Project

A systematic review of non-pharmaceutical interventions for reducing the risk of transmission of respiratory infection in early childhood education and care settings

Prepared for

The Commonwealth of Australia

as represented by

NHMRC | Staying Healthy Advisory Committee

Evaluation Report

prepared by

HTANALYSTS Pty Ltd

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Report information

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Dates

This evidence evaluation report and accompanying technical report received approval from the NHMRC Staying Healthy Advisory Committee (SHAC) on 14 February 2023.

The protocol for the evidence evaluation received approval from the NHMRC SHAC on 14 September 2022.

History

The ONHMRC is seeking to update the evidence underpinning the *2013 Staying Healthy – Preventing infectious diseases in early childhood education and care services* (Staying Healthy) resource. The NHRMC's SHAC has met twice to consider the information provided by the sector, through stakeholder surveys, email enquiries and preliminary scoping reviews of the literature. While there are many topics outlined in this resource, the SHAC has identified two key priority areas that require a systematic review of the literature to provide evidence-based guidance.

To support the ONHMRC in the conduct of the systematic review, **HT**ANALYSTS has been engaged to conduct a systematic review for research question one, which focuses on the non-pharmaceutical measures to prevent respiratory illnesses among healthy children, educators and other staff.

The Research Protocol, developed by **HT**ANALYSTS in conjunction with the ONHMRC and SHAC, provided a framework that outlined the methodology to be used to review the evidence about non-pharmaceutical measures used to prevent respiratory illnesses. All associated materials were developed in a robust and transparent manner in accordance with relevant best practice standards (1-3).

Table of Contents

List of tables

List of figures

List of abbreviations

AMSTAR	A measurement tool to assess systematic reviews
ARI	Acute respiratory infection
ASI	Average number of secondary infections
CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HEPA	High efficiency particulate air
HR	Hazard ratio
ILI	Influenza like illness
JBI	Joanna Briggs Institute
MD	Mean difference
MeSH	Medical Subject Headings
ONHMRC	The Office of National Health and Medical Research Council
NICE	The National Institute for Health and Care Excellence
NRSI	Nonrandomised study of an intervention
OR	Odds ratios
PICO	Population, Intervention, Comparator, Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised controlled trial
RoB	Risk of bias
RR	Risk ratio
SARS	Severe acute respiratory syndrome
SD	Standard deviation
SHAC	Staying Healthy Advisory Committee
SHIC	Staying healthy in childhood
systematic review	Systematic review

Executive summary

Background

Many children first enter education and care services at a time when their immune systems are still developing. The 2013 *Staying Healthy – preventing infectious disease in early childhood education and care services* resource that provides advice on minimising spread of disease in early childhood education and care services for educators and other staff working in these settings. Non-pharmaceutical interventions act as an adjunct to pharmaceutical interventions and are designed to interrupt the different modes of transmission of respiratory illnesses, and thereby mitigate the spread of these pathogens.

Objectives

The overall objective of the systematic review was to evaluate what non-pharmacological interventions are effective in reducing the risk of transmission of respiratory infection in early childhood education and care settings.

The purpose of the review was to update and enhance the evidence for the use of these interventions in reducing the risk of transmission of respiratory infections. Guidelines will be updated to include advice on the use of non-pharmaceutical interventions which were not addressed in the 2013 *Staying Healthy* guidelines.

Search methods

Embase, MEDLINE, CENTRAL, CINAHL and PubMed were searched between 15 and 20 September 20, 2022. Simple text searches of databases including Clinical trial registries, and international and national agencies were also searched. Additional studies were identified by a search of the Epistemonikos database and backward citation searching.

Selection criteria

Eligible studies were systematic reviews, RCTs and observational studies that examined the effectiveness of non-pharmaceutical interventions for reducing transmission of respiratory infection in early childhood education and care services compared to control or an alternative, or less intense intervention. A systematic review was considered the highest level of evidence. If the top tier evidence effectively addresses the specified outcomes of interest, assessment of RCTs and nonrandomised comparative studies was not conducted.

Data collection and analysis

Risk of bias assessment for systematic reviews used the AMSTAR-2 tool, ROBINS-1 tool for RCTs and JBI critical appraisal tool. Across each population, the certainty of the evidence was assessed for important outcomes using the GRADE approach and any data synthesis from eligible RCT's was performed using RevMan.

Main results

Fifteen studies, including ten systematic reviews, two randomised controlled trials and three modelling studies were included in the evidence synthesis. The settings of the primary studies identified by the included systematic reviews were varied, and, while an effort was made to select reviews relevant to the child-care setting, studies in this setting were limited and included studies were set in the broader community. This included primary and high school settings, households, and university halls. Four of the included systematic reviews were assessed to be of high quality, four of moderate quality and two of low quality. Identified RCTs were assessed as having some concerns of bias, and all modelling studies were assessed to be at moderate risk of bias.

The evidence on outcomes related to respiratory illnesses in the childcare setting were as follows:

Hand hygiene: there is a moderate certainty of evidence that hand hygiene probably reduces the transmission of acute respiratory illness and there is low certainty evidence that hand sanitiser is no more effective than soap and water for reducing transmission of respiratory infections. The evidence for hand hygiene on reducing absenteeism or causing adverse events is of very low certainty.

Face masks: there is low certainty evidence that suggests face masks (cloth, medical or surgical) do not reduce transmission related outcomes for respiratory illnesses. There was also evidence of very low certainty that eye protection (face shield, goggles) may reduce transmission-related outcomes in the childcare setting.

Environmental cleaning/ surface/ object disinfection (with or without hand hygiene): there is low certainty evidence that suggests the intervention may have little to no effect on reducing transmission or absenteeism related to respiratory illness.

The evidence for respiratory hygiene (including gargling and nasopharyngeal wash), for screening and testing at entry, and for air filtration and ventilation is of very low certainty. The available evidence suggests respiratory hygiene or screening at entry likely have little to no effect on reducing transmission of respiratory infections. The effect of air filtration and ventilation on transmission related outcomes and absenteeism is uncertain

For combined interventions, such as face masks and hand hygiene there is a moderate certainty of evidence that the intervention likely results in little to no difference in transmission-related outcomes.

No studies were identified for any non-pharmaceutical intervention reporting evidence about the effect of the intervention on illness severity or changes in behaviour.

Conclusions

The evidence provides general low certainty of evidence for the effect of non-pharmaceutical interventions on the transmission of respiratory illnesses, or the effect on absenteeism due to respiratory illness in the childcare setting. The low certainty of the evidence means the true effect estimate may be different from the observed estimate and that it is likely that any new evidence could give different results. Additionally, there is a paucity of high-quality evidence available for the effect of non-pharmaceutical interventions on safety and severity of illness outcomes.

1 Background

The ONHMRC is updating the 2013 *Staying Healthy – preventing infectious disease in early childhood education and care services* resource to ensure that they reflect the best available evidence relevant to the current Australian context. This update will enable ONHMRC to provide up to date advice to the sector on the management of infectious diseases in early childhood education and care settings.

Many children first enter education and care services at a time when their immune systems are still developing. They may not have been exposed to common pathogens and may be too young to be vaccinated against certain diseases. The scope of the *Staying Healthy* resource is to provide advice on minimising spread of disease in early childhood education and care services for educators and other staff working in these settings. This includes providing advice on infection prevention and control practice and what to do in the presence of specific infections.

This review will focus on assessing what non-pharmaceutical interventions are effective in reducing the risk of transmission of respiratory infections in early childhood education and care settings.

The process for conducting the review is built upon the following framework:

1. source the clinical evidence by performing a systematic literature search,
2. identify the best available evidence published in English and indexed in English language databases,
3. incorporate additional literature identified through non-database sources including grey literature, reports and guidelines from reputable international and national agencies,
4. critically appraise and present the evidence, and
5. determine the certainty in the evidence base for each question, using a structured assessment of the body of evidence in accordance with GRADE methodology (3).

1.1 Description of the condition and setting

Respiratory infections are viral, bacterial or fungal microorganisms that infect the cells within the respiratory tract, including the nose, throat and lungs. Acute respiratory infections are the most common illnesses experienced by people of all ages worldwide, and younger children will experience a higher frequency of infection than adults or older children. Children under two years of age may experience an average of 5 to 6 infections per year (4). Common respiratory tract infections (RTIs) include viral influenza, bacterial *Haemophilus influenzae*, human respiratory syncytial virus, *Streptococcus pneumoniae*, severe acute respiratory syndrome (SARS) and COVID-19 (5). Respiratory illness contribute to a significant burden of morbidity in children, in severe cases respiratory infections may develop to impact normal breathing that requires hospitalisation (4).

Children in childcare settings are at increased risk of transmission of respiratory infections. The spread of these infections in childcare centres is facilitated by the regular daily activities and play of children in these settings, usually involving proximity of children and/or carers. The risk of respiratory infection increases as the area available per child in a childcare setting decreases (6). Children may also not practice common hygiene behaviours such as covering mouth and nose while coughing or sneezing. Children are also more likely to have an aberrant innate immune response to these pathogens. In particular, younger children may have a naïve immune system and be unable to mount an appropriate immune response to prevent illness developing. Additionally children in childcare settings may be too young to receive vaccination for some of the viruses which cause respiratory infection (7).

In addition to causing infection in the children themselves, transmission of respiratory infections can also occur to the families and siblings of the children in childcare, including the adults who work at or enter the facilities. This population includes 'at risk' individuals, such as pregnant women, or immunocompromised adults and children. RTIs in children therefore have wider reaching consequences beyond illness in the children themselves, including parental absence from work, and potential misuse/overuse of antibiotics (8).

1.2 Description of intervention

Non-pharmaceutical interventions act as an adjunct to pharmaceutical interventions such as vaccines, antibiotics or antivirals to reduce the risk of transmission of respiratory conditions. In other cases, non-pharmaceutical interventions are the only option to reduce the spread of a respiratory infection for conditions where there are no licensed or appropriate pharmaceutical interventions. This may be particularly relevant in the context of those diseases which have the potential to become epidemic or pandemic in nature and may be novel or have no existing or robust treatment pathway (including antibiotic resistant bacteria).

Non-pharmaceutical interventions can be employed irrespective of specific pathogen type to mitigate transmission risks. Hand hygiene, respiratory hygiene, masks, gloves, exclusion, isolation, cohorting, physical distancing, screening at entry, ventilation, air filtration, outdoor play, environmental cleaning are all examples of non-pharmaceutical interventions

The chance of transmission of respiratory illness is determined by characteristics of the pathogen itself, host and environmental factors. These respiratory infections may be transmitted by four modes: (i) direct (physical contact), (ii) indirect contact (fomites[1]), (iii) (large) droplets and (iv) (fine) aerosols (9).

Transmission control measures focus on interrupting these modes to mitigate the spread of these illnesses. Non-pharmaceutical interventions for preventing the transmission of respiratory illness between individuals may involve forming a barrier, increasing the distance between individuals to reduce the likelihood of aerosolised droplets transferring from an infected individual to a yet uninfected individual, or cleaning/sterilising communal surfaces where transfer may occur. Interventions may also focus on air filtration or purification as another means of reducing aerosol transmission.

1.3 How the intervention might work

Non-pharmaceutical interventions focus on physical disruption of transfer of the infective agent. Hand sanitisation with soaps or alcohol-based sanitisers will kill or inactivate bacteria or viruses, reducing the likelihood of transmission of the infective agent through physical and indirect contact. Environmental cleaning with alcohol-based products or other surface disinfectants seeks to minimise transmission via fomites and may also affect aerosolised transmission, which could occur through resuspension of the pathogen (e.g. due to walking/door opening).

Masks, gloves and other personal protective equipment act as barriers to respiratory secretions as well as large and fine aerosolised droplets. Face covering can assist in containing infections when worn by an infected individual or reduce exposure to the infective agent when worn by a healthy individual. Face-coverings may also reduce the frequency of hands touching respiratory mucosa. Ventilation mitigates aerosol transmission by dilution, and usually involves the intentional incorporation of external air into a space. Air filtration attempts to mitigate aerosol transmission by removing particles/the infectious agent from the air in a space.

[1] objects or materials such as bedding, clothes, or utensil that are likely to carry infection.

Exclusion, isolation and physical distancing approaches focus on removing or isolating the infected individual from healthy individuals to minimise the chance of spread via all potential modes. The duration of exclusion periods and timing of imposing exclusion (e.g. prior to or at first symptoms) will differ on a case-by-case basis, depending on the cause of the infection.

1.4 Why it is important to do this review

In Australia, many children first enter education and care services at a time when their immune systems are still developing. They may not have been exposed to common pathogens and may be too young to be vaccinated against certain diseases. The spread of certain infectious diseases can be reduced by minimising contact between a person, known to be infectious, from others who are at risk of catching the infection.

Alongside various prevention and control strategies, the 2013 *Staying Healthy* guidelines provide advice on non-pharmaceutical interventions for the prevention of infectious diseases that commonly impact children and adults in education and child care services. The evidence for these measures is largely based on studies conducted in community settings and limited to literature published before 2013. Following the recent global pandemic, children in education and childcare settings are now also at risk of infection with COVID-19.

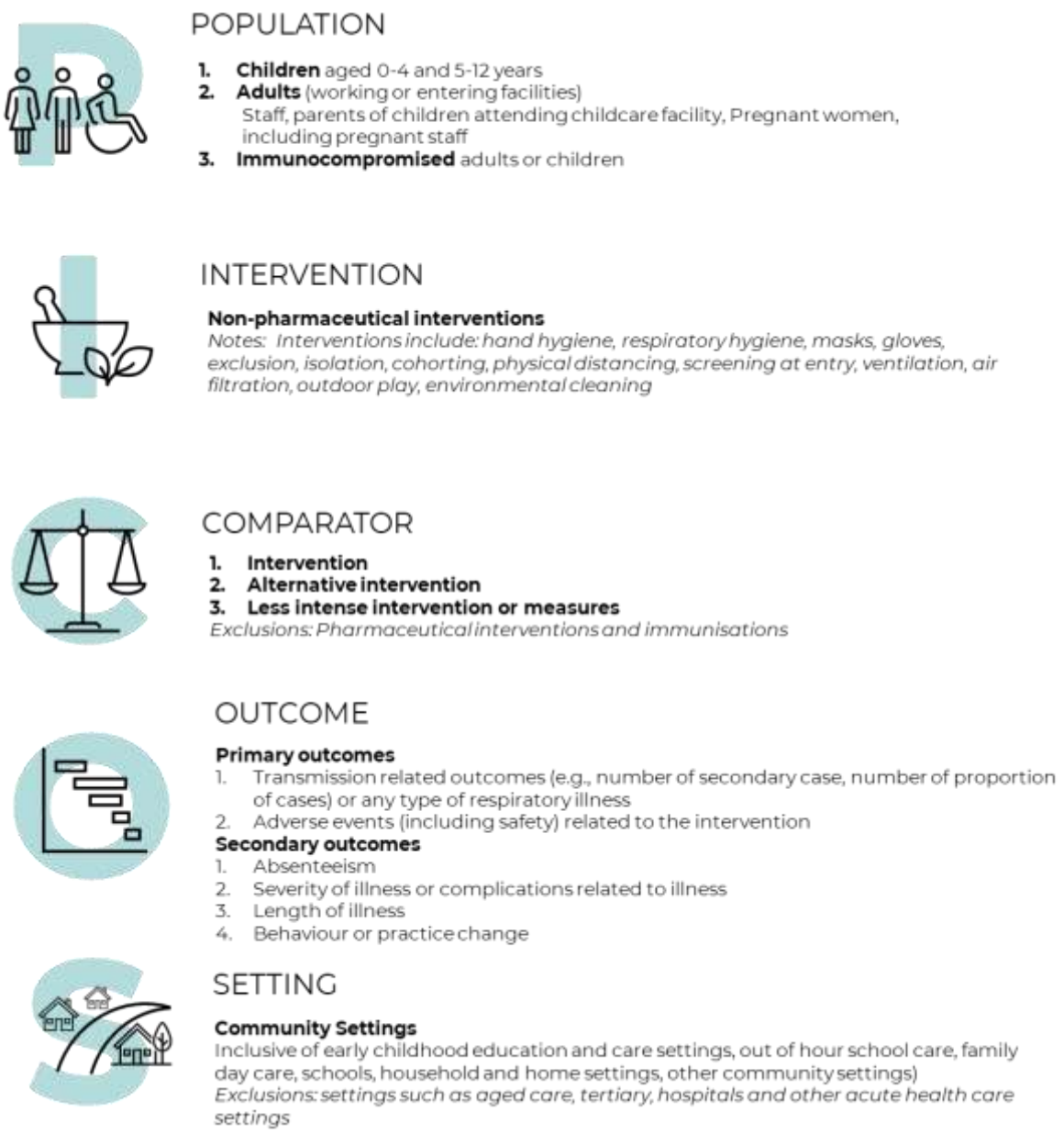
The purpose of this review is to update and enhance the evidence for the use of these interventions in reducing the risk of transmission of respiratory infections. Guidelines will be updated to include advice on the use of non-pharmaceutical interventions which were not addressed in the 2013 *Staying Healthy* guidelines, including masks, air filtrations, improved ventilation, physical distancing and cohorting. The guidelines will be updated to provide evidence and guidance for the use of non-pharmaceutical interventions to reduce the risk of transmission of COVID-19 in addition to and update of the advice for other respiratory conditions.

