Masks for prevention of viral respiratory infections among health care workers and the public

PEER umbrella systematic review

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Abstract

Objective To determine the effect of mask use on viral respiratory infection risk.

Data sources MEDLINE and the Cochrane Library.

Study selection Randomized controlled trials (RCTs) included in at least 1 published systematic review comparing the use of masks with a control group, either in community or health care settings, on the risk of viral respiratory infections.

Synthesis In total, 11 systematic reviews were included and 18 RCTs of 26 444 participants were found, 12 in the community and 6 in health care workers. Included studies had limitations and were deemed at high risk of bias. Overall, the use of masks in the community did not reduce the risk of influenza, confirmed viral respiratory infection, influenzalike illness, or any clinical respiratory infection. However, in the 2 trials that most closely aligned with mask use in real-life community settings, there was a significant risk reduction in influenzalike illness (risk ratio [RR] = 0.83; 95% CI 0.69 to 0.99). The use of masks in households with a sick contact was not associated with a significant infection risk reduction in any analysis, no matter if masks were used by the sick individual, the healthy family members, or both. In health care workers, surgical masks were superior to cloth masks for preventing influenzalike illness (RR = 0.12; 95% CI 0.02 to 0.98), and N95 masks were likely superior to surgical masks for preventing influenzalike illness (RR = 0.78; 95% CI 0.61 to 1.00) and any clinical respiratory infections (RR = 0.95; 95% CI 0.90 to 1.00).

Conclusion This systematic review found limited evidence that the use of masks might reduce the risk of viral respiratory infections. In the community setting, a possible reduced risk of influenzalike illness was found among mask users. In health care workers, the results show no difference between N95 masks and surgical masks on the risk of confirmed influenza or other confirmed viral respiratory infections, although possible benefits from N95 masks were found for preventing influenzalike illness or other clinical respiratory infections. Surgical masks might be superior to cloth masks but data are limited to 1 trial.

Editor's key points

▸ There is growing advocacy for the use of masks in the community to prevent transmission of viral respiratory infections. This systematic review found limited evidence that the use of masks might prevent viral respiratory infections.

▸ The use of masks by a group in the community setting appears to reduce influenzalike illness in those wearing masks. The pooled analysis showed a significant risk reduction (number needed to treat [NNT] = 24). Using masks within a family 1 to 3 days after someone has developed symptoms of a viral respiratory infection does not appear to prevent transmission to family members, no matter if the masks are used by the sick individual, the healthy family members, or both.

▸ Surgical masks are likely superior to cloth masks for preventing influenzalike illness in health care workers (NNT = 50) but the results are drawn from a single trial. N95 masks are likely superior to surgical masks for preventing influenzalike illness (NNT = 100) and clinical respiratory infections (NNT = 40) in health care workers.

Points de repère du rédacteur

‣ Le port du masque est de plus en plus préconisé pour prévenir la transmission des infections respiratoires virales. Cette revue systématique a trouvé un nombre limité de données pour soutenir que l'utilisation d'un masque est susceptible de prévenir les infections respiratoires virales.

‣ Le port du masque par un groupe dans un milieu communautaire semble réduire les affections pseudo-grippales chez les personnes qui portent le masque. L'analyse regroupée a démontré une réduction significative du risque (nombre de sujets à traiter [NST] = 24). Porter un masque au sein d'une famille de 1 à 3 jours après que l'un des membres a développé des symptômes d'une infection respiratoire virale ne semble pas prévenir la transmission aux autres membres de la famille, peu importe si le masque est porté par la personne malade, par les membres en santé de la famille ou par tous.

‣ Les masques chirurgicaux sont probablement supérieurs aux masques en tissu pour prévenir les affections pseudo-grippales chez les travailleurs de la santé (NST = 50), mais ces résultats proviennent d'un seul essai. Les masques N95 sont probablement supérieurs aux masques chirurgicaux pour prévenir les affections pseudo-grippales (NST = 100) et les infections respiratoires cliniques (NST = 40) chez les travailleurs de la santé.

Les masques pour prévenir les infections respiratoires virales chez les travailleurs de la santé et la population

Revue-cadre systématique du groupe PEER

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Résumé

Objectif Déterminer les effets du port du masque sur le risque d'infections respiratoires virales.

Sources des données MEDLINE et la Bibliothèque Cochrane.

