured by RT-PCR.	Three air samples (20%) were positive for viral RNA. All positive samples were from the COVID-19 patient room and near the patient.
Tan (2020) (74) Biological monitoring study China Mar 2020 *new*	Air samples (n=12) were collected from ICU and isolation wards of COVID-19 cases in hospital, and corridors. Air samples were collected at 1 meter from a patient's head.	A single air sample from a patient care area, collected when the patient was undergoing intubation, was positive for viral RNA.

Gehrke (2021) (61) *Preprint* Biological monitoring study Germany Oct 2020 - Jan 2021 *new* Note: Additional results on viral RNA in community setting air samples are summarized in Table 6.	Air samples were collected from patient rooms in two COVID-19 isolation units, and an outpatient endoscopy facility using non-powered cold traps. Viral RNA was quantified by RT-PCR.	Hospital setting samples: No viral RNA was isolated from the first isolation unit ventilated permanently by two windows. Viral RNA was detected in samples collected from a non-ventilated corridor next to the isolation room. In the second isolation unit samples, SARS-CoV-2 RNA levels reached concentrations of 10^5/mL in non-ventilated rooms, but when windows were open to increase ventilation SARS-CoV-2 RNA concentrations in samples were reduced to 10^4/mL or less. In the endoscopy facility, 50% of cold traps were positive for viral RNA (n=6/12). 57% of cold traps (n=4/7) from endoscopy operation rooms were positive for SARS-CoV-2, but RNA concentrations (initially at 12 copies/ml) and the number of positive samples were reduced when the ventilation levels in the room was increased.
Zhou (2021) (80) Biological monitoring study China Feb- Mar 2020 *new* Note: Additional results on viral RNA in exhaled breath samples are summarized in Table 4.	Air samples (and exhaled breath samples) of hospitalized COVID-19 patients were collected from multiple hospital sites. Air samples were collected from hospital corridors, waste storage rooms, ICU rooms, toilets, medical preparation rooms, clinical observation rooms, and general wards. Air samples were collected using the Air-nCoV-Watch (ACW) system and viral RNA quantified by RT-PCR.	6.8% of the air samples (n =3/ 44) were positive for viral RNA at digital PCR concentration levels ranging from 9-219 viruses/m^3.
Yarahmadi (2021) (64)	Air samples were collected (n=20) from an ICU ward at, 1) a	50% (n=2/4) of samples from the patient breathing zone were positive for

Biological monitoring study Iran Feb 2021* *new*	COVID-19 patient breathing zone (i.e., side table next to patient's head), general area (10 meters from the ICU unit), and breathing zone of health care personnel near the COVID-19 patient's bed, and 1 meter from the patient's bed. Samples were collected using NIOSH and ASHRAE bioaerosol samplers. Viral RNA was detected by RT-PCR.	viral RNA. The positive samples were from a confirmed case, and negative samples were from a suspected case. 12.5% (n=1/8) of samples from health care personnel breathing zone were positive for viral RNA. 12.5% (n=1/8) of samples from the general area were positive for viral RNA. Authors suggest bioaerosols maybe present due to the re-aerosolization of previously airborne SARS-CoV-2 particles from health care personnel walking between different wards and stations of the ICU.
Ong (2021) (93) Biological monitoring study Singapore Jan 2021*	Air samples were collected from AIIR in a hospital and community isolation facility (naturally ventilated) housing confirmed COVID-19 patients, at 1 meter away from the patient. Air samples were collected using a BioSpot-VIVAS BSS300-P bioaerosol sampler (collecting particles <4.34 µm in size). NIOSH aerosol samplers were used to validate the Biospot results. SARS-CoV-2 RNA was detected by RT-PCR, and cultured using Vero C1008 cell culture.	50% of BioSpot air samples from hospital AIIR (n=6/12) were positive for SARS-CoV-2 RNA (concentrations ranging from 178.9 to 2,738.4 copies/m^3). Positive samples were collected from rooms with at least one symptomatic patient (<7 days post symptom onset). NIOSH aerosol samplers detected SARS-CoV-2 RNA in aerosols <1 µm, 1–4 µm, and >4 µm in diameter. Only 1 of 9 samples from the community isolation facility was positive for SARS-CoV-2 RNA, with a concentration of 978.3 copies/m^3. Virus cultures of all positive samples were negative.
Dumont-Leblond (2020) (21) Biological monitoring study Canada Mar-June 2020	Sampled air from AIIR rooms from a Quebec hospital housing non-severe COVID-19 patients (n=22). Air samples were collected (with 3 µm gelatine filters and 0.8 µm polycarbonate filters) using a SASS 3100 dry sampler, at 1.5m	11% (n=11/100) of air samples collected at the bedside of 6 patients were positive for viral RNA. These patients had higher frequency of fever, dyspnoea, and cough compared to others in the sample. Most were males

new	away from the patient bedside. Viral contamination was measured by RT-PCR and Vero E6 cell culture.	and had a slightly longer duration of hospitalization. Average SARS-CoV-2 viral load in the positive sample rooms was estimated at 4.86E+4 virus genomes per hour. No virus isolated from air samples could be cultured.
Binder (2020) (75) Biological monitoring study USA Apr-May 2020 *new*	Environmental swabs and aerosol samples were collected from single patient hospital rooms housing COVID-19 patients (n=20, 16 symptomatic and 4 asymptomatic) within a dedicated COVID-19 ward. Bioaerosols were collected using a NIOSH BC 251 sampler placed at different distanced from the patients' heads (1, 1.4, 2.2, and 3.2 meters). Empty hospital rooms, hallways, staff break room and staff workstations were sampled as controls. SARS-CoV-2 viral contamination was measured by RT-PCR, and Vero EC6 cell culture.	Three samples collected from three of the COVID-19 patient rooms were positive for viral RNA; samples were collected at 1.4-2.2 meters from the patients. These patients were 4-10 days post symptom onset (runny nose, headache, fever, cough, difficulty breathing, fatigue, loss of smell, gastrointestinal symptoms). Viable virus could not be identified in bio aerosols samples via cell culture. Samples from other area were negative for SARS-CoV-2 RNA.
Passos (2021) (76) Biological monitoring study May-Aug 2020 *new*	Air samples were collected from two different hospital environments (n=52) using active and passive aerosol sampling methods. Active sampling used multiple portable/hand-held air sampler models (AIRIDEAL 3P, MD-8 AirPort, HANDI-VOL) and filter types (cellulose, PTFE or quartz microfiber filters). The passive method used petri dishes for the collection of sedimentable particles. Both hospitals housed	Air samples from four areas sampled in one hospital (at 100% ICU occupancy at the time of sampling) were positive for viral RNA in suspended particles (filter pore size >0.2 µm and >0.3 µm), as well as 11% of sedimentable particles (n=4/36). Positive suspended air particle samples were detected from inside the COVID-19 ICU ward (concentration of 0.33 genomic units m^{-3} @ distance >2 from patient), in a protective apparel removal room (0.14 genomic units m^{-3}), storage room for patient mobile toilets and

	COVID-19 patients in dedicated ICU wards at the time of sample collection. Aerosol samples were also collected from multiple outdoor public spaces using high-volume air samplers (AGV, Energética). SARS-CoV-2 RNA in samples was detected by RT-PCR.	soiled patient linens (0.19 genomic units m^{-3}). The storage room was open to natural ventilation. SARS-CoV-2 RNA positive sedimentable particles were detected in samples collected from an external corridor adjacent to the COVID-19 dedicated ICU. All outdoor air samples and samples collected at the other hospital (i.e., Hospital 1) l (at 33% occupancy at the time of sampling) were negative for SARS-CoV-2 RNA.
Lane (2021) (65) Biological monitoring study Jan 2021* *new*	Air samples were collected from multiple hospital units, AIIR, ICU nursing stations, family/visitor corridors outside of ICUs, medical unit, and patient room hallways. NIOSH 251 2-stage cyclone samplers collected air samples (limit of detection of 8 viral copies/m^3 of air). Two patient rooms housing COVID-19 patients were used as positive control samples. Viral RNA was detected by RT-PCR.	The two positive control samples collected from two confirmed COVID-19 patient rooms were positive for viral RNA. None of the air samples (n=528) from other sampling area were positive for SARS-CoV-2 RNA.
Liu (2020) (77) Biological monitoring study China Feb-Mar 2020	SARS-CoV-2 RNA concentration and aerosol size distributions in air samples (n=30) from multiple sites within or near a hospital and field hospital. All aerosol samples (n=30) were collected on pre-sterilized gelatin filters (Sartorius). Three size-segregated aerosol samples were collected using a miniature cascade impactor (all sampled	SARS-CoV-2 contamination in air samples was low to undetectable. In the field hospital setting, the greatest suspended SARS-CoV-2 RNA in aerosols was identified in a temporary patient toilet room (1 m^2 area) with low ventilation, likely from the patient breathing or aerosolization of virus from feces and urine of infected patients. Samples from the field hospital staff personal rooms demonstrated the

	from staff areas). Viral RNA was detected by RT-PCR.	greatest virus concentrations. Aerosols from 0.25 to > 2.5 µm were identified. The authors hypothesize this came from healthcare worker PPE surfaces and apparel. Low but detectable viral RNA concentrations were found at a department store entrance and an outdoor site near the hospital suggesting this may have occurred due to high traffic flow and crowding. Note: The specific concentrations of airborne SARS-CoV-2 in each aerosol sample by site are provided in the publication.
Chia (2020) (78) Biological monitoring study Singapore Spring 2020*	Detection of air contamination by SARS-CoV-2 in airborne infection isolation rooms (AIIR) housing COVID-19 patients, in hospital settings. Air samples were collected, and aerosol sizes were measured by NIOSH BC 251 bio-aerosol samplers. Viral RNA was detected by PCR.	66% (n=2/3) of the air samples collected from AIIR environments were SARS-CoV-2 RNA positive. The smallest aerodynamic size fraction that contained detectable levels of SARS-CoV-2 RNA was 1–4 µm. Total SARS-CoV-2 concentrations in air ranged from 1.84×10^3 to 3.38×10^3 RNA copies per m^3 air sampled. The authors suggest the presence of SARS-CoV-2 in the sampled air is likely highest during the first week of illness, when respiratory viral load is high.
Jin (2021) (79) Biological monitoring study China Feb-Mar 2020 *new*	Air samples were collected from an ICU housing a single ready-for-discharge COVID-19 patient, 2 days after the patient tested negative for SARS-CoV-2. Air samples were collected from the isolation room and staff PPE dressing room. High-volume air samples were collected using a WA 400 Portable viral aerosol	A single air sample from the ICU ward isolation room was positive (1/7, 14.29%) for viral RNA. The authors state their findings suggest the virus may be shed via aerosol for days, even after a patient has tested negative.

	sampler. Viral RNA in samples was detected using RT-PCR.	
Zhou (2020) (81) Biological monitoring study UK Apr 2020	Three to five air samples were collected from multiple hospital environments using a Coriolis air sampler, viral RNA was measured by RT-PCR, Vero E6 and Caco2 cells cultures were used to culture virus.	38.7% (n=14/31) of the collected air samples were positive for viral RNA, but SARS-CoV-2 virus could not be cultured due to low recovered viral loads. The odds of contamination in public areas was lower than areas immediately occupied by a COVID-19 patient (OR 0.5 95% CI 0.2-0.9).
Orenes-Piñero (2020) (81) Biological monitoring study Spain Spring 2020*	Investigators develop and apply "COVID traps" to measure the capacity of SARS-CoV-2 aerosol transmission in hospital patient care settings. "COVID traps" were placed 1 meter away from patients in ICU and ward settings. Viral RNA was detected by RT-PCR.	In the ICU, none of the "COVID traps" were positive for COVID-19; all COVID-19 patients were intubated. In the ward setting, two "COVID traps" were positive for SARS-CoV-2, both were near a patient requiring the use of respiratory assistance. The authors conclude it was unequivocally the result of virus transmission in air.
Feng (2020) (52) Biological monitoring study China Feb-Mar 2020 Note: Additional results on viral RNA in exhaled breath samples are summarized in Table 4.	Environmental air from the rooms of recovering COVID-19 patients in isolation hospital wards and ICU were sampled using a NIOSH sampler. Air samples (n=12) were collected and aerosol size measured. Samplers were also placed on a tripod 1.2 m in height and 0.2 m away from the bed at the side of the patient's head for 30 minutes.	SARS-CoV-2 RNA was detected in a single air sample from SARS-CoV-2 patients. The maximum viral RNA concentrations detected in the positive air sample by particle size was 1112 copies/m^3 (<1 µm) and 745 copies/m^3 (>4 µm). The authors attribute minimal contamination of viral RNA in study samples to reduced respiratory viral shedding among patients in later stages of infection.
Ding (2020) (53) *Preprint* Biological monitoring study Hong Kong Feb 2020	Air samples (n=46) were collected from airborne infection isolation rooms (AIIR) housing COVID-19 patients, nursing stations, corridor and air-conditioning units at a hospital treating COVID-19 cases. Multiple air samplers were used	A single air sample (n=1/46) from the corridor outside a storage room with a medical waste bin was weakly positive for SARS-CoV-2 RNA. All other tested air samples from patient rooms, washrooms, and air supply inlets were negative.

Note: Additional results on viral RNA in exhaled breath samples are summarized in Table 4.	for sample collection, which was conducted on different days, and RNA was detected by RT-PCR.	RNA copies for the weakly positive sample was not quantified.
Guo (2020) (82) Biological monitoring study China Feb-Mar 2020	Air samples were collected from hospital ICU (n=40) and general wards housing (n=6) COVID-19 patients, at different distances from patients and the doctors office (n=8). Air samples were collected using a SASS 2300 Wetted Wall Cyclone Sampler.	SARS-CoV-2 virus particles were identified in 35% (n=14/40) of ICU air samples, 12.5% (n=2/16) of general ward air samples. SARS-CoV-2 aerosol was detected in 35.7% (n=5/14) of samples near air outlets, 44.4% (n=8/18) of samples in patients' rooms, and 12.5% (n=1/8) in the doctors' office area. No SARS-CoV-2 virus were identified in patient corridor air samples. Based on site(s) of positive air sample collection authors conclude virus-laden aerosols to concentrate near and downstream from patients, and the maximum transmission distance of virus laden aerosols to be 4 meters.
Nissen (2020) (83) Biological monitoring study - Hospital setting Sweden Spring 2020*	Open liquid containing petri dishes were placed at air entrances to ward rooms and near exhaust filters of a hospital's ventilation system for 24 hrs to collect viable virus. Infectivity was assessed using Vero E6 cell culture.	SARS-CoV-2 RNA was detected in fluid samples placed in the ventilation system, and in 33% of samples (n=1/3) placed near air entrances of wards. Viability of the isolated virus could not be established by cell culture.
Zhang (2020) (84) *Preprint* Biological monitoring study - Hospital setting China Mar-Apr 2020	The study sampled outdoor environment aerosols (n=16) at three hospitals receiving COVID-19 patients. Aerosol samples were collected using bioaerosol samplers WA-15. Viral RNA was quantified by RT-PCR.	SARS-CoV-2 virus was identified within sampled aerosols at 285-1,130 copies/m^3 concentrations, similar to contamination levels observed in ICU units. Viral RNA was identified up to 5 meters away from outpatient buildings (n=1/2),

		as well as in hospital waste water treatment areas (n=1/3).
No SARS-CoV-2 RNA in samples		
Dumont-Leblond (2021) (22) Biological monitoring study Canada Spring 2020 *new*	Air and no-touch surfaces of 31 rooms from multiple long-term care facilities (n=7) in Quebec were sampled. The air samples were collected 8 to 30 days after the residents' symptom onset using an IOM Multidust sampler attached to a portable pump Gillian Air 5, placed ~2m from SARS-CoV-2 positive residents. The sampled rooms did not have significant aerosol mitigation measures in place. SARS-CoV-2 RNA was quantified by RT-PCR, and cultured by Vero E6 cells. Note: the distance of surfaces from SARS-CoV-2 patients was not provided.	All air samples (n=31) were negative, but viral RNA was recovered from 32% (n= 20/62) no-touch surface samples of door frames and shelving units (concentrations range 13-36,612 genomes/surface). Authors suggested the viral load recovered from the no touch surfaces without direct contact to be indicative of viruses spread through air. Virus could not be cultured from positive samples.
Song (2020) (85) Biological monitoring study China Feb 2020 *new*	Air samples were collected from Airborne infection isolation rooms (AIIR) housing COVID-19 cases. Air samples were collected using the automatic sampling system Derenda PNS 16T-3.1, at approximately 1 meter from patient beds. Viral RNA in samples was measured by RT-PCR.	All of the samples were negative for SARS-CoV-2 RNA.
Faridi (2020) (86) Biological monitoring study Iran Mar 2020 *new*	Air samples (n=10) were collected from COVID-19 patient wards housing individuals with server and critical symptoms. Air samples were collected into the sterile standard midget impingers using a vacuum pump.	All of the samples were negative for SARS-CoV-2 RNA.

	Air samplers placed 1.5 to 1.8 m above the floor and approximately 2 to 5 m away from patients' beds. Some patients coughed during the sample collection. Viral RNA in samples was measured by RT-PCR.	
Declementi (2020) (87) Biological monitoring study Italy Sept 2020* *new*	Air samples (n=8) were collected from a COVID-19 non-Intensive Care Unit, following cleaning and disinfection processes. Viral RNA in samples was measured by RT-PCR. Note: The sampler model, the presence of COVID-19 cases during sampling nor the sampling distance from cases are provided.	All of the samples were negative for SARS-CoV-2 RNA.
Anh (2020) (88) Biological monitoring study Korea Mar 2020 *new*	Air samples were collected from the isolation rooms of severe COVID-19 patients requiring mechanical ventilation or high-flow oxygen therapy. Samples were collected using a SKC BioSampler and swab sampler. Viral RNA was measured by RT-PCR.	All of the samples were negative for SARS-CoV-2 RNA.
Masoumbeigi (2020) (89) Biological monitoring study Iran Sept 2020* *new*	Air sampling (n=31) was conducted in a hospital with COVID-19 patients; all of the patients had a severe form of cough and sneezing. Air samples were collected from Emergency wards, ICU, CT-SCAN, and laundry unit. Air sampling was performed by all-glass impinger (AGI) at ~0.5-4 m away from patients' beds. Viral RNA was detected by RT-PCR.	All of the samples were negative for SARS-CoV-2 RNA.

Alsved (2020) (90) Biological monitoring study Sweden* Spring 2020*	SARS-CoV-2 RNA measured from COVID-19 cases (n=2) within 2 days of symptom onset. Air samples were collected 0.8 meters away from the case, as the individual was talking or singing. The measurements were carried out in an experimental airtight chamber with human volunteers.	Air samples collected within 0.8 meters of COVID-19 cases were negative for viral RNA. Viral loads in subject airways at the time of the experiment could not be obtained. Authors state qPCR Ct values of 22–25 to have been reported in clinical reports for the subjects within 24hrs of the experiment.
Cheng (2020) (91) Biological monitoring study China Jan-Apr 2020	Air samples were collected within 10 cm of asymptomatic and symptomatic COVID-19 patients (n=6) with and without surgical masks in AIIR were tested for SARS-CoV-2 contamination. Viral loads in respiratory patient fluid samples were also tested by having patients sneeze and spit into gelatin filters within air samplers. Viral loads were measured using assays (not specified) and RT-PCR.	No virus was detected in air samples from rooms with both surgical masked and non-masked patients. Except for one patient who had a respiratory fluid viral load of 2.54×10^4 copies/ml, all other patients' samples from sneezing were negative for virus RNA. Authors suggest aerosol transmission is not the predominate mode of infection transmission in the sampled settings. Appropriate PPE use, environmental disinfection, and single occupancy within AIIR are provided as reasons for observed results.
Kim (2020) (92) Biological monitoring study South Korea Mar-Apr 2020	Air samples (n=52) were collected 2 meters away from COVID-19 patients (n=8), before admission, and on hospital days 3, 5, and 7 using a MD8 Airport Portable Air Sampler. Some patients were housed in negative pressure rooms (e.g. AIIR). RNA was measured by RT-PCR.	All collected air samples were negative for viral RNA.
Ong (2020) (93) Biological monitoring study	Air samples were collected from COVID-19 patients (n=3) in AIIR at a dedicated SARS-CoV-2	No air samples were positive for SARS-CoV-2 viral RNA.

Singapore Jan-Feb 2020	outbreak center between day 4 and day 11 from symptom onset using SKC Universal pumps a Sartorius MD8 microbiological sampler. RNA was measured using RT-PCR.	
Ma (2020) (51) *Preprint* Biological monitoring study China Spring 2020* Note: Additional results on viral RNA in exhaled breath samples and community setting air samples are summarized in Table 4 and Table 6.	Air samples (n=26) were collected from hospital settings and unventilated quarantine hotel rooms of cases using a robot. RNA was detected by RT-PCR.	No air samples from hospital settings were positive for SARS-CoV-2 viral RNA.

Table 6: Biological monitoring studies investigating SARS-CoV-2 within air in community settings (n=9)

SARS-CoV-2 in cell culture samples		
Lednicky (2021) (23) *Preprint* Biological monitoring study USA Jan 2021* *new*	Air samples were collected from a car driven by a COVID-19 patient (mildly symptomatic, no cough) using a Sioutas personal cascade impactor sampler at multiple sampling stages of aerosol sizes (PCIS); the sampler was attached to the sun-visor on the passenger side of the car and approximately 3 feet from the subject's face. The air conditioner in the car was on during the 15 minute long drive.	SARS-CoV-2 viral RNA was detectable at all PCIS aerosol size sample stages, at concentrations ranging from 1.24E+03 to 3.14E+04 genome/ m^3 of air. These findings suggest virions are present in different sized respiratory secretions. SARS-CoV-2 was cultured from the sampling stages collecting particles in the 0.25 to 0.50µm size range.

	SARS-CoV-2 RNA was detected by RT-PCR, virus viability measured by Vero E6 cell culture, as well as genome sequencing.	
SARS-CoV-2 RNA in samples		
Munoz-Price (2021) (24) Biological monitoring study US Spring 2021* *new* Note: Additional results on viral RNA in environmental air from patient care settings are summarized in Table 5.	Air samples (n=9) collected from households occupied by confirmed COVID-19 cases. Air samples were collected using the Sartorius MD8 airscan sampler, positioned at 0.3 -1.8 meters from patients' head. Viral RNA in samples was measured by RT-PCR.	55% (n=5/9) of air samples, collected from three different households, were positive for viral RNA. The odds of positive air samples in household settings, when compared to hospital settings, were estimated to be 8.75 [95% CI 1.21–63.43; P = .058]. The median number of days from the last positive SARS-CoV-2 test to the day of air sampling was 3 (range, 2.5–5). Of the households with positive air samples, one had A/C running and all three had opened windows or doors immediately prior to air sampling. Anecdotally, most households felt warm and humid at the time of sample collection.
Gehrke (2021) (61) *Preprint* Biological monitoring study Germany Oct 2020 - Jan 2021 *new* Note: Additional results on viral RNA in hospital settings air samples are summarized in Table 5.	Air samples were collected from a concert hall and a shopping mall for 6 hours during operation using non-powered cold traps. Viral RNA was quantified by RT-PCR in an area with high community transmission in an effort to identify potential hotspots for transmission.	Indoor COVID-19 hotspots were found in non-ventilated areas and in zones that are predisposed to a buoyancy (chimney) effect. In the concert hall, 1/10 cold traps were positive for viral RNA. In the shopping mall, 35% of traps were positive for viral RNA (n=5/14) located on the ground floor, 2nd and 3rd kiosk area as well as around the escalators. The 4th floor fashion section that usually has 25% capacity was negative. The highest viral concentration (2.7-5.4 x10^3 copies/mL) was found on the ground level between the escalators. However, follow-up measurements where cold

		traps were placed directly under 2 inflows and 2 outflows on the 3rd floor (to exclude any contamination of the central ventilation system) were negative. Samples taken on Friday with a high volume of patrons were twice as high as those taken on Monday.
Moreno (2021) (69) Biological monitoring study Spain May- Jul 2020 *new*	Air samples were collected from subway trains and buses during operation. Ambient air ($PM_{2.5}$) was sampled using Teflon filters with PEM (Personal Environmental Monitor) equipment, A/C filters were also sampled. Viral RNA in samples was measured by RT-PCR.	2/6 subway train air samples were SARS-CoV-2 positive and none of the air conditioner filter samples were positive. 1/6 bus air samples and 4/9 air-conditioning filters were positive. Cleaning and disinfection results indicated this process was successful at decontamination.
de Rooij (2021) (66) *Preprint* Biological monitoring study Netherlands Apr-Jun 2020 *new*	Air samples were collected from mink farms with ongoing COVID-19 outbreaks (3 farms at late stage of outbreak, 1 at early stage of outbreak). Samples were collected from indoor farm environments, outdoors at the farm premises, and nearby residential sites. Air samples were collected using teflon filters, and in parallel with particulate size fraction PM_{10} (<10µm) and inhalable dust (<100µm) collection. Personal air samples from the investigation field staff were also collected. Viral contamination in air samples was measured by RT-PCR.	Based on sample contamination the investigators conclude mink farms to be highly contaminated with viral RNA inside but the dispersion of virus outdoors and to nearby areas to be negligible. Farm in acute stage of outbreak: - SARS-CoV-2 RNA was detected in 62.5% (n=5/8) of the inhalable dust samples and 50% (n=4/8) of PM_{10} samples collected inside the farm. All (n=2) personal air samples were positive for viral RNA. - SARS-CoV-2 RNA was also detected in outdoor samples at 1.5-10 meters from the farm's open entrance, but samples collected at 20m from this entrance were negative. Farms in late stage of outbreak:

		- Viral RNA was detected in 9.8% (n=4/41) of inhalable dust samples, at ~4x10^3 copies/m^3. SARS-CoV-2 RNA was not detected in the inhalable dust samples collected outside the mink houses (n=9) or from the PM_{10} samples collected inside the farm (n=9) or near the mink houses (n=9). One of the personal air samples was positive for SARS-CoV-2 RNA. - All of air samples from residential sites were negative for SARS-CoV-2 RNA.
Ma (2020) (51) *Preprint* Biological monitoring study China Spring 2020* Note: Additional results on viral RNA in exhaled breath samples and hospital settings air samples are summarized in Table 4 and Table 5.	Air samples (n=26) were collected from hospital settings and unventilated quarantine hotel rooms of cases using a robot. RNA was detected by RT-PCR.	A single positive air sample (3.8%) was identified in an unventilated quarantine hotel toilet room.
NO SARS-CoV-2 RNA in samples		
Wong (2020) (67) *Preprint* Biological monitoring study Singapore Feb-Mar 2020	Air samples (n=6) were collected from accommodation rooms, corridors, toilets and elevators used by COVID-19 cases in community settings (not specified). Viral RNA in samples was measured by RT-PCR.	All air samples were negative for viral RNA.

new		
Döhal (2020) (68) *Preprint* Biological monitoring study Germany Mar 2020 *new*	Environmental air from 21 quarantine households (n=15) were collected by cyclone sampling using a Coriolis 154 Micro Air sampler. Viral RNA in samples was measured by RT-PCR and Vero-E6 cell culture. Note: At least one person in each included household was positive for SARS-CoV-2 at the time of sample collection.	All air samples were negative for viral RNA.
Di Carlo (2020) (94) Biological monitoring study Italy May 2020 *new*	Samples were collected on a city bus in a town which had a high number of COVID-19 cases, during the last week of lockdown and first week of gradual opening (approx. 1100 passengers used the bus during the study period). Air was sampled using microbiological gelatin membrane sample filters of 80 mm. Viral RNA in samples was measured by RT-PCR.	No air samples (or surface samples) were positive for SARS-CoV-2. Public health measures in place included hand sanitized upon entry to the bus, mandatory masks and keeping the bus windows open. Authors state these precautions prevented SARS-CoV-2 circulation and detection in the investigation.

*Estimated based on author affiliations and publication date.

SARS-COV-2 VIRAL LOADS IN RESPIRATORY PARTICLES

A systematic review and meta-analysis informed a model to estimate the relationship between viable SARS-CoV-2 virus, case viral loads, and virus laden droplet and aerosol emission (55). This review found that peak viral load occurred between one day before to five days post symptom onset (55). The model estimated the likelihood of viable virus in respiratory aerosols expelled by an individual at peak viral load was ≤61.1% (95% CI: 51.8-70.4%), and the likelihood estimate was substantially lower, at ≤ 0.69% (95% CI: 0.43-0.95%), for an individual with a mean viral load.

Table 7: SARS-CoV-2 viral load in respiratory particles (n=1)

STUDY	METHOD	KEY OUTCOMES
Chen (2020) (55) *Preprint* Systematic Review informed *in-silico* analysis Canada* Aug 2020	A systematic review and meta-analysis were conducted (Aug 2020) to developed a dataset and summarize data on SARS-CoV-2 respiratory viral load (rVL). A model was developed to estimate the likelihood of respiratory droplets and aerosols containing viable virus assuming different viral load estimates, and different activities.	The meta-analysis showed there was a large degree of heterogeneity in viral loads across individuals, studies, and stages of infection. This suggests intrinsic virological factors mediate the over dispersion seen in the pandemic. Many cases present minimal transmission risk, whereas highly infectious individuals were estimated to shed 9.84 (95% CI 9.17-10.56,) $\log_{10}$ SARS-CoV-2 virions/ml via droplets and aerosols while breathing, talking and singing. The model estimates coughing increased the contagiousness of symptomatic cases. The likelihood of viable virus in respiratory aerosols at peak viral load was estimated to be ≤61.1% (95% CI: 51.8-70.4%) for the most infectious cases, and ≤ 0.69% (95% CI: 0.43-0.95%) for cases with mean viral load.

*Estimated based on author affiliations and publication date.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an excel list that can be searched. Targeted keyword searching is conducted within the COVID-19 database to identify relevant citations using search terms: aerosol, airborne, droplet.

Each potentially relevant citation was examined for relevance, the full text of potentially relevant research was examined to confirm relevance and a synopsis of the study was extracted into the review. This review contains research published up to March 12, 2020.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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Nouveaux éléments de preuve sur la COVID-19

Revue rapide sur la transmission par les aérosols du SRAS-CoV-2, Mise à jour 2

Introduction

Quelles sont les preuves émergentes en ce qui concerne les grappes de cas ou les éclosions, ainsi que les preuves expérimentales et biologiques en lien avec la transmission du SRAS-CoV-2 par les aérosols?

Les preuves scientifiques et la compréhension des modes de transmission du SRAS-CoV-2 ont évolué rapidement au cours de la dernière année. Les particules respirables expulsées contenant des agents pathogènes infectieux peuvent se présenter sous différentes tailles et les particules respirables plus petites (souvent appelées aérosols) peuvent rester en suspension dans l'air et se disperser sur de plus grandes distances que les grosses gouttelettes respiratoires. Il a été établi que d'autres agents pathogènes connus pour être principalement transmis par de grosses gouttelettes (par exemple, la grippe, le SRAS-CoV-1, la pneumonie pneumococcique et la légionellose) peuvent également se propager par des aérosols dans certains milieux et conditions (1 à 6). Ainsi, un éventail de données probantes a été produit pour décrire les caractéristiques et l'importance relative des aérosols dans la transmission du SRAS-CoV-2 dans différents milieux et conditions.

La présente synthèse en bref résume la documentation scientifique qui fournit des données probantes sur la transmission du SRAS-CoV-2 par les aérosols publiées jusqu'au 12 mars 2021. Elle comprend différentes sections portant sur les données probantes suivantes :

1) Les enquêtes sur les grappes de cas ou les éclosions de SRAS-CoV-2 associées à la transmission par les aérosols;
2) Les expériences sur la transmission indirecte du virus SRAS-CoV-2 à l'aide de modèles animaux;
3) Les preuves expérimentales sur la stabilité et la viabilité du virus du SRAS-CoV-2 dans les aérosols;
4) Les études de biosurveillance portant sur l'ARN du SRAS-CoV-2 dans des échantillons d'air expiré;
5) Les études de suivi biologique de l'ARN du SRAS-CoV-2 et de sa viabilité dans des échantillons d'air ambiant prélevés dans des milieux de soins aux malades et dans la collectivité (c.-à-d. milieux non hospitaliers/soins aux patients).

La section sur les données probantes portant sur les simulations dynamiques des fluides et les analyses *in silico* a été omise de cette mise à jour en raison de la quantité croissante de données empiriques à l'appui du potentiel de transmission du SRAS-CoV-2 par les aérosols.

Quoi de neuf

- Cette mise à jour a relevé 46 nouvelles études prépubliées et publiées entre le 6 novembre 2020 (la dernière date de mise à jour) et le 12 mars 2021 sur le potentiel de transmission du SRAS-CoV-2 par les aérosols. Ces études sont résumées ci-dessous et portent la mention *nouvelle* dans les tableaux présentant les données probantes.
- La mise à jour comprend également douze nouveaux rapports d'enquête portant sur des éclosions ou des grappes de cas de SRAS-CoV-2 dans des contextes réels (tableau 1). Ces événements avec transmission par les aérosols se seraient produits dans un hôtel où se trouvaient des voyageurs en quarantaine, dans une maison de soins infirmiers, dans l'unité d'hématologie d'un hôpital, dans un autobus avec passagers, dans un restaurant, dans des installations de conditionnement physique, dans un grand magasin et dans des appartements à la verticale dans une tour d'habitation (7 à 16). Ces rapports indiquaient notamment que le masque ou le couvre-visage était peu porté ou qu'il était porté de façon inadéquate au moment de la transmission présumée par les aérosols, alors que les cas index en étaient aux stades présymptomatiques ou symptomatiques précoces de l'infection.
- Deux nouvelles expériences fondées sur des modèles animaux ont fait état de multiples modes de transmission du SRAS-CoV-2, incluant les aérosols, entre des paires de hamsters infectés et vulnérables (17, 18). Une étude suggérait même que l'exposition aux aérosols avait entraîné une réplication précoce du virus, l'excrétion dans les tissus respiratoires et des manifestations plus aiguës de la maladie chez les hamsters, comparativement aux expositions fomites et intranasales (17). L'autre étude a révélé que les aérosols provenant de hamsters naïfs infectés pouvaient infecter des hamsters ayant déjà été infectés, ce qui indique que la guérison, après avoir eu une infection primaire au SRAS-CoV-2, n'éliminait pas le risque d'infection subséquente par des aérosols (18).
- Une étude expérimentale nouvellement incluse sur la viabilité et les taux de désintégration du virus SRAS-CoV-2 dans les aérosols a révélé que l'infectiosité du virus dans les aérosols dépendait fortement des conditions environnementales, selon l'ordre d'influence suivant : (mi-journée en été, mi-journée au printemps, intérieur/soirée) >température (entre 10 et 40 °C)> humidité (20 à 70 %) (19). L'on a estimé qu'il fallait 4,8 minutes (à 40 °C, avec 20 % d'humidité relative) avec une exposition à la lumière du soleil en mi-journée pour réduire de 90 % les virus infectieux alors que sans exposition à la lumière du soleil (c.-à-d. à l'intérieur ou la nuit), il fallait plus de 2 heures (à 40 °C, avec une humidité relative de 20 %) pour atteindre le même niveau de réduction. La lumière du soleil a eu la plus grande influence sur le taux de désintégration, mais on a aussi noté une plus grande désintégration à 30 °C avec un taux élevé d'humidité (70 %) ou à 40 °C sans égard à l'humidité.
- Une nouvelle étude de suivi biologique portant sur les échantillons d'air expiré de cinq patients a révélé que l'ARN viral n'avait été détecté que dans les échantillons provenant de patients atteints

de la COVID-19 ayant obtenu des résultats positifs lorsque l'échantillonnage avait inclus des prélèvements oropharyngés, naso-pharyngés ou salivaires (20).