2 Objectives

The overall objective of the systematic review is to evaluate what non-pharmaceutical interventions are effective in reducing the risk of transmission of respiratory infection in early childhood education and care settings.

The primary and secondary outcomes are outlined in the PICO framework below (see Figure 1) and focused on the evidence for populations in community and care settings relevant to inform the *Staying Healthy* guidelines.

Figure 1 PICO framework for the research objective



3 Methods

Methods used in this systematic review are based on that described in the *Cochrane Handbook for Systematic Reviews of Interventions* (10) and relevant sections in the JBI Manual for Evidence Synthesis (11, 12). Covidence (www.covidence.org), a web-based platform for producing systematic reviews, was used for screening citations and recording decisions made. Covidence is compatible with EndNote and Microsoft Excel, which were used for managing citations and data extraction, respectively. Where appropriate, RevMan (13) was used for the main analyses. GRADEpro GDT software (www.gradepro.org) was used to record decisions and derive an overall assessment of the certainty of evidence for each outcome guided by GRADE methodology (3).

To identify the evidence base for the clinical question, a systematic search of published medical literature was conducted. All potentially relevant studies were identified after applying prespecified inclusion and exclusion criteria as outlined in **Appendix A4**. systematic reviews, RCTs and observational studies as well as grey literature, reports and guidelines from reputable agencies were considered for inclusion.

Further details on the methods and approach used to conduct the evidence evaluation are provided in in the technical report, including: **Appendix A** (searching, selection criteria and screening results) and **Appendix B** (methods used for data appraisal, collection and reporting) and **Appendix F** (differences between protocol and review).

4 Results

4.1 Description of studies

4.1.1 Flow of studies

The literature was searched on 15 September 2022 to identify relevant studies published from database inception to the literature search date. The results of the literature search and the application of the study selection criteria are provided in **Appendix A1 – A5**.

A PRISMA flow summarising the screening results is provided in Figure 2. The PRISMA flow diagram shows the number of studies at each stage of search and screening process, including: the initial search; studies considered irrelevant based on the title and/or abstract; studies found not to be relevant when reviewed at full text; studies which met the eligibility criteria for inclusion in the review and the number of studies which were in considered in the analysis.

4.1.2 Excluded studies

A total of ten studies were identified that met the prespecified eligibility criteria but where not included because full texts could not be accessed.

As per Cochrane guidelines, details of citations which are likely to be considered eligible but are not, are presented in **Appendix C1**. Note that some studies may have been out of scope for more than one reason, but only one reason is listed for each.

4.1.3 Studies awaiting classification

Completed studies identified as potentially eligible for inclusion that could not be retrieved, were not translated, or did not provide complete or adequate data are listed in the *Characteristics of studies awaiting classification* tables (see **Appendix C4**). This includes one study published in languages other than English (German) (**Appendix C4.2**) that is probably eligible for inclusion (pending translation into English), this study provides information on the effect of mobile air filter systems on aerosol concentration in classrooms and the risk of COVID-19. 10 studies that were not able to be retrieved (**Appendix C4.3**), these studies provide information on hand hygiene, or broadly information about infectious disease prevention in day care, seven of these studies were published prior to 2000.

4.1.4 Ongoing studies

Ongoing studies that did not have published results at the time of the search are listed in the *Characteristics of ongoing studies* table (see **Appendix C5, Table C.12**). There one study currently 'recruiting', and one protocol for a scoping review being conducted from August 2021 to November 2021 with no published results.

The recruiting clinical trial is examining strategies to improve safety for children returning to schools, including child and family and staff COVID-19 screening and the impact of outdoor learning via garden education. The trial is being conducted in the United States, Arizona. The aim of the scoping review was to provide an overview of existing studies and evidence on the impact of school closures and reopening's during the COVID-19 pandemic.

4.1.5 Included studies

There were 28 RCTs, 27 NRSIs, 5 modelling studies and 45 systematic reviews identified as eligible for inclusion in this review. RCTs, NRSIs and modelling studies were not included in the review where there was a systematic review available for that outcome.

For hand hygiene, respiratory hygiene, face masks and eye protection, environmental cleaning and combined interventions there was systematic review evidence available. For hand hygiene, face masks and environmental cleaning overlap tables were generated to assess the overlap between primary studies included in each systematic review and select which reviews were included in the evidence synthesis (see **Appendix A5**). For ventilation, one systematic review was supplemented with one RCT and one NRSI/modelling study, for the screening at entry outcome, NRSI and modelling studies were included.

An overview of the conditions identified and the evidence for each intervention in summarised in Table 1.

Figure 2 Literature screening results

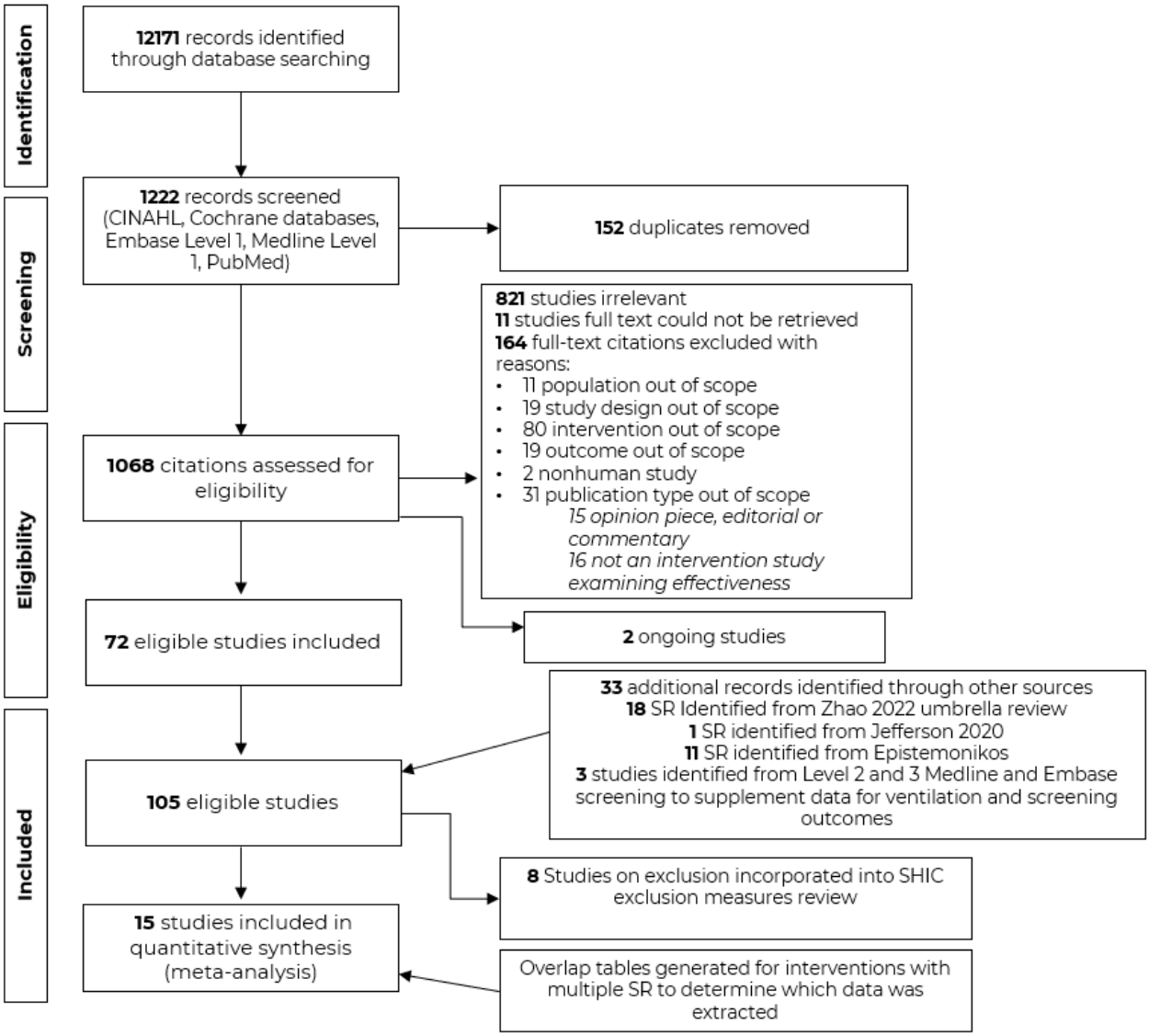


Table 1 Studies identified per outcome and included studies

Intervention	Number/ type of studies identified in literature search	Number/ type of studies included in the review
Hand hygiene	17 SR 25 RCTs 20 NRSI	4 SR
Respiratory hygiene	2 SR 1 RCT	2 SR
Face masks	21 SR 3 RCTs 10 NRSIs	6 SR
Eye protection	1 SR	1 SR
Screening at entry	1 RCT 1 NRSI 1 modelling study	1 RCT 1 NRSI 1 modelling study
Ventilation	1 SR 1 RCT 1 NRSI/modelling	1 SR 1 RCT 1 NRSI/modelling
Environmental cleaning	2 SR 1 RCT	2 SR
Combined interventions	5 SR	5 SR

Abbreviations: NRSI, nonrandomised study of an intervention; RCT, randomised controlled trial; SR, systematic review

4.2 Hand Hygiene

4.2.1 Description of studies

Sixteen systematic reviews were identified which reviewed the hand hygiene as an intervention to reduce the risk of transmission of respiratory infection. Four systematic reviews were included based on the overlap in the primary studies and information included in each systematic review.

One systematic review (Jefferson 2020) of RCTs, cluster RCTs or quasi-RCTs reviewed studies conducted in heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country. The studies reviewed were conducted in Japan, Denmark, Saudi Arabia, Egypt, USA, Israel, France, New Zealand, Thailand, Pakistan, Finland, Germany, Hong Kong. Jefferson 2020 examined any physical intervention to prevent respiratory virus transmission, including screening at entry ports, isolation, quarantine, physical distancing, personal protection, hand hygiene, face masks, and gargling) to prevent respiratory virus transmission compared with no or another intervention. For hand hygiene as an intervention, the review examined hand hygiene compared to control, hand hygiene plus medical/surgical masks compared to control, hand hygiene plus medical surgical masks compared to hand hygiene and soap and water compared to sanitiser and different types of sanitisers. The systematic review searched CENTRAL, PubMed, Embase, CINAHL on 1 April 2020 and ClinicalTrials.gov, and the WHO ICTRP on 16 March 2020, authors also conducted a backwards and forwards citation analysis on the newly included studies. This systematic review is an update to the first review of the same name, first published in 2007 (14).

Another systematic review (Abdullahi 2020) examined intervention studies and observational studies conducted in the community setting in low- and middle- income countries. The studies reviewed were conducted in China, Bangladesh, Thailand, Romania, Serbia, Madagascar, Mexico and Peru. The systematic review examined community measures to control infectious diseases, including hand hygiene, face masks and social distancing. For hand hygiene as an intervention, the systematic review compared hand hygiene to no hand hygiene, face masks and hand hygiene compared to hand hygiene only, and face masks and hand hygiene compared with no intervention. The systematic review searched PubMed, Google scholar, the WHO website, MEDRXIV and google, no date limits were applied to the search, and the date of search was not provided.

A third systematic review (Xiao 2020) of observational studies was conducted for studies in the community settings in the USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland and Denmark. The systematic review assessed the effectiveness of non-pharmaceutical personal protective measures and environment hygiene measures on the incidence of laboratory confirmed influenza, or influenza like illness. Measures included hand hygiene, respiratory etiquette, face masks, and surface and object cleaning. For hand hygiene as an intervention, the systematic review compared hand hygiene with control, hand hygiene compared to face masks, hand hygiene with or without face masks compared control and the effect of hand hygiene by setting. The systematic review searched Medline, PubMed, EMBASE, and CENTRAL for literature in all languages for RCTs on 14 August 2018 to identify literatures that were available during January 1, 2013–August 13, 2018. For hand hygiene, Wong 2014 (15), a systematic review on hand hygiene and risk of influenza virus infections in the community setting, was used as the reference base of the review.

A fourth systematic review (Munn 2020) reviewed RCTs conducted in preschools, day care centres and elementary or primary schools. 8 studies were conducted in the USA, two in Spain, and one each in China, Colombia, Finland, France, Kenya, Bangladesh, New Zealand, Sweden, and Thailand. The review assessed the effectiveness of rinse free handwash, compared to no or conventional handwashing intervention, in children in preschools or day care centres, and children in elementary or primary schools, and its impact on absenteeism due to any illness. The systematic review searched CENTRAL, MEDLINE, Embase, CINAHL, 12 other databases and three clinical trial registries were searched in February 2020.

A fifth systematic review (Wang 2017) examined RCTs, non-randomised and cross-over studies in elementary schools, 12 of the reviewed studies were conducted in the USA, the seven additional studies were conducted in Denmark, China, Egypt, New Zealand, Spain or Thailand. The review authors assessed the effect of hand hygiene on infectious disease related absenteeism, for gastrointestinal or acute respiratory illness, in school children aged between 4 and 15 years, comparing hand sanitiser alone, hand sanitiser and hand hygiene education, soap alone, soap and hand hygiene education, and hand hygiene education alone. The systematic review searched ScienceDirect, Academic search complete. Academic onefile, agEcon search and Web of Science, no date of search was provided.

Results for hand hygiene compared to control (no or alternative less intense intervention), and soap and water compared to hand sanitiser are provided in the Summary of Findings table (see **Section 4.2.3.1**).

4.2.2 Risk of Bias – per item

The risk of bias of included systematic reviews for hand hygiene is presented in Appendix D.

Two reviews (Jefferson 2020, Munn 2020) were assessed as high quality, one study (Xiao 2020) was assessed as moderate quality, the study did not justify excluded studies in the literature search or adjust for confounding in the meta-analysis including NRSIs. Two additional reviews (Abdullahi 2020, and Wang 2017) were assessed as low quality. Abdullahi 2020 did not assess the impact of risk of bias assessment on the metanalysis or account for risk of bias in reporting the results, or account for heterogeneity. Wang 2017 did not assess risk of bias of included RCTs.

4.2.3 Main comparison (vs control)

Jefferson 2020 identified 15 RCTs comparing hand hygiene to control. To supplement data for hand hygiene compared to control from Jefferson 2020 data from one RCT identified by Abdullahi 2020, one RCT from Xiao 2020 on the transmission of ILI was included. Other included studies were consistent between systematic reviews. Additionally, data from Jefferson 2020 is presented in Figure 4, this shows subgroup analysis of the evidence for hand hygiene compared to with control for reducing the transmission of viral illness, stratified into two groups, children or adults. Data from two RCTs identified by Munn 2020 were added to the three RCTs identified for the absenteeism outcome. In addition, Munn, Tufanaru (16) presented data for the effectiveness of rinse free hand wash vs control on reducing absenteeism, stratified by the age of the child. This data is shown in Figure 6. Jefferson 2020 also presented data from 2 RCTs for the comparison between soap and water hand hygiene compared to hand sanitiser.

