SENATE SELECT COMMITTEE ON COVID-19
Australian Government's response to the COVID-19 pandemic
THURSDAY, 25 JUNE 2020

Raina MacIntyre

I would like to add a supplementary statement to Dr Collignon's statement where he refers to me by name "*As to Raina's data, my understanding is that N95 masks, for the vast majority of people, have no benefit over surgical masks but are better than cloth masks. Surgical masks seem to me to be the thing you need to have large numbers of, but obviously you do need N95s for certain people as well. But we need an appropriate stockpile that's looked after adequately.* "

I am not certain to what Dr Collignon is referring. To state that N95 respirators are no better than surgical masks "but better than cloth masks" is not aligned with the available scientific evidence. I wish to clarify this, as his use of my name may mislead others to believe I am in agreement with his opinion.

I have published the largest body of randomised clinical trials of masks and respirators in the world, and two large health worker trials which I published show that respirators protect but surgical masks do not. I have attached a systematic review I published in 2020 summarising that and other evidence, as well as the misconstrued argument that surgical masks and respirators are equivalent.

In addition, the WHO-commissioned study by Chu et al in the Lancet (attached) shows that respirators provide 96% protection and surgical masks, 67%. My commentary in the Lancet is also attached, which discusses implications for health workers. I also cite in this commentary the clear evidence that SARS-CoV-2 is aerosol transmitted. The continued denial of this evidence places our health workers at risk. The guidelines should recommend a respirator for health workers caring for COVID-19 patients. A surgical mask is not adequate and places Australian health workers at risk of infection. We should employ the precautionary principle in protecting them.

Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis

*Derek K Chu, Elie A Akl, Stephanie Duda, Karla Solo, Sally Yaacoub, Holger J Schünemann, on behalf of the COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors**

Summary

Background Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19 and is spread person-to-person through close contact. We aimed to investigate the effects of physical distance, face masks, and eye protection on virus transmission in health-care and non-health-care (eg, community) settings.

Methods We did a systematic review and meta-analysis to investigate the optimum distance for avoiding person-to-person virus transmission and to assess the use of face masks and eye protection to prevent transmission of viruses. We obtained data for SARS-CoV-2 and the betacoronaviruses that cause severe acute respiratory syndrome, and Middle East respiratory syndrome from 21 standard WHO-specific and COVID-19-specific sources. We searched these data sources from database inception to May 3, 2020, with no restriction by language, for comparative studies and for contextual factors of acceptability, feasibility, resource use, and equity. We screened records, extracted data, and assessed risk of bias in duplicate. We did frequentist and Bayesian meta-analyses and random-effects meta-regressions. We rated the certainty of evidence according to Cochrane methods and the GRADE approach. This study is registered with PROSPERO, CRD42020177047.

Findings Our search identified 172 observational studies across 16 countries and six continents, with no randomised controlled trials and 44 relevant comparative studies in health-care and non-health-care settings (n=25 697 patients). Transmission of viruses was 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). Face mask use could result in a large reduction in risk of infection (n=2647; aOR 0·15, 95% CI 0·07 to 0·34, RD −14·3%, −15·9 to −10·7; low certainty), with stronger associations with N95 or similar respirators compared with disposable surgical masks or similar (eg, reusable 12–16-layer cotton masks; $p_{interaction}$=0·090; posterior probability >95%, low certainty). Eye protection also was associated with less infection (n=3713; aOR 0·22, 95% CI 0·12 to 0·39, RD −10·6%, 95% CI −12·5 to −7·7; low certainty). Unadjusted studies and subgroup and sensitivity analyses showed similar findings.

Interpretation The findings of this systematic review and meta-analysis support physical distancing of 1 m or more and provide quantitative estimates for models and contact tracing to inform policy. Optimum use of face masks, respirators, and eye protection in public and health-care settings should be informed by these findings and contextual factors. Robust randomised trials are needed to better inform the evidence for these interventions, but this systematic appraisal of currently best available evidence might inform interim guidance.

Funding World Health Organization.

Introduction

As of May 28, 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected more than 5·85 million individuals worldwide and caused more than 359 000 deaths.[1] Emergency lockdowns have been initiated in countries across the globe, and the effect on health, wellbeing, business, and other aspects of daily life are felt throughout societies and by individuals. With no effective pharmacological interventions or vaccine available in the imminent future, reducing the rate of infection (ie, flattening the curve) is a priority, and prevention of infection is the best approach to achieve this aim.

SARS-CoV-2 spreads person-to-person through close contact and causes COVID-19. It has not been solved if

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See Online for appendix

Research in context

Evidence before this study

We searched 21 databases and resources from inception to May 3, 2020, with no restriction by language, for studies of any design evaluating physical distancing, face masks, and eye protection to prevent transmission of the viruses that cause COVID-19 and related diseases (eg, severe acute respiratory syndrome [SARS] and Middle East respiratory syndrome [MERS]) between infected individuals and people close to them (eg, household members, caregivers, and health-care workers). Previous related meta-analyses have focused on randomised trials and reported imprecise data for common respiratory viruses such as seasonal influenza, rather than the pandemic and epidemic betacoronaviruses causative of COVID-19 (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), SARS (SARS-CoV), or MERS (MERS-CoV). Other meta-analyses have focused on interventions in the health-care setting and have not included non-health-care (eg, community) settings. Our search did not retrieve any systematic review of information on physical distancing, face masks, or eye protection to prevent transmission of SARS-CoV-2, SARS-CoV, and MERS-CoV.

Added value of this study

We did a systematic review of 172 observational studies in health-care and non-health-care settings across 16 countries and six continents; 44 comparative studies were included in a meta-analysis, including 25 697 patients with COVID-19, SARS, or MERS. Our findings are, to the best of our knowledge, the first to rapidly synthesise all direct information on COVID-19 and, therefore, provide the best available evidence to inform optimum use of three common and simple interventions to help reduce the rate of infection and inform non-pharmaceutical interventions, including pandemic mitigation in non-health-care settings. Physical distancing of 1 m or more was associated with a much lower risk of infection, as was use of face masks (including N95 respirators or similar and surgical or similar masks [eg, 12–16-layer cotton or gauze masks]) and eye protection (eg, goggles or face shields). Added benefits are likely with even larger physical distances (eg, 2 m or more based on modelling) and might be present with N95 or similar respirators versus medical masks or similar. Across 24 studies in health-care and non-health-care settings of contextual factors to consider when formulating recommendations, most stakeholders found these personal protection strategies acceptable, feasible, and reassuring but noted harms and contextual challenges, including frequent discomfort and facial skin breakdown, high resource use linked with the potential to decrease equity, increased difficulty communicating clearly, and perceived reduced empathy of care providers by those they were caring for.

Implications of all the available evidence

In view of inconsistent guidelines by various organisations based on limited information, our findings provide some clarification and have implications for multiple stakeholders. The risk for infection is highly dependent on distance to the individual infected and the type of face mask and eye protection worn. From a policy and public health perspective, current policies of at least 1 m physical distancing seem to be strongly associated with a large protective effect, and distances of 2 m could be more effective. These data could also facilitate harmonisation of the definition of exposed (eg, within 2 m), which has implications for contact tracing. The quantitative estimates provided here should inform disease-modelling studies, which are important for planning pandemic response efforts. Policy makers around the world should strive to promptly and adequately address equity implications for groups with currently limited access to face masks and eye protection. For health-care workers and administrators, our findings suggest that N95 respirators might be more strongly associated with protection from viral transmission than surgical masks. Both N95 and surgical masks have a stronger association with protection compared with single-layer masks. Eye protection might also add substantial protection. For the general public, evidence shows that physical distancing of more than 1 m is highly effective and that face masks are associated with protection, even in non-health-care settings, with either disposable surgical masks or reusable 12–16-layer cotton ones, although much of this evidence was on mask use within households and among contacts of cases. Eye protection is typically underconsidered and can be effective in community settings. However, no intervention, even when properly used, was associated with complete protection from infection. Other basic measures (eg, hand hygiene) are still needed in addition to physical distancing and use of face masks and eye protection.

SARS-CoV-2 might spread through aerosols from respiratory droplets; so far, air sampling has found virus RNA in some studies[2–4] but not in others.[5–8] However, finding RNA virus is not necessarily indicative of replication-competent and infection-competent (viable) virus that could be transmissible. The distance from a patient that the virus is infective, and the optimum person-to-person physical distance, is uncertain. For the currently foreseeable future (ie, until a safe and effective vaccine or treatment becomes available), COVID-19 prevention will continue to rely on non-pharmaceutical interventions, including pandemic mitigation in community settings.[9] Thus, quantitative assessment of physical distancing is relevant to inform safe interaction and care of patients with SARS-CoV-2 in both health-care and non-health-care settings. The definition of close contact or potentially exposed helps to risk stratify, contact trace, and develop guidance documents, but these definitions differ around the globe.

To contain widespread infection and to reduce morbidity and mortality among health-care workers and others in contact with potentially infected people, jurisdictions have issued conflicting advice about physical or social distancing. Use of face masks with or

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without eye protection to achieve additional protection is debated in the mainstream media and by public health authorities, in particular the use of face masks for the general population;[10] moreover, optimum use of face masks in health-care settings, which have been used for decades for infection prevention, is facing challenges amid personal protective equipment (PPE) shortages.[11]

Any recommendations about social or physical distancing, and the use of face masks, should be based on the best available evidence. Evidence has been reviewed for other respiratory viral infections, mainly seasonal influenza,[12,13] but no comprehensive review is available of information on SARS-CoV-2 or related betacoronaviruses that have caused epidemics, such as severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS). We, therefore, systematically reviewed the effect of physical distance, face masks, and eye protection on transmission of SARS-CoV-2, SARS-CoV, and MERS-CoV.

Methods

Search strategy and selection criteria

To inform WHO guidance documents, on March 25, 2020, we did a rapid systematic review.[14] We created a large international collaborative and we used Cochrane methods[15] and the GRADE approach.[16] We prospectively submitted the systematic review protocol for registration on PROSPERO (CRD42020177047; appendix pp 23–29). We have followed PRISMA[17] and MOOSE[18] reporting guidelines (appendix pp 30–33).

From database inception to May 3, 2020, we searched for studies of any design and in any setting that included patients with WHO-defined confirmed or probable COVID-19, SARS, or MERS, and people in close contact with them, comparing distances between people and COVID-19 infected patients of 1 m or larger with smaller distances, with or without a face mask on the patient, or with or without a face mask, eye protection, or both on the exposed individual. The aim of our systematic review was for quantitative assessment to ascertain the physical distance associated with reduced risk of acquiring infection when caring for an individual infected with SARS-CoV-2, SARS-CoV, or MERS-CoV. Our definition of face masks included surgical masks and N95 respirators, among others; eye protection included visors, faceshields, and goggles, among others.

We searched (up to March 26, 2020) MEDLINE (using the Ovid platform), PubMed, Embase, CINAHL (using the Ovid platform), the Cochrane Library, COVID-19 Open Research Dataset Challenge, COVID-19 Research Database (WHO), Epistemonikos (for relevant systematic reviews addressing MERS and SARS, and its COVID-19 Living Overview of the Evidence platform), EPPI Centre living systematic map of the evidence, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, relevant documents on the websites of governmental and other relevant organisations, reference lists of included papers, and relevant systematic reviews.[19,20] We hand-searched (up to May 3, 2020) preprint servers (bioRxiv, medRxiv, and Social Science Research Network First Look) and coronavirus resource centres of *The Lancet*, *JAMA*, and *N Engl J Med* (appendix pp 3–5). We did not limit our search by language. We initially could not obtain three full texts for evaluation, but we obtained them through interlibrary loan or contacting a study author. We did not restrict our search to any quantitative cutoff for distance.

Data collection

We screened titles and abstracts, reviewed full texts, extracted data, and assessed risk of bias by two authors and independently, using standardised prepiloted forms (Covidence; Veritas Health Innovation, Melbourne, VIC, Australia), and we cross-checked screening results using artificial intelligence (Evidence Prime, Hamilton, ON, Canada). We resolved disagreements by consensus. We extracted data for study identifier, study design, setting, population characteristics, intervention and comparator characteristics, quantitative outcomes, source of funding