- Vingt-huit nouvelles études de suivi biologique portant sur la contamination par le virus du SRAS-CoV-2 dans des échantillons d'air ambiant prélevés dans des milieux de soins aux patients (y compris des études sur les hôpitaux et les soins de longue durée) et dans des milieux communautaires (c.-à-d. soins non prodigués aux patients) sont incluses dans la présente mise à jour.
    - Deux études canadiennes ont révélé une contamination par l'ARN viral dans des échantillons d'air ambiant prélevés dans un hôpital (à environ 3 mètres de patients atteints de la COVID-19) et sur des surfaces sans contact dans des foyers de soins de longue durée (21, 22) indiquant que le SRAS-CoV-2 peut se propager dans les aérosols.
    - Une nouvelle étude a confirmé la présence d'un virus viable dans des échantillons d'air prélevés dans une voiture conduite par un individu légèrement symptomatique (23). Cela met en évidence le fait que le virus du SRAS-CoV-2 peut être expulsé dans l'air ambiant, même chez une personne atteinte d'une forme légère, pendant une courte période de temps (23).
    - Une autre étude a comparé des échantillons d'air ambiant prélevés dans des chambres d'hôpital et chez des ménages en quarantaine où se trouvaient des cas actifs (24). On a estimé que les échantillons d'air ambiant provenant des ménages étaient environ huit fois (RC 8,75 [IC à 95 % 1,21 à 63,43; p = 0,058]) plus susceptibles d'être contaminés par de l'ARN viral que les échantillons d'air provenant des hôpitaux. D'après les résultats de l'étude, les experts cliniques suggèrent que les différences dans les échanges d'air et la ventilation sont une différence clé plus importante que l'acuité même de la maladie, en ce qui concerne la contamination de l'air ambiant.

Points clés

- Au total, 84 études sur le potentiel de transmission par les aérosols ont été recensées dans les publications et préimpressions. Des enquêtes effectuées dans les cas d'éclosions multiples et de grappes de cas suggèrent que la transmission du SRAS-CoV-2 par les aérosols peut se produire dans certains contextes. De nouvelles preuves expérimentales chez des animaux séparés indiquent que l'infection peut se propager à la suite d'une exposition aux aérosols, et que le virus infectieux peut demeurer stable et viable dans les aérosols en suspension. Des études de suivi biologique confirment la présence d'ARN viral dans des échantillons d'air expiré et d'air ambiant. Une revue systématique et une méta-analyse fondées sur des données cliniques permettent d'estimer la durée pendant laquelle le virus respiratoire du SRAS-CoV-2 est viable.
- Vingt-six enquêtes sur vingt éclosions ou grappes de cas différentes de COVID-19 dans différents contextes réels (p. ex., une maison de soins infirmiers, l'unité d'hématologie d'un hôpital, un hôtel ou

un établissement où se trouvaient des voyageurs en quarantaine, des usines de transformation de viande, une pratique d'un groupe de chorale qui avait lieu à l'intérieur, un restaurant, un navire de croisière, un autobus avec passagers, des installations de conditionnement physique, une tour d'habitation et un centre commercial) ont contribué à la transmission par les aérosols parmi les cas (tableau 1). Les enquêtes épidémiologiques suggèrent que la transmission par les aérosols est amplifiée ou plus susceptible de se produire dans certains environnements et dans certaines conditions, comme dans des espaces intérieurs mal ventilés ou surpeuplés, lorsque des personnes symptomatiques ou présymptomatiques précoces sont présentes ou lorsque les personnes prennent part à différentes activités physiques (par exemple, chanter, faire du conditionnement physique).

- Une revue systématique et une méta-analyse des estimations cliniques ont révélé que la probabilité qu'un virus viable soit présent dans les aérosols respiratoires expulsés par une personne ayant une charge virale maximale était de 61,1 % (IC à 95 % : 51,8 à 70,4 %), alors que les estimations de vraisemblance étaient très inférieures à ≤ 0,69 % (IC à 95 % : 0,43 à 0,95 %) pour une personne ayant une charge virale moyenne. On a estimé que le pic de la charge virale se produisait entre un jour après l'apparition des symptômes et cinq jours après l'apparition de ceux-ci (tableau 7). Cette constatation est conforme à celles qui ont été obtenues pour l'ensemble des éclosions dans lesquelles le cas index était habituellement présymptomatique ou à un stade précoce de la maladie symptomatique lors de la transmission.
- Les études sur les animaux fournissent des preuves de l'infection par les aérosols et de la transmission de l'infection même lorsque les animaux infectés et vulnérables sont séparés par des cages ou des barrières. Les experts cliniques responsables de l'étude ont déterminé que cette transmission indirecte de l'infection était au moins partiellement attribuable aux aérosols et à la circulation d'air (tableau 2).
- Trois études font état de la stabilité et de la viabilité du virus dans les aérosols, ainsi que de l'influence des facteurs environnementaux (p. ex., température, humidité et exposition à la lumière du soleil) sur la persistance du virus dans les aérosols (tableau 3). Des preuves expérimentales ont démontré la viabilité prolongée pendant plusieurs heures (entre 2 et 16 heures) du virus du SRAS-CoV-2 dans les aérosols en laboratoire.
- Les études de biosurveillance mesurent l'ARN viral dans des échantillons d'haleine expirés provenant de personnes infectées (tableau 4) ainsi que dans l'air ambiant dans des milieux communautaires et de soins aux patients (tableaux 5 et 6). Le nombre croissant d'études qui confirment la présence du SRAS-CoV-2 dans l'air ambiant fournit des preuves supplémentaires à l'appui de la transmission par les aérosols dans les collectivités. Les quelques études qui ont confirmé la viabilité du virus dans la culture cellulaire ont aussi mentionné la collecte d'échantillons d'air ambiant près des personnes infectées (< 2 mètres) (tableaux 5 et 6).

Vue d'ensemble des éléments de preuve

Les éléments de preuves disponibles en ce qui concerne la transmission potentielle du SRAS-CoV-2 par les aérosols dans les documents publiés et en préimpression évoluent rapidement. La présente revue comprend les études (n = 84) consultées jusqu'au 12 mars 2021 et jugées pertinentes par un seul examinateur. La qualité globale des éléments de preuve examinés est décrite de manière générale ci-dessous pour chacune des sections des éléments de preuve présentés selon le plan d'étude, la quantité et l'uniformité des données présentées. En gros, la hiérarchie des données probantes et les évaluations générales de la qualité jugent que les essais contrôlés randomisés effectués de façon appropriée sont de grande qualité en raison de leur faible risque de biais. D'autres études expérimentales qui peuvent être vues comme étant de qualité moyenne peuvent également être déclassées en raison de problèmes associés à l'autorité ou à la conduite des études. Les expériences utilisant des modèles animaux sont vues comme des preuves de faible qualité. Les études d'observation sont, quant à elles, généralement considérées comme présentant un risque élevé de biais et, par conséquent, une faible qualité, mais certaines grandes études de cohorte prospectives bien menées peuvent être évaluées comme présentant un risque modéré ou faible de biais, et peuvent donc être vues comme de qualité modérée à élevée.

Parmi toutes les études, 26 études d'enquête sur des éclosions ou des grappes de cas portant sur 20 différentes éclosions chez les humains suggèrent une transmission du SRAS-CoV-2 par les aérosols (tableau 1). Il s'agit d'études d'observation rétrospectives qui risquent de comporter de nombreux biais. La nature rétrospective de ces enquêtes et le manque de données de génotypage pour la majorité des cas indiqués signifient que les inférences sur la transmission par les aérosols se limitent aux liens épidémiologiques. Les études en grappes multiples incluent une description de l'enquête et des simulations *in silico* qui explorent le potentiel de transmission par les aérosols dans des contextes réels.

Les modèles animaux fournissent des données expérimentales sur l'infection découlant de l'exposition à des aérosols, en évaluant la transmission indirecte des animaux infectés à des animaux vulnérables en raison de l'écoulement d'air passif ou dirigé, lorsqu'ils ne sont séparés que par des cages et des barrières (tableau 2). Ces études n'ont cependant pas fourni suffisamment de détails sur les symptômes et les comportements des animaux infectés (p. ex., éternuements et transfert de liquide respiratoire par reniflement ou léchage des barrières) ou la configuration expérimentale pour exclure la transmission de l'infection par contact avec les liquides respiratoires et buccaux dans la plupart des expériences. Dans l'ensemble, les modèles animaux de transmission offrent la plus faible qualité de données probantes sur la transmission par les aérosols.

Trois études expérimentales fournissent des preuves confirmant la stabilité et la viabilité du virus infectieux dans les aérosols artificiellement générés et en suspension (tableau 3). Bien que ces études fournissent des preuves solides qui appuient la longévité du virus infectieux en laboratoire pendant une période pouvant aller jusqu'à 16 heures, l'application de ces résultats à des contextes réels par l'entremise d'études de suivi biologique demeure en grande partie non établie.

La majorité des études de suivi biologique indiquées recherchaient l'ARN viral du SRAS-CoV-2 dans l'air expiré (tableau 4) et dans des échantillons d'air ambiant provenant de différents milieux (tableaux 5 et 6). Ces données fournissent des preuves de qualité modérée indiquant que l'ARN viral peut se déplacer dans l'air ou y demeurer à une certaine distance d'une personne infectée dans certains milieux et dans certaines conditions. Il y a un nombre limité de rapports sur la concentration du virus dans les échantillons positifs, sur la distance d'échantillonnage des personnes infectées et sur la viabilité du virus documentée grâce à la culture cellulaire. L'absence de ces détails limite donc le caractère généralisable des données de suivi biologique à tous les environnements intérieurs et à toutes les personnes infectées et entrave la détermination des paramètres et des conditions qui favorisent une augmentation de la concentration du virus viable se trouvant dans l'air expiré et des particules aérosolisées dans l'air. Il est également probable que la vaste gamme de milieux dans lesquels les échantillons ont été prélevés (p. ex., milieux de soins aux patients ou milieux communautaires) et de différentes techniques de prélèvement (p. ex., air expiré ou condensat de l'air expiré) ait influé sur la sensibilité de la quantification de l'ARN viral et des tests viables de détection de virus utilisée dans les échantillons de suivi biologique. Des recherches supplémentaires sont donc nécessaires pour confirmer l'infectiosité et la viabilité du SRAS-CoV-2 dans les échantillons d'air afin de savoir où et quand augmente le risque de transmission du SRAS-CoV-2 par les aérosols.

Cette revue résume donc les données probantes sur la transmission du SRAS-CoV-2 par les aérosols et caractérise les milieux et conditions ayant été étudiés. D'autres données probantes sont cependant nécessaires pour combler les lacunes dans les connaissances sur la transmission du SRAS-CoV-2 par les aérosols :

1) Quantification de la dose infectieuse de SRAS-CoV-2;

2) Caractéristiques du cas et conditions environnementales dans lesquelles un virus viable est susceptible d'être présent dans l'air expiré, de demeurer en suspension dans l'air ambiant et d'y circuler;

3) Données génomiques tirées des enquêtes sur les grappes de cas et les éclosions qui suggèrent une transmission indirecte de l'infection par le SRAS-CoV-2 chez les humains;

4) Confirmation du lien entre les cas grâce aux données de génotypage, et données de meilleure qualité appuyant la transmission par les aérosols dans les éclosions ou grappes de cas visées;

5) Examen officiel de la documentation sur la dynamique des fluides effectuée par des experts dans ce domaine afin qu'ils puissent mieux décrire les conditions environnementales et les activités comportementales qui augmentent (ou diminuent) l'émission d'aérosols respiratoires et la transmission des infections, et quantification des estimations des risques de transmission par les aérosols.

TABLE DES MATIÈRES

ENQUÊTES SUR LES GRAPPES DE CAS ET LES ÉCLOSIONS

Cette section présente un résumé de vingt-six études décrivant vingt grappes de cas ou éclosions de COVID-19 différentes dans des contextes réels qui soutiennent épidémiologiquement la transmission d'infections par les aérosols (tableau 1). Dans un certain nombre d'études, les mêmes grappes de cas ou éclosions de COVID-19 ont été étudiées par des groupes distincts d'expert clinique qui ont tous conclu que les aérosols ou la transmission indirecte longue distance du virus avaient joué un rôle dans la propagation de l'infection entre les cas. Ces éclosions ont été organisées en fonction du milieu dans lequel les experts cliniques responsables de l'étude ont supposé que la transmission de l'infection s'était produite. Les installations comprenaient une unité d'hématologie dans un hôpital, un hôtel où des voyageurs restaient en quarantaine, des autobus avec passagers, des cours et des installations de conditionnement physique, une usine de transformation de viande, des restaurants avec salle à manger, une pratique d'un groupe de chorale, un navire de croisière, des grands magasins et différentes tours d'habitation. Les preuves incluent des enquêtes épidémiologiques, des analyses et des simulations dynamiques numériques des fluides, des images de surveillance vidéo ou une analyse spatiale des cas pendant l'événement de transmission.

Il est intéressant de noter que plusieurs grappes de cas et éclosions de COVID-19 se sont produites dans des milieux semblables, ce qui laisse entendre qu'ils pourraient être plus favorables à la transmission par les aérosols. Les caractéristiques communes étaient des espaces fermés avec ventilation minimale (c.-à-d. peu ou pas de fenêtres, ventilation et circulation d'air insuffisantes), la présence de cas index présymptomatiques ou avec symptômes précoces et la propagation des virions au-delà des deux mètres favorisée par un débit d'air artificiel, des systèmes de ventilation, des conduits d'air, des tuyaux d'évacuation ou une ventilation inefficace. De plus, dans certains cas, tant l'infecteur que les personnes infectées participaient à des activités qui augmentaient généralement les taux d'expiration (p. ex., exercice physique, chant) ou se trouvaient dans des espaces surpeuplés pendant les événements de transmission.

Il est également important de noter qu'à l'exception d'une des études résumées, aucune ne déclarait les séquences génétiques du virus isolé dans les cas d'éclosion ou de grappe de cas, sans oublier que nombreuses études ne décrivent pas le port du couvre-visage ou du masque pendant les événements d'exposition. Il s'agit là de lacunes importantes dans les données probantes existantes, car les données de génotypage confirmeraient le lien entre les cas, tandis que les données sur le port des couvre-visages ou des masques donneraient une idée de l'efficacité de cette mesure de prévention. Le fait que ces informations ne figurent pas dans le résumé des enquêtes sur les éclosions et les grappes de cas est l'une des principales limites de cette preuve.

Tableau 1 : Enquêtes sur les grappes de cas ou les éclosions de SRAS-CoV-2 associées à la transmission par les aérosols (n = 26)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Unité d'hématologie dans un hôpital		
Saidel-Odes (2021) (25) Enquête sur les grappes Israël Septembre et octobre 2020 *nouvelle*	Enquête sur une éclosion de COVID-19 liée à un cas de référence qui était immunodéprimé en raison d'un myélome multiple et qui a subi une greffe de cellules souches. Le patient a été traité dans une chambre d'isolement des infections aéroportées après un diagnostic de COVID-19, et le personnel médical a revêtu l'EPI approprié (c.-à-d. masque N95, écran facial, blouse et gants) avant d'entrer dans la salle d'isolement du patient. Tous les membres du personnel de l'unité portaient des blouses, des gants et des masques.	Sept membres du personnel soignant de l'unité de transplantation qui hébergeait le cas de référence ont eu un diagnostic d'infection, soit un taux d'attaque de 19 % (n = 7 sur 37). Le personnel infecté comprenait deux médecins, quatre infirmières et un préposé à l'entretien ménager. Deux des employés qui ont eu un résultat positif n'ont signalé aucun contact direct avec le cas de référence. L'enquête épidémiologique et l'analyse univariée ont révélé que les travailleurs de la santé infectés étaient plus susceptibles d'avoir dit avoir passé du temps dans le corridor de l'unité ou au poste d'infirmières ([RR], R = 7,2; IC à 95 %, 1,22 à 42,49; P = 0,018), mais pas dans la chambre du cas de référence. Selon les experts cliniques, la transmission par les aérosols est la seule explication plausible de cette éclosion.

Quarantaine dans un hôtel et voyages en avion		
Eichler (2021) (14) Enquête sur les grappes Nouvelle-Zélande Septembre 2020 *nouvelle*	Enquête sur une éclosion de COVID-19 qui s'est produite pendant le rapatriement, dans un établissement d'isolement et de quarantaine obligatoire (hôtel) et parmi les contacts des ménages dans la collectivité. Les personnes qui revenaient d'autres pays étaient tenues de se soumettre à une quarantaine et à un isolement obligatoires dans un établissement pendant 14 jours après leur arrivée à destination.	L'utilisation des données de vidéosurveillance et de l'analyse génomique virale des grappes de cas a permis aux experts cliniques de dire qu'il devait y avoir plusieurs chaînes de transmission. Les sites de transmission soupçonnés étaient les vols internationaux et intérieurs, l'installation dans laquelle a eu lieu la quarantaine et les ménages. Bien que la transmission par les aérosols ait pu être le mode de transmission dans chacun des événements de transmission, une enquête approfondie a permis de conclure que la transmission par les aérosols était le principal mode de transmission de l'infection dans l'hôtel utilisé pour la quarantaine. Les expositions ou transmissions de cas dans l'éclosion sont présumées être les suivantes : - 2 cas de référence infectés au moment du rapatriement de l'Inde à Christchurch, en Nouvelle-Zélande. 1 cas d'exposition pendant le vol vers Christchurch, 2 cas d'exposition dans le couloir de l'hôtel utilisé pour la quarantaine (par les aérosols, plus de détails ci-dessous), 1 cas d'exposition pendant le vol de Christchurch à Auckland (transmission à partir des deux cas ayant été exposés aux aérosols qui avaient reçu un résultat de test négatif le jour 12 de leur quarantaine), ainsi que des cas supplémentaires parmi les contacts du ménage pour les trois derniers cas. En fonction des séquences vidéo obtenues, les experts cliniques ont pu conclure que la transmission par les aérosols avait eu lieu à la porte de deux chambres d'hôtel différentes où se trouvaient des personnes en quarantaine et cette transmission découlait des aérosols en suspension dans l'air. On a supposé que la transmission s'était produite pendant une fenêtre de 50 secondes

		entre le moment où la porte d'une chambre a été fermée dans un cas et l'ouverture de la porte de la chambre dans l'autre cas. Remarque : Un examen du système de ventilation de l'hôtel a révélé que les chambres en question avaient une pression positive nette par rapport au corridor, de sorte que l'air s'écoulait probablement dans le corridor lorsque la porte était ouverte.
Maison de soins infirmiers		
de Man (2020) (15) LTE Enquête sur les grappes Pays-Bas Juin et juillet 2020 *nouvelle*	Enquête sur une éclosion de COVID-19 dans une unité d'une maison de retraite néerlandaise comprenant sept unités.	Au total, 17 des 21 résidents de l'unité, 13 des 34 travailleurs de la santé œuvrant dans cette unité et 4 autres travailleurs de laboratoire ont été confirmés comme étant des cas liés à la grappe; le taux d'attaque parmi les résidents était de 81 % alors qu'il était de 50 % parmi les travailleurs de la santé. Les 106 travailleurs de la santé et les 95 résidents des autres unités ont tous continué à recevoir des résultats négatifs pour la COVID-19. Les travailleurs de la santé portaient des masques lorsqu'ils s'occupaient des patients et travaillaient dans des salles désignées pour limiter les contacts. L'éclosion s'est limitée à une seule unité (sur les sept que compte l'établissement) avec un système de ventilation qui recirculait l'air non filtré. Le système de ventilation était neuf et a permis de surveiller les concentrations de CO_2 pour déterminer à quel moment l'air devait être rafraîchi avec de l'air provenant de l'extérieur. L'ARN viral a été détecté dans le système de ventilation (climatiseurs et filtres à poussière du système de ventilation). Les experts cliniques ont déclaré que la transmission par les aérosols était probablement le résultat d'une mauvaise ventilation de l'unité, compte tenu de la détection simultanée d'un grand nombre de cas limités à une seule unité, et

		qu'elle s'est produite pendant une période de faible transmission dans la communauté.
Autobus pour passagers		
Luo (2020) (7) Enquête sur les grappes Chine Janvier 2020 *nouvelle*	Enquête sur une éclosion de COVID-19 liée à de multiples trajets en autobus du cas index à Hunan, en Chine.	Un total de 12 cas ont été recensés à la suite de l'enquête sur 243 personnes qui étaient associées épidémiologiquement à de multiples trajets en autobus effectués par le cas index, avec un taux d'attaque de 7,0 %. La distance à laquelle les personnes infectées se sont assises pendant les déplacements en autobus variait de 1 à 4,5 mètres du cas index. Le trajet de 2,5 heures en autobus a entraîné huit cas qui n'étaient pas tous assis les uns près des autres pendant le trajet. L'infection a également été décelée chez une personne qui se serait assise (probablement) sur le même siège que le cas index, une fois que cette personne soit débarquée de l'autobus. Deux cas ont été identifiés après le trajet d'une heure en autobus. Deux cas étaient des cas tertiaires pour l'une des personnes ayant été infectées dans l'autobus. Aucun des cas déterminés n'a déclaré avoir porté de couvre-visage pendant les déplacements en autobus. Les experts cliniques suggèrent que le fait que les aérosols puissent parcourir plus de deux mètres et la circulation de l'air ont influencé la transmission de l'infection dans l'environnement bondé et fermé de ces autobus.
Shen (2020) (26) Cluster Investigation China Jan 2020	A COVID-19 outbreak among 128 people driven to a worship event in Eastern China on two separate buses. Round trip was 100 minutes on the bus.	None of the passengers on Bus 1 were infected, 24 of the 68 passengers on Bus 2 developed COVID-19. Passengers riding Bus 2 with the index case had an attack rate of 34.3% (95% CI, 24.1%-46.3%), compared to passengers on bus 1. Although sitting near bus windows and doors appeared to have had a protective effect on

	Attack rates were measured for Bus 1 vs. Bus 2 that had the index case. Air conditioning systems of both buses were on recirculation mode. Spatial analysis of passenger seating was estimated.	infection transmission, the authors conclude, the lack of a significant increase in infection risk between individuals sitting in high risk zones (i.e. closer to the index case) and low risk zones, and elevated attack rates among bus passengers riding with the index case, to be partially explained by aerosol transmission of infection.
Usine de transformation de viande		
Guenther (2020) (27) *préimpression* Enquête sur les grappes de cas Allemagne Printemps 2020*	Enquête sur un événement de super-contamination parmi les travailleurs d'une usine de transformation de la viande, comprenant : les voies de transmission possibles, la relation spatiale entre les travailleurs, les conditions de climat et de ventilation, le partage des habitations et du transport, et le type génétique des échantillons prélevés dans la gorge.	L'analyse des cas index (colocataires) et de 18 cas de collègues de travail suggère que le fait de travailler au poste du matin (140 travailleurs de l'équipe du matin) est la source commune d'infection. Des taux d'infection statistiquement significatifs ont été observés chez les employés travaillant dans un rayon de 8 mètres autour du cas index suspect. Les auteurs concluent que les environnements intérieurs confinés, le travail physique exigeant et les conditions environnementales de l'installation (c'est-à-dire l'air constamment en recirculation et refroidi à 10 °C, avec un faible taux d'échange d'air) ont tous créé des conditions propices à la transmission par les aérosols. Remarque : aucune évaluation quantitative des risques n'a été fournie.
Restaurant		
Kwon (2020) (8) Enquête sur les grappes Corée Juin 2020 *nouvelle*	Enquête sur un groupe de trois clients dans un restaurant. L'enquête a tenu compte des données épidémiologiques, des images fournies par la télévision, des patrons de	Les experts cliniques ont conclu que la transmission de l'infection s'était produite d'un client infecté à deux personnes se trouvant dans le restaurant, avec un taux d'attaque de 15,4 % (2 sur 13). On a présumé que la date de l'exposition (et la source de l'exposition) a eu lieu une journée avant l'apparition des symptômes chez le cas index. Les aérosols étaient le mode de

	flux d'air et l'emplacement des téléphones cellulaires.	transmission présumé puisqu'ils ont pu parcourir plus de 6,5 mètres en raison du courant d'air créé par le climatiseur à l'intérieur du restaurant. Le temps d'exposition entre l'infecteur et l'infecté est d'environ 5 minutes. On précise que le port du masque ou du couvre-visage est inapproprié parmi les membres du personnel et les clients.
Lu (2020) (28) Enquête sur les grappes de cas Chine Janvier-février 2020	Analyse d'une grappe de cas de COVID-19 dans des petits restaurants offrant le dîner. L'enquête comprenait une analyse spatiale de la disposition des tables dans les restaurants et de l'endroit où les cas étaient assis.	Une éclosion parmi 91 personnes dans un restaurant; 83 personnes assises à 15 tables, et les huit personnes restantes étaient des membres du personnel. Un seul cas asymptomatique a conduit à neuf infections à la COVID-19 parmi les clients des familles A, B et C. Aucune des familles ne s'était rencontrée auparavant et n'avait eu de contact étroit pendant le dîner. Aucun cas supplémentaire n'a été identifié pendant les 14 jours de quarantaine des clients restants. L'analyse spatiale des tables de cas pendant le dîner (c'est-à-dire l'événement d'exposition) a révélé que les tables touchées avaient été disposées en fonction du flux d'air provenant d'une unité de climatisation. Les auteurs suggèrent que la transmission de l'infection ne pouvait pas être expliquée uniquement par les gouttelettes, et que les aérosols voyageant avec le flux d'air pourraient avoir contribué à la transmission de l'infection.
Li (2020) (29) *préimpression* Étude in silico Chine Février 2020	Une enquête et une analyse d'un grappe de cas de COVID-19 parmi trois familles qui ont mangé dans le même restaurant. L'analyse comprenait : des données épidémiologiques, une analyse spatiale de la	Dix personnes de trois familles différentes assises à des tables différentes ont été infectées par le SRAS-CoV-2 à la suite d'un dîner de la veille du Nouvel An chinois (24 janvier 2020). Aucun des serveurs ou des clients des autres tables n'a été infecté. Le taux de ventilation a été estimé à 0,75-1,04 L/s par personne.

Remarque : Voir également une analyse distincte de la grappe de cas décrite par Lu (2020).	disposition des tables du restaurant, des données de surveillance vidéo, et des simulations informatiques de la dynamique des fluides et des gaz traceurs de la propagation des fines gouttelettes lors de l'événement.	Aucun contact étroit ou contact avec des matières contaminées n'a été observé parmi les cas, à part le fait que certains clients s'asseyaient dos à dos. À l'aide de simulations informatiques, les auteurs démontrent que la distribution de l'infection est conforme au schéma de propagation des aérosols de virus expirés. Une mauvaise ventilation dans le restaurant peut également avoir contribué à la propagation de l'infection.
Pratique de chorale		
Charlotte (2020) (16) Enquête sur les grappes France Mars 2020 *nouvelle*	L'enquête sur une éclosion de COVID-19 liée à une pratique chorale, à Whir au Val, en France.	Vingt-sept participants (25 chanteurs, un chef d'orchestre et un accompagnateur) ont assisté à la pratique de la chorale à l'intérieur, pratique qui s'est déroulée dans un espace non ventilé de 45 m^2. Aucun participant n'a déclaré avoir eu de symptômes dans les 14 jours ayant précédé la date de la pratique. 19 participants sur 27 ont développé une infection à la COVID-19 entre 1 et 12 jours après la date de la pratique (médiane de 5,1 jours). Le taux d'attaque secondaire était de 70 % parmi tous les participants. Les experts cliniques supposent que la transmission de l'infection s'est produite par des aérosols provenant de personnes présymptomatiques ou asymptomatiques qui ont assisté à la pratique, puisque le cas de référence n'a pas été identifié de façon définitive.
Hamner (2020) (30) Enquête sur les grappes de cas États-Unis Mars 2020 Remarque : Voir également une	Une enquête épidémiologique sur un groupe de cas liés à une chorale, dans le comté de Skagit, Washington. La pratique était d'une durée deux heures trente. Pendant la pratique, les	Parmi les 61 choristes présents à la pratique, au moins une personne était un cas symptomatique de COVID-19. L'enquête épidémiologique a fait état de 53 cas (33 cas confirmés, 20 cas probables). Les taux d'attaque secondaire étaient de 53,3 % parmi les cas confirmés et de 86,7 % parmi l'ensemble des cas.

analyse distincte de la grappe de cas décrite par Miller (2020).	gens ont chanté et se sont assis à une distance de 15 à 25 cm les uns des autres, ils se sont réunis autour d'une collation et ont empilé des chaises. Aucun des participants n'a signalé de contact physique.	La probabilité d'infection était de 125,7 fois (IC à 95 % : 31.7-498.9) plus importante parmi les membres qui ont assisté à la pratique du 10 mars (événement d'exposition supposé). Les enquêteurs introduisent la possibilité de transmission de la COVID-19 par les aérosols pendant le chant dans la documentation sur la COVID-19.
Miller (2020) (31) Étude in silico États-Unis Mars 2020 Remarque : Voir également une analyse distincte de la grappe de cas décrite par Hamner (2020).	Des simulations de Monte Carlo et une modélisation mathématique ont été utilisées pour estimer les taux d'émission des aérosols dans l'éclosion liée à une pratique de chorale, dans le comté de Skagit. Le modèle appliqué suppose que la transmission de l'infection lors de l'éclosion a été dominée par l'inhalation d'aérosols dans un environnement intérieur bien distribué (c'est-à-dire que les aérosols étaient répartis uniformément dans l'air). La charge virale émise a été exprimée sous forme de taux d'émission *quanta* (*quanta* par heure) où *quantum* a été défini comme la dose de noyaux de gouttelettes dans les aérosols nécessaire pour provoquer une infection	L'analyse in silico a soutenu la transmission des aérosols en se basant sur l'hypothèse que des taux d'émission élevés se produisaient étant donné le taux d'attaque élevé (53-87 %), qui était plus élevé que ce à quoi on pourrait s'attendre si la transmission était due à des vecteurs passifs ou à de grosses gouttelettes respiratoires. Le modèle estime le taux moyen d'émission d'aérosols pour un seul cas infecté lors de l'exposition à 970 [EI 680-1190] quanta par heure. Remarque : Les conclusions de l'étude sont en accord avec les résultats de Buonanno, 2020.

	chez 63 % des personnes sensibles.	
Éclosions multiples		
Buonanno (2020) (32) Étude in silico Chine et États-Unis (sites d'éclosions) Février-mars 2020 Remarque : Une analyse différente des éclosions dans les restaurants et les pratiques de chorales décrite ci-dessus.	Il s'agit d'un modèle d'émission et d'exposition qui utilise une approche par étapes pour quantifier le risque individuel d'infection parmi les sujets sensibles exposés à un cas asymptomatique ou peu symptomatique dans une chorale et un restaurant. La méthode de Monte Carlo a également été utilisée; les risques d'infection individuels ont été calculés en fonction des caractéristiques d'émission *quanta*.	Le modèle a illustré l'augmentation du risque d'infection individuel en fonction des taux de ventilation, des activités et de la quantité de virus expirée. Par exemple, des activités sédentaires pendant une heure peuvent présenter un risque d'infection de 2,1 %, qui peut passer à 27 % avec des taux d'émission plus élevés. Sur la base de l'approche d'évaluation des risques et des données disponibles, les taux d'émission *quanta* ont été estimés à 61 *quanta* par heure pour le restaurant et à 341 *quanta* par heure pour la chorale de Skagit Valley. Dans les deux exemples, varier la ventilation n'aurait pas permis d'atteindre un risque individuel <0,1. Les auteurs ont conclu que la transmission par les aérosols représente la principale voie de transmission pour les deux éclosions.
Kriegel (2020) (33) Étude in silico Allemagne, Chine, États-Unis (sites d'éclosions) Février-mars 2020 Remarque : Comprend les grappes de cas suivantes : Usine de transformation de la viande –Guenther (2020), Pratique de chorale –Hamner	Une extension de l'équation de Wells-Riley a été utilisée pour estimer le risque d'infection prévisible par les aérosols dans 12 éclosions de COVID-19 publiées et non publiées. Les prédictions des risques d'infection ont été comparées aux taux d'attaque observés dans chaque événement. Pour estimer un intervalle de crédibilité pour les prédictions de risques d'infection par le modèle, le taux d'émission *quanta*,	Dans neuf des douze éclosions, les taux d'attaque observés étaient conformes aux prédictions de risques d'infection par les aérosols et aux fourchettes correspondantes (avec la variation des conditions limites). Prédiction du risque d'infection par les aérosols (PIRA)/taux d'attaque (TA) Usine de transformation de la viande : 25 % (17-35)/26 % Chorale : 97 % (88-99)/87 % Restaurant : 40 % (35-56)/45 % autocar : 35 % (19-58)/34 % Les taux d'attaque de toutes ces éclosions seraient conformes à la prédiction du risque d'infection par les aérosols.

