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Physical interventions to interrupt or reduce the spread of respiratory viruses (Review)

Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, van Driel ML, Nair NS, Jones MA, Thorning S, Conly JM

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TABLE OF CONTENTS

[Intervention Review]

Physical interventions to interrupt or reduce the spread of respiratory viruses

Tom Jefferson[1], Chris B Del Mar[2], Liz Dooley[3], Eliana Ferroni[4], Lubna A Al-Ansary[5], Ghada A Bawazeer[6], Mieke L van Driel[7,8], N Sreekumaran Nair[9], Mark A Jones[10], Sarah Thorning[11], John M Conly[12,13]

[1]Centre for Evidence Based Medicine, University of Oxford, Oxford, UK. [2]Centre for Research in Evidence-Based Practice (CREBP), Bond University, Gold Coast, Australia. [3]Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia. [4]Epidemiological System of the Veneto Region, Regional Center for Epidemiology, Veneto Region, Padova, Italy. [5]Department of Health Metrics and Measurement, World Health Organization, Geneva, Switzerland. [6]Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia. [7]Primary Care Clinical Unit, Faculty of Medicine, The University of Queensland, Brisbane, Australia. [8]Department of Public Health and Primary Care, Ghent University, Ghent, Belgium. [9]Department of Medical Biometrics & Informatics (Biostatistics), Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) (Institution of National Importance Under Ministry of Health and Family Welfare, Government of India), Dhanvantri Nagar, India. [10]Institute for Evidence-Based Healthcare, Bond University, Gold Coast, Australia. [11]GCUH Library, Gold Coast Hospital and Health Service, Southport, Australia. [12]Foothills Medical Centre, Room 930, North Tower, Calgary, Canada. [13]Department of Global Alert and Response - Health Security and Environment, WHO. Infection Prevention and Control in Health Care, Geneva, Switzerland

Contact address: Tom Jefferson, Centre for Evidence Based Medicine, University of Oxford, Oxford, OX2 6GG, UK. jefferson.tom@gmail.com.

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ABSTRACT

Background

Viral epidemics or pandemics of acute respiratory infections like influenza or severe acute respiratory syndrome pose a global threat. Antiviral drugs and vaccinations may be insufficient to prevent their spread.

Objectives

To review the effectiveness of physical interventions to interrupt or reduce the spread of respiratory viruses.

Search methods

We searched *The Cochrane Library*, the Cochrane Central Register of Controlled Trials (CENTRAL 2010, Issue 3), which includes the Acute Respiratory Infections Group's Specialised Register, MEDLINE (1966 to October 2010), OLDMEDLINE (1950 to 1965), EMBASE (1990 to October 2010), CINAHL (1982 to October 2010), LILACS (2008 to October 2010), Indian MEDLARS (2008 to October 2010) and IMSEAR (2008 to October 2010).

Selection criteria

In this update, two review authors independently applied the inclusion criteria to all identified and retrieved articles and extracted data. We scanned 3775 titles, excluded 3560 and retrieved full papers of 215 studies, to include 66 papers of 67 studies. We included physical interventions (screening at entry ports, isolation, quarantine, social distancing, barriers, personal protection, hand hygiene) to prevent respiratory virus transmission. We included randomised controlled trials (RCTs), cohorts, case-controls, before-after and time series studies.

Data collection and analysis

We used a standardised form to assess trial eligibility. We assessed RCTs by randomisation method, allocation generation, concealment, blinding and follow up. We assessed non-RCTs for potential confounders and classified them as low, medium and high risk of bias.

Main results

We included 67 studies including randomised controlled trials and observational studies with a mixed risk of bias. A total number of participants is not included as the total would be made up of a heterogenous set of observations (participant people, observations on participants and countries (object of some studies)). The risk of bias for five RCTs and most cluster-RCTs was high. Observational studies were of mixed quality. Only case-control data were sufficiently homogeneous to allow meta-analysis. The highest quality cluster-RCTs suggest respiratory virus spread can be prevented by hygienic measures, such as handwashing, especially around younger children. Benefit from reduced transmission from children to household members is broadly supported also in other study designs where the potential for confounding is greater. Nine case-control studies suggested implementing transmission barriers, isolation and hygienic measures are effective at containing respiratory virus epidemics. Surgical masks or N95 respirators were the most consistent and comprehensive supportive measures. N95 respirators were non-inferior to simple surgical masks but more expensive, uncomfortable and irritating to skin. Adding virucidals or antiseptics to normal handwashing to decrease respiratory disease transmission remains uncertain. Global measures, such as screening at entry ports, led to a non-significant marginal delay in spread. There was limited evidence that social distancing was effective, especially if related to the risk of exposure.

Authors' conclusions

Simple and low-cost interventions would be useful for reducing transmission of epidemic respiratory viruses. Routine long-term implementation of some measures assessed might be difficult without the threat of an epidemic.

PLAIN LANGUAGE SUMMARY

Physical interventions to interrupt or reduce the spread of respiratory viruses

Although respiratory viruses usually only cause minor disease, they can cause epidemics. Approximately 10% to 15% of people worldwide contract influenza annually, with attack rates as high as 50% during major epidemics. Global pandemic viral infections have been devastating. In 2003 the severe acute respiratory syndrome (SARS) epidemic affected around 8000 people, killed 780 and caused an enormous social and economic crisis. In 2006 a new avian H5N1, and in 2009 a new H1N1 'swine' influenza pandemic threat, caused global anxiety. Single and potentially expensive measures (particularly the use of vaccines or antiviral drugs) may be insufficient to interrupt the spread. Therefore, we searched for evidence for the effectiveness of simple physical barriers (such as handwashing or wearing masks) in reducing the spread of respiratory viruses, including influenza viruses.

We included 67 studies including randomised controlled trials and observational studies with a mixed risk of bias. A total number of participants is not included as the total would be made up of a varied set of observations: participant people and observations on participants and countries (the object of some studies). Any total figure would therefore be misleading. Respiratory virus spread can be reduced by hygienic measures (such as handwashing), especially around younger children. Frequent handwashing can also reduce transmission from children to other household members. Implementing barriers to transmission, such as isolation, and hygienic measures (wearing masks, gloves and gowns) can be effective in containing respiratory virus epidemics or in hospital wards. We found no evidence that the more expensive, irritating and uncomfortable N95 respirators were superior to simple surgical masks. It is unclear if adding virucidals or antiseptics to normal handwashing with soap is more effective. There is insufficient evidence to support screening at entry ports and social distancing (spatial separation of at least one metre between those infected and those non-infected) as a method to reduce spread during epidemics.

BACKGROUND

Description of the condition

Pandemic viral infections pose a serious threat to all nations. There have been several recently, including pandemic influenza (one of which has just occurred) (Jefferson 2009; WHO 2009) and a novel coronavirus causing severe acute respiratory syndrome (SARS) (Shute 2003).

Even non-epidemic acute respiratory infections (ARIs) place a serious burden on the health of nations. In total these cause much of the 7% of total deaths in the world that are attributed to lower respiratory tract infections (representing four million deaths worldwide, mostly occurring in low-income countries). In addition there is a huge burden from ARIs on morbidity and nations' healthcare systems (www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html).

High viral load and infectiousness probably increase the spread of acute respiratory infection outbreaks (Jefferson 2006a). Stopping the spread of virus from person to person may be effective at preventing these outbreaks. This can be achieved in a number of ways. However, single interventions (such as vaccination or antiviral drugs) may be inadequate (Jefferson 2005a; Jefferson 2005b; Jefferson 2005c; Jefferson 2006a).

Description of the intervention

There is increasing evidence (Jefferson 2005a; Jefferson 2005b; Jefferson 2005c; Jefferson 2006a; Thomas 2010) that single measures (such as the use of vaccines or antivirals) may be insufficient to interrupt the spread of influenza. However, a recent trial showed that handwashing may be effective in diminishing mortality due to respiratory disease (Luby 2005). The possible effectiveness of public health measures during the 'Spanish Flu' pandemic of 1918 to 1919 (Bootsma 2007) in US cities led us to wonder what evidence exists on the effectiveness of combined public health measures such as isolation, distancing and barriers. We also considered the major social implications for any community adopting them (CDC 2005a; CDC 2005b; WHO 2006). Given the potential global importance of interrupting viral transmission, up-to-date, concise estimates of effectiveness are necessary to inform planning and decision-making. We could find no previous systematic review of such evidence.

How the intervention might work

Epidemics and pandemics are more likely during antigenic shift in the virus (especially influenza), when the viral genes sufficiently alter to create a new subtype against which there is little circulating natural immunity (Smith 2006). This may happen when viruses cross from animal species such as ducks or pigs to infect humans (Bonn 1997). Minor changes in viral antigenic configurations, known as 'drift', cause local or more circumscribed epidemics (Smith 2006).

High viral load and high viral infectiousness are likely to be the drivers of such epidemics and pandemics (Jefferson 2006a).

Physical means might prevent the spread of virus by **aerosols or large droplets** from infected to susceptible people (such as by using masks and distancing measures) and by **contact** (such as by using handwashing, gloves and protective gowns). Such public health measures were widely adopted during the 'Spanish Flu' pandemic of 1918 to 1919 (Bootsma 2007).

Why it is important to do this review

Although the benefits of physical methods seem self-evident, they require establishing and quantifying. Physical methods have several possible advantages over other methods of suppressing acute respiratory infection outbreaks: they can be instituted rapidly and may be independent of any specific type of infective agent including novel viruses.

OBJECTIVES

To systematically review the evidence of effectiveness of physical interventions to interrupt or reduce the spread of acute respiratory viruses.

METHODS

Criteria for considering studies for this review

Types of studies

We considered trials (individual-level or cluster-randomised, or quasi-randomised), observational studies (cohort and case-control designs) and any other comparative design, provided some attempt had been made to control for confounding, carried out in people of all ages.

Types of participants

People of all ages.

Types of interventions

We included any intervention to prevent viral animal-to-human or human-to-human transmission of respiratory viruses (screening at entry ports, isolation, quarantine, social distancing, barriers, personal protection and hand hygiene) compared with doing nothing or with another intervention. We excluded vaccines and antivirals.

Types of outcome measures

1. Deaths.
2. Numbers of cases of viral illness.
3. Severity of viral illness in the compared populations. In children and healthy adults we measured burden by consequences of influenza, for example, losses in productivity due to absenteeism by parents. For the elderly in the community, we measured the burden by repeated primary healthcare contacts, hospital admissions and the risk of complications.
4. Any proxies for these (for example, clinical symptoms as a proxy for viral illness and confirmed viral polymerase chain reaction (PCR) testing or viral serological tests).

Search methods for identification of studies

Electronic searches

In this 2010 update we searched, as we have done previously, the Cochrane Central Register of Controlled Trials (CENTRAL) 2010, Issue 3, which includes the Acute Respiratory Infections Group's Specialised Register, MEDLINE (April 2009 to October week 2, 2010), EMBASE (April 2009 to October 2010) and CINAHL (January 2009

to October 2010). Details of previous searches are in Appendix 1. In addition, to include more of the literature of low-income countries in this update, we ran searches in LILACS (2008 to October 2010), Indian MEDLARS (2008 to October 2010) and IMSEAR (2008 to October 2010).

We used the following search strategy (updated to include new and emerging respiratory viruses) to search MEDLINE and CENTRAL. We combined the MEDLINE search strategy with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) (Ovid format) (Lefebvre 2009). We also included an additional search strategy based on the work of Fraser, Murray and Burr (Fraser 2006) to identify observational studies. The search strategies were adapted for Embase.com (Appendix 2), CINAHL (Appendix 3), LILACS (Appendix 4), Indian MEDLARS (Appendix 5) and IMSEAR (Appendix 6).

MEDLINE (Ovid)

1 Influenza, Human/
2 exp Influenzavirus A/
3 exp Influenzavirus B/
4 Influenzavirus C/
5 (influenza* or flu).tw.
6 Common Cold/
7 common cold*.tw.
8 Rhinovirus/
9 rhinovir*.tw.
10 adenoviridae/ or mastadenovirus/ or adenoviruses, human/
11 adenoviridae infections/ or adenovirus infections, human/
12 adenovir*.tw.
13 coronavirus/ or coronavirus 229e, human/ or coronavirus oc43, human/ or infectious bronchitis virus/ or sars virus/
14 coronavir*.tw.
15 coronavirus infections/ or severe acute respiratory syndrome/
16 (severe acute respiratory syndrome* or sars).tw.
17 respiratory syncytial viruses/ or respiratory syncytial virus, human/
18 Respiratory Syncytial Virus Infections/
19 (respiratory syncytial virus* or rsv).tw.
20 Pneumovirus Infections/
21 parainfluenza virus 1, human/ or parainfluenza virus 3, human/
22 parainfluenza virus 2, human/ or parainfluenza virus 4, human/
23 (parainfluenza* or para-influenza* or para influenza).tw.
24 enterovirus a, human/ or exp enterovirus b, human/ or enterovirus c, human/ or enterovirus d, human/
25 Enterovirus Infections/
26 enterovir*.tw.
27 Human bocavirus/
28 bocavirus*.tw.
29 Metapneumovirus/
30 metapneumovir*.tw.
31 Parvovirus B19, Human/
32 parvoviridae infections/ or erythema infectiosum/
33 parvovirus*.tw.
34 Parechovirus/
35 parechovirus*.tw.
36 acute respiratory tract infection*.tw.
37 acute respiratory infection*.tw.
38 or/1-37
39 Handwashing/
40 (handwashing or hand washing or hand-washing).tw.
41 hand hygiene.tw.
42 (sanitiser* or sanitizer*).tw.
43 (cleanser* or disinfectant*).tw.
44 gloves, protective/ or gloves, surgical/
45 glov*.tw.
46 masks/ or respiratory protective devices/
47 (mask or masks or respirator or respirators).tw.
48 Protective Clothing/
49 Protective Devices/
50 Patient Isolators/
51 Patient Isolation/
52 patient isolat*.tw.
53 (barrier* or curtain* or partition*).tw.
54 negative pressure room*.tw.
55 ((reverse barrier or reverse-barrier) adj3 (nurs* or unit or isolation)).tw.
56 Cross Infection/pc [Prevention & Control]
57 (cross infection* adj2 prevent*).tw.
58 Communicable Disease Control/
59 Infection Control/
60 (school* adj3 (clos* or dismissal*)).tw.
61 temporary closur*.tw.
62 mass gathering*.tw.
63 (public adj2 (gathering* or event*)).tw.
64 (bans or banning or banned or ban).tw.
65 (outbreak adj3 control*).tw.
66 distancing*.tw.
67 Quarantine/
68 quarantine*.tw.
69 (protective adj2 (cloth* or garment* or device* or equipment)).tw.
70 ((protective or preventive) adj2 (procedure* or behaviour* or behavior*)).tw.
71 personal protect*.tw.
72 (isolation room* or isolation strateg*).tw.
73 (distance adj2 patient*).tw.
74 ((spatial or patient) adj separation).tw.
75 cohorting.tw.
76 or/39-75
77 38 and 76
78 (animals not (animals and humans)).sh.
79 77 not 78

Searching other resources

There were no language restrictions. Study design filters designed to retrieve RCTs, cohort case-control and cross-over studies, and before-after and time series trials were used in the original searches but we applied no filters to the searches carried out for this update. We scanned the references of all included studies to identify other potentially relevant studies. We also accessed the archives of the former MRC Common Cold Unit (Jefferson 2005d) as a possible source for interruption of transmission evidence.