Table 2 Description of studies: hand hygiene

Review ID	Study design	Setting	Location	Condition	Intervention/ Comparator	Outcomes
Jefferson 2020 (14)	SR	Heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country	Japan. Denmark. Saudi Arabia. Egypt. USA, Israel. France. New Zealand. Thailand. Pakistan. Finland. Germany. Hong Kong	Laboratory confirmed influenza, influenza like illness	N/A	Primary outcomes 1. Numbers of cases of viral illness (including ARIs, influenza-like illness, and laboratory confirmed influenza, or other viral pathogens). 2. Adverse events related to the intervention. Secondary outcomes 1. Deaths. 2. Severity of viral illness as reported in the studies. 3. Absenteeism. 4. Hospital admissions. 5. Complications related to the illness, e.g. pneumonia.
Abdullahi 2020 (17)	SR/MA	Low- and Middle-income countries Households Schools General Community	China, Bangladesh, Thailand, Romania, Serbia, Madagascar, Mexico, Peru	SARS, influenza	N/A	SARS and influenza incidence
Xiao 2020 (18)	SR/MA	Community	USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland, Denmark	Laboratory confirmed influenza	N/A	Incidence of laboratory confirmed influenza
Munn 2020 (16)	SR	Six studies were conducted in preschools or day care centres, with the remaining 13 conducted in elementary or primary schools	USA, Spain, China, Colombia, Finland, France, Kenya, Bangladesh, New Zealand, Sweden, and Thailand	Acute gastrointestinal or respiratory illness	Rinse free handwash / No rinse free handwashing program: No hand washing Conventional handwashing with soap and water, or other hand hygiene strategies.	Absenteeism for any reason (within the study period) Absenteeism due to any illness (within the study period) Adverse skin reactions (within the study period) Absenteeism due to acute respiratory illness (within the study period) Absenteeism due to acute gastrointestinal illness (within the study period) Compliance with the intervention or program Perception of the hand hygiene strategy or stratification with the hand hygiene strategy
Wang 2017 (19)	SR	Elementary schools	USA, Denmark, China, Egypt, New Zealand, Spain or Thailand	Acute gastrointestinal or respiratory illness	N/A	Absenteeism

4.2.3.1 Summary of findings

Hand hygiene compared to control (no intervention) for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: hand hygiene
Comparison: control (no intervention)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control (no intervention)	Risk with hand hygiene				
Transmission related outcomes (assessed with acute respiratory illness)	380 per 1,000	**319 per 1,000** (312 to 327)	**RR 0.84** (0.82 to 0.86)	44129 (8 RCTs)	⊕⊕⊕◯ Moderate[a]	Hand hygiene probably reduces acute respiratory illnesses
Transmission related outcomes (assessed with acute Influenza-like illness)	63 per 1,000	**63 per 1,000** (55 to 73)	**RR 1.00** (0.87 to 1.16)	33127 (11 RCTs)	⊕◯◯◯ Very low[a,b,c]	Hand hygiene may have little to no effect on acute Influenza-like illness, but the evidence is very uncertain.
Transmission related outcomes (assessed with acute: Laboratory confirmed influenza)	89 per 1,000	**73 per 1,000** (50 to 107)	**RR 0.82** (0.56 to 1.20)	9988 (9 RCTs)	⊕⊕◯◯ Low[b,c]	The evidence suggests that hand hygiene results in little to no difference in acute laboratory confirmed influenza.
Transmission related outcomes (assessed with acute: Transmission of SARS)	177 per 1,000	**213 per 1,000** (46 to 971)	**RR 1.20** (0.26 to 5.47)	1365 (2 observational studies)	⊕◯◯◯ Very low[d]	Hand hygiene likely results in no difference in transmission related outcomes (as assessed with acute: transmission of SARS)
Absenteeism	Low		**incidence rate ratio 0.91** (0.82 to 1.01)	19605 (2 RCTs)	⊕◯◯◯ Very low[c,e]	Hand hygiene likely results no difference in absenteeism. [f]
	32 per 1,000	**29 per 1,000** (26 to 32)				
Safety	Data were insufficient to conduct meta-analysis.1 study reported that no adverse events were observed (Correa 2012), and another study (Priest 2014) reported that skin reaction was recorded for 10.4% of participants in the hand sanitiser group versus 10.3% in the control group.			(2 RCTs)	⊕◯◯◯ Very low[a,g,h]	Hand hygiene likely results in no difference in safety or adverse events

Hand hygiene compared to control (no intervention) for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: hand hygiene
Comparison: control (no intervention)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control (no intervention)	Risk with hand hygiene				
Severity of illness - not reported	-	-	-	-	-	
Behaviour or practice change - not reported	-	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

a. Lack of blinding in assessment of the outcome. Certainty of evidence downgraded.
b. Some statistical heterogeneity (I^2=73%). Certainty of evidence downgraded.
c. Wide confidence intervals (upper and lower bounds overlap with both effect and no effect). Certainty of evidence downgraded.
d. Significant statistical heterogeneity (I^2=99%). Certainty of evidence downgraded.
e. High risk of performance bias and detection bias relating to students, parents of students and teachers being aware of treatment assignment. Both studies are also at high risk of attrition bias. Certainty of evidence downgraded two levels.
f. Risk ratio calculated using data from one RCT (Priest 2014). Adjusted risk ratios were presented by Stebbins (2011) and could not be used.
g. Inconsistent results reported for outcomes across studies.
h. No meta-analysis conducted.

Soap and water compared to hand sanitiser for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: soap and water
Comparison: hand sanitiser

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hand sanitiser	Risk with soap and water				
Transmission related outcomes	In one RCT (Azor-Martinez 2018), acute respiratory illness incidence was significantly higher in the soap-and-water group compared with the hand sanitiser group (rate ratio 1.21, 95% CI 1.06 to 1.39). In another RCT, there was no significant difference between interventions in Savolainen-Kopra 2012.			(2 RCTs)	⨁⨁◯◯ Low[a,b]	There is little to no evidence that hand sanitiser is more effective than soap and water for reducing transmission related outcomes for respiratory infections
Safety	One RCT stated that no adverse events were observed (Savolainen-Kopra 2012).			(1 RCT)	⨁⨁⨁◯ Moderate[a]	It is likely that soap and water vs hand sanitiser results in no difference in safety or adverse effect outcomes
Absenteeism	One RCT (Azor-Martinez 2018) observed a significant benefit for hand sanitiser in reduction in days absent, Another RCT (Savolainen-Kopra 2012) found no difference between intervention groups.			(2 RCTs)	⨁⨁◯◯ Low[a,b]	There is little to no evidence that hand sanitiser is more effective than soap and water for reducing absenteeism
Severity of illness - not reported	-	-	-	-	-	
Behaviour or practice change - not reported	-	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

a. Lack of blinding in assessment of the outcome. Certainty of evidence downgraded.
b. Inconsistent results reported for outcomes across studies.

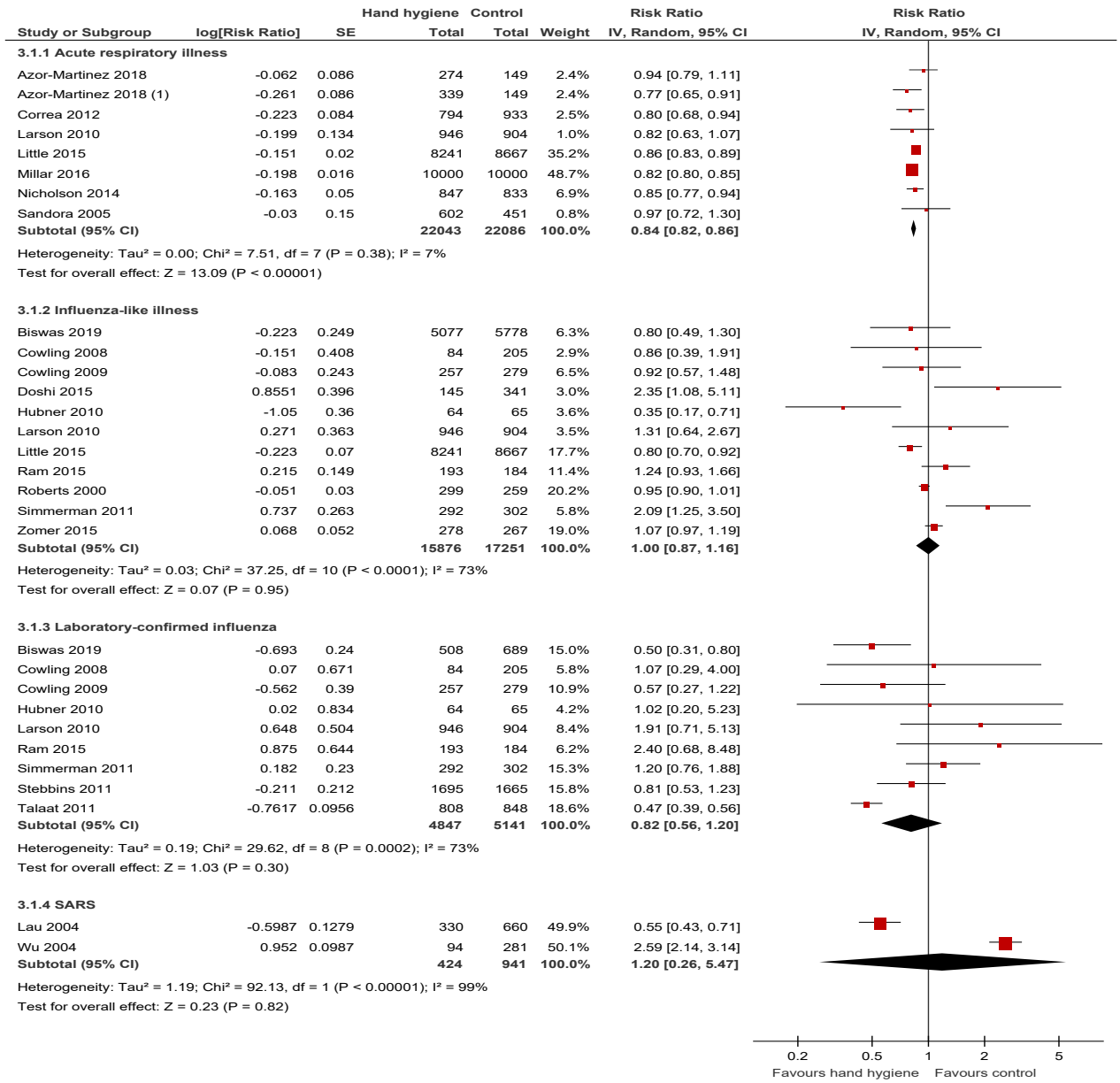
4.2.3.2 Forest Plots

Outcome results related to hand hygiene for transmission related outcomes, viral illness is presented in Figure 3.

Outcome results related to hand hygiene for absenteeism is presented in Figure 5.

Outcome results from Munn 2020 related to hand hygiene for absenteeism, stratified by age of the child is presented in Figure 7.

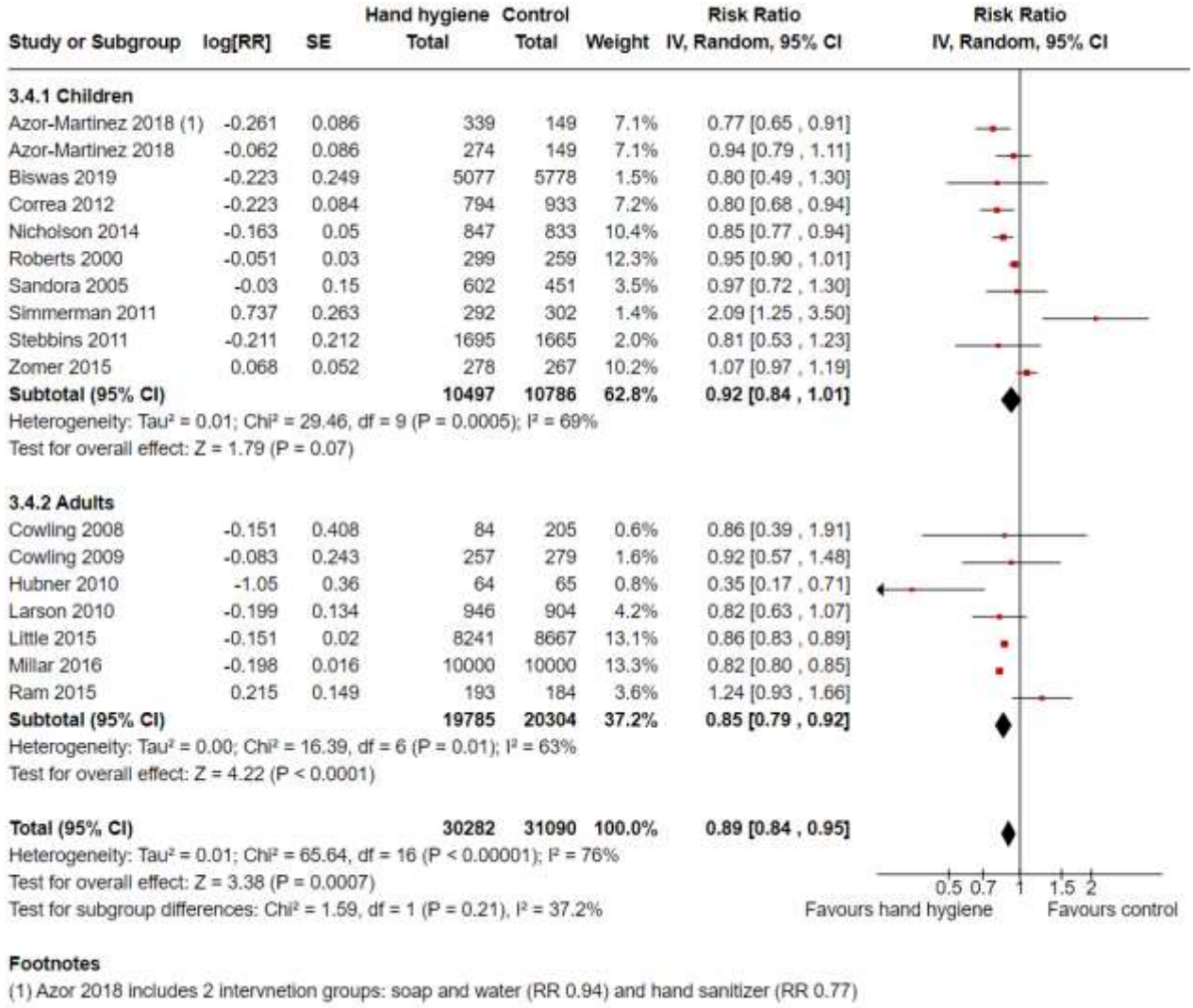
Figure 3 Forest plot of comparison: Hand hygiene vs control: Viral illness



Footnotes

(1) Azor 2018 included 2 hand-washing groups: one using soap and water (RR 0.94) and the other using hand sanitizer (RR 0.77)

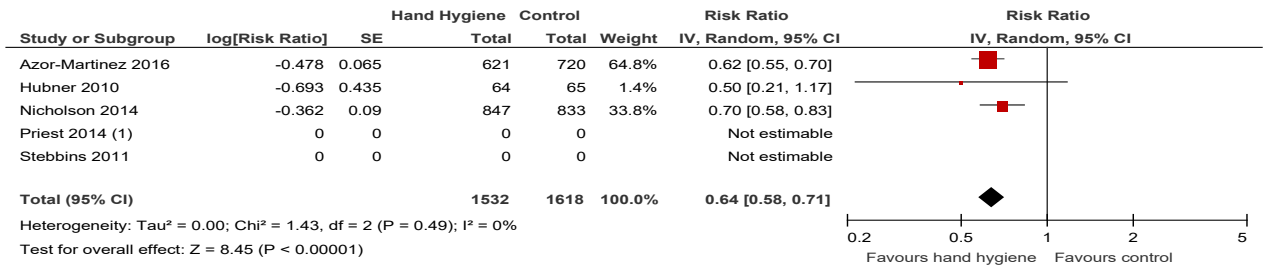
Figure 4 Forest plot of comparison: Hand hygiene vs control: Viral illness - subgroup analysis, children and adults.