(2020), passagers d'autocar –Shen (2020), et restaurant –Lu (2020).	la fréquence respiratoire ainsi que les débits volumétriques de l'air ont été variés. L'analyse suppose une transmission par les aérosols à longue distance dans un environnement idéalement homogène.	
Navires de croisière		
Azimi (2021) (34) Étude in silico Bateau de croisière Janvier-février 2020 Remarque : Même éclosion décrite par Almilaji (2020) et Xu (2020).	Analyse des données sur les cas de l'éclosion du Diamond Princess à l'aide d'un cadre qui applique une chaîne de Markov stochastique et un modèle de la relation dose-réponse exponentielle négative avec des données empiriques, afin d'informer une version modifiée du modèle de Reed-Frost sur les épidémies, pour prédire les taux de comptage des cas. La période d'incubation effective a été estimée à 6-15 jours, et considérée comme ayant différents modes de transmission. Remarque : Les données des cas du 20 janvier au 24 février 2020 ont été incluses dans l'analyse.	Il y a eu 712 cas de COVID-19 parmi 3 711 passagers et membres d'équipage (taux d'attaque de 19 %). Les contributions moyennes des gouttelettes et des aérosols à courte distance (35 %), des aérosols à longue distance (35 %) et des vecteurs passifs (30 %) aux modes de transmission de l'infection à bord du bateau ont été estimées, tout comme les contributions des grosses gouttelettes respiratoires (41 %) et des petits aérosols (59 %). Sur la base des estimations de l'analyse modélisée, les auteurs concluent que les transmissions par les aérosols à courte et à longue distance sont les principaux modes de transmission de l'infection dans l'éclosion. La mise en quarantaine des passagers dans leurs cabines a fait chuter la valeur Rt à presque zéro. Les auteurs suggèrent que sur le bateau de croisière, la transmission par les aérosols était le mode de transmission dominant (>70 % des cas) malgré les taux de renouvellement d'air (9 à 12 renouvellements d'air par heure) sans recirculation de l'air.
Almilaji (2020) (35)	Analyse des données cliniques et du nombre de	Les taux parmi les passagers des cabines sans cas infectés étaient de 5,4 %, ce qui était plus élevé

Enquête sur les grappes de cas Bateau de croisière Janvier-février 2020 Remarque : Même éclosion décrite par Azimi (2020) et Xu (2020).	cas de l'éclosion du bateau de croisière Diamond Princess. Les taux d'apparition des infections symptomatiques après quarantaine parmi les cas confirmés en laboratoire ont été examinés et la conception du système de climatisation du bateau de croisière a été étudiée. Remarque : Les données des cas jusqu'au 20 février 2020 ont été incluses dans l'analyse.	que les taux parmi les passagers des cabines avec des cas confirmés 2,4 %. La différence entre les taux était de -3,1 % ($IC_{élevé}$ de 95 %; 9,1 %). En se basant sur cette différence, les auteurs suggèrent que la transmission par les aérosols du SRAS-CoV-2 par le système de ventilation du bateau de croisière pourrait avoir contribué à l'éclosion. Remarque : Tous les cas dans les deux types de cabines se sont produits dans les dix jours suivant le début de la quarantaine sur le bateau. L'utilisation d'une période d'incubation de six jours par l'auteur a conduit aux résultats ci-dessus.
Xu (2020) (36) *préimpression* Enquête sur les grappes de cas Bateau de croisière Janvier-février 2020 Remarque : Une analyse différente de la grappe de cas décrite par Azimi (2020) et Almilaji (2020).	L'analyse des données des cas de COVID-19 de l'éclosion du bateau de croisière Diamond Princess a été effectuée sur la base des facteurs de risque individuels, de l'occupation des cabines et du système de climatisation (c'est-à-dire CVCA) du bateau afin d'explorer les modes de transmission les plus plausibles. Les données des cas du 20 janvier au 18 février 2020 ont été incluses dans cette analyse.	Les taux d'infection quotidiens des cas de passagers (n = 146) ont été prédits sur la base de l'état de contact étroit par rapport à l'état de sans contact étroit, et des données avant et après la quarantaine (le 5 février étant le début de la quarantaine). Les enquêteurs ont conclu que la plupart des cas de passagers ont probablement été exposés avant la mise en quarantaine et que le système de climatisation du bateau de croisière n'a pas joué de rôle dans la transmission de la COVID-19 par les aérosols à longue distance.
Centres de conditionnement physique/centre sportif		

Groves (2021) (9) Enquête sur les grappes États-Unis Juin 2020 *nouvelle*	Enquête sur une épidémie de COVID-19 associée à de multiples événements d'exposition à Hawaï entre un instructeur dans des cours sur vélo stationnaire, un instructeur de kick-boxing/entraînement personnel et leurs clients. Remarque : Au moment de l'éclosion, le taux de transmission moyen dans la collectivité était de 2 à 3 cas par 100 000 personnes par jour, ce qui porte à croire qu'il était peu probable qu'il y ait d'autres expositions.	Vingt cas ont été liés à deux instructeurs de conditionnement physique présymptomatiques, dans différents cours. L'instructeur de kickboxing/entraînement personnel était un cas secondaire de l'instructeur responsable des cours sur vélo stationnaire. L'instructeur, le cas index, portait un couvre-visage pendant le cours sur vélo stationnaire, mais pas les participants. L'instructeur était à plus de 6 pieds de distance des participants et leur faisait face pendant le cours. Les fenêtres et les portes de la salle étaient fermées et les ventilateurs au sol (pour le refroidissement) envoyaient de l'air sur les participants. On suppose que les événements de transmission avec le deuxième instructeur se sont produits pendant les séances de kickboxing en petits groupes et les séances d'entraînement personnel alors que l'instructeur ne portait pas de couvre-visage et que peu de participants en portaient un. Les deux instructeurs ont donné des cours avant l'apparition des symptômes et les taux d'attaque globaux suivants ont été calculés : - < 1 jour avant l'apparition des symptômes (taux d'attaque de 95 %). - 1 à < 2 jours avant l'apparition des symptômes (taux d'attaque de 13 %). - ≥ 2 jours avant l'apparition des symptômes (taux d'attaque de 0 %). Les experts cliniques responsables de l'enquête épidémiologique indiquent que la transmission de l'infection a été facilitée par le fait que presque personne de portait de couvre-visage, qu'il y a eu des contacts étroits et prolongés, qu'il y avait une mauvaise ventilation dans la pièce et qu'il y a eu

		émission d'aérosols pendant l'activité physique et lorsque l'instructeur criait pour se faire entendre.
Lendacki (2021) (10) Enquête sur les grappes États-Unis Août et septembre 2020 *nouvelle*	Enquête sur une éclosion de COVID-19 associée à des cours de conditionnement physique à l'intérieur, cours qui ont été donnés à 25 % de la capacité maximale (c.-à-d. de 10 à 15 personnes) et dont les participants se trouvaient à 2 m (6 pi) les uns des autres. Remarque : le bâtiment n'a pas été conçu à l'origine pour des cours de conditionnement physique et son système de ventilation n'a pas été évalué.	55 cas de COVID-19 (49 cas confirmés et 6 cas probables) ont été identifiés parmi les 81 personnes qui ont suivi des cours avec exercices haute intensité à l'intérieur, avec un taux d'attaque de 68 %. On a signalé que peu de gens portaient un couvre-visage pendant les cours, soit environ 75 % des participants. L'éclosion a été attribuée à deux cas de référence qui ont suivi plusieurs cours alors qu'ils étaient symptomatiques et étaient potentiellement infectieux. Les deux participants ont déclaré porter un couvre-visage 60 % du temps pendant les cours (port peu fréquent). La probabilité du port peu fréquent du couvre-visage comparativement au port constant de ce dernier pendant les cours était plus fréquente chez les participants qui avaient eu la COVID-19 que chez ceux qui ne l'avaient pas eu (RC = 3,5; IC à 95 % = 0,9 à 15,1). Les participants ayant reçu un diagnostic de COVID-19 ont également déclaré suivre un plus grand nombre de cours (médiane de 5 par rapport à 3 cours). Les auteurs suggèrent que le port peu fréquent du couvre-visage, l'augmentation de l'effort respiratoire pendant l'exercice, la transmission par les aérosols et une ventilation sous-optimale peuvent avoir contribué à la transmission de l'infection pendant cette éclosion.
Jang (2020) (37) Enquête sur les grappes de cas Corée du Sud Février-mars 2020	Enquête sur une éclosion de COVID-19 associée à des cours de Zumba dans 12 lieux différents d'installations de conditionnement physique, suite à un atelier	La transmission initiale est supposée avoir eu lieu entre les instructeurs lors d'un atelier de quatre heures où 8 des 27 participants ont été testés positifs pour le SRAS-CoV-2. Dans les semaines qui ont suivi, le nombre de cas associés à des instructeurs infectés a atteint 112 cas dans plusieurs centres de conditionnement physique.

	pour les instructeurs à Cheonan, en Corée du Sud.	Le taux d'attaque lors de l'atelier était de 26,3 % (IC de 95 % 20,9 %-32,5 %) et le taux d'attaque secondaire de huit instructeurs était de 4,10 % (IC de 95 % 2,95 %-5,67 %, 830 contacts étroits). Les enquêteurs déclarent qu'environ la moitié des cas identifiés (50,9 %) étaient dus à une transmission par des instructeurs à des participants à des cours de conditionnement physique; 38 cas (33,9 %) étaient des transmissions au sein de la famille par des instructeurs et des clients; et 17 cas (15,2 %) étaient des transmissions lors de rencontres avec des collègues ou des connaissances. Aucun cas secondaire n'a été observé parmi les clients des cours de Pilates et de yoga, donnés par un instructeur infecté. Les auteurs affirment qu'une activité physique intense, le grand nombre de participants à un cours de conditionnement physique (c'est-à-dire un espace bondé) et le milieu chaud et humide de l'installation sportive peuvent avoir contribué aux taux élevés d'infection dans l'éclosion.
Brlek (2020) (38) Enquête sur les grappes de cas Slovénie Février-mars 2020	Enquête sur une grappe de cas de SRAS-CoV-2 lié à un court de squash.	La grappe de cas comprenait six cas censés être liés par une transmission indirecte de l'infection. L'enquête épidémiologique a indiqué que le cas index a développé des symptômes pendant la partie de squash, et que quatre cas confirmés et un cas suspect étaient liés à la même salle de squash et potentiellement aux mêmes vestiaires. Aucun des cas ne partageait des équipements sportifs ou n'avait de contact avec le personnel de l'établissement. Aucun autre cas n'a été identifié. Les auteurs suggèrent que la transmission de l'infection au sein de la grappe de cas s'est probablement produite en raison de l'aérosolisation du virus dans un environnement intérieur, notamment dans un espace restreint,

		une ventilation inadéquate et une activité physique intense.
Immeubles d'habitation		
Hwang (2021) (11) Enquête sur les grappes Corée du Sud Août 2020 *nouvelle*	Enquête sur le rôle de la transmission par les aérosols dans une éclosion de COVID-19 associée à une tour d'habitation à Séoul.	10 cas de COVID-19 dans 7 ménages ont été identifiés dans des appartements situés sur deux lignes verticales dans une tour d'habitation. Chaque ligne d'appartements était reliée par une seule conduite d'air installée dans la salle de bain pour assurer une ventilation naturelle. Taux d'attaque de 2 % chez les résidents de la tour d'habitation (n = 10 sur 437). Aucune des surfaces testées, incluant les grilles de ventilation et les drains domestiques, n'a révélé la présence d'ARN viral. On a supposé que la transmission par gouttelettes, lorsque les personnes se trouvaient dans un même espace commun (p. ex., un ascenseur), était peu probable en raison de la disposition spatiale des logements. Les responsables de l'enquête épidémiologique présument que la circulation verticale de l'air dans une seule conduite d'air qui traverse la salle de bain (ce qui correspond à la circulation d'air dans un puits vertical) a propagé l'infection aux résidents des appartements dans le haut et dans le bas de la tour.
Lin (2021) (12) Enquête sur les grappes Chine Janvier et février 2020 *nouvelle*	Étude d'une grappe de COVID-19 liée à des familles vivant dans trois appartements sur une même ligne verticale dans une tour d'habitation. La famille de référence a déclaré une exposition possible à la suite d'un voyage à Wuhan, mais les deux autres familles qui	10 cas de COVID-19 ont été identifiés dans 3 ménages et l'analyse phylogénétique a confirmé que tous les cas avaient été infectés par la même souche. Les images de surveillance vidéo n'ont pas permis d'identifier d'expositions entre les membres du ménage de référence et d'autres cas. Les experts cliniques concluent que la transmission de l'infection s'est probablement produite en raison des tuyaux d'évacuation

Remarque : Analyse différente de la grappe décrite par Kang (2020).	ont eu des cas subséquents n'y sont pas allées. Un gaz traceur a été utilisé pour simuler le débit d'air entre les unités.	raccordés aux toilettes qui étaient ensuite raccordés aux tuyaux d'égout et aux drains de crue, un système que se partageaient les appartements se trouvant sur une même ligne verticale.
Kang 2020 (39) Enquête sur les grappes Chine Janvier et février 2020 *nouvelle* Remarque : Analyse différente de la grappe décrite par Lin (2021).	Enquête sur la transmission de l'infection entre trois familles qui vivaient dans le même immeuble. La famille de référence a déclaré une exposition possible à la suite d'un voyage à Wuhan, mais les deux autres familles qui ont eu des cas subséquents n'y sont pas allées. Les experts cliniques ont utilisé l'éthane comme gaz traceur en remplacement du gaz dans le système d'évacuation des bâtiments et ont calculé la dynamique des fluides pour étudier les sources possibles d'infection et de transmission entre les familles.	10 cas de COVID-19 dans trois familles qui vivaient dans des appartements se trouvant sur la même ligne verticale et reliés par des tuyaux d'évacuation dans les salles de bain principales. Taux d'attaque de 4 % chez les résidents et les membres du personnel de la tour d'habitation (n = 10 sur 217) Aucune exposition provenant des ascenseurs du bâtiment n'a été identifiée, et l'ARN viral n'a pas été détecté sur les boutons des ascenseurs ou sur les surfaces de ventilation. Les surfaces les plus fréquemment contaminées par de l'ARN viral se trouvaient dans les salles de bain principales, ce qui suggère que ces zones sont probablement des sites de transmission d'infection. Sur la base des analyses épidémiologiques et *in silico*, les experts cliniques supposent que la transmission de l'infection de la famille index aux deux autres familles s'est probablement produite par des aérosols fécaux dans la tuyauterie verticale. Remarque : aucun des échantillons d'air prélevés dans cette installation n'était positif pour l'ARN viral.
Centres commerciaux/magasins		
Jiang (2020) (13) Enquête sur les grappes Chine	Enquête sur 43 cas de SRAS-CoV-2 liés à une grappe dans un grand magasin à Baodi, en Chine. L'enquête a tenu compte des données épidémiologiques, des	43 cas de COVID-19 liés à une éclosion dans un grand magasin : 6 vendeurs, 18 clients et 19 de leurs proches. On a déterminé que les cas avec contact étroit étaient des cas secondaires dont l'exposition n'était pas liée au magasin.

Janvier et février 2020 *nouvelle*	images de surveillance vidéo, de l'aménagement du magasin et des conditions de ventilation.	Les experts cliniques ont conçu que les aérosols ont été un mode de transmission important parmi 11 cas dans cette éclosion. Le cas index n'a pas été identifié, mais on a supposé qu'il s'agissait d'un des vendeurs infectés.
Cai 2020 (40) Enquête sur les grappes de cas Chine Janvier 2020	Enquête sur une grappe de cas de SRAS-CoV-2 liée à un centre commercial. Les données cliniques, épidémiologiques et de laboratoire (méthode RT-PCR) des cas ont été analysées pour évaluer les modes possibles de transmission de l'infection.	Deux collègues du centre commercial étaient les cas index : cela a été associé à sept infections parmi les collègues du même étage, sept membres du personnel d'autres étages, dix clients du centre commercial et deux contacts étroits à l'extérieur du centre commercial. Les clients et les collègues des autres étages ont dit ne pas avoir eu de contact étroit avec les cas répertoriés. Sur la base des données disponibles, les auteurs suggèrent que la propagation de l'infection pourrait avoir résulté d'une propagation par vecteur passif ou par aérosolisation du virus dans un espace public confiné (par exemple, toilettes ou ascenseurs).

LTE = lettre à la rédaction

EXPÉRIENCES SUR LES ANIMAUX DE LABORATOIRE ET EXPOSITION PAR LES AÉROSOLS ET TRANSMISSION DU SRAS-COV-2

La présente section résume les six études sur les modèles animaux qui ont fourni des preuves expérimentales à l'appui de la transmission du SRAS-CoV-2 par les aérosols (tableau 2). Les modèles animaux utilisés dans les études étaient des primates non humains, des putois et des hamsters qui ont tous été établis comme modèles animaux appropriés pour l'étude de la transmission du SRAS-CoV-2 chez l'homme (41, 42)

Deux expériences ont porté sur l'exposition contrôlée de primates non humains et de hamsters à des aérosols infectieux générés artificiellement à différentes concentrations de virus afin de déterminer s'il peut y avoir infection et de suivre le cours clinique chez les animaux hôtes infectés (17, 43). Ces études démontrent que l'infection par le SRAS-CoV-2 peut se produire par l'exposition à des aérosols infectieux dans un milieu contrôlé. L'une des études sur les hamsters, qui comparait de multiples modes de transmission (c.-à-d. aérosols, fomite et intranasal) a indiqué que la réplication et l'excrétion du virus chez les animaux étaient liées au type d'exposition. Les auteurs ont observé une réplication virale antérieure, une charge virale plus élevée, une manifestation aiguë des symptômes respiratoires et des modèles différents d'excrétion virale dans les tissus respiratoires des animaux infectés par les aérosols comparativement aux animaux infectés par les modes d'exposition intranasaux et fomites (17).

Cinq expériences ont porté sur la transmission du SRAS-CoV-2 entre des animaux hôtes infectés et vulnérables (c.-à-d. des paires de transmission) qui étaient physiquement séparés par des barrières et des cages différentes (17, 18, 44 à 46). Dans la plupart des expériences, les paires de transmission étaient séparées par des barrières qui empêchaient le contact direct, mais permettaient la circulation de l'air. Ainsi, 25 à 100 % des animaux sensibles ont été infectés après une certaine durée d'exposition. Ces expériences fournissent des preuves à l'appui de la transmission par les aérosols chez les animaux hôtes dans un milieu expérimental.

Des preuves supplémentaires tirées de deux expériences démontrent comment la circulation de l'air et la ventilation peuvent avoir une incidence sur la transmission indirecte de l'infection (17, 45). Dans l'une de ces expériences, des paires de putois étaient logées dans des cages séparées physiquement, mais qui se partageaient de l'air amené par des conduits d'air connectés, ce qui a mené à l'infection de 50 % des animaux vulnérables (45). Dans le cadre d'une autre expérience, l'influence de la direction du flux d'air sur la probabilité de transmission de l'infection a été étudiée, et les résultats montrent que l'infection ne s'est produite que chez le hamster susceptible installé en aval de l'air que respirait le hamster infecté (17).

La petite taille des échantillons, les animaux n'aient pas été séparés par de grandes distances, le manque de détails sur le comportement des animaux pendant l'expérience (p. ex., symptômes de toux ou d'éternuement chez les animaux infectés), et parfois le manque de détails concernant la perméabilité des

barrières de séparation aux fluides respiratoires et oraux, aux mouvements des particules fécales et alimentaires, limite cette preuve de la transmission des aérosols.

Tableau 2 : Expériences sur les animaux de laboratoire en ce qui concerne l'exposition par les aérosols et la transmission indirecte du SRAS-CoV-2 (n = 6)

RÉFÉRENCE	MÉTHODE	RÉSULTATS PERTINENTS
Edwards (2020) (43) Expérience de simulation États-Unis Octobre 2020* Remarque : Des résultats supplémentaires sur les émissions d'aérosols sont résumés dans le tableau 7.	Huit primates non humains (Macaca mulatta [macaque rhésus] et Chlorocebus aethiops [singe vert]) ont été infectés par des aérosols (≈2 µm) contenant le SRAS-CoV-2 (~2,5x103 DICT50) en utilisant un système d'inhalation de laboratoire.	L'échantillonnage des muqueuses par écouvillonnage nasal a montré que l'ARN viral était détecté dès le jour suivant l'exposition à l'aérosol infectieux. La production de particules par l'air expiré a commencé trois jours après l'infection, a augmenté jusqu'au septième jour et a diminué jusqu'au 14e jour chez les primates. Il y avait une association significative entre les particules respiratoires expirées et la charge virale chez la plupart des primates et une corrélation avec la cinétique virale. L'ARN viral était indétectable dans les échantillons de prélèvement nasal des primates infectés au 28e jour suivant l'infection.
Port (2020) (17) *Préimpression* *Étude in vivo* États-Unis Décembre 2020* *nouvelle*	Trois groupes de femelles de *Mesocricetus auratus* (hamsters syriens) (n = 36) ont été infectés par des aérosols du virus SRAS-CoV-2 et par d'autres types d'expositions (c.-à-d. fomites et intranasal). Les animaux infectés ont été comparés aux témoins non exposés (n = 12). L'exposition aux aérosols du SRAS-CoV-2 (1,5 x 103 $DICT_{50}$) a été causée par une collision de 3 jets envoyés par nébulisation avec une	Les auteurs ont constaté que le mode de transmission utilisé par l'infection par le SRAS-CoV-2 jouait un rôle dans la gravité de la maladie, la charge virale et l'excrétion du virus dans le modèle animal. Une réplication précoce du virus (1 jour après l'infection), une excrétion respiratoire maximale du virus 2 jours après l'exposition et une charge virale précoce plus élevée dans les tissus pulmonaires et trachéaux (p = < 0,0001), ont été observées chez les animaux exposés aux aérosols comparativement aux autres types d'expositions. Les titres viraux dans les tissus pulmonaires ont montré une relation positive avec la pathologie des voies respiratoires supérieures et inférieures et la perte de poids, ce qui a amené les auteurs à suggérer que l'excrétion respiratoire précoce (observée chez les animaux

	taille des particules variant de 1 à 5 µm. Mesure des tendances en ce qui concerne l'élimination du virus et les modèles de réplication dans les tissus respiratoires et avec des écouvillons oropharyngés et fécaux. Dans des expériences distinctes de transmission aéroportée, deux paires de transmission (n = 4) ont été hébergées ensemble dans des cages séparées par une cloison en plastique perforé qui empêchait tout contact direct. Les animaux sensibles ont été placés dans la direction du flux d'air des animaux infectés ou à l'inverse de celui-ci; quatre paires de transmission (n = 8). Infection détectée d'après la séroconversion sérique.	infectés par des aérosols) pouvait prédire la manifestation aiguë de la maladie. Dans les expériences avec contacts indirects utilisées pour évaluer la transmission fondée sur le flux d'air, aucun symptôme lié à l'infection n'a été observé chez les animaux sensibles, mais 25 % (n = 1 sur 4) ont eu une séroconversion. Cette séroconversion (c.-à-d. l'exposition au virus) a été liée au flux d'air directionnel provenant des animaux infectés vers les animaux hôtes. Il convient de noter qu'on a observé que la transmission fomite était liée à une manifestation tardive de la maladie, soit à une période plus longue entre l'exposition et la réplication virale dans les tissus respiratoires, ce qui a réduit la gravité de la maladie.
Zhang (2021) (18) *Préimpression* *Étude in vivo* États-Unis Janvier 2021* *nouvelle*	Enquête sur le risque de transmission de l'infection par le SRAS-CoV-2 attribuable à l'exposition par les aérosols, et sur le risque de réinfection lors d'une reprise entre les paires de transmission naïves infectées et les paires de *Mesocricetus*	Des expériences ont révélé que le SRAS-CoV-2 était efficacement transmis des hamsters naïfs infectés aux hamsters précédemment infectés par transmission aéroportée, dans toutes les paires de transmission. En se fondant sur les concentrations d'ARN viral présentes dans les tissus respiratoires, les experts cliniques concluent que l'infection antérieure a fourni une bonne immunité protectrice, mais pas une immunité complète contre la réinfection au

	auratus (hamsters syriens) ayant déjà été infectées. Dans les expériences de transmission par les aérosols, les hamsters infectés et les hamsters donneurs (n = 6) se trouvaient dans des cages de transmission munies de cloisons à mailles métalliques qui empêchent le contact direct et indirect entre les animaux, mais permettent une circulation d'air. Les niveaux de virus vivants dans les tissus respiratoires au cours de la période suivant l'exposition ont été mesurés pour confirmer la réinfection.	moment de la reprise puisqu'un virus vivant était présent chez les animaux réinfectés.
Sia (2020) (44) Étude in vivo Hong-Kong* Mai 2020*	Étude expérimentale pour étudier la transmission du SRAS-CoV-2 par les aérosols. Les hamsters dorés infectés et sensibles qui étaient logés dans des cages grillagées adjacentes placées à 1,8 cm les unes des autres (trois paires différentes) ont été exposés les uns aux autres pendant huit heures.	Une transmission indirecte efficace de l'infection à des hamsters sensibles s'est produite pour les trois paires dans un cadre expérimental. La charge virale maximale chez le hamster exposé par des aérosols a été atteinte trois jours après le contact.
Kutter (2020) (45) *Préimpression*	Une installation d'étude expérimentale dans laquelle quatre cages de	La transmission indirecte du SRAS-CoV-2 entre deux furets à plus d'un mètre de distance a été confirmée dans deux des quatre paires de

Étude *in vivo* Pays-Bas* Octobre 2020*	paires de donneurs et de receveurs indirects ont été reliées par un système de conduits durs composé de tuyaux horizontaux et verticaux à multiples coudes. Le flux d'air était dirigé vers le haut depuis le donneur vers les animaux receveurs indirects. L'air a parcouru en moyenne 118 cm dans les systèmes de tubes.	transmissions indépendantes. L'infection a été confirmée par la détection d'ARN viral dans des prélèvements de gorge et de nez.
Kim (2020) (46) Étude *in vivo* Corée du Sud* Mai 2020*	Étude expérimentale de la transmission de furet à furet du SRAS-CoV-2 en laboratoire. Le contact indirect des furets a été réalisé par une cloison perméable entre les cages pour séparer les furets sensibles et les furets infectés.	Deux des six furets de contact indirect étaient positifs pour l'ARN viral dans les lavages nasaux et les échantillons de selles. Les auteurs suggèrent que la transmission par les aérosols s'est produite chez les furets de contact indirect.

*Estimation basée sur les affiliations des auteurs et la date de publication.

VIABILITÉ DU SRAS-COV-2 DANS LES AÉROSOLS

Trois études ont mesuré la demi-vie des particules virales en suspension dans des aérosols artificiels dans le cadre d'études expérimentales et confirmé la viabilité du virus dans des aérosols artificiels grâce à des essais sur plaque et à la culture cellulaire (19, 47, 48). Ces études ont révélé que les titres viraux du SRAS-CoV-2 sont demeurés stables dans des aérosols créés artificiellement jusqu'à des périodes de 2 à 16 heures (19, 47, 48). La stabilité et l'infectiosité du virus dans les aérosols artificiels semblent dépendre de facteurs environnementaux comme la température, l'humidité et les niveaux simulés de lumière du soleil, comme cela a été suggéré précédemment dans certaines analyses générées par ordinateur. Une étude expérimentale a démontré que la lumière du soleil simulée avait l'effet le plus important sur le taux de désintégration, que les températures élevées (seules les températures variant entre 10 °C et 40 °C ont été testées) avaient un effet modéré et une interaction significative avec la lumière du soleil, tandis que l'humidité relative avait le moins d'influence sur la désintégration globale et seulement à un niveau élevé (70 %) humidité relative (19).

Tableau 3 : Preuves expérimentales confirmant la viabilité du SRAS-CoV-2 dans les aérosols (n = 3)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Dabisch (2020) (19) Expériences de simulation États-Unis* Août 2020* *nouvelle*	Mesure de la viabilité et de la persistance du SRAS-CoV-2 dans des aérosols générés artificiellement dans une chambre à aérosol à tambour à différentes températures (10 °C, 20 °C, 30 °C et 40 °C), avec différents niveaux d'humidité relative (20 %, 45 % et 70 %) et différents niveaux d'ensoleillement simulés, soit irradiation UVB intégrée nulle (c'est-à-dire intérieur, nuit, obscurité), avec rayonnement UVB de 0,9 W/m^2 et rayonnement UVB intégré de 1,9 W/m^2 (c'est-à-dire la lumière du soleil le midi, en été). La concentration virale s'est maintenue à une valeur moyenne de 2,3 ± 0,4 $\log_{10}$ $DICT_{50}$ /L d'air pendant l'expérience. L'infectiosité du virus dans les aérosols a été mesurée à l'aide d'un essai de microtitrage et de cellules Vero. Les résultats de l'expérience ont permis d'obtenir un modèle de régression prévoyant la désintégration du SRAS-CoV-2 en aérosol dans des conditions variables.	Le temps nécessaire pour obtenir une réduction de 90 % du virus infectieux à 40 °C, avec une humidité relative de 20 % est passé de 4,8 minutes avec une lumière du soleil correspondant à celle du midi, un jour d'été clair à l'extérieur, à plus de 2 heures dans des conditions représentant l'intérieur ou la nuit. Pour d'autres niveaux de température et d'humidité, la décomposition par minute dans les simulations avec soleil du midi allait de 38,1 % ± 8,9 % par minute à 40 °C avec une humidité relative de 20 %, à 18,9 ± 4,8 % par minute à 10 °C avec une humidité relative de 20 %. Pour la lumière modérée du soleil correspondant à l'intensité que l'on voit au printemps et à l'automne à 40 °C, les taux de désintégration variaient de 18,0 ± 6,2 % par minute à 30 °C avec une humidité relative de 45 %, à 11,1 ± 4,6 % par minute à 10 °C avec une humidité relative de 20 %. En l'absence de lumière du soleil, un taux de désintégration (moyen) inférieur à 2 % par minute a été estimé, pour la plupart des niveaux de température et d'humidité testés. Il y a eu des exceptions dans les plages de température ou d'humidité plus élevées : - Le taux de désintégration à 30 °C avec une humidité relative de 70 % était de 6,3 ± 2,6 % par minute.

		- Le taux de désintégration à 40 °C avec une humidité relative de 20 % était de 3,9 ± 0,4 %. Dans l'analyse de régression, la lumière du soleil a eu la plus grande influence sur la désintégration, suivie de la température et de l'interaction entre la lumière du soleil et la température. L'humidité (relative ou absolue) a eu l'influence la plus faible sur la constante de désintégration. Ainsi, la lumière plus intense du soleil et les températures élevées supérieures à 30 °C ont entraîné un taux de désintégration plus rapide.
Fears (2020) (47) Expériences de simulation États-Unis Sep 2020*	La persistance à long terme des suspensions d'aérosols viraux de SRAS-CoV-2 générées artificiellement a été mesurée à différents intervalles de temps. Le contenu viral a été quantifié par la méthode RT-PCR, et l'infectiosité du virus a été mesurée par la méthode des plages de lyse. Les échantillons ont été évalués qualitativement par microscopie électronique.	Le SRAS-CoV-2 infectieux a été détecté à 10 minutes, 30 minutes, 2, 4 et 16 heures au cours de l'expérience de stabilité de la suspension d'aérosol. Une réduction minimale des copies du génome viral dans les échantillons d'aérosols (mesurée par la méthode RT-PCR) a été constatée pour les points de temps mesurés. Une fraction mineure, mais constante du SRAS-CoV-2 en aérosols a maintenu la capacité de réplication à tous les points de mesure, y compris à 16 heures. L'évaluation qualitative de l'intégrité des virions a révélé que les virions étaient de forme ovoïde ou sphérique, et qu'ils conservaient les morphologies prévues jusqu'à 16 heures en suspension dans les aérosols.
Van Doremalen (2020) (48)	Dans cette expérience, la stabilité et la décomposition des titres des virus SRAS-CoV-	Le virus SRAS-CoV-2 est resté viable dans des aérosols générés de manière expérimentale jusqu'à trois heures (durée de

Lettre à l'éditeur Expérience de simulation États-Unis* Printemps 2020*	2 et SRAS-CoV-1 ont été mesurées à partir d'aérosols générés artificiellement. L'analyse a utilisé un modèle de régression bayésienne.	l'expérience), avec une réduction du titre infectieux de $10^{3,5}$ à $10^{2,7}$ DICT50 par litre d'air. Dans les aérosols, la demi-vie du virus SRAS-CoV-2 a été estimée à 1,1-1,2 avec un intervalle de crédibilité de 95 % de 0,64-2,64.

*Estimation basée sur les affiliations des auteurs et la date de publication.
LTE = lettre à la rédaction

ARN DU SRAS-COV-2 DANS L'AIR EXPIRÉ

Six études ont examiné la présence de l'ARN viral du SRAS-CoV-2 dans des échantillons d'air expiré ou les échantillons de condensat d'air expiré provenant de cas humains (20, 50 à 53).

Deux techniques différentes d'échantillonnage de l'air expiré ont été cernées dans l'ensemble des études : certaines études ont permis de prélever des échantillons de condensat d'air expiré, tandis que d'autres ont recueilli des échantillons d'air expiré des personnes infectées. Les techniques de récupération de condensat expiré permettent de recueillir de 1 à 2 ml de condensat par le refroidissement et la condensation de l'air expiré pendant la respiration silencieuse. Certains chercheurs ont suggéré que la technique du condensat respiratoire expiré convenait mieux pour déterminer les biomarqueurs expulsés des voies respiratoires inférieures, et entraînerait une réduction des faux négatifs obtenus par RT-PCR (50, 54).