Data collection and analysis

Selection of studies

We scanned the titles and abstracts after conducting the searches. We obtained full-text articles if a study appeared to meet our eligibility criteria (or when there was insufficient information to exclude it). We then used a standardised form to assess the eligibility of each study, based on the full article.

Data extraction and management

For this 2010 update, two review authors (TOJ, JMC) independently applied inclusion criteria to all identified and retrieved articles and extracted data. CDM checked the procedure and arbitrated. MJ carried out data analysis.

Assessment of risk of bias in included studies

For the 2009 update (Jefferson 2009) we contacted one trial author (Dr Michael Broderick) to better understand the risk of bias in his study (Broderick 2008). For this 2010 update Drs Aiello and Larson were contacted and provided additional information.

A common problem in these studies was a lack of reporting of viral circulation in the reference population, making interpretation and generalisability of their conclusions questionable.

Randomised studies

Three RCTs were poorly reported with no description of randomisation sequence, concealment or allocation in three studies (Gwaltney 1980; Turner 2004a; Turner 2004b). Satomura 2005 reported the generation of randomisation but the very nature of the intervention (gargling with water with or without povidone iodine versus standard gargling with no attempt at masking the taste of iodine) made blinding impossible. The design of two trials was so artificial that their results cannot be generalised to everyday situations (Turner 2004a; Turner 2004b). One trial (Satomura 2005) is linked to a subsequent brief report which provides contradictory information which is difficult to reconcile (Kitamura 2007).

The quality of the cluster-randomised trials varied. Only the best reported cluster coefficients and conducted analysis of data by unit of (cluster) allocation instead of by individuals (Luby 2005; Roberts 2000; Sandora 2005). Analysing cluster-randomised trials at the individual level leads to spuriously narrow confidence intervals around the estimates of effect (Grimshaw 2004). Other frequent problems were a lack of description of randomisation procedure, partial reporting of outcomes, unclear numerators or denominators and unexplained attrition (Carabin 1999; Kotch 1994; Morton 2004; White 2001), and either complete failure of double-blinding (Farr 1988a; Farr 1988b) or inappropriate choice of placebo (Longini 1988). Three cluster-randomised trials involving the use of face masks (Cowling 2008; Cowling 2009; MacIntyre 2009) by influenza-like illness (ILI) contacts had poor compliance. This shows the difficulty of conducting clinical trials using bulky equipment in the absence of the perception of a real threat. One trial (Cowling 2008) was also conducted in a period of low viral circulation and randomisation was carried out on the basis of two different sequences. The other study (MacIntyre 2009) was underpowered to detect differences in effect between different types of masks.

The cluster-randomised trial by Sandora and colleagues (Sandora 2008) is at low risk of bias with careful evaluation of compliance in the intervention arm (hand sanitiser wipes and disinfection of surfaces).

Of the four RCTs in the 2010 update, one was classified at low risk of bias (Loeb 2009), one at medium risk of bias (Aiello 2010a) and two (Jacobs 2009; Larson 2010) at high risk of bias.

Non-randomised studies

These were assessed for the presence of potential confounders using the appropriate Newcastle-Ottawa Scales (NOS) (Wells 2005) for case-control and cohort studies and a three-point checklist for controlled before and after and ecological studies (Khan 2000).

Case-control studies

We classified five of the nine case-control studies as having medium risk of bias (Lau 2004a; Seto 2003; Wu 2004; Yin 2004; Yu 2007) and two as at low risk of bias (Nishiura 2005; Teleman 2004), mostly because of inconsistencies in the text and lack of adequate description of controls. Two were at high risk of bias (Chen 2009; Liu 2009).

Prospective cohort studies

Six of the 16 prospective cohort studies were classified as at low risk of bias (Agah 1987; Dick 1986; Falsey 1999; Leung 2004; Madge 1992; Somogyi 2004), six as of medium risk (Broderick 2008; Dyer 2000; Kimel 1996; Murphy 1981; White 2003, Yen 2006), and four as of high risk of bias (Makris 2000; Master 1997; Niffenegger 1997; Wang 2007). One was a very brief report of a small study with insufficient details to allow assessment (Derrick 2005).

Retrospective cohort studies

All six retrospective cohort studies had high risk of bias (Cowling 2010, Doherty 1998; Foo 2006; Isaacs 1991; Ou 2003; Yen 2006). In general, retrospective designs are prone to recall bias.

Time series studies

Six of the 13 controlled before-after studies were at low risk of bias (Hall 1981a; Leclair 1987; Macartney 2000; Pang 2003; Ryan 2001; Simon 2006), two of medium risk (Krasinski 1990; Pelke 1994) and five at high risk (Gala 1986; Hall 1981b; Heymann 2004; Krilov 1996; Snydman 1988).

Measures of treatment effect

When possible, we performed a quantitative analysis and summarised effectiveness as odds ratio (OR) using 95% confidence intervals (CI). We expressed absolute intervention effectiveness as a percentage using the formula intervention effectiveness = 1 - OR, whenever significant. In studies which could not be pooled, we used the effect measures reported by the trial authors (such as risk ratio (RR) or incidence rate ratio (IRR) with 95% CI or, when these where not available, relevant P values).

Unit of analysis issues

Outcome measures varied from incidence of experimentally-induced rhinovirus infections, to the incidence of naturally occurring undifferentiated acute respiratory infections (ARIs). This was measured in a variety of ways, including numbers of ARIs per time period, or number of ARIs per household per time period. In some studies the ARIs were replaced by influenza-like illness (ILI). Other included studies focused on SARS specifically, or respiratory syncytial virus (RSV).

Proxy measures of illness included absenteeism.

Dealing with missing data

Whenever details of studies were unclear or studies were only known to us by abstracts or communications at meetings we corresponded with first or corresponding authors.

Assessment of heterogeneity

Aggregation of data was dependent on study design, types of comparisons, sensitivity and homogeneity of definitions of exposure, populations and outcomes used. We calculated the I^2 statistic for each pooled estimate to assess the presence of statistical heterogeneity (Higgins 2002; Higgins 2003).

Assessment of reporting biases

Given the limited nature of our quantitative synthesis and the widely disparate nature of our evidence base, we limited our assessment of possible reporting biases to funnel plot visual inspection.

Data synthesis

We systematically described and reviewed included studies separately by study design. In other words randomised studies were described and reviewed separately from case-control studies which were described and reviewed separately from prospective cohort studies, and so on. If possible and appropriate, we combined studies within a particular study design in a meta-analysis. We used fixed-effect meta-analysis providing there was no evidence of heterogeneity, otherwise we used random-effects meta-analysis.

Subgroup analysis and investigation of heterogeneity

An a priori subgroup analysis was planned for:

1. pandemic influenza outbreaks;
2. seasonal influenza; and
3. other epidemics (for example, SARS).

We had sufficient data to carry out only the last.

Sensitivity analysis

We aimed to perform a sensitivity analysis on the results of our meta-analysis. We assessed the robustness of the conclusions from the evidence of the effects of each intervention by comparing the results across the original multivariable analysis, looking for consistency of findings.

Summary of findings and assessment of the certainty of the evidence

RESULTS

Description of studies

Results of the search

We scanned 3775 titles, excluded 3560 and retrieved full papers of 215 studies, to include 66 papers of 67 studies.

Included studies

See Summary of main results section for a summary table of interventions and types of evidence.

In 2010 we included seven new studies and listed three trials as awaiting assessment. The seven newly included studies are four RCTs (Aiello 2010a; Jacobs 2009; Larson 2010; Loeb 2009), one retrospective cohort (Cowling 2010) and two case-control studies (Chen 2009; Liu 2009).

Excluded studies

We excluded 36 additional studies. The most frequent reasons for exclusion were no reporting of original data/non-comparative design, confounding by use of antivirals or other medication and in vitro studies (carried out without live patients).

Risk of bias in included studies

Three RCTs were poorly reported with no description of randomisation sequence, concealment or allocation (Gwaltney 1980; Turner 2004a; Turner 2004b). The design of two trials by one author means their results may not be generalised to everyday situations. This is due to the artefactual delivery of the interventions tested (see Quality of the evidence in the Discussion section) (Turner 2004a; Turner 2004b).

The quality of the cluster-randomised trials varied. Only the highest quality trials (Cowling 2009; Luby 2005; Roberts 2000; Sandora 2005) reported cluster coefficients and conducted analysis of data by unit of (cluster) allocation instead of by individuals. Analysing cluster-randomised trials at the individual level leads to spuriously narrow CIs around the estimates of effect (Grimshaw 2004). Other common problems were a lack of description of randomisation procedure, partial reporting of outcomes, unclear numerators or denominators and unexplained attrition (Carabin 1999; Kotch 1994; Morton 2004; White 2001) and either complete failure of double-blinding (Farr 1988a; Farr 1988b) or inappropriate choice of placebo (Longini 1988). Jacobs 2009 is an underpowered individual randomised trial carried out in Japan. Its open design means that due to lack of accounting for drop outs and definitions of outcomes the trial is at high risk of bias. In addition, no guidance as to the generalisability of its results to other settings and countries is provided to readers.

Aiello 2010a is at medium risk of bias. Despite logistical and design problems the trial appears to show an effectiveness gradient of mask-wearing and hand sanitation combined versus instruction on hand sanitation and mask-wearing in student halls. The last cluster-randomised trial (Larson 2010) compared the effects of education alone versus education plus the use of an alcohol-based hand sanitiser versus education plus the use of an alcohol-based hand sanitiser plus the use of medical face masks on the interruption of self-reported upper respiratory tract infection (URTI), ILI and laboratory-confirmed influenza or other viral pathogen by culture or polymerase chain reaction (PCR) in US immigrant Latino households. Due to design issues, difficulty interpreting whether there was an intention-to-treat (ITT) analysis and lack of sufficient details of dropouts and other reporting problems, we classified it at high risk of bias.

Loeb 2009 is a low risk of bias non-inferiority trial directly comparing the effects of surgical mask wearing versus N95 fit-tested respirators in nurses in acute units in Ontario Canada. The outcomes measured range from symptomatic and asymptomatic influenza to physician visits and ILI caused by non-influenza agents. This is possibly the most reliable piece of evidence available for this 2010 update.

We classified five of the nine case-control studies as having medium risk of bias (Lau 2004a; Seto 2003; Wu 2004; Yin 2004; Yu 2007) and two as at low risk of bias (Nishiura 2005; Teleman 2004), mostly because of inconsistencies in the text and lack of adequate description of controls. Two case-control studies (Chen 2009; Liu 2009) were at high risk of bias. Their interpretation is not straightforward. Both studies assess the effects of multiple factors as risk and protective measures for SARS during the epidemic in China. They appeared to be searching for associations and lacked precision with respect to conducting true matched blinded assessments.

Only live cases were considered when we know that between 10% to 20% of infected healthcare workers died in the first weeks of the epidemic (Liu 2009 mentions the high mortality rate in the Introduction). However, the studies did ascertain the cases and controls of SARS by performing confirmatory laboratory testing rather than relying on a clinical diagnosis.

Six of the 16 prospective cohort studies were classified as at low risk of bias (Agah 1987; Dick 1986; Falsey 1999; Leung 2004; Madge 1992; Somogyi 2004), four as of medium risk (Dyer 2000; Kimel 1996; Murphy 1981; White 2003) and three as of high risk of bias (Makris 2000; Master 1997; Niffenegger 1997). One was a very brief report of a small study (Derrick 2005) and two recent studies (Broderick 2008; Wang 2007) report insufficient details to allow assessment.

Four retrospective cohort studies exploring the effect of barrier interventions (Doherty 1998; Isaacs 1991; Ou 2003; Yen 2006) and one study reporting on adverse effects of barrier interventions (Foo 2006) had a high risk of bias. The other high risk of bias retrospective cohort study is Cowling 2010, mainly due to the nature of its design, heavily dependent on web availability of information.

Six of the 13 controlled before-after studies were at low risk of bias (Hall 1981a; Leclair 1987; Macartney 2000; Pang 2003; Ryan 2001; Simon 2006), two of medium risk (Krasinski 1990; Pelke 1994) and five at high risk (Gala 1986; Hall 1981b; Heymann 2004; Krilov 1996; Snydman 1988).

The most common problem in all of these studies was a lack of reporting of viral circulation in the reference population, making interpretation and generalisability of their conclusions questionable.

The results of a GRADE evaluation (the GRADE Working Group available from http://www.gradeworkinggroup.org/index.htm) of the case-control studies categorised them as providing low to very low quality evidence and categorised the updated RCTs as very low quality with the exception of two studies which were considered of moderate quality.

The overall risk of bias is presented graphically in Figure 1 and summarised in Figure 2.

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included RCTs.

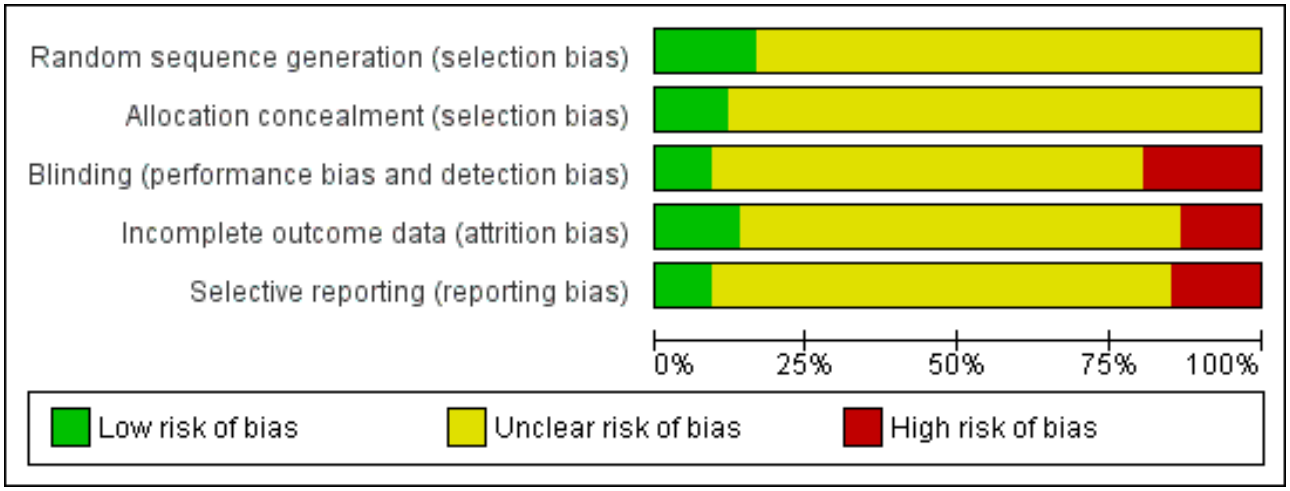


Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included RCT.