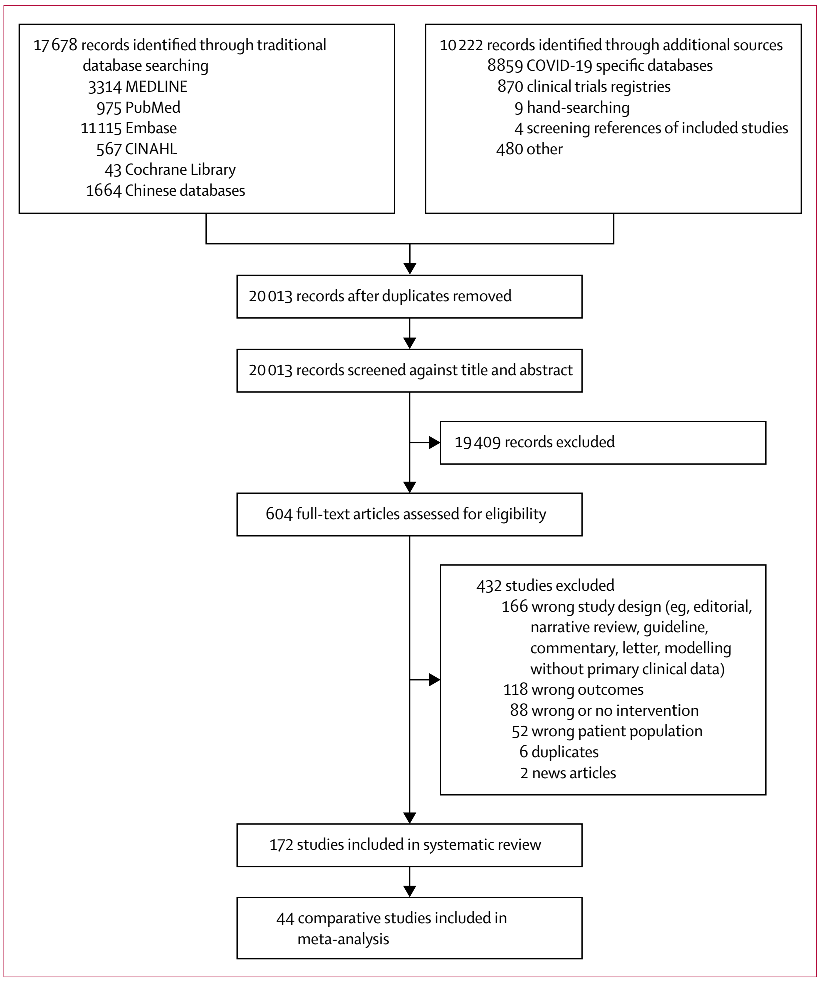

Figure 1: **Study selection**

	Population size (n)	Country	Setting	Disease caused by virus	Case definition (WHO)	Adjusted estimates	Risk of bias*
Alraddadi et al (2016)[34]	283	Saudi Arabia	Health care	MERS	Confirmed	Yes	********
Arwady et al (2016)[35]	79	Saudi Arabia	Non-health care (household and family contacts)	MERS	Confirmed	No	******
Bai et al (2020)[36]	118	China	Health care	COVID-19	Confirmed	No	*****
Burke et al (2020)[37]	338	USA	Health care and non-health care (including household and community)	COVID-19	Confirmed	No	****
Caputo et al (2006)[38]	33	Canada	Health care	SARS	Confirmed	No	*****
Chen et al (2009)[39]	758	China	Health care	SARS	Confirmed	Yes	*******
Cheng et al (2020)[40]	226	China	Non-health care (household and family contacts)	COVID-19	Confirmed	No	******
Ha et al (2004)[42]	117	Vietnam	Health care	SARS	Confirmed	No	**
Hall et al (2014)[43]	48	Saudi Arabia	Health care	MERS	Confirmed	No	***
Heinzerling et al (2020)[44]	37	USA	Health care	COVID-19	Confirmed	No	****
Ho et al (2004)[45]	372	Taiwan	Health care	SARS	Confirmed	No	********
Ki et al (2019)[47]	446	South Korea	Health care	MERS	Confirmed	No	******
Kim et al (2016)[48]	9	South Korea	Health care	MERS	Confirmed	No	*****
Kim et al (2016)[49]	1169	South Korea	Health care	MERS	Confirmed	No	******
Lau et al (2004)[50]	2270	China	Non-health care (households)	SARS	Probable	Yes	******
Liu et al (2009)[51]	477	China	Health care	SARS	Confirmed	Yes	*****
Liu et al (2020)[52]	20	China	Non-health care (close contacts)	COVID-19	Confirmed	No	*******
Loeb et al (2004)[53]	43	Canada	Health care	SARS	Confirmed	No	**
Ma et al (2004)[54]	426	China	Health care	SARS	Confirmed	Yes	*********
Nishiura et al (2005)[55]	115	Vietnam	Health care	SARS	Confirmed	Yes	********
Nishiyama et al (2008)[56]	146	Vietnam	Health care	SARS	Confirmed	Yes	******
Olsen et al (2003)[57]	304	China	Non-health care (airplane)	SARS	Confirmed	No	******
Park et al (2004)[58]	110	USA	Health care	SARS	Confirmed	No	**********
Park et al (2016)[59]	80	South Korea	Health care	MERS	Confirmed and probable	No	***
Peck et al (2004)[60]	26	USA	Health care	SARS	Confirmed	No	*********
Pei et al (2006)[61]	443	China	Health care	SARS	Confirmed	No	********
Rea et al (2007)[62]	8662	Canada	Non-health care (community contacts)	SARS	Probable	No	****
Reuss et al (2014)[63]	81	Germany	Health care	MERS	Confirmed	No	*****
Reynolds et al (2006)[64]	153	Vietnam	Health care	SARS	Confirmed	No	***
Ryu et al (2019)[65]	34	South Korea	Health care	MERS	Confirmed	No	******
Scales et al (2003)[66]	69	Canada	Health care	SARS	Probable	No	**
Seto et al (2003)[67]	254	China	Health care	SARS	Confirmed	Yes	********
Teleman et al (2004)[68]	86	Singapore	Health care	SARS	Confirmed	Yes	********
Tuan et al (2007)[69]	212	Vietnam	Non-health care (household and community contacts)	SARS	Confirmed	Yes	******
Van Kerkhove et al (2019)[46]	828	Saudi Arabia	Non-health care (dormitory)	MERS	Confirmed	Yes	********
Wang et al (2020)[41]	493	China	Health care	COVID-19	Confirmed	Yes	****

(Table 1 continues on next page)

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	n	Country	Setting	Disease caused by virus	Case definition (WHO)	Adjusted estimates	Risk of bias*
(Continued from previous page)							
Wang et al (2020)[70]	5442	China	Health care	COVID-19	Confirmed	No	*****
Wiboonchutikul et al (2016)[71]	38	Thailand	Health care	MERS	Confirmed	No	*****
Wilder-Smith et al (2005)[72]	80	Singapore	Health care	SARS	Confirmed	No	********
Wong et al (2004)[73]	66	China	Health care	SARS	Confirmed	No	*****
Wu et al (2004)[74]	375	China	Non-health care (community)	SARS	Confirmed	Yes	********
Yin et al (2004)[75]	257	China	Health care	SARS	Confirmed	Yes	******
Yu et al (2005)[76]	74	China	Health care	SARS	Confirmed	No	*******
Yu et al (2007)[77]	124 wards	China	Health care	SARS	Confirmed	Yes	*******

Across studies, mean age was 30–60 years. SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome. *The Newcastle-Ottawa Scale was used for the risk of bias assessment, with more stars equalling lower risk.

Table 1: **Characteristics of included comparative studies**

and reported conflicts of interests, ethics approval, study limitations, and other important comments.

Outcomes

Outcomes of interest were risk of transmission (ie, WHO-defined confirmed or probable COVID-19, SARS, or MERS) to people in health-care or non-health-care settings by those infected; hospitalisation; intensive care unit admission; death; time to recovery; adverse effects of interventions; and contextual factors such as acceptability, feasibility, effect on equity, and resource considerations related to the interventions of interest. However, data were only available to analyse intervention effects for transmission and contextual factors. Consistent with WHO, studies generally defined confirmed cases with laboratory confirmation (with or without symptoms) and probable cases with clinical evidence of the respective infection (ie, suspected to be infected) but for whom confirmatory testing either had not yet been done for any reason or was inconclusive.

Data analysis

Our search did not identify any randomised trials of COVID-19, SARS, or MERS. We did a meta-analysis of associations by pooling risk ratios (RRs) or adjusted odds ratios (aORs) depending on availability of these data from observational studies, using DerSimonian and Laird random-effects models. We adjusted for variables including age, sex, and severity of source case; these variables were not the same across studies. Because between-study heterogeneity can be misleadingly large when quantified by I^2 during meta-analysis of observational studies,[21,22] we used GRADE guidance to assess between-study heterogeneity.[21] Throughout, we present RRs as unadjusted estimates and aORs as adjusted estimates.

We used the Newcastle-Ottawa scale to rate risk of bias for comparative non-randomised studies corresponding to every study's design (cohort or case-control).[23,24] We planned to use the Cochrane Risk of Bias tool 2.0 for randomised trials,[25] but our search did not identify any eligible randomised trials. We synthesised data in both narrative and tabular formats. We graded the certainty of evidence using the GRADE approach. We used the GRADEpro app to rate evidence and present it in GRADE evidence profiles and summary of findings tables[26,27] using standardised terms.[28,29]

For more on the **GRADEpro app** see https://www.gradepro.org

We analysed data for subgroup effects by virus type, intervention (different distances or face mask types), and setting (health care *vs* non-health care). Among the studies assessing physical distancing measures to prevent viral transmission, the intervention varied (eg, direct physical contact [0 m], 1 m, or 2 m). We, therefore, analysed the effect of distance on the size of the associations by random-effects univariate meta-regressions, using restricted maximum likelihood, and we present mean effects and 95% CIs. We calculated tests for interaction using a minimum of 10 000 Monte Carlo random permutations to avoid spurious findings.[30] We formally assessed the credibility of potential effect-modifiers using GRADE guidance.[21] We did two sensitivity analyses to test the robustness of our findings. First, we used Bayesian meta-analyses to reinterpret the included studies considering priors derived from the effect point estimate and variance from a meta-analysis of ten randomised trials evaluating face mask use versus no face mask use to prevent influenza-like illness in health-care workers.[31] Second, we used Bayesian meta-analyses to reinterpret the efficacy of N95 respirators versus medical masks on preventing influenza-like illness after seasonal viral (mostly influenza) infection.[13] For these sensitivity analyses, we used hybrid Metropolis-Hastings and Gibbs sampling, a 10 000 sample burn-in, 40 000 Markov chain Monte Carlo samples, and we tested non-informative and sceptical priors (eg, four time variance)[32,33] to inform

	Country	Respirator (0=no)	Distance (m)	Events, further distance (n/N)	Events, shorter distance (n/N)	RR (95% CI)	% weight (random)
MERS							
Van Kerkhove et al (2019)[46]	Saudi Arabia	0	0	8/774	11/54	0·05 (0·02–0·12)	5·5
Arwady et al (2016)[35]	Saudi Arabia	0	1	1/10	8/20	0·25 (0·04–1·73)	2·6
Ki et al (2019)[47]	South Korea	1	2	2/29	4/42	0·72 (0·14–3·70)	3·2
Park et al (2016)[59]	South Korea	0	2	0/3	5/25	0·59 (0·04–8·77)	1·6
Hall et al (2014)[43]	Saudi Arabia	1	1	0/5	0/43	(Not calculable)	0
Wiboonchutikul et al (2019)[71]	Thailand	1	1	0/16	0/22	(Not calculable)	0
Reuss et al (2014)[63]	Germany	1	2	0/12	0/69	(Not calculable)	0
Ryu et al (2019)[65]	South Korea	1	2	0/7	0/27	(Not calculable)	0
Random, subtotal (I^2=75%)				**11/856**	**28/302**	**0·23 (0·04–1·20)**	**12·9**
SARS							
Scales et al (2003)[66]	Canada	0	0	1/12	6/19	0·35 (0·05–2·57)	2·6
Ma et al (2004)[54]	China	1	0*	4/149	43/294	0·18 (0·07–0·50)	5·0
Nishiyama et al (2008)[56]	Vietnam	0	0	1/12	26/73	0·23 (0·03–1·57)	2·7
Tuan et al (2007)[69]	Vietnam	0	0	3/123	6/57	0·23 (0·06–0·89)	3·9
Rea et al (2007)[62]	Canada	0	1	18/3493	41/647	0·08 (0·05–0·14)	6·6
Chen et al (2009)[39]	China	0	1*	28/314	63/445	0·63 (0·41–0·96)	6·9
Lau et al (2004)[50]	China	0	1	39/965	136/1124	0·33 (0·24–0·47)	7·1
Liu et al (2009)[51]	China	0	0	14/133	39/341	0·92 (0·52–1·64)	6·5
Pei et al (2006)[61]	China	0	1	8/61	139/382	0·36 (0·19–0·70)	6·2
Wong et al (2004)[73]	China	0	1	0/4	3/3	0·11 (0·01–1·63)	1·7
Teleman et al (2004)[68]	Singapore	1	1	4/9	32/77	1·07 (0·49–2·33)	5·8
Reynolds et al (2006)[64]	Vietnam	0	1	5/38	17/29	0·22 (0·09–0·54)	5·5
Olsen et al (2003)[57]	China	0	1·5	9/84	11/35	0·34 (0·16–0·75)	5·8
Wong et al (2004)[73]	China	0	2	0/4	4/8	0·20 (0·01–3·00)	1·6
Loeb et al (2004)[53]	Canada	1	2*	0/11	8/40	0·20 (0·01–3·24)	1·6
Yu et al (2005)[76]	China	1	2	17/54	13/20	0·48 (0·29–0·81)	6·6
Peck et al (2004)[60]	USA	1	1	0/3	0/38	(Not calculable)	0
Random, subtotal (I^2=75%)				**151/5469**	**587/3632**	**0·35 (0·23–0·52)**	**76·1**
COVID-19							
Bai et al (2020)[36]	China	1	0	0/76	12/42	0·02 (0·001–0·37)	1·5
Burke et al (2020)[37]	USA	0	0	0/13	2/2	0·04 (0·003–0·68)	1·6
Liu et al (2020)[52]	China	0	1	0/17	2/3	0·04 (0·003–0·76)	1·5
Cheng et al (2020)[40]	Taiwan	0	1*	5/47	7/36	0·55 (0·19–1·58)	4·8
Heinzerling et al (2020)[44]	USA	0	1·8	0/4	3/33	0·97 (0·06–16·14)	1·5
Burke et al (2020)[37]	USA	1	0	0/50	0/76	(Not calculable)	0
Burke et al (2020)[37]	USA	0	2	0/41	0/37	(Not calculable)	0
Random, subtotal (I^2=59%)				**5/248**	**26/229**	**0·15 (0·03–0·73)**	**10·9**
Unadjusted estimates, overall (I^2=73%)				**167/6573**	**641/4163**	**0·30 (0·20–0·44)**	**100·0**
Adjusted estimates, overall (1 MERS, 8 SARS)						**aOR 0·18 (0·09–0·38)**	
						aRR 0·20 (0·10–0·41)	
Interaction by type of virus p=0·49							

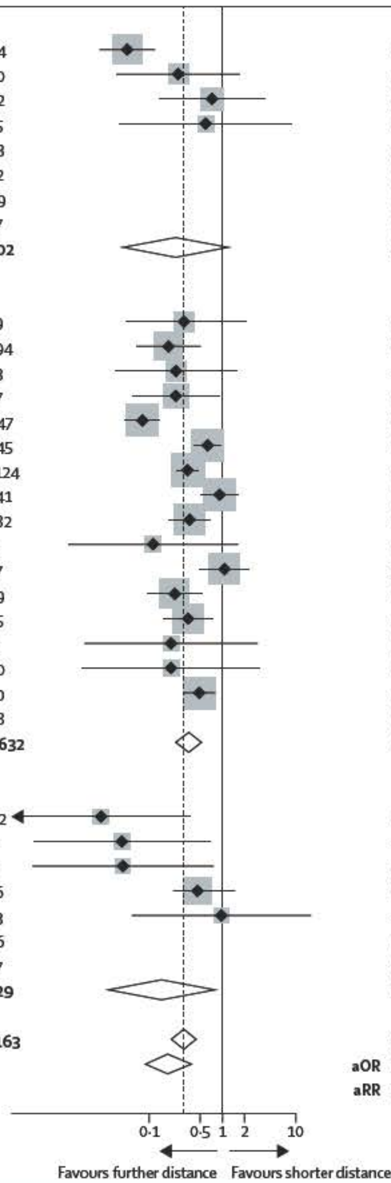

Figure 2: **Forest plot showing the association of COVID-19, SARS, or MERS exposure proximity with infection**
SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome. RR=relative risk. aOR=adjusted odds ratio. aRR=adjusted relative risk. *Estimated values; sensitivity analyses excluding these values did not meaningfully alter findings.

mean estimates of effect, 95% credibility intervals (CrIs), and posterior distributions. We used non-informative hyperpriors to estimate statistical heterogeneity. Model convergence was confirmed in all cases with good mixing in visual inspection of trace plots, autocorrelation plots, histograms, and kernel density estimates in all scenarios. Parameters were blocked, leading to acceptance of approximately 50% and efficiency greater than 1% in all cases (typically about 40%). We did analyses using Stata version 14.3.