Sélection des études Les essais contrôlés randomisés (ECR) inclus dans au moins 1 revue systématique publiée comparant le port du masque avec cette pratique dans un groupe témoin, soit en milieu communautaire ou en milieu de soins de santé, portant sur le risque d'infections respiratoires virales.

Synthèse Au total, 11 revues systématiques ont été incluses, et 18 ECR auprès de 26 444 participants ont été recensés, 12 dans la communauté et 6 chez des travailleurs de la santé. Les études retenues comportaient certaines limites et étaient jugées à risque élevé de biais. Dans l'ensemble, le port du masque dans la communauté n'a pas réduit le risque de grippe, d'infections respiratoires virales confirmées, d'affections pseudo-grippales ou de toute autre infection respiratoire clinique. Toutefois, dans 2 essais qui concordaient le plus étroitement avec le port du masque dans des milieux communautaires de la vie réelle, il s'est produit une réduction significative du risque d'affections pseudo-grippales (risque relatif [RR] = 0,83; IC à 95 % de 0,69 à 0,99). Dans les analyses, le port du masque dans les familles en contact avec un membre malade n'était pas associé à une réduction significative du risque d'infection, que le masque soit utilisé ou non par le malade, par les membres en santé de la famille ou par tous. Chez les travailleurs de la santé, les masques chirurgicaux étaient supérieurs aux masques en tissu pour prévenir les affections pseudo-grippales (RR = 0,12; IC à 95 % de 0,02 à 0,98), et les masques N95 étaient probablement supérieurs aux masques chirurgicaux pour prévenir les affections pseudo-grippales (RR = 0,78; IC à 95 % de 0,61 à 1,00) et les autres infections respiratoires cliniques (RR = 0,95; IC à 95 % de 0,90 à 1,00).

Conclusion Cette revue systématique a dégagé des données probantes limitées selon lesquelles le port du masque pourrait réduire le risque d'infections respiratoires virales. Dans la communauté, une réduction possible du risque d'affections pseudo-grippales a été observée chez les porteurs de masque. Chez les travailleurs de la santé, les résultats n'ont démontré aucune différence entre les masques N95 et les masques chirurgicaux quant au risque de grippe confirmée ou d'autres infections respiratoires virales confirmées, quoique des bienfaits possibles puissent être attribués aux masques N95 pour prévenir les affections pseudo-grippales ou d'autres infections respiratoires cliniques. Les masques chirurgicaux pourraient être supérieurs aux masques en tissu, mais les données proviennent de 1 seul essai.

In the management of infectious disease, prevention is clearly preferred to treatment. For viral respiratory infections, the list of preventive options includes vaccines, physical distancing, isolation (of those who are sick), quarantine (of those who are exposed), hand hygiene, masks, and a host of other interventions. For health care workers, masks are one part of personal protective equipment (PPE), but the amount of PPE varies based on the clinical environment, current risk level, and local directives. As the coronavirus disease 2019 (COVID-19) pandemic continues to spread, so has advocacy for public mask use, with rationale based on simple precautionary principles and the potential for benefit over harm.[1,2]

In observational studies, wearing masks is associated with a lower risk of contracting viral respiratory infections.[3,4] For example, in a 2011 Cochrane systematic review published by Jefferson et al, the use of masks in case-control studies was associated with an important risk reduction (odds ratio=0.32; 95% CI 0.26 to 0.39).[3] However, the observational design is at high risk of confounding and mask use might simply be a surrogate measure for comparing more careful versus less careful people. Experimental laboratory-based studies of masks and mask types seem to provide promising and important information, but translation into meaningful clinical differences is often lacking.[5] To reduce confounding and determine the true effects of masks on infection prevention, randomized controlled trial (RCT) data are required. While there are a number of recent systematic reviews of RCTs, some meta-analyzed studies had differing designs or settings, which led to increased heterogeneity, while others focused on a very specific question.[6-9] Some meta-analyses also did not appear to account for cluster-randomized designs.[4,6,8]

Trials are under way to determine if masks can reduce the spread of COVID-19 (**ClinicalTrials.gov**: NCT04296643 and NCT04337541); however, none were published at the time of writing.[10] This systematic review examines if masks can reduce the risk of viral respiratory infections in members of the public or in health care workers. In addition, this review will examine if the type of mask influences the risk of viral respiratory infections.