Cinq des études incluses ont rapporté au moins un échantillon d'air expiré positif pour l'ARN viral. Parmi les études qui ont confirmé la présence d'ARN viral dans certains échantillons expirés, quatre ont utilisé la technique du condensat d'air expiré, tandis que deux se fondaient sur un échantillonnage de l'air expiré. La positivité de l'échantillon variait entre 16 % et 93,5 % dans les études d'échantillonnage de condensats d'haleine expirés et jusqu'à 40 % dans l'étude d'échantillonnage unique d'air expiré avec des résultats positifs. Une étude n'a révélé aucun échantillon positif, tant pour les techniques de prélèvement de condensat d'air expiré que pour celles du prélèvement de l'air expiré (53). La variabilité de la positivité de l'ARN viral dans les échantillons d'air expiré peut être liée à l'évolution infectieuse des personnes échantillonnées. Toutefois, le manque d'information clinique sur les dates d'exposition et d'apparition des symptômes, les symptômes, ainsi que la charge virale et la réplication virale dans les tissus respiratoires, au moment du prélèvement des échantillons, limite les inférences entre l'exhalation virale et l'infection. Les données probantes indiquant que la charge virale maximale se produit entre un jour avant l'apparition des symptômes et jusqu'à cinq jours après celle-ci ou chez les personnes hospitalisées ou symptomatiques plusieurs jours après le début de l'infection peuvent ne pas être un échantillon approprié pour mesurer l'ARN viral dans l'air expiré (43, 55). Il se peut que les personnes hospitalisées ne

soient plus contagieuses au moment du prélèvement de l'échantillon, ce qui ne doit pas être interprété comme un manque de preuves à l'appui de l'émission d'infection par l'air expiré pendant la période d'infection précoce.

Tableau 4 : Études de biosurveillance portant sur la présence du virus SRAS-CoV-2 dans l'air expiré (n = 3)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Présence du SRAS-CoV-2 dans les échantillons		
Ryan (2020) (50) Étude de surveillance du condensat de l'air expiré Irlande Avril et mai 2020 *nouvelle*	Des échantillons de condensat d'air expiré ont été prélevés sur des patients atteints de la COVID-19 à l'aide de tubes pour condensat RTube. L'échantillon comprenait des écouvillons naso-pharyngés positifs (n = 16) et négatifs avec diagnostic clinique de patients atteints de la COVID (n = 15). D'autres échantillons prélevés avant le SRAS-CoV-2 ont été inclus comme témoins (n = 14). Le virus dans les échantillons a été détecté par RT-PCR et différents tests génétiques viraux. Remarque : Les diagnostics cliniques de COVID-19 étaient fondés sur l'expertise clinique et les résultats d'imagerie.	93,5 % (29 sur 31) des échantillons d'air expiré prélevés sur des patients atteints du SRAS-CoV-2 (résultats cliniques confirmés ou résultat positif obtenu par écouvillonnage du nasopharynx) étaient positifs parce que le test RT-PCR ciblait les quatre gènes (E, S, N, ORF1ab). Tous les échantillons témoins prélevés avant la pandémie étaient négatifs. Dans cette étude, il a été démontré que l'air expiré est un type d'échantillon sensible et non invasif. La positivité des échantillons variait selon la séquence cible du test RT-PCR chez des patients séronégatifs (n = 15) : - Positivité de 66 % (10 sur 15) pour l'enveloppe virale (E)/les tests de gènes des protéines de spicule (S) (utilisés pour l'écouvillonnage du nasopharynx). - Positivité de 73 % (11 sur 15) pour les tests sur gènes nucléocapsides viraux (N)/cadre de lecture ouvert (ORF1ab). Les résultats combinés correspondaient à 14 cas sur 15 ayant obtenu un résultat clinique positif après au moins un test.
Zhou (2021) (49) Étude de surveillance du condensat de l'air expiré	Les patients atteints de la COVID-19 (n = 10) qui étaient sur le point d'obtenir leur congé de l'hôpital (après un	22,2 % des 9 patients du COVID-19 sur le point d'obtenir leur congé de l'hôpital présentaient du SRAS-CoV-2 à une concentration d'environ 105 copies ARN/m^3

Chine Février et mars 2020 *nouvelle* Remarque : Les résultats supplémentaires sur la présence d'ARN viral dans les échantillons d'air sont résumés au tableau 5.	écouvillonnage négatif du nez et de la gorge) ont été recrutés dans plusieurs établissements hospitaliers. Un échantillon de condensat d'air expiré a été prélevé à l'aide d'un appareil BioScreen II. L'ARN du SRAS-CoV-2 dans les échantillons d'air expiré a été quantifié par RT-PCR.	dans l'échantillon d'air expiré obtenu. Les deux patients avaient plus de 70 ans. On a estimé que certains patients atteints de la COVID-19 inclus dans l'échantillon exhalaient le virus à un taux d'environ 1 400 copies d'ARN par minute au moment de leur congé.
Ma (2020) (51) *Préimpression* Étude de biosurveillance Chine Printemps 2020* Remarque : D'autres résultats sur l'ARN viral dans des échantillons d'air ambiant sont résumés dans le tableau 5.	Des échantillons de condensats d'air exhalé ont été prélevés chez des patients atteints de la COVID-19 (n = 30) à l'aide d'un dispositif de BioScreen.	L'étude confirme l'émission d'ARN du SRAS-CoV-2 dans l'air à partir du condensat de l'air exhalé par les personnes infectées (16,7 % n = 5/30). Les échantillons positifs ont été détectés soit <3 jours après l'apparition des symptômes (n = 3), soit dans les 7 à 14 jours suivant l'apparition des symptômes (n = 2). Les niveaux de SRAS-CoV-2 dans l'air expiré ont été estimés à 105-107 copies/m3 si l'on suppose un rythme respiratoire moyen de 12 l/min et qu'il est le plus élevé pendant les premiers stades de l'infection.
Di Carlo (2021) (20) Étude de surveillance de l'air expiré Italie Avril à juin 2020 Remarque : Les résultats supplémentaires sur la présence d'ARN viral	Évalue la quantité d'ARN du SRAS-CoV-2 émise dans l'air pendant la respiration normale – sans tousser, éternuer ou parler chez les personnes infectées (n = 5). Tous ces cas étaient des patients hospitalisés pour des symptômes non liés à la COVID qui ont ensuite	Le nombre de jours qui s'est écoulé entre l'apparition des symptômes et le prélèvement de l'échantillon variait de 7 à 56 dans l'échantillon de patients. Les écouvillons oropharyngés et naso-pharyngés de 4 patients étaient positifs au moment de l'échantillonnage. L'ARN viral a été détecté à 1 cm de la bouche de deux patients (40 % n = 2 sur 5). Les deux avaient des écouvillons oropharyngés, naso-

dans les échantillons d'air ambiant sont résumés au tableau 5. *nouvelle*	développé des symptômes de COVID pendant leur séjour à l'hôpital. Les personnes échantillonnées se trouvaient dans des chambres d'isolement des infections aéroportées et les échantillons d'air expiré ont été prélevés à l'aide d'un échantillonneur Sartorius AirPort. Des écouvillons oropharyngés, naso-pharyngés et salivaires ont également été prélevés avec les échantillons d'air expiré.	pharyngés et salivaires positifs. Les prélèvements de salive étaient négatifs chez les patients dont les échantillons d'air expiré étaient négatifs, même s'ils sont été déclarés infectés à partir d'échantillons positifs obtenus par la suite. Chez l'un de ces patients, le port d'un masque chirurgical a effectivement bloqué la détection de l'ARN viral à 1 cm (des échantillons obtenus lorsque la personne portait un masque n'ont pas été prélevés sur l'autre patient ayant obtenu des échantillons d'air expiré positifs). Les échantillons d'air prélevés à 1 cm chez des patients ayant obtenu des résultats négatifs au test RT-PCR ne contenaient pas d'ARN viral.
Feng (2020) (52) Étude de biosurveillance Chine Février-mars 2020 Remarque : D'autres résultats sur l'ARN viral dans des échantillons d'air ambiant sont résumés dans le tableau 5.	Échantillonnage de l'air expiré et de l'air ambiant de patients atteints de la COVID-19 à l'aide d'un échantillonneur de bioaérosols du NIOSH. Le condensat de l'air exhalé a été prélevé à l'aide d'un système de prélèvement stérile fabriqué en laboratoire. Les échantillons d'air ont été séparés par taille d'aérosols. Des échantillons ont été prélevés sur des patients atteints de la COVID-19 dans les derniers stades de l'infection en milieu hospitalier.	L'ARN du SRAS-CoV-2 n'a été détecté dans aucun des échantillons d'air expiré des patients (n = 0/9). L'ARN a été isolé dans le condensat de l'air exhalé (n = 2/8), et dans des échantillons d'air au chevet (n = 1/12). Les auteurs ont attribué la contamination minimale de l'ARN viral dans les échantillons de l'étude à la réduction de l'excrétion virale respiratoire chez les patients aux stades ultérieurs de l'infection.
Aucune présence de SRAS-CoV-2 dans les échantillons		

Ding (2020) (53) *Préimpression* Étude de biosurveillance Hong Kong Février 2020 Remarque : D'autres résultats sur l'ARN viral dans des échantillons d'air ambiant sont résumés dans le tableau 5.	Des échantillons de condensat exhalé (n = 2) et des échantillons d'air expiré (n = 2) ont été prélevés sur des patients atteints de la COVID-19 hébergés dans des chambres d'isolement des infections aérogènes. Plusieurs dispositifs ont été utilisés pour le prélèvement d'échantillons d'air (n = 27), qui a été effectué à des jours différents. Remarque : les distances de prélèvement des échantillons par rapport aux patients ne sont pas indiquées.	Tous les échantillons de condensat exhalé et les échantillons d'air expiré recueillis étaient négatifs pour l'ARN du SRAS-CoV-2.

*Estimation basée sur les affiliations des auteurs et la date de publication.

ARN DU SRAS-COV-2 DANS L'AIR AMBIANT

Quarante-neuf études de suivi biologique ont évalué des échantillons d'air prélevés dans des établissements de soins aux patients, comme les chambres d'isolement des infections aéroportées, les unités de soins intensifs, les salles d'urgence, les services hospitaliers, les maisons de soins infirmiers, les zones de diagnostic (p. ex., tomodensitométrie) et les cliniques externes, pour déterminer s'ils contenaient ou non des traces de SRAS-CoV-2 (tableau 5). Elles indiquent toutes la présence de cas confirmés à proximité du prélèvement des échantillons. La majorité des études (n = 29 sur 40) ont signalé l'isolement de l'ARN viral d'au moins un échantillon d'air prélevé par RT-PCR. Trois études ont réussi à mettre en culture des particules de virus isolées à partir d'un très petit nombre d'échantillons d'air positifs, ce qui a permis d'obtenir des preuves de la viabilité du virus dans l'air (56 à 58). Tous ces échantillons d'air contenant un virus viable ont été prélevés à proximité (moins de 2 mètres) de cas confirmés. De plus, des échantillons d'air prélevés à une distance variant entre 1 et 4,8 m de cas confirmés ont systématiquement identifié l'ARN du SRAS-COV-2, avec des concentrations plus élevées d'ARN viral lorsque l'appareil de collecte était placé plus près du cas (21, 56 à 61, 64, 65, 93).

Une seule étude dans un milieu de soins aux patients a démontré que l'ouverture des fenêtres dans la chambre du patient atteint de COVID-19 était bénéfique et avait réduit la concentration virale dans l'échantillon d'air de 10^5/ml à moins de 10^4 (61). Une autre étude a comparé des échantillons d'air

ambiant prélevés dans des chambres d'hôpital et chez des ménages en quarantaine où se trouvaient des cas actifs (24). On a estimé que les échantillons d'air ambiant provenant des ménages étaient environ huit fois (RC 8,75 [IC à 95 % 1,21 à 63,43; p = 0,058]) plus susceptibles d'être contaminés par de l'ARN viral que les échantillons d'air provenant des hôpitaux. Les chercheurs ont suggéré que la variabilité des échanges d'air et de la ventilation entre les milieux de soins aux patients et les milieux communautaires était la principale différence qui influençait la contamination de l'air entre les deux milieux. Il a été suggéré que la ventilation de la salle soit un facteur plus important que la gravité de la maladie en ce qui concerne la contamination de l'air ambiant.

Neuf études de suivi biologique de la présence du SRAS-CoV-2 dans des échantillons d'air provenant de milieux communautaires (c.-à-d. une voiture conduite par une personne infectée, un centre commercial, une salle de concert, des chambres d'hôtel utilisées pour la quarantaine et des ménages, un élevage de visons, des autobus publics et des métros) ont été identifiées (tableau 6). La majorité d'entre elles (n = 5 sur 9) ont utilisé un test RT-PCR pour confirmer la présence d'ARN viral alors qu'une étude a indiqué qu'une culture cellulaire à partir d'un virus isolé de COVID-19 a pu être effectuée à partir des échantillons d'air pris dans une voiture (23). L'étude portant sur la voiture met en évidence le fait que des quantités importantes de SRAS-CoV-2 viables peuvent être expulsées par des cas, même légers, sur de courtes périodes de temps (23). Une étude réalisée dans un élevage de visons dans laquelle l'éclosion continue a mis en évidence des niveaux élevés de virus dans l'élevage, ce qui représente un risque pour les travailleurs, mais si le risque à l'extérieur de l'élevage était faible pour la collectivité (66). L'identification d'échantillons d'air positifs prélevés dans des ménages en quarantaine et dans des chambres d'hôtel où se trouvaient des cas actifs était variable et exigera donc un examen plus approfondi, puisque certaines études ont relevé des échantillons positifs, tandis que d'autres ne l'ont pas fait (24, 67, 68). Deux études ayant prélevé des échantillons d'air ambiant dans des lieux publics, ce qui inclut une salle de concert, un centre commercial, des autobus publics et des métros, confirment également la présence d'ARN viral dans les échantillons d'air (61, 69). Fait intéressant, ces études ne confirment pas la présence de cas à proximité des échantillons d'air prélevés, mais indiquent des niveaux élevés de transmission communautaire dans les milieux échantillonnés (61, 69).

Diverses méthodes d'échantillonnage de l'air ont été utilisées dans le cadre des études de suivi biologique incluses. Certaines études ont utilisé différents modèles d'échantillonneurs d'air, tandis que d'autres ont utilisé des boîtes de Pétri remplies de liquide, des filtres en gélatine, des plaques d'Agar et de nouveaux pièges à COVID-19 pour échantillonner l'air ambiant. La variabilité des méthodes d'échantillonnage peut avoir contribué aux différences observées dans la détection de l'ARN viral, la confirmation de la viabilité du virus et de l'infectiosité dans les échantillons d'air ambiant. Seul un petit nombre d'études ont confirmé la viabilité du virus en culture cellulaire et tous les échantillons avaient été prélevés très près (moins de 2 mètres) des personnes infectées.

Les auteurs qui n'ont signalé aucune contamination virale dans les échantillons d'air prélevés dans les milieux de soins aux patients ont souvent suggéré une désinfection efficace, une ventilation d'air à haut rendement et des systèmes de filtration adaptés aux chambres d'isolement des infections aéroportées

comme raisons possibles des résultats négatifs. Cette justification est également appuyée par une étude de suivi biologique qui n'a pas permis de détecter d'ARN viral dans les échantillons prélevés lorsque l'entrée de l'échantillonneur d'air était recouverte d'un filtre HEPA (56).

Parmi les études identifiées, la concentration d'ARN viral dans les échantillons contaminés, la taille et les fractions des particules d'aérosol isolées, la distance d'échantillonnage des cas de COVID-19, le volume de l'échantillon d'air et toute tentative de culture de particules de virus isolées n'ont pas été déclarés de façon uniforme. De plus, la majorité des études n'ont pas fourni d'information clinique, comme des données sur l'apparition des symptômes ou la présence de symptômes respiratoires, sur les cas présents pendant le prélèvement d'échantillons d'air ni sur la ventilation et le débit d'air dans le milieu échantillonné. En raison de ces lacunes dans les données, il est difficile de déterminer les conditions dans lesquelles les virus infectieux présents dans les échantillons d'air ambiant deviennent plus fréquents.

Tableau 5 : Études de suivi biologique sur la présence du virus SRAS-CoV-2 dans l'air (n = 17) dans les milieux de soins aux patients (n = 40)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Présence du SRAS-CoV-2 dans les échantillons de culture cellulaire		
Lednicky (2020) (56) Étude de biosurveillance États-Unis* Novembre 2020*	Des échantillons d'air ont été prélevés dans les chambres d'hôpital des patients atteints de la COVID-19 en l'absence d'interventions générant des aérosols. Les échantillons d'air en trois exemplaires ont été prélevés à l'aide d'un échantillonneur d'air de VIVAS, à une distance de 2 à 4,8 mètres de la tête des patients. Les échantillons d'air ont été prélevés avec et sans filtre HEPA sur le tube d'entrée de l'échantillonneur d'air. Les génomes des virus isolés ont été séquencés.	La présence du virus dans des échantillons d'air isolés a été mesurée par la méthode RT-PCR, et l'infectiosité a été mesurée sur la base des effets cytopathologiques en culture cellulaire (LLC-MK2 et Vero-E6). Tous les échantillons d'air prélevés sans filtre HEPA étaient positifs pour l'ARN viral. Une seule séquence virale presque complète a été isolée à partir des échantillons d'air. Cette séquence génétique correspondait à la souche du virus isolé à partir d'un échantillon nasopharyngé d'un des deux patients qui occupaient la chambre lors du prélèvement. Au moment du prélèvement de l'échantillon d'air, le patient correspondant avait une infection aiguë.

Santarpia (2020) (57) *Préimpression* Étude de biosurveillance États-Unis Avril 2020	Les aérosols générés par les patients en milieu hospitalier ont été recueillis à l'aide d'un échantillonneur d'aérosols NIOSH BC251 au pied des lits de patients atteints de la COVID-19. La taille des aérosols et la concentration ont été mesurées lors de la collecte des échantillons à l'aide d'un spectromètre de particules aérodynamique. Les aérosols se distinguent par la proportion de tailles différentes (>4,1 µm, 1-4 µm, et <1 µm) parmi les échantillons.	De l'ARN a été détecté dans les six chambres de patients, et comprenait toutes les fractions de tailles de particules des aérosols (définies comme >4,1 µm, 1-4 µm, et <1 µm). La réplication du virus en culture cellulaire a été observée chez la plupart des d'échantillons d'aérosols <1 µm, deux des échantillons d'aérosols 1-4 µm et deux des échantillons >4,1µm. L'analyse par le transfert Western et la microscopie électronique à transmission de ces échantillons a montré la présence de protéines virales et de virions intacts.
Santarpia (2020) (58) Étude de biosurveillance États-Unis Mars 2020	Des échantillons d'air provenant de lieux d'isolement à pression négative et de salles abritant des cas de COVID-19 ont été prélevés à l'aide d'un échantillonneur AirPort MD8 de Sartorius et testés par la méthode RT-PCR pour détecter l'ARN viral du SRAS-CoV-2. Un sous-ensemble d'échantillons positifs a été examiné pour la propagation du virus dans les cellules Vero E6. Plusieurs indicateurs ont été utilisés pour déterminer la réplication virale, notamment l'effet cytopathologique, la détection par immunofluorescence, le surnageant de culture de cellules par PCR quantitative et la microscopie électronique.	63,2 % des échantillons d'air ambiant étaient positifs par la méthode RT-PCR (concentration moyenne de 2,42 copies/L d'air). Deux échantillons placés à proximité d'un patient, dont un à moins de 2 mètres du patient, étaient positifs. La concentration virale était plus élevée dans l'échantillon d'air prélevé plus près du patient (4,07 par rapport à 2,48 copies/L d'air). 58,3 % des échantillons d'air prélevés dans les couloirs étaient positifs (concentration moyenne de 2,51 copies/L d'air). Dans un seul échantillon positif provenant d'un couloir, on a constaté une certaine présence de réplication virale.
ARN du SRAS-CoV-2 dans les échantillons		

Munoz-Price (2021) (24) Étude de suivi biologique États-Unis Printemps 2021* *nouvelle* Remarque : Les résultats supplémentaires sur la présence de l'ARN viral dans l'air ambiant dans les maisons des ménages sont résumés au tableau 6.	Échantillons d'air (n = 16) prélevés dans les chambres des patients hospitalisés aux soins intensifs occupées par des cas confirmés de COVID-19. Des échantillons d'air ont été prélevés à l'aide de l'échantillonneur d'air Sartorius MD8, placé entre 0,3 et 1,8 mètre de la tête des patients. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	12,5 % (n = 2 sur 16) des échantillons d'air prélevés à l'hôpital n'étaient positifs que pour l'ARN viral. Ces échantillons ont été prélevés à 0,3 m des cas confirmés. Les patients présentaient une forme légère de la maladie et ne prenaient pas d'oxygène d'appoint au moment du prélèvement de l'échantillon.
Razzini (2020) (70) Étude de suivi biologique Italie Avril 2020* *nouvelle*	Échantillons d'air (n=5) prélevés avec un échantillonneur d'air portatif MD8 Airport avec filtres en gélatine à membrane dans des zones de l'hôpital où l'on retrouvait des cas de COVID-19. Les échantillons ont été prélevés dans trois zones contaminées (corridor pour les patients et soins intensifs), semi-contaminées (salle de déshabillage) et propres (vestiaires et vestiaires du personnel médical). L'ARN viral dans les échantillons a été mesuré par RT-PCR.	Tous les échantillons d'air prélevés dans l'unité des soins intensifs et le couloir où l'on trouvait des cas de COVID-19 étaient positifs pour l'ARN viral alors que les autres étaient négatifs. La concentration virale (Ct médian) dans les échantillons d'air prélevés dans l'unité des soins intensifs était de 22,6 alors qu'elle était de 31,1 pour les échantillons d'air prélevés dans le corridor.
Ge (2020) (71) Étude de suivi biologique Chine Juin 2020* *nouvelle*	Des échantillons d'air (n = 33) ont été prélevés à l'aide de l'échantillonneur pour bioaérosols BC251 du NIOSH. Les milieux qui ont été échantillonnés comprenaient l'USI, les cliniques d'hémodialyse, les cliniques pour	Tous les échantillons d'air (n = 3) provenant de l'USI étaient positifs pour l'ARN viral. Les concentrations virales dans les échantillons avaient un Ct variant entre 36,5 et 37,8.

	la fièvre et les salles du service respiratoire. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	
Hu (2020) (72) Étude de suivi biologique Février et mars 2020 Chine *nouvelle*	Des échantillons d'air (aérosols) ont été prélevés dans plusieurs hôpitaux à l'aide d'un échantillonneur centrifugeur aérosol-hydrosol (n = 123). L'ARN viral présent dans les échantillons a été mesuré par RT-PCR et sa viabilité par culture cellulaire Vero E6.	Huit échantillons d'air (21 %) provenant de l'unité des soins intensifs et un échantillon identique provenant de la salle de tomodensitométrie (16 %) étaient positifs pour l'ARN viral. La plage de concentrations du virus dans les échantillons d'air positif (aérosols) variait entre 1,11 x 10^3 et 1,12 x 10^4 copies d'ARN m^{-3}. Le virus n'a pas pu être cultivé à partir des échantillons positifs.
Seyyed (2020) (73) Étude de suivi biologique Iran Mai 2020* *nouvelle*	Des échantillons d'air (n=10) ont été prélevés dans le service des soins intensifs où se trouvaient des patients atteints de la COVID-19 à l'aide d'une pompe d'échantillonnage munie d'une tige agitatrice poreuse. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	60 % des échantillons d'air étaient positifs pour l'ARN viral. Les concentrations d'ARN les plus élevées ont été mesurées dans des échantillons prélevés entre des lits des patients (3 913 copies par ml). Il s'agissait d'échantillons d'air prélevés entre 1,5 et 2 mètres des lits des patients.
Moore (2020) (59) Étude de suivi biologique Angleterre Mars à mai 2020 *nouvelle*	Des échantillons d'air (n = 55) ont été prélevés dans huit hôpitaux différents chez des patients atteints de la COVID-19 qui avaient, ou non, des symptômes respiratoires. Les milieux échantillonnés comprenaient les chambres d'isolement des infections aéroportées, les salles générales où se trouvaient des patients atteints de la COVID-19 général et les autres salles. Les échantillons ont été collectés à l'aide d'un échantillonneur d'air µ	7 % (n = 4) des échantillons d'air étaient positifs pour l'ARN viral, bien qu'à de faibles concentrations variant entre < 10 et 460 copies génomiques/m^3 d'air. Le virus n'a pas pu être cultivé à partir des échantillons positifs. Tous les échantillons positifs ont été prélevés à 1 mètre de distance des patients, et le nombre de jours écoulés depuis l'apparition des symptômes chez les patients variait de 8 à 10 jours.

	Coriolis ou d'un échantillonneur d'air Sartorius MD8. L'ARN viral présent dans les échantillons a été mesuré par RT-PCR et sa viabilité par culture cellulaire Vero E6.	
Hernández López (2021) (60) Étude de suivi biologique Janvier 2021* Mexique *nouvelle*	Des échantillons d'air (n = 15) provenant des salles d'urgence, des salles de médecine interne, des chambres dans lesquelles se trouvaient des patients atteints de la COVID-19 et des salles avec plusieurs lits dans deux hôpitaux ont été prélevés à l'aide d'un échantillonneur Millipore. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	Trois échantillons d'air (20 %) étaient positifs pour l'ARN viral. Tous les échantillons positifs provenaient des chambres des patients atteints de la COVID-19 et avaient été prélevés près des patients.
Tan (2020) (74) Étude de suivi biologique Chine Mars 2020 *nouvelle*	Des échantillons d'air (n = 12) ont été prélevés dans les unités de soins intensifs et les salles d'isolement pour les patients atteints de la COVID-19 et dans les corridors. Des échantillons d'air ont été prélevés à 1 mètre de la tête d'un patient.	Un seul échantillon d'air prélevé dans une zone de soins au patient lors d'une intubation était positif pour l'ARN viral.
Gehrke (2021) (61) *Préimpression* Étude de suivi biologique Allemagne Octobre 2020 à janvier 2021 *nouvelle*	Des échantillons d'air ont été prélevés dans des chambres de patients dans deux unités d'isolement pour les patients atteints de la COVID-19 et dans une salle d'endoscopie ambulatoire utilisant des pièges à froid non alimentés. L'ARN viral a été quantifié par RT-PCR.	Échantillons prélevés en milieu hospitalier : Aucun ARN viral n'a été isolé dans la première unité d'isolation ventilée en permanence par deux fenêtres. L'ARN viral a été détecté dans des échantillons prélevés dans un couloir non identifié à proximité de la salle d'isolement. Dans les échantillons prélevés dans la deuxième unité d'isolement, les concentrations d'ARN du SRAS-CoV-2 ont atteint 10^5/ml dans les pièces non ventilées, mais lorsque les fenêtres

Remarque : Les résultats supplémentaires sur la présence d'ARN viral dans les échantillons d'air en milieu communautaire sont résumés au tableau 6.		étaient ouvertes pour augmenter la ventilation, les concentrations d'ARN du SRAS-CoV-2 dans les échantillons sont passées à 10^4/ml ou moins. Dans la salle d'endoscopie, 50 % des pièges à froid étaient positifs pour l'ARN viral (n = 6 sur 12). 57 % des pièges à froid (n = 4 sur 7) dans les salles d'endoscopie étaient positifs pour le SRAS-CoV-2, mais les concentrations d'ARN (initialement à 12 copies/ml) et le nombre d'échantillons positifs ont été réduits lorsque les niveaux de ventilation dans la salle ont été augmentés.
Zhou (2021) (80) Étude de suivi biologique Chine Février et mars 2020 *nouvelle* Remarque : Les résultats supplémentaires sur l'ARN viral dans les échantillons d'air expiré sont résumés au tableau 4.	Des échantillons d'air (et des échantillons d'air expiré) provenant de patients hospitalisés atteints de la COVID-19 ont été prélevés dans plusieurs établissements hospitaliers. Des échantillons d'air ont été prélevés dans les couloirs d'hôpitaux, les salles d'entreposage des déchets, les salles des soins intensifs, les toilettes, les salles de préparation des médicaments, les salles d'observation clinique et les salles générales. Des échantillons d'air ont été prélevés à l'aide du système Air-nCoV-Watch (ACW) et l'ARN viral a été quantifié par RT-PCR.	6,8 % des échantillons d'air (n = 3 sur 44) étaient positifs pour l'ARN viral à des concentrations numériques variant de 9 à 219 virus/m^3.
Yarahmadi (2021) (64) Étude de suivi biologique Iran Février 2021*	Des échantillons d'air ont été prélevés (n = 20) dans une unité de soins intensifs, précisément dans une zone de respiration d'un patient atteint de COVID-19 (c.-à-	50 % (n = 2 sur 4) des échantillons prélevés dans la zone respiratoire du patient étaient positifs pour l'ARN viral. Les échantillons positifs provenaient

nouvelle	d. une table installée à côté de la tête du patient), dans une zone générale (à 10 mètres de l'unité des soins intensifs) et dans une zone de respiration du personnel soignant près du lit du patient atteint de COVID-19, ainsi qu'à 1 mètre du lit du patient. Les échantillons ont été prélevés à l'aide d'échantillonneurs d'aérosols biologiques du NIOSH et de l'ASHRAE. L'ARN viral a été détecté par RT-PCR.	d'un cas confirmé et les échantillons négatifs d'un cas soupçonné. 12,5 % (n = 1 sur 8) des échantillons prélevés dans la zone respiratoire du personnel soignant étaient positifs pour l'ARN viral. 12,5 % (n = 1 sur 8) des échantillons prélevés dans la région générale étaient positifs pour l'ARN viral. Les auteurs suggèrent que des bioaérosols pourraient être présents en raison de la nouvelle aérosolisation des particules de SRAS-CoV-2 en suspension dans l'air provenant du personnel de soins de santé qui se promène entre différents services et différents postes des soins intensifs.
Ong (2021) (93) Étude de biosurveillance Singapour Jan 2021*	Des échantillons d'air ont été prélevés dans une chambre d'isolement des infections aéroportées d'un hôpital et d'une installation d'isolement communautaire (à ventilation naturelle) hébergeant des patients ayant reçu un diagnostic positif de COVID-19, à 1 mètre de distance du patient. Les échantillons d'air ont été prélevés à l'aide d'un échantillonneur de bioaérosols BioSpot-VIVAS BSS300-P (prélevant des particules d'une taille <4,34 µm). Les échantillonneurs d'aérosols du NIOSH ont été utilisés pour valider les résultats du Biospot. L'ARN du SRAS-CoV-2 a été détecté par RT-PCR, et cultivé à	50 % des échantillons d'air BioSpot de la chambre d'isolement des infections aéroportées de l'hôpital (n=6/12) étaient positifs pour l'ARN du SRAS-CoV-2 (concentrations allant de 178,9 à 2 738,4 copies/m^3). Les échantillons positifs ont été prélevés dans les chambres où se trouvait au moins un patient symptomatique (<7 jours après l'apparition des symptômes). Les échantillonneurs d'aérosols du NIOSH ont détecté l'ARN du SRAS-CoV-2 dans les aérosols de <1 µm, 1-4 µm et >4 µm de diamètre. Seul 1 des 9 échantillons provenant de l'installation d'isolement communautaire était positif pour l'ARN du SRAS-CoV-2, avec une concentration de 978,3 copies/m3. Les cultures virales de tous les échantillons positifs étaient négatives.

	l'aide de la culture cellulaire Vero C1008.	
Dumont-Leblond (2020) (21) Étude de suivi biologique Canada Mars à juin 2020 *nouvelle*	Échantillons d'air prélevés dans les chambres d'isolement des infections aéroportées d'un hôpital du Québec où se trouvaient des patients non atteints de la COVID-19 (n = 22). Des échantillons d'air ont été prélevés (avec des filtres en gélatine de 3 µm et des filtres en polycarbonate de 0,8 µm) à l'aide d'un échantillonneur sec SASS 3100 installé à 1,5 m du chevet du patient. La contamination virale a été mesurée par RT-PCR et par la culture cellulaire Vero E6.	11 % (n = 11 sur 100) des échantillons d'air prélevés au chevet de 6 patients étaient positifs pour l'ARN viral. Ces patients présentaient de la fièvre, de la dyspnée et une toux plus élevée que les autres patients de l'échantillon. La plupart étaient de sexe masculin et ont été hospitalisés un peu plus longtemps. La charge virale moyenne du SRAS-CoV-2 dans les échantillons positifs prélevés dans les salles a été estimée à 4,86E +4 génomes viraux par heure. Aucun virus isolé dans les échantillons d'air n'a pu être cultivé.
Binder (2020) (75) Étude de suivi biologique États-Unis Avril et mai 2020 *nouvelle*	Des échantillons d'air ambiant et d'aérosols ont été prélevés dans les chambres d'hôpital de patients individuels où se trouvaient des patients atteints de la COVID-19 (n = 20, 16 symptomatiques et 4 asymptomatiques) dans un service réservé aux patients atteints de la COVID-19. Les bioaérosols ont été prélevés à l'aide d'un échantillonneur NIOSH BC 251 placé à différentes distances de la tête des patients (1, 1,4, 2,2 et 3,2 mètres). Les chambres d'hôpital vides, les couloirs, la salle de repos du personnel et les postes de travail du personnel ont été échantillonnés comme zones témoins. La contamination virale par le SRAS-CoV-2 a été mesurée	Trois échantillons prélevés dans trois des chambres de patients atteints de la COVID-19 étaient positifs pour l'ARN viral. Les échantillons avaient été prélevés à une distance variant entre 1,4 et 2,2 mètres des patients. Il s'était écoulé de 4 à 10 jours depuis l'apparition des symptômes (nez qui coule, maux de tête, fièvre, toux, difficulté à respirer, fatigue, perte d'odorat, symptômes gastro-intestinaux). Aucun virus viable n'a pu être identifié dans les échantillons de bioaérosols par culture cellulaire. Les échantillons prélevés dans d'autres régions étaient négatifs pour l'ARN du SRAS-CoV-2.

	par RT-PCR et par la culture cellulaire Vero EC6.	
Passos (2021) (76) Étude de suivi biologique De mai à août 2020 *nouvelle*	Des échantillons d'air ont été prélevés dans deux hôpitaux différents (n = 52) à l'aide de méthodes d'échantillonnage actif et passif des aérosols. L'échantillonnage actif a utilisé plusieurs modèles d'échantillonneurs d'air portatifs (AIRIDEAL 3P, MD-8 AirPort, HANDI-VOL) et types de filtres (filtres en cellulose, en PTFE ou en microfibre de quartz). La méthode passive a utilisé des boîtes de Pétri pour recueillir des particules sédimentaires. On trouvait, dans les deux hôpitaux, des patients atteints de la COVID-19 dans des services de soins intensifs spécialisés au moment du prélèvement de l'échantillon. Des échantillons d'aérosols ont également été prélevés dans plusieurs espaces publics extérieurs à l'aide d'échantillonneurs d'air à grand débit (AGV, Energética). L'ARN du SRAS-CoV-2 dans les échantillons a été détecté par RT-PCR.	Des échantillons d'air provenant de quatre zones d'échantillonnage dans un hôpital (dont les soins intensifs étaient occupés à 100 % au moment de l'échantillonnage) étaient positifs pour l'ARN viral dans les particules en suspension (taille des pores du filtre > 0,2 µm et > 0,3 µm), ainsi que dans 11 % des particules sédimentables (n = 4 sur 36). Des échantillons positifs de particules d'air en suspension ont été détectés dans la salle des soins intensifs réservée aux patients atteints de la COVID-19 (concentration de 0,33 unité génomique m^{-3} à une distance supérieure à 2 par rapport au patient), dans une salle de retrait des vêtements de protection (0,14 unité génomique m^{-3}), une salle de rangement pour les toilettes mobiles destinées aux patients et pour le linge souillé des patients (0,19 unité génomique m^{-3}). La salle de rangement profitait d'une ventilation naturelle. Des particules sédimentables positives à l'ARN du SRAS-CoV-2 ont été détectées dans des échantillons prélevés dans un couloir extérieur adjacent à l'unité des soins intensifs réservée aux patients atteints de la COVID-19. Tous les échantillons d'air extérieur et les échantillons prélevés dans l'autre hôpital (c.-à-d. L'hôpital 1) (taux d'occupation de 33 % au moment de

		l'échantillonnage) étaient négatifs pour l'ARN du SRAS-CoV-2.
Lane (2021) (65) Étude de suivi biologique Janvier 2021* *nouvelle*	Des échantillons d'air ont été prélevés dans plusieurs unités de l'hôpital, dans les chambres d'isolement des infections aéroportées, dans les postes de soins infirmiers des soins intensifs, dans les couloirs pour les familles et les visiteurs à l'extérieur de l'unité des soins intensifs, dans l'unité de médecin et dans les couloirs près des chambres des patients. Des échantillonneurs cycloniques NIOSH 251 à 2 étapes ont été utilisés pour prélever des échantillons d'air (limite de détection de 8 copies virales/m^3 d'air). Deux chambres de patients atteints de la COVID-19 ont été utilisées comme échantillons témoins positifs. L'ARN viral a été détecté par RT-PCR.	Les deux échantillons témoins positifs prélevés dans les deux chambres des patients dont la COVID-19 a été confirmée étaient positifs pour l'ARN viral. Aucun des échantillons d'air (n = 528) provenant d'une autre zone d'échantillonnage n'était positif pour l'ARN du SRAS-CoV-2.
Liu (2020) (77) Étude de biosurveillance Chine Février-mars 2020	Concentration d'ARN du SRAS-CoV-2 et distribution de la taille des aérosols dans les échantillons d'air (n = 30) provenant de plusieurs sites à l'intérieur ou à proximité d'un hôpital et d'un hôpital de campagne. Tous les échantillons d'aérosols (n = 30) ont été prélevés sur des filtres en gélatine préstérilisés (Sartorius). Trois échantillons d'aérosols de tailles différentes ont été prélevés à l'aide d'un impacteur en cascade miniature	La contamination par le SRAS-CoV-2 dans les échantillons d'air des soins aux patients était faible à indétectable. Dans le cas de l'hôpital de campagne, le plus grand ARN en suspension du SRAS-CoV-2 en aérosols a été identifié dans une salle de toilette temporaire (1 m^2) avec une faible ventilation, probablement due à la respiration du patient ou à l'aérosolisation du virus à partir des excréments et de l'urine des patients infectés.