Role of the funding source

The funder contributed to defining the scope of the review but otherwise had no role in study design and data collection. Data were interpreted and the report drafted and submitted without funder input, but according to contractual agreement, the funder provided review at the time of final publication. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

	Studies and participants	Relative effect (95% CI)	Anticipated absolute effect (95% CI), eg, chance of viral infection or transmission		Difference (95% CI)	Certainty*	What happens (standardised GRADE terminology)[29]
			Comparison group	Intervention group			
Physical distance ≥1 m *vs* <1 m	Nine adjusted studies (n=7782); 29 unadjusted studies (n=10 736)	aOR 0·18 (0·09 to 0·38); unadjusted RR 0·30 (95% CI 0·20 to 0·44)	Shorter distance, 12·8%	Further distance, 2·6% (1·3 to 5·3)	–10·2% (–11·5 to –7·5)	Moderate†	A physical distance of more than 1 m probably results in a large reduction in virus infection; for every 1 m further away in distancing, the relative effect might increase 2·02 times
Face mask *vs* no face mask	Ten adjusted studies (n=2647); 29 unadjusted studies (n=10 170)	aOR 0·15 (0·07 to 0·34); unadjusted RR 0·34 (95% CI 0·26 to 0·45)	No face mask, 17·4%	Face mask, 3·1% (1·5 to 6·7)	–14·3% (–15·9 to –10·7)	Low‡	Medical or surgical face masks might result in a large reduction in virus infection; N95 respirators might be associated with a larger reduction in risk compared with surgical or similar masks§
Eye protection (faceshield, goggles) *vs* no eye protection	13 unadjusted studies (n=3713)	Unadjusted RR 0·34 (0·22 to 0·52)¶	No eye protection, 16·0%	Eye protection, 5·5% (3·6 to 8·5)	–10·6% (–12·5 to –7·7)	Low‖	Eye protection might result in a large reduction in virus infection

Table based on GRADE approach.[26,29] Population comprised people possibly exposed to individuals infected with SARS-CoV-2, SARS-CoV, or MERS-CoV. Setting was any health-care or non-health-care setting. Outcomes were infection (laboratory-confirmed or probable) and contextual factors. Risk (95% CI) in intervention group is based on assumed risk in comparison group and relative effect (95% CI) of the intervention. All studies were non-randomised and evaluated using the Newcastle-Ottawa Scale; some studies had a higher risk of bias than did others but no important difference was noted in sensitivity analyses excluding studies at higher risk of bias; we did not further rate down for risk of bias. Although there was a high I^2 value (which can be exaggerated in non-randomised studies)[21] and no overlapping CIs, point estimates generally exceeded the thresholds for large effects and we did not rate down for inconsistency. We did not rate down for indirectness for the association between distance and infection because SARS-CoV-2, SARS-CoV, and MERS-CoV all belong to the same family and have each caused epidemics with sufficient similarity; there was also no convincing statistical evidence of effect-modification across viruses; some studies also used bundled interventions but the studies include only those that provide adjusted estimates. aOR=adjusted odds ratio. RR=relative risk. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. SARS-CoV=severe acute respiratory syndrome coronavirus. MERS-CoV=Middle East respiratory syndrome coronavirus. *GRADE category of evidence; high certainty (we are very confident that the true effect lies close to that of the estimate of the effect); moderate certainty (we are moderately confident in the effect estimate; the true effect is probably close to the estimate, but it is possibly substantially different); low certainty (our confidence in the effect estimate is limited; the true effect could be substantially different from the estimate of the effect); very low certainty (we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect). †The effect is very large considering the thresholds set by GRADE, particularly at plausible levels of baseline risk, which also mitigated concerns about risk of bias; data also suggest a dose–response gradient, with associations increasing from smaller distances to 2 m and beyond, by meta-regression; we did not rate up for this domain alone but it further supports the decision to rate up in combination with the large effects. ‡The effect was very large, and the certainty of evidence could be rated up, but we made a conservative decision not to because of some inconsistency and risk of bias; hence, although the effect is qualitatively highly certain, the precise quantitative effect is low certainty. §In a subgroup analysis comparing N95 respirators with surgical or similar masks (eg, 12–16-layer cotton), the association was more pronounced in the N95 group (aOR 0·04, 95% CI 0·004–0·30) compared with other masks (0·33, 0·17–0·61; $p_{interact\ on}$=0·090); there was also support for effect-modification by formal analysis of subgroup credibility. ¶Two studies[54,75] provided adjusted estimates with n=295 in the eye protection group and n=406 in the group not wearing eye protection; results were similar to the unadjusted estimate (aOR 0·22, 95% CI 0·12–0·39). ‖The effect is large considering the thresholds set by GRADE assuming that ORs translate into similar magnitudes of RR estimates; this mitigates concerns about risk of bias, but we conservatively decided not to rate up for large or very large effects.

Table 2: **GRADE summary of findings**

Results

We identified 172 studies for our systematic review from 16 countries across six continents (figure 1; appendix pp 6–14, 41–47). Studies were all observational in nature; no randomised trials were identified of any interventions that directly addressed the included study populations. Of the 172 studies, 66 focused on how far a virus can travel by comparing the association of different distances on virus transmission to people (appendix pp 42–44). Of these 66 studies, five were mechanistic, assessing viral RNA, virions, or both cultured from the environment of an infected patient (appendix p 45).

44 studies were comparative[34–77] and fulfilled criteria for our meta-analysis (n=25 697; figure 1; table 1). We used these studies rather than case series and qualitative studies (appendix pp 41–47) to inform estimates of effect. 30 studies[34,37,41–45,47–51,53–56,58–61,64–70,72,74,75] focused on the association between use of various types of face masks and respirators by health-care workers, patients, or both with virus transmission. 13 studies[34,37–39,47,49,51,54,58,60,61,65,75] addressed the association of eye protection with virus transmission.

Some direct evidence was available for COVID-19 (64 studies, of which seven were comparative in design),[36,37,40,41,44,52,70] but most studies reported on SARS (n=55) or MERS (n=25; appendix pp 6–12). Of the 44 comparative studies, 40 included WHO-defined confirmed cases, one included both confirmed and probable cases, and the remaining three studies included probable cases. There was no effect-modification by case-definition (distance $p_{interaction}$=0·41; mask $p_{interaction}$=0·46; all cases for eye protection were confirmed). Most studies reported on bundled interventions, including different components of PPE and distancing, which was usually addressed by statistical adjustment. The included studies all occurred during recurrent or novel outbreak settings of COVID-19, SARS, or MERS.

Risk of bias was generally low-to-moderate after considering the observational designs (table 1), but both within studies and across studies the overall findings were similar between adjusted and unadjusted estimates. We did not detect strong evidence of publication bias in the body of evidence for any intervention (appendix pp 15–18). As we did not use case series data to inform estimates of effect of each intervention, we did not systematically rate risk of bias of these data. Therefore, we report further only those studies with comparative data.

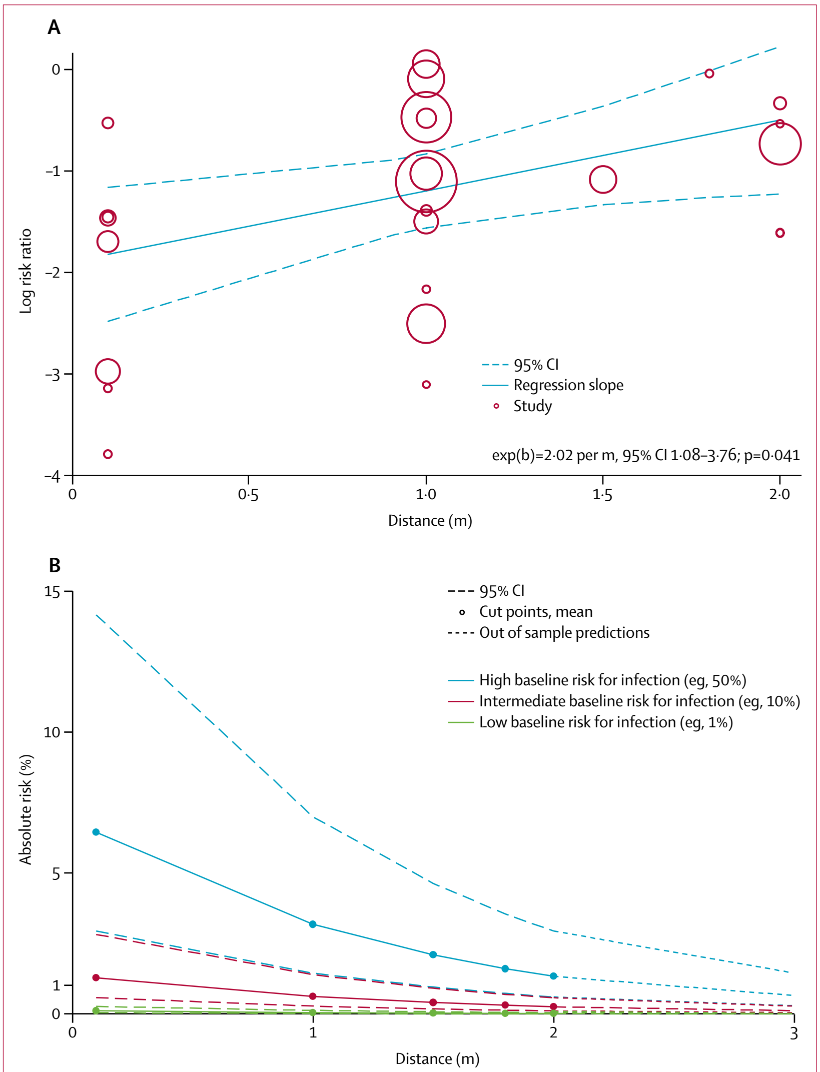

Figure 3: **Change in relative risk with increasing distance and absolute risk with increasing distance**
Meta-regression of change in relative risk with increasing distance from an infected individual (A). Absolute risk of transmission from an individual infected with SARS-CoV-2, SARS-CoV, or MERS-CoV with varying baseline risk and increasing distance (B). SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. SARS-CoV=severe acute respiratory syndrome coronavirus. MERS-CoV=Middle East respiratory syndrome coronavirus.

Across 29 unadjusted and nine adjusted studies,[35–37,39,40,43,44,46,47,50–54,56,57,59–66,68,69,71,73,76] a strong association was found of proximity of the exposed individual with the risk of infection (unadjusted n=10736, RR 0·30, 95% CI 0·20 to 0·44; adjusted n=7782, aOR 0·18, 95% CI 0·09 to 0·38; absolute risk [AR] 12·8% with shorter distance *vs* 2·6% with further distance, risk difference [RD] –10·2%, 95% CI –11·5 to –7·5; moderate certainty; figure 2; table 2; appendix p 16). Although there were six studies on COVID-19, the association was seen irrespective of causative virus ($p_{interaction}$=0·49), health-care setting versus non-health-care setting ($p_{interaction}$=0·14), and by type of face mask ($p_{interaction}$=0·95; appendix pp 17, 19). However, different studies used different distances for the intervention. By meta-regression, the strength of association was larger with increasing distance (2·02 change in RR per m, 95% CI 1·08 to 3·76; $p_{interaction}$=0·041; moderate credibility subgroup effect; figure 3A; table 2). AR values with increasing distance given different degrees of baseline risk are shown in figure 3B, with potential values at 3 m also shown.

Across 29 unadjusted studies and ten adjusted studies,[34,37,41–45,47–51,53–56,58–61,64–70,72,74,75] the use of both N95 or similar respirators or face masks (eg, disposable surgical masks or similar reusable 12–16-layer cotton masks) by those exposed to infected individuals was associated with a large reduction in risk of infection (unadjusted n=10 170, RR 0·34, 95% CI 0·26 to 0·45; adjusted studies n=2647, aOR 0·15, 95% CI 0·07 to 0·34; AR 3·1% with face mask *vs* 17·4% with no face mask, RD –14·3%, 95% CI –15·9 to –10·7; low certainty; figure 4; table 2; appendix pp 16, 18) with stronger associations in health-care settings (RR 0·30, 95% CI 0·22 to 0·41) compared with non-health-care settings (RR 0·56, 95% CI 0·40 to 0·79; $p_{interaction}$=0·049; low-to-moderate credibility for subgroup effect; figure 4; appendix p 19). When differential N95 or similar respirator use, which was more frequent in health-care settings than in non-health-care settings, was adjusted for the possibility that face masks were less effective in non-health-care settings, the subgroup effect was slightly less credible ($p_{interaction}$=0·11, adjusted for differential respirator use; figure 4). Indeed, the association with protection from infection was more pronounced with N95 or similar respirators (aOR 0·04, 95% CI 0·004 to 0·30) compared with other masks (aOR 0·33, 95% CI 0·17 to 0·61; $p_{interaction}$=0·090; moderate credibility subgroup effect; figure 5). The interaction was also seen when additionally adjusting for three studies that clearly reported aerosol-generating procedures ($p_{interaction}$=0·048; figure 5). Supportive evidence for this interaction was also seen in within-study comparisons (eg, N95 had a stronger protective association compared with surgical masks or 12–16-layer cotton masks); both N95 and surgical masks also had a stronger association with protection versus single-layer masks.[38,39,51,53,54,61,66,67,75]

We did a sensitivity analysis to test the robustness of our findings and to integrate all available information on face mask treatment effects for protection from COVID-19. We reconsidered our findings using random-effects Bayesian meta-analysis. Although non-informative priors showed similar results to frequentist approaches (aOR 0·16, 95% CrI 0·04–0·40), even using informative priors from the most recent meta-analysis on the effectiveness of masks versus no masks to prevent influenza-like illness (RR 0·93, 95% CI 0·83–1·05)[31] yielded a significant association with protection from COVID-19 (aOR 0·40, 95% CrI 0·16–0·97; posterior probability for RR <1, 98%). Minimally informing (25% influence with or without four-fold smaller mean effect size) the most recent and rigorous meta-analysis of the effectiveness of N95

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	Country	Respirator (0=no)	Infection	Events, face mask (n/N)	Events, no face mask (n/N)	RR (95% CI)	% weight (random)
Health-care setting							
Scales et al (2003)[66]	Canada	0	SARS	3/16	4/15	0·70 (0·19–2·63)	3·2
Liu et al (2009)[51]	China	0	SARS	8/123	43/354	0·54 (0·26–1·11)	6·7
Pei et al (2006)[61]	China	0	SARS	11/98	61/115	0·21 (0·12–0·38)	7·9
Yin et al (2004)[75]	China	0	SARS	46/202	31/55	0·40 (0·29–0·57)	10·3
Park et al (2016)[59]	South Korea	0	MERS	3/24	2/4	0·25 (0·06–1·06)	2·8
Kim et al (2016)[48]	South Korea	0	MERS	0/7	1/2	0·13 (0·01–2·30)	0·8
Heinzerling et al (2020)[44]	USA	0	COVID-19	0/31	3/6	0·03 (0·002–0·54)	0·9
Nishiura et al (2005)[55]	Vietnam	0	SARS	8/43	17/72	0·79 (0·37–1·67)	6·5
Nishiyama et al (2008)[56]	Vietnam	0	SARS	17/61	14/18	0·36 (0·22–0·58)	9·0
Reynolds et al (2006)[64]	Vietnam	0	SARS	8/42	14/25	0·34 (0·17–0·69)	6·7
Loeb et al (2004)[53]	Canada	1	SARS	3/23	5/9	0·23 (0·07–0·78)	3·6
Wang et al (2020)[41]	China	1	COVID-19	0/278	10/215	0·04 (0·002–0·63)	0·9
Seto et al (2003)[67]	China	1	SARS	0/51	13/203	0·15 (0·01–2·40)	0·9
Wang et al (2020)[70]	China	1	COVID-19	1/1286	119/4036	0·03 (0·004–0·19)	1·7
Alraddadi et al (2016)[34]	Saudi Arabia	1	MERS	6/116	12/101	0·44 (0·17–1·12)	5·0
Ho et al (2004)[45]	Singapore	1	SARS	2/62	2/10	0·16 (0·03–1·02)	1·9
Teleman et al (2004)[68]	Singapore	1	SARS	3/26	33/60	0·21 (0·07–0·62)	4·2
Wilder-Smith et al (2005)[72]	Singapore	1	SARS	6/27	39/71	0·40 (0·19–0·84)	6·5
Ki et al (2019)[47]	South Korea	1	MERS	0/218	6/230	0·08 (0·005–1·43)	0·8
Kim et al (2016)[49]	South Korea	1	MERS	1/444	16/308	0·04 (0·01–0·33)	1·6
Hall et al (2014)[43]	Saudi Arabia	1	MERS	0/42	0/6	(Not calculable)	0
Ryu et al (2019)[65]	South Korea	1	MERS	0/24	0/10	(Not calculable)	0
Park et al (2004)[58]	USA	1	SARS	0/60	0/45	(Not calculable)	0
Peck et al (2004)[60]	USA	1	SARS	0/13	0/19	(Not calculable)	0
Burke et al (2020)[37]	USA	1	COVID-19	0/64	0/13	(Not calculable)	0
Ha et al (2004)[42]	Vietnam	1	SARS	0/61	0/1	(Not calculable)	0
Random subtotal (I^2=50%)				**126/3442**	**445/6003**	**0·30 (0·22–0·41)**	**81·9**
Non-health-care setting							
Lau et al (2004)[50]	China	0	SARS	12/89	25/98	0·53 (0·28–0·99)	7·5
Wu et al (2004)[74]	China	0	SARS	25/146	69/229	0·57 (0·38–0·85)	9·7
Tuan et al (2007)[69]	Vietnam	0	SARS	0/9	7/154	1·03 (0·06–16·83)	0·9
Random subtotal (I^2=0%)				**37/244**	**101/481**	**0·56 (0·40–0·79)**	**18·1**
Unadjusted estimates, overall (I^2=48%)				**163/3686**	**546/6484**	**0·34 (0·26–0·45)**	**100·0**
Adjusted estimates, overall (1 COVID-19, 1 MERS, 8 SARS)						**aOR 0·15 (0·07–0·34)**	
						aRR 0·18 (0·08–0·38)	