—— Methods ——

We followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for completion of this systematic review.[11] Our search was modified to improve efficiency, similar to our previous systematic reviews.[12,13]

Search

Two team members (J.T. and D.P.) performed a search of MEDLINE via Ovid from inception to May 5, 2020. This search was limited to systematic reviews and used both key and MeSH terms related to masks and infectious disease transmission. In addition to MEDLINE, the search was carried out on the same date in the Cochrane Library, using the same terminology and limited to Cochrane systematic reviews. A search for RCTs published in MEDLINE or added to the MedRxiv preprint database from January 1, 2020, to May 5, 2020, was also performed to identify any new trials not captured by the included systematic reviews. Full details of the search strategy, including MeSH terms, are in Appendix 1, available from **CFPlus**.*

Study selection

For added efficiency, our modified approach involved identifying systematic reviews of studies examining the use of masks for the prevention of viral respiratory infections. Systematic reviews were included if they were published in English and they reported at least 1 RCT comparing any mask use, either alone or in combination with other interventions, with a control group. Systematic reviews were reviewed by 2 team members and disagreements were resolved by consensus and consultation with a third author when necessary. Once all relevant systematic reviews were located, RCTs from each were reviewed and included if they studied mask use for the prevention of viral respiratory infections, either in health care workers or in people in the community. The same inclusion criteria were applied to individual RCTs found in the additional search for RCTs that were published in 2020. We excluded observational studies and laboratory or surrogate experimental studies.

Data extraction

Data extraction was performed by a single reviewer, with a second author reviewing for accuracy. Extracted data included country, setting, population enrolled, population details (eg, age, sex), cluster details when appropriate (eg, universities, schools, tents), number of participants randomized, number of participants analyzed, duration of study, types of masks used, who was directed to wear masks, direction on when to wear masks (eg, all of the time, 5 hours per day), adherence to mask use, and data on 4 outcomes (confirmed influenza, any confirmed viral respiratory infection, influenzalike illness, and any clinical respiratory infection).

Quality assessment

Risk of bias for each RCT was assessed by 2 reviewers (N.D. and G.M.A.) using the Cochrane Collaboration risk-of-bias assessment tool.[14]

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*The full PRISMA flow diagram (**Appendix 1**); forest plots for all analyses (**Appendix 2**); all original trial data, cluster sizes, intracluster correlation coefficients, adjusted events, and sample sizes (**Appendix 3**); and **Table 1** and **Figure 2** are available at **www.cfp.ca**. Go to the full text of the article online and click on the **CFPlus** tab.

Analysis

We focused on 4 primary end points: confirmed influenza, confirmed viral respiratory tract infection, influenzalike illness (defined by RCT authors), and any clinical respiratory tract infection. For all RCTs, we extracted the number of events for each outcome when available and the number of participants analyzed in both the intervention group and the control group. In studies where the participants were randomized individually, we applied those values directly into our analysis. For cluster RCTs, we adjusted those values to account for clustering by dividing the numbers by the design effect, with the design effect calculated using the following equation: design effect = 1 + ([cluster size - 1] × ICC), where ICC is the intracluster correlation coefficient.[15] Cluster size was calculated by dividing the number of patients by the number of clusters. The ICC was identified in the trials whenever possible: first, if the authors provided an ICC they calculated for a specific outcome; or second, if the authors provided an expected ICC when determining sample size. If the trial did not provide an ICC, we used the ICC estimate from a similar study. This approach allowed all results to be analyzed in a similar fashion.

Meta-analyses were performed to calculate risk ratios (RRs) by pooling adjusted events and numbers. When a study had multiple arms used in the same analysis, we divided the total number of participants in the control group by the number of intervention groups to avoid counting participants more than once. Subgroup analyses were performed based on setting (community or clinical setting), mask type, control group, and who wore masks (eg, only sick people, only healthy people). Because similar designs and settings were pooled, fixed-effects models were used. We also performed random-effects sensitivity analyses in the comparisons of N95 and surgical masks, as different approaches to wearing N95 masks were used (such as fit-tested versus non–fit-tested masks, or masks worn only for higher-risk clinical scenarios versus worn all day). Absolute risks of events and numbers needed to treat (NNTs) were calculated by pooling the unadjusted event rates in the control groups (baseline risk) and applying cluster-adjusted, meta-analyzed, relative-effects estimates to attain absolute benefits.