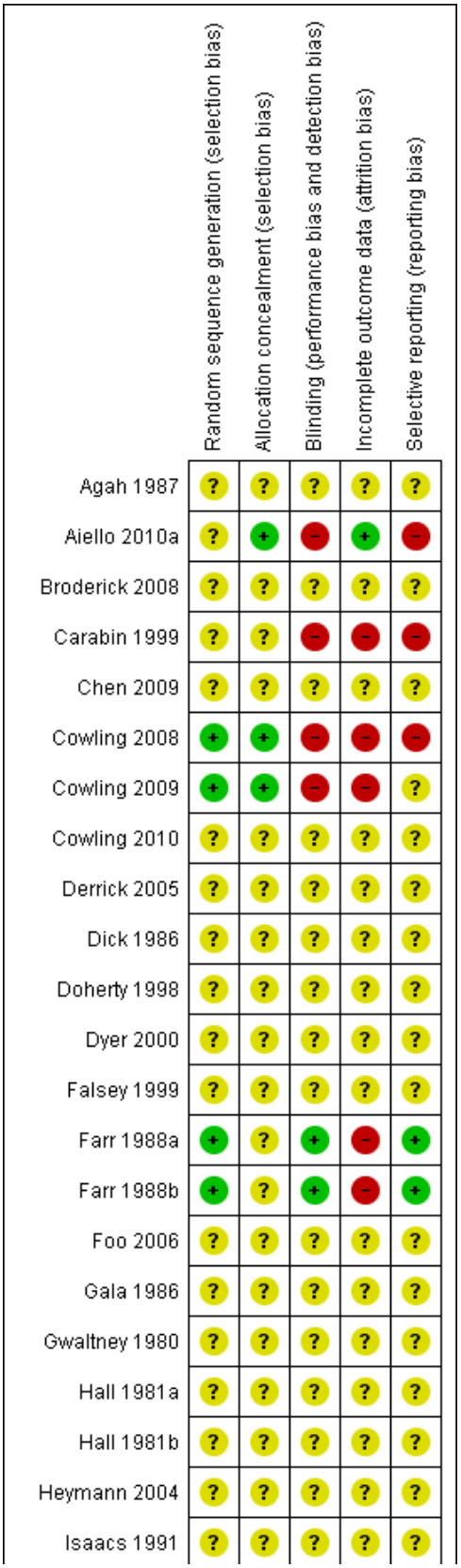


Figure 2. (Continued)

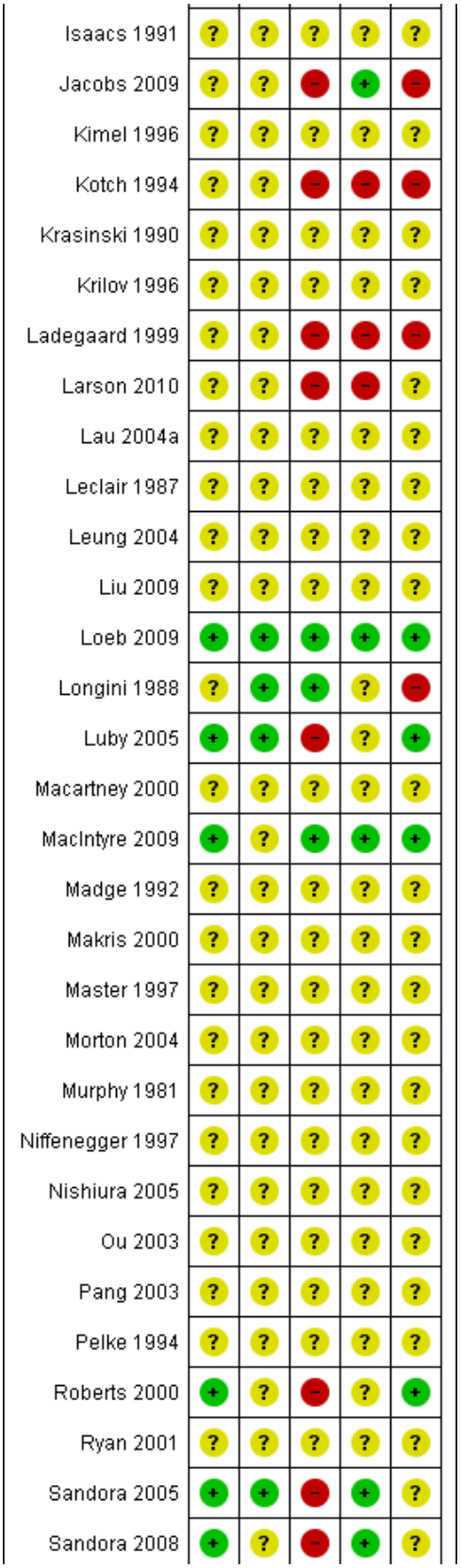
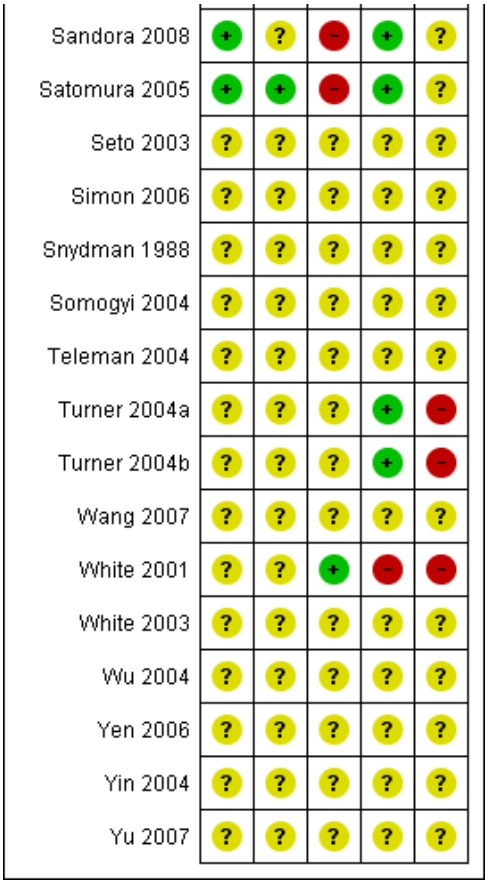


Figure 2. (Continued)



Effects of interventions

We scanned 3775 titles, excluded 3560 and retrieved the full papers of 215 studies, to include 66 papers of 67 studies. Four trials were listed in the Studies awaiting classification section. For one trial currently being submitted for publication we had insufficient information for assessment (Aiello 2010b). Two studies (Hubner 2009; Savolainen-Kopra 2010) assessed the effects of handwashing practices which were of less interest at this time than the use of the physical interventions featured in this update. Another study was identified after our searches had been conducted (Raboud 2010).

Reported results from randomised studies

Three studies tested the effects of hand-cleaning on inactivating the virus and preventing experimental rhinovirus colds. These resulted in either a reduction in the incidence of rhinovirus infection among volunteers treated using different combinations of the acids used for cleaning (P = 0.025) (Turner 2004a) or did not reach statistical significance (13% versus 30% with combined denominator of only 60) (Turner 2004b). Using iodine treatment of fingers, one out of 10 volunteers were infected compared to six out of 10 in the placebo preparation arm (P = 0.06 with Fisher's exact test) (Gwaltney 1980). One study found that gargling with water or povidone-iodine solution in addition to handwashing is effective in preventing URTIs, but not influenza-like illnesses (Satomura 2005).

Three cluster-randomised studies tested the effects of virucidal cleaning disposable handkerchief wipes on the incidence and spread of ARIs. One reported a reduced incidence of ARIs in the household over 26 weeks, from 14% to 5% (Farr 1988a). A similar study reported a small non-significant (5%) drop across families (Farr 1988b). However, since the drop in incidence was confined to primary illness, unaffected by tissue use, we might assume they were ineffective. A community trial also reported a non-significant reduction in ARI secondary attack rates (18.7% versus 11.8%) during a time of high circulation of influenza H3N2 and rhinoviruses in the community (Longini 1988). This result is likely to be an underestimate because of any barrier effect of the inert tissue wipes used in controls.

Eight cluster-randomised studies tested educational programmes to promote handwashing, with or without the adjunct of antiseptic agents, on the incidence of ARIs either in schools or in households. Because of different definitions, comparisons, lack of reporting of cluster coefficients and (in two cases) missing participant data (Carabin 1999; Kotch 1994), we judged it improper to meta-analyse the data. Two of these trials reported a lack of effect: RR for the prevention of acute respiratory illness of 0.94 (95% CI -2.43 to 0.66) (Kotch 1994); and 0.97 (95% CI 0.72 to 1.30) (Sandora 2005). Nevertheless, the highest quality trials reported a significant decrease in respiratory illness in children up to 24 months (RR 0.90, 95% CI 0.83 to 0.97), although the decrease was not significant in older children (RR 0.95, 95% CI 0.89 to 1.01) (Roberts 2000); and a 50% (95% CI -65% to -34%) lower incidence of pneumonia in children aged less than five years of age in a low-income country (Luby 2005). Another study reported a decrease of 30% to 38% in respiratory infections with additional hand-rubbing (RR for illness absence incidence 0.69, RR for absence duration 0.71) (White 2001).

One study reported decreased school absenteeism of 43% with the additional use of alcohol gel as well as handwashing (Morton 2004). Two trials reported that repeated handwashing significantly reduced the incidence of colds by as much as 20% (Carabin 1999; Ladegaard 1999). One study found that in households in which interventions (handwashing with or without wearing a facemask) were implemented within 36 hours of symptom onset in the index patient, transmission of reverse transcription polymerase chain reaction (RT-PCR)-confirmed infection was reduced, an effect attributable to reductions in infection among participants using face masks plus hand hygiene (adjusted OR 0.33 (95% CI 0.13 to 0.87)) (Cowling 2009).

The findings of the cluster-randomised trial by Aiello et al (Aiello 2010a) suggest that face masks and hand hygiene may reduce respiratory illnesses in shared living settings and mitigate the impact of the influenza A (H1N1) pandemic compared to no intervention or hand sanitiser and education. This conclusion is based on a significantly lower level of ILI incidence in the mask and hand sanitiser arm compared to the other two arms after adjustment for covariates (30% to 50% less in arm one compared to controls in the last two weeks of the study). However, influenza virus circulation was very low during the study period.

The authors of Jacobs 2009 were unable to detect a difference in incidence of ILI of surgical mask wearing compared to no mask in healthcare workers in a Japanese hospital, possibly because of the study's lack of power.

The cluster-randomised trial by Larson et al (Larson 2010) tested the addition of mask and hand sanitiser use to hand sanitiser use alone to nothing other than education which was common to all three arms. Given the many biases in the design and reporting the results are difficult to interpret: the hand sanitiser group was significantly more likely to report that no household member had symptoms (P = 0.01) but there were no significant differences in rates of infection by intervention group in multivariate analyses. Knowledge improved significantly more in the hand sanitiser group (P = 0.0001).

The credible results of the individual trial by Loeb et al (Loeb 2009) report that the use of surgical masks was not inferior to the use of N95 respirators against influenza.

Reported results from case-control studies

Nine case-control studies assessed the impact of public health measures to curb the spread of the SARS epidemic during February to June 2003 in China, Singapore and Vietnam. Homogeneity of case definition, agent, settings and outcomes allowed meta-analysis. We pooled binary data; one of the comparisons showed significant heterogeneity (handwashing), however we used a fixed-effect model. A random-effects model made no appreciable difference to the handwashing comparison. Although continuous data were often available, the variables were different and measured in different units with standard deviations usually missing, which prevented their meta-analysis.

Studies reported that disinfection of living quarters was highly effective in preventing the spread of SARS (OR 0.30, 95% CI 0.23 to 0.39) (Lau 2004a); handwashing for a minimum of 11 times daily prevented many cases (OR 0.54, 95% CI 0.44 to 0.67) (Analysis 1.2), based on seven studies (Chen 2009; Lau 2004a; Nishiura 2005; Seto 2003; Teleman 2004; Wu 2004; Yin 2004); simple mask-wearing was highly effective (OR 0.32, 95% CI 0.26 to 0.39) (Analysis 1.3), based on seven studies (Chen 2009; Lau 2004a; Liu 2009; Nishiura 2005; Seto 2003; Wu 2004; Yin 2004); three studies found N95 respirator-wearing even more effective (OR 0.17, 95% CI 0.07 to 0.43) (Analysis 1.4), (Seto 2003; Teleman 2004; Liu 2009); glove-wearing was effective (OR 0.32, 95% CI 0.23 to 0.45) (Analysis 1.5) (Chen 2009; Liu 2009; Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); gown-wearing was also effective (OR 0.33, 95% CI 0.24 to 0.45) (Analysis 1.6) (Chen 2009; Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); all means combined (handwashing, masks, gloves and gowns) achieved very high effectiveness (OR 0.09, 95% CI 0.02 to 0.35) (Analysis 1.7) (Nishiura 2005; Seto 2003); use of eye protection such as goggles or masks with goggles is protective (OR 0.10, 95% CI 0.05 to 0.17) (Analysis 1.8) (Chen 2009; Liu 2009; Yin 2004) and nose-washing was also protective (OR 0.30, 95% CI 0.16 to 0.57) (Analysis 1.9) (Chen 2009; Liu 2009). As the data are all based on univariable analyses, they may be subject to confounding. We have separately tested how many of these measures were statistically significant in multivariable analyses (Table 1).

These data suggest that wearing a surgical mask or a N95 mask is the measure with the most consistent and comprehensive supportive evidence. Seven out of eight studies included masks as a measure in their study and six out of seven of these studies found masks to be statistically significant in multivariable analysis. Handwashing was also included in seven of the studies with four studies showing handwashing to be statistically significant in multivariable analysis. All other measures were shown to be statistically significant in multivariable analysis on only one or two occasions.

Another case-control study from Hong Kong and Guangzhou hospital wards reported that a minimum distance between beds of less than one metre was a risk factor for transmission (Yu 2007). Disaggregated data were not reported and therefore we did not pool this study in the meta-analysis. All studies selected cases from hospitals, except for one (Lau 2004a) in which cases were people with probable SARS reported to the Department of Health in Hong Kong.

The detailed results of Chen 2009 report that avoiding face-to-face contact while caring for SARS patient (OR 0.30, 95% 0.15 to 0.60) and wearing gloves coupled with methods of ventilation are highly protective practices (various ORs for the various combinations intensity of wearing and ventilation methods, all significant). Liu 2009 reports that personal protective measures against droplet spread, such as wearing multiple layers of mask, are effective against the nosocomial spread of SARS.

Reported results from prospective cohort studies

Using an alcohol rub in students' communal residences resulted in significantly fewer symptoms (reductions of 14.8% to 39.9 %) and lower absenteeism (40% reduction) (White 2003). In a much-cited small experimental study, virucidal paper handkerchiefs containing citric acid interrupted the transmission of rhinovirus colds transmitted through playing cards: 42% of re-usable cotton handkerchief users developed colds compared with none using disposable virucidal tissues (Dick 1986).

Few identified studies reported interventions in the daycare setting, either in staff or patients. One staff educational programme

on handwashing in a daycare centre for adults was effective over a four-year period in reducing rates of respiratory infection in daycare patients from 14.5 to 10.4 per 100 person-months to 5.7 (P < 0.001), with an accompanying decline in viral isolates. This seems to be more effective than the use of additional portable virucidal hand foam as an adjunct to handwashing (Falsey 1999). This confirmed an earlier report of the effectiveness of a handwashing programme in reducing absenteeism for ILI in a primary school (Kimel 1996).

Two high risk of bias studies reported that education, a handwashing routine and encouragement for kindergarten children, parents and staff in correct sneezing and coughing procedure were effective, although there were considerable fluctuations in incidence of infections in the control and test centres (Niffenegger 1997); but the intervention was not effective in reducing absenteeism caused by ARIs (RR 0.79, P = 0.756) (Master 1997).

Dyer and colleagues reported a prospective, cluster, open-label, cross-over cohort study. The study assessed the effectiveness of a hand sanitiser in conjunction with at will soap-and-water handwashing in a private elementary school in California. Use of the sanitiser reduced illness absenteeism by 41.9% (reduction in respiratory illnesses of 49.7% over the 10-week period of the study) (Dyer 2000).