Interaction by setting, p=0·049; adjusted for N95 and distance, p=0·11

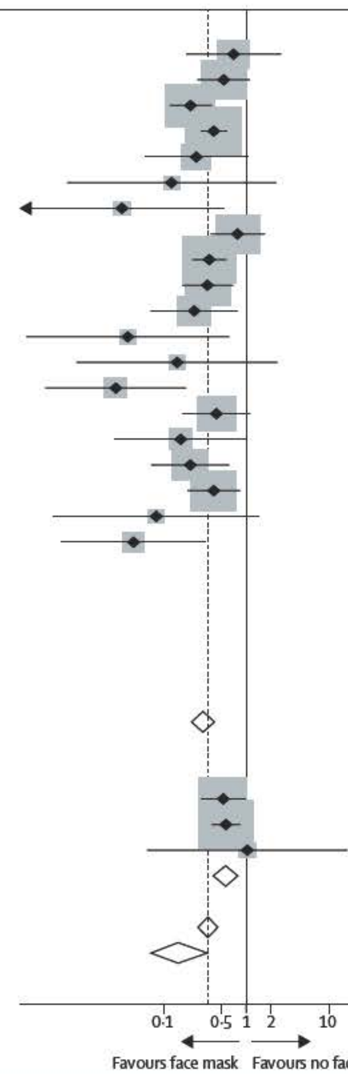

Figure 4: **Forest plot showing unadjusted estimates for the association of face mask use with viral infection causing COVID-19, SARS, or MERS**
SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome. RR=relative risk. aOR=adjusted odds ratio. aRR=adjusted relative risk.

respirators versus medical masks in randomised trials (OR 0·76, 95% CI 0·54–1·06)[13] with the effect-modification seen in this meta-analysis on COVID-19 (ratio of aORs 0·14, 95% CI 0·02–1·05) continued to support a stronger association of protection from COVID-19, SARS, or MERS with N95 or similar respirators versus other face masks (posterior probability for RR <1, 100% and 95%, respectively).

In 13 unadjusted studies and two adjusted studies,[34,37–39,47,49,51,54,58,60,61,65,75] eye protection was associated with lower risk of infection (unadjusted n=3713, RR 0·34, 95% CI 0·22 to 0·52; AR 5·5% with eye protection *vs* 16·0% with no eye protection, RD –10·6%, 95% CI –12·5 to –7·7; adjusted n=701, aOR 0·22, 95% CI 0·12 to 0·39; low certainty; figure 6; table 2; appendix pp 16–17).

Across 24 studies in health-care and non-health-care settings during the current pandemic of COVID-19, previous epidemics of SARS and MERS, or in general use, looking at contextual factors to consider in recommendations, most stakeholders found physical distancing and use of face masks and eye protection acceptable, feasible, and reassuring (appendix pp 20–22). However, challenges included frequent discomfort, high resource use linked with potentially decreased equity, less clear communication, and perceived reduced empathy of care providers by those they were caring for.

	Country	Virus	Setting	aOR (95% CI)	% weight (random)
N95 respirator or similar *vs* no face mask					
Seto et al (2003)[67]	China	SARS	Health care	0·08 (0·02–0·34)	9·0
Ma et al* (2004)[54]	China	SARS	Health care	0·01 (0·003–0·06)	8·9
Wang et al (2020)[41]	China	COVID-19	Health care	0·002 (0·000–0·02)	6·2
Alraddadi et al* (2016)[34]	Saudi Arabia	MERS	Health care	0·41 (0·13–1·26)	10·4
Random subtotal (I^2=87%)				**0·04 (0·004–0·30)**	**34·5**
Surgical face mask or similar (eg, 12–16-layer cotton) *vs* no face mask					
Wu et al (2004)[74]	China	SARS	Non-health care	0·30 (0·12–0·73)	11·2
Lau et al (2004)[50]	China	SARS	Non-health care	0·32 (0·17–0·61)	12·0
Yin et al (2004)[75]	China	SARS	Health care	0·78 (0·61–1·00)	12·8
Liu et al* (2009)[51]	China	SARS	Health care	0·22 (0·08–0·62)	10·8
Nishiura et al (2005)[55]	Vietnam	SARS	Health care	0·29 (0·11–0·75)	11·0
Nishiyama et al (2008)[56]	Vietnam	SARS	Health care	0·08 (0·01–0·50)	7·7
Random subtotal (I^2=76%)				**0·33 (0·17–0·61)**	**65·5**
Random overall (I^2=88%)				**0·15 (0·07–0·34)**	**100·0**
Bayesian overall (Jefferson[31] seasonal viruses)				**0·40 (0·16–0·97)**	

Interaction p=0·090; adjusted for setting, p=0·17; adjusted for AGP, p=0·048

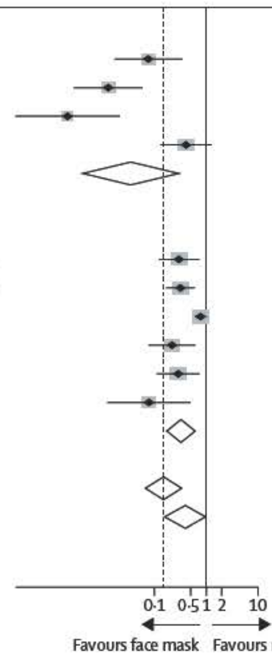

***Figure 5:* Forest plot showing adjusted estimates for the association of face mask use with viral infection causing COVID-19, SARS, or MERS**
SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome. RR=relative risk. aOR=adjusted odds ratio. AGP=aerosol-generating procedures. *Studies clearly reporting AGP.

Discussion

The findings of this systematic review of 172 studies (44 comparative studies; n=25 697 patients) on COVID-19, SARS, and MERS provide the best available evidence that current policies of at least 1 m physical distancing are associated with a large reduction in infection, and distances of 2 m might be more effective. These data also suggest that wearing face masks protects people (both health-care workers and the general public) against infection by these coronaviruses, and that eye protection could confer additional benefit. However, none of these interventions afforded complete protection from infection, and their optimum role might need risk assessment and several contextual considerations. No randomised trials were identified for these interventions in COVID-19, SARS, or MERS.

Previous reviews are limited in that they either have not provided any evidence from COVID-19 or did not use direct evidence from other related emerging epidemic betacoronaviruses (eg, SARS and MERS) to inform the effects of interventions to curtail the current COVID-19 pandemic.[13,19,31,78] Previous data from randomised trials are mainly for common respiratory viruses such as seasonal influenza, with a systematic review concluding low certainty of evidence for extrapolating these findings to COVID-19.[13] Further, previous syntheses of available randomised controlled trials have not accounted for cluster effects in analyses, leading to substantial imprecision in treatment effect estimates. In between-study and within-study comparisons, we noted a larger effect of N95 or similar respirators compared with other masks. This finding is inconsistent with conclusions of a review of four randomised trials,[13] in which low certainty of evidence for no larger effect was suggested. However, in that review, the CIs were wide so a meaningful protective effect could not be excluded. We harmonised these findings with Bayesian approaches, using indirect data from randomised trials to inform posterior estimates. Despite this step, our findings continued to support the ideas not only that masks in general are associated with a large reduction in risk of infection from SARS-CoV-2, SARS-CoV, and MERS-CoV but also that N95 or similar respirators might be associated with a larger degree of protection from viral infection than disposable medical masks or reusable multilayer (12–16-layer) cotton masks. Nevertheless, in view of the limitations of these data, we did not rate the certainty of effect as high.[21] Our findings accord with those of a cluster randomised trial showing a potential benefit of continuous N95 respirator use over medical masks against seasonal viral infections.[79] Further high-quality research, including randomised trials of the optimum physical distance and the effectiveness of different types of masks in the general population and for health-care workers' protection, is urgently needed. Two trials are registered to better inform the optimum use of face masks for COVID-19 (NCT04296643 [n=576] and

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	Country	Respirator (0=no)	Events, eye protection (n/N)	Events, no eye protection (n/N)	RR (95% CI)	% weight (random)
MERS						
Alraddadi et al (2016)[34]	Saudi Arabia	1	1/47	17/165	0·21 (0·03–1·51)	4·0
Ki et al (2019)[47]	South Korea	1	0/9	6/64	0·50 (0·03–8·21)	2·2
Kim et al (2016)[49]	South Korea	1	0/443	2/294	0·13 (0·01–2·76)	1·8
Ryu et al (2019)[65]	South Korea	1	0/24	0/10	(Not calculable)	0
Random subtotal (I^2=0%)			**1/523**	**25/533**	**0·24 (0·06–0·99)**	**8·0**
SARS						
Chen et al (2009)[39]	China	0	1/45	90/703	0·17 (0·02–1·22)	4·2
Liu et al (2009)[51]	China	0	17/221	34/256	0·58 (0·33–1·01)	21·2
Pei et al (2006)[61]	China	0	24/120	123/323	0·53 (0·36–0·77)	26·0
Yin et al (2004)[75]	China	0	10/120	67/137	0·17 (0·09–0·32)	19·4
Caputo et al (2006)[38]	Canada	1	2/46	4/32	0·35 (0·07–1·79)	5·6
Ma et al (2004)[54]	China	1	7/175	40/269	0·27 (0·12–0·59)	15·6
Park et al (2004)[58]	USA	1	0/30	0/72	(Not calculable)	0
Peck et al (2004)[60]	USA	1	0/13	0/19	(Not calculable)	0
Random subtotal (I^2=62%)			**61/770**	**358/1811**	**0·34 (0·21–0·56)**	**92·0**
COVID-19						
Burke et al (2020)[37]	USA	1	0/42	0/34	(Not calculable)	0
Random subtotal			**0/42**	**0/34**	**(Not calculable)**	**0**
Random overall (I^2=43%)			**62/1335**	**383/2378**	**0·34 (0·22–0·52)**	**100·0**
Adjusted estimates, overall (2 studies, Yin[75] and Ma[54])					**aOR 0·22 (0·12–0·39)**	
					aRR 0·25 (0·14–0·43)	
Interaction by virus, p=0·75						

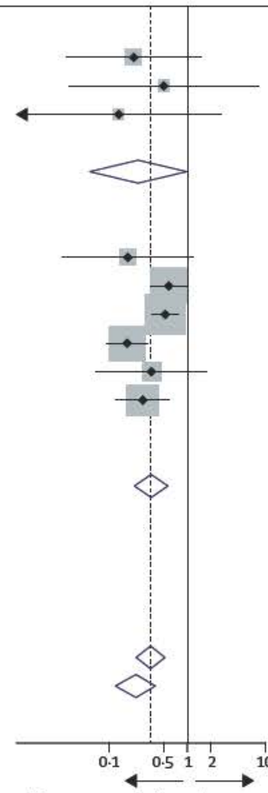

Figure 6: **Forest plot showing the association of eye protection with risk of COVID-19, SARS, or MERS transmission**
Forest plot shows unadjusted estimates. SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome. RR=relative risk. aOR=adjusted odds ratio. aRR=adjusted relative risk.

NCT04337541 [n=6000]). Until such data are available, our findings represent the current best estimates to inform face mask use to reduce infection from COVID-19. We recognise that there are strong, perhaps opposing, sentiments about policy making during outbreaks. In one viewpoint, the 2007 SARS Commission report stated:

> "...recognize, as an aspect of health worker safety, the precautionary principle that reasonable action to reduce risk, such as the use of a fitted N95 respirator, need not await scientific certainty".[80]

> "...if we do not learn from SARS and we do not make the government fix the problems that remain, we will pay a terrible price in the next pandemic".[81]

A counter viewpoint is that the scientific uncertainty and contextual considerations require a more nuanced approach. Although challenging, policy makers must carefully consider these two viewpoints along with our findings.

We found evidence of moderate certainty that current policies of at least 1 m physical distancing are probably associated with a large reduction in infection, and that distances of 2 m might be more effective, as implemented in some countries. We also provide estimates for 3 m. The main benefit of physical distancing measures is to prevent onward transmission and, thereby, reduce the adverse outcomes of SARS-CoV-2 infection. Hence, the results of our current review support the implementation of a policy of physical distancing of at least 1 m and, if feasible, 2 m or more. Our findings also provide robust estimates to inform models and contact tracing used to plan and strategise for pandemic response efforts at multiple levels.

The use of face masks was protective for both health-care workers and people in the community exposed to infection, with both the frequentist and Bayesian analyses lending support to face mask use irrespective of setting. Our unadjusted analyses might, at first impression, suggest use of face masks in the community setting to be less effective than in the health-care setting, but after accounting for differential N95 respirator use between health-care and non-health-care settings, we did not detect any striking differences in effectiveness of face mask use between settings. The credibility of effect-modification across settings was, therefore, low. Wearing face masks was also acceptable and feasible. Policy makers at all levels should, therefore, strive to address equity implications for groups with currently limited access to face masks and eye protection. One concern is that face mask use en masse could divert supplies from people at highest risk for infection.[10] Health-care workers are increasingly being asked to ration and reuse PPE,[82,83] leading to calls for government-directed repurposing of manufacturing capacity to overcome mask shortages[84] and finding solutions for mask use by the general public.[84] In this respect, some of the masks studied in our review were reusable 12–16-layer cotton or gauze masks.[51,54,61,75] At the moment, although there is consensus that SARS-CoV-2 mainly spreads through large droplets and contact, debate continues about the role of aerosol,[2–8,85,86] but our meta-analysis provides evidence (albeit of low certainty) that respirators might have a stronger protective effect than surgical masks. Biological plausibility would be supported by data for aerosolised SARS-CoV-2[5–8] and preclinical data showing seasonal coronavirus RNA detection in fine aerosols during tidal breathing,[87] albeit, RNA detection does not necessarily imply replication and infection-competent virus. Nevertheless, our findings suggest it plausible that even in the absence of aerosolisation, respirators might be simply more effective than masks at preventing infection. At present, there is no data to support viable virus in the air outside of aerosol generating procedures from available hospital studies. Other factors such as super-spreading events, the subtype of health-care setting (eg, emergency room, intensive care unit, medical wards, dialysis centre), if aerosolising procedures are done, and environmental factors such as ventilation, might all affect the degree of protection afforded by personal protection strategies, but we did not identify robust data to inform these aspects.

Strengths of our review include adherence to full systematic review methods, which included artificial intelligence-supported dual screening of titles and abstracts, full-text evaluation, assessment of risk of bias, and no limitation by language. We included patients infected with SARS-CoV-2, SARS-CoV, or MERS-CoV and searched relevant data up to May 3, 2020. We followed the GRADE approach[16] to rate the certainty of evidence. Finally, we identified and appraise a large body of published work from China, from which much evidence emerged before the pandemic spread to other global regions.