—— Synthesis ——

The search found 544 publications, out of which 11 relevant systematic reviews were identified. Three of these systematic reviews were published in 2020. Six systematic reviews focused on the effect of masks on influenza incidence.

From these 11 systematic reviews, 18 unique RCTs were identified, including a total of 26 444 participants. No additional RCTs published in 2020 were found. The full PRISMA flow diagram is available in Appendix 1.* All 18 RCTs involved using masks to prevent the spread of viral respiratory infections and were broken into 2 primary groups: community use (n = 12) and use by health care workers (n = 6). Details of the RCTs conducted in community settings are found in **Table 1**,[16-27] available from **CFPlus**.* Details of the RCTs conducted in health care settings are found in **Table 2**.[28-33] All trials were deemed at high risk of bias. Risk-of-bias assessment for each RCT is available in Appendix 1.*

All primary results for both settings are available in **Table 3.** Forest plots for all analyses are available in Appendix 2 from **CFPlus**.* All original trial data, cluster sizes, intracluster correlation coefficients, adjusted events, and sample sizes are provided in Appendix 3 from **CFPlus**.*

Community setting

All 12 community trials were cluster RCTs. Nine of these 12 community RCTS involved an index case. In 7 of those, the index case was identified after receiving a diagnosis of influenza or influenzalike illness by a health care professional.[19,21-25,27] The patient's family was then subsequently enrolled in the trial. In the intervention arms, mask use could be recommended for everyone, just the sick person, just the healthy family members at home, or both. In 1 RCT conducted during the Hajj in Saudi Arabia, index cases were pilgrims presenting with influenzalike illness and the enrolled contacts were the individuals sleeping within 2 metres of an index case in the accommodation tents.[26] In the intervention arm, both index cases and contacts had to wear masks. In 1 trial, masks were given to 509 households in New York, NY, and participants were told to start using masks if 1 household member developed influenzalike illness (masks for the ill person and the caretaker).[20] In the 3 remaining trials, masks were used in a prespecified healthy population group, either American university students randomized by residence hall or Australian Hajj pilgrims randomized by accommodation tent.[16-18]

The use of masks in community settings in general did not reduce the risk of confirmed influenza (RR = 0.97; 95% CI 0.75 to 1.25; $I^2 = 0\%$) or confirmed viral respiratory infection (RR = 1.28; 95% CI 0.87 to 1.89; $I^2 = 0\%$). Results were not statistically significant in any subgroup analysis (masks worn by all, just the sick person, or just the healthy family members at home). The use of masks in community settings did not result in a significant risk reduction of influenzalike illness (RR = 0.91; 95% CI 0.80 to 1.03; $I^2 = 0\%$) or any clinical respiratory infection (RR = 1.06; 95% CI 0.82 to 1.36; $I^2 = 0\%$). However, for influenzalike illness, the use of masks by everyone for 6 weeks during influenza season in 2 RCTs conducted in an American university appeared to reduce risk (RR = 0.83; 95% CI 0.69 to 0.99; $I^2 = 0\%$) (**Figure 1**).[16,17] From the unadjusted numbers in the trials, the pooled control event rate (risk of influenzalike illness) was 24.7% over 6 weeks. Applying the cluster-adjusted RR, mask use would reduce this to 20.5%, a 4.2% absolute risk reduction or an NNT of 24.

Table 2. Study characteristics of mask use in health care workers to prevent viral respiratory tract infections