Footnotes

(1) Azor 2018 includes 2 intervnetion groups: soap and water (RR 0.94) and hand sanitizer (RR 0.77)

Figure 5 Forest plot of comparison: Hand hygiene vs control: Absenteeism



Footnotes

(1) Data for Priest 2014 and Stebbins 2011 log(IRR) presented in seperate forest plot

Figure 6 Forest plot of comparison: Hand hygiene vs control: Absenteeism (logIRR)

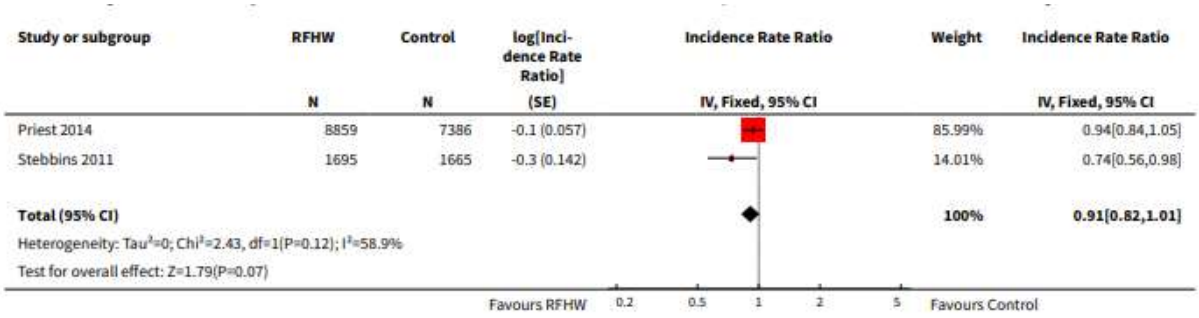
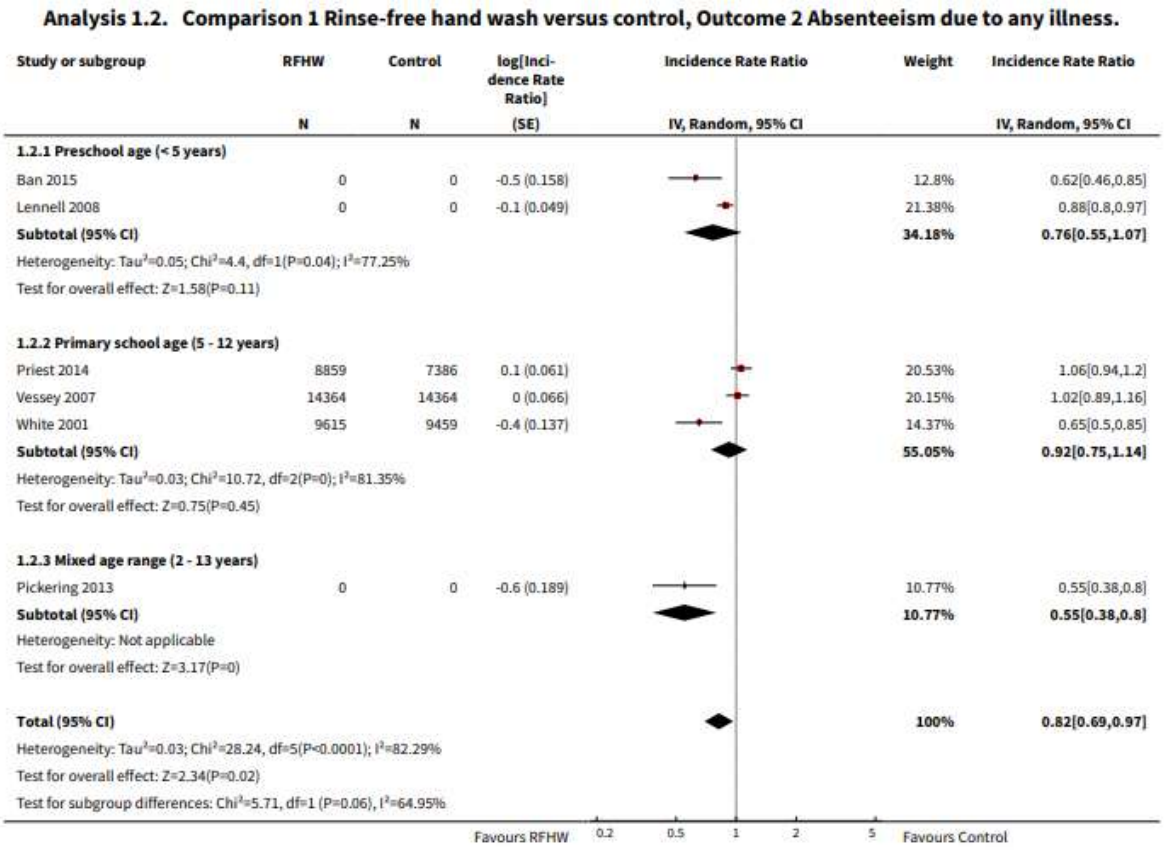


Figure 7 Forest plot of comparison: Rinse free handwash vs control: Absenteeism due to any illness



4.3 Respiratory Hygiene

4.3.1 Description of studies

One systematic review (Xiao 2020) of observational studies was conducted for studies in the community settings in the USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland and Denmark. The systematic review assessed the effectiveness of non-pharmaceutical personal protective measures and environment hygiene measures on the incidence of laboratory confirmed influenza, or influenza like illness. Measures included hand hygiene, respiratory etiquette, face masks, and surface and object cleaning. The study did not identify research evaluating the effectiveness of respiratory etiquette on influenza transmission. The systematic review searched Medline, PubMed, EMBASE, and CENTRAL for literature in all languages for RCTs on 14 August 2018 to identify literatures that were available during January 1, 2013–August 13, 2018.

Another systematic review (Jefferson 2020) reviewed RCTs, cluster RCTs or quasi-RCTs conducted in heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country. The studies reviewed were conducted in Japan, Denmark, Saudi Arabia, Egypt, USA, Israel, France, New Zealand, Thailand, Pakistan, Finland, Germany, Hong Kong. The systematic review examined any physical intervention to prevent respiratory virus transmission, including screening at entry ports, isolation, quarantine, physical distancing, personal protection, hand hygiene, face masks, and gargling) to prevent respiratory virus transmission compared with no or another intervention. The review compared the effect of gargling to control on the incidence of viral illness. The systematic review searched CENTRAL, PubMed, Embase, CINAHL on 1 April 2020 and ClinicalTrials.gov, and the WHO ICTRP on 16 March 2020, authors also conducted a backwards and forwards citation analysis on the newly included studies. This systematic review is an update to the first review of the same name, first published in 2007 (20).

Results for respiratory hygiene (gargling compared to control) are presented in the Summary of Findings table (see Section 4.2.3.1).

4.3.2 Risk of Bias – per item

The risk of bias of included studies for respiratory hygiene (respiratory etiquette, gargling and nasopharyngeal wash) is presented in Appendix D.

One review (Jefferson 2020) was assessed as high quality, and one review (Xiao 2020) was assessed as moderate quality, the study did not justify excluded studies in the literature search or adjust for confounding in the meta-analysis including NRSIs

4.3.3 Main comparison (vs control)

One systematic review (18) identified no studies which evaluated the effectiveness of respiratory etiquette on influenza transmission. Another systematic review (14) provided data from 2 RCTs for the effect of gargling on the transmission of respiratory disease.

Table 3 Description of studies – Respiratory hygiene

Review ID	Study design	Setting	Location	Condition	Intervention/ Comparator	Outcomes
Jefferson 2020 (14)	SR	Heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country	Japan. Denmark. Saudi Arabia. Egypt. USA, Israel. France. New Zealand. Thailand. Pakistan. Finland. Germany. Hong Kong	Laboratory confirmed influenza, influenza like illness	N/A	Primary outcomes 1. Numbers of cases of viral illness (including ARIs, influenza-like illness, and laboratory confirmed influenza, or other viral pathogens). 2. Adverse events related to the intervention. Secondary outcomes 1. Deaths. 2. Severity of viral illness as reported in the studies. 3. Absenteeism. 4. Hospital admissions. 5. Complications related to the illness, e.g. pneumonia.
Xiao 2020 (18)	SR/MA	Community	USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland, Denmark	Laboratory confirmed influenza	N/A	Incidence of laboratory confirmed influenza

4.3.3.1 Summary of findings

Gargling / nasopharyngeal rinsing compared to no or an alternative, or less intense intervention for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: gargling / nasopharyngeal rinsing
Comparison: no or an alternative, or less intense intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no or an alternative, or less intense intervention	Risk with gargling / nasopharyngeal rinsing				
Transmission related outcomes assessed with: Viral illness	379 per 1,000	**345 per 1,000** (0 to 0)	**RR 0.91** (0.63 to 1.31)	830 (2 RCTs)*	⨁◯◯◯ Very low [a,b,c,d]	Gargling / nasopharyngeal rinsing may have little to no effect on incidence of viral illness, but the evidence is very uncertain.
Safety - not reported				-	-	
Absenteeism - not reported				-	-	
Severity of illness	*Satomura (2015): mean peak score in bronchial symptoms was lower in the water gargling group (0.97) than in the povidone-iodine gargling group (1.41) and the control group (1.40), p = 0.055. Other symptoms were not significantly different between groups. *Goodall (2014): symptom severity was greater in the gargling group for clinical (225.3 vs 191.8) and laboratory confirmed URTI (210.5 vs 191.8), but this was not statistically significant *Ides (2014) did not report this outcome			830 (2 RCTs)	⨁◯◯◯ Very low [a,b,c]	
Behaviour or practice change - not reported				-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

Gargling / nasopharyngeal rinsing compared to no or an alternative, or less intense intervention for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: gargling / nasopharyngeal rinsing
Comparison: no or an alternative, or less intense intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no or an alternative, or less intense intervention	Risk with gargling / nasopharyngeal rinsing				

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

* Missing data from one RCT (Ides 2014) (total 747 participants) that reported adjusted data. Laboratory confirmed (adjusted OR 0.69, 95% CI 0.37 to 1.28; P = 0.24); Clinically defined influenza (adjusted OR 0.75, 95% CI 0.50 to 1.13; P = 0.17).
a. One study at low risk of bias and one study at moderate risk of bias. Certainty of evidence not downgraded.
b. Some statistical heterogeneity (I^2=62%). Certainty of evidence downgraded.
c. The available evidence is in university students and healthy adults and may not be applicable to children in the childcare setting (relating to application of the intervention). Certainty of evidence downgraded.
d. Wide confidence intervals (upper and lower bounds overlaps with both effect and no effect). Certainty of evidence downgraded.

4.3.3.2 Forest Plots

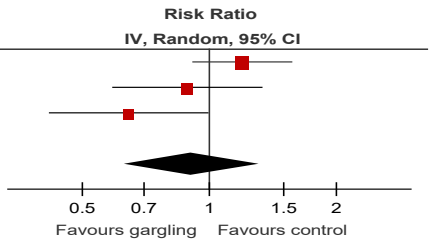
Outcome results related to respiratory hygiene (gargling) for transmission related outcomes (viral illness) is presented in Figure 8.

Figure 8 Forest plot of comparison: Respiratory hygiene (gargling) vs inactive control: Viral illness

Study or Subgroup	log[Risk Ratio]	SE	Gargling Total	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Goodall 2014	0.18	0.137	256	236	39.5%	1.20 [0.92, 1.57]
Satomura 2005	-0.12	0.207	119	58	31.0%	0.89 [0.59, 1.33]
Satomura 2005 (1)	-0.44	0.22	104	57	29.5%	0.64 [0.42, 0.99]
Total (95% CI)			**479**	**351**	**100.0%**	**0.91 [0.63, 1.31]**

Heterogeneity: Tau² = 0.07; Chi² = 6.01, df = 2 (P = 0.05); I² = 67%

Test for overall effect: Z = 0.52 (P = 0.61)



Footnotes

(1) Satomura 2005 included 2 intervention groups

4.4 Face masks and eye protection

4.4.1 Description of studies

One systematic review (Nanda 2021) of one preclinical, one observational cohort clinical study and 12 RCTs conducted in the USA, Saudi Arabia, Face, Hong Kong, Australia, Thailand, and Germany examined the efficacy of surgical masks or cloth masks in the prevention of viral transmission. The studies were conducted in settings including the community, households, university residence halls and the Hajj mass gathering. The systematic review examined face masks alone to no face masks, face masks with or without hand hygiene to no face masks, and face masks and hand hygiene to no face masks. The systematic review searched PubMed, Cochrane CENTRAL, and Embase with the on the 15 August 2020. Studies of SARS-CoV-2 and facemasks and RCTs (n≥50) for other respiratory illnesses were included.

Another systematic review (Jefferson 2020) reviewed RCTs, cluster RCTs or quasi-RCTs conducted in heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country. The studies reviewed were conducted in Japan, Denmark, Saudi Arabia, Egypt, USA, Israel, France, New Zealand, Thailand, Pakistan, Finland, Germany, Hong Kong. The systematic review examined any physical intervention to prevent respiratory virus transmission, including screening at entry ports, isolation, quarantine, physical distancing, personal protection, hand hygiene, face masks, and gargling) to prevent respiratory virus transmission compared with no or another intervention. For face masks as an intervention, the review examined face masks compared to control. The systematic review searched CENTRAL, PubMed, Embase, CINAHL on 1 April 2020 and ClinicalTrials.gov, and the WHO ICTRP on 16 March 2020, authors also conducted a backwards and forwards citation analysis on the newly included studies.

A third systematic review (Chu 2020) of comparative studies in health care and non-healthcare settings, studies were conducted across 17 countries (Saudi Arabia, China, USA, Vietnam, Canada, Taiwan, South Korea, Singapore, Germany, Thailand, Australia, UAE, Iran, Malaysia, Brazil, Hong Kong, Netherlands) with the majority of studies from China. The study examined the effect of physical distancing, face masks, and eye protection to prevent transmission of the viruses that cause COVID-19 and related diseases (e.g., SARS and Middle East respiratory syndrome [MERS]). The systematic review compared face masks with control (no masks). The systematic review also presented evidence assessing the effectiveness of eye protection (face shields and googles) compared to no eye protection, however all evidence available for eye protection was from a healthcare setting. The systematic review 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. Authors also 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.

A fourth systematic review (Abdullahi 2020) examined intervention studies and observational studies conducted in the community setting in low- and middle- income countries. The studies reviewed were conducted in China, Bangladesh, Thailand, Romania, Serbia, Madagascar, Mexico and Peru. The systematic review examined community measures to control infectious diseases, including hand hygiene, face masks and social distancing. The systematic review presented comparisons for face masks compared to no facemasks, face masks and hand hygiene compared to no intervention, and face mask and hand hygiene vs hand hygiene only. The systematic review searched PubMed, Google scholar, the WHO website, MEDRXIV and google, no date limits were applied to the search, and the date of search was not provided.

Another systematic review (Xiao 2020) of observational studies was conducted for studies in the community settings in the USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland and Denmark. The systematic review assessed the effectiveness of non-pharmaceutical personal protective measures and environment hygiene measures on the incidence of laboratory confirmed influenza, or influenza like illness. Measures included hand hygiene, respiratory etiquette, face masks, and surface and object cleaning. The study presented comparisons for face masks alone compared with control, face masks and hand hygiene compared with control, and face masks with or without hand hygiene, compared to control. The systematic review searched Medline, PubMed, EMBASE, and CENTRAL for literature in all languages for RCTs on 14 August 2018 to identify literatures that were available during January 1, 2013–August 13, 2018.

Another systematic review (Chou 2020) of RCTs and observational studies reviewed the effectiveness of N95, surgical, and cloth masks in community and health care settings for preventing respiratory virus infections. Eight trials were conducted in Asia, and four in the USA, the remaining were conducted in Canada, Australia, Europe, Saudi Arabia. The study examined the efficacy of respirators (N95 or equivalent), face (surgical) and cloth masks for SARS-CoV-2, SARS-CoV-1 and MERS-CoV, or influenza, ILI and other viral respiratory infections in community or healthcare settings. A search of PubMed, MEDLINE, and Elsevier Embase (from 2003 through 14 April 2020) was conducted, authors also searched the WHO COVID-19 database and the medRxiv preprint server and reviewed reference lists of relevant articles. This study is a 'living review', whereby the literature search has been updated monthly for a year from the initial search date, the latest search was conducted on 21 July 2020.

The results for face masks compared to control (no intervention), and face masks plus hand hygiene compared to control (no intervention) and eye protection compared to control (no intervention) are presented in the Summary of findings table (see Section 4.4.3.1).