The primary limitation of our study is that all studies were non-randomised, not always fully adjusted, and might suffer from recall and measurement bias (eg, direct contact in some studies might not be measuring near distance). However, unadjusted, adjusted, frequentist, and Bayesian meta-analyses all supported the main findings, and large or very large effects were recorded. Nevertheless, we are cautious not to be overly certain in the precise quantitative estimates of effects, although the qualitative effect and direction is probably of high certainty. Many studies did not provide information on precise distances, and direct contact was equated to 0 m distance; none of the eligible studies quantitatively evaluated whether distances of more than 2 m were more effective, although our meta-regression provides potential predictions for estimates of risk. Few studies assessed the effect of interventions in non-health-care settings, and they primarily evaluated mask use in households or contacts of cases, although beneficial associations were seen across settings. Furthermore, most evidence was from studies that reported on SARS and MERS (n=6674 patients with COVID-19, of 25 697 total), but data from these previous epidemics provide the most direct information for COVID-19 currently. We did not specifically assess the effect of duration of exposure on risk for transmission, although whether or not this variable was judged a risk factor considerably varied across studies, from any duration to a minimum of 1 h. Because of inconsistent reporting, information is limited about whether aerosol-generating procedures were in place in studies using respirators, and whether masks worn by infected patients might alter the effectiveness of each intervention, although the stronger association with N95 or similar respirators over other masks persisted when adjusting for studies reporting aerosol-generating medical procedures. These factors might account for some of the residual statistical heterogeneity seen for some outcomes, albeit I^2 is commonly inflated in meta-analyses of observational data,[21,22] and nevertheless the effects seen were large and probably clinically important in all adjusted studies.

Our comprehensive systematic review provides the best available information on three simple and common interventions to combat the immediate threat of COVID-19, while new evidence on pharmacological treatments, vaccines, and other personal protective strategies is being generated. Physical distancing of at least 1 m is strongly associated with protection, but distances of up to 2 m might be more effective. Although direct evidence is limited, the optimum use of face masks, in particular N95 or similar respirators in health-care settings and 12–16-layer cotton or surgical masks in the community, could depend on contextual factors; action is needed at all levels to address the paucity of better evidence. Eye protection might provide additional benefits. Globally collaborative and well conducted studies, including randomised trials, of different personal protective strategies are needed regardless of the challenges, but this systematic appraisal of currently best available evidence could be considered to inform interim guidance.

Contributors

DKC, EAA, SD, KS, SY, and HJS designed the study. SY, SD, KS, and HJS coordinated the study. SY and LH designed and ran the literature search. All authors acquired data, screened records, extracted data, and assessed risk of bias. DKC did statistical analyses. DKC and HJS wrote the report. All authors provided critical conceptual input, analysed and interpreted data, and critically revised the report.

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Declaration of interests

ML is an investigator of an ongoing clinical trial on medical masks versus N95 respirators for COVID-19 (NCT04296643). All other authors declare no competing interests.

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References

1 Worldometer. COVID-19 coronavirus pandemic. 2020. https://www.worldometers.info/coronavirus/ (accessed May 28, 2020).
2 Guo ZD, Wang ZY, Zhang SF, et al. Aerosol and surface distribution of severe acute respiratory syndrome coronavirus 2 in hospital wards, Wuhan, China, 2020. *Emerg Infect Dis* 2020; published online April 10. DOI:10.3201/eid2607.200885.
3 Chia PY, Coleman KK, Tan YK, et al. Detection of air and surface contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in hospital rooms of infected patients. *medRxiv* 2020; published online April 9. DOI:10.1101/2020.03.29.20046557 (preprint).
4 Santarpia JL, Rivera DN, Herrera V, et al. Transmission potential of SARS-CoV-2 in viral shedding observed at the University of Nebraska Medical Center. *medRxiv* 2020; published online March 26. DOI:10.1101/2020.03.23.20039446 (preprint).
5 Cheng V, Wong S-C, Chen J, et al. Escalating infection control response to the rapidly evolving epidemiology of the coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 in Hong Kong. *Infect Control Hosp Epidemiol* 2020; **41:** 493–98.
6 Wong SCY, Kwong RT-S, Wu TC, et al. Risk of nosocomial transmission of coronavirus disease 2019: an experience in a general ward setting in Hong Kong. *J Hosp Infect* 2020; **105:** 119–27.
7 Faridi S, Niazi S, Sadeghi K, et al. A field indoor air measurement of SARS-CoV-2 in the patient rooms of the largest hospital in Iran. *Sci Total Environ* 2020; **725:** 138401.
8 Ong SWX, Tan YK, Chia PY, et al. Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. *JAMA* 2020; **323:** 1610–12.
9 Qualls N, Levitt A, Kanade N, et al. Community mitigation guidelines to prevent pandemic influenza: United States, 2017. *MMWR Recomm Rep* 2017; **66:** 1–34.
10 Feng S, Shen C, Xia N, Song W, Fan M, Cowling BJ. Rational use of face masks in the COVID-19 pandemic. *Lancet Respir Med* 2020; **8:** 434–36.
11 MacIntyre R, Chughtai A, Tham CD, Seale H. COVID-19: should cloth masks be used by healthcare workers as a last resort? April 9, 2020. https://blogs.bmj.com/bmj/2020/04/09/covid-19-should-cloth-masks-be-used-by-healthcare-workers-as-a-last-resort/ (accessed May 12, 2020).
12 Loeb M, Dafoe N, Mahony J, et al. Surgical mask *vs* N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA* 2009; **302:** 1865–71.
13 Bartoszko JJ, Farooqi MAM, Alhazzani W, Loeb M. Medical masks vs N95 respirators for preventing COVID-19 in healthcare workers: a systematic review and meta-analysis of randomized trials. *Influenza Other Respir Viruses* 2020; published online April 4. DOI:10.1111/irv.12745.
14 Schünemann HJ, Moja L. Reviews: rapid! Rapid! Rapid! . . . and systematic. *Syst Rev* 2015; **4:** 4.
15 Cochrane Training. Cochrane handbook for systematic reviews of interventions, version 6. 2019. https://training.cochrane.org/handbook/current (accessed May 12, 2020).
16 Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336:** 924–26.
17 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009; **62:** 1006–12.
18 Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000; **283:** 2008–12.
19 Jefferson T, Del Mar CB, Dooley L, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database Syst Rev* 2011; **7:** CD006207.
20 Offeddu V, Yung CF, Low MSF, Tam CC. Effectiveness of masks and respirators against respiratory infections in healthcare workers: a systematic review and meta-analysis. *Clin Infect Dis* 2017; **65:** 1934–42.
21 Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines, 7: rating the quality of evidence—inconsistency. *J Clin Epidemiol* 2011; **64:** 1294–302.
22 Iorio A, Spencer FA, Falavigna M, et al. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. *BMJ* 2015; **350:** h870.
23 Moskalewicz A, Oremus M. No clear choice between Newcastle-Ottawa Scale and Appraisal Tool for Cross-Sectional Studies to assess methodological quality in cross-sectional studies of health-related quality of life and breast cancer. *J Clin Epidemiol* 2020; **120:** 94–103.
24 Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2019. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed May 12, 2020).
25 Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; **366:** l4898.
26 Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines, 1: introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; **64:** 383–94.
27 Guyatt GH, Thorlund K, Oxman AD, et al. GRADE guidelines, 13: preparing summary of findings tables and evidence profiles—continuous outcomes. *J Clin Epidemiol* 2013; **66:** 173–83.
28 Santesso N, Carrasco-Labra A, Langendam M, et al. Improving GRADE evidence tables part 3: detailed guidance for explanatory footnotes supports creating and understanding GRADE certainty in the evidence judgments. *J Clin Epidemiol* 2016; **74:** 28–39.
29 Santesso N, Glenton C, Dahm P, et al. GRADE guidelines, 26: informative statements to communicate the findings of systematic reviews of interventions. *J Clin Epidemiol* 2020; **119:** 126–35.

30 Higgins JP, Thompson SG. Controlling the risk of spurious findings from meta-regression. *Stat Med* 2004; **23:** 1663–82.

31 Jefferson T, Jones M, Al Ansari LA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses, part 1: face masks, eye protection and person distancing—systematic review and meta-analysis. *medRxiv* 2020; published online April 7. DOI:10.1101/2020.03.30.20047217 (preprint).

32 Sutton AJ, Abrams KR. Bayesian methods in meta-analysis and evidence synthesis. *Stat Methods Med Res* 2001; **10:** 277–303.

33 Goligher EC, Tomlinson G, Hajage D, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome and posterior probability of mortality benefit in a post hoc Bayesian analysis of a randomized clinical trial. *JAMA* 2018; **320:** 2251–59.

34 Alraddadi BM, Al-Salmi HS, Jacobs-Slifka K, et al. Risk factors for Middle East respiratory syndrome coronavirus infection among healthcare personnel. *Emerg Infect Dis* 2016; **22:** 1915–20.

35 Arwady MA, Alraddadi B, Basler C, et al. Middle East respiratory syndrome coronavirus transmission in extended family, Saudi Arabia, 2014. *Emerg Infect Dis* 2016; **22:** 1395–402.

36 Bai Y, Wang X, Huang Q, et al. SARS-CoV-2 infection in health care workers: a retrospective analysis and a model study. *medRxiv* 2020; published online April 1. DOI:10.1101/2020.03.29.20047159 (preprint).

37 Burke RM, Balter S, Barnes E, et al. Enhanced contact investigations for nine early travel-related cases of SARS-CoV-2 in the United States. *medRxiv* 2020; published online May 3. DOI:10.1101/2020.04.27.20081901 (preprint).

38 Caputo KM, Byrick R, Chapman MG, Orser BJ, Orser BA. Intubation of SARS patients: infection and perspectives of healthcare workers. *Can J Anaesth* 2006; **53:** 122–29.

39 Chen WQ, Ling WH, Lu CY, et al. Which preventive measures might protect health care workers from SARS? *BMC Public Health* 2009; **9:** 81.

40 Cheng H-Y, Jian S-W, Liu D-P, Ng T-C, Huang W-T, Lin H-H. High transmissibility of COVID-19 near symptom onset. *medRxiv* 2020; published online March 19. DOI:10.1101/2020.03.18.20034561 (preprint).

41 Wang X, Pan Z, Cheng Z. Association between 2019-nCoV transmission and N95 respirator use. *J Hosp Infect* 2020; **105:** 104–05.

42 Ha LD, Bloom SA, Hien NQ, et al. Lack of SARS transmission among public hospital workers, Vietnam. *Emerg Infect Dis* 2004; **10:** 265–68.

43 Hall AJ, Tokars JI, Badreddine SA, et al. Health care worker contact with MERS patient, Saudi Arabia. *Emerg Infect Dis* 2014; **20:** 2148–51.

44 Heinzerling A, Stuckey MJ, Scheuer T, et al. Transmission of COVID-19 to health care personnel during exposures to a hospitalized patient: Solano County, California, February 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69:** 472–76.

45 Ho KY, Singh KS, Habib AG, et al. Mild illness associated with severe acute respiratory syndrome coronavirus infection: lessons from a prospective seroepidemiologic study of health-care workers in a teaching hospital in Singapore. *J Infect Dis* 2004; **189:** 642–47.

46 Van Kerkhove MD, Alaswad S, Assiri A, et al. Transmissibility of MERS-CoV infection in closed setting, Riyadh, Saudi Arabia, 2015. *Emerg Infect Dis J* 2019; **25:** 1802–09.

47 Ki HK, Han SK, Son JS, Park SO. Risk of transmission via medical employees and importance of routine infection-prevention policy in a nosocomial outbreak of Middle East respiratory syndrome (MERS): a descriptive analysis from a tertiary care hospital in South Korea. *BMC Pulm Med* 2019; **19:** 190.

48 Kim T, Jung J, Kim SM, et al. Transmission among healthcare worker contacts with a Middle East respiratory syndrome patient in a single Korean centre. *Clin Microbiol Infect* 2016; **22:** e11–13.

49 Kim CJ, Choi WS, Jung Y, et al. Surveillance of the Middle East respiratory syndrome (MERS) coronavirus (CoV) infection in healthcare workers after contact with confirmed MERS patients: incidence and risk factors of MERS-CoV seropositivity. *Clin Microbiol Infect* 2016; **22:** 880–86.

50 Lau JTF, Lau M, Kim JH, Tsui HY, Tsang T, Wong TW. Probable secondary infections in households of SARS patients in Hong Kong. *Emerg Infect Dis* 2004; **10:** 235–43.

51 Liu W, Tang F, Fang LQ, et al. Risk factors for SARS infection among hospital healthcare workers in Beijing: a case control study. *Trop Med Int Health* 2009; **14** (suppl 1)**:** 52–59.

52 Liu ZQ, Ye Y, Zhang H, Guohong X, Yang J, Wang JL. Analysis of the spatio-temporal characteristics and transmission path of COVID-19 cluster cases in Zhuhai. *Trop Geogr* 2020; published online March 12. DOI:10.13284/j.cnki.rddl.003228.

53 Loeb M, McGeer A, Henry B, et al. SARS among critical care nurses, Toronto. *Emerg Infect Dis* 2004; **10:** 251–55.

54 Ma HJ, Wang HW, Fang LQ, et al. A case-control study on the risk factors of severe acute respiratory syndromes among health care workers. *Zhonghua Liu Xing Bing Xue Za Zhi* 2004; **25:** 741–44 (in Chinese).

55 Nishiura H, Kuratsuji T, Quy T, et al. Rapid awareness and transmission of severe acute respiratory syndrome in Hanoi French Hospital, Vietnam. *Am J Trop Med Hyg* 2005; **73:** 17–25.

56 Nishiyama A, Wakasugi N, Kirikae T, et al. Risk factors for SARS infection within hospitals in Hanoi, Vietnam. *Jpn J Infect Dis* 2008; **61:** 388–90.

57 Olsen SJ, Chang HL, Cheung TY, et al. Transmission of the severe acute respiratory syndrome on aircraft. *N Engl J Med* 2003; **349:** 2416–22.

58 Park BJ, Peck AJ, Kuehnert MJ, et al. Lack of SARS transmission among healthcare workers, United States. *Emerg Infect Dis* 2004; **10:** 244–48.

59 Park JY, Kim BJ, Chung KH, Hwang YI. Factors associated with transmission of Middle East respiratory syndrome among Korean healthcare workers: infection control via extended healthcare contact management in a secondary outbreak hospital. *Respirology* 2016; **21** (suppl 3)**:** 89 (abstr APSR6-0642).

60 Peck AJ, Newbern EC, Feikin DR, et al. Lack of SARS transmission and U.S. SARS case-patient. *Emerg Infect Dis* 2004; **10:** 217–24.

61 Pei LY, Gao ZC, Yang Z, et al. Investigation of the influencing factors on severe acute respiratory syndrome among health care workers. *Beijing Da Xue Xue Bao Yi Xue Ban* 2006; **38:** 271–75.

62 Rea E, Laflèche J, Stalker S, et al. Duration and distance of exposure are important predictors of transmission among community contacts of Ontario SARS cases. *Epidemiol Infect* 2007; **135:** 914–21.

63 Reuss A, Litterst A, Drosten C, et al. Contact investigation for imported case of Middle East respiratory syndrome, Germany. *Emerg Infect Dis* 2014; **20:** 620–25.

64 Reynolds MG, Anh BH, Thu VH, et al. Factors associated with nosocomial SARS-CoV transmission among healthcare workers in Hanoi, Vietnam, 2003. *BMC Public Health* 2006; **6:** 207.

65 Ryu B, Cho SI, Oh MD, et al. Seroprevalence of Middle East respiratory syndrome coronavirus (MERS-CoV) in public health workers responding to a MERS outbreak in Seoul, Republic of Korea, in 2015. *Western Pac Surveill Response J* 2019; **10:** 46–48.

66 Scales DC, Green K, Chan AK, et al. Illness in intensive care staff after brief exposure to severe acute respiratory syndrome. *Emerg Infect Dis* 2003; **9:** 1205–10.

67 Seto WH, Tsang D, Yung RWH, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003; **361:** 1519–20.

68 Teleman MD, Boudville IC, Heng BH, Zhu D, Leo YS. Factors associated with transmission of severe acute respiratory syndrome among health-care workers in Singapore. *Epidemiol Infect* 2004; **132:** 797–803.

69 Tuan PA, Horby P, Dinh PN, et al. SARS transmission in Vietnam outside of the health-care setting. *Epidemiol Infect* 2007; **135:** 392–401.