Curiously, an infection-control education programme reinforcing handwashing and other hygienic measures in a nosocomial setting reported reducing the number of organisms present on hands and surfaces, and ARIs, although the data tabled suggested the opposite (an incidence rate of 4.15/1000 patient-days in the test homes versus 3.15/1000 in the control homes) (Makris 2000).

A study found wearing a goggle-mask apparatus in healthcare workers visiting and caring for children aged up to five with respiratory syncytial virus (RSV) and symptoms of respiratory disease was effective (5% illness rate in goggle wearers against 61% in no-goggle controls) (Agah 1987).

Rapid laboratory diagnosis, cohort nursing and the wearing of gowns and gloves for all contacts with RSV-infected children significantly reduced the risk of nosocomial RSV infection (OR 0.013 to 0.76) (Madge 1992), although another similar study reported no effect of adding the use of both gown and mask to the usual handwashing routine on the development of illness in personnel caring for infants with respiratory disease (4 out of 30 in the handwashing group alone compared to 5 out of 28 in the handwashing, gown and masking group, P > 0.20); although the authors described poor compliance with the barrier protocol (Murphy 1981).

Strict procedures of triage and infection control to stop transmission of SARS from infected children to carers and visitors of a large hospital at the height of the epidemic in 2003 in Hong Kong was reported effective at interrupting the transmission of SARS, as no healthcare worker became ill, in contrast to experiences in other institutions (Leung 2004).

A tiny study comparing the N95 respirator with paper surgical masks in volunteers found that surgical masks, even when worn in multiple layers (up to five), filtered ambient particles poorly (Derrick 2005); this principle was confirmed in another small study of air filtration to prevent droplet spread (Somogyi 2004).

Reported results from retrospective cohort studies

Two studies investigated isolating together children less than three years of age with suspected RSV. In one, transmission was diminished by "up to 60%" (Isaacs 1991), while the statement that nosocomial transmission "was minimised" was not supported by data in the other study (Doherty 1998).

Isolation of cases during the 2003 epidemic of SARS in China was reported to limit transmission only to those contacts who actually had home or hospital contact with a symptomatic SARS patient (attack rate 31.1%, 95% CI 20.2 to 44.4 for carers; 8.9%, 95% CI 2.9 to 22.1 for visitors; 4.6%, 95% CI 2.3 to 8.9 for those living with a SARS case) but not to contacts living in the same building, working with cases, or without contact with SARS cases during the incubation period. This suggests extending quarantine only for contacts of symptomatic SARS cases (Ou 2003).

Another brief report carried out in 2003 during the SARS epidemic, in a military hospital in Taiwan, China and 86 control hospitals, compared an integrated infection-control policy to protect healthcare workers against infection; only two from the military hospital were infected with SARS compared to 43 suspected and 50 probable cases in the control hospitals (Yen 2006).

Cowling 2010 reports a marginal (one to two weeks) non-significant benefit in delaying spread of novel A/H1N1 autochthonous pandemic influenza by various means of entry screening. The high risk of bias is mainly due to the nature of its design, heavily dependent on web availability of information. However, it is difficult to see how else a similar study could have been conducted.

Reported results from controlled before and after studies

Two small studies by the same first author assessed means of nosocomial transmission of RSV in small children and the effects of introducing distancing and barriers: one with low risk of bias reported effective physical distancing and room separation (0 infected out of 14 who sat away from RSV-infected infants compared with five out of seven who cuddled and four out of 10 who touched infected infants) (Hall 1981a). The second with high risk of bias reported no incremental benefits of gowns and masks (32% infection versus 41%) (Hall 1981b). Adding disposable plastic eye-nose goggles to other respiratory infection-control procedures (isolating infected from uninfected people, handwashing) also reduced transmission of RSV (6% versus 42% of controls) (Gala 1986). Screening and subsequent isolation of infected from uninfected people ('cohorting') also reduced nosocomial RSV transmission in older children (from 5.33 infections per 1000/patient days of care to 1.23 infections per 1000/patient days after introduction of screening) (Krasinski 1990). A similar study reported that increased compliance with a policy of glove and gown isolation precautions reduced the high rate of nosocomial RSV transmission on an infant and toddler ward (RR for pre- and post-intervention periods infection rates 2.9, 95% CI 1.5 to 5.7) (Leclair 1987).

A study of protective gowning did not protect neonatal intensive care unit infants from RSV or any other type of infection, or affect mortality (1.21 per 100 patient-days of gowning compared to 1.38 of none), although selection bias was likely with 17% of participating children lost to follow up (Pelke 1994).

A German study conducted over three seasons reported a decrease of nosocomial RSV infections, from 1.67/1000 patient-days in the first season to 0.18/1000 patient-days in the last season, after instituting enhanced surveillance and feedback, rapid diagnosis, barriers and isolation, and disinfection of surfaces (Simon 2006). A similar study but with high risk of bias reported a decrease from eight confirmed RSV cases per 1000 patient-days to none (Snydman 1988). A better conducted study over eight years implemented a combination of education with high index of suspicion for case-finding (contact precautions), with barriers (but no goggles or masks) and handwashing for patients and staff reduced RSV infections in a hospital in Philadelphia, USA: RR 0.61, 95% CI 0.53 to 0.69 (Macartney 2000).

One small study with serious potential biases assessed training and a sanitary programme (handwashing, disinfection of school buses, appliances and toys) in a special-needs daycare facility for children with Downs Syndrome, a pupil to staff ratio of five or six to one, and reported reductions in: respiratory illnesses from a mean of 0.67 to 0.42 per child per month ($P < 0.07$); physician visits from 0.50 to 0.33 ($P < 0.05$); mean courses of antibiotics prescribed from 0.33 to 0.28 ($P < 0.05$); and days of school missed because of respiratory infections from 0.75 to 0.40 ($P < 0.05$) (Krilov 1996).

A very large study of military recruits reported that a structured top-down programme of handwashing at least five times daily nearly halved the incidence of ARIs. Recruits who handwashed less frequently reported more episodes of ARIs (OR 1.5, 95% CI 1.2 to 1.8), which represents a difference of 4.7 versus 3.2 mean infections per recruit per year, and more hospitalisations (OR 10.9, 95% CI 2.7 to 46.2). However, implementation was difficult (Ryan 2001).

An ecological study analysed the effects of quarantine and port of entry screening on the SARS epidemic in early 2003 in Beijing, China, from data collected centrally. Hospitals were the initial sources of transmission of the SARS virus. The shape of the epidemic suggests these measures may have reduced SARS transmission although only 12 cases identified out of over 13 million people screened puts in doubt the direct effectiveness of entry port checks at airports and railway stations, and screening was probably more important (Pang 2003).

An Israeli study of 186,094 children aged six to 12 years reported that school closure was temporally associated with a 42% decreased morbidity from respiratory tract infections, a consequent 28% decrease in visits to physicians and to emergency departments, and a 35% reduction in purchase of medications (Heymann 2004).

DISCUSSION

Quality issues

Several features need consideration before drawing generalisations from these studies.

The settings of the studies, conducted over four decades, were heterogeneous and ranged from suburban schools (Carabin 1999; Dyer 2000; Heymann 2004; Niffenegger 1997) to military barracks (Ryan 2001), emergency departments, intensive care units and paediatric wards (Gala 1986; Leclair 1987; Loeb 2009) in high-income countries; slums in low-income countries (Luby 2005); an upper Manhattan immigrant Latino neighbourhood (Larson 2010) and special-needs daycare centres with a very high teacher to pupil ratio (Krilov 1996). Few attempts were made to obtain socio-economic diversity by (for example) involving more schools in the evaluations of the same programme (Dyer 2000). We were able to identify few studies from low-income countries where the vast majority of the burden lies, and where cheap interventions are so critical. Even in high-income countries, such as Israel, the dramatic fall in ARIs subsequent to school closure may have been related to that country's high child population (34%). Additionally, limited availability of over-the-counter medications and national universal comprehensive health insurance provided with consequent physician prescription of symptomatic treatment may further limit generalisability of findings (Heymann 2004).

The variable quality of the methods of these studies is striking. Hasty design of interventions for public health crises, particularly the SARS case-control studies, is understandable but less so when no randomisation - not even of clusters - was carried out in several unhurried cohort and before and after studies. Randomisation could often have involved minimal disruption to service delivery. Inadequate reporting especially made interpretation difficult of before-after studies. Incomplete or no reporting of randomisation (Turner 2004a), blinding (Farr 1988a; Farr 1988b), numerators and denominators (Carabin 1999; Kotch 1994), interventions, outcomes (White 2003), participant attrition (Makris 2000), confidence intervals (CIs) (Madge 1992) and cluster coefficients in the relevant trials (Carabin 1999) led to a considerable loss of information. Potential biases (such as cash incentives given to participants (White 2003)) were not discussed. Some trial authors even confused cohort with before-after designs to elaborate conclusions unsupported by their data (Makris 2000). Methodological quality was sometimes eroded by the need to deliver behavioural interventions in the midst of service delivery (Niffenegger 1997).

Nonetheless, even when suboptimal designs were selected, trial authors rarely attempted to articulate potential confounders. A commonly ignored confounder, specific to this area, is the huge variability in viral incidence (Heymann 2004; Isaacs 1991). Sometimes this was addressed in the study design (Falsey 1999), even in controlled before and after studies (one attempted correlation between respiratory syncytial virus (RSV) admissions and RSV circulating in the community) (Krasinski 1990). Another attempted linking exposure (measured as nasal excretion) and infection rate in the pre- and post-intervention periods (Leclair 1987).

Inappropriate placebos caused design problems. In some studies the placebo probably carried sufficient intervention effect apparently to dilute the intervention effects (Longini 1988). Two valiant attempts probably failed because placebo handkerchiefs were impregnated with a dummy compound which stung the users' nostrils (Farr 1988a; Farr 1988b).

Some studies used impractical interventions. Volunteers subjected to the intervention hand cleaner (organic acids) were not allowed to use their hands between cleaning and virus challenge, so the effect of normal use of the hands on the intervention remains unknown (Turner 2004a; Turner 2004b). Two per cent aqueous iodine painted on the hands, although a successful antiviral intervention, causes unacceptable cosmetic staining, impractical for all but those at the highest risk of epidemic contagion (Gwaltney 1980).

Compliance with interventions, especially educational programmes, was a problem for several studies despite the importance of many such low-cost interventions. Overall the logistics of carrying out trials in immigrant neighbourhoods or students' halls of residence are demanding and recognition should be given to all those who planned and carried out studies in very difficult circumstances (as in the middle of an epidemic).

The evidence

The highest quality cluster-randomised trials indicate most effect on preventing respiratory virus spread from hygienic measures in younger children. Perhaps this is because younger children are least capable of hygienic behaviour themselves (Roberts 2000), and have longer-lived infections and greater social contact, thereby acting as portals of infection into the household (Monto 1969). Additional benefit from reduced transmission from them to other members of the household is broadly supported by the results of other study designs where the potential for confounding is greater.

The pooled case-control studies, which focused on the SARS coronavirus (SARS CoV), suggest that implementing barriers to transmission, isolation and hygienic measures are effective with the use of relatively cheap interventions to contain respiratory virus epidemics. We found limited evidence of the superior effectiveness of devices such as the N95 respirator over simple surgical masks. This evidence is supported by a high quality hospital-based trial (Loeb 2009) which reports non-inferiority between face barriers. Overall masks were the best performing intervention across populations, settings and threats. More expensive and uncomfortable (especially if worn for long periods) than simple surgical masks, N95 respirators may be useful in very high-risk situations but additional studies are required to define these situations.

It is uncertain whether the incremental effect of adding virucidals or antiseptics to normal handwashing actually decreased the respiratory disease burden outside the confines of the rather atypical studies, upon which we reported. The extra benefit may have been, at least in part, accrued by confounding additional routines.

Studies preventing transmission of RSV and similar viruses appeared to be closer to real life and suggest good effectiveness. However, methodological quality concerns of the controlled before and after studies, mentioned previously, suggest benefits may have been due to population differences, especially virus infection rates. These were poorly reported in most studies.

Routine long-term implementation of some of the measures assessed in this review would be problematic, particularly maintaining strict hygiene and barrier routines for long periods of time. This would probably only be feasible in highly motivated environments, such as hospitals, without a real threat of a looming epidemic. Most of the trial authors commented on the major logistic burden that barrier routines imposed at the community level. However, the threat of a looming epidemic may provide stimulus for their inception.

A disappointing finding was the lack of proper evaluation of global and highly resource-intensive measures such as screening at entry ports and social distancing. The handful of studies (mostly conducted during the SARS epidemic) do not allow us to reach any firm conclusions. It is remarkable that despite a long lead time to the declaration of a pandemic, an international, prospective study to evaluate entry screening practices was not set up. The study by Cowling et al is a good contribution to our evidence base but no substitute for a well designed and conducted trial (Cowling 2010). Finally, few studies reported harms from the interventions studied. Harms affect compliance, which may decrease even if the intervention is merely cumbersome (such as a mask) and the threat is unclear.

Summary of main results

See Table 2.

Overall completeness and applicability of evidence

See Discussion.

Quality of the evidence

See Discussion.

Potential biases in the review process

Through the World Health Organization (WHO), we made inquiries to identify a list of manufacturers of the interventions assessed in this review. However, no such list appears to exist. The low-tech (i.e. locally manufacturable) nature of some of the interventions, the lack of effective regulation in some settings and the possible endless number of manufacturers make the compilation and updating of such a list in a satisfactory manner very difficult. As a consequence it is impossible to gauge the existence of unpublished data. Low-tech device marketing is poorly regulated and incompletely understood.

Agreements and disagreements with other studies or reviews

We are not aware of systematic reviews of the same evidence.

AUTHORS' CONCLUSIONS

Implications for practice

The following effective interventions should be implemented, preferably in a combined fashion, to reduce transmission of viral respiratory disease:

1. frequent handwashing with or without adjunct antiseptics;
2. barrier measures such as gloves, gowns and masks with filtration apparatus; and
3. suspicion diagnosis with isolation of likely cases.

Special efforts should be focused on implementing the three above interventions in order to reduce transmission from young children, who are generally the most fecund sources of respiratory viruses.