RCT (CLUSTER: YES OR NO)	COUNTRY, SETTING	POPULATION (AGE)	SAMPLE SIZE ENROLLED (ANALYZED)	CLUSTERS (RANDOM-IZED)	INTERVENTIONS	WHO WORE THE MASKS	MASK USE RECOMMENDATION	ADHERENCE
Jacobs et al,[28] 2009 (no)	Japan, tertiary care hospital	Health care workers (mean 35.5 y)	33 (32)	NA	Mask (17), no mask (15)	Health care workers (not sick)	Health care workers wear masks while on hospital property and performing their roles	84.3% of participants self-reported "full compliance," with the remaining complying 79% to 99% of the time (applies to both mask use and nonuse)
Loeb et al,[29] 2009 (no)	Canada, tertiary hospitals	Nurses (mean 36 y)	446 (422)	NA	Surgical masks (212), N95 masks (210)	Nurses	When caring for patients with febrile respiratory illness	All 11 participants allocated to surgical masks wore them when caring for patients admitted to unit in droplet precautions for influenza
MacIntyre et al,[30] 2011 (yes)	China, hospital (ED and respiratory wards)	Nurses, doctors, ward clerks (mean 34 y)	1441 (1441)	Cluster: unit of random-ization was hospital (15 hospitals involved, 5 per study arm)	Surgical masks (492), N95 fit-tested masks (461), N95 masks not fit-tested (488)	Health care workers	Every shift (given 3 surgical masks daily or 2 N95 masks daily)	Worn > 80% on working days: surgical, 76% (5 h/day); N95 fit, 74% (5.2 h/day); N95 no fit, 68% (4.9 h/day)
MacIntyre et al,[31] 2013 (yes)	China, hospitals (ED and respiratory wards)	Nurses, doctors (mean 33.1 y)	Surgical mask = 572 (572), targeted use of N95 = 561 (516), N95 = 581 (581), total = 1669 (166)	68 wards at 19 sites	Surgical masks (572), targeted use of N95 masks (516), N95 masks (581)	Nurses, doctors	All the time (surgical masks), as needed (targeted N95 masks), all the time (N95 masks)	66% for surgical masks, 82% for N95 targeted masks, 57% for N95 masks
MacIntyre et al,[32] 2015 (yes)	Vietnam, hospitals (ED, ICU, ID or respiratory wards, pediatric ward)	Nurse or doctor (mean 36 y)	1607 (1607)	74 wards at 14 sites	Surgical masks (580), cloth masks (2-layer cotton) (569), control (458)—"standard practice" of mask use	Nurses or doctors	Surgical masks: all the time on shift; cloth masks: all the time on shift; control: standard practice	Surgical masks 56.6%, cloth masks 56.8%, standard practice 23.6%
Radonovich et al,[33] 2019 (yes)	US, outpatient sites (clinics, primary care clinics, EDs)	Health care personnel (mean 43 y)	5180 health care personnel seasons = 4051 participants (5180 seasons)	380 clusters at 137 sites	Surgical masks (2668 person-seasons), N95 masks (2512 person-seasons)—note that 1 person could be in different arms each of the 4 seasons	Those involved in direct patient care	Whenever positioned within 6 ft of a patient with suspected or confirmed respiratory illness	N95: 65.2% always, 24.2% sometimes; surgical: 65.1% always, 25.1% sometimes

ED—emergency department, ICU—intensive care unit, ID—infectious disease, NA—not applicable, RCT—randomized controlled trial, US—United States.

Table 3. Outcomes for mask use to prevent viral respiratory tract infections

MASK USERS	CONFIRMED INFLUENZA		CONFIRMED VIRAL RESPIRATORY INFECTION		INFLUENZALIKE ILLNESS		ANY RESPIRATORY INFECTION	
	RCTS (N*)	RR[†] (95% CI)	RCTS (N*)	RR[†] (95% CI)	RCTS (N*)	RR[†] (95% CI)	RCTS (N*)	RR[†] (95% CI)
Community								
• Community members	2 (1683)	0.93 (0.50-1.75)	0 (0)	NA	2 (1683)	0.83 (0.69-0.99)	0 (0)	NA
• Families—sick wearing masks	0 (0)	NA	1 (597)	0.98 (0.06-15.54)	2 (794)	0.89 (0.48-1.66)	1 (597)	0.65 (0.19-2.28)
• Families—healthy wearing masks	1[‡] (220)	2.18 (0.25-19.16)	1[‡] (220)	2.96 (0.67-13.02)	1[‡] (220)	1.17 (0.62-2.18)	0 (0)	NA
• Families—healthy and sick wearing masks	4 (1168)	0.95 (0.71-1.26)	0 (0)	NA	4 (1377)	1.09 (0.86-1.37)	0 (0)	NA
• Communities staying in tents	1 (2317)	1.24 (0.33-4.59)	2 (2386)	1.18 (0.79-1.78)	1 (69)	0.56 (0.29-1.08)	1 (1810)	1.08 (0.83-1.40)
• Families—given masks before illness	0 (0)	NA	0 (0)	NA	1 (789)	0.90 (0.60-1.34)	0 (0)	NA
Health care workers								
• Masks vs nothing	1 (431)	Not estimable	1 (431)	0.90 (0.33-2.44)	1 (431)	0.26 (0.01-6.42)	2 (463)	0.74 (0.36-1.54)
• N95 masks vs surgical masks	4[§] (6039)	1.10 (0.91-1.32)	4[§] (6059)	0.95 (0.83-1.07)	4[§] (6662)	0.78 (0.61-1.00)	3[§] (5033)	0.95 (0.90-1.00)
• Surgical masks vs cloth masks	1 (717)	0.98 (0.06-15.62)	1 (717)	0.62 (0.31-1.26)	1 (717)	0.12 (0.02-0.98)	1 (717)	0.62 (0.34-1.11)