70 Wang Q, Huang X, Bai Y, et al. Epidemiological characteristics of COVID-19 in medical staff members of neurosurgery departments in Hubei province: a multicentre descriptive study. *medRxiv* 2020; published online April 24. DOI:10.1101/2020.04.20.20064899 (preprint).

71 Wiboonchutikul S, Manosuthi W, Likanonsakul S, et al. Lack of transmission among healthcare workers in contact with a case of Middle East respiratory syndrome coronavirus infection in Thailand. *Antimicrob Resist Infect Control* 2016; **5:** 21.

72 Wilder-Smith A, Teleman MD, Heng BH, Earnest A, Ling AE, Leo YS. Asymptomatic SARS coronavirus infection among healthcare workers, Singapore. *Emerg Infect Dis* 2005; **11:** 1142–45.

73 Wong TW, Lee CK, Tam W, et al. Cluster of SARS among medical students exposed to single patient, Hong Kong. *Emerg Infect Dis* 2004; **10:** 269–76.

74 Wu J, Xu F, Zhou W, et al. Risk factors for SARS among persons without known contact with SARS patients, Beijing, China. *Emerg Infect Dis* 2004; **10:** 210–16.
75 Yin WW, Gao LD, Lin WS, et al. Effectiveness of personal protective measures in prevention of nosocomial transmission of severe acute respiratory syndrome. *Zhonghua Liu Xing Bing Xue Za Zhi* 2004; **25:** 18–22.
76 Yu ITS, Wong TW, Chiu YL, Lee N, Li Y. Temporal-spatial analysis of severe acute respiratory syndrome among hospital inpatients. *Clin Infect Dis* 2005; **40:** 1237–43.
77 Yu IT, Xie ZH, Tsoi KK, et al. Why did outbreaks of severe acute respiratory syndrome occur in some hospital wards but not in others? *Clin Infect Dis* 2007; **44:** 1017–25.
78 Verbeek JH, Rajamaki B, Ijaz S, et al. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. *Cochrane Database Syst Rev* 2019; **7:** CD011621.
79 MacIntyre CR, Wang Q, Seale H, et al. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. *Am J Respir Crit Care Med* 2013; **187:** 960–66.
80 Campbell A. Chapter eight: it's not about the mask: SARS Commission final report, volume 3. December, 2006. http://www.archives.gov.on.ca/en/e_records/sars/report/v3-pdf/Vol3Chp8.pdf (accessed May 12, 2020).
81 Webster P. Ontario issues final SARS Commission report. *Lancet* 2007; **369:** 264.
82 Rimmer A. COVID-19: experts question guidance to reuse PPE. *BMJ* 2020; **369:** m1577.
83 Mackenzie D. Reuse of N95 masks. *Engineering* 2020; published online April 13. DOI:10.1016/j.eng.2020.04.003.
84 Greenhalgh T, Schmid MB, Czypionka T, Bassler D, Gruer L. Face masks for the public during the covid-19 crisis. *BMJ* 2020; **369:** m1435.
85 Bahl P, Doolan C, de Silva C, Chughtai AA, Bourouiba L, MacIntyre CR. Airborne or droplet precautions for health workers treating coronavirus disease 2019? *J Infect Dis* 2020; published online April 16. DOI:10.1093/infdis/jiaa189.
86 Schünemann HJ, Khabsa J, Solo K, et al. Ventilation techniques and risk for transmission of coronavirus disease, including COVID-19: a living systematic review of multiple streams of evidence. *Ann Intern Med* 2020; published online May 22. DOI:10.7326/M20-2306.
87 Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat Med* 2020; **26:** 676–80.

Comment

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Physical distancing, face masks, and eye protection for prevention of COVID-19

The choice of various respiratory protection mechanisms, including face masks and respirators, has been a vexed issue, from the 2009 H1N1 pandemic to the west African Ebola epidemic of 2014,[1] to the current COVID-19 pandemic. COVID-19 guidelines issued by WHO, the US Centers for Disease Control and Prevention, and other agencies have been consistent about the need for physical distancing of 1–2 m but conflicting on the issue of respiratory protection with a face mask or a respirator.[2] This discrepancy reflects uncertain evidence and no consensus about the transmission mode of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). For eye protection, data are even less certain. Therefore, the systematic review and meta-analysis by Derek Chu and colleagues in *The Lancet*[3] is an important milestone in our understanding of the use of personal protective equipment (PPE) and physical distancing for COVID-19. No randomised controlled trials were available for the analysis, but Chu and colleagues systematically reviewed 172 observational studies and rigorously synthesised available evidence from 44 comparative studies on SARS, Middle East respiratory syndrome (MERS), COVID-19, and the betacoronaviruses that cause these diseases.

The findings showed a reduction in risk of 82% with a physical distance of 1 m in both health-care and community settings (adjusted odds ratio [aOR] 0·18, 95% CI 0·09–0·38). Every additional 1 m of separation more than doubled the relative protection, with data available up to 3 m (change in relative risk [RR] 2·02 per m; $p_{interaction}$=0·041). This evidence is important to support community physical distancing guidelines and shows risk reduction is feasible by physical distancing. Moreover, this finding can inform lifting of societal restrictions and safer ways of gathering in the community.

The 1–2 m distance rule in most hospital guidelines is based on out-of-date findings from the 1940s, with studies from 2020 showing that large droplets can travel as far as 8 m.[4] To separate droplet and airborne transmission is probably somewhat artificial, with both routes most likely part of a continuum for respiratory transmissible infections.[4] Protection against presumed droplet infections by use of respirators, but not masks,[5] supports a continuum rather than discrete states of droplet or airborne transmission. Both experimental and hospital studies have shown evidence of aerosol transmission of SARS-CoV-2.[6–8] One study found viable virus in the air 16 h after aerosolisation and showed greater airborne propensity for SARS-CoV-2 compared with SARS-CoV and MERS-CoV.[6]

Chu and colleagues reported that masks and respirators reduced the risk of infection by 85% (aOR 0·15, 95% CI 0·07–0·34), with greater effectiveness in health-care settings (RR 0·30, 95% CI 0·22–0·41) than in the community (0·56, 0·40–0·79; $p_{interaction}$=0·049). They attribute this difference to the predominant use of N95 respirators in health-care settings; in a sub-analysis, respirators were 96% effective (aOR 0·04, 95% CI 0·004–0·30) compared with other masks, which were 77% effective (aOR 0·33, 95% CI 0·17–0·61; $p_{interaction}$=0·090). The other important finding for health workers by Chu and colleagues was that eye protection resulted in a 78% reduction in infection (aOR 0·22, 95% CI 0·12–0·39); infection via the ocular route might occur by aerosol transmission or self-inoculation.[9]

For health-care workers on COVID-19 wards, a respirator should be the minimum standard of care. This study by Chu and colleagues should prompt a review of all guidelines that recommend a medical mask for health workers caring for COVID-19 patients. Although medical masks do protect, the occupational health and safety of health workers should be the highest priority and the precautionary principle should be applied. Preventable infections in health workers can result not only in deaths but also in large numbers of health workers being quarantined and nosocomial outbreaks. In the National Health Service trusts in the UK, up to one in five health workers have been infected with COVID-19,[10] which is an unacceptable risk for front-line workers. To address global shortages of PPE, countries should take responsibility for scaling up production rather than expecting health workers to work in suboptimum PPE.[11]

Chu and colleagues also report that respirators and multilayer masks are more protective than are single layer masks. This finding is vital to inform the proliferation of home-made cloth mask designs, many

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of which are single-layered. A well designed cloth mask should have water-resistant fabric, multiple layers, and good facial fit.[12] This study supports universal face mask use, because masks were equally effective in both health-care and community settings when adjusted for type of mask use. Growing evidence for presymptomatic and asymptomatic transmission of SARS-CoV-2[13] further supports universal face mask use and distancing. In regions with a high incidence of COVID-19, universal face mask use combined with physical distancing could reduce the rate of infection (flatten the curve), even with modestly effective masks.[14] Universal face mask use might enable safe lifting of restrictions in communities seeking to resume normal activities and could protect people in crowded public settings and within households. Masks worn within households in Beijing, China, prevented secondary transmission of SARS-CoV-2 if worn before symptom onset of the index case.[15] Finally, Chu and colleagues reiterate that no one intervention is completely protective and that combinations of physical distancing, face mask use, and other interventions are needed to mitigate the COVID-19 pandemic until we have an effective vaccine. Until randomised controlled trial data are available, this study provides the best specific evidence for COVID-19 prevention.

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1 MacIntyre CRC, Chughtai AA, Seale H, Richards GA, Davidson PM. Respiratory protection for healthcare workers treating Ebola virus disease (EVD): are facemasks sufficient to meet occupational health and safety obligations? *Int J Nurs Stud* 2014; **51:** 1421–26.

2 Chughtai AA, Seale H, Islam MS, Owais M, Macintyre CR. Policies on the use of respiratory protection for hospital health workers to protect from coronavirus disease (COVID-19). *Int J Nurs Stud* 2020; **105:** 103567.

3 Chu DKA, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet* 2020; published online May 26. https://doi.org/10.1016/S0140-6736(20)31142-9.

4 Bahl P, Doolan C, de Silva C, Chughtai AA, Bourouiba L, MacIntyre CR. Airborne or droplet precautions for health workers treating COVID-19? *J Infect Dis* 2020; published online April 16. DOI:10.1093/infdis/jiaa189.

5 MacIntyre CR, Chughtai AA, Rahman B, et al. The efficacy of medical masks and respirators against respiratory infection in healthcare workers. *Influenza Other Respir Viruses* 2017; **11:** 511–17.

6 Fears AC, Klimstra WB, Duprex P, et al. Comparative dynamic aerosol efficiencies of three emergent coronaviruses and the unusual persistence of SARS-CoV-2 in aerosol suspensions. *medRxiv* 2020; published online April 18. DOI:10.1101/2020.04.13.20063784 (preprint).

7 Guo Z-D, Wang Z-Y, Zhang S-F, et al. Aerosol and surface distribution of severe acute respiratory syndrome coronavirus 2 in hospital wards, Wuhan, China, 2020. *Emerg Infect Dis* 2020; published online April 10. DOI:10.3201/eid2607.200885.

8 Santarpia JL, Rivera DN, Herrera V, et al. Transmission potential of SARS-CoV-2 in viral shedding observed at the University of Nebraska Medical Center. *medRxiv* 2020; published online March 26. DOI:10.1101/2020.03.23.20039446 (preprint).

9 Lu CW, Liu XF, Jia ZF. 2019-nCoV transmission through the ocular surface must not be ignored. *Lancet* 2020; **395:** e39.

10 Hunter E, Price DA, Murphy E, et al. First experience of COVID-19 screening of health-care workers in England. *Lancet* 2020; **395:** e77–78.

11 Greenhalgh T, Schmid MB, Czypionka T, Bassler D, Gruer L. Face masks for the public during the covid-19 crisis. *BMJ* 2020; **369:** m1435.

12 MacIntyre R, Chughtai A, Tham CD, Seale H. Covid-19: Should cloth masks be used by healthcare workers as a last resort? April 9, 2020. https://blogs.bmj.com/bmj/2020/04/09/covid-19-should-cloth-masks-be-used-by-healthcare-workers-as-a-last-resort/ (accessed May 14, 2020).

13 He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020; **26:** 672–75.

14 Ngonghala CN, Iboi E, Eikenberry S, et al. Mathematical assessment of the impact of non-pharmaceutical interventions on curtailing the 2019 novel Coronavirus. *Math Biosci* 2020; **325:** 108364.

15 Wang Y, Tian H, Zhang L, et al. Reduction of secondary transmission of SARS-CoV-2 in households by face mask use, disinfection and social distancing: a cohort study. *BMJ Glob Health* (in press).

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A rapid systematic review of the efficacy of face masks and respirators against coronaviruses and other respiratory transmissible viruses for the community, healthcare workers and sick patients

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ABSTRACT

Background: The pandemic of COVID-19 is growing, and a shortage of masks and respirators has been reported globally. Policies of health organizations for healthcare workers are inconsistent, with a change in policy in the US for universal face mask use. The aim of this study was to review the evidence around the efficacy of masks and respirators for healthcare workers, sick patients and the general public.

Methods: A systematic review of randomized controlled clinical trials on use of respiratory protection by healthcare workers, sick patients and community members was conducted. Articles were searched on Medline and Embase using key search terms.

Results: A total of 19 randomised controlled trials were included in this study – 8 in community settings, 6 in healthcare settings and 5 as source control. Most of these randomised controlled trials used different interventions and outcome measures. In the community, masks appeared to be effective with and without hand hygiene, and both together are more protective. Randomised controlled trials in health care workers showed that respirators, if worn continually during a shift, were effective but not if worn intermittently. Medical masks were not effective, and cloth masks even less effective. When used by sick patients randomised controlled trials suggested protection of well contacts.

Conclusion: The study suggests that community mask use by well people could be beneficial, particularly for COVID-19, where transmission may be pre-symptomatic. The studies of masks as source control also suggest a benefit, and may be important during the COVID-19 pandemic in universal community face mask use as well as in health care settings. Trials in healthcare workers support the use of respirators continuously during a shift. This may prevent health worker infections and deaths from COVID-19, as aerosolisation in the hospital setting has been documented.

What is already known about the topic?

- Masks and respirators are commonly used to protect from respiratory infections in three different indications – for healthcare workers, sick patients and well community members.
- Currently there is debate and conflicting guidelines around the use of masks and respirators in healthcare and community settings.

What this paper adds

- In the community, masks may be more protective for well people.
- In healthcare settings continuous use of respirators, is more protective compared to the medical masks, and medical masks are more protective than cloth masks. Depending on the fabric and design, some cloth masks may not be safe for healthcare workers.
- The use of masks by sick patients is likely protective, and coronaviruses can be emitted in normal breathing, in fine airborne particles.

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1. Introduction

The use of personal protective equipment for coronavirus disease (COVID-19) has been controversial, with differing guidelines issued by different agencies (Chen et al., 2020). COVID-19 is caused by severe acute respiratory syndrome coronavirus2 (SARS-CoV-2), a beta-coronavirus, similar to severe acute respiratory syndrome coronavirus (SARS CoV) (Chen et al., 2020). Seasonal alpha and beta coronaviruses cause common colds, croup and broncholitis. The transmission mode of coronaviruses in humans is similar, thought to be by droplet, contact and sometimes airborne routes (Ong et al., 2020; Zhang et al., 2020; Zou et al., 2020). The World Health Organization recommends surgical mask for health workers providing routine care to a coronavirus disease patient (World Health Organisation (WHO) 2020), whilst the US Centers for Disease Control and Prevention recommended a respirator (Center for Disease Control and Prevention CDC, 2020). Most authorities, except the US CDC, are recommending that community members not wear a mask, and that a mask should only be worn by a sick patient (also referred to as *source control*) (Chughtai et al., 2020). There are more randomised controlled trials of community use of masks in well people than studies of the use by sick people (*source control*). The aim of this study was to review the randomised controlled trials evidence for use of masks and respirators by the community, health care workers and sick patients for prevention of infection.

2. Methods

We searched Medline and EmBase for clinical trials on masks and respirators using the key words “mask”, “respirator”, and “personal protective equipment”. The search was conducted between 1 March to April 17 2020, and all randomised controlled trials published before the search date were included. Two authors (CRM and AAC) reviewed the title and abstracts to identify randomised controlled trials on masks and respirators. We also searched relevant papers from the reference lists of previous clinical trials and systematic reviews. Studies that were not randomised controlled trials, were about anesthesia, or not about prevention of infection were excluded. Animal studies, experimental and observational epidemiologic studies were also excluded. Studies published in English language were included.