Implications for research

Public health measures can be highly effective, especially when they are part of a structured programme that includes instruction and education and when they are delivered together. There is a clear requirement to carry out further large, pragmatic trials to evaluate the best combinations in the community and in healthcare settings and with other respiratory viruses. RCTs with a pragmatic design, similar to the Luby et al trial, should be

carried out whenever possible (Luby 2005). Nevertheless, this systematic review of the available research does provide some important insights. Perhaps the impressive effect of the hygienic measures aimed at younger children derives from the children's poor capability with their own hygiene. The variable quality and small scale of some studies is known from descriptive studies (Aiello 2002; Fung 2006; WHO 2006) and systematic reviews of selected interventions (Meadows 2004). More research is needed to evaluate the most effective strategies to implement successful physical interventions in practice, both on a small scale and at a population level. More attention should be paid to describing and quantifying the harms of the interventions assessed in this review and their relationship with compliance.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agah 1987

Methods	Prospective cohort study carried out in California hospital during the autumn 1984 to spring 1985 season. The study assessed the efficacy of healthcare workers (HCW) wearing goggle-mask apparatus while visiting and caring for children aged up to 5 with RSV and symptoms of respiratory disease compared to do nothing. Children admitted with a RSV diagnosis were assigned to the 2 arms balanced for age and sex
Participants	168 HCW caring for children < 5 years with differential diagnosis of RSV
Interventions	Mask and goggles (sometimes gowns too) versus normal care
Outcomes	RSV illness reduced from 61% (controls) to 5% (intervention) Laboratory: swabs for RSV diagnosis Effectiveness: RSV illness Safety: n/a
Notes	Risk of bias: low Notes: the authors conclude that wearing mask and goggles significantly reduced transmission to HCWs and other children of RSV (61% versus 5% illness rate). Analysis is also given by number of contacts (data not extracted). A reasonably reported if difficult to conduct study. Standard procedures such as handwashing should not have acted as a confounder given 100% coverage among HCWs

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Aiello 2010a

Methods	Cluster-randomised trial assessing the effects of hand sanitiser and masks with masks or no intervention on ILI symptoms. The trial was conducted in University halls of residence with more than 100 student residents in a US university during the 2006 to 2007 influenza “season”. It lasted 6 weeks The units of randomisation were 7 of the 15 halls. One hall was very large (1240 residents) and the 6 remaining ones which had between 110 and 830 residents were combined into 2 clusters roughly equivalent in size. The 3 clusters were then randomised by random extraction of the clustered halls’ names out of a container. The largest hall (single-cluster) was randomised to the mask and hand sanitiser arm, the 4 halls cluster received masks and the remaining 2 halls were assigned as controls
Participants	Willing, consenting residents aged 18 or more. Recruitment of students began in November 26 but the trial did not go “live” with distribution of intervention materials until 22 January 2007 when the first

Aiello 2010a *(Continued)*

	case of influenza was confirmed on campus by laboratory tests. Enrolment continued until 16 February 2007 and the study was completed on 16 March 2007. During the study period there was a 1-week break when the majority of residents left campus. There were 1327 eligible participants, of which 1297 had a complete baseline survey and at least 1 weekly survey result (367, 378 and 552 in the mask and hand sanitiser, mask only and control groups respectively, giving a total of 1297). It is unclear what the ineligibility criteria were for the 30 missing (1327 minus 1297) but the explanation may be in the appendix.
Interventions	Alcohol-based hand sanitiser (62% ethyl alcohol in a gel base) in a squeeze bottle and TECNOL procedure masks with ear loops (KC Ltd) and educational material or masks and educational material or no intervention. Compliance was encouraged within halls and outside. Sleep wearing was optional All participants received basic video-linked instruction on cough etiquette and hand sanitation. At baseline and weekly during the study participants were asked to fill in a web-based survey collecting demographic and ILI symptom data. This was supplemented by direct observation of compliance by staff Compliance with "optimal handwashing" (at least 20 seconds 5 or more times a day) was significantly higher in the sanitiser and mask arm
Outcomes	Laboratory details are described in appendix Effectiveness: ILI, defined as cough and at least 1 constitutional symptom (fever/feverishness, chills, headache, myalgia). ILI cases were given contact nurses phone numbers to record the illness and paid USD 25 to provide a throat swab. 368 participants had ILI and 94 of these had a throat swab analysed by PCR. 10 of these were positive for influenza (7 for A and 3 for B), respectively by arm 2, 5 and 3 using PCR, 7 using cell culture Safety: n/a
Notes	The authors conclude that "These findings suggest that face masks and hand hygiene may reduce respiratory illnesses in shared living settings and mitigate the impact of the influenza A (H1N1) pandemic". This conclusion is based on a significantly lower level of ILI incidence in the mask and hand sanitiser arm compared to the other 2 arms after adjustment for covariates (30% to 50% less in arm 1 compared to controls in the last 2 weeks of the study) Comparison with the ILI rate of the control arm may not be a reflection of the underlying rate of ILI because the intervention arm received instruction on hand sanitation and hand etiquette The play of adjustments is unclear. The intra cluster correlation coefficient is reported in the footer of Table 4. Its very small size suggests lack of clustering within halls The role of the spring break is mentioned in the Discussion as are the results of this study compared to other studies included in our review (Cowling 2008 and MacIntyre 2009) The authors report that 147 of 1297 participants (11.3%) "at baseline" had ILI symptoms and were excluded from analysis. During the 6 weeks of the study 368 of 1150 participants (32%) had ILI. This averages out at about 5% per week. It is unclear what the term "at baseline" means. Presumably this means during the 2 to 3 weeks of participant enrolment. If this is so, the reason for the triggering of the interventions (tied to influenza isolation) are obscure as the trial is supposedly about ILI and an ILI outbreak was already underway "at baseline"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as randomised but sequence generation not reported
Allocation concealment (selection bias)	Low risk	The residence hall units were randomised by blindly selecting a uniform ticket with the name of each hall out of a container (A.S.M. and A.A.) for randomisation assignment to each study arm

Aiello 2010a *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition is reported as follows: 9, 11 and 19 ineligible and 26, 52 and 21 lost to follow up (respectively by arm). This makes a total of 39 and 99 for each cause of attrition. In total, 1297 (97%) of 1331 participants completed a baseline and at least 1 weekly survey The text reports an ITT analysis with only one ILI episode included by participant No reasons for the attrition of participants and swab volunteers are reported (were the swabs taken from a random sample or not?)
Selective reporting (reporting bias)	High risk	There is no information on the causes of ILI other than the reporting on the 10 influenza PCR-positive swabs of 94 out of 368 students with ILI. This is a very low rate (and the Discussion confirms that the influenza season was mild) but investigation of the other known causes of ILI is not even mentioned in the text. This is especially important because stress, alcohol intake levels and influenza vaccination were a significant predictor of ILI symptoms (Table 1). The reason for selective testing and/or reporting of influenza viruses tests over the other causes of ILI are unclear especially as the study objective was focused on ILI. The text also is difficult to follow, weaving the reporting of ILI and influenza without a clear rationale

Broderick 2008

Methods	Prospective, cohort study carried out in a military recruit training centre during the first 4 weeks of recruit training. Data were collected between February 2004 and March 2005 (duration of recruit training is not reported) It is not clear how the recruits were assigned to 'experimental' (closed) or control (open). Recruits were assigned to units on the basis of arrival order with no particular allocation scheme The study assessed if social distancing would reduce the incidence of febrile respiratory illness (FRI). Data were collected over 4 weeks for each new group of recruits Housing units (n = 196 units) were divided into closed units (n = 30) (experiment/intervention) or open units (n = 166) (control). For description of how the closed units were selected and geographical position in the training centre see notes Microbiological samples from physical structures (tables, surfaces, angles of surfaces, handles) of some units were done. However, it is not mentioned if these units were selected from among the closed or open units
Participants	Male military recruits (n = 13,114), distributed among 196 housing units (166 open units and 30 closed units) took part in the study. Unit size ranged from 44 to 88 recruits per unit. Reported denominators add up to 13488 recruits not 13114 (closed: 329/2099 versus open: 1586/11389). No exclusions were reported. Dimensions of the units are not described (space/subject or space/unit). The average number of subjects/unit in the closed units was not reported 10% of medical convalescent unit (MCU) subjects (762) and 6% of physical conditioning unit (PCU) subjects (395) were positive for adenovirus 4 by PCR
Interventions	To test the effect of social distancing: participants were either assigned (allocation process not clear) to closed or open units. The closed units did not introduce any new participants once their personnel had been assigned (socially-distant); sick recruits were removed but if their symptoms did not require

Broderick 2008 *(Continued)*

	placement in the MCU, the recruits returned to their units. The open units accepted recovering subjects after being discharged from MCU and PCU To test an environmental aetiology: some of the units, which were vacant after 4 weeks of occupation, were swabbed. The MCU was also swabbed. The samples were tested by PCR and were cultured
Outcomes	Laboratory: (MicroTest M4 Transport; Remel) polymerase chain reaction (PCR) culture for Ad-4 virus Not used to confirm FRI in all index cases. Adenovirus was the only microorganism tested for and isolated Effectiveness: cases of FRI were defined either by a body temperature of > 38°C and 1 respiratory symptom or by the presence of non-febrile pneumonia Cases were reported as number of cases of FRI per 100 persons per week, averaged over the 4 weeks Safety: n/a
Notes	The institutional review board of the Naval Health Research Centre classified the protocol of this study as a non-research public health endeavour. Given the flaws of the study design (the disparity between the number of closed and open units, testing 2 different 'aetiological' hypothesis using different methodologies and lack of information on how the units were selected), one gets the impression that this study was probably carried out at least retrospectively instead of being carried out as a prospective study as claimed by the authors. The authors conclude that social distancing did not reduce FRI and that environmental contamination rather than person to person transmission is the culprit in the spread of FRI. The method used for social distancing, however, did not exclude those that were little bit sick but did not require placement in the MCU. In other words, sick people were allowed to remain in the closed unit (? as well as in the open units); only apparently healthy recruits were allowed to rejoin the open units after being placed in the MCU and PCU The study put emphasis on the importance of environmental cleaning. In addition to that crowded areas increase the risk of transmission of viruses. In the study, however, it was not clear if open and closed units are similar or different as pathogen reservoir. Also, analysis of closed units according to the population size was not done and information about the location of the closed units (all over the centre or localised in certain (isolated) area) is lacking. Despite these clear limitations this pragmatic study's findings may be interpreted in a variety of different ways. Perhaps the most interesting interpretation is that environmental conditions are determinants of adenoviral infectivity but not entry and exit from a community. In other words virological and presumably bacterial agents persist in the environment, they are not "brought" in and do not "arrive" and do not directly and invariably cause one-on-one disease. This hypothesis challenges the current simplistic interpretation of the postulates of Henle-Koch (one agent = one disease and suggests that the presence of microorganism may only be one of the many variables which determine infectious disease. This interpretation is comforted by the relatively small number of isolates found in studies of ILI causes (so called pie studies) The corresponding author provided the following additional information: each week a new cohort of about 500 recruits arrives at the camp, all of whom arrive by Wednesday. On Thursday the recruits are assigned to 6 platoons (each platoon housed in its own large room - called "housing units" in the article). Each cohort's 6 housing units are numbered from 1 to 6, with no particular distinction between them. Each house is given approximately the same number of recruits. The placement of the recruits into the housing units is based somewhat on the order of their arrival to the camp, but otherwise there are no criteria for placement, although relatives and friends are allowed to be in the same platoon. The recruits at MCRD San Diego tend to be from west of the Mississippi. There is no particular order of arrival at the camp from different regions. The number of the closed housing unit assigned in each cohort varied. In the majority of cases it was 1 or 2 Each building contains 4 wings of 3 floors each. From the sky, the buildings form an H shape. The line in the middle of the H connects the sides of the H, and on each side the half above the middle line is one wing and below the middle line is the other wing. If you go on maps.google.com and type in 'san diego ca mcrd' and zoom in on C you can see how big the buildings are. The housing units for each cohort typically occupy 2 wings one building, but occasionally one housing unit will be in a different building. E.g. if there are 6 housing units in a cohort, the cohort will occupy 3 floors of wing A and 3 floors of wing C. The map gives you an idea of the geography of horizontal distance between each wing, and each floor is about 10 feet high. Although the housing units are relatively close to each other, the platoons do

Broderick 2008 *(Continued)*

	not typically interact with each other. They are large permanent buildings each consisting of 12 large rooms and a hallway

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Carabin 1999

Methods	Cluster-randomised controlled trial carried out in daycare centres (DCC) in the Canadian province of Quebec between 1 Sept 1996 and 30 November 1997 (15 months). The aim was to test the effects of a hygiene programme on the incidence of diarrhoea and fecal contamination (data not extracted) and on colds and URTIs. The design included before and after periods analysed to assess the Hawthorne effect of study participation on control DCCs. Unit of randomisation was DCC but analysis was also carried out at classroom and single child level. This is a common mistake in C-RCT analysis. DCCS were stratified by URTI incidence preceding the trial and randomised by location. Cluster coefficients are not reported
Participants	1729 children aged 18 to 36 months in 47 DCCs (83 toddler classrooms)
Interventions	Training session (1 day) with washing of hands, toy cleaning, window opening, sand pit cleaning and repeated exhortations to handwash
Outcomes	Laboratory: n/a Effectiveness: diarrhoea and coliform contamination (data not extracted) Colds (nasal discharge with at least one of the following: fever, sneezing, cough, sore throat, earache, malaise, irritability) URTI (cold of at least 2 days' duration) Surveillance was carried out by educators, annotating absences or illness on calendars. Researchers also filled in a phone questionnaire with answers by DCC directors Safety: n/a
Notes	Risk of bias: high (no description of randomisation; partial reporting of outcomes, numerators and denominators) Notes: the authors conclude that the intervention reduced the incidence of colds (IRR 0.80, 95% CI 0.68 to 0.93). Confusingly written study with unclear interweaving of 2 study designs. For unclear reasons analysis was only carried out for the first autumn. Unclear why colds are not reported in the results. Cluster-coefficients and randomisation process not described

Risk of bias

Carabin 1999 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomisation of DCC according to region, but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not possible (hygiene session plus educational material versus none)
Incomplete outcome data (attrition bias) All outcomes	High risk	Originally 52 eligible DCCs with 89 classrooms agreed to take part but 5 dropped out (2 closed, 1 was sold, 2 either did not provide data or the data were "unreliable" and 6 classrooms had insufficient data). Forty-three children failing to attend DCC for at least 5 days in the autumn were also excluded. ITT analysis was carried out including an additional DCC whose director refused to let staff attend the training session No correction for clustering made
Selective reporting (reporting bias)	High risk	Denominators unclear and not explained

Chen 2009

Methods	Case-control study to test the association between SARS onset and a range of causative and protective variables in Sun Yan Tzen University hospitals in Guanzhou, Southern China The study collected information on cases and controls retrospectively during the first phase of the SARS epidemic in China (March to May 2003) but there is also a prospective element with antibody confirmation of SARS infection. Analysis plan was similar to that of Liu 2009 with a univariate and multivariate analysis conducted to assess risk factors
Participants	Description of cases. Probable SARS cases were defined using the criteria by the China Health Ministry. Criteria for probable and suspected SARS cases included travel to a SARS epidemic area in the 2 weeks before the onset of symptoms or close contact with a probable SARS patient; fever of ≥ 38°C; chest X-ray abnormalities; normal or decreased leukocyte count; and no response to treatment by antimicrobial drugs. In this study what appears to have happened is that available Sun Yan Tzen University hospitals HCWs who were willing to be interviewed were bled and those with raised IgG against SARS-CoV were included as cases. Cases enrolled were 90 out of the possible 112 who had SARS (80%) and 758/846 controls (89%). The choice criterion for interview of cases and controls was availability i.e. being “off duty” during the survey. It is unclear what this means and why such bias was knowingly introduced Description of controls. Controls were SARS-CoV negative HCW who had worked in the 2 hospitals attending SARS cases
Interventions	An extensive number of exposure and interventions variables were elicited and quantified with discrete scores. Definitions are absent in most cases *Use of personal protective and control measures* Number of gowns worn 0 = single, 1 = double Number of multilayered cotton mask worn 0 = single, 1 = double Number of pairs of gloves worn 0 = single, 1 = double Frequency of wearing shoe cover 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of wearing cap 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of face shield in SARS ward 0 = never, 1 = sometimes, 2 = often, 3 = every time