NA—not applicable, RCT—randomized controlled trial, RR—risk ratio.
*The number of patients is modified (reduced) to account for clustering.
[†]Results calculated using a fixed-effects model.
[‡]One RCT had 2 arms.
[§]Two of the included RCTs had 2 arms, so 4 RCTs would be 6 arms and 3 RCTs would be 5 arms.

Note that the definition of influenzalike illness in these trials was broad: cough and at least 1 constitutional symptom such as chills or fever.
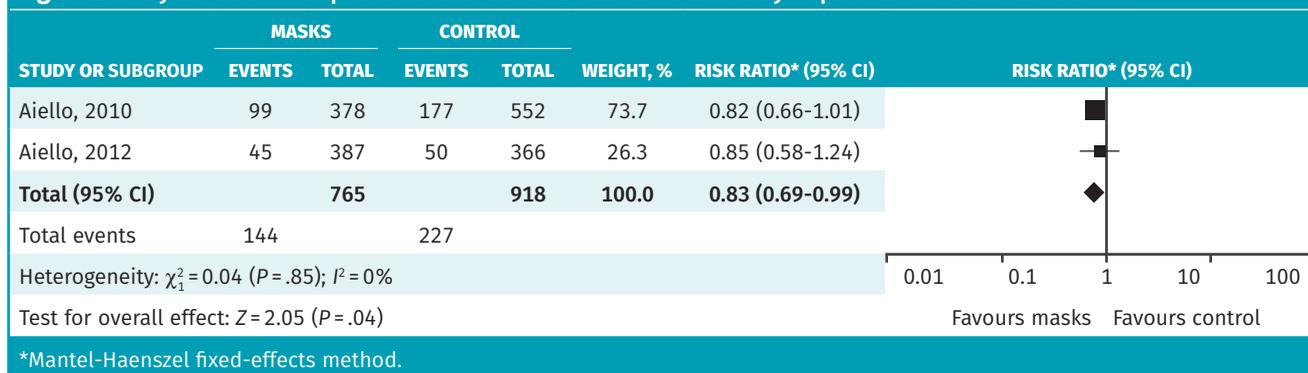
Health care setting

Of the 6 RCTs examining the use of masks by health care workers, only 2 had a control group assigned to "no mask."[28,32] In these trials, masks did not reduce influenzalike illness (RR=0.26; 95% CI 0.01 to 6.42; 1 trial), any clinical respiratory infection (RR=0.74; 95% CI 0.36 to 1.54; I^2=0%), confirmed influenza (RR=not estimable), or confirmed viral respiratory infection (RR=0.90; 95% CI 0.33 to 2.44; 1 trial), compared with no masks. However, 1 of the 2 trials was small (32 participants) and the overall number of events were low (only 62 cases of clinical respiratory infections in a total of 1160 individuals), leading to imprecision (see analysis 2 in Appendix 2 for forest plots*). Also, in the larger trial (n=1038 for the "masks" vs "no mask" comparison), there was a

high contamination rate, with 99% of the participants assigned to the control group reporting use of some kind of mask at some point.[32]

In the only trial comparing surgical masks to cloth masks, results favoured surgical masks over cloth masks for reduction in clinical or laboratory-confirmed viral respiratory infections; however, results were not statistically significant (see analysis 3 in Appendix 2 for forest plots*).[32] Influenzalike illness risk was significantly reduced with surgical masks compared with cloth masks (RR=0.12; 95% CI 0.02 to 0.98) but again event rates were low, explaining the large CI and limiting the certainty of this result. The event rate in the cloth mask group (risk of influenzalike illness) was 2.3% over 4 weeks. Applying the cluster-adjusted RR, surgical mask use would reduce this risk to 0.3%, a 2% absolute risk reduction or an NNT of 50.