We found 602 papers on Medline and 250 on Embase. 820 papers were excluded by title and abstract review. Full texts were reviewed for 32 papers and 19 were selected in this review. Results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria (Moher et al., 2015).

3. Results

In general, the results show protection for healthcare workers and community members, and likely benefit of masks used as source control. We found eight clinical trials (Aiello et al., 2012; Simmerman et al., 2011; Larson et al., 2010; Aiello et al., 2010; MacIntyre et al., 2009; Cowling et al., 2008; Suess et al., 2012; Cowling et al., 2009) on the use of masks in the community (Table 1). In the community, masks appear to be effective with and without hand hygiene, and both together are more protective (Aiello et al., 2012; Aiello et al., 2010; MacIntyre et al., 2009). However, some randomised controlled trials which measured both hand hygiene and masks measured the effect of hand hygiene alone, but not of masks alone (Simmerman et al., 2011, Cowling et al., 2009). In more than one trial, interventions had to be used within 36 hours of exposure to be effective (Cowling et al., 2009; Suess et al., 2012).

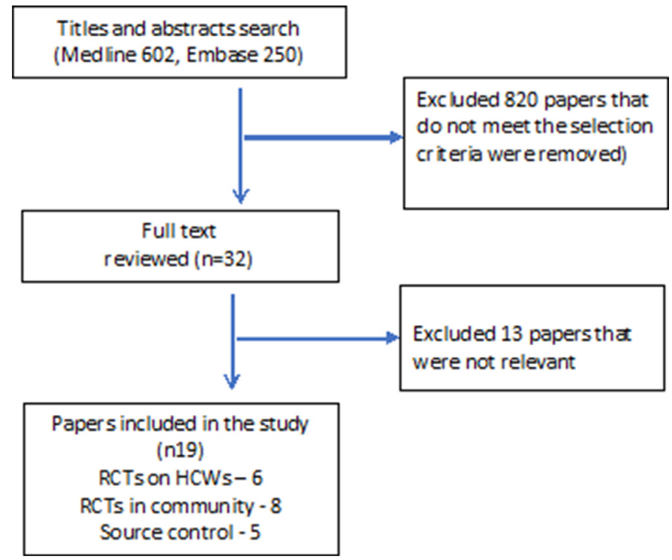

Fig. 1. Search strategy and selection of papers.

To date, six randomised controlled trials (Radonovich et al., 2019; Jacobs et al., 2009, Loeb et al., 2009; MacIntyre et al., 2011, 2013, 2015) have been conducted on the use of masks and/or respirators by healthcare workers in health care settings (Table 2). The healthcare worker trials (Table 2) used different interventions and different outcome measures, and one was in the outpatient setting. A Japanese study had only 32 subjects, and likely was underpowered to find any difference between masks and control (Jacobs et al., 2009). Two North American trials of masks and respirators against influenza infection found no difference between the arms, but neither had a control arm to differentiate equal efficacy from equal inefficacy (Radonovich et al., 2019, Loeb et al., 2009). Neither trial can prove equivalence, as this requires one intervention to be already proven efficaceous against placebo. Without a control group to determine rates of influenza in unprotected healthcare workers, neither study is able to determine efficacy if no difference was observed between the two interventions. A serologic study showed that up to 23% of unprotected healthcare workers (a rate identical to that observed in Loeb the trial, which also used serology) contract influenza during outbreaks (Elder et al., 1996), which suggests lack of efficacy. Studies of nosocomial influenza generally find lower influenza attack rates in unprotected healthcare workers than observed in the Loeb trial (Salgado et al., 2002).

Further problems with this study are that the majority of subjects were defined as having influenza on the basis of serological positivity (Loeb et al., 2009). The 10% seroconversion to pandemic H1N109 (with no pandemic virus isolation or positive PCR) observed in the trial, suggests that pandemic H1N109 was circulating in Ontario before April 2009, which is unlikely.

A serological definition of influenza can be affected by vaccination. The authors claim they excluded influenza vaccinated subjects in the outcome, but according to figure 1 in the Loeb trial, (Loeb et al., 2009) these subjects (130 in total) are included in the analysis. If they had been excluded and even if no other subjects were excluded, the total analysed would be 348, which is lower than the 422 subjects analysed (Loeb et al., 2009). These 130 vaccinated subjects should have been excluded entirely from the analysis. The vaccination status of subjects with seropositivity is not provided in the paper, but it appears people with positive serology due to vaccination may have been misclassified as influenza cases (Loeb et al., 2009).

Table 1
Community mask trials.

Author, year	N, country	Interventions	Results
Cowling et al. (2008)	198 Households Hong Kong	Medical masks Hand washing Control	NS – this was a preliminary report of the 2009 trial.
MacIntyre et al. (2009)	143 Households Australia	Medical masks P2 masks Control	Intention to treat non-significant. Adherence with mask wearing low (25-30% by day 5). In sub-analysis, masks/P2 protective if adherent.
Cowling et al., 2009)	407 households Hong Kong	Hand hygiene Masks + hand hygiene Control	Intention to treat not significant. Masks plus hand hygiene protective against lab confirmed influenza if used within 36 hours. Hand hygiene alone not significant.
Aiello et al. (2010)	1437 college students, United States of America	Masks Masks + hand washing Control	Intention to treat non-significant. Masks + handwashing protective in week 4 -6 of observation and beyond.
Aiello et al. (2012)	1178 college students, United States of America	Masks Masks + hand hygiene Control	Intention to treat non-significant. Masks + hand hygiene protective in week 3 of observation and beyond. Masks alone not protective.
Larson et al. (2010)	617 households, United States of America	Health education (HE) Hand hygiene + HE Masks + hand hygiene +HE	Masks + hand hygiene + HE protective against secondary transmission measured by confirmed influenza and ILI. Mean secondary attack rates for HE, HE + HH, HE+HH+M groups were 0.023, 0.020, and 0.018, respectively
Simmerman et al. (2011)	465 index patients and their families, Thailand	Hand hygiene Masks + hand hygiene Control	No significant difference in confirmed influenza infection
Suess et al. (2012)	84 index cases and 218 household contacts, Germany	Masks Masks + hand hygiene Control	Intention to treat analysis was non-significant. Where used within 36 h, secondary infection in the pooled M and MH groups was significantly lower compared to the control group. In multivariable analysis for predictors of qRT-PCR confirmed influenza infection and clinical influenza among included households in separate models allowing for within household correlation, M and MH were protective against Influenza AH1N1pdm09.

Table 2
Trials of mask and respirator use by health care workers.

Author, year	N healthcare workers, Country	Interventions	Results
Jacobs et al. (2009)	32 Japan	Medical masks Control	NS
Loeb et al. (2009)	446 Canada	Medical masks, targeted N95	No significant difference between Masks and targeted N95
MacIntyre et al. (2011)	1441 China	Masks N95 respirators, fit tested N95 respirators, non-fit tested Control	Continuous N95 protective against clinical, viral and bacterial endpoints
MacIntyre et al. (2013)	1669 China	Medical Mask N95 (continuous) N95 (targeted)	Continuous N95 protective No difference between targeted N95 and medical masks
MacIntyre et al. (2015)	1607 Vietnam	Medical masks, cloth masks, control	Medical masks protective or Cloth masks increase risk of infection
Radonovich et al. (2019)	2862 United States of America	Medical masks, targeted N95 (when 2 m from confirmed respiratory infection) in Outpatient setting.	No significant difference between Masks and targeted N95

In both the North American trials, the intervention comprised wearing the mask or respirator when in contact with recognized ILI or when doing a high risk procedure, which is a targeted strategy (Radonovich et al., 2019, Loeb et al., 2009). One was in an outpatient setting. (Radonovich et al., 2019) We conducted a randomised controlled trial comparing the targeted strategy tested in the two North American studies, with the wearing of respiratory protection during an entire shift, and showed efficacy for continual (but not targeted) use of a respirator (MacIntyre et al., 2013). The study also did not show efficacy for a surgical mask worn continually, and therefore no difference between a surgical mask and targeted use of a respirator (MacIntyre et al., 2013), which is consistent with the findings of the North American trials (Radonovich et al., 2019, Loeb et al., 2009). In summary, the evidence is consistent that a respirator must be worn throughout the shift to be protective. Targeted use of respirators only when doing high risk procedures and medical mask use is not protective. Another randomised controlled trial we conducted in China showed efficacy for continual use of a respirator, but not for a mask, and also found fit-testing of the respirator did not affect efficacy (MacIntyre et al., 2011). However, this may be specific to the quality of the tested product, and is not generalisable to other respirators – fit testing is a necessary part of respirator use (Chughtai et al., 2015).

For healthcare workers, there is evidence of efficacy of respirators if worn continually during a shift, but no evidence of efficacy of a mask (MacIntyre et al., 2011, 2013). For hospitals where COVID-19 patients are being treated, there is growing evidence of widespread contamination of the ward environment, well beyond 2 m from the patient, as well as aerosol transmission (Ong et al., 2020; Santarpia et al., n.d.; Guo et al., 2020). Several studies have

Table 3
Trials of Masks used by a sick patient as source control.

Author, year	*N*, country	Interventions	Results
Johnson et al. (2009)	9 subjects with confirmed influenza, Australia	Medical mask N95 (participants coughed 5 times onto a Petri dish wearing each device)	NS - Surgical and N95 masks were equally effective in preventing the spread of PCR-detectable influenza
Canini et al. (2010)	105 index cases and 306 household contacts, France	Medical mask Control	No significant difference, but trial terminated early
MacIntyre et al. (2016)	245 index cases and 597 household contacts,	Medical mask worn by sick case Control (no mask) Household contacts Followed for infection.	Intention to treat analysis not significant. Mask protective if worn
Barasheed et al. (2014)	Hajj Setting. 22 tents were randomised to 'mask' ($n = 12$) or 'control' ($n = 10$) 75 pilgrims in 'mask' and 89 in 'control' group Saudi Arabia	Mask and control	Less ILI among the contacts of mask users compared to the control tents (31% versus 53%, $p = 0.04$). Laboratory results did not show any difference between the two groups
Leung et al. (2020)	Experimental study of 246 subjects randomised to surgical mask and no mask	Mask and control	111 were infected by human (seasonal) coronavirus. Coronavirus found in exhaled breath of no-mask subjects but not in mask wearers. More virus was found in fine aerosols than large droplets

found SARS-CoV-2 on air vents and in air samples in intensive care units and COVID-19 wards (Santarpia et al., n.d.; Chia et al., 2020; Liu et al., 2020), and an experimental study showed the virus in air samples three hours after aerosolization (van Doremalen et al., 2020). The weight of this evidence and the precautionary principle (MacIntyre et al., 2014a; 2014b), favors respirators for healthcare workers. We showed lower rates of infection outcomes in the medical mask arm compared to control, but the difference was not significant (MacIntyre et al., 2011). It could be that larger trials are needed to demonstrate efficacy of a mask, but any protection is far less than from a respirator. A trial we conducted in Vietnam of 2-layered cotton cloth masks compared to medical masks showed a lower rate of infection in the medical mask group, and a 13 times higher risk of infection in the cloth mask arm (MacIntyre et al., 2015). The study suggests cloth masks may increase the risk of infection (MacIntyre et al., 2015), but may not be generalizable to all homemade masks. The material, design and adequacy of washing of cloth masks may have been a factor (Macintyre et al., 2020). There are no other randomised controlled trial of cloth masks published at this time, but if any protection is offered by these it would be less than even a medical mask.

Table 3 shows the trials of source control. There were five randomised controlled trials identified of masks used by sick patients (Johnson et al., 2009, Barasheed et al., 2014; Leung et al., 2020; MacIntyre et al., 2016; Canini et al., 2010). One was an experimental study of 9 influenza patients, which did not measure clinical endpoints (Johnson et al., 2009). Participants with confirmed influenza coughed onto culture medium wearing a N95 respirator or a mask. No influenza grew on the medium. A trial of 105 sick patients wearing a mask (or no mask) in the household found no significant difference between arms (Canini et al., 2010). However, the trial was terminated prematurely and did not meet recruitment targets, so was probably underpowered. One randomised controlled trial was conducted among Hajj pilgrims, with both well and sick pilgrims wearing masks, and low rates of ILI were reported among contact of mask pilgrims (Barasheed et al., 2014). Our randomised controlled trial is the largest available with clinical endpoints, and studied 245 patients randomised to mask or control (MacIntyre et al., 2016). Compliance was suboptimal in the mask group and some controls wore masks. The intention to treat analysis showed no difference, but when analysed by actual mask use, the rate of infection in household contacts was lower in those who wore masks (MacIntyre et al., 2016). A trial with an experimental design was published in April 2020, examining a range of viruses including seasonal human coronaviruses (Leung et al., 2020). This showed that coronaviruses are preferentially found in aerosolized particles compared to large droplets, and could be expelled by normal tidal breathing. Wearing a surgical mask prevented virus from being exhaled.

4. Discussion

There are more randomised controlled trials of community use of masks in well people (Aiello et al., 2012; Simmerman et al., 2011; Larson et al., 2010; Aiello et al., 2010; MacIntyre et al., 2009; Cowling et al., 2008, Suess et al., 2012, Cowling et al., 2009) than studies of the use by sick people (also referred to as "*source control*"), and these trials are larger than the few on source control (Johnson et al., 2009, Leung et al., 2020; MacIntyre et al., 2016). The evidence suggests protection by masks in high transmission settings such as household and college settings, especially if used early, in some trials if combined with hand hygiene and if wearers are compliant (Aiello et al., 2012; Aiello et al., 2010; MacIntyre et al., 2009; Cowling et al., 2008, 2009; Suess et al., 2012). If masks protect in high transmission settings, they should also protect in crowded public spaces, including workplaces, buses, trains, planes and other closed settings. The trial which did not show efficacy used influenza as the outcome measure (Simmerman et al., 2011), which is a rare outcome, so requires a larger sample size for adequate power and may have been underpowered.

For healthcare workers, the only trials to show a difference between respirators and masks demonstrated efficacy for continuous use of a respirator through a clinical shift, but not masks (MacIntyre et al., 2011, 2013). The two trials which showed no difference are widely cited as evidence that masks provide equal protection as respirators (Radonovich et al., 2019, Loeb et al., 2009). However, without a control arm, the absence of difference between arms could reflect equal efficacy or inefficacy, and it is not possible to draw any conclusions about efficacy. The outpatient setting in the US trial may have had lower exposure risk than the inpatient setting of other trials. (Radonovich et al., 2019) In both the North American trials, the intervention comprised wearing the mask or respirator intermittently when in contact with recognized ILI or when doing a high risk procedure (Radonovich et al., 2019, Loeb et al., 2009). The underlying assumption that the majority of infections in healthcare workers occur during self-identified high-risk exposures is not supported by any evidence. It assumes healthcare workers can accurately identify when they are risk in a busy, clinical setting, when the majority of infections may occur when healthcare workers are unaware of the risk (such as when walking through a busy emergency room or ward where aerosolized virus may be present). Conversely, infections could occur outside the workplace. This could explain the lack of difference if there was no actual efficacy of either arm and if much of the infection occurs in unrecognized situations of risk either within or outside the workplace.

In practice, hospital infection control divides infections into droplet or airborne spread, and recommends droplet (mask) or airborne (respirator) precautions accordingly (MacIntyre et al., 2017). In a pooled analysis of both healthcare worker trials, we showed that continual use of a respirator is more efficacious in protecting healthcare workers even against infections assumed to be spread by the droplet route (MacIntyre et al., 2017). Medical masks did not significantly protect against viral, bacterial, droplet or other infection outcomes. However, the summary odds ratio for masks was less than one, which suggests a low level of protection. Targeted use of respirator protected against bacterial and droplet infections, but not against viral infections, suggesting viral infections may be more likely to be airborne in the hospital setting (MacIntyre et al., 2017).