Table 4 Description of studies: Face masks and eye protection

Review ID	Study design	Setting	Location	Condition	Intervention/ Comparator	Outcomes
Nanda 2021 (21)	SR	Community Households University residence halls Hajj mass gathering	USA, Saudi Arabia, France, Hong Kong, Australia, Thailand, Germany	Influenza, influenza like illness	N/A	Incidence of Laboratory confirmed respiratory viral illness Influenza like illness
Jefferson 2020 (14)	SR	Heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country	Japan. Denmark. Saudi Arabia. Egypt. USA, Israel. France. New Zealand. Thailand. Pakistan. Finland. Germany. Hong Kong	Laboratory confirmed influenza, influenza like illness	N/A	Primary outcomes 1. Numbers of cases of viral illness (including ARIs, influenza-like illness, and laboratory confirmed influenza, or other viral pathogens). 2. Adverse events related to the intervention. Secondary outcomes 1. Deaths. 2. Severity of viral illness as reported in the studies. 3. Absenteeism. 4. Hospital admissions. 5. Complications related to the illness, e.g. pneumonia.
Chu 2020 (22)	SR	Health care and community settings	Saudi Arabia, China, USA, Vietnam, Canada, Taiwan, South Korea, Singapore, Germany, Thailand, Australia, UAE, Iran, Malaysia, Brazil, Hong Kong, Netherlands	SARS-CoV-2	N/A	Risk of transmission (ie, WHO defined confirmed or probable COVID-19, SARS, or MERS) to people in healthcare or non-healthcare settings by those infected Contextual factors such as acceptability, feasibility, effect on equity and resource considerations
Abdullahi 2020 (17)	SR/MA	Low- and Middle-income countries Households Schools General Community	China, Bangladesh, Thailand, Romania, Serbia, Madagascar, Mexico, Peru	SARS, influenza	N/A	SARS and influenza incidence
Xiao 2020 (18)	SR/MA	Community	USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland, Denmark	Laboratory confirmed influenza	N/A	Incidence of laboratory confirmed influenza
Chou 2020 (23)	SR	Community or healthcare settings in all geographic areas	USA, Australia, Saudi Arabia, Canada, Europe	SARS-CoV-2, SARS-CoV-1 or MERS-CoV, influenza, influenza like illness and other viral respiratory infection	N/A	Efficacy of respirators

4.4.2 Risk of Bias – per item

The risk of bias of included studies for masks wearing, mask wearing plus hand hygiene and eye protection presented in Appendix D. One study (Jefferson 2020) was assessed as high quality, and four studies (Nanda 2021, Chu 2020, Xiao 2020 and Chou 2020) were assessed as moderate quality, Chu 2020 did not describe the included studies in adequate detail, while Chou 2020 did not assess risk of bias of included studies and a meta-analysis of the studies was not conducted, with a narrative reporting of results. Nanda 2021 did not provide the population or review methods in detail. Xiao 2020 did not justify excluded studies in the literature search or adjust for confounding in the meta-analysis including NRSIs. One study (Abdullahi 2020) was assessed as low quality, the study did not assess the impact of risk of bias assessment on the metanalysis or account for risk of bias in reporting the results, or account for heterogeneity

4.4.3 Main comparison (vs control)

Information for face masks compared to control one RCT from Nanda 2021 the 9 RCTs identified by Jefferson 2020 for the comparison between face masks and control. Evidence from three RCTs for the effect of masks on the transmission of SARS was incorporated from Chu 2020 and Abdullahi 2020. Additional narrative data from Chou 2020, who did not perform a meta-analysis found there were no studies which evaluated masks for the prevention of SARS-CoV02 infections in community settings, at the time of the literature search in April 2020.

Chou 2020 (24) is a living rapid review, at the time of the latest literature search update in July 2022 there is additional evidence from 2 RCTs and 11 observational studies. Data from the two RCTs showed mask wearing reduced symptomatic SARS-CoV-2 infections (adjusted prevalence ratio 0.9, 95 % CI 0.82, 0.995) in one study, and little benefit was observed in another (OR 0.82, 95% CI 0.52, 1.23). As most of the additional evidence were from observational studies and had methodological limitation, the evidence benefits of mask use versus no use for the prevention of SARS-CoV-2 infection in the community was of moderate to low certainty.

One systematic review (Xiao 2020) reviewed eye protection as an intervention for preventing the transmission of respiratory infections, with all studies conducted in the health care setting. Jefferson 2020 found no RCT's which assessed the effectiveness and safety of eye protection.

4.4.3.1 Summary of findings

Facemasks compared to control (no intervention) for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: facemasks
Comparison: control (no intervention)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control (no intervention)	Risk with facemasks				
Transmission related outcomes assessed with: Influenza-like illness	126 per 1,000	**126 per 1,000** (106 to 151)	**RR 1.00** (0.84 to 1.20)	4341 (10 RCTs)	⨁⨁◯◯ Low[a,b]	The evidence suggests that facemasks do not reduce transmission related outcomes.
Transmission related outcomes assessed with: Laboratory confirmed influenza	40 per 1,000	**36 per 1,000** (26 to 50)	**RR 0.91** (0.66 to 1.26)	3005 (6 RCTs)	⨁⨁⨁◯ Moderate[b]	Facemasks probably results in little to no difference in transmission related outcomes.
Transmission related outcomes assessed with: transmission of SARS	210 per 1,000	**118 per 1,000** (84 to 166)	**RR 0.56** (0.40 to 0.79)	725 (3 observational studies)	⨁⨁◯◯ Low	The evidence suggests facemasks result in a slight reduction in the transmission of SARS in non-healthcare settings.
Safety	not reported	-	-	-	-	
Absenteeism	not reported	-	-	-	-	
Severity of illness	not reported	-	-	-	-	
Behaviour or practice change	not reported	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

a. Lack of blinding in assessment of the outcome. Certainty of evidence downgraded.
b. Wide confidence intervals (upper bound overlaps with no effect). Certainty of evidence downgraded.

Eye protection (face shield, goggles) compared to control (no intervention) for reducing the transmission of respiratory infection

Patient or population: reducing the transmission of respiratory infection
Setting: early childhood education settings
Intervention: eye protection (face shield, goggles)
Comparison: control (no intervention)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control (no intervention)	Risk with eye protection (face shield, goggles)				
Transmission related outcomes assessed with: Change of viral infection or transmission	161 per 1,000	**55 per 1,000** (35 to 84)	**RR 0.34** (0.22 to 0.52)	3713 (13 observational studies)	⨁◯◯◯ Very low[a,b,c]	Eye protection (face shield, goggles) may reduce transmission related outcomes in the childcare setting, but the evidence is very uncertain.
Safety	not reported	-	-	-	-	
Absenteeism	not reported	-	-	-	-	
Severity of illness	not reported	-	-	-	-	
Behaviour or practice change	not reported	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

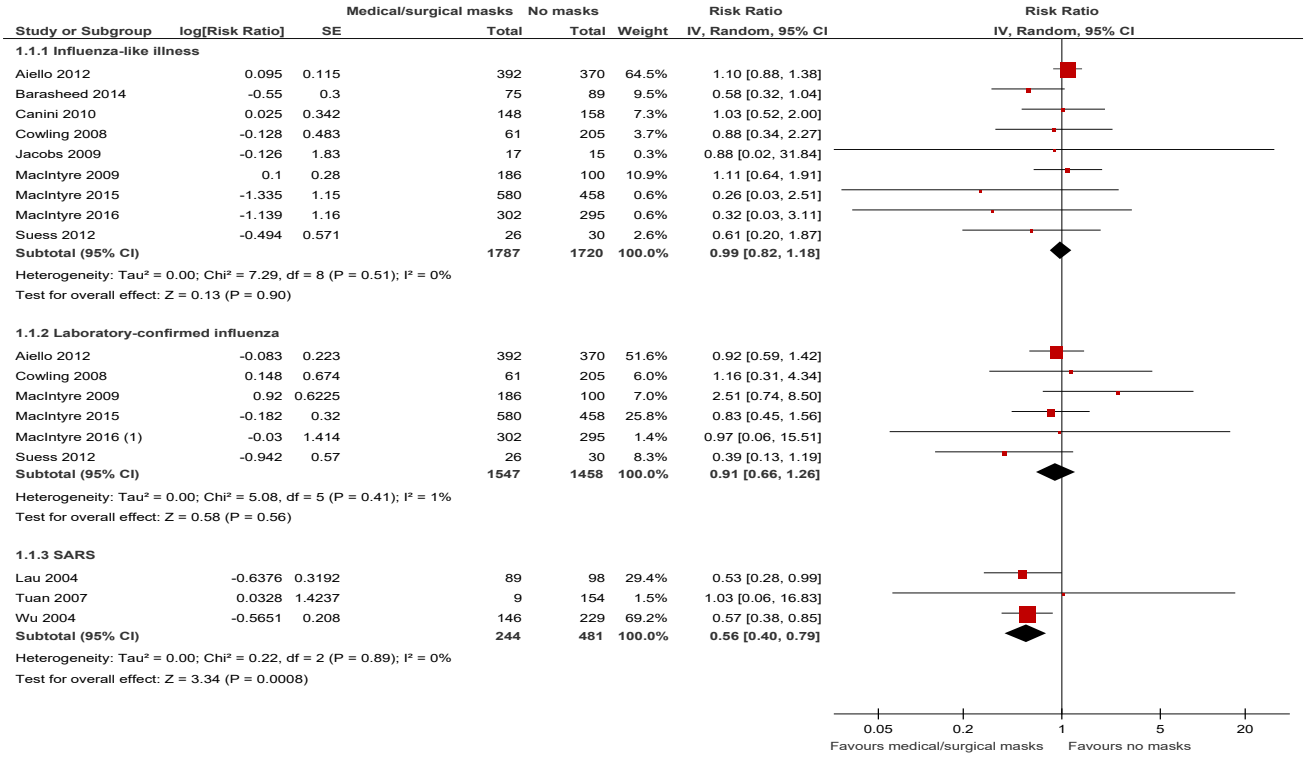
a. All studies were judged to be at low to moderate risk of bias. Certainty of evidence not downgraded.
b. No serious heterogeneity (I^2=43%). Certainty of evidence not downgraded
c. Very serious indirectness. All included studies were conducted in adult healthcare workers. Certainty of evidence downgraded two levels.

4.4.3.2 Forest Plots

Outcome results related to face masks for transmission related outcomes (viral illness) is presented in Figure 9.

Outcome results related to the association between eye protection and risk of COVID-19, SARS, or MERS transmission is presented in Figure 10.

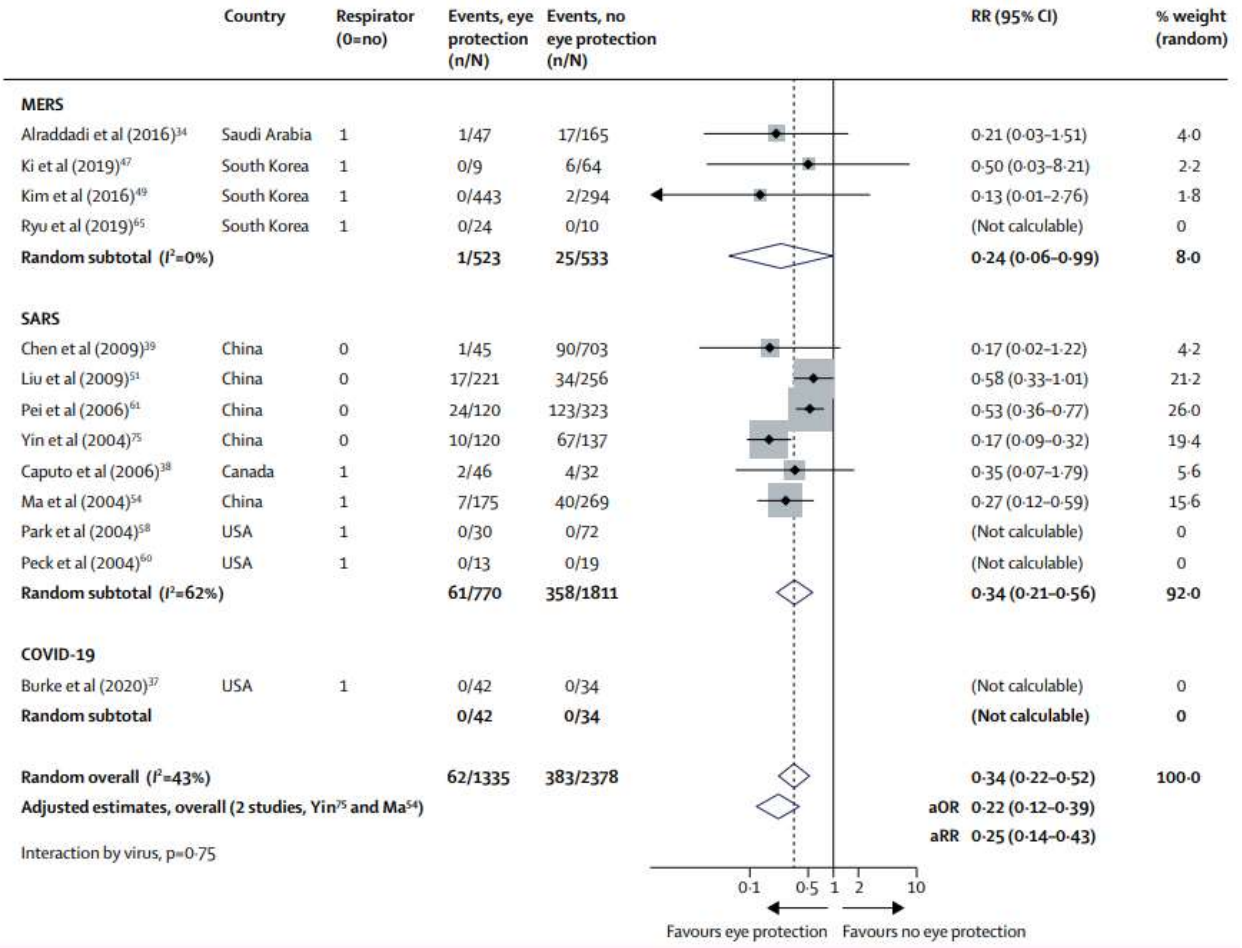
Figure 9 Forest plot of comparison: face masks vs no masks transmission related outcomes, viral illness.



Footnotes

(1) Both MacIntyre studies reported on laboratory confirmed respiratory virus infection

Figure 10 Forest plot of comparison: association of eye protection with risk of COVID-19, SARS, or MERS transmission



4.5 Screening at entry

4.5.1 Description of studies

One open label, cluster-randomised controlled trial (Young 2021) assessed the effectiveness of voluntary daily later flow device testing for 7 days in secondary schools and further education colleges in England, with LFD-negative contacts remaining at the school. This was compared with the self-isolation of school based COVID-19 contacts for 10 days. The study examined the effect of the intervention on COVID-19 related absenteeism.

Two studies using the same data (Bilinksi 2021, Bilinski 2022) modelled the effectiveness of screening children in elementary and middle school in the US for COVID-19 on transmission outcomes. One non-randomised controlled trial/modelling study (Forster 2022) examined the feasibility of SARS-CoV-2 surveillance testing among children and childcare workers across 9-day care centres in Germany, the study also modelled the estimated number of secondary infections resulting from different testing schedules.

The results for screening at entry compared to control or alternative intervention are presented in the Summary of findings table (see Section 4.5.3.1)

Table 5 Description of studies: Screening at entry

Review ID	Study design	Setting	Location	Condition	Intervention/ Comparator	Outcomes
Young 2021 (25)	Open label, cluster-randomised controlled trial	Secondary schools and further education colleges	England	SARS-CoV-2	Voluntary daily later flow device testing for 7 days with LFD-negative contacts remaining at the school/ self-isolation of school based COVID-19 contacts for 10 days	Primary outcomes: Number of COVID-19 related school absences among those otherwise eligible to be in school The extent of in school SARS-CoV-2 transmission
Bilinksi 2021/2022 (26, 27)	Modelling study	Elementary and middle school communities	USA	SARS-CoV-2	Screening for COVID-19/ No screening	Cumulative incidence of SARS-CoV-2 infection; proportion of cases detected; proportion of planned and unplanned days out of school; and the cost of testing programs and of childcare costs associated with different strategies
Forster 2022 (28)	Non-randomised control trial/ modelling study	Multicentre: 9 day care centres	Wuerzburg, Germany	SARS-CoV-2	Continuous surveillance of asymptomatic children and childcare workers by SARS-CoV-2 PCR testing of either mid-turbinate nasal swabs twice weekly, or once weekly or self-sampled saliva samples twice weekly / testing of symptomatic participants	The primary outcomes were acceptance of the respective surveillance protocols (feasibility study) and the estimated number of secondary infections (ASI) (mathematical modelling)

4.5.2 Risk of Bias – per item

The risk of bias of included studies for screening at entry is presented in Appendix D.

Two studies (Young 2021 and Forster 2022) were assessed to have some concerns for risk of bias, both studies has bias arising from the patient selection, Young 2021 also had bias related to measurement of the outcome. An additional study (Bilinksi 2021, Bilinski 2022) was assessed as moderate risk of bias, the modelling study did not present strategies to deal with confounding.

4.5.3 Main comparison (vs control)

No systematic reviews were identified that assessed screening/ testing entry for reducing the transmission of respiratory infections. Data for this outcome was compiled from one nRCT/modelling study (28), one modelling study (26, 29) and one open label cluster-randomised controlled trial (30).