Chen 2009 *(Continued)*

	Frequency of wearing goggles while performing operation for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time *Health-related behaviours* Frequency of washing uncovered skin after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of washing hands after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of washing nasal cavity after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of washing oral cavity after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time *SARS patient care* Special training for SARS 0 = no, 1 = yes Performing tracheotomy 0 = no, 1 = yes Performing tracheal intubations 0 = no, 1 = yes Caring for "Super Spreading Patient" 0 = no, 1 = Yes Avoiding face to face while caring for patient 0 = never, 1 = sometimes, 2 = often, 3 = every time *Other relevant control measures* Method of air ventilation in offices and SARS wards 1 = artificial central ventilation (windows were closed in wards), 2 = natural ventilation (windows were opened in wards), 3 = natural ventilation and additional electronic exhaust fan (windows were opened in wards, at the same time, electronic exhaust fans were used for improving air circulation in wards) Type of equipment for washing hands 1 = automatic tap, 2 = non-automatic tap, 3 = other
Outcomes	N/A
Notes	The authors conclude that “Some measures, particularly good air ventilation in SARS wards, may be effective in minimising or preventing SARS transmission among HCWs in hospitals”. The study is biased by the selection of cases and controls (enrolment only of available personnel) and the non-eligibility (and lack of mention) of HCW who died of SARS (which may be up to 20% of people who were ill during the first wave of SARS). The design and analysis are very similar to those of Ma 2004/Liu 2009 and the design also lacks focus. i.e. it does not test a defined hypothesis, but trawls through large numbers of variables looking for associations. There is no attempt at matching cases with controls and part of the design is prospective (IgG estimation). As a consequence the design distinction between a case-control and a cohort study is blurred. There is no mention of whether interviewers were blinded to case or control status of interviewees Data extracted are from the univariate analysis table 3 which is the table reporting both numerators and denominators for cases and controls. Table 4 (multivariate logistic analysis) reports the significant multiple protective associations: caring for super spreading patient and avoiding face to face contact while caring for SARS patient (OR 0.30, 0.15 to 0.60) and wearing gloves coupled with methods of ventilation (various ORs for the various combinations intensity of wearing and ventilation methods, all significant). In the light of so many biases it is difficult to interpret the data but there does seem to be a gradient favouring multiple interventions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias)	Unclear risk	N/A

Chen 2009 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Cowling 2008

Methods	Cluster-randomised controlled trial carried out in Hong Kong SARS between February and September 2007. The study assessed the effects of non-pharmaceutical interventions on the household transmission of influenza over a 9-day period. ILI cases whose family contacts had been symptom-free for at least 2 weeks rapid tested for influenza A and B were used and randomised to 3 interventions carried out. Randomisation was carried out in 2 different schedules (2:1:1 for the first 100 households and subsequently 8:1:1) but it is unclear why and how
Participants	946 index subjects aged 2 years or more in 122 clusters (households). 116 households were included in the analysis, 6 were excluded because subsequent laboratory testing (culture) were negative. There were 350 household contacts in the analysis but there 370 household contacts at randomisation. Attrition is not explained. Index cases were defined as subjects presented with at least 2 influenza-like symptoms of at least 48 hour duration (such as fever more or equal to 38 degrees, cough, headache, coryza , sore throat, muscle aches and pains) and positive influenza A+B rapid test
Interventions	Households were randomised to either wearing face masks with education (as the control group plus education about face mask use) or handwashing with special medicated soap (with alcohol sanitiser) with education (as the control group plus education about handwashing) or education about general healthy lifestyle and diet (control group). The soap was distributed in special containers which were weighed at the start and the end of the study. Interventions visits to the households were done on average 1 day after randomisation of index case household
Outcomes	Laboratory: QuickVue RTI MDCK culture Samples were harvested using NTS, but the text refers to a second procedure from June 2007 onwards testing for non-influenza viruses but no data were reported Effectiveness: secondary attack ratios (SAR): SAR is the proportion of household contacts of an index case who subsequently were ill with influenza (symptomatic contact individuals with at least 1 NTS positive for influenza by viral culture or PCR) Three clinical definitions were used for secondary analysis: 1. Fever more or equal to 38 degrees or at least 2 of following symptoms, headache, coryza , sore throat, muscle aches and pains 2. At least 2 of the following S/S: fever more or equal to 37.8 degrees, cough, headache, sore throat and muscle aches and pains 3. Fever of more or equal to 37.8 degrees plus cough or sore throat Safety: no harms were reported in any of the arms
Notes	The authors conclude that “The secondary attack ratios were lower than anticipated, and lower than reported in other countries, perhaps due to differing patterns of susceptibility, lack of significant antigenic drift in circulating influenza virus strains recently, and/or issues related to the symptomatic recruitment design. Lessons learnt from this pilot have informed changes for the main study in 2008” Although billed as a pilot study the text is highly confusing and at times contradictory. The intervention was delivered at a home visit up to 36 hours after the index case was seen in the outpatients. This is a

Cowling 2008 *(Continued)*

	long time and perhaps the reason for the failure of the intervention. Practically, the intervention will have to be organised before even seeking medical care – i.e. people know to do it when the kid gets sick at home

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computer-generated by a biostatistician "A pre-specified table of random numbers will be used to assign one of the three interventions to the household of the index case."
Allocation concealment (selection bias)	Low risk	The households of eligible study index patients were allocated to 3 groups in a 1:1:1 ratio under a block randomisation structure with randomly permuted block sizes of 18, 24 and 30 by using a random-number generator. Allocation was concealed from treating physicians and clinics and implemented by study nurses at the time of the initial household visit
Blinding (performance bias and detection bias) All outcomes	High risk	Participants and people who administered the interventions were not blinded to the interventions, but participants were not informed of the specific nature of the interventions applied to other participating households
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout was accounted for. Dropout from randomised population was high: 32% in control group, 37.5% in hand hygiene group and 39.4% in the face masks and hand hygiene group. Reasons for dropout distributed evenly over the 3 groups Authors report follow up as proportion of patients remaining in the study after initial dropout
Selective reporting (reporting bias)	High risk	The choice of season, change in randomisation schedules and unexplained dropouts among contacts, the use of QuickVue which proved unreliable, reporting bias on non-influenza isolates make this study at high risk of bias

Cowling 2009

Methods	Cluster-randomised controlled trial
Participants	Households in Hong Kong From 45 outpatient clinics in both the private and public sectors across Hong Kong, they enrolled persons who reported at least 2 symptoms of acute respiratory illness (temperature 37.8 °C, cough, headache, sore throat, or myalgia); had symptom onset within 48 hours; and lived in a household with at least 2 other people, none of whom had reported acute respiratory illness in the preceding 14 days. After participants gave informed consent, they provided nasal and throat swab specimens. 2750 patients were eligible and tested between 2 January through 30 September 2008. Included were 407 people with influenza-like illness who were positive for influenza A or B virus by rapid testing (index patients) and 794 household members (contacts) in 331 households
Interventions	Participants with a positive rapid test result and their household contacts were randomly assigned to 1 of 3 study groups: control (lifestyle measures - 134 households), control plus enhanced hand hygiene only (136 households) and control plus face masks and enhanced hand hygiene (137 households) for all household members. No detailed description of the instructions given to participants
Outcomes	Influenza virus infection in household contacts, as confirmed by reverse transcription polymerase chain reaction (RT-PCR) or diagnosed clinically after 7 days

Cowling 2009 *(Continued)*

	"The primary outcome measure was the secondary attack ratio at the individual level: that is, the proportion of household contacts infected with influenza virus. We evaluated the secondary attack ratio using a laboratory definition (a household contact with a nose and throat swab specimen positive for influenza by RT-PCR) as the primary analysis and 2 secondary clinical definitions of influenza based on self-reported data from the symptom diaries as secondary analyses." Statistical analysis: adjusted for clustering Results: no significant difference in secondary attack ratio between groups in total population. Statistically significant reduction in RT-PCR confirmed influenza virus infections in the household contacts in 154 households in which the intervention was applied within 36 hours of symptom onset in the index patient. Adherence to hand hygiene between 44% and 62%. Adherence of index patient to wearing a face mask between 15% and 49%
Notes	"In an unintentional deviation from that protocol, 49 of the 407 randomly allocated persons had a household contact with influenza symptoms at recruitment (a potential co-index patient). We also randomly assigned 6 of 407 persons who had symptoms for slightly more than 48 hours." The authors conclude that "Hand hygiene and face masks seemed to prevent household transmission of influenza virus when implemented within 36 hours of index patient symptom onset. These findings suggest that non-pharmaceutical interventions are important for mitigation of pandemic and interpandemic influenza. "

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computer-generated by a biostatistician "A pre-specified table of random numbers will be used to assign one of the three interventions to the household of the index case."
Allocation concealment (selection bias)	Low risk	The households of eligible study index patients were allocated to 3 groups in a 1:1:1 ratio under a block randomisation structure with randomly permuted block sizes of 18, 24 and 30 by using a random-number generator. Allocation was concealed from treating physicians and clinics and implemented by study nurses at the time of the initial household visit
Blinding (performance bias and detection bias) All outcomes	High risk	Participants and people who administered the interventions were not blinded to the interventions, but participants were not informed of the specific nature of the interventions applied to other participating households
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout was accounted for. Dropout from randomised population was high: 32% in control group, 37.5% in hand hygiene group and 39.4% in the face masks and hand hygiene group. Reasons for dropout distributed evenly over the 3 groups Authors report follow up as proportion of patients remaining in the study after initial dropout
Selective reporting (reporting bias)	Unclear risk	In general good reporting

Cowling 2010

Methods	Retrospective cohort study carried out to test whether entry screening practices delayed the onset of endogenous (i.e. not linked with travel of travel contacts) cases of nH1N1 during the recent influenza pandemic in countries which had introduced them compared to countries which had not

Cowling 2010 *(Continued)*

Participants	35 countries which reported more than 100 cases of nH1N1 influenza to WHO by 6 July 2009 and for which entry policies could be ascertained or date of first untraceable local case (n = 26 countries). Participants excluded Mexico and US where transmission seemingly occurred earlier
Interventions	Dates and types of entry screening: temp check prior to disembarkation, health questionnaires from traveller with H1N1 cases, observation of arrivals for symptoms and thermal body imaging. There was wide variation in implementation with China and Japan implemented all 4, and 5 other nations none (Table 1)
Outcomes	Laboratory: n/a Effectiveness: dates of first imported pandemic influenza case and confirmation of first untraceable case (identified by Google and sundry searches) Safety: n/a
Notes	The authors conclude that entry screening provided an additional 1 to 2 weeks' delay with distributions delay ranging from 0 to 30 days (the CIs of median days of delay overlap). The authors question the cost-effectiveness of entry screening given the uncertainty of its effects and the enormous amounts of resources required to implement it This an interesting broad-brush study, heavily dependent on web-based searches but with a wide-ranging scope reflected in the multilingual capabilities of the study group. Its many weaknesses are known to the authors and are discussed.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Derrick 2005

Methods	Prospective cohort study testing the performance of 1, 2, 3, 4 and 5 surgical masks worn in layers against the droplet filtration capacity of a N95 respirator. The study is described as cross-over trial when all volunteers wore the combinations of layers, but this is not further described
Participants	6 volunteers who wore the masks and had their droplet count taken
Interventions	Pleated rectangular 3-ply surgical mask

Derrick 2005 *(Continued)*

Outcomes	Laboratory
Notes	Risk of bias: high (report too brief to allow assessment) Notes: the authors conclude that the best combination of 5 surgical masks scored a fit factor of 13.7, well below the minimum level of 100 required for a half face respirator. The reduction in particle count went from 2.7 for a singe mask to 5.5 for 5 masks worn at the same time. Multiple surgical masks filter ambient particles poorly. They should not be used as a substitute for N95 respirator unless there is no alternative. Cautiously the authors state that they cannot comment on the capacity of 5 layers of masks to stop infections such as SARS as the infective count of the SARS-CoV is unknown Fascinating small study with no details of assignment so it was classified as a cohort study. Unfortunately there is no indication of how comfortable 5 masks are to wear in a layer and no description of the volunteers

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Dick 1986

Methods	Prospective cohort study involving men ˜ 18 years of age. The objective of the study was to determine whether rhinovirus 16 colds could be stopped from spreading with the use of an highly virucidal paper handkerchief (CMF tissues) containing citric acid and other virucidal ingredients. 20 to 25 men ˜ 18 years of age were inoculated intranasally with a safety tested R16. The laboratory-induced cold was in all aspects comparable to natural colds. 8 of them with the most severe colds (donors) played cards with 12 antibody-free men (recipients) in a experiment room. Four experiments were conducted, in experiments B and C volunteers used CMF tissues to prevent spreading of R16 colds. In the 2 control experiments (A and D) volunteers were permitted to use cotton handkerchiefs
Participants	Males ˜ 18 years of age with a laboratory-induced R 16 cold (donors) and 12 antibody-free men (recipients)
Interventions	Use of virucidal paper handkerchief (CMF tissues), containing citric acid and other virucidal ingredients to stop the spreading of R16 colds versus normal cotton handkerchiefs
Outcomes	Laboratory: serological evidence (serum samples or viral isolation) Effectiveness: rhinovirus colds Safety: n/a
Notes	Risk of bias: low

Dick 1986 *(Continued)*

	Notes: the authors concluded that the use of CMS tissues has been successful, because it determined a complete interruption of transmission of R16 among participants, stopping the spreading in an environment in which possibilities for transfer of virus were constant, and in which the rate of transmission was predictably high under standard conditions (42% of cotton handkerchief users developed colds, but no user of virucidal tissues did so)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Doherty 1998

Methods	Retrospective cohort study carried out in North Staffordshire hospital (UK) during 2 periods: from 1 November 1994 to 31 January 1995 and from 1 November 1995 to 31 January 1996. The study assessed the use at admission of assigning children to a cohort once a rapid enzyme immunoassay or immunofluorescence testing had identified RSV-positive patients. The incidence of RSV illness was compared in cohorted and uncohorted children. The authors believed that this procedure would aid clinical management and minimise cross-infection from affected to susceptible patients. Nasopharyngeal aspirates were obtained from infants and young children with an acute respiratory illness. Aspirates were sent for rapid diagnostic testing. RSV-positive patients were cohorted into 6-bedded bays on the paediatric ward. All carers observed standard routines (handwashing and gown wearing)
Participants	Children less than 3 years of age with an acute respiratory illness on admission. During the study periods a total of 222 patients in 1994 to 1995 and 291 patients in 1995 to 1996 had positive rapid tests
Interventions	RSV diagnosis and cohorting versus normal care
Outcomes	Laboratory: aspirates for RSV diagnosis Effectiveness: RSV illness (developed at least 5 days since admission) Safety: n/a "RSV infection reduced" (but data tabled do not support this conclusion)
Notes	Risk of bias: high (poor descriptions) Notes: the authors conclude that cohorting has been shown to reduce nosocomial transmission of RSV infections (no OR or other measures of strength are reported: "nosocomial transmission was minimised"). The study presents many inconsistencies between text and table and data were not extracted. The objective of the study is not well-defined. Part of the results is in the discussion. Most of all it is unclear who the intervention and control arms were (i.e. cohorting of RSV-infected children to prevent infection in whom?)