The five available studies of mask use by sick patients suggest a benefit, but are much smaller trials than the community trials, two without clinical endpoints, and with less certainty around the findings (Johnson et al., 2009, Barasheed et al., 2014; Leung et al., 2020; MacIntyre et al., 2016; Canini et al., 2010). Only 3/5 trials examined clinical outcomes in close contacts (Barasheed et al., 2014; MacIntyre et al., 2016; Canini et al., 2010) and suggest a benefit

Many systematic reviews have been conducted on masks, respirators and other PPE in past (Cowling et al., 2010; Bin-Reza et al., 2012; Gralton and McLaws, 2010; Gamage et al., 2005; Jefferson et al., 2009; Jefferson et al., 2011; Jefferson et al., 2008; Aledort et al., 2007; Lee et al., 2011; Verbeek et al., 2020). These reviews generally examined multiple interventions (e.g. masks and hand hygiene etc.), often combined different outcome measures that were not directly comparable and were inconclusive. Moreover, most of these reviews did not include more recent randomised controlled trials (Radonovich et al., 2019, MacIntyre et al., 2015). This systematic review only focuses on masks and respirators and contains all new studies.

In summary, there is a growing body of evidence supporting all three indications for respiratory protection – community, healthcare workers and sick patients (source control). The largest number of randomised controlled trials have been done for community use of masks by well people in high-transmission settings such as household or college settings. There is benefit in the community if used early, with hand hygiene and if compliant.

Respirators protect healthcare workers if worn continually, but not if worn intermittently in self-identified situations of risk. This supports the suggestion that the health care environment is a risk to healthcare workers even when not doing aerosol generating procedures or caring for a known infectious patient. For COVID-19 specifically, the growing body of evidence showing aerosolisation of the virus in the hospital ward highlights the risk of inadvertent exposure for healthcare workers and supports the use of airborne precautions at all times on the ward (Santarpia et al., n.d.; Chia et al., 2020; Liu et al., 2020). Further, the rule of 1–2 m of spatial separation is not based on good evidence, with most research showing that droplets can travel further than 2 m, and that infections cannot be neatly separated into droplet and airborne (MacIntyre et al., 2017; Bahl et al., 2020). In the UK, one healthcare trust found almost one in five healthcare workers to be infected with COVID-19 (Keeley et al., 2020). The deaths of healthcare workers from COVID-19 reflect this risk (Zhan et al., 2020). The use of masks by sick people, despite being the WHO's only recommendation for mask use by community members during COVID-19 pandemic, is supported by the smallest body of evidence. Source control is probably a sensible recommendation given the suggestion of protection and given specific data on coronaviruses showing protection (Leung et al., 2020). It may help if visitors and febrile patients wear a mask in the healthcare setting, whether in primary care or hospitals. Universal face mask use is likely to have the most impact on epidemic growth in the community, given the high risk of asymptomatic and pre-symptomatic transmission (He et al., 2020).

Conflict of Interest

C Raina MacIntyre receives funding from NHMRC (centre for Research Excellence and Principal Research Fellowship) and Sanofi currently. She has received funding from 3M more than 10 years ago for face mask research.

Abrar Ahmad Chughtai had testing of filtration of masks by 3M for his Ph.D. more than 10 years ago. 3M products were not used in his research. He also has worked with CleanSpace Technology on research on fit testing of respirators (no funding was involved).

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References

Aiello, A.E., Perez, V., Coulborn, R.M., Davis, B.M., Uddin, M., Monto, A.S., 2012. Facemasks, hand hygiene, and influenza among young adults: a randomized intervention trial. PLoS ONE 7 (1).
Aiello, A.E., Murray, G.F., Perez, V., Coulborn, R.M., Davis, B.M., Uddin, M., et al., 2010. Mask use, hand hygiene, and seasonal influenza-like illness among young adults: a randomized intervention trial. J. Infect. Dis. 201 (4), 491–498.
Aledort, J.E., Lurie, N., Wasserman, J., Bozzette, S.A., 2007. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. BMC Public Health 7, 208.
Bahl, P., Doolan, C., de Silva, C., Chughtai, A.A., Bourouiba, L., MacIntyre, C.R., 2020. Airborne or droplet precautions for health workers treating COVID-19? J. Infect. Dis..
Barasheed, O., Almasri, N., Badahdah, A.M., Heron, L., Taylor, J., McPhee, K., et al., 2014. Pilot randomised controlled trial to test effectiveness of facemasks in preventing influenza-like illness transmission among Australian Hajj Pilgrims in 2011. Infect. Disord. Drug Targets. 14 (2), 110–116.
Bin-Reza, F., Lopez Chavarrias, V., Nicoll, A., Chamberland, M.E., 2012. The use of masks and respirators to prevent transmission of influenza: a systematic review of the scientific evidence. Influenza Other Respir. Viruses 6 (4), 257–267.
Canini L., Andreoletti L., Ferrari P., D'Angelo R., Blanchon T., Lemaitre M., et al. Surgical mask to prevent influenza transmission in households: a cluster randomized trial. PLoS ONE [Electronic Resource]. 2010. 5(11):e13998.
Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., et al., 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet 395 (10223), 507–513.
Center for Disease Control and Prevention (CDC). Interim healthcare infection prevention and control recommendations for patients under investigation for 2019 novel coronavirus. 2020. January 2020 [Available from: https://www.cdc.gov/coronavirus/2019-nCoV/infection-control.html.
Chughtai, A.A., Seale, H., Islam, M.S., Owais, M., Macintyre, C.R., 2020. Policies on the use of respiratory protection for hospital health workers to protect from coronavirus disease (COVID-19). Int. J. Nurs. Stud. 105, 103567.
Chia, P.Y., Coleman, K.K., Tan, Y.K., Ong, S.W.X., Gum, M., Lau, S.K., et al., 2020. Detection of Air and Surface Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Hospital Rooms of Infected Patients. medRxiv doi:10.1101/2020.03.29.20046557.
Chughtai, A.A., MacIntyre, C.R., Zheng, Y., Wang, Q., Toor, Z.I., Dung, T.C., et al., 2015. Examining the policies and guidelines around the use of masks and respirators by healthcare workers in China, Pakistan and Vietnam. J. Infect. Prev. 16 (2), 68–74.
Cowling, B.J., Chan, K.H., Fang, V.J., Cheng, C.K., Fung, R.O., Wai, W., et al., 2009. Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial. Ann. Intern. Med. 151 (7), 437–446.
Cowling, B.J., Fung, R.O., Cheng, C.K., Fang, V.J., Chan, K.H., Seto, W.H., et al., 2008. Preliminary findings of a randomized trial of non-pharmaceutical interventions to prevent influenza transmission in households. PLoS ONE 3 (5), e2101.
Cowling, B.J., Zhou, Y., Ip, D.K., Leung, G.M., Aiello, A.E., 2010. Face masks to prevent transmission of influenza virus: a systematic review. Epidemiol. Infect. 138 (4), 449–456.

Elder, A.G., O'Donnell, B., McCruden, E.A., Symington, I.S., Carman, W.F., 1996. Incidence and recall of influenza in a cohort of Glasgow healthcare workers during the 1993-4 epidemic: results of serum testing and questionnaire. BMJ (Clin. Res. Ed.) 313 (7067), 1241–1242.

Gamage, B., Moore, D., Copes, R., Yassi, A., Bryce, E., 2005. Protecting health care workers from SARS and other respiratory pathogens: a review of the infection control literature. Am. J. Infect. Control 33 (2), 114–121.

Gralton, J., McLaws, M.L., 2010. Protecting healthcare workers from pandemic influenza: N95 or surgical masks? Crit. Care Med. 38 (2), 657–667.

Guo, Z., Wang, Z., Zhang, S., Li, X., Li, L., Li, C., et al., 2020. Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020. Emerg. Infect. Dis. 26 (7).

He, X., Lau, E.H., Wu, P., Deng, X., Wang, J., Hao, X., et al., 2020. Temporal dynamics in viral shedding and transmissibility of COVID-19. medRxiv doi:10.1038/s41591-020-0869-5.

Jacobs, J.L., Ohde, S., Takahashi, O., Tokuda, Y., Omata, F., Fukui, T., 2009. Use of surgical face masks to reduce the incidence of the common cold among health care workers in Japan: a randomized controlled trial. Am. J. Infect. Control 37 (5), 417–419.

Jefferson, T., Del Mar, C., Dooley, L., Ferroni, E., Al-Ansary, L.A., Bawazeer, G.A., et al., 2009. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ (Clin. Res. Ed.) 339, b3675.

Jefferson, T., Del Mar, C.B., Dooley, L., Ferroni, E., Al-Ansary, L.A., Bawazeer, G.A., et al., 2011. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochr. Database Syst. Rev. (7), CD006207.

Jefferson, T., Foxlee, R., Del Mar, C., Dooley, L., Ferroni, E., Hewak, B., et al., 2008. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ (Clin. Res. Ed.) 336 (7635), 77–80.

Johnson, D., Druce, J.D., Birch, C., Grayson, M.L., 2009. A quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection. Clin. Infect. Dis. 49 (2), 275–277.

Keeley, A.J., Evans, C., Colton, H., Ankcorn, M., Cope, A., Bennett, T., et al., 2020. Roll-out of SARS-CoV-2 testing for healthcare workers at a large NHS Foundation Trust in the United Kingdom, March 2020. Eurosurveillance 25 (14), 2000433.

Larson, E.L., Ferng, Y.-H., Wong-McLoughlin, J., Wang, S., Haber, M., Morse, S.S., 2010. Impact of non-pharmaceutical interventions on URIs and influenza in crowded, urban households. Public Health Rep. 125 (2), 178–191.

Lee K.M., Shukla V.K., Clark M., Mierzwinski-Urban M., Pessoa-Silva C.L., Conly J. Physical Interventions to Interrupt or Reduce the Spread of Respiratory Viruses - Resource Use Implications: a Systematic Review. Ottawa ON: 2011 Cadth.; 2011 Dec.

Leung, N.H., Chu, D.K., Shiu, E.Y., Chan, K.-H., McDevitt, J.J., Hau, B.J., et al., 2020. Respiratory virus shedding in exhaled breath and efficacy of face masks. Nat. Med. 1–5.

Liu, Y., Ning, Z., Chen, Y., Guo, M., Liu, Y., Gali, N.K., et al., 2020. Aerodynamic characteristics and RNA concentration of SARS-CoV-2 aerosol in Wuhan hospitals during COVID-19 outbreak. bioRxiv doi:10.1101/2020.03.08.982637.

Loeb, M., Dafoe, N., Mahony, J., John, M., Sarabia, A., Glavin, V., et al., 2009. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. JAMA 302 (17), 1865–1871.

MacIntyre, C.R., Cauchemez, S., Dwyer, D.E., Seale, H., Cheung, P., Browne, G., et al., 2009. Face mask use and control of respiratory virus transmission in households. Emerg. Infect. Dis. 15 (2), 233.

MacIntyre, C.R., Chughtai, A.A., Seale, H., Richards, G.A., Davidson, P.M., 2014. Respiratory protection for healthcare workers treating Ebola virus disease (EVD): are facemasks sufficient to meet occupational health and safety obligations? Int. J. Nurs. Stud. 51 (11), 1421–1426.

MacIntyre, C.R., Chughtai, A.A., Seale, H., Richards, G.A., Davidson, P.M., 2014. Uncertainty, risk analysis and change for Ebola personal protective equipment guidelines. Int. J. Nurs. Stud. 52 (5), 899–903.

MacIntyre, C.R., Chughtai, A.A., Rahman, B., Peng, Y., Zhang, Y., Seale, H., et al., 2017. The efficacy of medical masks and respirators against respiratory infection in healthcare workers. Influenza Other Respir. Viruses 11 (6), 511–517.

Macintyre, R., Chughtai, A., Tham, C.D., Seale, H., 2020. Covid-19: Should cloth masks be used by healthcare workers as a last resort? BMJ (Clin. Res. Ed.) [Internet][cited 2020]. https://blogs.bmj.com/bmj/2020/04/09/covid-19-should-cloth-masks-be-used-by-healthcare-workers-as-a-last-resort/.

MacIntyre, C.R., Seale, H., Dung, T.C., Hien, N.T., Nga, P.T., Chughtai, A.A., et al., 2015. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. BMJ Open 5 (4), e006577.

MacIntyre, C.R., Wang, Q., Cauchemez, S., Seale, H., Dwyer, D.E., Yang, P., et al., 2011. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. Influenza Other Respir. Viruses 5 (3), 170–179.

MacIntyre, C.R., Wang, Q., Seale, H., Yang, P., Shi, W., Gao, Z., et al., 2013. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. Am. J. Respir. Crit. Care Med. 187 (9), 960–966.

MacIntyre, C.R., Zhang, Y., Chughtai, A.A., Seale, H., Zhang, D., Chu, Y., et al., 2016. Cluster randomised controlled trial to examine medical mask use as source control for people with respiratory illness. BMJ Open 6 (12), e012330.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., et al., 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst. Rev. 4 (1), 1.

Ong, S.W.X., Tan, Y.K., Chia, P.Y., Lee, T.H., Ng, O.T., Wong, M.S.Y., 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. JAMA: J. Am. Med. Assoc. doi:10.1001/jama.2020.3227.

Radonovich, L.J., Simberkoff, M.S., Bessesen, M.T., Brown, A.C., Cummings, D.A.T., Gaydos, C.A., et al., 2019. N95 respirators vs medical masks for preventing influenza among health care personnel: a randomized clinical trial. JAMA J. Am. Med. Assoc. 322 (9), 824–833.

Salgado, C.D., Farr, B.M., Hall, K.K., Hayden, F.G., 2002. Influenza in the acute hospital setting. Lancet Infect. Dis. 2 (3), 145–155.

Santarpia, J.L., Rivera, D.N., Herrera, V., Morwitzer, M.J., Creager, H., Santarpia, G.W., et al., medRxiv. 2020. Transmission Potential of SARS-CoV-2 in Viral Shedding Observed at the. University of Nebraska Medical Center doi:10.1101/2020.03.23.20039446.

Simmerman, J.M., Suntarattiwong, P., Levy, J., Jarman, R.G., Kaewchana, S., Gibbons, R.V., et al., 2011. Findings from a household randomized controlled trial of hand washing and face masks to reduce influenza transmission in Bangkok, Thailand. Influenza Other Respir. Viruses 5 (4), 256–267.

Suess, T., Remschmidt, C., Schink, S.B., Schweiger, B., Nitsche, A., Schroeder, K., et al., 2012. The role of facemasks and hand hygiene in the prevention of influenza transmission in households: results from a cluster randomised trial; Berlin, Germany, 2009-2011. BMC Infect. Dis. 12, 26.

van Doremalen, N., Bushmaker, T., Morris, D.H., Holbrook, M.G., Gamble, A., Williamson, B.N., et al., 2020. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. New Engl. J. Med. 382 (16), 1564–1567. doi:10.1056/NEJMc2004973.

Verbeek, J.H., Rajamaki, B., Ijaz, S., Sauni, R., Toomey, E., Blackwood, B., et al., 2020. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. Cochr. Database Syst. Rev. (4).

World Health Organisation (WHO). Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected. Interim guidance 2020 [Available from: https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected.

Zhan, M., Qin, Y., Xue, X., Zhu, S., 2020. Death from Covid-19 of 23 Health Care Workers in China. New Engl. J. Med. doi:10.1056/NEJMc2005696.

Zhang, W., Du, R.-H., Li, B., Zheng, X.-S., Yang, X.-L., Hu, B., et al., 2020. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg. Microbes Infect. 9 (1), 386–389.

Zou, L., Ruan, F., Huang, M., Liang, L., Huang, H., Hong, Z., et al., 2020. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. New Engl. J. Med. 382 (12), 1177–1179. doi:10.1056/NEJMc2001737.