4.5.3.1 Summary of findings

Screening/ testing at entry compared to no or an alternative, or less intense intervention for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood and care services
Intervention: screening/ testing at entry
Comparison: no or an alternative, or less intense intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no or an alternative, or less intense intervention	Risk with screening/ testing at entry				
Transmission related outcomes assessed with: average number of secondary infections (ASI) follow up: 12 weeks	*One nRCT/modelling study (Forster 2021) found continuous surveillance of asymptomatic children and childcare workers by SARS-CoV-2 PCR testing of mid-turbinate nasal swabs is a feasible strategy for reducing the ASI in day care centres, compared to no testing. More frequent testing was associated with less secondary infections, however authors determined under realistic conditions (biweekly testing including Monday as a testing day, with >50% participation rate) can reduce the ASI to less than 1. *One modelling study (Bilinksi 2021/2022) estimated once weekly, or twice weekly screening of children in elementary and middle schools can reduce the difference in the proportion of whole school population infected per month by -0.0013 and -0.0017, respectively.			(2 observational studies)	⨁◯◯◯ Very low [a,b]	The evidence is very uncertain about the effect of screening/ testing at entry on transmission related outcomes.
Safety	not reported		-	-		
Absenteeism	not reported		-	-		
Severity of illness	not reported		-	-		
Behaviour or practice change	not reported		-	-		

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

a. Population includes students from middle and high school settings in the US Certainty of evidence downgraded.
b. Two modelling studies with serious concerns of bias, certainty of evidence downgraded.

4.6 Ventilation

4.6.1 Description of studies

One systematic review (Hammond 2000) of any study type compared the use of portable, commercially available air filters in any indoor community setting, with no air filter use within the same setting on the incidence of respiratory infection and removal or aerosolised bacteria and viruses from the air. The two included studies were conducted in Beijing and the USA, in an office building and emergency room, respectively. The systematic review searched Medline, Embase and Cochrane for articles published in any language between January 2000 and March 2021.

One cluster-RCT (Curtius 2021) assessed the effect of operating four air purifiers equipped with HEPA filters in a high school classroom while classes are taking place on aerosol load. This was compared with air purifiers without HEPA filters. The study was conducted in Germany over the course of a week (Monday to Friday).

One prospective cohort/modelling study (Mendell 2013) estimated the relationship between daily illnesses absence and ventilation rates in Californian elementary schools over a period of two years.

The results for ventilation compared to control (no or alternative, less intense intervention) are presented in the Summary of findings table (see Section 4.6.3.1).

Table 6 Study details: Ventilation

Review ID	Study design	Setting	Location	Condition	Intervention/ Comparator	Outcomes
Hammond 2021 (31)	SR	Office building Emergency room	Beijing, USA	SARS-CoV-2 and other respiratory illness	Portable, commercially available air filters, including high efficiency particulate air (HEPA) filters / No air filter use within the same setting (for example randomised controlled trial of air filters in a classroom or office) or not applicable if observational study	Incidence of respiratory infection Whether filters capture/ remove aerosolised bacteria and viruses from the air, including information of what is captured
Curtius 2021 (32)	Cluster-RCT	School setting – Air filters in place Monday to Friday.	Germany	SARS-CoV-2	Operating four air purifiers equipped with HEPA filters in a high school classroom while classes are taking place/ air purifiers without HEPA filters	Aerosol number concentration for particles >3nm at two locations in the room and aerosol size distribution in the range from 10 mm to 10 µm, PM_{10} and CO_2 concentration
Mendell 2013 (33)	Prospective cohort/ modelling	162 3rd-5th grade classrooms in 28 schools in three school districts: South Coast, Bay Area and Central Valley.	Californian elementary school	Any infection	N/A	Daily illness absence count in each classroom CO_2 concentration Temperature Relative humidity Estimated VR per person (Vo) in l/s-person in each classroom for each school day during the study

4.6.2 Risk of Bias – per item

The risk of bias of included studies for ventilation is summarised in Appendix D. One study (Hammond 2021) was assessed as high quality and two additional modelling studies (Mendell 2013, Curtius 2021) were assessed at moderate risk of bias. The studies did not assess confounding, Curtius 2021 only assessed the impact of air purifiers in the school setting over a short period of one week.

4.6.3 Main comparison (vs control)

One systematic review (31) identified no studies which reported the effect of air filters on respiratory infection or transmission in a community setting, identifying one study in an office setting and one in a health care setting. The data from Hammond 2000 was supplemented with findings from one cluster-RCT (Curtius 2021) and one modelling study (Mendell 2013) which examined the effect of air filtration and ventilation in a school setting.

4.6.3.1 Summary of findings

Air filtration/ increased ventilation compared to no or an alternative, or less intense intervention for reducing transmission of respiratory infections

Patient or population: reducing transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: air filtration/ increased ventilation
Comparison: no or an alternative, or less intense intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no or an alternative, or less intense intervention	Risk with air filtration/ increased ventilation				
Transmission related outcomes assessed with: incidence of respiratory infections	*One SR (Hammond 2021) (literature search to March 2021) found there is a considerable gap in evidence around whether portable air filters reduce the incidence of respiratory infections, including SARS-CoV-2. The SR identified two RCTs that found portable air filtration does capture airborne bacteria and reduced the amount of airborne bacteria in the air. *No studies were identified that investigated the effects of portable, commercially available air filters on the incidence of respiratory infection in the community.			4 (2 RCTs)	⨁◯◯◯ Very low a,b,c	The evidence is very uncertain about the effect of air filtration/ increased ventilation on transmission related outcomes.
Transmission related outcomes assessed with: inhaled dose of airborne SARS-CoV-2 RNA	*One RCT (Curtius 2021) reported the effect of mobile air purifiers in a school classroom for reducing the airborne transmission risk for SARS-CoV-2. The authors estimate that the inhaled dose of airborne SARS-CoV-2 RNA is reduced by a factor of six when using air purifiers with an air exchange rate of 5.7 per hour, compared to no purifiers.			2 (1 RCT)	⨁◯◯◯ Very low[b,c]	
Safety	not reported			-	-	

Air filtration/ increased ventilation compared to no or an alternative, or less intense intervention for reducing transmission of respiratory infections

Patient or population: reducing transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: air filtration/ increased ventilation
Comparison: no or an alternative, or less intense intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no or an alternative, or less intense intervention	Risk with air filtration/ increased ventilation				
Absenteeism	One prospective cohort study (Mendell 2013) suggested higher ventilation rates in classroom settings were associated with decreased illness absence for school students and teachers.			162 (1 observational study)	⨁◯◯◯ Very low [d,e,f]	The evidence is very uncertain about the effect of air filtration/ increased ventilation on absenteeism.
Severity of viral illness	not reported			-	-	
Behaviour or practice change	not reported			-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

a. RCTs with some concerns of bias not considered to seriously effect the results. Certainty of evidence not downgraded.
b. Evidence from two RCTs identified by Hammond 2021 were in a workplace and emergency room setting. Evidence from one RCT was in high school in Germany. Certainty of evidence downgraded.
c. Evidence is limited by the small number or classrooms/workplaces studied. Curtius (2021) used evidence collected from HEPA filters place in one classroom over a period of one week. Certainty of evidence downgraded two levels.
d. One study at moderate risk of bias, certainty of evidence not downgraded.
e. Mendell (2013) conducted study in 28 school (total 162 3rd-5th grade classrooms) across three school districts in the USA. Certainty of evidence downgraded.
f. Evidence is limited by the small number or classrooms/workplaces studied. Certainty of evidence downgraded two levels.

4.7 Environmental cleaning

4.7.1 Description of studies

One systematic review (Jefferson 2020) reviewed of RCTs, cluster RCTs or quasi-RCTs conducted in heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country. The studies reviewed were conducted in Japan, Denmark, Saudi Arabia, Egypt, USA, Israel, France, New Zealand, Thailand, Pakistan, Finland, Germany, Hong Kong. The systematic review examined any physical intervention to prevent respiratory virus transmission, including screening at entry ports, isolation, quarantine, physical distancing, personal protection, hand hygiene, face masks, and gargling) to prevent respiratory virus transmission compared with no or another intervention. The systematic review examined surface/object disinfection (with or without hand hygiene) compared to control. The systematic review searched CENTRAL, PubMed, Embase, CINAHL on 1 April 2020 and ClinicalTrials.gov, and the WHO ICTRP on 16 March 2020, authors also conducted a backwards and forwards citation analysis on the newly included studies. This systematic review is an update to the first review of the same name, first published in 2007 (14)

Another systematic review (Xiao 2020) of observational studies was conducted for studies in the community settings in the USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland and Denmark. The systematic review assessed the effectiveness of non-pharmaceutical personal protective measures and environment hygiene measures on the incidence of laboratory confirmed influenza, or influenza like illness. Measures included hand hygiene, respiratory etiquette, face masks, and surface and object cleaning. The systematic review assessed the effect of surface and object cleaning on the prevention of laboratory confirmed influenza. The systematic review searched Medline, PubMed, EMBASE, and CENTRAL for literature in all languages for RCTs on 14 August 2018 to identify literatures that were available during January 1, 2013–August 13, 2018.

The results for environmental cleaning compared to control (no or alternative, less intense intervention) are presented in the Summary of findings table (see Section 4.7.3.1).

4.7.2 Risk of Bias – per item

The risk of bias of included studies for environmental cleaning is presented in Appendix D. One study (Jefferson 2020) was assessed as high quality, another study (Xiao 2020) was assessed as of moderate quality, the study did not justify excluded studies in the literature search or adjust for confounding in the meta-analysis including NRSIs

4.7.3 Main comparison (vs control)

Two systematic review reviewed environmental cleaning, or surface/object disinfection. Jefferson 2020 identified six trials on surface/object disinfection, which could not be pooled due to heterogeneity in outcome reporting. Xiao 2020 identified three studies which examined surface and object cleaning, two of which were included by Jefferson 2020 with the inclusion of an additional observational study.

Table 7 Study details environmental cleaning

Review ID	Study design	Setting	Location	Condition	Intervention/ Comparator	Outcomes
Jefferson 2020 (14)	SR	Heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country	Japan. Denmark. Saudi Arabia. Egypt. USA, Israel. France. New Zealand. Thailand. Pakistan. Finland. Germany. Hong Kong	Laboratory confirmed influenza, influenza like illness	N/A	Primary outcomes 1. Numbers of cases of viral illness (including acute respiratory infections, influenza-like illness, and laboratory confirmed influenza, or other viral pathogens). 2. Adverse events related to the intervention. Secondary outcomes 1. Deaths. 2. Severity of viral illness as reported in the studies. 3. Absenteeism. 4. Hospital admissions. 5. Complications related to the illness, e.g. pneumonia.
Xiao 2020 (18)	SR/MA	Community	USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland, Denmark	Laboratory confirmed influenza	N/A	Incidence of laboratory confirmed influenza

4.7.3.1 Summary of findings

Environmental cleaning/ surface/ object disinfection (with or without hand hygiene) compared to no or an alternative, or less intense intervention for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: environmental cleaning/ surface/ object disinfection (with or without hand hygiene)
Comparison: no or an alternative, or less intense intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no or an alternative, or less intense intervention	Risk with environmental cleaning/ surface/ object disinfection (with or without hand hygiene)				
Transmission related outcomes - respiratory infections	Five of the six trials combined disinfection with other interventions such as hand hygiene education, provision of hand hygiene products, and audits. *Ban 2015 utilised a combination of provision of hand hygiene products, and cleaning and disinfection of surfaces, and demonstrated a significant reduction in ARI in the intervention group (OR 0.47, 95% CI 0.48 to 0.65). *A similar result was seen in Carabin 1999 with a significant reduction in episodes of acute respiratory infections (ARI). *Two studies tested multicomponent interventions and observed no significant difference in ARI outcomes (Kotch 1994; McConeghy 2017). *One trial compared disinfection alone to usual care (Ibfelt 2015). This study demonstrated a significant reduction in some viruses detected on surfaces in the childcare centres (adenovirus, rhinovirus, respiratory syncytial virus, and metapneumovirus), but not in other viruses, including coronavirus.			(6 RCTs)	⊕⊕◯◯ Low[a,b]	The evidence suggests that environmental cleaning/ surface/ object disinfection (with or without hand hygiene) results in little to no difference in transmission related outcomes.
Safety	not reported	-	-	-	-	
Absenteeism	250 per 1,000	**275 per 1,000** (243 to 310)	-	285 (1 RCT)	⊕⊕◯◯ Low[c,d]	The evidence suggests that environmental cleaning/ surface/ object disinfection (with or without hand hygiene) results in little to no difference in absenteeism related to respiratory illnesses.
Severity of illness	not reported	-	-	-	-	

Environmental cleaning/ surface/ object disinfection (with or without hand hygiene) compared to no or an alternative, or less intense intervention for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: environmental cleaning/ surface/ object disinfection (with or without hand hygiene)
Comparison: no or an alternative, or less intense intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no or an alternative, or less intense intervention	Risk with environmental cleaning/ surface/ object disinfection (with or without hand hygiene)				
Behaviour or practice change	not reported	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

a. Lack of blinding in assessment of the outcome. Certainty of evidence downgraded.
b. Inconsistent results reported for outcomes across studies. Certainty of evidence downgraded.
c. Lack of blinding in assessment of the outcome., some issues with allocation concealment and selective reporting. Certainty of evidence downgraded.
d. Evidence is limited to one small study. Certainty of evidence downgraded.

4.8 Combined interventions

4.8.1 Description of studies

One systematic review (Nanda 2021) of 12 RCTs and one preclinical, one observational cohort study conducted in the USA, Saudi Arabia, Face, Hong Kong, Australia, Thailand, and Germany examined the efficacy of surgical masks or cloth masks in the prevention of viral transmission. The studies were conducted in settings including the community, households, university residence halls and the Hajj mass gathering. The systematic review examined face masks alone to no face masks, face masks with or without hand hygiene to no face masks, and face masks and hand hygiene to no face masks. The systematic review searched PubMed, Cochrane CENTRAL, and Embase with the on the 15 August 2020. Studies of SARS-CoV-2 and facemasks and RCTs of n ≥ 50 for other respiratory illnesses were included.

Another systematic review (Jefferson 2020) reviewed RCTs, cluster RCTs or quasi-RCTs conducted in heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country. The studies reviewed were conducted in Japan, Denmark, Saudi Arabia, Egypt, USA, Israel, France, New Zealand, Thailand, Pakistan, Finland, Germany, Hong Kong. The systematic review examined any physical intervention to prevent respiratory virus transmission, including screening at entry ports, isolation, quarantine, physical distancing, personal protection, hand hygiene, face masks, and gargling) to prevent respiratory virus transmission compared with no or another intervention. The systematic review examined face masks with hand hygiene compared to no masks. The systematic review searched CENTRAL, PubMed, Embase, CINAHL on 1 April 2020 and ClinicalTrials.gov, and the WHO ICTRP on 16 March 2020, authors also conducted a backwards and forwards citation analysis on the newly included studies.

A third systematic review (Abdullahi 2020) examined intervention studies and observational studies conducted in the community setting in low- and middle- income countries. The studies reviewed were conducted in China, Bangladesh, Thailand, Romania, Serbia, Madagascar, Mexico and Peru. The systematic review examined community measures to control infectious diseases, including hand hygiene, face masks and social distancing. The systematic review presented comparisons for face masks compared to no facemasks, face masks and hand hygiene compared to no intervention, and face mask and hand hygiene vs hand hygiene only. The systematic review searched PubMed, Google scholar, the WHO website, MEDRXIV and google, no date limits were applied to the search, and the date of search was not provided.

Another systematic review (Xiao 2020) of observational studies was conducted for studies in the community settings in the USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland and Denmark. The systematic review assessed the effectiveness of non-pharmaceutical personal protective measures and environment hygiene measures on the incidence of laboratory confirmed influenza, or influenza like illness. Measures included hand hygiene, respiratory etiquette, face masks, and surface and object cleaning. The study presented comparisons for face masks alone compared with control, face masks and hand hygiene compared with control, and face masks with or without hand hygiene, compared to control. The systematic review searched Medline, PubMed, EMBASE, and CENTRAL for literature in all languages for RCTs on 14 August 2018 to identify literatures that were available during January 1, 2013–August 13, 2018.

One systematic review (Krishnaratne 2020) assessed the effectiveness of measures implemented in school settings to safely reopen schools, or keep schools open, or both, during the COVID-19 pandemic. Schools were considered any setting with the primary purpose to provide regular education to children between 4 and 18 years of age, given this definition childcare setting were not included. The systematic review included 33 modelling studies, three observational studies, one quasi-experimental and one experimental study with modelling components. The studies reviewed were carried out in a range of countries, including the USA, Canada, Germany, the UK, France, China, Chile, Denmark, Israel, the Netherlands, Sweden, and Switzerland. The evidence synthesis was divided into four broad categories (i) measures reducing the opportunity for contacts; (ii) measures making contacts safer; (iii) surveillance and response measures; and (iv) multicomponent measures. The systematic review assessed transmission related outcomes, healthcare utilisation outcomes and societal, economic and ecological outcomes. The systematic review searched Medline, Embase, CENTRAL, Educational resources information centre, the Cochrane COVID-19 study register and the WHO COVID-19 global literature on coronavirus disease, search year was limited to 2020.