Four RCTs compared the use of surgical and N95 masks in health care workers.[29-31,33] In these trials, we

Figure 1. Daily mask use compared with no mask use in the community to prevent influenzalike illness

| STUDY OR SUBGROUP | MASKS | | CONTROL | | WEIGHT, % | RISK RATIO* (95% CI) | RISK RATIO* (95% CI) |
	EVENTS	TOTAL	EVENTS	TOTAL			
Aiello, 2010	99	378	177	552	73.7	0.82 (0.66-1.01)	
Aiello, 2012	45	387	50	366	26.3	0.85 (0.58-1.24)	
Total (95% CI)		**765**		**918**	**100.0**	**0.83 (0.69-0.99)**	
Total events	144		227				
Heterogeneity: $\chi_1^2 = 0.04$ ($P = .85$); $I^2 = 0\%$							0.01 0.1 1 10 100
Test for overall effect: $Z = 2.05$ ($P = .04$)							Favours masks Favours control

*Mantel-Henszel fixed-effects method.

found no difference between surgical and N95 masks for confirmed influenza (RR = 1.10; 95% CI 0.91 to 1.32; $I^2 = 0\%$) or confirmed viral respiratory infections (RR = 0.95; 95% CI 0.83 to 1.07; $I^2 = 0\%$). N95 masks appeared to reduce influenzalike illness (RR = 0.78; 95% CI 0.61 to 1.00; $I^2 = 0\%$) and any clinical respiratory infection risk (RR = 0.95; 95% CI 0.90 to 1.00; $I^2 = 55\%$) (**Figure 2**, available from **CFPlus***). The pooled control event rate for influenzalike illness from the unadjusted numbers in the trials was 4.6% over 4 to 12 weeks (1 study looking at 12 weeks each year for 4 years for a total of 48 weeks, but using individual seasons as their unit of analysis) of wearing surgical masks. Applying the cluster-adjusted RR, N95 masks would reduce this risk to 3.6%, a 1% absolute risk reduction or an NNT of 100. The pooled control event rate for clinical respiratory infections from the unadjusted numbers in the trials was 49.4% over 4 to 12 weeks of wearing surgical masks. Applying the cluster-adjusted RR, N95 masks would reduce this risk to 46.9%, meaning a 2.5% absolute risk reduction or an NNT of 40. To account for differences in trials comparing N95 masks with surgical masks, the random-effects model demonstrated a more conservative estimate with wider CIs, reducing the certainty of a positive effect for both influenzalike illness (RR = 0.79, 95% CI 0.62 to 1.02; $I^2 = 0\%$) and for any clinical respiratory infections (RR = 0.69, 95% CI 0.47 to 1.03; $I^2 = 55\%$) (see analyses 4 and 5 in Appendix 2 for full details*).

—— Discussion ——

Overall, we found limited evidence regarding the effect of masks on viral respiratory infections both in the community and in health care settings, and most of our analyses showed no statistically significant differences. Particularly in the community setting, we wanted to see if there was any evidence of benefit from systematic use of masks by the general public outside the home, but we found no such evidence. Our review still identified 4 potentially important results. First, the use of masks by a group in the community setting appears to reduce influenzalike illness in those wearing masks. While community

trials that most closely aligned with mask use in real-life community settings[16,17] did not show significant effects individually, our pooled analysis showed a significant risk reduction (NNT = 24). Although the same analysis showed no significant risk reduction in confirmed influenza or confirmed viral infection, we believe influenzalike illness to be an important patient-oriented outcome. Second, using masks within a family 1 to 3 days after someone has developed symptoms of a viral respiratory infection does not appear to prevent transmission to family members, no matter if the masks are used by the sick individual, the healthy family members, or both. Third, surgical masks are likely superior to cloth masks for preventing influenzalike illness in health care workers (NNT = 50) but our results are drawn from a single study.[32] Finally, N95 masks are likely superior to surgical masks for preventing influenzalike illness (NNT = 100) and clinical respiratory infections (NNT = 40) in health care workers.