	(tous les échantillons ont été prélevés dans les zones du personnel). L'ARN viral a été détecté par la méthode RT-PCR.	Les échantillons prélevés dans les chambres personnelles des employés de l'hôpital de campagne ont montré les plus grandes concentrations de virus. Des aérosols de 0,25 à > 2,5 µm ont été identifiés. Les auteurs émettent l'hypothèse que cela provient des surfaces des EPI et des vêtements des travailleurs de la santé. Des concentrations d'ARN viral faibles, mais détectables ont été trouvées à l'entrée d'un grand magasin et sur un site extérieur près de l'hôpital, ce qui suggère que cela pourrait être dû à un flux de circulation élevé et à la foule. Remarque : Les concentrations spécifiques du SRAS-CoV-2 dans l'air dans chaque échantillon d'aérosol par site sont fournies dans la publication.
Chia (2020) (78) Étude de biosurveillance Singapour Printemps 2020*	Détection de la contamination de l'air par le SRAS-CoV-2 dans les chambres d'isolement des infections aérogènes accueillant des patients atteints de la COVID-19, en milieu hospitalier. Des échantillons d'air ont été prélevés et la taille des aérosols a été mesurée par les échantillonneurs de bioaérosols NIOSH BC 251. L'ARN viral a été détecté au moyen d'une épreuve PCR.	66 % (n = 2/3) des échantillons d'air prélevés dans les environnements des chambres d'isolement des infections aéroportées étaient positifs pour l'ARN du SRAS-CoV-2. La plus petite fraction de taille aérodynamique qui contenait des niveaux détectables d'ARN du SRAS-CoV-2 était de 1 à 4 µm. Les concentrations totales du SRAS-CoV-2 dans l'air variaient entre $1,84 \times 10^3$ à $3,38 \times 10^3$ copies d'ARN par m^3 d'air échantillonné. Les auteurs suggèrent que la présence du SRAS-CoV-2 dans les échantillons d'air est probablement la plus élevée pendant la première semaine de la maladie, lorsque la charge virale respiratoire est élevée.

Jin (2021) (79) Étude de suivi biologique Chine Février et mars 2020 *nouvelle*	Des échantillons d'air ont été prélevés dans une unité de soins intensifs où se trouvait un seul patient ayant eu la COVID-19 et prêt à recevoir son congé, deux jours après que ce patient eut obtenu un résultat négatif au test de dépistage du SRAS-CoV-2. Des échantillons d'air ont été prélevés dans la chambre d'isolement et dans le vestiaire pour EPI du personnel. Des échantillons d'air à grand volume ont été prélevés à l'aide d'un échantillonneur d'aérosols portatif WA 400. L'ARN viral dans les échantillons a été détecté par RT-PCR.	Un seul échantillon d'air provenant de la chambre d'isolement dans l'unité des soins intensifs était positif (1 sur 7, 14,29 %) pour l'ARN viral. Les auteurs indiquent que leurs résultats laissent entendre que le virus peut être transmis par aérosol pendant des jours, même après qu'un patient ait obtenu un test négatif.
Zhou (2020) (81) Étude de biosurveillance Royaume-Uni Avril 2020	Trois à cinq échantillons d'air ont été prélevés dans plusieurs milieux hospitaliers à l'aide d'un échantillonneur d'air de Coriolis, la présence d'ARN du SRAS-CoV-2 a été quantifiée par la méthode RT-PCR, puis des cultures de cellules Vero E6 et Caco-2 ont été utilisées pour cultiver le virus.	38,7 % (n = 14/31) des échantillons d'air prélevés étaient positifs pour l'ARN viral, mais le SRAS-CoV-2 n'a pas pu être mis en culture en raison de la faible charge virale récupérée. La probabilité de contamination dans les zones publiques était plus faible que dans les zones immédiatement occupées par un patient atteint de la COVID-19 (OR 0,5 IC de 95 % 0,2-0,9).
Orenes-Piñero (2020) (81) Étude de biosurveillance Espagne Printemps 2020*	Les chercheurs mettent au point et appliquent des pièges à COVID-19 pour mesurer la capacité de transmission du SRAS-CoV-2 par les aérosols dans les établissements de soins hospitaliers. Des pièges à COVID-19 ont été placés à un mètre des patients dans les unités de soins intensifs et les chambres	Dans l'unité de soins intensifs, aucun des pièges à COVID-19 n'était positif; tous les patients atteints de la COVID-19 étaient intubés. Dans les chambres communes, deux pièges à COVID-19 étaient positifs pour le SRAS-CoV-2, tous deux se trouvaient à proximité d'un patient nécessitant une assistance respiratoire. Les auteurs concluent que c'est sans équivoque le résultat de la transmission du virus dans l'air.

	communes. L'ARN viral a été détecté par la méthode RT-PCR.	
Feng (2020) (52) Étude de biosurveillance Chine Février-mars 2020 Remarque : D'autres résultats sur l'ARN viral dans des échantillons d'air expiré sont résumés dans le tableau 4.	L'air ambiant des chambres des patients atteints de la COVID-19 en convalescence dans les unités d'isolement des hôpitaux et aux soins intensifs a été échantillonné à l'aide d'un échantillonneur du NIOSH. Des échantillons d'air (n = 12) ont été prélevés et la taille des aérosols a été mesurée. Les échantillonneurs ont également été placés sur un trépied de 1,2 m de hauteur et à 0,2 m du lit, du côté de la tête du patient, pendant 30 minutes.	L'ARN du SRAS-CoV-2 a été détecté dans un seul échantillon d'air provenant de patients atteints du SRAS-CoV-2. La concentration maximale d'ARN viral détectée dans l'échantillon d'air positif par taille de particules était de 1 112 copies/m^3 (<1 µm) et 745 copies/m^3 (>4 µm). Les auteurs ont attribué la contamination minimale de l'ARN viral dans les échantillons de l'étude à la réduction de l'excrétion virale respiratoire chez les patients aux stades ultérieurs de l'infection.
Ding (2020) (53) *Préimpression* Étude de biosurveillance Hong Kong Février 2020 Remarque : D'autres résultats sur l'ARN viral dans des échantillons d'air expiré sont résumés dans le tableau 4.	Des échantillons d'air (n = 46) ont été prélevés dans les chambres d'isolement des infections aérogènes accueillant des patients atteints de la COVID-19, dans les postes de soins infirmiers, dans les couloirs et dans les unités de climatisation d'un hôpital traitant des cas de COVID-19. Plusieurs échantillonneurs d'air ont été utilisés pour le prélèvement des échantillons, qui a été effectué à des jours différents, et l'ARN a été détecté par la méthode RT-PCR.	Un seul échantillon d'air (n = 1/46) provenant du couloir à l'extérieur d'une salle d'entreposage avec une poubelle pour les déchets médicaux avait un résultat positif faible pour l'ARN du SRAS-CoV-2. Tous les autres échantillons d'air testés dans les chambres des patients, les toilettes et les entrées d'air étaient négatifs. Les copies d'ARN pour l'échantillon faiblement positif n'ont pas été quantifiées.
Guo (2020) (82) Étude de biosurveillance Chine Février-mars 2020	Des échantillons d'air ont été prélevés dans l'unité de soins intensifs d'un hôpital (n = 40) et dans les unités de soins généraux hébergeant des patients atteints de la COVID-19 (n = 6), à différentes distances des patients	Des particules du SRAS-CoV-2 ont été identifiées dans 35 % des échantillons d'air des unités de soins intensifs, 12,5 % des échantillons d'air des unités de soins généraux et 12,5 % des échantillons d'air du bureau du médecin. Aucun virus du SRAS-CoV-2

	et du bureau du médecin (n = 8). Des échantillons d'air ont été prélevés à l'aide d'un échantillonneur avec cyclone humide SASS 2300.	n'a été identifié dans les échantillons d'air du couloir des patients. Sur la base du ou des sites de prélèvement d'échantillons d'air positifs, les auteurs concluent que les aérosols chargés de virus se concentrent à proximité et en aval des patients, et que la distance maximale de transmission des aérosols chargés de virus est de 4 mètres.
Nissen (2020) (83) Étude de biosurveillance Suède Printemps 2020*	Des boîtes de Pétri ouvertes contenant du liquide ont été placées à l'entrée d'air des salles de soins et près des filtres d'évacuation du système de ventilation d'un hôpital pendant 24 heures afin de recueillir des virus viables. L'infectivité a été évaluée à l'aide de la culture cellulaire Vero E6.	L'ARN du SRAS-CoV-2 a été détecté dans des échantillons de fluides placés dans le système de ventilation, et dans 33 % des échantillons (n = 1/3) placés près des entrées d'air des salles. La viabilité du virus isolé n'a pas pu être établie par culture cellulaire.
Zhang (2020) (84) *Préimpression* Étude de biosurveillance Chine Mars-avril 2020	L'étude a consisté à échantillonner les aérosols de l'environnement extérieur (n = 16) dans trois hôpitaux recevant des patients atteints de la COVID-19. Les échantillons d'aérosols ont été prélevés à l'aide d'échantillonneurs de bioaérosols. L'ARN viral a été quantifié par la méthode RT-PCR. Remarque : Il n'a pas été signalé que l'infectiosité du virus récupéré a été mesurée.	Le SRAS-CoV-2 a été identifié dans les aérosols échantillonnés à des concentrations de 285-1 130 copies/m^3, similaires aux niveaux de contamination observés dans les unités de soins intensifs. L'ARN viral a été identifié jusqu'à 5 mètres de distance des bâtiments de soins ambulatoires, ainsi que dans les zones de traitement des eaux usées des hôpitaux.
Aucun ARN du SRAS-CoV-2 dans les échantillons		

Dumont-Leblond (2021) (22) Étude de suivi biologique Canada Printemps 2020 *nouvelle*	Des échantillons d'air et des échantillons provenant de surfaces sans contact ont été prélevés dans 31 chambres de plusieurs établissements de soins de longue durée (n = 7) au Québec. Les échantillons d'air ont été prélevés 8 à 30 jours après l'apparition des symptômes des résidents à l'aide d'un échantillonneur IOM Multidust attaché à une pompe portable Gillian Air 5, placée à environ 2 mètres des résidents positifs au SRAS-CoV-2. Les salles échantillonnées ne comportaient aucune mesure importante d'atténuation des aérosols. L'ARN SRAS-CoV-2 a été quantifié par RT-PCR et une culture avec cellules Vero E6 a été effectuée. Remarque : la distance entre les surfaces et les patients atteints du SRAS-CoV-2 n'a pas été fournie.	Tous les échantillons d'air (n = 31) étaient négatifs, mais de l'ARN viral a pu être récupéré sur 32 % (n = 20 sur 62) des échantillons de surface sans contact, soit les cadres de porte et étagères dans les chambres (concentrations variant entre 13 et 36 612 génomes/surface). Les auteurs ont suggéré que la charge virale récupérée sur les surfaces sans contact direct était un indice de la propagation des virus dans l'air. Le virus n'a pas pu être cultivé à partir des échantillons positifs.
Song (2020) (85) Étude de suivi biologique Chine Février 2020 *nouvelle*	Des échantillons d'air ont été prélevés dans des chambres d'isolement des infections aéroportées où se trouvaient des patients atteints de la COVID-19. Des échantillons d'air ont été prélevés à l'aide du système d'échantillonnage automatique Derenda PNS 16T-3.1, à environ 1 mètre des lits des patients. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	Tous les échantillons étaient négatifs pour l'ARN du SRAS-CoV-2.
Faridi (2020) (86)	Des échantillons d'air (n = 10) ont été prélevés dans des salles où se	Tous les échantillons étaient négatifs pour l'ARN du SRAS-CoV-2.

Étude de suivi biologique Iran Mars 2020 *nouvelle*	trouvaient des patients atteints de la COVID-19 présentant des symptômes aigus et critiques. Des échantillons d'air ont été prélevés dans les mini-impacteurs standards stériles à l'aide d'une pompe à vide. Les échantillonneurs d'air étaient placés de 1,5 à 1,8 m au-dessus du plancher et à environ 2 à 5 m des lits des patients. Certains patients ont toussé pendant le prélèvement de l'échantillon. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	
Declementi (2020) (87) Étude de suivi biologique Italie Septembre 2020* *nouvelle*	Des échantillons d'air (n = 8) ont été prélevés dans une unité de soins non intensifs pour des patients atteints de la COVID-19, après la mise en place de processus de nettoyage et de désinfection. L'ARN viral dans les échantillons a été mesuré par RT-PCR. Remarque : Ni le modèle de l'échantillonneur, ni la présence ou l'absence de cas de COVID-19 pendant l'échantillonnage ni la distance avec les cas au moment de l'échantillonnage ne sont indiqués.	Tous les échantillons étaient négatifs pour l'ARN du SRAS-CoV-2.
Anh (2020) (88) Étude de suivi biologique Corée Mars 2020 *nouvelle*	Des échantillons d'air ont été prélevés dans les chambre d'isolement où se trouvaient des patients atteints d'une forme grave de la COVID-19 qui ont dû avoir recours à une ventilation mécanique ou à une	Tous les échantillons étaient négatifs pour l'ARN du SRAS-CoV-2.

	oxygénothérapie à haut débit. Les échantillons ont été prélevés à l'aide d'un BioSampler SKC et d'un échantillonneur pour écouvillon. L'ARN viral a été mesuré par RT-PCR.	
Masoumbeigi (2020) (89) Étude de suivi biologique Iran Septembre 2020* *nouvelle*	Un échantillonnage d'air (n = 31) a été effectué dans un hôpital où se trouvaient des patients atteints de la COVID-19; tous les patients avaient une forme grave avec toux et éternuements. Des échantillons d'air ont été prélevés dans les salles d'urgence, l'unité des soins intensifs, la salle du tomodensitomètre et la buanderie. L'échantillonnage de l'air a été effectué par un impacteur en verre (AGI) à une distance d'environ 0,5 à 4 m des lits des patients. L'ARN viral a été détecté par RT-PCR.	Tous les échantillons étaient négatifs pour l'ARN du SRAS-CoV-2.
Alsved (2020) (90) Étude de biosurveillance Suède* Printemps 2020*	ARN du SRAS-CoV-2 mesuré à partir des cas de COVID-19 (n = 2) dans les deux jours suivant l'apparition des symptômes. Des échantillons d'air ont été prélevés à 0,8 mètre du cas, alors que l'individu parlait ou chantait. Les mesures ont été effectuées dans une chambre expérimentale étanche à l'air avec des volontaires humains.	Les échantillons d'air prélevés dans un rayon de 0,8 mètre des cas de COVID-19 étaient négatifs pour l'ARN viral. Les charges virales dans les voies respiratoires des sujets au moment de l'expérience n'ont pas pu être obtenues. Les auteurs affirment que des valeurs de Ct qPCR de 22-25 ont été rapportées dans les rapports cliniques des sujets dans les 24 heures suivant l'expérience.
Cheng (2020) (91)	Des échantillons d'air ont été prélevés à moins de 10 cm de patients asymptomatiques et	Aucun virus n'a été détecté dans les échantillons d'air provenant de pièces

Étude de biosurveillance Chine Janvier-avril 2020	symptomatiques (n = 6) atteints de la COVID-19, avec ou sans masque chirurgical, dans une chambre d'isolement des infections aérogènes, afin de détecter une contamination par le SRAS-CoV-2. Les charges virales dans les échantillons de fluides respiratoires des patients ont également été testées en faisant éternuer et cracher les patients sur des filtres en gélatine dans les échantillonneurs d'air. Les charges virales ont été mesurées à l'aide de tests (non spécifiés) et par la méthode RT-PCR.	où se trouvaient des patients avec ou sans masque. À l'exception d'un patient dont la charge virale du liquide respiratoire était de 2,54 x10^4 copies/ml, les échantillons de tous les autres patients ayant éternué étaient négatifs pour l'ARN du virus. Les auteurs suggèrent que la transmission par les aérosols n'est pas le mode prédominant de transmission de l'infection dans les milieux échantillonnés. L'utilisation appropriée des EPI, la désinfection de l'environnement et l'occupation unique dans une chambre d'isolement des infections aéroportées sont les raisons des résultats observés.
Kim (2020) (92) Étude de biosurveillance Corée du Sud Mars-avril 2020	Des échantillons d'air (n = 52) ont été prélevés à deux mètres des patients atteints de la COVID-19 (n = 8), avant leur admission et les jours 3, 5 et 7 de l'hospitalisation, à l'aide d'un échantillonneur d'air portable AirPort MD8. Certains patients étaient logés dans des chambres à pression négative (par exemple, les chambres d'isolement des infections aéroportées). L'ARN a été mesuré par la méthode RT-PCR.	Tous les échantillons d'air prélevés étaient négatifs pour l'ARN viral.
Ong (2020) (93) Étude de biosurveillance	Des échantillons d'air ont été prélevés chez des patients atteints de la COVID-19 (n = 3) dans une chambre d'isolement des	Aucun échantillon d'air n'était positif pour le SRAS-CoV-2.

Singapour Janvier-février 2020	infections aérogènes à pression négative d'un centre dédié aux éclosions de SRAS-CoV-2 entre le 4e et le 11e jour de leur maladie, à l'aide de pompes de SKC Universal et d'un échantillonneur microbiologique MD8 de Sartorius. L'ARN a été mesuré par la méthode RT-PCR.	
Ma (2020) (51) *Préimpression* Étude de suivi biologique Chine Printemps 2020* Note : Des résultats supplémentaires sur l'ARN viral dans les échantillons d'haleine expirée et les échantillons d'air de la communauté sont résumés dans les tableaux 4 et 6.	Des échantillons d'air (n=26) ont été prélevés dans les hôpitaux et dans les chambres d'hôtel de quarantaine non ventilées des cas à l'aide d'un robot. L'ARN a été détecté par RT-PCR.	Aucun échantillon d'air provenant du milieu hospitalier n'était positif pour l'ARN viral du SRAS-CoV-2.

Tableau 6 : Études de suivi biologique portant sur le SRAS-CoV-2 dans l'air en milieu communautaire (n = 9)

Présence du SRAS-CoV-2 dans les échantillons de culture cellulaire		
Lednicky (2021) (23) *Préimpression* Étude de suivi biologique États-Unis Janvier 2021* *nouvelle*	Des échantillons d'air ont été prélevés dans une voiture conduite par un patient atteint de COVID-19 (légèrement symptomatique, sans toux) à l'aide d'un échantillonneur en cascade personnel Sioutas à plusieurs stades d'échantillonnage	L'ARN viral du SRAS-CoV-2 était détectable à tous les stades d'échantillonnage des aérosols avec le SIPC, à des concentrations allant de 1,24E+03 à 3,14E+04 génome/m^3 d'air.

	pour différentes tailles d'aérosols (SIPC). L'échantillonneur était fixé au pare-soleil du côté passager de la voiture, soit à environ 1 mètre du visage du sujet. Le climatiseur de la voiture était en marche pendant la course de 15 minutes. L'ARN du SRAS-CoV-2 a été détecté par la RT-PCR, la viabilité du virus mesurée par la culture cellulaire Vero E6, tout comme le séquençage du génome.	Ces résultats suggèrent que les virions sont présents dans des sécrétions respiratoires de différentes tailles. Le SRAS-CoV-2 a été mis en culture à partir des stades d'échantillonnage dans lesquels on a recueilli des particules de 0,25 à 0,50 µm.
ARN du SRAS-CoV-2 dans les échantillons		
Munoz-Price (2021) (24) Étude de suivi biologique États-Unis Printemps 2021* *nouvelle* Remarque : D'autres résultats sur l'ARN viral dans l'air ambiant dans les milieux de soins aux patients sont résumés au tableau 5.	Les échantillons d'air (n = 9) ont été prélevés auprès de ménages où l'on trouvait des cas confirmés de COVID-19. Des échantillons d'air ont été prélevés à l'aide de l'échantillonneur d'air Sartorius MD8, placé entre 0,3 et 1,8 mètre de la tête des patients. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	55 % (n = 5 sur 9) des échantillons d'air prélevés auprès de trois ménages différents étaient positifs pour l'ARN viral. La probabilité de résultats positifs pour les échantillons d'air dans les ménages, comparativement aux milieux hospitaliers, a été estimée à 8,75 [IC à 95 %, 1,21 à 63,43; P = 0,058]. Le nombre médian de jours entre le dernier test positif pour le SRAS-CoV-2 et le jour de l'échantillonnage de l'air était de 3 (plage de 2,5 à 5). Parmi les ménages dont les échantillons d'air étaient positifs, l'un avait un climatiseur en marche et les trois avaient ouvert des fenêtres ou des portes immédiatement avant l'échantillonnage d'air. Soit dit en passant, la plupart des maisons étaient chaudes et humides au moment du prélèvement de l'échantillon.
Gehrke (2021) (61) *Préimpression*	Des échantillons d'air ont été prélevés dans une salle de concert et un centre commercial pendant	On a trouvé des points chauds pour la COVID-19 dans des zones non visibles

Étude de suivi biologique Allemagne Octobre 2020 à janvier 2021 *nouvelle* Remarque : Le tableau 5 résume les résultats supplémentaires sur l'ARN viral tirés des échantillons d'air prélevés en milieu hospitalier.	6 heures au moyen de pièges à froid non alimentés. L'ARN viral a été quantifié par RT-PCR dans une zone à forte transmission dans la communauté afin d'identifier les points chauds potentiels pour la transmission.	et dans des zones prédisposées à un effet de flottabilité (cheminée). Dans la salle de concert, 1 des pièges à froid sur 10 était positif pour l'ARN viral. Dans le centre commercial, 35 % des pièges qui se trouvaient au rez-de-chaussée, dans les zones de kiosques aux 2e et au 3e étages, ainsi qu'autour des escaliers mécaniques étaient positifs pour l'ARN viral (n = 5 sur 14). La section de mode du 4e étage, qui a habituellement une capacité de 25 %, était négative. La concentration virale la plus élevée (2,7 à 5,4 x 10^3 copies/ml) a été trouvée au niveau du sol entre les escaliers mécaniques. Toutefois, les mesures de suivi pour les pièges à froid placés directement sous 2 entrées et 2 sorties d'air au 3e étage (pour exclure toute contamination du système de ventilation central) étaient négatives. Les échantillons prélevés le vendredi où l'on retrouvait un plus grand nombre de clients étaient deux fois plus élevés que ceux prélevés le lundi.
Moreno (2021) (69) Étude de suivi biologique Espagne Mai à juillet 2020 *nouvelle*	Des échantillons d'air ont été prélevés dans des métros et des autobus utilisés. L'air ambiant ($PM_{2,5}$) a été échantillonné à l'aide de filtres en téflon et d'équipement de surveillance individuelle de l'environnement (PEM). Des filtres de climatisation ont également été échantillonnés. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	2 échantillons d'air du métro sur 6 étaient positifs pour le SRAS-CoV-2, mais aucun des échantillons du filtre du climatiseur n'était positif. 1 échantillon d'air sur 6 provenant des autobus et 4 échantillons sur 9 provenant des filtres de climatisation étaient positifs. Les résultats du nettoyage et de la désinfection ont indiqué que ce processus a réussi la décontamination.
de Rooij (2021) (66)	Des échantillons d'air ont été prélevés dans des élevages de	En se fondant sur la contamination des échantillons, les chercheurs ont conclu

Préimpression Étude de suivi biologique Pays-Bas Avril à juin 2020 *nouvelle*	visons où on a vu des éclosions de COVID-19 (3 élevages à la fin de l'éclosion, 1 au début de l'éclosion). Des échantillons ont été prélevés dans des salles d'élevage à l'intérieur, à l'extérieur sur les lieux de l'élevage et dans des sites résidentiels avoisinants. Des échantillons d'air ont été prélevés à l'aide de filtres en téflon et en parallèle avec le prélèvement de particules PM_{10} (< 10 µm) et de poussières inhalables (< 100 µm). Des échantillons d'air ont également été prélevés sur les membres du personnel effectuant l'enquête sur le terrain. La contamination virale dans les échantillons d'air a été mesurée par RT-PCR.	que les élevages de visons étaient fortement contaminés par de l'ARN viral à l'intérieur, mais que la dispersion du virus à l'extérieur et dans les zones avoisinantes était négligeable. Élevage à un stade aigu de l'éclosion : - L'ARN du SRAS-CoV-2 a été détecté dans 62,5 % (n = 5 sur 8) des échantillons de poussière inhalables et dans 50 % (n = 4 sur 8) des échantillons de PM^{10} prélevés dans l'élevage. Tous les échantillons d'air prélevés sur les membres du personnel (n = 2) étaient positifs pour l'ARN viral. - L'ARN du SRAS-CoV-2 a également été détecté dans des échantillons prélevés à l'extérieur, soit à une distance variant entre 1,5 et 10 mètres de l'entrée ouverte de l'élevage, mais les échantillons prélevés à 20 m de l'entrée étaient négatifs. Élevage à un stade tardif de l'éclosion : - L'ARN viral a été détecté dans 9,8 % (n = 4 sur 41) des échantillons de poussière inhalables, à environ 4×10^3 copies/m^3. L'ARN du SRAS-CoV-2 n'a pas été décelé dans les échantillons de poussière inhalables prélevés à l'extérieur des espaces où se trouvaient les visons (n = 9) ou dans les échantillons de PM^{10} prélevés dans l'élevage (n = 9) ou près des espaces où se trouvaient les visons (n = 9). L'un des échantillons d'air prélevés auprès

		des membres du personnel était positif pour l'ARN du SRAS-CoV-2. - Tous les échantillons d'air provenant de sites résidentiels étaient négatifs pour l'ARN du SRAS-CoV-2.
Ma (2020) (51) *Préimpression* Étude de biosurveillance Chine Printemps 2020* Remarque : D'autres résultats sur l'ARN viral dans des échantillons d'air expiré sont résumés dans le tableau 4 et le tableau 5.	Des échantillons d'air ont été prélevés à l'aide d'un robot dans des hôpitaux et des chambres d'hôtel non ventilées utilisées pour la quarantaine. L'ARN a été détecté par la méthode RT-PCR.	Un seul échantillon d'air positif (3,8 % n = 26) a été identifié dans les toilettes non ventilées d'un hôtel utilisé pour la quarantaine.
AUCUN ARN du SRAS-CoV-2 dans les échantillons		
Wong (2020) (67) *Préimpression* Étude de suivi biologique Singapour Février et mars 2020 *nouvelle*	Des échantillons d'air (n = 6) ont été prélevés dans des chambres, des couloirs, des toilettes et des ascenseurs utilisés par les patients atteints de la COVID-19 dans des milieux communautaires (non précisés). L'ARN viral dans les échantillons a été mesuré par RT-PCR.	Tous les échantillons d'air étaient négatifs pour l'ARN viral.
Döhal (2020) (68) *Préimpression* Étude de suivi biologique Allemagne Mars 2020	L'air ambiant dans 21 foyers où se trouvaient des personnes en quarantaine (n = 15) a été prélevé par échantillonnage cyclonique à l'aide d'un échantillonneur Coriolis 154 Micro Air. L'ARN viral dans les échantillons a été mesuré	Tous les échantillons d'air étaient négatifs pour l'ARN viral.

nouvelle	par la RT-PCR et par la culture cellulaire Vero-E6. Remarque : Au moins une personne dans chaque ménage inclus dans l'étude était séropositive pour le SRAS-CoV-2 au moment du prélèvement de l'échantillon.	
Di Carlo (2020) (94) Étude de suivi biologique Italie Mai 2020 *nouvelle*	Des échantillons ont été prélevés dans un autobus de la ville dans lequel on trouvait un grand nombre de patients atteints de la COVID-19, pendant la dernière semaine de confinement et la première semaine de réouverture graduelle (environ 1 100 passagers ont pris l'autobus pendant la période de l'étude). L'air a été échantillonné à l'aide de filtres à membrane de gélatine microbiologique de 80 mm. L'ARN viral dans les échantillons a été mesuré par RT-PCR.	Aucun échantillon d'air (ou de surface) n'a été positif pour le SRAS-CoV-2. Les mesures de santé publique en place comprenaient une désinfection des mains à l'entrée de l'autobus, le port obligatoire du couvre-visage et le fait de garder les fenêtres de l'autobus ouvertes. Les auteurs affirment que ces précautions ont empêché la circulation et la détection du SRAS-CoV-2 pendant la période de l'enquête.

*Estimation basée sur les affiliations des auteurs et la date de publication.

CHARGES VIRALES DU SRAS-COV-2 DANS LES PARTICULES RESPIRATOIRES

Un examen systématique et une méta-analyse ont permis de créer un modèle pour estimer la relation entre le virus viable du SRAS-CoV-2, les charges virales des cas et les gouttelettes chargées de virus et les émissions d'aérosols (55). Cet examen a révélé que la charge virale maximale se situait entre un jour avant et cinq jours après l'apparition des symptômes (55). Le modèle a estimé que la probabilité de trouver un virus viable dans les aérosols respiratoires expulsés par une personne ayant une charge virale maximale était ≤ 61,1 % (IC à 95 % : 51,8 à 70,4 %), et l'estimation de la probabilité était considérablement plus faible, soit 0,69 % (IC à 95 % : 0,43 à 0,95 %), lorsque la personne avait une charge virale moyenne.

Tableau 7 : Charge virale du SRAS-CoV-2 dans les particules respiratoires (n = 1)

ÉTUDE	MÉTHODE	RÉSULTATS PERTINENTS
Chen (2020) (55) *Préimpression* Analyse in silico éclairée par l'examen systématique Canada* Août 2020	Un examen systématique et une méta-analyse ont été réalisés (août 2020) pour élaborer un ensemble de données et résumer les données sur la charge virale respiratoire (rVL) du SRAS-CoV-2. Un modèle a été développé pour estimer la probabilité que les gouttelettes respiratoires et les aérosols contiennent des virus viables, en supposant différentes estimations de la charge virale et différentes activités.	La méta-analyse a montré une grande hétérogénéité des charges virales entre les individus, les études et les stades d'infection. Cela suggère que des facteurs virologiques intrinsèques sont à l'origine de la dispersion observée lors de la pandémie. De nombreux cas présentent un risque de transmission minime, alors que les individus hautement infectieux ont libéré 9,84 (IC de 95 %, 9,17-10,56,) $\log_{10}$ de virions du SRAS-CoV-2/ml via des gouttelettes et des aérosols en respirant, en parlant et en chantant. Le modèle estime que la toux a augmenté la contagiosité des cas symptomatiques. La probabilité de présence d'un virus viable dans les aérosols au pic de la charge virale a été estimée à ≤61,1 % (IC de 95 %) : 51,8-70,4 %) pour les cas les plus infectieux, et ≤ 0,69 % (IC de 95 % : 0,43-0,95 %) pour les cas ayant une charge virale moyenne.

*Estimation basée sur les affiliations des auteurs et la date de publication.