The results for hand hygiene and face masks compared to control (no or alternative, less intense intervention) are presented in the Summary of findings table (see Section 4.8.3.1).

Table 8 Study details combined interventions

Review ID	Study design	Setting	Location	Condition	Intervention/ Comparator	Outcomes
Nanda 2021 (21)	SR	Community Households University residence halls Hajj mass gathering	USA, Saudi Arabia, France, Hong Kong, Australia, Thailand, Germany	Influenza, influenza like illness	N/A	Incidence of Laboratory confirmed respiratory viral illness Influenza like illness
Jefferson 2020 (14)	SR	Heterogeneous settings, ranging from suburban schools to hospital wards in high-income countries; crowded inner city settings in low-income countries; and an immigrant neighbourhood in a high-income country	Japan. Denmark. Saudi Arabia. Egypt. USA, Israel. France. New Zealand. Thailand. Pakistan. Finland. Germany. Hong Kong	Laboratory confirmed influenza, influenza like illness	N/A	Primary outcomes 1. Numbers of cases of viral illness (including ARIs, influenza-like illness, and laboratory confirmed influenza, or other viral pathogens). 2. Adverse events related to the intervention. Secondary outcomes 1. Deaths. 2. Severity of viral illness as reported in the studies. 3. Absenteeism. 4. Hospital admissions. 5. Complications related to the illness, e.g. pneumonia.
Abdullahi 2020 (17)	SR/MA	Low- and Middle-income countries Households Schools General Community	China, Bangladesh, Thailand, Romania, Serbia, Madagascar, Mexico, Peru	SARS, influenza	N/A	SARS and influenza incidence
Xiao 2020 (18)	SR/MA	Community	USA, Thailand, Bangladesh, Hong Kong, Germany, Egypt, Saudi Arabia, Australia, Finland, Denmark	Laboratory confirmed influenza	N/A	Incidence of laboratory confirmed influenza
Krishnaratne 2020	SR	Schools	USA, Canada, Germany, the UK, France, China, Chile, Denmark, Israel, the Netherlands, Sweden, and Switzerland	SARS-CoV-2	Measures reducing the opportunity for contacts Measures making contacts safer Surveillance and response measures Multicomponent measures/ no intervention	

4.8.2 Risk of Bias – per item

The risk of bias of included studies for combined interventions is presented in Appendix D. Two studies (Jefferson 2020, and Krishnaratne 2020) were assessed as high quality, two studies (Nanda 2021 and Xiao 2020) were assessed as moderate quality, Nanda 2021 did not provide the population or review methods in detail. Xiao 2020 did not justify excluded studies in the literature search or adjust for confounding in the meta-analysis including NRSIs. An additional study (Abdullahi 2020) was assessed as low quality, The study did not assess the impact of risk of bias assessment on the metanalysis or account for risk of bias in reporting the results, or account for heterogeneity

4.8.3 Main comparison (vs control)

The combination of masks and hand hygiene was examined by a number of systematic reviews. Data from Jefferson 2020 was supplemented with one RCT identified by two systematic reviews (18, 21). Included studies were otherwise consistent between systematic reviews.

There were 23 modelling studies assessing measures to reduce the opportunity for contacts, the studies were largely consistent in predicting positive effects on transmission related outcomes (e.g. a reduction in the number or proportion of cases, reproduction number) and healthcare utilisation outcomes (i.e. fewer hospitalisations) and mixed or negative effects on societal, economic and ecological outcomes (i.e. fewer number of days spent in school). There were some differences in the direction of the effect for different types of interventions to reduce the opportunity for contacts (i.e. alternating attendance schedules, staggered start/finish times).

There were 11 modelling studies and two real-world studies looking at measures making contacts safer, such as mask wearing in schools, cleaning, handwashing, and ventilation. Overall evidence shows a reduction in transmission related outcomes resulting from these interventions; however, the certainty of the evidence was low. Two studies assessing handwashing policies showed either negative or no effects, with one study of low certainty showing an increase in hand eczema due to a handwashing policy introduced once schools reopened and another study of very low certainty showing no effect, although results were only presented graphically. Evidence on interventions combining multiple measures to make contacts safer was of very low certainty and showed mixed results in terms of a reduction in the number of cases, reduction in the number of deaths, shift in pandemic development, as well as days of school missed, however, they did show a reduction in the reproduction number and the number or proportion of hospitalisations.

There were 12 modelling studies and one real-world study assessing surveillance and response measures. Overall, the studies yielded positive outcomes. However, these measures were often implemented alongside other transmission mitigation measures, such as physical distancing and cohorting strategies which may have moderated the effects of the testing and isolation strategies. Furthermore, the effectiveness of measures was also dependent on the level of community transmission. The most effective testing and isolation strategies used a combination of early testing together with symptom screening and isolation of symptomatic cases, with one study finding that opening schools was likely to increase the death count more rapidly if asymptomatic testing and tracing strategies were not implemented. There was mixed evidence on the costs and human resource costs of surveillance measures, but there was generally evidence that surveillance and response measures could reduce the number of hospitalisations and the number of school days missed. Studies that assess symptom-based screening and isolation measures also showed some evidence to suggest that such measures could reduce the number or proportion of infections and could reduce the peak number of people infected during the pandemic, however the certainty of evidence was very low.

There were three studies that looked at multicomponent interventions, where it was not possible to determine the effect of each individual intervention. Two observational/quasi-experimental studies with very low certainty evidence, showed mixed results on the impact of these measures on reducing the number or proportion of cases, but this is likely due to the comparator used in both studies was full school closure. One modelling study with very low certainty evidence, showed that reopening schools with such measures in place would still lead to a higher number or proportion of cases as compared to when schools were closed.

4.8.3.1 Summary of findings

Facemasks PLUS hand hygiene compared to control (no intervention) for reducing the transmission of respiratory infections

Patient or population: reducing the transmission of respiratory infections
Setting: Early childhood education and care services
Intervention: facemasks PLUS hand hygiene
Comparison: control (no intervention)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control (no intervention)	Risk with facemasks PLUS hand hygiene				
Transmission related outcomes assessed with: Influenza-like illness	0 per 1,000	**0 per 1,000** (0 to 0)	**RR 1.03** (0.78 to 1.34)	5307 (7 RCTs)	⨁⨁◯◯ Low[a,b]	The evidence suggests facemasks PLUS hand hygiene results in little to no difference in transmission related outcomes.
Transmission related outcomes assessed with: Laboratory confirmed influenza	0 per 1,000	**0 per 1,000** (0 to 0)	**RR 0.97** (0.69 to 1.36)	3121 (4 RCTs)	⨁⨁⨁◯ Moderate[b]	Facemasks PLUS hand hygiene likely results in little to no difference in transmission related outcomes.
Safety	not reported	-	-	-	-	
Absenteeism	not reported	-	-	-	-	
Severity of illness	not reported	-	-	-	-	
Behaviour or practice change	not reported	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades 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 likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may 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.

Explanations

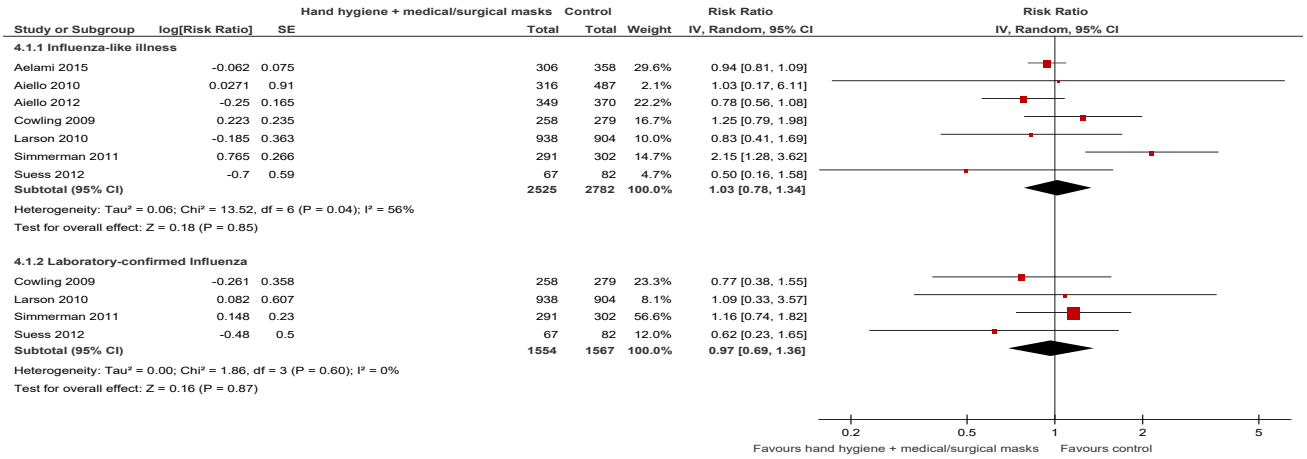
a. Serious imprecision. High statistical heterogeneity (I^2=56%). Certainty of evidence downgraded.
b. Wide confidence intervals (upper and lower bounds overlap with both effect and no effect). Certainty of evidence downgraded.

4.8.3.2 Forest Plots

Outcome results related to hand hygiene plus face masks for viral transmission is presented in Figure 11.

Outcome results related to hand hygiene and face masks transmission of influenza like illness or laboratory confirmed influenza is presented in Figure 11.

Figure 11 Forest plot of comparison: Hand hygiene and face masks compared with control



5 Discussion

5.1 Summary of main results

5.1.1 Hand hygiene compared to no or alternative, less intense intervention

The pooled estimates of effect from RCTs and cluster RCTs for hand hygiene compared to control (no or an alternative, or less intense intervention) for reducing the transmission of respiratory illness (assessed by the incidence of acute respiratory illness) suggest hand hygiene probably reduces acute respiratory illness (RR 0.84, 95% CI 0.82, 0.86). However, the evidence for the effect of hand hygiene of reducing the transmission of respiratory infections when assessed with the incidence of acute influenza like illness suggests hand hygiene may have little to no effect (RR 1.00, 95% CI 0.87, 1.16). There is an observed estimate of effect in favour of hand hygiene for transmission related outcomes measured by laboratory confirmed influenza (RR 0.82, 95% CI 0.56, 1.20), but the large confidence intervals may be a consequence of smaller sample sizes in conjunction with a more rigorous outcome measure, suggesting there is likely little to no effect. The evidence also suggests hand hygiene likely results in no difference in absenteeism due to the transmission of respiratory infections (IRR 0.91, 95% CI 0.82, 1.01)

There were too few trials comparing different types of hand hygiene interventions to be certain of any true differences between soap and water, alcohol-based hand sanitisers, or other types of interventions.

5.1.2 Respiratory etiquette

One systematic review (Xiao 2020) found no evidence evaluating the effectiveness of respiratory etiquette, defined as covering the nose and mouth with a tissue or a mask (but not a hand) when coughing or sneezing, followed by proper disposal of used tissues, and proper hand hygiene after contact with respiratory secretions, on influenza transmission. One systematic review found three RCTs that assessed the use of gargling in preventing respiratory infections. Although the trials used a variety of liquids and different outcomes, pooling the results of the two trials that compared gargling with tap water versus control did not show a favourable effect in reducing upper respiratory tract infections (RR 0.91, 95% CI 0.63, 1.31).

5.1.3 Face masks compared to control

Evidence for the use of face masks (cloth, surgical or medical) compared to no masks suggests that face masks do no reduce transmission of respiratory infections, assessed with the incidence of influenza like illness (RR 1.00, 95% CI 0.84, 1.20), or laboratory confirmed illness (RR 0.91, 95% CI 0.66, 1.26). The evidence suggests facemask results in a slight reducing in the transmission of SARS (RR 0.56, 95% CI 0.40, 0.79)

5.1.4 Eye protection (face shield, goggles) compares to control

The evidence from 13 comparative studies suggest that eye protection (face shields, goggles) may reduce transmission of MERS, SARS and COVID-19 viral infections (RR 0.34, 95% CI 0.22, 0.52). However only one of these studies was conducted in a non-health care (community) setting, and the evidence in the childcare setting is very uncertain.

5.1.5 Screening/ testing at entry compared to no or alternative, less intense intervention

There was limited evidence available for the effectiveness of screening/ testing at entry on reducing the transmission of respiratory infections, with all evidence being for SARS-CoV-2. One prospective cohort study showed screening/ testing at entry may reduce transmission related outcomes by increasing case detection, but the evidence is very uncertain. Evidence from one nRCT and one modelling study found screening children and workers for SARS-CoV-2 can reduce the number of secondary infections, however the evidence is very uncertain.

5.1.6 Ventilation/ air filtration compared to no or alternative, less intense intervention

One systematic review which conducted a review of the literature current to March 2021 found there is a considerable gap in the evidence around whether portable air filters reduce the incidence of respiratory infections, including SARS-CoV-2. The evidence identified showed air filters can reduce the amount of airborne bacteria, but these were not conducted in a community setting. As such the evidence is very uncertain about the effect of air filtration or increased ventilation on transmission related outcomes. One prospective cohort study suggested higher ventilation rates were associated with reduced absenteeism in a school setting, however the evidence was very uncertain.

5.1.7 Combined interventions

The estimate of effect of combined hand hygiene and mask interventions compared to control in six (mostly small) trials suggested that the intervention may make little or no difference for the transmission related outcomes, assessed with the incidence of influenza like illness (RR 1.03, 95% CI 0.77, 1.37) and laboratory confirmed influenza (four trials) (RR 0.97, 95% CI 0.69, 1.36).

The assessment of implementing school measures on SARS-CoV-2/COVID-19 related transmission and other outcomes was assessed by Krishnaratne 2022 (34). Interventions were divided into four broad categories i) measures reducing the opportunity for contacts; ii) measures making contacts safer; iii) surveillance and response measures; and iv) multicomponent measures. Overall, the majority of included studies were modelling studies. While studies showed variable reductions in transmission and healthcare utilisation-related outcomes, the evidence available at the time the searches were conducted was of limited quality. For measures reducing the opportunity for contacts, the studies included consistently predicted outcomes in a positive direction with regards to transmission related outcomes and healthcare utilisation outcomes; they also showed a reduction in the number of days spent in school due to the intervention, but in some cases, the initial reduction in days spent in school was offset by an increase the number of intended days spent in school due to their ability to prevent days lost due to quarantine or isolation. Overall, very low certainty evidence showed a reduction in the number of cases, reproductive number, hospitalisations, and ICU admissions, as well as days of school missed.

For measures making contacts safer, overall, the evidence showed a reduction in the number of cases, reproduction number, hospitalisations, and ICU admissions, as well as days of school missed, but the certainty of evidence was very low for studies assessing mask wearing policies, modification of activities, and cleaning and ventilation procedures and systems. For surveillance and response measures, a very low certainty of evidence showed that implementing measures to detect, trace, and quarantine cases within schools could lead to reductions in the COVID-19 infection/transmission rate among students, teachers, and staff, and could also slow or prevent a second wave of the epidemic and reduce the reproduction number and number or proportion of deaths. For multicomponent measures, three studies with very low certainty of evidence found there was limited effectiveness of combined measures to make contacts safer or reduce the opportunity for contacts with measures reducing the number of contacts and surveillance and response measures.

5.2 Overall completeness and applicability of evidence

The main barrier for the direct applicability of the evidence presented in this review is the settings of the studies reviewed by the systematic reviews. The studies were conducted between the years 2000 and 2022 and were conducted in a range of settings, included the Hajj pilgrimage (Aelami 2015), University Hall residences (Aiello 2010), primary schools (Alzaher 2018), kindergartens (Ban 2015), childcare facilities (Correa 2012), households (Cowling 2009), and a range of health care settings. Of the trials assessing the effect of masks, six were carried out in those at greater exposure (i.e. health care workers) (Jacobs 2009; Loeb 2009; MacIntyre 2011; MacIntyre 2013; MacIntyre 2015; Radonovich 2019). Additionally, all studies identified by Xiao 2020 (18) assessing the effect of eye protection were conducted in a health care setting.

In terms of the studies that were conducted in a school setting, studies assessed measures implemented both in primary and secondary school settings but also looked at outcomes in the wider community. Most studies did not differentiate between different school types (i.e. primary and secondary) and evidence was limited in child care settings. There are various differences in contextual conditions between school types, such as changing classrooms, size of the buildings, commuting styles, and children's age which can affect reporting of transmission related outcomes.