Doherty 1998 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Dyer 2000

Methods	Prospective, cluster open-label cross-over cohort study of programmed use of a hand sanitiser in conjunction with at-will soap-and-water handwashing conducted in a private elementary school in California. The aim of the study was to assess the effectiveness of the SAB sanitiser at reducing illness absenteeism in a school setting. Subjects were grouped by classroom without formal randomisation. 7 classes received the instant sanitiser, while the remaining 7 classes were assigned to the control group. Male-to-female ratios and age distributions of the 2 groups did not differ significantly Prior to study commencement all students participated in an educational programme about germs and the importance of handwashing to prevent illnesses. Children in the hand sanitiser group received a spray to use under teacher supervision to supplement normal, at-will handwashing with soap and water. The control group was instructed to wash hands with water and soap, and it was not supervised. Data were collected for 10 weeks. After this period, there was a 2-week wash-out period, during which neither group of students used SAB sanitiser. Then SAB sanitiser was distributed to the student group that had previously served as the control and the study proceeded for another 4 weeks
Participants	420 children in a private elementary school in California aged 5 to 12 years; cluster, open-label, cross-over cohort study over 10 weeks
Interventions	Educational programme plus the SAB (surfactant, allantoin and benzalkonium chloride) spray hand sanitiser in 1 oz bottles fitted with a pump spray top and with at-will soap-and-water handwashing versus nothing
Outcomes	Laboratory: serological evidence: n/a Effectiveness: days of absences from school for respiratory illness (and gastrointestinal illness - data not extracted) Safety: n/a Respiratory illness and gastrointestinal illness: reduced absenteeism by 41.9%; respiratory illnesses by 49.7%
Notes	Risk of bias: medium Notes: the authors conclude that daily use of the SAB instant hand sanitiser with at-will handwashing using soap and water significantly decreased absences due to acute communicable illness. Use of the sanitiser reduced illness absenteeism by 41.9% (reduction in respiratory illnesses of 49.7% over the 10-week period of the study). The authors also described some limitations of the study, as limited so-

Dyer 2000 *(Continued)*

	cio-economic diversity in the study population, limitation to a single study site and lack of blinding. Further soap-and-water washing was not monitored. Generalisability of the results is questionable as all participants underwent the educational programme

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Falsey 1999

Methods	Prospective cohort study conducted at 3 adult daycare centres in Rochester, New York. The study assessed the value of a staff educational programme combined with the use of a portable virucidal hand foam for the reduction of respiratory infections in daycare participants. The authors report in the same paper an ecological study of the incidence of ILI in 3 previous seasons (1992 to 1996) which does not report numerators and denominators and was not extracted
Participants	In December 1995 when the study started there were centre 1: 69 elderly and 36 staff members; centre 2: 67 elderly and 45 staff members; centre 3: 68 elderly and 16 staff members
Interventions	Addition of virucidal hand foam as a supplement versus normal handwashing and educational programme
Outcomes	Laboratory: serological evidence and virology cultures (Table 1 reports a series of isolated pathogens, with no tie in with actual cases) Effectiveness: viral pathogens: influenza A/B, RSV, coronavirus, parainfluenza, rhinovirus Safety: n/a
Notes	Risk of bias: low Notes: the authors conclude that the educational programme for staff was associated with an almost 50% decrease in the infection rate in daycare attendees. The programme was effective only in the last of the 4 years of the programme (rates of infection in daycare patients fell from 14.5 to 10.4 per 100 person-months to 5.7 per 100 person months, $P < 0.001$). This is a conclusion based on an ecological study of the incidence of ILI in 3 previous seasons which the authors report in the same paper, but which does not report numerators and denominators and was not extracted. The lower infection rate is likely to reflect the combination of interventions and education, which increased staff awareness and more broadly changed behaviour. There was no apparent additional benefit from the virucidal foam. This is one of the few identified studies reporting circulating viruses in the daycare setting, both in staff and patients. The decline in influenza-like illness episodes across the 4 study years is reflected in the de-

Falsey 1999 *(Continued)*

	cline in viral isolates, suggesting that aspecific measures such as handwashing are effective against the main respiratory viruses

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Farr 1988a

Methods	The study was a 6-month cluster-randomised, controlled, double-blind trial of the efficacy of virucidal nasal tissues in the prevention of natural cold, and it was conducted in Charlottesville, Virginia, USA. Many of the families were enrolled, because one or more members worked at the State Farm Insurance Company; the remaining families were recruited from the Charlottesville community by advertisement in a local newspaper. Families were randomly assigned by the sponsoring company to receive boxes of treated tissues, placebo tissues or no tissues. The randomisation was performed by computer. Study participants and investigators were unaware of the type of tissues which each family was randomised to receive. Blinding efficacy was tested using a questionnaire: the mothers in each family were asked twice if she believed her family was using virucidal or placebo tissues Participants in the treated and placebo groups were instructed to use only tissues received through the study, while families in the additional control group without tissues were allowed to continue their usual practice of personal hygiene. Each family member kept a daily listing of respiratory symptoms on a record card. A nurse epidemiologist visited each family monthly to encourage recording
Participants	186 families, 58 in the active group, 59 in the placebo group and 69 in the no tissues group. A total of 302 families were originally recruited, 116 families who did not comply with the study protocol, lost their surveillance cards, could not complete the protocol were excluded from the analysis
Interventions	Use of virucidal tissues versus placebo tissues versus no tissues. The treated tissues were impregnated with malic and citric acids and sodium lauryl sulphate, while placebo tissues contained saccharin
Outcomes	Laboratory: serological evidence: no Effectiveness: respiratory illness Safety: n/a
Notes	Notes: the authors conclude that virucidal tissues have only a small impact upon the overall rate of natural acute respiratory illnesses. The total illness rate was lower in families using virucidal tissues than in both of the other 2 study groups, but only the difference between active and placebo groups was statistically significant (3.4 illness per person versus 3.9 for placebo group, P = 0.04 and 3.6 for no tissues control group P = 0.2, and overall 14% to 5% reduction). The questionnaire results suggest that some bias may have been present since a majority of mothers in the virucide group believed they were re-

Farr 1988a *(Continued)*

	ceiving the "active" tissues. Another possible explanation of the low effectiveness of virucidal tissues is poor compliance by children in the use of virucidal tissues. A well-designed and honestly reported study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The randomisation was performed by computer in each trial."
Allocation concealment (selection bias)	Unclear risk	"In trial I, families were randomly assigned by the sponsoring company to receive boxes of treated tissues, placebo tissues or no tissues." "Families with one or two children were randomised in one stratum, and families with three or more children were randomised in a second stratum in trial I." Concealment of allocation not described
Blinding (performance bias and detection bias) All outcomes	Low risk	"Study participants and investigators were unaware of the type of tissues which each family was randomised to receive in both trials. In trial I, the mother in each family was asked twice if she believed her family was using active or placebo tissues, first after three months and then at the end of the study."
Incomplete outcome data (attrition bias) All outcomes	High risk	"A total of 116 of the 302 families were excluded from the analysis. Families were excluded if they lost their surveillance cards or did not conscientiously record data, did not comply with the study protocol, or simply could not complete the protocol for family reasons. It was discovered that families with five or more members had so many colds that it was not possible to distinguish primary and secondary illnesses. These large families were therefore excluded from the analysis in trial I and were excluded from enrolment in trial II."
Selective reporting (reporting bias)	Low risk	All indicated outcomes are reported

Farr 1988b

Methods	The study was a 6-month randomised, controlled, double-blind trial of the efficacy of virucidal nasal tissues in the prevention of natural cold and it was conducted in Charlottesville, Virginia. Families were recruited from the Charlottesville community by advertisement in a local newspaper. Families were randomly assigned by the sponsoring company to receive either virucidal tissues, or placebo-treated tissues. Stratified randomisation was performed by computer and the strata were defined by total number in the family. Study participants and investigators were unaware of the type of tissues which each family was randomised to receive. Each family member kept a daily listing of respiratory symptoms on a record card. A nurse epidemiologist visited each family monthly to encourage recording. In addition a study monitor visited each family bimonthly to further encourage compliance and reporting of symptoms
Participants	98 families, 58 in the active group and 40 in the placebo group. 231 families were initially recruited, 222 completed the trial, data of 98 families were analysed. The others were excluded from the analysis since they complained of side effects (sneezing, etc.) or reported not using the tissues regularly
Interventions	Use of virucidal tissues versus placebo tissues. The treated tissues were impregnated with malic and citric acids and sodium lauryl sulphate, while placebo tissues contained succinic acid. Participants in the treated and placebo groups were instructed to use only tissues received through the study

Farr 1988b *(Continued)*

Outcomes	Laboratory: serological evidence: no Effectiveness: respiratory illness Safety: n/a
Notes	Notes: the study suggests that virucidal tissues have only a small impact upon the overall rate of natural acute respiratory illnesses. The total illness rate was lower in families using virucidal tissues than in the other study group, but the difference between active and placebo groups was not statistically significant. There was a small non-significant drop in illness rates across families (5%). The tissues appeared ineffective as the drop was confined to primary illness unaffected by tissue use. Placebo (succinic acid) was not inert, and it was associated with cough and nasal burning. This impacted on allocation concealment. A well-designed and honestly reported study marred by transparent allocation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The randomisation was performed by computer in each trial."
Allocation concealment (selection bias)	Unclear risk	"In trial II, families were randomly assigned by the sponsor to receive either virucidal tissues or placebo treated tissues." "In trial II, stratified randomisation was again used, but this time the strata were defined by total number in the family (i.e., one stratum for two-member families, another stratum for three-member families, and a final one for four-member families)." Concealment of allocation not described
Blinding (performance bias and detection bias) All outcomes	Low risk	"Study participants and investigators were unaware of the type of tissues which each family was randomised to receive in both trials."
Incomplete outcome data (attrition bias) All outcomes	High risk	"A total of 222 (of 231) families completed trial II; 9 families were terminated early (table 1). In 124 families, one or more family members reported not using the tissues regularly and/or reported having significant side effects. The data from these families were not analysed, leaving 58 families (177 persons) and 40 families (114 persons) for analysis in the virucide and placebo groups, respectively."
Selective reporting (reporting bias)	Low risk	All indicated outcomes are reported

Foo 2006

Methods	Retrospective cohort survey carried out in Singapore to assess the harm associated with the use of the personal protective equipment in healthcare staff working in a “SARS-designated hospital” from March 2003 to middle 2004. Three departments from the hospital were surveyed the National Skin Centre (NSC), Department of Emergency (A&E) and the intensive care unit (ICU) Control group: unclear Control group: none
Participants	340 healthcare staff were surveyed, 322 responded (60 from the NSC, 77 from the TTSH A&E, and 185 from the TTSH ICU)

Foo 2006 *(Continued)*

Interventions	Use of personal protective equipment (PPE), namely, masks, gloves and gowns. Adverse skin reactions to PPE
Outcomes	Laboratory: none Effectiveness: not applicable Safety: adverse skin reactions (ASR) from the use of 3 types of PPE (masks (respirator, surgical or paper masks), plastic gloves and disposable gowns) developed with prolonged use (8.4, 9.4 and 8.8 months, respectively)
Notes	The authors conclude that prolonged use of PPEs (N95 respirators, rubber gloves) is associated with high frequency of ASR. The authors reported that there were no significant differences in adverse skin reactions to masks and gloves due to sex, race or profession. Some differences were reported by age as follows: • Those who developed acne with masks were younger (mean of 29.5 years) compared with those who did not (mean of 33.2; P < 0.001) • Those who developed dry skin with gloves were younger (mean of 28.7 years) compared with those who did not (mean of 33.2; P < 0.002) • Those who developed itch with gloves were younger (mean of 29.5 years) compared with those who did not (mean of 33.2; P < 0.001) Survey results show that acne, itch and rash are the most common harms reported after wearing a N95 respirator (59.6%, 51.4% and 35.8%) and that dry skin, itch and rash were reported by (73.4%, 56.3% and 37.5%, respectively) glove users. Other harms were reported by very small numbers of users (4 or below). This study, although a retrospective survey is important as it suggests that barrier intervention-using carries harms and such harms may affect compliance with the intervention

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Gala 1986

Methods	The purpose of this study was to evaluate whether the use of a disposable plastic goggle designed to cover the eyes and nose could help reduce the rate of nosocomial infections during an outbreak of RSV infection. The rates of RSV infection in staff members and infants were determined on an infant and toddler ward during a seven-week study. Two 3-week study periods were compared: period 1, during which all staff members used the goggles, and period 2, were no goggles were worn. The respiratory infection control procedures were the same during both periods of study: handwashing, isolation and cohorting. In reality although on report, Gala and colleagues are conducting 2 studies. The first is a non-concurrent cohort study, in which 2 different population of children are assessed separated by a

Gala 1986 *(Continued)*

	1-week 'wash-out' period and the intervention (goggles) on staff. The play of confounders here is too heavy and uncontrolled to include the data in the study. The second is a controlled before and after on the 40-odd members of staff (32 of whom took part in both periods). Here the play of confounders should be partly reduced. We extracted data relating to the second study only
Participants	74 children and 40 staff members in period 1; 77 children and 41 staff members in period 2. During the study 151 children were admitted to the ward; their mean age was 12.9 months, 59% were boys. During period 174 infants were examined, 15 were admitted with RSV infections, the remaining 59 constituted the group potentially susceptible to a nosocomial RSV infection. Seventeen infants were hospitalised for sufficient time for a nosocomial infection and in 1 nosocomial RSV infection was detected. During period 277 babies were studied, 17 of whom were admitted with RSV infection. Of the remaining 60, 39 children were excluded, 21 were considered susceptible, and in 9 of them nosocomial RSV infection was detected. Forty staff members were examined in period 1 and 41 during period 2. During period 2, 2 of the ward staff acquired RSV infection and were not considered susceptible
Interventions	Use of a disposable plastic eye-nose goggle and respiratory infection control procedures versus only respiratory infection control procedures (cohorting, isolation and handwashing)
Outcomes	Laboratory: serological evidence Effectiveness: RSV infection (symptoms and laboratory confirmation) Safety: n/a
Notes	Risk of bias: high Notes: the use of the disposable eye-nose goggles appeared to be associated with a significant decrease in nosocomial RSV infections (6% versus 42% of contacts when the goggles were used compared to when they were not). The expense of such goggles will have to be determined and compared with the cost of nosocomial infections. The study has an orgy of confounders, is it difficult to see how such studies can be carried out without disrupting patient care? Why not randomise staff to goggles or standard care?