Méthodologies :

Une analyse documentaire quotidienne (ouvrages publiés et en prépublication) est effectuée par le Groupe des sciences émergentes de l'ASPC. L'analyse a compilé les ouvrages sur la COVID-19 depuis le début de l'éclosion et est mise à jour quotidiennement. Les recherches visant à extraire les ouvrages pertinents sur la COVID-19 sont menées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN et Research Square, et les résultats sont recoupés avec les ouvrages figurant sur la liste de la documentation sur la COVID de l'Organisation mondiale de la Santé et des centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier et Wiley. Le résumé quotidien et les résultats complets de l'analyse sont conservés dans une base de données RefWorks et dans une liste Excel consultable. Une recherche ciblée par mot-clé a été effectuée dans ces bases de données pour recenser les citations pertinentes sur la COVID-19 et le SRAS-CoV-2 à l'aide des termes de recherche suivants, soit aerosol, airborne, droplet.

Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle comportait des données pertinentes, qui ont été extraites dans la revue. Le texte intégral de la recherche potentiellement pertinente a été examiné pour confirmer sa pertinence et un synopsis de l'étude a été extrait dans la revue. La présente revue contient des recherches publiées jusqu'au 12 mars 2020.

Examen par les pairs

Ce document a fait l'objet d'un examen par les pairs dirigé par un expert en la matière et d'un examen en ce qui concerne la rédaction et la science par le Bureau de la Conseillère scientifique en chef.

Préparée par : Chatura Prematunge et Lisa Waddell. LNM, Groupe des sciences émergentes, ASPC.

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May 14, 2021

Evidence Snapshot:

Evidence Brief on the Risk of COVID-19 Transmission in Flight, Update 2

Context

Many changes have been implemented by airlines during the pandemic to reduce the risk of SARS-CoV-2 transmission during air travel. This evidence brief updates the literature on in-flight transmission of SARS-CoV-2, and the strategies developed to mitigate transmission during boarding, flight and disembarkation.

Key Findings

Sixty-four studies were identified in total including 29 studies published between October 2020 and April 26, 2021.

- Most in-flight transmission events occurred on flights early in the pandemic when mandatory use of face masks in flights was not yet in place. Those seated within two rows of an index case were at higher risk of acquiring SARS-CoV-2. Overall, increasing the time duration of a trip increased infection transmission risk which may be partially due to removing one's mask during meal service or walking around on longer flights.
- Multiple interventions maximally reduced the risk of transmission. Enhanced protective measures included: enhanced cleaning; universal face masks; hand hygiene; reduced flight capacities; physical distancing on embarkation and disembarkation; designated crew only areas; and quarantine areas for unwell passengers and crew.
- The risk of transmission in simulation models was higher on flights near capacity compared with those with empty middle seats that allowed for more physical distancing. Symptom checks were not always effective due to lack of compliance by passengers.
- Airplane ventilation systems quickly refresh cabin air, reducing opportunities for transmission. Environmental studies estimated that in-flight particle concentrations in the air in airplanes were lower than that of retail/grocery stores, restaurants, office spaces, homes, and other forms of transportation.

Considerations

Effective ventilation and layering multiple interventions with enhanced protective measures have significantly reduced the risk of COVID-19 transmission during air travel. Future research needs to assess both the effect of emerging variants on transmissibility risk and vaccination status of both travellers and airline staff in mitigating risk.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evidence Brief of the Evidence on the Risk of COVID-19 Transmission in Flight, Update 2; May 2021. Full report available from: **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Evidence Snapshot:

Evidence Brief on SARS-CoV-2 Variants of Concern and Transmission in Children

Context

Several SARS-CoV-2 variants of concern (VOCs) that have acquired enhanced infectivity and transmissibility have been identified since December 2020. This review gathered evidence up to March 26, 2021 regarding the transmission of the VOCs in children and their impact on in-school transmission.

Key Findings

The evidence brief includes results of web-scraped media data of school-related COVID-19 outbreaks across Canada and nine studies on transmission of the VOCs in children. Of these, five assessed only VOC transmission in children, three assessed the impact on in-school transmission, and one evaluated both.

- There were an increasing number of VOC related school outbreaks reported in the media in Canada between January to March 2021. All published studies were on B.1.1.7 transmission in the UK during November 2020 to January 2021. There was increased transmissibility of the VOC in both adults and children but B.1.1.7 did not disproportionately affect children and youth < 20 years. Transmission in school-aged children was strongly correlated with the level of community transmission. Both a modelling study and epidemiological evidence identified that children did not drive variant transmission.
- Among children who were hospitalized, there was no evidence of more severe disease with B.1.1.7 infection. A single report estimated that children under ten are about half as likely as adults to transmit the variant similar to the original SARS-CoV-2 variant findings.
- Modelling studies found that B.1.1.7 transmission in children was inversely proportional to the stringency of public health measures other than school closures, and the stringency of public health measures was the most important determinate of epidemic trajectory.

Considerations

Community transmission appears to be the biggest predictor of VOC transmission in children and transmission patterns in schools. To date, B.1.1.7 appears to be more transmissible in children but does not appear to be more severe than the original strain and whether schools are open or closed appears to have minimal impact on the epidemic course overall. A key knowledge gap in this research is the lack of high-quality transmission studies of all the current VOCs in children and VOC transmission patterns in schools.

Reference: Emerging Science Group of the Public Health Agency of Canada. Evidence Brief on SARS-CoV-2 Variants of Concern and Transmission in Children. March 26, 2021. Full report available from: **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

mars 8, 2021

Aperçu des éléments de preuve :

Synthèse en bref des données probantes sur les variants préoccupants du SRAS-CoV-2 et la transmission chez les enfants

Contexte

Plusieurs variants préoccupants du SRAS-CoV-2 qui ont acquis une plus grande infectivité et une plus grande transmissibilité ont été identifiés depuis décembre 2020. Cette synthèse en bref inclut donc les éléments de preuve disponibles jusqu'au 26 mars 2021 sur la transmission des variants préoccupants chez les enfants et l'impact sur la transmission dans les écoles.

Principales constatations

La synthèse en bref inclut les données des médias recueillis sur le Web à propos des éclosions de COVID-19 dans les écoles partout au Canada, ainsi que neuf études sur la transmission des variants préoccupants chez les enfants. De ce nombre, cinq ont évalué uniquement la transmission des variants préoccupants chez les enfants, trois ont évalué l'impact sur la transmission à l'école et un a évalué les deux.

- De janvier à mars 2021, les médias ont fait état d'un nombre croissant d'éclosions de variants préoccupants dans les écoles du Canada. Toutes les études publiées portaient sur la transmission du variant B.1.1.7 au Royaume-Uni entre novembre 2020 et janvier 2021. On a pu voir une augmentation de la transmissibilité des variants préoccupants chez les adultes et les enfants, mais le variant B.1.1.7 n'a pas touché de façon disproportionnée les enfants et les jeunes de moins de 20 ans. La transmission chez les enfants d'âge scolaire était cependant fortement corrélée avec le niveau de transmission dans la collectivité. Tant une étude de modélisation que des signes épidémiologiques ont révélé que les enfants n'étaient pas responsables de la transmission des variants.
- Parmi les enfants qui ont été hospitalisés, il n'y avait aucun signe de maladie plus grave en raison d'une infection par le variant B.1.1.7. Un seul rapport a estimé que les enfants de moins de dix ans étaient deux fois moins susceptibles que les adultes de transmettre le variant SRAS-CoV-2 que la souche originale.
- Les études de modélisation ont révélé que la transmission du variant B.1.1.7 chez les enfants était inversement proportionnelle à la rigueur des mesures de santé publique autres que la fermeture des écoles et que la rigueur de ces mesures était le déterminant le plus important de la trajectoire de l'épidémie.

Facteurs dont il faut tenir compte

La transmission communautaire semble être le plus important prédicteur tant de la transmission des variants préoccupants chez les enfants que des modes de transmission dans les écoles. À ce jour, le variant B.1.1.7 semble être plus transmissible chez les enfants, mais ne semble pas avoir de plus graves répercussions que la souche originale. Le fait que les écoles soient ouvertes ou fermées ne semble avoir qu'un impact minime sur le cours de l'épidémie dans son ensemble. L'absence d'études de grande qualité sur la transmission de tous les variants préoccupants chez les enfants et sur les modes de transmission dans les écoles représente une lacune clé de cette recherche.

Référence : Groupe des sciences émergentes de l'Agence de la santé publique du Canada. Synthèse en bref des données probantes sur les variants préoccupants du SRAS-CoV-2 et leur transmission chez les enfants. 26 mars 2021. Rapport complet disponible auprès de : **phac.ocsoevidence-bcscdonneesprobantes.aspc@canada.ca**

Nouvelles éléments de preuve sur la COVID-19

Résumé évolutif à propos des variants préoccupants du SRAS-CoV-2

Faits saillants jusqu'au 28 avril 2021

Introduction

Les **variants préoccupants** (*variants of concern* ou VOC en anglais) du SRAS-CoV-2 sont des variants en circulation qui ont été signalés par des organisations de santé publique nationales ou internationales. Ces VOC sont préoccupants par rapport aux variants originaux du SRAS-CoV-2, car leur complément de mutations entraîne une transmissibilité et une virulence accrue (morbidité ou mortalité), des changements dans la présentation clinique de la maladie, une évasion immunitaire, une efficacité réduite des traitements, des vaccins ou des mesures de santé publique et des échecs de détection diagnostique (1, 2). L'objectif de ce résumé à jour de la littérature sur les VOC du SRAS-CoV-2 est de mettre en évidence les nouvelles données à ce sujet, leur épidémiologie et la manière dont les attributs des variants préoccupants peuvent avoir un impact sur la gestion de la pandémie. L'accent sera mis sur les changements de paramètres épidémiologiques (par exemple, les taux de transmission, les résultats cliniques de la gravité et de la mortalité, les changements dans les groupes d'âge touchés ou les proportions asymptomatiques), les impacts sur les tests de diagnostic, l'évasion immunitaire/l'efficacité des vaccins et les impacts sur d'autres mesures de santé publique.

TABLEAU 1 : VARIANTS ACTUELS PRÉOCCUPANTS (VOC)

Nom de l'OMS (05-21)	Lignée Pango	Clade de la prochaine souche	Clade GISAID	Autre nom	Première détection	Premiers échan-tillons	Mutations de pointe caractéristiques
Alpha	B.1.1.7	20I/501Y.V1	GR/501Y.V1	VOC 202012/01	Royaume-Uni	Sept. 2020	69/70del, 144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Bêta	B.1.351	20H/501Y.V2	GH/501Y.V2	VOC 202012/02	Afrique du Sud	Août 2020	D80A, D215G, 241/243del, K417N, E484K, N501Y, D614G, A701V
Gamma	P.1, B.1.1.28.1	20J/501Y.V3	GR/501Y.V3	VOC 202101/02	Brésil et Japon	Déc. 2020	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y,

							D614G H655Y, T1027I, V1176F
Delta	B.1.617.[21]		G/452R.V3		Inde	Octobre 2020	L452R, D614G, P681R, ± (E484Q, Q107H, T19R, del157/158, T478K, D950N)

[1] Le B.1.617.2 a été ajouté à la liste des VOC le 11 mai 2021. Un profil sera établi pour ce VOC dans la prochaine mise à jour mensuelle.

Les **variants d'intérêt** (*variants of interest* ou VOI en anglais), également appelés variants en cours d'investigation (*variants under investigation* ou VUI en anglais), sont une désignation utilisée pour signaler un variant qui a le potentiel d'être une VOC, mais qui nécessite une étude ou des preuves supplémentaires. Les indicateurs pour la désignation d'un VOI comprennent un changement phénotypique ou l'acquisition de mutations avec une implication phénotypique établie ET qui a été la cause d'une transmission communautaire/d'amas ou qui est détectée dans plusieurs pays OU qui est évaluée comme un VOI par une autorité telle que l'OMS (1, 2). Les données sur les VOI sont collectées, mais ne sont pas mises en évidence dans ce résumé. L'ensemble complet de données en format Excel est accessible ici et filtré par VOI.

Ce résumé se veut un portrait à jour des données probantes clés sur la façon dont les VOC peuvent avoir un impact sur la pandémie, y compris sur les changements dans l'épidémiologie, l'évasion immunitaire ou les échecs des tests de diagnostic.

Points clés

Au 28 avril 2021, 218 études faisaient état d'un VOC ou d'un VOI et 156 études identifiées faisaient rapport d'un B.1.1.7, P.1 ou d'un B.1.351, et elles ont été incluses dans les résumés ci-dessous. Les observations cliniques, et les estimations de prévalence ponctuelle (n=23) et les études sur les VOI n'ont pas été résumées. Des résumés généraux sont présentés dans le tableau des points clés ci-dessous, et des résumés plus détaillés de chaque VOC figurent dans les sections d'examen. Les détails des études individuelles se trouvent dans l'ensemble de données en format Excel et accessibles ici. Dans l'ensemble, la prédominance des preuves disponibles concernait le variant B.1.1.7 (142 études) par rapport au variant B.1.351 (66 études) et au P.1 (34 études).

Transmissibilité :

- Toutes les études ont montré une augmentation de la transmissibilité pour les variants B.1.1.7, B.1.351 et P.1 par rapport au variant original, bien que l'étendue soit très variable. Pour le B.1.1.7, deux études canadiennes ont rapporté une transmissibilité accrue de 34 % (3) et des taux d'attaque secondaire plus élevés de 31 % (4).

Gravité clinique :

- Les études portant sur les trois variants ont montré une augmentation du risque d'hospitalisation et d'admission en unité de soins intensifs (USI). Toutefois, ces données sont basées sur un nombre limité d'études.
- Pour les indicateurs de gravité, quelques études ont rapporté un risque d'hospitalisation stratifié par âge et une probabilité accrue dans les groupes d'âge adulte entre 20 et 59 ans. D'autres études n'ont pas signalé d'association avec l'âge. Plusieurs études ont également rapporté une proportion plus faible de conditions préexistantes parmi les cas de VOC, à l'exception de l'obésité.
- En ce qui concerne la mortalité, les données relatives au P.1 et au B.1.1.7 ont montré que le risque de mortalité était globalement inférieur à celui du variant original. Une seule étude de surveillance sur le B.1.351 n'a montré aucune différence dans l'ensemble quant aux risques de mortalité. Le risque de mortalité aurait augmenté dans certains groupes d'âge adulte.
- Par rapport au variant original, la charge virale était systématiquement de 2 à 10 fois plus élevée pour le B.1.1.7, et était plus élevée pour le P.1 et le B.1.351 que le variant original, mais plus faible que la charge virale du B.1.1.7.
- Il n'y a pas eu d'études évaluant la période infectieuse pour le P.1 et le B.1.351 et seulement une petite étude qui a trouvé que l'infection moyenne au B.1.1.7 a duré 13,3 jours contre 8,2 jours pour les autres variants. Il n'y a pas eu d'études sur la période d'incubation pour aucun des VOC.

- D'autres catégories liées à la performance diagnostique et à la recherche épidémiologique sur la diffusion et l'impact des interventions non pharmaceutiques sont résumées dans les sections approfondies sur les VOC.
    - Aucune étude évaluant les tests de diagnostic ou de détection du SRAS-CoV-2 n'a décrit des problèmes d'échec ou de performance pour la détection des VOC, en dehors de l'abandon du gène S bien caractérisé pour le B.1.1.7.
    - Peu d'études portaient sur des interventions non pharmaceutiques. Bien qu'une plus grande rigueur ait été nécessaire pour contrôler les VOC en raison d'une transmissibilité plus élevée, aucune modification des interventions individuelles n'a été nécessaire.
    - Les études sur l'introduction et la propagation des VOC dans une région géographique n'ont pas été incluses dans le tableau ci-dessous, mais des résumés sont disponibles dans les profils des VOC individuels, tout comme les résumés des modèles animaux et des études *in vitro* sur la réinfection, la protection vaccinale et l'impact potentiel des VOC sur la thérapeutique.

Les catégories de preuves dans les tableaux ci-dessous comprennent les éléments suivants s'ils sont signalés :

La **transmissibilité** comprend les changements dans la transmissibilité, les taux d'attaque secondaire et les estimations de l'avantage sélectif.

La **gravité clinique** comprend la proportion d'infections qui sont symptomatiques, la proportion de maladie grave et de mortalité, ainsi que les facteurs de risque de maladie grave ou de mortalité, la charge virale, la

période infectieuse, la période d'incubation. Il convient de noter que les facteurs de risque de maladie grave incluent des populations spéciales, par exemple les personnes enceintes, si elles sont signalées.

L'**échappement immunitaire** comprend les modifications de l'efficacité des vaccins, le risque de réinfection chez l'humain, les modèles animaux, les expériences *in vitro* ou *in silico*, ainsi que les impacts sur la thérapeutique s'ils sont signalés.

Les **échecs des tests de diagnostic/détection** sont saisis dans les sections individuelles, et ne seront inclus dans le tableau 2 que si la performance du test est préoccupante.

Autre épidémiologie comprend toutes les études qui documentent l'émergence et la propagation des VOC dans une zone géographique, les études écologiques qui examinent la propagation des VOC et les facteurs de risque pour les points chauds, et les études sur les interventions de santé publique efficaces contre les VOC, l'épidémiologie génomique comme sous-catégories.

TABLEAU 2 : RÉSUMÉ DES PREUVES CLÉS DU VOC P.1 (GAMMA) (N=34), DU VOC B.1.351 (BETA) (N=66) ET DU VOC B.1.1.7 (ALPHA) (N=142)

Catégorie	P.1 (Gamma)	B.1.351 (Bêta)	B.1.1.7(Alpha)
EFFICACITÉ DE LA TRANSMISSION			
Transmissibilité Par rapport au variant original	Quatre rapports de données de surveillance : • 27 % de plus en France (combiné P.1/B.1.351) (5) • 160 % - 100 % plus élevé au Brésil (6, 7) • Un modèle étudiant le P.1 en Italie a rapporté une transmissibilité supérieure de 12 à 39 % selon que le P.1 présente ou non une évasion immunitaire (8). Faible niveau de preuve.	Quatre rapports de données de surveillance : • 27 % plus élevé en France (combiné P.1/B.1.351) (5), • 55 % (9, 10) et 20-100 % plus élevé en Afrique du Sud (11) Faible niveau de preuve	24 études de surveillance et d'observation : • Variation relative de la transmissibilité du B.1.1.7 ($_{1-Rvoc/Variant\ original}$) entre 34 et 118 % d'une étude à l'autre, une partie de la variation étant due à l'époque (12) et au pays (plus élevée au Royaume-Uni) (10) : ○ Canada : 34 % (IC 95 % : 31-38) (3), É.-U. : 35-59 % (13, 14). ○ Royaume-Uni : de 43 à 118 % (10, 12, 13, 15-17), de 13,4 à 41,3 % dans les régions du Royaume-Uni en décembre 2020 (18). ○ Europe : France 41 -52 % (5, 19), Danemark 55 %, Suisse 54-74 % (13), (20), Norvège 24 % (21), Italie 55-57 % (22), Pays de Galles et É.-U. 65-72 % (10). ○ Israël 45 % (23). ○ Le Japon a estimé une augmentation de 60 % de la transmissibilité relative aux VOC (non spécifiés) (24). • De même, les ratios des taux d'attaque secondaire parmi les études sur la transmission par les ménages étaient de 30 à 70 % plus élevés au Canada (4), en Norvège (21) et au Danemark (25). Niveau de preuve faible à modéré

SÉVÉRITÉ CLINIQUE			
Virulence/gravité ou durée de la maladie Par rapport au variant original	Deux (2) études de surveillance : • Une proportion plus élevée de cas d'hospitalisation (p<0,001) (26). • Plus grande probabilité d'être admis à l'hôpital (aOR 2,6, 95 % CI 1,4-4,8) (26). • Probabilité plus élevée d'être admis en soins intensifs (aOR 2,2, 95 % CI 1,8-2,9) (26). • Une croissance exponentielle des cas hospitalisés a été signalée à Rio Grande do Sul et Porto Alegre (27). Faible niveau de preuve.	Une (1) étude de surveillance européenne : • Aucune différence dans la proportion de personnes symptomatiques. • Plus grande probabilité d'être admis à l'hôpital (aOR 3,6, 95 % CI 2,1-6,2) (26) • Probabilité plus élevée d'être admis en soins intensifs (aOR 3,3, 95 % CI 1,9-5,7) (26). Faible niveau de preuve.	Dix (10) études de surveillance et d'observation : • Des données contradictoires sur la prévalence de la maladie symptomatique n'ont révélé aucune différence entre les deux dans une étude et moins de cas symptomatiques (p<0,001) dans une autre (26, 28). • Cinq études ont révélé une probabilité plus élevée d'être admis à l'hôpital (aOR 1,36 - 1,7 et aHR 1,34) (26, 29-32). • Deux études ont révélé une probabilité plus élevée d'admission en soins intensifs (aOR 2,3, aHR 1,99) (26, 33). • Parmi les cas hospitalisés, il n'y avait pas d'association entre le B.1.1.7 et la maladie grave et le décès (aPR 1-02) (34). • Des taux plus élevés d'hypoxie à l'admission à l'hôpital ont été signalés dans deux études (35, 36). Niveau de preuve modéré.
Facteurs de risque sur la gravité Par rapport au variant original	Trois (3) études d'observation • Les cas de P.1 avaient une probabilité d'hospitalisation de 3,0 à 13,1 fois plus élevée dans les	Une (1) étude de surveillance européenne • Risques d'hospitalisation de 3,5 à 3,6 fois plus élevés pour les groupes d'âge 40-79 ans (26)	Cinq (5) études d'observation : • Une étude sur les cas de COVID-19 hospitalisés a rapporté une plus grande proportion de femmes (48,0 % contre 41,8 %, p=0,01), moins de patients fragiles (14,5 % contre 22,4 %, p=0,001) et une plus grande proportion de cas obèses (30,2 %

	groupes d'âge 20-79 ans (26). • L'admission en USI était 2,9 -13,9 fois plus élevée dans les groupes d'âge ≥ 40 ans (26). • Les conditions préexistantes étaient plus faibles : 27,8 % dans le P.1 contre 89 % dans le variant original, p<0,001 (26). • Les cas graves chez les personnes de moins de 60 ans sont passés de 39 % lors de la première vague à 47 % lors de la deuxième vague (37). • Deux études n'ont pas trouvé d'augmentation de la proportion de personnes hospitalisées dans aucun groupe d'âge (26, 38). Faible niveau de preuve.	• L'admission en USI des personnes âgées de 40 à 59 ans était plus élevée (aOR 8, IC 95 % 3,7-17,3). • Les conditions préexistantes étaient plus faibles (79,6 % B.1.351, contre 89 %, p<0,001) (26). Faible niveau de preuve.	contre 24,8 %, p=0,048), mais aucune différence selon l'âge ou l'ethnie (35). • Une autre étude n'a signalé aucune différence significative en ce qui concerne l'âge et le sexe des patients, ainsi que la durée médiane du séjour à l'hôpital (31). La différence d'âge était statistiquement significative dans une autre étude (37 contre 39 ans) (39). • Une étude a rapporté un ratio de probabilités d'hospitalisation 3,0 fois plus élevé chez les 20-39 ans et 2,3 fois plus élevé chez les 40-59 ans, et que les conditions préexistantes étaient plus faibles (44,8 % contre 89 % p<0,001) (26). • Une étude hospitalière réalisée en France a révélé que l'âge moyen était de 59,2 ans, en baisse par rapport à 70,7 ans, et que le nombre de patients sans comorbidité avait augmenté de 16 % à 42 % (p=0,007) (36). Niveau de preuve faible à modéré.
Mortalité	Deux (2) études observationnelles et 1 modèle prédictif :	Une (1) étude de surveillance européenne :	Neuf (9) études de surveillance et d'observation :

Par rapport au variant original	• Le P.1 présentait une probabilité de mortalité globale plus faible (aOR 0,6, IC 95 % 0,3-1,0) (26). • Taux de mortalité hospitalière plus élevé chez les jeunes adultes (38). • Le modèle prédictif a estimé que la mortalité moyenne était 1,5 (50 % CrI 1,2-1,9) fois plus élevée après l'émergence du P.1, (7). Faible niveau de preuve	• Pas de différence dans les risques de décès (26). Faible niveau de preuve.	• Trois études n'ont signalé aucune différence significative en matière de mortalité globale (2,1 vs 4,1 %) (28), (31), ou après 28 jours (OR : 0,90, IC 95 % 0,57-1,41, p=0,64) (32) • Une étude a fait état d'un risque de mortalité plus faible (aOR 0,5, IC 95 % 0,3-0,9) (26) • Cinq études ont fait état d'un risque de mortalité plus élevé : risque plus élevé de décès à 28 jours (55 %, IC 95 % : 39-72 %) (40), aHR 1,59 (IC 95 % 1,25-2,03) (33), aHR 1,67 (IC 95 % 1,34 - 2,09; P <0,0001) (34). HR 1,64 (IC 95 % 1,32 - 2,04, p <0,001) ce qui équivaut à une augmentation de 2,5 à 4,1 décès pour 1 000 cas détectés (41) et une étude écologique a estimé que le B.1.1.7 était 33 % plus mortel au Royaume-Uni (42) Niveau de preuve modéré.
Facteurs de risque de mortalité par rapport au variant original	Une (1) étude de surveillance au Brésil : • La mortalité chez les cas de COVID-19 <60 ans a augmenté de 18 % en novembre 2020 à 28 % en février 2021 (37). • La mortalité chez les personnes ne présentant aucune condition préexistante	Aucune étude	Deux (2) études de surveillance et de cohorte rétrospective : • Une étude a révélé que la mortalité était plus élevée dans les groupes d'âge plus jeunes que dans les groupes plus âgés (59,0 % chez les 1-34 ans contre 55,4 % chez les 85 ans ou plus) et qu'elle était plus élevée chez les Noirs (69,6 %), les personnes d'origine ethnique mixte ou inconnue (64,8 %), les Blancs (58,0 %) et les Asiatiques (57,6 %) (40). • Une autre étude n'a trouvé aucune augmentation de la mortalité en fonction du

	était plus élevée après l'émergence du P.1 chez les femmes (RR 5,65, IC 95 % 2,9 - 11,03; p <0,0001) et chez les 40 - 59 ans (RR 7,7, IC 95 % 5,01-11,83; p <0,0001) (37). Faible niveau de preuve.		sexe (p = 0,90), du groupe ethnique (p = 0,64) ou du groupe d'âge (p = 0,15) (33). Faible niveau de preuve.
Charge virale Par rapport au variant original	Deux (2) études de surveillance : • La charge virale des cas de P.1 était environ 10 fois plus élevée, indépendamment de l'âge et du sexe (43). • La charge virale était plus élevée (mais inférieure à celle des échantillons B.1.1.7) (5). Faible niveau de preuve.	Deux (2) études avec des résultats secondaires : • La charge virale était plus élevée (mais inférieure à celle des échantillons de B.1.1.7) (5, 44). Niveau de preuve très faible.	Treize études d'observation et analyses de surveillance : • On a toujours trouvé des valeurs de Ct plus faibles ou des charges virales estimées plus élevées. L'ordre de grandeur médian supérieur varie selon les études et la protéine cible de 2 à 10 fois la différence (5, 28, 31, 39, 44-49, 49-51). Niveau de preuve faible à modéré.
Période infectieuse par rapport au variant original	Aucune étude	Aucune étude	Une petite étude a calculé que les infections durent en moyenne 13,3 jours contre 8,2 jours pour les autres variants (47). Niveau de preuve très faible
Période d'incubation	Aucune étude	Aucune étude	Aucune étude

ÉCHAPPEMENT IMMUNITAIRE —Impact potentiel sur l'efficacité du vaccin, possibilité de réinfection			
Réinfection à partir d'une infection naturelle par rapport au variant original	Une (1) étude de surveillance au Brésil : • En supposant que 78 % de la population était déjà infectée, on estime que 28 % des cas à Manaus sont des réinfections (6). • Une (1) observation clinique de réinfection (52). Niveau de preuve faible/très faible.	Deux (2) observations cliniques de réinfection (53, 54). Niveau de preuve très faible.	Deux (2) études ont montré que le B.1.1.7 n'échappe pas à l'immunité naturelle : • Un taux de réinfection estimé à 0,7 % (IC 95 % : 0.6-0.8) (55). • Une étude britannique n'a trouvé aucune preuve que le B.1.1.7 modifiait l'étendue de la protection positive à l'infection par PCR chez les personnes séropositives (aIRR 0,40, IC 95 %0,10-1,64, p=0,20) (56). Niveau de preuve modéré.
Infection découverte après la vaccination/efficacité ou efficience du vaccin par rapport au variant original	Une (1) étude cas-témoins : • La vaccination avec au moins une dose de CoronaVac a été associée à une réduction d'un facteur 0,50 (EV ajustée, 49,6 %; IC 95 %, 11,3 - 71,4) des chances d'infection symptomatique par le SRAS-CoV-2 14 jours après la première dose (57).	Deux (2) ECR : • AstraZeneca : Efficacité de 10,4 % pour la prévention de la maladie symptomatique (58) • Novavax : Efficacité de 50-60 % pour la prévention de la maladie symptomatique (59) • Johnson and Johnson : l'efficacité était de 52 % et 64 % pour la maladie modérée et	Neuf (9) études comprenant des ECR, des cohortes et des études de surveillance : • L'efficacité du vaccin dans un ECR britannique d'AstraZeneca était de 70,4 % (CI 9 5 % 43,6 — 84,5) contre 81,5 % (67,9 - 89,4) dans les variants originaux (62). • En Israël, où 94 % des cas étaient le B.1.1.7, l'efficacité du vaccin Pfizer était >96 % 14 jours après la deuxième dose (63), mais il y avait un risque accru de percées infectieuses entre la première dose et jusqu'à 14 jours après la deuxième dose (aOR 2,4 (IC 95 %): 1,2 à 5,1) (61). • Une étude britannique n'a pas trouvé de différence dans la protection après une

	Faible niveau de preuve.	de 73 % et 82 % pour la maladie grave à 14 jours et 28 jours respectivement (60) • Aucune percée infectieuse n'a été identifiée >14 jours après la deuxième dose (principalement Pfizer) dans une étude cas-témoins menée en Israël (61) Niveau de preuve modéré.	première dose de vaccin (aIRR=1,84, IC 95 % 0,75-4,49, p=0,18) (56). Niveaux de preuve variables, allant des ECR (modérés à élevés) aux observations cliniques (très faibles).

CFR = taux de létalité, IC= intervalle de confiance, Ct = seuil de cycle, USI = unité de soins intensifs, OR = rapport des cotes, PCR = réaction en chaîne par polymérase, EV = efficacité du vaccin, aOR= rapport des cotes ajusté, aHR = rapport de risque ajusté, aPR= rapport de prévalence ajusté

Aperçu des données probantes

Les modèles d'étude inclus dans ce résumé vont des essais cliniques randomisés en double aveugle à faible risque de biais à un certain nombre de modèles d'étude par observation différents. Les études par observation offrent des preuves faibles à modérées, selon la conception spécifique de l'étude et la cohérence entre les études. Les études descriptives incluses dans ce rapport, telles que les séries de cas et les observations cliniques, les modèles prédictifs, les études écologiques, les modèles animaux et les études *in vitro*, présentent un niveau de preuve faible à très faible et ne peuvent généralement être utilisées que pour générer des hypothèses qui doivent être examinées plus avant avec un plan d'étude différent. Compte tenu de cette très grande variation, une indication du niveau de confiance des preuves est fournie pour un résultat particulier. Les plans d'étude sont fournis, mais aucune évaluation formelle du risque de biais n'a été réalisée.

Il y a plusieurs lacunes dans les connaissances ou des domaines où très peu de recherche figure dans le tableau des points clés, et des recherches supplémentaires sont nécessaires pour améliorer la confiance dans les résultats sommaires, en particulier pour le B.1.351 et le P.1.

CONTENU

P.1 (GAMMA)

L'ensemble de données en format Excel comprend les résumés des études individuelles et est accessible ici. Le profil détaillé des preuves élaboré pour le P.1 est présenté ci-dessous. Il couvre les données sur les modifications de l'efficacité de la transmission, les modifications de la gravité clinique, l'échappement immunitaire, les tests et les diagnostics, ainsi que d'autres études épidémiologiques portant principalement sur la propagation des VOC.