While most studies reported on transmission related outcomes, other outcomes which were considered of importance such safety was poorly reported. While no studies reported data for behaviour or practice change, or severity of the illness.

5.3 Certainty of the evidence

The evidence provides general low certainty of evidence for the effect of non-pharmaceutical interventions on the transmission of respiratory illnesses, or the effect on absenteeism due to respiratory illness in the childcare setting. There is a paucity of high-quality evidence available for the effect of non-pharmaceutical interventions on safety and severity of illness outcomes.

The systematic review's included in this review were generally of high or moderate quality, meaning they likely provide an accurate summary of the results of the available evidence. Included RCT's and modelling studies, were mostly determined to be at moderate risk of bias. For RCTs assessed by the systematic review's or included in the evidence synthesis, the nature of most of the interventions being assessed meant that blinding of treatment allocation after randomisation was rarely achieved. Additionally, most outcomes, including transmission-related outcomes such as influenza-like illness, were self-reported, with few studies using laboratory confirmed outcomes, increasing reliability of the reporting. The quality of evidence from studies was often downgraded for indirectness, due to lack of applicability between the study setting and the desired setting specified in the PICO.

5.4 Potential biases in the review process

To ensure the correct scope of this review, the protocol for this review was endorsed by the NHMRC SHIC committee. Multiple databases were comprehensively searched and the literature screened in a stepwise manner to capture the best available evidence. Included studies were not limited by study design, and the highest quality evidence for each outcome was considered; however this approach means there is a potential to miss primary studies if they have not been identified by other systematic review authors, or to double count evidence included in multiple systematic reviews. Overlap tables were generated to determine which primary studies were included in each systematic review and avoid repetition in the evidence presented. The most recent systematic reviews were included in the evidence synthesis, however there was still some overlap in the studies presented for each outcome..

As mentioned previously, many of the studies that were identified assessed the impact of measures implemented within the school setting on outcomes within the broader community, even if they did not have any direct connection with the school setting, this and the lack of studies conducted in childcare settings are a main source of bias.

5.5 Agreements and disagreements with other studies or reviews

An umbrella review (35) of non-pharmaceutical interventions to prevent viral respiratory infection in community settings searched the literature between the years 2000 and 2020 and identified 11 systematic reviews and meta-analyses, 12 systematic reviews without meta-analyses and one standalone meta-analysis. The reviews identified in this umbrella review were also included in the evidence synthesis for this review. The studies were graded according to AMSTAR 2, which identified seven low quality studies and 17 critically low quality studies. This is inconsistent with the AMSTAR ratings assigned in this review, which found some of the studies such as Jefferson 2020 and Xiao 2020 to be of high or moderate quality. The umbrella review determined the evidence suggests hand hygiene is protective against respiratory viral infection. The use of hand hygiene and facemasks, facemasks alone and physical distancing were interventions with inconsistent evidence. These finding as generally consistent with our review. Interventions such as school closures, oral hygiene or nasal saline rinses were shown to be effective in reducing the risk of influenza; however, the evidence is sparse and mostly of low and critically low quality. The umbrella review did not perform a GRADE review of the evidence or pool the available data to perform a meta-analysis.

5.6 Limitations

5.6.1 At study and outcome level

The main limitation at the study and outcome level was the limited evidence available for the effect of the interventions on absenteeism and safety, and that no evidence was identified reporting on behaviour/practice change or severity of illness. There was also no evidence identified for glove wearing, and limited data available for ventilation.

The trials included for review by the systematic review's generally reported few events and were conducted mostly during non-epidemic periods. The large study by Radonovich 2019 is an exception as it crossed over two of the highest reporting years for influenza in the USA between 2010 and 2017. Some trials such as Aiello 2010 were conducted during influenza seasons. Most studies reporting on SARS-CoV-2 were conducted during the early stages of the pandemic, where vaccination rates may have been low to none. Therefore, there is a need for more data from the later staged of the pandemic and acknowledgment of nuances related to the prevalence of different strains of SARS-CoV-2 at different times.

Compliance with interventions, especially educational programmes, was a problem for many studies despite the importance of many such low-cost interventions. Compliance with mask wearing varied; it was generally around 60% to 80% but was reported to be as low as 40%. Overall, the logistics of carrying out trials that involve sustained behaviour change are demanding, particularly in challenging settings such as immigrant neighbourhoods or students' halls of residence. The identified trials provided sparse and unsystematic data on adverse effects of the intervention, and few of the RCTs measured or reported compliance with the intervention, which is especially important for the use of medical/surgical masks or N95 respirators. No studies investigated how the level of adherence may have influenced the effect size. For the hand hygiene intervention comparators for hand hygiene ranged from usual hand washing practice, education about hand washing or none, where none was specified as the comparator it is unlikely participants did not engage in hand hygiene behaviour, participants likely engaged in a less intense hand hygiene intervention to the one specified in the trial. There was variability between the different interventions administered in the studies. For the trials investigating hand hygiene, hand sanitiser, soap and water, hand washing education were all variably used, the intervention lacks consistency in the products used for hand hygiene, in addition to the method and comparators. For some interventions, it was difficult to draw conclusions on a small number of systematic reviews and meta-analyses on individual non-pharmaceutical interventions such as nasal rinses and hypertonic saline gargles for respiratory hygiene.

Where modelling studies were included, including for ventilation and screening outcomes, it should be noted that in modelling the population, setting, context and interventions, modelling studies all make a series of assumptions; some of these are closer to real-world conditions than others. Indeed, most modelling studies across all intervention categories considered outcomes in the general population, but not always within the population in which the measure was implemented (i.e. students and school staff).

5.6.2 At review level

This review is limited to the assessment of non-pharmaceutical interventions to prevent respiratory disease transmission in childcare settings to inform the SHAC for the updated Staying Healthy in Childhood guidelines. This review is not designed to assess the effectiveness of these interventions in other settings or populations.

Interventions were grouped broadly, hand hygiene encompassed all forms of hand hygiene including sanitisers, soap and water, and in some circumstances, this was supplemented with education about hand hygiene. Evidence presented for face masks did not distinguish between face mask type, including cloth, surgical or N95. The main comparator of interest was the intervention compared to no or alternate, less intense interventions. In the case of some interventions this comparison was clear (masks vs no masks), in other cases such as hand hygiene, the control is less certain, it is unlikely that participants did not engage in any hand hygiene practices.

Most of the data for the effectiveness of the interventions is against influenza, and influenza-like illness, with limited data available for SARS, SARS-CoV-2, or other respiratory viruses.

6 Authors' conclusions

6.1 Implications for policy

This report was commissioned by the SHAC as part of the Staying Healthy in Childhood Guidelines review, with findings in intended to inform decisions relating to the upcoming version of the SHIC. As such, specific recommendations are not provided.

The majority of studies for interventions such as hand hygiene and mask wearing were conducted for influenza or influenza-like illness, as such the applicability of the evidence for the interventions and risk of SARS-CoV-2 and other viral illnesses is uncertain. The observed lack of effect of mask wearing in interrupting the spread of influenza or influenza like illness may be due to poor study design; insufficiently powered studies arising from low viral circulation in some studies; lower compliance with mask wearing, especially among children; quality of the masks used; self-contamination of the mask by hands; lack of protection from eye exposure from respiratory droplets (allowing a route of entry of respiratory viruses into the nose via the lacrimal duct); saturation of masks with saliva from extended use (promoting virus survival in proteinaceous material); and risk compensation behaviour leading to an exaggerated sense of security The applicability of evidence on influenza and influenza-like illness to SARS-CoV-2 could be reduced owing to differential transmission dynamics, lower mask adherence, or limited use of other personal protective equipment

While it was shown within one study that air purifiers do reduce the dose of particles containing RNA virus in an experimental scenario (32), the quality of this evidence was low. Installing air purifiers in schools might entail significant costs and resources (e.g. energy, disposal of used filters), whilst at the same time contributing to widening inequalities with regards to access to ventilators/air purifiers.

6.2 Implications for research

To improve consistency between the studies, there is a need to provide outcomes with explicitly defined clinical criteria for acute respiratory illnesses and discrete laboratory confirmed outcomes of viral acute respiratory illness using molecular diagnostic tools which are now widely available. Studies should also consider the sociocultural factors that might affect compliance with the interventions, especially those in a community setting. There are several research gaps related to non-pharmaceutical interventions, including the optimal duration of the use of physical interventions to prevent the spread of viruses; the effectiveness of respiratory etiquette (i.e. coughing/sneezing into tissues or a sleeved bent elbow); use of frequent disinfection techniques appropriate to the setting (high-touch surfaces in the environment). As noted in the July 2022 update to Chou 2020 (24), there is still a paucity of high-quality mask studies on SARS-CoV-2

Trials which conduct large, pragmatic trials to evaluate the best combinations of interventions in the community, beyond the combinations of face masks and hand hygiene. For studies conducted in school settings, most of the studies we identified either used data from, or were focused on, high-income countries, but regional differences, or even school-level differences relating to socioeconomic status, might influence how interventions are implemented and taken up, and this was rarely examined within the identified studies.

As previously mentioned, when studies addressing the effect of the interventions on COVID-19m were conducted, vaccine coverage was not high. The implications of the vaccine on future practices surrounding the control of the pandemic in the school setting will need to be evaluated in future research.

References

1. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.
2. Higgins J, Lasserson T, Chandler J, Tovey D, Thomas J, Flemyng E, et al. Methodological Expectations of Cochrane Intervention Reviews. London: Cochrane; 2019. Available from: https://community.cochrane.org/mecir-manual.
3. Schünemann H, Brożek J, Guyatt G, Oxman A. GRADE Handbook. Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach [Internet]. 2013; (Updated October 2013). Available from: https://gdt.gradepro.org/app/handbook/handbook.html.
4. Toivonen L, Karppinen S, Schuez-Havupalo L, Teros-Jaakkola T, Vuononvirta J, Mertsola J, et al. Burden of Recurrent Respiratory Tract Infections in Children: A Prospective Cohort Study. The Pediatric Infectious Disease Journal. 2016;35(12).
5. Boncristiani HF, Criado MF, Arruda E. Respiratory Viruses. Encyclopedia of Microbiology. 2009:17.
6. Alexandrino AS, Santos R, Melo C, Bastos JM. Risk factors for respiratory infections among children attending day care centres. Family Practice. 2016;33(2):161-6.
7. Jaspan HB, Lawn SD, Safrit JT, Bekker L-G. The maturing immune system: implications for development and testing HIV-1 vaccines for children and adolescents. AIDS. 2006;20(4).
8. Schuez-Havupalo L, Toivonen L, Karppinen S, Kaljonen A, Peltola V. Daycare attendance and respiratory tract infections: a prospective birth cohort study. BMJ Open. 2017;7(9):e014635.
9. Leung NHL. Transmissibility and transmission of respiratory viruses. Nature Reviews Microbiology. 2021;19(8):528-45.
10. Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019): Cochrane; 2019. Available from: www.training.cochrane.org/handbook.
11. Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. https://jbi-global-wiki.refined.site/space/MANUAL/4687404/About+this+Manual: Joanna Briggs Institute; 2020.
12. Tufanaru C, Munn Z, Aromataris E, Campbell J, Hopp L. Chapter 3: Systematic reviews of effectiveness. In: Aromataris E, Munn Z, editors. Joanna Briggs Institute Reviewer's Manual: The Joanna Briggs Institute; 2017.
13. Review Manager (RevMan) [Computer program]. Version 5.4. ed: The Cochrane Collaboration; 2020.
14. Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database of Systematic Reviews. 2020(11).
15. Wong VW, Cowling BJ, Aiello AE. Hand hygiene and risk of influenza virus infections in the community: a systematic review and meta-analysis. Epidemiol Infect. 2014;142(5):922-32.
16. Munn Z, Tufanaru C, Lockwood C, Stern C, McAneney H, Barker TH. Rinse-free hand wash for reducing absenteeism among preschool and school children. Cochrane database of systematic reviews. 2020;4.
17. Abdullahi L, Onyango JJ, Mukiira C, Wamicwe J, Githiomi R, Kariuki D, et al. Community interventions in Low—And Middle-Income Countries to inform COVID-19 control implementation decisions in Kenya: A rapid systematic review. PLOS ONE. 2020;15(12):e0242403.
18. Xiao J, Shiu EYC, Gao H, Wong JY, Fong MW, Ryu S, et al. Nonpharmaceutical Measures for Pandemic Influenza in Nonhealthcare Settings-Personal Protective and Environmental Measures. Emerg Infect Dis. 2020;26(5):967-75.
19. Wang Z, Lapinski M, Quilliam E, Jaykus L-A, Fraser A. The effect of hand-hygiene interventions on infectious disease-associated absenteeism in elementary schools: A systematic literature review. Am J Infect Control. 2017;45(6):682-9.
20. Jefferson T, Foxlee R, Mar CD, Dooley L, Ferroni E, Hewak B, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ. 2008;336(7635):77-80.

21. Nanda A, Hung I, Kwong A, Man VC, Roy P, Davies L, et al. Efficacy of surgical masks or cloth masks in the prevention of viral transmission: Systematic review, meta-analysis, and proposal for future trial. J Evid Based Med. 2021;14(2):97-111.

22. Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ, 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. The Lancet. 2020;395(10242):1973-87.

23. Masks for Prevention of Respiratory Virus Infections, Including SARS-CoV-2, in Health Care and Community Settings. Annals of Internal Medicine. 2020;173(7):542-55.

24. Chou R, Dana T, Jungbauer R, Weeks C, McDonagh MS. Masks for Prevention of Respiratory Virus Infections, Including SARS-CoV-2, in Health Care and Community Settings : A Living Rapid Review. Ann Intern Med. 2020;173(7):542-55.

25. Young BC, Eyre DW, Kendrick S, White C, Smith S, Beveridge G, et al. Daily testing for contacts of individuals with SARS-CoV-2 infection and attendance and SARS-CoV-2 transmission in English secondary schools and colleges: an open-label, cluster-randomised trial. Lancet. 2021;398(10307):1217-29.

26. Bilinski A, Ciaranello A, Fitzpatrick MC, Giardina J, Shah M, Salomon JA, et al. Estimated Transmission Outcomes and Costs of SARS-CoV-2 Diagnostic Testing, Screening, and Surveillance Strategies Among a Simulated Population of Primary School Students. JAMA Pediatrics. 2022;176(7):679-89.

27. Bilinski A, Salomon JA, Giardina J, Ciaranello A, Fitzpatrick MC. Passing the Test: A Model-Based Analysis of Safe School-Reopening Strategies. Annals of Internal Medicine. 2021;174(8):1090-100.

28. Forster J, Streng A, Rudolph P, uuml;cker V, Wallstabe J, Timme S, et al. Feasibility of SARS-CoV-2 Surveillance Testing Among Children and Childcare Workers at German Day Care Centers: A Nonrandomized Controlled Trial. JAMA network open. 2022;Vol.5(1):e2142057p.

29. Bilinski A, Ciaranello A, Fitzpatrick MC, Giardina J, Shah M, Salomon JA, et al. SARS-CoV-2 testing strategies to contain school-associated transmission: model-based analysis of impact and cost of diagnostic testing, screening, and surveillance. medRxiv. 2021.

30. Young BC, Eyre DW, Kendrick S, White C, Smith S, Beveridge G, et al. Daily testing for contacts of individuals with SARS-CoV-2 infection and attendance and SARS-CoV-2 transmission in English secondary schools and colleges: an open-label, cluster-randomised trial. Lancet (london, england). 2021;Vol.398(10307):1217-29p.

31. Hammond B, Ali Y, Fendler E, Dolan M, Donovan S. Effect of hand sanitizer use on elementary school absenteeism. Am J Infect Control. 2000;28(5):340-6.

32. Curtius J, Granzin M, Schrod J. Testing mobile air purifiers in a school classroom: Reducing the airborne transmission risk for SARS-CoV-2. Aerosol Science and Technology. 2021;55(5):586-99.

33. Mendell MJ, Eliseeva EA, Davies MM, Spears M, Lobscheid A, Fisk WJ, et al. Association of classroom ventilation with reduced illness absence: a prospective study in California elementary schools. Indoor Air. 2013;23(6):515-28.

34. Krishnaratne S, Littlecott H, Sell K, Burns J, Rabe JE, Stratil JM, et al. Measures implemented in the school setting to contain the COVID-19 pandemic. Cochrane Database of Systematic Reviews. 2022;1:CD015029.

35. Zhao H, Jatana S, Bartoszko J, Loeb M. Nonpharmaceutical interventions to prevent viral respiratory infection in community settings: an umbrella review. ERJ Open Research. 2022;8(2):00650-2021.