There are many potential reasons why RCTs of masks have historically struggled to find statistically significant differences. The first reason might simply be that masks do not prevent viral respiratory infection transmission. Some have postulated this is because people are not using them properly, are touching their face while wearing one, or are wearing it below their nose. Some also postulated that people using masks might feel protected and might be less likely to follow other recommendations such as hand hygiene. A host of other reasons are also mentioned; however, these reasons remain hypotheses and are unproven. Second, many studies use a cluster-randomized design, which reduces the power of these studies and the ability to achieve statistical significance if indeed there is a difference. Third, adherence to wearing masks is generally poor. For example, most community studies found that mask use averaged 5 hours or less per day or that 50% of participants or less reported regular use. And even if the rate of adherence was high, most studies had particular instructions about when to wear masks. For example, all studies in health care workers instructed participants in the mask group to wear a mask when at work. These individuals could therefore get infected outside work, while not wearing

a mask, influencing the overall results. In other studies, mask use in the control arm also occurred. For example, in the Alfelali et al study,[18] masks were used by 25% of the individuals in the mask arm and 14% of the individuals in the no-mask arm, making any separation of effect less likely. Fourth, in some studies, event rates (eg, influenza cases) were low, with only a few cases in either arm, reducing the ability of the studies to determine statistical significance if there is a difference. This might explain why we found significant risk reduction in more common outcomes such as influenzalike illness and any clinical respiratory infection, but not in confirmed influenza or confirmed viral infection. Fifth, many community studies were designed to start mask use after the index patient was seen by a health care provider. This means patients might have already been sick at home for 1 to 3 days, potentially transmitting infection to family members and making mask introduction potentially useless. Sixth, in health care workers, the comparison of N95 and surgical masks might not reach clear statistical significance simply because both interventions might be beneficial and differences between the 2 might be small. It might also be because in all but 1 study, N95 masks and surgical masks were used either all the time at work or when caring for patients with respiratory illness, not only in particularly high-risk situations (eg, intubation) where N95 masks might be more warranted.

Strengths and limitations

This review has some limitations and notable remaining uncertainties. Our search strategy pertaining to articles published before January 1, 2020, was limited to systematic reviews and might have kept us from finding additional RCTs. Our review did not identify any study examining if wearing masks in a large community such as a city prevents the spread of infection to others. The studies of sick individuals wearing masks to prevent secondary infection of family members did not find benefit but had many limitations as mentioned above; therefore, we do not yet know if wearing masks will reduce transmission to others. Our review did not find any RCTs investigating the use of cloth masks in the community. Pertaining to the use of masks by health care workers, we found no studies conducted in primary care and almost no evidence comparing wearing a mask to not wearing a mask. The last is not surprising, as having a "no mask" group raises ethical issues. Regarding our analysis, the most correct way to perform these meta-analyses is debatable. We chose to pool event rates adjusted only for clustering rather than pooling adjusted effect estimates (eg, odds ratios). We did this to minimize other adjustments and to avoid selecting results with different levels of adjustment, thereby maintaining consistency in our analysis. Also, we tried to pool studies into similar clinical scenarios and believed fixed-effects models for analysis were the most appropriate.

We did, however, perform random-effects sensitivity analyses when some design heterogeneity remained (as in the comparison of N95 and surgical masks in health care workers). We looked at multiple outcomes and did numerous analyses, therefore increasing the probability that our positive results are owing to chance. Our review focused on masks and did not account for the benefits of other preventive interventions such as hand hygiene or additional PPE.

Our review also had a number of strengths including using only RCTs, adjustment for cluster design, and pooling based on clinical similarities.

None of the studies in this review included patients with COVID-19. Future research on masks for the prevention of COVID-19 in health care and community settings is very much needed. In addition, the effect of cloth masks on community prevention of any viral respiratory illness should be studied, as no RCTs exist to assess their benefit.

Conclusion

Our systematic review found limited evidence that the use of masks might reduce the risk of viral respiratory infections. In the community setting, we found no evidence regarding the use of masks by the general public outside the home, but found a possible reduction on the risk of influenzalike illness when masks are used at least a few hours a day by a population in a specific area. In health care workers, the best available evidence shows no difference between N95 masks and surgical masks on the risk of confirmed influenza or other confirmed viral respiratory infections, although our results suggest a possible benefit from N95 masks for preventing influenzalike illness or other clinical respiratory infections. Surgical masks might be superior to cloth masks but data are limited to 1 trial. ✺

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