Tableau 3 : Profil d'évidence du P.1 (Gamma) VOC (n=34)

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	APERÇU DES DONNÉES PROBANTES
Efficacité de la transmission		

Transmissibilité par rapport au variant original	Une transmissibilité accrue par rapport au variant original : • 27 % de plus en France pour le combiné P.1 et B.1.351 (5). • 2.6 (IC 95 % : 2.4-2,8) fois plus élevée (6) et 2,0 (50 % CrI 1,7 - 2,4) fois plus transmissible avec une immunité croisée médiane estimée à 68 % (50 % CrI 54-79 %) au Brésil (7). • 1,12 (IC 95 % 1,03-1,23) fois plus transmissible avec une évasion immunitaire complète à 1,39 (IC 95 % 1,26-1,56) avec une protection croisée complète en Italie (8).	Quatre études ont fourni des estimations de la transmissibilité du P.1, notamment : deux analyses de données de surveillance du Brésil, une étude transversale de la France, et un modèle prédictif de l'Italie. Il y a peu de cohérence entre les études. L'hétérogénéité des estimations de la transmissibilité accrue peut être due à des facteurs tels que l'emplacement géographique et les moments où les estimations ont été faites. Faible niveau de preuve.
Gravité clinique		
Virulence/gravité ou durée de la maladie par rapport au variant original	• Une proportion plus élevée de cas de P.1 hospitalisés a été signalée par rapport au variant original (20 % contre 7,5 % p<0,001) (26). • Une étude a rapporté un rapport de cotes ajusté (aOR 2,6, IC 95 % 1,4-4,8) plus élevé de cas de P.1 admis à l'hôpital par rapport au variant original ou en USI (aOR 2,2, IC 95 % 1,8-2,9) (26). • Il y a eu croissance exponentielle des hospitalisations dans le Rio Grande do Sul, avec un temps de doublement moyen de 13,4 jours et un taux de croissance quotidien de 5,3 %. • Une croissance exponentielle similaire (temps de doublement de 13,3 jours, taux de croissance quotidien de 5,4 %) pour les hospitalisations a été signalée dans la ville de Porto Alegre (27).	Deux (2) études de données de surveillance en Europe et au Brésil. Faible niveau de preuve.
Facteurs de risque de gravité par rapport au variant original	• Dans l'analyse stratifiée par âge, les cas de P.1 avaient une probabilité d'hospitalisation 3,0 à 13,1 fois plus élevée dans les groupes d'âge 20-39, 40-59 et 60-79 (26). • Une étude a indiqué qu'il y a eu augmentation du nombre de personnes de moins de 60 ans parmi les cas graves dans une proportion de 39 % lors de la première	Deux (2) études provenant de pays européens et de données de surveillance du Brésil et une (1) étude écologique. Faible niveau de preuve.

	vague et de 47 % lors de la deuxième vague (37). • D'autres études n'ont pas indiqué d'augmentation de la proportion de personnes hospitalisées, quel que soit le groupe d'âge (38). • Les probabilités d'admission en USI étaient 2,9 à 13,9 fois plus élevées dans les groupes d'âge 40-59 ans, 60-79 ans et ≥ 80 ans (26). • Les conditions préexistantes étaient plus faibles : 27,8 % dans le P.1 contre 89 % dans le variant original, p<0,001 (26).	
Mortalité par rapport au variant original	• Diminution du risque de mortalité dû au P.1 par rapport au variant original dans l'analyse multivariable (aOR 0,6, IC 95 % 0,3-1,0) (26). • Une augmentation différenciée de la mortalité des jeunes adultes suggère la possibilité d'une plus grande sévérité du variant P.1 dans cette population. Les hospitalisations et les décès à l'hôpital chez les jeunes adultes étaient corrélés à des taux élevés de mortalité hospitalière >10 % (38). • Le modèle prédictif a estimé que les infections à P.1 ont un risque médian de 1,5 (50 % CrI 1,2-1,9) fois plus élevé risquant d'entraîner la mortalité dans la période suivant l'émergence du P.1, par rapport à avant (7).	Une (1) étude à partir des données de surveillance des pays européens, et des études du Brésil; une (1) étude écologique, un (1) modèle prédictif. Faible niveau de preuve.
Facteurs de risque de mortalité par rapport au variant original	La mortalité des cas de COVID-19 de <60 ans a augmenté de 18 % en novembre 2020 à 28 % en février 2021 (37). Le taux de létalité (CFR) a augmenté le plus chez les personnes âgées de 20 à 59 ans et chez les patients sans condition à risque préexistante. La proportion de patients sans condition à risque préexistante parmi les cas graves était plus élevée en février (33 %, contre 25 % auparavant). Par rapport à nov./déc. 2020, les femmes âgées de 20 à 39 ans, sans condition de risque préexistante, avaient un risque de décès 5,65 (IC 95 % 2,9 - 11,03; p <0,0001) fois plus élevé en février 2021 et	Une (1) étude à partir des données de surveillance du Brésil. Faible niveau de preuve.

	7,7 fois plus élevé (IC 95 % 5,01-11,83; p <0,0001) chez les 40 - 59 ans (37).	
Charge virale par rapport au variant original	La charge virale (mesurée par les valeurs CT) des échantillons de P.1 était inférieure à celle des échantillons de B.1.1.7 et supérieure à celle des variants originaux (5). La charge virale des cas de P.1 par rapport aux cas de variant original était environ 10 fois plus élevée dans le cas de P.1 (43). Les charges virales étaient plus élevées dans les infections à P.1, indépendamment de l'âge et du sexe (43).	Deux (2) études à partir des données de surveillance de la France et du Brésil. Faible niveau de preuve.
Période infectieuse	Aucune étude	
Période d'incubation	Aucune étude	
Échappement immunitaire - Impact potentiel sur l'efficacité du vaccin, possibilité de réinfection		
Réinfection à partir d'une infection naturelle par rapport au variant original	• On a estimé que 28 % des cas à Manaus au Brésil étaient des réinfections, étant donné que 78 % de la population était déjà infectée (6). • Des observations cliniques de réinfection par le P.1 ont également été rapportées (52).	Une (1) étude des données de surveillance du Brésil. Faible niveau de preuve. Un (1) rapport de cas : niveau de preuve très faible
Infection découverte après la vaccination/efficacité ou efficience du vaccin par rapport au variant original	• La vaccination avec au moins une dose de CoronaVac a été associée à une réduction d'un facteur 0,50 (EV ajustée, 49,6 %; IC 95 %, 11,3 - 71,4) des chances d'infection symptomatique par le SRAS-CoV-2 pendant la période de 14 jours ou plus après avoir reçu la 1re dose. Le sexe féminin (OR, 0,50; IC à 95 %, 0,38 - 0,81) et un test RT-PCR ou antigène du SRAS-CoV-2 positif au cours de la période précédant l'étude (OR, 0,38; IC à 95 %, 0,17 - 0,87) ont été associés à une probabilité réduite d'infection symptomatique par le SRAS-CoV-2 (57).	Une (1) étude cas-témoins.
Études *in vitro*	La plupart des sérums de convalescents ont montré une activité neutralisante réduite pour le P.1 par rapport au variant original ou au B.1.1.7. Certains vaccins ont montré une activité neutralisante modeste ou nulle contre le P.1 (64-66). *Note : De nombreuses études in vitro ont été identifiées et toutes n'ont pas été extraites dans cette version.*	Niveau de preuve très faible. La réponse immunitaire est complexe, et l'absence ou la réduction des anticorps neutralisants ne signifie pas un manque de protection immunitaire. D'autres recherches sont nécessaires (voir l'examen des sciences émergentes de

		l'ASPC sur l'immunité protectrice).
Tests et diagnostics		
Test et détection par rapport au variant original	Aucun échec de test n'a été signalé pour la PCR du P.1, les tests d'antigènes ou les tests sérologiques (67).	
Épidémiologie de la propagation		
Émergence des VOC au fil du temps	De nombreuses études font état de « détections » de P.1 qui n'ont pas été résumées. Trois études montrent la croissance de P.1 dans différentes régions d'Italie et du Brésil, dont une étude axée sur le personnel de santé vacciné (22, 43, 68).	Une (1) étude de surveillance, un (1) modèle prédictif et une (1) étude transversale. Faible niveau de preuve.

CFR = taux de létalité, CI = intervalle de confiance, Ct = seuil de cycle, ICU = unité de soins intensifs, OR = rapport de cotes, PCR = réaction en chaîne par polymérase, EV = efficacité du vaccin, OR= rapport de cotes, aOR= rapport de cotes ajusté

B.1.351 (BETA)

L'ensemble de données en format Excel comprend les résumés des études individuelles et est accessible ici. Le profil détaillé des preuves élaboré pour le B.1.351 est présenté ci-dessous. Il couvre les données sur les modifications de l'efficacité de la transmission, les modifications de la gravité clinique, l'échappement immunitaire, les tests et les diagnostics, ainsi que d'autres études épidémiologiques portant principalement sur la propagation des VOC.

Tableau 4 : Profil d'évidence du B.1.351 (Beta) VOC (n=66)

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	APERÇU DES DONNÉES PROBANTES
Efficacité de la transmission		
Transmissibilité par rapport au variant original	Une transmissibilité accrue par rapport au variant original : 27 % en France pour le combiné B.1.351 et P.1 (5), 55 % (9, 10) et 20-100 % (jusqu'à 175 %) en Afrique du Sud (11)	Ces chiffres ont été estimés à partir de quatre analyses de données de surveillance. Il y a peu de cohérence entre les études. L'hétérogénéité des estimations de la transmissibilité accrue peut être due à de nombreux facteurs, notamment le moment où sont prises les estimations de la pandémie. Faible niveau de preuve.
Taux d'attaque secondaire par rapport au variant original	76.9 % ($_{Reff=4}$) (69)	Une (1) enquête sur l'épidémie. Faible niveau de preuve.
Gravité clinique		
Virulence / Gravité ou durée de la maladie par rapport au variant original	Proportion symptomatique : B.1.351 (90,3 %; 28/31) par rapport aux cas de variant original (81,4 %; 547/672, p = 0,2) (26). Hospitalisations dues B.1.351 (19,3 %) par rapport au variant original (7,5 %) p<0,001 (26). Analyse multivariable : Plus grande probabilité d'hospitalisation en raison du B.1.351 par rapport aux cas de variants originaux (aOR 3,6, IC 95 % 2,1-6,2) (26). La proportion de cas de B.1.351 en USI (2,3 %) par rapport au variant original (0,6 %), p=0,001, était plus élevée que pour le variant original (aOR 3,3, IC 95 % 1,9-5,7) (26).	Une (1) étude, données de surveillance des pays européens. Faible niveau de preuve.

Facteurs de risque de gravité par rapport au variant original	Dans une analyse stratifiée par âge, les cas de B.1.351 présentaient une probabilité d'hospitalisation 3,5 à 3,6 fois plus élevée pour les groupes d'âge 40-59 ans et 60-79 ans par rapport aux cas du variant original du même âge (26). L'admission en USI était significativement plus probable pour les cas de B.1.351 (aOR 8, IC de 95 % 3,7-17,3) âgés de 40-59 ans (26). Les conditions préexistantes étaient plus faibles pour les trois VOC (79,6 % pour le B.1.351, contre 89 % pour le variant original, p<0,001) (26).	Une (1) étude, données de surveillance des pays européens. Faible niveau de preuve.
Mortalité par rapport au variant original	Aucune différence dans les chances de décès pour les cas de B.1.351 par rapport au variant original dans l'analyse multivariable (aOR 1,1, IC 95 % 0,4-3,4) (26).	Une (1) étude, données de surveillance des pays européens. Faible niveau de preuve.
Facteurs de risque de mortalité	Aucune étude	
Charge virale par rapport au variant original	La charge virale (mesurée par les valeurs CT) des échantillons de B.1.351 était inférieure à celle des échantillons de B.1.1.7 et supérieure à celle des variants originaux (5, 44).	Deux (2) études, résultats secondaires. Niveau de preuve très faible.
Période infectieuse	Aucune étude	
Période d'incubation	Aucune étude	
Échappement immunitaire - Impact potentiel sur l'efficacité du vaccin, possibilité de réinfection		
Réinfection à partir d'une infection naturelle par rapport au variant original	Deux cas de réinfection par B.1.351 ont été signalés (53, 54).	Deux (2) observations cliniques. Niveau de preuve très faible
Infection découverte après la vaccination/efficacité ou efficience du vaccin par rapport au variant original	AstraZeneca : 10,4 % d'efficacité pour la prévention de la maladie symptomatique (58). Novavax : 57,7 % d'efficacité pour la prévention de la maladie symptomatique chez les participants séronégatifs (59). Johnson et Johnson : Les estimations de l'efficacité en Afrique du Sud étaient plus faibles que dans les autres pays. L'efficacité du vaccin (EV) contre le B.1.351 était de 52 % et 64 % pour la maladie modérée et de 73 % et 82 % pour la maladie sévère à 14 jours et 28 jours respectivement (60).	Deux (2) ECR Niveau de preuve modéré, car il n'y avait qu'une seule étude par vaccin à partir d'ECR. Des essais supplémentaires sont nécessaires pour améliorer la confiance dans ces estimations.

	Aucune percée de B.1.351 n'a été identifiée >14 jours après la deuxième dose (principalement Pfizer) dans une étude cas-témoins menée en Israël (61).	
Modèles animaux	Dans des modèles animaux soumis à l'épreuve du B.1.351, des hamsters préalablement infectés ou vaccinés ont montré une protection contre la maladie clinique (70, 71).	Deux (2) modèles animaux. Niveau de preuve très faible.
Études *in vitro*	La plupart des vaccins et des sérums de convalescence ont montré une activité neutralisante réduite pour le B.1.351 par rapport au variant original ou au B.1.1.7. Dans la plupart des études, le B.1.351 a une neutralisation plus réduite que le P.1. *Il existe de nombreuses expériences in vitro et toutes n'ont pas encore été extraites.*	Niveau de preuve très faible. La réponse immunitaire est complexe, et l'absence ou la réduction des anticorps neutralisants ne signifie pas un manque de protection immunitaire. D'autres recherches sont nécessaires (voir l'examen du groupe scientifique émergent de l'ASPC sur l'immunité protectrice).
Tests et diagnostics		
Test et détection par rapport au variant original	Aucun échec de test n'a été signalé pour la PCR du B.1.351, les tests d'antigènes ou les tests sérologiques (67).	Une étude DTA a évalué les performances de ces tests. Faible niveau de preuve.
Épidémiologie de la propagation		
Émergence des VOC au fil du temps	Les études qui font état d'une « détection » de B. 1.351 n'ont pas été résumées. Deux études montrent la croissance du B.1.351 dans différentes régions d'Afrique du Sud et de Colombie-Britannique, Canada (72, 73).	Deux (2) analyses de données de surveillance. Faible niveau de preuve.

B.1.1.7 (ALPHA)

L'ensemble de données en format Excel comprend les résumés des études individuelles et est accessible ici. Le profil détaillé des preuves élaboré pour le B.1.1.7 est présenté ci-dessous et couvre les données sur les changements dans l'efficacité de la transmission et dans la sévérité clinique, l'échappement immunitaire, les tests et les diagnostics, et d'autres études épidémiologiques portant principalement sur la propagation des VOC.

Tableau 5 : Profil de preuves de B.1.1.7 (Alpha) VOC (n=142)

CATÉGORIE	RÉSUMÉ DES PRINCIPAUX RÉSULTATS	APERÇU DES DONNÉES PROBANTES
Efficacité de la transmission		
Transmissibilité par rapport au variant original	Les estimations de la transmissibilité relative accrue ($_{1\text{-Rvoc/Variant original}}$) varient entre 34 et 118 % d'une étude à l'autre, une partie de la variation étant due au moment où les données ont été tirées dans l'émergence du B.1.1.7. Une étude note une variation dans le temps (12) et la plupart des estimations du Royaume-Uni sont plus élevées que celles des autres pays (10) : • Canada : 34 % (IC 95 % : 31-38) (3). • Royaume-Uni : 50-100 % (12), 75 % (CrI 95 % 70-80 %) (15), 52 % (IC 95 % 46 - 58 %) (16), 43-90 % (gamme CrI : 38-130 %) (13), 44-55 % (IC 95 % 38-61%) (17), 83-118 % (71-140 %) à travers le Royaume-Uni (10), 13,4-41,3 % à travers les régions du Royaume-Uni en décembre 2020 (18). • Europe : France 41 % (IC 95 % 38-44) (5) et 52 % (CrI 95 % 54-66 %) (19), Danemark 55 % (CrI 45-66 %), Suisse 74 % (CrI 66-82 %) (13) et 54 % (IC 95 % 49-65 %) (20), Norvège 24 % (IC 95 % 0-52 %) (21), Italie 55-57 % (IC 95 % 45-66 %) (22), Pays de Galles et É.-U. 65-72 % (46-104 %) (10). • É.-U. : 59 % (CrI 56-63 %) (13), 35-46 % (14). • Israël : 45 % (IC 95 % 20-60) (23). • Le Japon a estimé une augmentation de 60 % de la transmissibilité relative des VOC (non spécifiés) par rapport aux variants originaux (24). Certaines études ne fournissent pas suffisamment de données pour calculer l'efficacité accrue de la transmission, mais indiquent qu'elle était plus élevée (55). Une revue de cadrage sur la transmissibilité a inclus des études jusqu'au 21 février 2021 (9).	Cette section s'appuie sur 21 études par observation, dont des analyses de données de surveillance, des études transversales, des études de cohorte rétrospectives et des études écologiques. Ces études sont considérées comme étant de qualité faible à modérée et présentent un risque de biais de sélection, d'information et de confusion qui n'ont pas été pris en compte de manière cohérente dans toutes les études. On s'accorde à dire que le B.1.1.7 est plus transmissible et il y a un chevauchement assez important dans les estimations de l'ampleur.
Avantage sélectif	Selon un modèle d'avantage sélectif, on a estimé que le B.1.1.7 présentait un avantage	Un (1) modèle prédictif. Faible niveau de preuve.

	sélectif de 0,337 (0,336-0,339) par rapport aux variants originaux au Royaume-Uni (74).	
Taux d'attaque secondaire par rapport au variant original	• Dans une étude canadienne sur la transmission domestique, le B.1.1.7 avait un taux d'attaque secondaire (SAR) qui était RR=1,31 (IC 95 % 1,14-1,49) fois plus élevé que les non VOC et le risque était accentué pour les cas de référence asymptomatiques (RR=1,91, IC 95 % 0,96-3,80) et les cas présymptomatiques (RR=3,41, IC 95% 1,13-10,26) (4). • Dans les ménages norvégiens, le B.1.1.7 était 60 % (20 % — 114 %) plus transmissible que les variants originaux et, dans l'ensemble, le SAR était de 0,13 pour le variant original et de 0,15 pour le B.1.1.7, ce qui équivaut à 16 % (-6 % — 43 %) plus infectieux (rapport des SAR), même en tenant compte de l'âge (21). • Une étude danoise a rapporté une transmission plus élevée parmi les ménages de B.1.1.7, soit 1,50 à 1,70 fois les variantes originales. Elle a constaté que la transmissibilité en fonction de l'âge suivait un modèle en forme de U. La transmission la plus faible était celle des cas primaires dans la tranche d'âge de 10 à 30 ans, la plus élevée étant celle des enfants plus jeunes, et la plus élevée étant celle des cas âgés (25).	Trois études sur la transmission au sein des ménages. Le rapport des taux d'attaque secondaire a également été fourni comme mesure d'une transmissibilité plus élevée pour le B.1.1.7 dans certaines études basées sur des études de recherche de contacts. Les résultats étaient contradictoires dans les trois études résumées.
Interventions non pharmaceutiques par rapport au variant original	• Un modèle SEIR basé sur la situation en France décrit l'incapacité des interventions non pharmaceutiques telles que le couvre-feu et les mesures de distanciation physique à réduire le Ro du B.1.1.7 sous 1, alors que les mêmes interventions ont réussi contre les variants originaux (75). • Un modèle permettant d'examiner les scénarios de quarantaine et de test pour contrôler les importations de SRAS-CoV-2 aux États-Unis rapporte que le B.1.1.7 ne modifie pas l'efficacité des stratégies de quarantaine et de test (76).	Deux (2) modèles prédictifs. Les modèles prédictifs sont d'excellents outils pour comparer les options, mais il convient de faire preuve de prudence lors de l'extrapolation des résultats au-delà des scénarios de comparaison des modèles. Faible niveau de preuve.
Gravité clinique		

Virulence/gravité ou durée de la maladie par rapport au variant original	Cinq études montrent qu'il y a eu plus de cas d'hospitalisations liés au B.1.1.7 et deux études effectuées sur la population en général, plus d'admission en USI. • Les preuves sont contradictoires quant à savoir si le B. 1.1.7 entraîne davantage d'infections asymptomatiques : La prévalence de la maladie symptomatique était la même dans une étude italienne (28). Proportion symptomatique : 72,6 % cas de B.1.1.7 (5 365/7 390) par rapport aux cas de variants originaux (81,4 %; 547/672; p < 0.001) (26). • Plusieurs études ont fait état d'un nombre plus élevé d'hospitalisations et d'admissions en USI lié au B.1.1.7 : ○ Hospitalisation de B.1.1.7 par rapport au variant original (11 % contre 7,5 % p<0,001) et probabilité plus élevée d'hospitalisation des cas de B.1.1.7 par rapport au variant original (aOR 1,7, 95 I % CI 1,0-2,9) (26); OR 1,64 (IC 95 % 1,32-2,04) (29); OR 1,58 (IC 95 % 1,50 - 1,67) (30); (OR 1,36 IC 95 % 1,16-1,60, p=0,0002) (31). Le rapport de risque pour l'hospitalisation due au variant B.1.1.7 par rapport au variant original (aHR 1,34, IC 95 % 1,07-1,66) et la durée du séjour étaient similaires dans les deux groupes p=0,07 (32). ○ L'admission en USI était de 1,4 % pour le B.1.1.7 contre 0,6 % pour le variant original, p=0,002, ce qui représente une probabilité plus élevée d'admission en USI pour le B.1.1.7 aOR 2,3 (IC 95 % 1,4-3,5) (26). Admission en soins intensifs pour le B.1.1.7 aHR : IC 1,99 95 % 1,59 - 2,49 par rapport au variant original (33). • Parmi les cas hospitalisés, il n'y avait pas d'association entre la maladie grave et le décès parmi les variants B.1.1.7 et les variants originaux, PR ajusté 1-02 (IC 95 % : 0·76–1·38) (34).	Dix (10) études sur la sévérité, parmi lesquelles des analyses de données de surveillance, des cohortes prospectives, des cohortes rétrospectives et des études transversales, dont la plupart ont été menées au Royaume-Uni. Niveau de preuve modéré.

	• L'hypoxie (70,0 % contre 62,5 %, p=0,029) et des taux respiratoires plus élevés (p=0,001) ont été signalés parmi les admissions de cas B.1.1.7 dans deux études (35, 36).	
Facteurs de risque de gravité par rapport au variant original	Il n'y avait pas d'accord entre les études pour savoir si des facteurs de risque étaient associés à la gravité du B.1.1.7, y compris l'âge et le sexe, mais plusieurs études ont rapporté que les personnes infectées au B.1.1.7 étaient moins susceptibles d'avoir des comorbidités : • Une étude réalisée aux États-Unis n'a pas signalé de différence significative en ce qui concerne l'âge et le sexe des patients, ainsi que la durée médiane du séjour à l'hôpital (31). Dans une autre étude, la différence d'âge était statistiquement significative (37 contre 39 ans) (39). • Dans les modèles stratifiés par âge, les cas de B.1.1.7/SGTF des groupes d'âge 20-39 ans et 40-59 ans avaient, respectivement, une probabilité d'hospitalisation 3,0 et 2,3 fois plus élevée que les cas du variant original (26). • Une cohorte hospitalière entre décembre 2020 et janvier 2021 en France décrit des patients plus jeunes (63 % de >65 ans, contre 50 %) avec un âge moyen de 59,2 ans contre 70,7 ans; les patients sans comorbidité ont augmenté de 16 % à 42 % (p=0,007) (36). Les conditions préexistantes étaient plus faibles avec le B.1.1.7, par rapport au variant original (44,8 % contre 89 % p<0,001) (26). • Une étude des cas de COVID-19 hospitalisés a rapporté une plus grande proportion de femmes atteintes du B.1.1.7 (48,0 % contre 41,8 %, p=0,01), moins de patients fragiles (14,5 % contre 22,4 %, p=0,001) et une plus grande proportion de cas obèses (30,2 % contre 24,8 %, p=0,048), mais aucune différence selon l'âge ou l'ethnie (35).	Cinq (5) études sur les facteurs de risque de gravité. Il s'agit notamment d'analyses de données de surveillance, de cohortes prospectives, de cohortes rétrospectives et d'études transversales, dont la plupart ont été menées au Royaume-Uni. Niveau de preuve modéré.

Mortalité par rapport au variant original	Il existe des preuves contradictoires sur l'association entre la mortalité et l'infection B.1.1.7 : • Trois études n'ont rapporté aucune différence significative dans la mortalité globale : Italie (2,1 contre 4,1 %) (28), États-Unis (31) et aucune association avec la mortalité à 28 jours au Royaume-Uni (OR : 0,90, IC 95 % 0,57-1,41, p=0,64) (32). • Le B.1.1.7 présentait une probabilité de mortalité plus faible que le variant original dans l'analyse multivariable (aOR 0,5, IC 95 % 0,3-0,9) (26). • Cinq études ont fait état d'un risque de mortalité plus élevé : risque plus élevé de décès à 28 jours (55 %, IC 95 % : 39-72 %) (40), aHR 1,59 (IC 95 % 1,25-2,03) (33), aHR 1,67 (IC 95 % 1,34 - 2,09; P <0,0001) (34). HR 1,64 (IC 95 % 1,32 - 2,04, p <0,001), ce qui équivaut à une augmentation de 2,5 à 4,1 décès pour 1 000 cas détectés (41). • Une étude écologique du Royaume-Uni estime que le B.1.1.7 est 33 % plus mortel (42)	Neuf (9) ont fait état de la mortalité; il s'agissait d'analyses de données de surveillance, d'études écologiques, de cohortes prospectives, de cohortes rétrospectives et d'études transversales, dont la plupart ont été menées au Royaume-Uni. Niveau de preuve modéré.
Facteurs de risque de mortalité par rapport au variant original	• Les données démographiques sur les décès liés au B.1.1.7 étaient similaires chez les hommes et les femmes, mais la prévalence était plus élevée dans les groupes d'âge plus jeune que dans les groupes d'âge plus âgés (59,0 % chez les 1-34 ans contre 55,4 % chez les 85 ans ou plus) (40). Il y avait également des variations selon l'origine ethnique : noire (69,6 %), mixte ou d'origine ethnique inconnue (64,8 %), blanche (58,0 %) et asiatique (57,6 %). La variation était la plus faible dans le quintile le plus défavorisé de l'indice de privation multiple (53,9 %) (40). • Aucune preuve d'une association significative entre le B.1.1.7 et le sexe (p = 0,90), le groupe ethnique (p = 0,64) ou le groupe d'âge (p = 0,15) (33).	Une analyse des données de surveillance et une cohorte rétrospective chacune. Faible niveau de preuve.

Charge virale par rapport au variant original	Plusieurs études (n=13) ont mesuré la charge virale en tant que Ct ou copies estimées/mL pour différentes protéines cibles (généralement N et ORF1ab). Ils indiquent systématiquement que les échantillons de B.1.1.7 sont plus susceptibles de présenter des valeurs Ct plus faibles ou des charges virales estimées plus élevées. L'ordre de grandeur médian supérieur varie selon les études et la protéine cible de 2 à 10 fois la différence (5, 28, 31, 39, 44-49, 49-51).	Treize études qui étaient principalement des analyses de données de surveillance, des études de cohorte ou transversales qui ont analysé les valeurs Ct de la PCR entre les échantillons du B.1.1.7 et les échantillons autres que le B.1.1.7. Cette mesure est indirecte et toutes les études sont conçues sur la base d'observations, cependant la conclusion que les cas B.1.1.7 ont des valeurs Ct plus basses était cohérente entre les études. Le niveau de preuve est donc faible à modéré.
Période infectieuse	Les infections durent en moyenne 13,3 jours, contre 8,2 jours pour les autres variants, selon une petite étude (47).	Preuve très faible, nécessite une évaluation plus approfondie avec un échantillon plus grand et une gamme de cas plus étendue.
Période d'incubation	*Aucune étude*	
Échappement immunitaire - Impact potentiel sur l'efficacité du vaccin, possibilité de réinfection		
Réinfection à partir d'une infection naturelle par rapport au variant original	Deux études estiment le taux de réinfection à 0,7 % (IC 95 % : 0.6-0,8) (55) et chez les travailleurs de la santé du Royaume-Uni, rien ne prouve que le B.1.1.7 modifie l'étendue de la protection contre toute infection positive à la PCR chez les personnes séropositives (aIRR 0,40, IC 95 % 0,10-1,64, p=0,20) (56).	Deux études de réinfection ont inclus une analyse sur le B.1.1.7 et s'accordent à dire que le B.1.1.7 n'échappe pas à l'immunité naturelle. Ces études de cohorte sont de niveau de preuve modéré.
Modèle animal de réinfection par rapport au variant original	Les hamsters infectés par le SRAS-CoV-2 original et guéris ont tous été protégés contre une réinfection par le B.1.1.7 (70, 77).	En accord avec les études humaines et les études *in vitro*, les deux modèles animaux offrent des niveaux de preuve cohérents, mais faibles, concernant la protection contre la réinfection.
Études *in vitro* avec sérums convalescents comparés au variant original	Réduction minime de la neutralisation (64) (78) (62, 79, 80). Les sérums convalescents des cas symptomatiques légers par rapport aux cas asymptomatiques avaient un pouvoir	Il existe de nombreuses études *in vitro* et cette liste n'est pas exhaustive à ce jour. Les études *in vitro* ont systématiquement montré des

	neutralisant significativement plus élevé p=0.0005 (81)	réductions minimes ou faibles de la neutralisation du B.1.1.7 par rapport au variant original. Les études *in vitro* offrent un faible niveau de preuve même si les résultats sont cohérents.
Infection découverte après la vaccination/efficacité ou efficience du vaccin par rapport au variant original	• L'efficacité du vaccin dans un ECR britannique d'AstraZeneca était de 70,4 % (IC 95 % 43,6 - 84,5) contre la COVID-19 symptomatique causé par le variant B.1.1.7 et de 81,5 % (67,9 - 89,4) contre la COVID-19 symptomatique causé par les variants originaux (62). Dans le cas d'une infection asymptomatique ou à symptôme inconnu, l'efficacité du vaccin était plus élevée pour les infections non-B.1.1.7 (69,7 %, 33,0-86,3) que pour les infections au B.1.1.7 (28,9 %, -77,1-71,4) (62). • En Israël, où 94 % des cas étaient B.1.1.7, l'efficacité du vaccin Pfizer était >96 % 14 jours après la deuxième dose (63, 82). Les infections notées entre la première dose et jusqu'à 14 jours après la deuxième dose en Israël ont entraîné un risque plus élevé ajusté d'être positif à la PCR avec le B.1.1.7 (aOR 2,4 (IC 95 % : 1,2 à 5,1) (61). • Dans une étude britannique sur les travailleurs de la santé, rien ne prouve que le B.1.1.7 modifie l'étendue de la protection après une première dose de vaccin (aIRR=1,84, IC 95 % 0,75-4,49, p=0,18) (56). D'autres études en situation réelle au Royaume-Uni n'ont signalé aucune différence dans l'efficacité du vaccin (données combinées avec AstraZeneca et Pfizer) avec le B.1.1.7 (83). • Après la vaccination BNT162b2, la probabilité ajustée d'une activité de neutralisation inadéquate contre le variant B.1.1.7 dans le groupe d'âge le plus élevé (>80) par rapport aux travailleurs sanitaires adultes était de aOR 4,4 (1,5-12,6, p<0,007) (84).	Les ECR, les cohortes prospectives, l'analyse des données de surveillance peuvent constituer des niveaux de preuve élevés et modérés, et leur généralisation dépend de la représentativité de la population de l'échantillon par rapport à la population générale. Des conclusions cohérentes entre les études améliorent la certitude des résultats. Les séries de cas et les rapports constituent des niveaux de preuve très faibles et ne doivent être utilisés que pour formuler des hypothèses en vue de recherches ultérieures.

	• Des observations cliniques et des séries de cas font état d'infections par rupture asymptomatiques liées au B.1.1.7 chez des adultes (85) et des personnes âgées (86), ainsi que chez des travailleurs de la santé au Brésil après l'administration de CronaVac (68).	
Modèle animal de vaccination par rapport au variant original	Les hamsters vaccinés avec ChAdOx1, puis exposés au B.1.1.7 n'ont pas perdu de poids, n'ont pas présenté de pathologie pulmonaire, et aucun virus n'a été détecté dans les échantillons de tissus, alors que les témoins présentaient une pathologie pulmonaire étendue (71)	Une (1) étude en accord avec les études humaines et les études *in vitro* : ce modèle animal offre des niveaux de preuve cohérents, mais faibles, concernant la protection contre la réinfection.
Étude *in vitro* des sérums injectés par rapport au variant original	• Pfizer BNT162b2 : faible perte de neutralisation (2,1 fois) (79, 87-89). • Les personnes déjà infectées ont beaucoup plus d'anticorps neutralisants après la première dose (90). Trois semaines après la seconde dose, tous les individus vaccinés ont neutralisé le B.1.1.7 (91). • Moderna mRNA-1273 : petite perte de neutralisation (2,3 fois) (89). • AstraZeneca ChAdOx1 : petite perte de neutralisation (88). • Vaccin AZD1222/Covishield après la première dose 96,1 % avaient des anticorps (92). • Les sérums du vaccin Spoutnik V ont neutralisé efficacement le variant original du B.1.1.7 (93).	Il existe de nombreuses études *in vitro* et cette liste n'est pas exhaustive à ce jour. Les études *in vitro* ont systématiquement montré des réductions minimes ou faibles de la neutralisation du B.1.1.7 par rapport au variant original. Les études *in vitro* offrent un faible niveau de preuve même si les résultats sont cohérents.
Modèle animal de la thérapeutique par rapport au variant original	Un certain nombre d'anticorps monoclonaux testés ont protégé des souris et des hamsters contre le B.1.1.7 (94).	Les modèles animaux constituent un faible niveau de preuve.
Étude *in vitro* de la thérapeutique par rapport au variant original	Perte minime d'activité : plusieurs anticorps monoclonaux (94-97), CP polyclonaux ou préparations d'anticorps hCoV-2-IG purifiés (98).	Les études *in vitro* constituent un faible niveau de preuve offrant un aperçu préliminaire de ce qui est attendu *in vivo*.

Étude *in vitro* de l'infectivité par rapport au variant original	La capacité du pseudovirus porteur de la mutation UK-N501Y à transduire ses cellules cibles par rapport au variant original a été considérablement augmentée, jusqu'à neuf fois (79).	Les études *in vitro* constituent un faible niveau de preuve offrant un aperçu préliminaire de ce qui est attendu *in vivo*.
Tests et diagnostics		
Test et détection	La PCR est efficace pour détecter et distinguer le variant (67, 99-104). Détection du B.1.1.7 dans les eaux usées dans des proportions aussi faibles que 0,1 % du SRAS-CoV-2 (105). De multiples études font état de tests fiables pour la détection rapide des variants (67, 105).	Huit études, cinq études sur l'exactitude des tests de diagnostic, deux analyses de données de surveillance qui décrivaient également un nouveau test ou un ensemble d'amorces, et une étude *in silico* concevant des amorces. Comme elles décrivent toutes des tests différents, les études sont considérées comme individuelles et ne peuvent être résumées ensemble. Faible niveau de preuve.
Épidémiologie de la propagation		
Émergence des VOC au fil du temps	Trois études canadiennes détaillent que les cas de B.1.1.7 étaient initialement regroupés dans deux régions et ont rapidement augmenté (73). De même, deux études réalisées en Ontario ont documenté l'augmentation rapide du B.1.1.7 (3, 106). Des études ont été retenues dans de nombreux pays du monde, la plupart décrivent la première détection du B.1.1.7 à la mi-décembre ou à la fin décembre, suivie d'une augmentation rapide du variant sur 3,5 à 10 semaines. On a constaté qu'elle était devenue la souche dominante dans plusieurs études. Une étude israélienne a documenté un plateau et un déclin dans le groupe d'âge >60 ans, alors que >50 % de la population avait été vaccinée (1 dose Pfizer> 14 jours) (23). Les États-Unis ont documenté plusieurs introductions de B.1.1.7 dans le pays (14). Plusieurs études documentent la détection du B.1.1.7 dans les eaux usées (105, 107-109).	Quarante-trois études rendent compte de l'émergence et de la propagation du B.1.1.7 dans un pays ou une région au fil du temps. La plupart de ces études sont basées sur des données de surveillance, des cohortes prospectives souvent constituées de travailleurs de santé, des cohortes rétrospectives de dossiers hospitaliers, des études longitudinales et des études écologiques. Les rapports de prévalence ponctuelle ou de cas de voyageurs infectés ont été exclus de ce résumé.

Attribution au variant B.1.1.7	On a constaté qu'une augmentation de 0,1 de la proportion du B.1.1.7, en considérant la période de pré-pic, était associée à une augmentation de 35,8 % de la hauteur du pic de la deuxième vague. Au cours de la période du 1er janvier au 25 février 2021, une augmentation de 0,1 de la proportion du B.1.1.7 a été liée à une augmentation de 15,3 % du nombre cumulé de décès au cours de cette période (110).	Un modèle utilisé pour estimer la charge supplémentaire de COVID-19 due à l'augmentation de la forme physique du B.1.1.7. Preuve de faible niveau.
Facteurs de risque de propagation	Une étude écologique menée dans les régions de Toronto et de Peel, en Ontario, a montré que le taux de croissance du B.1.1.7 (11,3 %, 19,8 % et 30,8 %), l'ensemble des cas (19,0 %, 32,7 % et 48,3 %) et les cas de VOC (18,4 %, 30,8 % et 50,8 %) étaient positivement corrélés avec la proportion de travailleurs essentiels (30,4 %, 47,9 % et 63,2 %) et le revenu médian (33 000 $, 45 000 $ et 60 000 $ CAN) de la communauté, respectivement (111).	Une étude écologique est une preuve de faible niveau.
Analyse génomique de la propagation	Les résultats ne suggèrent pas que les mutations canoniques du VOC B.1.1.7 ont évolué indépendamment dans différents endroits, et indiquent une origine et une propagation du VOC B.1.1.7 à partir du Royaume-Uni (112).	Une (1) étude des données de surveillance génomique; faible niveau de preuve.

Méthodes :

Une analyse quotidienne de la littérature (publiée et prépubliée) est effectuée par le Groupe des sciences émergentes de l'ASPC. La littérature sur la COVID-19 compilée depuis le début de l'épidémie est mis à jour quotidiennement. Les recherches pour retrouver la littérature pertinente sur la COVID-19 sont effectuées dans Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square et croisées avec les centres d'information sur la COVID-19 gérés par Lancet, BMJ, Elsevier, Nature et Wiley. Le résumé quotidien et les résultats de l'analyse complète sont conservés dans une base de données Refworks et dans une liste en format Excel pouvant être consultée. L'un des objectifs est d'identifier les études sur les variants préoccupants ou faisant l'objet d'une étude. Les études ainsi identifiées figurent plus en détail dans notre base de données VOC/VOI, et les résultats sur les VOC sont extraits dans cette revue. Une vérification croisée des articles pertinents est également effectuée dans les bases de données à l'aide d'une recherche par mots clés ciblés. Ce tableau évolue au fur et à mesure que les preuves évoluent.

Variant préoccupant (VOC)	Termes de recherche
B.1.1.7, 202012/01, 501Y.V1, variant Kent (Mutations : Δ69/70, Δ144Y, (E484K*), (S494P*), N501Y, A570D, D614G, P681H)	B.1.1.7 OU 202012/02 OU 501Y.V1

* de nouveaux variants avec des mutations ont été signalés et sont classés dans la catégorie B.1.1.7 + E484K	
B.1.351, 501Y.V2, 20H/501.V2, Variant sud-africain (mutations : K417N, E484K, N501Y, D614G)	B.1.351 OU 501Y.V2
P.1, B.1.1.28.1, 501Y.V3, 20J/501Y.V3, variant du Brésil (mutations : K417N/T, E484K, N501Y, D614G)	P.1 OU B.1.1.28 OU 501Y.V3
Nouveau VOC au Royaume-Uni : 202102/02, B.1.1.7 avec mutation E484K (nom?)	Voir B.1.1.7
Variant en cours d'examen	
É.-U. : B.1.429 et B.1.427, 20C/S:452R, (mutations : L452R, D614G et S13I, W152C en 429 uniquement)	B.1.429 et B.1.427, 20C/S:452R, CAL.20C, L452R
P.2, B.1.1.28.2, au Brésil B.1.1.33	P.2 OU B.1.1.28 OU B.1.1.33
Royaume-Uni : A.28.1	A.28.1
Royaume-Uni, Mexique, Nigeria : B.1.525	B.1.525
Royaume-Uni : B.1.318	B.1.318
Russie : B.1.317	B.1.317
New York : B.1.526	B.1.526
Autres aux États-Unis : B.1.426, recombinant B.1.1.7 + B.1.429	B.1.426 et autres capturés avec la chaîne du B.1.429
P.3, VUI-21MAR-02 nommé aux Philippines (et possède les mutations E484, N501Y, P681H, LGV141-143)	P.3
B.1.617 Inde, sous-lignages : B.1.617.1 B.1.617.2 B.1.617.3 (double mutant E484Q et L452R)	B.1.617
B.1.618 Inde (triple mutant)	B.1.618

Cette revue contient les recherches publiées jusqu'au 28 avril 2021.
Chaque référence potentiellement pertinente a été examinée pour confirmer qu'elle contenait des données pertinentes et les données pertinentes ont été incluses dans l'examen.

Révision par les pairs

Le présent document a fait l'objet d'un examen par les pairs, par un expert en la matière, ainsi que d'un examen rédactionnel et d'un examen des aspects scientifiques et politiques par le Bureau du directeur scientifique.

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ANNEXE

a) LEXIQUE VOC/VOI DE L'OMS

Label de l'OMS (2021-05-27)	**Lignée Pango**	**Clade/lignée GISAID**	**Clade de souches suivantes**	**Les plus anciens échantillons documentés**	**Date de la désignation**
Alpha	B.1.1.7	GRY (anciennement GR/501Y.V1)	20I/S:501Y.V1	Royaume-Uni, sept. 2020	18-déc-2020
Bêta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	Afrique du Sud, mai-2020	18-déc-2020
Gamma	P.1	GR/501Y.V3	20J/S:501Y.V3	Brésil, nov. 2020	11-jan-2021
Delta	B.1.617.2	G/452R.V3	21A/S:478K	India, Oct-2020	VOI : 4-avril-2021

					VOC: 11 mai 2021
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	United States of America, Mar-2020	5 mars 2021
Zeta	P.2	GR	20B/S.484K	Brésil, avr-2020	17 mars 2021
Eta	B.1.525	G/484K.V3	20A/S484K	Plusieurs pays, Déc-2020	17 mars 2021
Thêta	P.3	GR	20B/S:265C	Philippines, Jan-2021	24 mars 2021
Iota	B.1.526	GH	20C/S:484K	États-Unis d'Amérique, Nov-2020	24 mars 2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	India, Oct-2020	4 avril 2021

b) AUTRES RESSOURCES

Référence	Description
Examen des preuves à ce jour sur les variants du SRAS-CoV-2 Australie En cours, dernier examen le 10 mars.	Ce tableau met en évidence les données pertinentes récentes dans les différentes catégories d'études, à l'instar de ce qui a été présenté dans les profils de cette revue.
CDC Page COV	Un résumé de chaque VOC disponible.
Rapports de situation de l'OMS; comprennent une section sur les VOC.	
Revue	
Transmission characteristics of SARS-CoV-2 variants of concern (MAR 2021) Curran, et al Data up to Feb 21, 2021	Examen rapide fait dans le cadre du reseau COVID-END.
Littérature grise	
Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 13. 2021 mai	Ce rapport a été publié pour continuer à partager la surveillance détaillée du VOC-21APR02 (B.1.617.2) et des informations sur un nouveau variant en cours d'investigation VUI-21MAY-02 (C.36.3).
Public Health England. SARS-CoV-2 variants of concern and variants under	Ce rapport a été publié pour continuer à partager la surveillance détaillée de VOC-21APR02 (B.1.617.2) et les

investigation in England. Technical briefing 12. 2021 May	renseignements sur un nouveau variant en cours d'investigation VUI-21MAY-02 (C.36.3).
ALL Public Health England. Research and analysis reports on Investigation of SARS-CoV-2 variants of concern technical briefings. 2020 Dec to present	Les rapports techniques compilent les renseignements provenant de diverses études et de la surveillance à travers le Royaume-Uni sur les COV et les VOI qui circulent. Ces rapports et publications de recherche se recoupent largement.
Public Health England. Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01 [Internet]. 2020 Dec	Le VOC (B.1.1.7) s'est développé rapidement au Royaume-Uni et a été évalué comme ayant une transmissibilité considérablement accrue.
Public Health England. Analysis of transmissibility based on genomics [Internet]. 2020 Dec	Indication que le B.1.1.7 croît de 71 % (IC 95% : 67%-75%) plus rapidement par génération (6,5 jours), mais une fréquence constante n'indique pas un avantage sélectif constant de B.1.1.7
NERVTAG. NERVTAG meeting on SARS-CoV-2 variant under investigation VUI-202012/01 [Internet]. 2020 Dec	Confiance modérée dans le fait que le B.1.1.7 démontre une augmentation substantielle de la transmissibilité par rapport aux autres variantes.
NERVTAG. Update note on B.1.1.7 severity [Internet]. 2021 Feb	Il est probable que l'infection par le VOC B.1.1.7 soit associée à un risque accru d'hospitalisations et de décès par rapport à l'infection par les virus du variant original.

Bradley, Kevin (HC/SC)

From: Tam, Dr Theresa (PHAC/ASPC) <drtheresa.tam@canada.ca>
Sent: 2021-01-02 4:23 PM
To: Stewart, Iain (PHAC/ASPC)
Cc: Njoo, Howard (PHAC/ASPC); Rendall, Jennifer (PHAC/ASPC); Ponic, Pamela (PHAC/ASPC)
Subject: Fwd: Ivermectin to treat people infected with COVID-19

This email is addressed to our Minister but perhaps something the Therapeutic task force can look at.

Sent from my iPad

Begin forwarded message:

From: [redacted]
Date: January 2, 2021 at 1:36:27 PM EST
To: patty.hajdu@parl.gc.ca
Cc: [redacted]"Tam, Dr Theresa (PHAC/ASPC)" <drtheresa.tam@canada.ca>, [redacted] justin.trudeau@parl.gc.ca
Subject: Ivermectin to treat people infected with COVID-19

The Honourable
Patty Hajdu
Member of Parliament
Minister of Health
Government of Canada

Dear Minister Hajdu,

With the backdrop of shocking death rates in Canada, even more shocking 500 daily deaths in California alone, and now a new variant of COVID-19 that has a huge increase in transmission, pretty much everybody knows that we are literally in a Global biological war. So when it came to my attention that there is the potential for a simple drug treatment in the form of oral tablets to treat people who have tested positive for COVID-19 I felt compelled to write to you.

My question is: Can Ivermectin (Stromectol) be used to treat COVID-19 or ANY coronavirus? You might find that the answer sounds extremely encouraging, and with emergency approval of its use in Canada for 'essential' working adults, we will have made a major step to help fight Covid-19 and thus ease, in a major way, the ongoing spread of the virus.

World Health Organization officials are predicting that the "destiny" of the COVID-19 virus is to become endemic, suggesting it could continue to spread through the population at a steady rate despite a global vaccination effort, and may never go away.

Several senior WHO officials also warned that the development of COVID-19 vaccines is no guarantee that the virus will be eradicated, proposing that a more realistic goal would be to reduce the threat of transmission to more manageable levels. This must be the ultimate goal in this war.

Ivermectin appears to be able to meet that goal. Ivermectin is a medication used to treat many types of parasite infestations. It can be taken by mouth or applied to the skin for external infestations. Ivermectin is used to treat infections in the body that are caused by certain parasites. The dose of this medicine will be different for different patients. Ivermectin is usually given as a single dose. To effectively treat your infection, you may need to take ivermectin again several months to a year after your first dose.

Ivermectin was discovered in 1975 and came into medical use in 1981. It is already on the WHO list of Essential Medicines with over 4 billion doses administered. Ivermectin is an FDA-approved anti-parasitic agent.

Ivermectin is currently being investigated as a treatment for coronavirus SARS-CoV-2, which is the virus that causes COVID-19. The trials so far have shown ivermectin reduces the number of cell-associated viral DNA by 99.8 % in 24 hours. Further studies are needed to determine the effectiveness of this medicine in humans with COVID-19.

Ivermectin has been trialled in treating the coronavirus SARS-CoV-2, which is the virus that causes COVID-19.
An in vitro trial has shown ivermectin reduces the number of cell-associated viral RNA by 99.8 % in 24 hours. An in vitro study is when they study cells in a laboratory and not in a living organism.
More studies are now needed to be done using ivermectin on people or animals to see how well ivermectin works against COVID-19. This is in vivo testing.

How does Ivermectin work on COVID-19?

- For the SARS-CoV-2 virus to make you sick, it has to first infect your cells.
- Then while inside the cell, the virus makes heaps of copies of itself, so it can spread around your body.
- The virus also has ways of reducing the way your body fights the infection.
- During the infection of the cell, some viral proteins go into the cell nucleus, and from here they can decrease the body's ability to fight the virus, which means the infection can get worse.
- To get into the nucleus the viral proteins need to bind a cargo transporter which lets them in.
- Ivermectin can block the cargo transporter, so the viral proteins can't get into the nucleus. This is how the scientists believe Ivermectin works against SARS-CoV-2 virus.
- By taking Ivermectin, it means the body can fight the infection like normal, because its antiviral response hasn't been reduced by the viral proteins.

About the FLCCC Alliance

The Front Line COVID-19 Critical Care Alliance was initially formed as a working group under "emergency" conditions of the early COVID-19 pandemic in response to multiple early reports of COVID patients with an inexplicably high need for prolonged mechanical ventilation and an excessive mortality associated with the prevailing "supportive care only" recommendations disseminated by the majority of national and international health care organizations.

In October 2020, the FLCCC Alliance identified, based on a review of the recent and rapidly emerging clinical trials evidence, that ivermectin has highly potent real-world, anti-viral, and anti-inflammatory properties against SARS-CoV-2 and COVID-19. This conclusion is based not only from multiple in-vitro and animal models, but from numerous clinical trials from centres and countries around the world showing repeated, consistent, large magnitude improvements in clinical outcomes when ivermectin is used not only as a prophylactic agent but also in mild, moderate, and even severe disease states. Further, data from large "natural experiments" that appear to have occurred when various regional health ministries and governmental authorities within South American countries initiated "ivermectin distribution" campaigns which then led to temporally associated decreases in case counts and case fatality rates.

Dr. Pierre Kory of the FLCCC Alliance calls on National Health authorities to immediately review medical evidence showing the efficacy of ivermectin for the prevention of COVID-19 and as an early outpatient treatment.

The FLCCC believes that their Critical Care team's testimony will help to immediately alter the trajectory of this pandemic. Take a closer look at the data and publish their findings, or those of now dozens of studies (and more to come) on the efficacy of Ivermectin in the prophylaxis and treatment of #COVID-19. The FLCCC Urges policymakers to take action.

They realize some people won't take the vaccine and not everybody responds to the vaccine. A person can still spread the virus after having received the vaccine. Ivermectin has been tested and appears effective.They take 12mg /70 kg bodyweight 1day and repeat in 3 days. Wait one month and repeat till the pandemic is under control.

When Ivermectin was used in a nursing home for scabies outbreak in France they found by accident nobody got COVID. The drug can be taken before during and after covid for those lasting symptoms. It is not 100% but it seems more effective than what they have now. It could take over a year for enough vaccine to be available, and you can get COVID again,

Again, the World Health Organization even says that COVID-19 may very well become Endemic, meaning that this virus will NEVER go away. This is an unimaginable prospect that requires everyone's attention now. Ivermectin appears to allow the world to get back on its feet, unless we think that every single living person on the planet will have been vaccinated. Realistically this never going to happen. The world needs a drug that can effectively treat the COVID-19 virus, including the seasonal flu virus, to prevent and mitigate the spread.

The data shows the ability of the drug Ivermectin to prevent COVID-19, to keep those with early symptoms from progressing to the hyper-inflammatory phase of the disease, and even to help critically ill patients recover. I ask that you urgently review the latest data and then issue guidelines for physicians, nurse-practitioners, and physician assistants to prescribe Ivermectin to battle COVID-19.

Please forward my comments to those who can work with Merck Canada, the makers of Stromectol (Ivermectin)Tablets , to start work on an effective oral dose to treat CANADIANS who have been infected with COVID-19 ASAP.

From my own perspective, this past year, I've heard and read about the COVID-19 virus thousands of times with sky high numbers of people infected and dead. Our Health Care system seems on the verge of collapse today. It is without a doubt a TOTAL DISASTER. Now all I am hearing about is catastrophic economic damage for small businesses and VACCINE, VACCINE, VACCINE thousands of times. Sounds like sheer panic to me, with politicians claiming that there is a light at the end of the tunnel or the end is in sight. What end, and how long is this tunnel? Politicians efforts to reassure the population that everything will be under control soon does not resonate with me at all. In fact, I believe the opposite is true. And I am a normally an optimistic retiree who is saving money right now. Surely we cannot keep shutting down our economies. So, the point is that vaccines

and human behaviour alone is not getting us to where we want and need to be, a FULL RECOVERY. The Government and medical scientists need to come up with a multi-pronged medical solution to end this war. As a relatively rich nation we are in a position where we can make this happen.

The I-MASK+ protocol will revolutionize the treatment of COVID-19"

The Front Line COVID-19 Critical Care Alliance has now developed a prophylactic and early outpatient combination treatment protocol for COVID-19 called I-Mask+. This protocol is centred around the use of Ivermectin, a well-known anti-parasite drug with recently discovered anti-viral and anti-inflammatory properties and a rapidly growing published medical evidence base demonstrating its unique and highly potent ability to inhibit SARS-CoV-2 replication.

Copy of the prophylaxis & Treatment Protocols for COVID-19 (Updated Dec 18, 2020) is in this link:

https://covid19criticalcare.com/wp-content/uploads/2020/11/FLCCC-Ivermectin-in-the-prophylaxis-and-treatment-of-COVID-19.pdf

PLEASE, PLEASE, get working TOGETHER on the emergency approval of Ivermectin drug for COVID-19 in Canada. I know we have all the scientific expertise and other resources we need. I am sure Dr. Kory will be happy to work with you.

Thank you,

[redacted]

c.c.
The Right Honourable Justin Trudeau, Prime Minister of Canada
Dr. Theresa Tam, Chief Public Health Officer, Government of Canada
Merck drug Representative, Merck Canada

ATIA - 19(1)

[redacted]

Bradley, Kevin (HC/SC)

From: Tam, Dr Theresa (PHAC/ASPC) <drtheresa.tam@canada.ca>
Sent: 2020-12-13 3:27 PM
To: Njoo, Howard (PHAC/ASPC)
Cc: Ponic, Pamela (PHAC/ASPC)
Subject: Fwd: Physician tells Senate, Ivermectin is a COVID "wonder drug." He states emphatically, "If You Take It, You Will Not Get Sick." (December 2020)

Can IDPCB take care of this and talk to the therapeutics task force secretariat as to whether they can review/ discuss ivermectin?

I don't know who at PHAC is linked to the work of this task force but Kim would know.

TT

Sent from my iPhone

Begin forwarded message:

> **From:** "Salvadori, Marina (PHAC/ASPC)" <marina.salvadori@canada.ca>
> **Date:** December 13, 2020 at 14:34:15 EST
> **To:** "Tam, Dr Theresa (PHAC/ASPC)" <drtheresa.tam@canada.ca>, "Njoo, Howard (PHAC/ASPC)" <howard.njoo@canada.ca>
> **Cc:** "Ponic, Pamela (PHAC/ASPC)" <pamela.ponic@canada.ca>
> **Subject: RE: Physician tells Senate, Ivermectin is a COVID "wonder drug." He states emphatically, "If You Take It, You Will Not Get Sick." (December 2020)**
>
> I kid you not, I have seen it all too - so we specifically asked the Therapeutics task Force to deal with it on Friday's meeting. [redacted]
> I would very much appreciate if you sent them an official request to make a recommendation.
> There is a lot of data, the drug is not authorized in Canada (though I have used it a ton by SAP in practice, and it is vet heartworm pill, which you can get in Canada)
>
> We have a large database on all the data. No media lines
> Marina
>
> ---
>
> **From:** Tam, Dr Theresa (PHAC/ASPC) <drtheresa.tam@canada.ca>
> **Sent:** 2020-12-13 2:24 PM
> **To:** Salvadori, Marina (PHAC/ASPC) <marina.salvadori@canada.ca>; Njoo, Howard (PHAC/ASPC) <howard.njoo@canada.ca>

Cc: Ponic, Pamela (PHAC/ASPC) <pamela.ponic@canada.ca>
Subject: Fwd: Physician tells Senate, Ivermectin is a COVID "wonder drug." He states emphatically, "If You Take It, You Will Not Get Sick." (December 2020)

Non urgent issue.

There seems to be an upswing of emails on ivermectin. Definitely a lot of enthusiasts (reminds me of the surge sometime back on hydroxy chloroquine) .

Do you know why there is a current blip in interest? Do we have lines developed on this topic?

TT

Sent from my iPhone

Begin forwarded message:

> **From:** [redacted]
> **Date:** December 13, 2020 at 14:04:01 EST
> **Subject: Physician tells Senate, Ivermectin is a COVID "wonder drug." He states emphatically, "If You Take It, You Will Not Get Sick." (December 2020)**
>
> https://www.cnsnews.com/article/national/susan-jones/physician-tells-senate-ivermectin-covid-wonder-drug-if-you-take-it-you

Bradley, Kevin (HC/SC)

From: Ministerial Services / Services Ministériels (HC/SC)
Sent: 2021-08-31 6:47 PM
Subject: HEADS UP: Advisory - Ivermectin not authorized to prevent or treat COVID-19; may cause serious health problems // Avis - L'ivermectine n'est pas homologuée pour la prévention ni pour le traitement de
Attachments: ROEB_PA_Ivermectin and COVID-19_2021-08_31_1746_FINAL_FR.docx; ROEB_PA_Ivermectin and COVID-19_2021-08_31_1746_FINAL_EN.docx

Please note that the attached *Advisory* will be issued shortly. / Veuillez noter que l'*Avis* ci-joint sera diffusé sous peu.

Merci. / Thank you.

Alexandre Richer-Brulé
(he / him | il / lui)

Communications Officer | Ministerial Communications Directorate (Ministerial Services)
Health Canada and the Public Health Agency of Canada
alexandre.richer-brule@hc-sc.gc.ca | 343-572-1833
Team email : Comms_Coordination@hc-sc.gc.ca

Agent de communications | Direction des communications ministériels (Services ministériels)
Santé Canada et l'Agence de la santé publique du Canada
alexandre.richer-brule@hc-sc.gc.ca | 343-572-1833
Courriel de l'équipe : Comms_Coordination@hc-sc.gc.ca

***Please note** emails to comms_coordination@hc-sc.gc.ca are monitored from 8 am – 9 pm during the week and from 9 am – 5 pm on weekends and holidays. The Ministerial Services inbox is only checked periodically. Please continue to cc comms_coordination@hc-sc.gc.ca on all approvals and requests.*
***Veuillez noter** que la boîte de réception comms_coordination@hc-sc.gc.ca est surveillée de 8 h à 21 h du lundi au vendredi, et de 9 h à 17 h les fins de semaine et les jours fériés. La boîte de réception des Services ministériels n'est vérifiée que périodiquement. Pour toute demande et approbation, veuillez continuer de mettre comms_coordination@hc-sc.gc.ca en cc.*

Santé Canada Health Canada

Avis

L'ivermectine n'est pas homologuée pour la prévention ni pour le traitement de la COVID-19 et peut entraîner de graves problèmes de santé

Résumé

Produit : L'ivermectine (pour usage vétérinaire ou humain), un agent antiparasitaire (comprimé, pâte, solution orale [soluté buvable], solution injectable, prémélange médicamenteux ou préparation topique).
Problème : Des consommateurs achètent de l'ivermectine à usage vétérinaire pour la prévention ou le traitement de la COVID-19.
Ce qu'il faut faire : N'utilisez pas d'ivermectine à usage vétérinaire pour prévenir ni traiter la COVID-19. Si vous avez acheté de l'ivermectine dans ce but, débarrassez-vous-en immédiatement. Consultez un professionnel de la santé si vous avez pris ce produit et que vous avez des préoccupations relatives à votre santé.

Problème

Santé Canada a reçu des signalements préoccupants concernant l'utilisation d'ivermectine à usage vétérinaire pour prévenir ou traiter la COVID-19. Les Canadiennes et les Canadiens ne devraient jamais consommer de produits de santé destinés aux animaux en raison des possibilités de graves risques de ces produits pour leur santé.

C'est pourquoi Santé Canada avise la population canadienne de ne pas prendre d'ivermectine (pour usage vétérinaire ou humain) pour la prévention ou le traitement de la COVID-19. Il n'existe pas de données probantes montrant que l'utilisation contre la COVID-19 d'ivermectine (pour usage vétérinaire ou humain) est sûre et efficace. La vente d'ivermectine à usage humain n'est permise au Canada que pour le traitement chez les gens d'infestations par vers, un type d'infection parasitaire.

L'ivermectine à usage vétérinaire peut être dangereuse pour les humains, surtout à dose élevée, et peut entraîner de graves problèmes de santé, comme des vomissements, de la diarrhée, une hypotension artérielle, des réactions allergiques, des étourdissements, des convulsions ou un coma, et même la mort. Les produits d'ivermectine destinés aux animaux contiennent des concentrations d'ivermectine plus élevées que les produits d'ivermectine destinés aux humains.

Le Ministère a connaissance de multiples signalements de personnes qui ont eu besoin d'aide médicale ou qui ont dû être hospitalisées après la prise d'ivermectine destinée aux chevaux (en anglais seulement).

Santé Canada suit de près tous les traitements curatifs envisagés contre la COVID-19, y compris les traitements faisant l'objet d'essais cliniques à l'international. Santé Canada n'a pas reçu à ce jour de présentation de médicament ni de demande d'essai clinique concernant l'utilisation d'ivermectine pour prévenir ou traiter la COVID-19.

Santé Canada encourage les fabricants de médicaments à faire des essais cliniques pour tout médicament qui pourrait être utile dans le traitement de la COVID-19; il s'agit d'une occasion pour le milieu des soins de santé de recueillir de l'information sur l'efficacité des traitements de même que les risques connexes.

Si un fabricant présentait à Santé Canada une demande concernant l'utilisation d'ivermectine pour la prévention ou le traitement de la COVID-19, le Ministère ferait une évaluation scientifique des éléments probants afin de déterminer la qualité, l'innocuité et l'efficacité de ce médicament.

Le Ministère continuera de suivre la situation et prendra les mesures qui s'imposent en temps opportun s'il obtient de nouveaux renseignements, dont de l'information sur des activités de publicité ou de vente illégales concernant l'ivermectine. Santé Canada communiquera aussi toute information relative à l'innocuité de l'ivermectine aux professionnels de la santé et aux consommateurs.

Santé Canada a déjà mis la population canadienne en garde contre les produits de santé assortis d'allégations fausses ou trompeuses sur leur capacité à traiter ou à guérir la COVID-19. Pour en savoir plus sur les vaccins et les traitements homologués par Santé Canada, consultez Canada.ca.

Contexte

La vente d'ivermectine (un médicament sur ordonnance) est permise au Canada pour le traitement chez les humains d'infestations par vers, un type d'infection parasitaire, en particulier l'anguillulose et l'onchocercose intestinales. L'ivermectine ne devrait être utilisée que pour cette indication et sous la supervision d'un professionnel de la santé. Une version pour usage vétérinaire de ce médicament est offerte pour le traitement d'infections parasitaires chez les animaux. Les humains ne devraient jamais utiliser la version pour usage vétérinaire de ce produit.

Ce que vous devriez faire

- Si vous avez acheté de l'ivermectine à usage vétérinaire pour prévenir ou traiter la COVID-19, arrêtez d'utiliser le produit et débarrassez-vous-en de l'une ou l'autre des façons ci-dessous.
    - Respectez les directives municipales ou régionales concernant l'élimination des produits chimiques et autres déchets dangereux.
    - Rapportez le produit au point de vente pour qu'il soit correctement éliminé.
- Consultez un professionnel de la santé si vous avez pris de l'ivermectine et que vous avez des préoccupations relatives à votre santé.
- Signalez tout effet secondaire de ce produit directement à Santé Canada.
- Faites une plainte à Santé Canada si vous avez de l'information concernant la publicité ou la vente illégale d'ivermectine ou de tout autre produit de santé au moyen du formulaire de plainte en ligne.

Renseignements aux médias
Santé Canada
613-957-2983
media@hc-sc.gc.ca

Renseignements au public
613-957-2991
1-866-225-0709
hcinfo.infosc@canada.ca

Health Canada Santé Canada

Advisory

Ivermectin not authorized to prevent or treat COVID-19; may cause serious health problems

Summary

Product: Ivermectin (veterinary or human versions), an antiparasitic agent (tablets, paste, oral solution, injectable solution, medicated premix or topical).
Issue: Consumers, are purchasing veterinary ivermectin to prevent or treat COVID-19.
What to do: Do not use veterinary ivermectin for the prevention or treatment of COVID-19. If you have purchased ivermectin for this purpose, discard it immediately. Consult a healthcare professional if you have used this product and have health concerns.

Issue

Health Canada has received concerning reports of the use of veterinary ivermectin to prevent or treat COVID-19. Canadians should never consume health products intended for animals because of the potential serious health dangers posed by them.

In this light, Health Canada is advising Canadians not to use either the veterinary or human drug versions of Ivermectin to prevent or treat COVID-19. There is no evidence that ivermectin in either formulation is safe or effective when used for those purposes. The human version of ivermectin is authorized for sale in Canada only for the treatment of parasitic worm infections in people.

The veterinary version of ivermectin, especially at high doses, can be dangerous for humans and may cause serious health problems such as vomiting, diarrhea, low blood pressure, allergic reactions, dizziness, seizures, coma and even death. Ivermectin products for animals have a higher concentrated dose than ivermectin products for people.

The Department is aware of multiple reports of patients in the U.S. who have required medical support and been hospitalized after using ivermectin intended for horses.

Health Canada is closely monitoring all potential therapeutic treatments for COVID-19, including treatments being studied in international clinical trials. To date, Health Canada has not received any drug submission or clinical trial application for ivermectin for the prevention or treatment of COVID-19.

For drugs that have the potential to be helpful in treating COVID-19, Health Canada encourages drug manufacturers to conduct clinical trials. This would provide an opportunity for the healthcare community to collect information on the effectiveness of the treatment and its associated risks.

Should a manufacturer provide a submission to Health Canada related to the use of ivermectin to prevent or treat COVID-19, Health Canada would conduct a scientific evaluation of the evidence to determine the drug's quality, safety and effectiveness.

Health Canada will continue to monitor the situation and will take appropriate and timely action should new information become available, including any information regarding the illegal advertising or sale of ivermectin. Health Canada will also communicate any new safety information to healthcare professionals and consumers.

Health Canada has previously warned Canadians about products making false and misleading claims to treat or cure COVID-19. For information on Health Canada authorized vaccines and treatments, visit Canada.ca.

Background

Ivermectin, a prescription drug product, is authorized for sale in Canada for the treatment of parasitic worm infections in humans, specifically intestinal strongyloidiasis and onchocerciasis, and should only be used for this purpose, under the supervision of a healthcare professional. A veterinary version of this medication is available to treat parasitic infections in animals. People should never use the veterinary version of this product.

What you should do:

- If you have purchased ivermectin for the prevention or treatment of COVID-19, stop using it and discard it:
  - Follow municipal or regional guidelines on how to dispose of chemicals and other hazardous waste; or
  - Return the product to the point of sale for proper disposal.
- Consult a healthcare professional if you have used ivermectin and have health concerns.
- Report any side effects from this product directly to Health Canada.
- Submit a complaint to Health Canada should you have any information regarding the illegal advertising or sale of ivermectin or any other health product using its online complaint form.

Media enquiries
Health Canada
(613) 957-2983
media@hc-sc.gc.ca

Public enquiries
(613) 957-2991
1-866 225-0709
hcinfo.infosc@canada.ca

IVERMECTIN
BACKGROUNDER (January 4, 2021)

Ivermectin

- Ivermectin is an antiparasitic-drug approved for use in Canada in both people and animals.
- The Merck manufactured drug stromectol (ivermectin) was authorized by Health Canada in September 2018 to treat intestinal strongyloidiasis and onchocerciasis (parasitic worms), and proven or suspected microfilaremia in patients with lymphatic filariasis caused by Wuchereria bancrofti.
- Ivermectin is widely available due to its inclusion on the WHO model list of essential medicines.
- Before the 2018 Notice of Compliance, the drug was only accessible in Canada through the Special Access Program.

COVID-19 and Clinical Trials

- Ivermectin is not approved for use in Canada or in the USA for the prevention or treatment of COVID-19. In April 2020, the USA FDA issued guidance not to use it to prevent or treat COVID-19.
- Completed clinical trials to test the use of ivermectin as a therapy to treat COVID-19 to date have had negative results (Camprubi et al, Public Library of Science, November 11, 2020). Several additional clinical trials are underway.
- A recent Australian article in Antiviral Research noted the positive impacts ivermectin had as an inhibitor of COVID-19 in vitro. It notes that more research is needed, and their work does not mean it should be used in humans.
- In Latin America, countries such as Peru, Bolivia, and Guatemala, ivermectin is over-the-counter, and has been been popularly used as a preventative against COVID-19. Its use there is so widespread that it may make clinical trials in those countries difficult.
- There are currently no authorized COVID-19 ivermectin clinical trials in Canada.

Therapeutics Task Force

- At the last TTF meeting (December 11, 2020), the TTF was asked to investigate ivermectin given recent attention to its potential utility in COVID-19 treatment.

- TTF members had a brief discussion about ivermectin, including both research studies and clinical trials, as well as its use in practice. Members found that its use as either a prophylactic or treatment lacked evidence of effectiveness. They concluded that it was not a promising therapy and that it required further investigation.
- Health Canada and Public Health Agency of Canada officials continue to be in dialogue with the TTF about further evidence, if additional clinical data emerges.