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Gwaltney 1980

Methods	The study assessed the effectiveness of aqueous iodine applied to the fingers in blocking hand transmission of experimental infection with rhinovirus from one volunteer to another. Healthy, young adult volunteers were recruited from the general population at the University of Virginia, Charlottesville. Volunteers were not informed about the contents of the hand preparation until after the study. Two exper-

Gwaltney 1980 *(Continued)*

	iments were conducted to evaluate the virucidal activity of aqueous iodine applied to the fingers immediately before viral contamination. Another 2 experiments were conducted to determine whether there was sufficient residual activity of aqueous iodine after 2 hours to interrupt viral spread by the hand route. Volunteers who were donors of virus for the hand exposures were challenged intranasally on 3 consecutive days with strain HH rhinovirus. Recipients were randomly assigned to receive iodine or placebo. The donors contaminated their hands with nasal secretions by finger to nose contact before the exposure. Hand contact was made between a donor and a recipient by stroking of the fingers for 10 seconds. Donors and recipients wore masks during the exposure period
Participants	15 and 20 volunteers in 2 experiments
Interventions	Treatment of fingers with iodine versus placebo. The virucidal preparation used was aqueous iodine(2% iodine and 4% potassium iodide). The placebo was an aqueous solution of food colours
Outcomes	Experimental rhinovirus infection reduced (P = 0.06) Laboratory: serological evidence Effectiveness: rhinovirus infection (based on serology, isolation and clinical symptoms) with high score clinical illness. Score was published elsewhere Safety: N/A
Notes	Risk of bias: high (poor description of randomisation process, concealment, or allocation) Notes: the study suggests that aqueous iodine applied to the fingers was effective in blocking transmission by hand contact of experimental infection with rhinovirus for up to 2 hours after application (1 out 10 volunteers were infected compared to 6 out of 10 in the placebo preparation arm, P = 0.06 with Fisher's exact test). The effectiveness of iodine treatment of the fingers in interrupting viral transmission in volunteers recommends its use for attempting to block transmission of rhinovirus under natural conditions. Although the cosmetic properties of 2% aqueous iodine make it impractical for routine use, it can be used as an epidemiologic tool to study the importance of the hand transmission route and to develop an effective cosmetically acceptable hand preparation. A summarily reported study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Hall 1981a

Methods	Cohort study to determine the possible modes of spread a RSV to young adult volunteers working on a paediatric ward who were exposed in different manners to infants with RSV. Volunteers were divided into 3 groups: "cuddlers", exposed to an infected infant over 2 to 4 hours by caring for the baby in the usual manner, wearing gowns, but no mask or gloves; "touchers", exposed with the infant out of the

Hall 1981a *(Continued)*

	room by touching surfaces contaminated with the baby's secretions; "sitters", exposed to an infected baby by sitting at a distance of more than 6 feet from an infant's bed, and they wore gowns and gloves, but no masks. In order to control for possible differences in infectivity among infants, a volunteer from each of the 3 groups was exposed to each infant, or to this environment in the case of touchers. In addition, volunteers from each group were exposed to more than one infant. After exposure volunteers were followed for 12 days
Participants	31 volunteers: 7 in the cuddler group, 10 in toucher group and 14 in the sitter group
Interventions	Exposure to infants admitted with bronchiolitis or pneumonia during a community outbreak of RSV isolation
Outcomes	Laboratory: serological evidence Effectiveness: RSV infection demonstrated by viral isolation and serology. Clinical symptom diary collected with questionnaires. Symptomatic, asymptomatic and febrile symptomatic data reported separately Safety: n/a
Notes	Risk of bias: low Notes: the authors concluded that the spread of RSV may occur by close contact with direct inoculation of large droplets or by self-inoculation after touching contaminated surfaces. Infection does not appear to occur after more distant contact requiring small particle aerosols (0 infected out of 14 "sitters", those that sat away from RSV infected infants, compared with 5 out of 7 who cuddled and 4 out of 10 who touched the infected infants). Ancillary procedures that may be helpful include the care of contaminated surfaces and gowns, cohorting of staff and infants, and limiting the traffic in and out of the infants' room. With limited facilities, isolation rooms might best be reserved for uninfected infants with underlying disease who, should they acquire nosocomial RSV infection, are at risk for severe disease

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Hall 1981b

Methods	Controlled before and after study designed to evaluate the efficacy of infection-control procedures with the use of masks and gowns compared with procedures not using mask and gowns on the rate of nosocomial RSV infection in both infants and staff. The study, conducted at Strong Memorial Hospital in Rochester, NY, USA, in 1979, was begun 12 days after the hospital admission of the first infant infected by RSV, and was continued for the next 2 months. All patients and staff on the ward for children less than 3 years of age were included. During the first 4 weeks (period 1) of the study the infection-control

Hall 1981b *(Continued)*

	procedures for infants with respiratory illness included handwashing and the use of mask and gowns by the staff on entering the room, with a change of gowns between contacts with each infant. After 4 weeks the wearing of gowns and masks was discontinued and handwashing alone was used for the final 5 weeks of the study. Throughout the study handwashing, cohorting and isolation were employed and emphasised. The number of nosocomial infections in patients and staff for period 1 were compared with the period 2 (last 4 weeks of the study). Infections that occurred in the interval week were not counted
Participants	162 patients suspected with RSV infections from infected infants; 78 admitted in the period 1 and 84 in period 2. The age range was 2 weeks to 3 years. 55% were male. Of 78 (period 1), 24 were admitted for RSV infections and the remaining 24 became the contacts. (Due to lack of comparability of children and an unclear text children data were not extracted) 39 ward personnel were included, 30 in the period 1 and 27 of these were also studied during period 2 along with 9 other personnel. Thus a total of 36 staff members were studied during period 2
Interventions	Use of gowns and masks and standard infection-control procedures (handwashing, cohorting, isolation) versus standard infection-control procedures only to prevent transmission of RSV infections from infected infants
Outcomes	Laboratory: serological evidence Effectiveness: RSV infection demonstrated by symptoms, viral isolation and serology Safety: n/a
Notes	Risk of bias: high Notes: the authors concluded that the use of masks and gowns as additional infection-control procedures for RSV infection shows no appreciable benefit in preventing nosocomial spread of RSV to infants or to the ward personnel. The nosocomial infection rate in the 2 periods was not significantly different in either the infants or staff (32% infection versus 41%). Both of the study periods appeared to be equal in terms of potential for transmission or exposure to RSV. The number of infants admitted during both periods was similar. Furthermore these 2 groups of contacts were alike in age and types of underlying diseases. The routine use of masks and gowns does not seem warranted in view of the considerable cost. A very poorly reported study with an unclear eligibility procedure and a lack of description of denominators. Why not use randomisation?

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Heymann 2004

Methods	Controlled before and after study to evaluate the effect of school closure on the occurrence of respiratory infection among children ages 6 to 12 years and its impact on healthcare services. The study was conducted in Maccabi healthcare services, which has a nationwide network of > 3000 independent physicians connected by a unified computer system. The authors assembled a retrospective cohort of all 6 to 12 year old children comprising 186,094 children. The computerised data were examined for three 2-week periods: before school closure, during closure and after closure. The occurrence of respiratory tract infections was determined according to recorded diagnoses, including cough, upper respiratory tract infection, common cold, sore throat and viral infection
Participants	186,094 children aged 6 to 12 years
Interventions	Effect of a school closure on the occurrence of respiratory infection during an "influenza" outbreak
Outcomes	Laboratory: no Effectiveness: respiratory tract infections Safety: n/a
Notes	Risk of bias: high Notes: the authors concluded that school closure was temporally associated with 42% decreased morbidity from respiratory tract infections, a consequent 28% decrease in visits to physicians and to emergency departments and a 35% reduction in purchase of medications. Limits of this study are: the fact that in Israel 33.8% of the population are children, hence these results may not be applicable to high-income countries with lower percentage of children. In addition there may be a difference in parental attitudes toward respiratory illness symptoms in other cultures that affect health care utilisation. Another reason for such a difference may be the basic structure of the health system in Israel, where comprehensive health insurance is universal and provided by the law. Finally there is limited availability of over-the-counter medications, and to obtain symptomatic therapeutic agents children are generally seen by a physician. The biggest limit to this study is not mentioned by the authors: the assumption that the circulation of respiratory viruses is constant throughout the study period. Although in the Discussion the authors mention some surveillance data on national diffusion of an H3N2 epidemic but this took place in December 1999 Observed effects may be due to school closure or they may be due to lower circulation of the viruses

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Isaacs 1991

Methods	Retrospective and prospective cohort study was conducted to evaluate the effectiveness of cohorting and educational programme (handwashing) in reducing the incidence of nosocomial respiratory syncytial virus infections Data on all children with RSV infection on any of the paediatric wards in winter of 1986 to 1987 were retrospectively collected. In order to define the population at risk of developing RSV infection it was determined the number of children under 2 years of age hospitalised on the 2 paediatric wards and the paediatric intensive care unit and the number they spent in hospital. For the next 2 winters (1987 to 1988 and 1988 to 1989) the same data were prospectively collected. In addition some interventions were made to try to reduce the incidence of hospital-acquired RSV infection. Children admitted with suspected RSV infection were nursed in a specific area until the result of an indirect immunofluorescent test. It was not possible to cohort babies on the paediatric intensive care unit. Staff were instructed on the importance of handwashing and this was reinforced on ward rounds. An educational leaflet was prepared and given to the parents of every child admitted with the infection
Participants	Children < 2 years of age: 425 in period 1; 840 in period 2; 552 in period 3
Interventions	Isolation and handwashing versus normal care
Outcomes	Laboratory: indirect immunofluorescence on nasopharyngeal secretions or by culture of secretions Effectiveness: RSV infection Safety: n/a
Notes	Risk of bias: high (poor descriptions) Notes: the authors concluded that handwashing and cohorting reduced at least 66% in the number of hospital acquired infections due to RSV in the 2 intervention winters. One minor problem with cohorting was that babies could not remain in the accident and emergency department until a diagnosis of RSV was virologically confirmed. Hence they were cohorted on the basis of a clinical diagnosis of bronchiolitis. The authors also underline the importance of a more rapid antigen test for RSV. It is doubtful whether the non-exposed cohort is similar to its hospital peers, especially because there are several cardiac children in the exposed cohort. The biggest limit to this study is mentioned by the authors in the Discussion: the assumption that the circulation of RSV is constant throughout the study period. Exposure however is not the same in the 3 seasons and observed effect may be due to cohorting or to the different viral circulation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Jacobs 2009

Methods	Open randomised controlled trial lasting 77 days from January 2008 to test "superiority" of face masks in preventing URTI. This term appears as an acronym in the introduction and is not explained. It is assumed it stands for "upper respiratory infections" but it is preceded in the text by the term "common cold" which is also lacking a definition. Randomisation was carried out in blocks within each of 3 professional figures (physicians, nurses and "co-medical" personnel)
Participants	33 HCWs mainly females aged around 34 to 37 in a tertiary healthcare hospital in Tokyo, Japan. HCW with "predisposing conditions" (undefined) to "URTI" and those taking antibiotics were excluded A baseline descriptive survey was carried out including "quality of life" 1 participant dropped out at end of week 1 but no reason is reported nor the allocation arm
Interventions	Surgical mask MA-3 (Osu Sangyo, Japan) during all phases of hospital work (n = 17) or no mask (n = 15) (except when specifically required by hospital SOPs)
Outcomes	Laboratory; n/a Effectiveness: URTI is defined on the basis of a symptoms score with a score >14 being a URTI according to Jackson's 1958 criteria ("Jackson score"). These are not explained in text although the symptoms are listed in Table 3 (any, sore throat, runny nose, stuffy nose, sneeze, cough, headache, ear ache, feel bad) together with their mean and scores SD by intervention arm Safety: the text does not mention or report harms. These appear to be indistinguishable from URTI symptoms (e.g. headache which is reported as of significantly longer duration in the intervention arm). Compliance is self-reported as high (84.3% of participants)
Notes	The authors conclude that "Face mask use in healthcare workers has not been demonstrated to provide benefit in terms of cold symptoms or getting colds. A larger study is needed to definitively establish non-inferiority of no mask use" This is a small, badly reported trial. The purpose of trials is to test hypotheses not to prove or disprove "superiority" of interventions. There is no power calculation and CIs are not reported (although there is a mention in Discussion). No accurate definitions of a series of important variables (e.g. URTI, runny nose etc.) are reported and the Jackson scores are not explained, nor their use in Japanese personnel or language validated Intervention arm data not extracted because of the uncertainty of its meaning

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Open randomised controlled trial, but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	"Mask and no mask groups were formed using block randomisation of subjects within their respective job categories: nurses, doctors, and co-medical personnel." Concealment of allocation not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible (mask wearing or not)
Incomplete outcome data (attrition bias) All outcomes	Low risk	One dropout in each group accounted for. "Analyses were performed following the principles of intention-to-treat."

Jacobs 2009 *(Continued)*

Selective reporting (reporting bias)	High risk	NB: influenza vaccine coverage in mask group was 100% and only 81% in the non-mask wearing group

Kimel 1996

Methods	Prospective cohort study conducted in a school of Chicago, USA, to evaluate the effectiveness of a handwashing programme in reducing the absenteeism caused by flu-like illness. The school was located in a predominantly white, middle to upper middle class suburb. All 4 kindergarten and 5 first-grade classes were included in the study. No significant differences were found between participating classes for size, male-female ratio, percentage of low-income students, or students with chronic health problems. Teachers were surveyed to determine classroom handwashing activities. The influenza season usually occurs during December and January. The handwashing programme was planned for presentation just prior to this time. The effectiveness of the programme was determined by comparing absentee rates among participants and non-participating classes (the control group). Absentee rates were determined by reviewing the computerised daily school absence logs. Entries that listed flu-like symptoms were counted. A take-home handwashing chart was also given to each student to encourage follow-through with handwashing at home
Participants	199 children of kindergarten and first grade schools
Interventions	Handwashing and educational programme versus no intervention
Outcomes	Laboratory: no Effectiveness: flu-like illness Safety: n/a Absenteeism from influenza-like illness was approximately double in the control arm (P = 0.01)
Notes	Risk of bias: medium Notes: the authors concluded that handwashing education can decrease absenteeism even among kindergarten and first grade students. This study did not control for health and hygiene practices at home or exposure to ILI outside of school. Furthermore the student population at the school was generally healthy, probably because families were able to provide adequate health and hygiene resources. Another problem of the study is that the flu season was later than usual (February), and this represented a confounding variable. The teacher surveys indicated problems with handwashing facilities

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Kotch 1994

Methods	Pair-matched cluster-randomised, controlled trial conducted in the period 19 October 1988 to 23 May 1989 in 24 childcare centres in North Carolina, USA. The trial tested the effects of a handwashing and environment sterilising programme on diarrhoea (data not extracted) and ARIs. Child daycare centres had to care for 30 children or less, at least 5 of whom had to be in nappies and intending to stay open for at least another 2 years. Randomisation is not described, nor are cluster coefficients reported
Participants	389 children aged 3 years or less in daycare for at least 20 hours a week. There were some withdrawals but the attrition on participants is not stated, only that in the end data for 31 intervention classrooms and 36 control classrooms were available. There were 291 children aged up to 24 months and 80 over 24 months that took part. The text is very confusing as 371 seem to be the total of the number of families that took part. No denominator breakdown by arm is reported and numerators are only reported as new episodes per child-year
Interventions	Structured handwashing and environment (including surfaces, sinks, toilets and toys) disinfecting programme with waterless disinfectant scrub
Outcomes	Laboratory: N/A Effectiveness: ARI (coughing, runny nose, wheezing, sore throat or earache) Safety: N/A
Notes	Risk of bias: high (poor reporting of randomisation; outcomes; numerators and denominators) Notes: the authors conclude that the fully adjusted RR for prevention of ARIs was 0.94 (-2.43 to 0.66). A poorly reported study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Pair-matched cluster-randomised, controlled trial', but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Centres were matched in pairs and then randomly allocated to either intervention or control programmes. Allocation concealment not reported.
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible (intervention was training session)
Incomplete outcome data (attrition bias) All outcomes	High risk	18 families were dropped, denominator not clear
Selective reporting (reporting bias)	High risk	Denominators not clearly reported

Krasinski 1990

Methods	Controlled before and after study conducted in Bellevue Hospital Center, New York, USA, to determine the effectiveness of screening for RSV and assignment to a cohort at admission to reduce nosocomial transmission of RSV infections. Children who were 3 years of age and older were admitted to a paediatric ward that is equipped with private rooms for the control of communicable diseases. Children younger than 3 years of age were admitted to a separate ward without private rooms, where as many as 4 children shared a room. All paediatric patients hospitalised on or before 31 December 1986 were

Krasinski 1990 *(Continued)*

	regarded as potentially infected with RSV and were constituted as an RSV-infected cohort. A second cohort, free of infection with RSV, was established on the toddlers' ward to segregate high-risk patients from RSV-infected patients. Patients requiring hospital admission and assignment to the high-risk cohort were screened for evidence of RSV infection by means of a rapid ELISA method. No gloves or masks were used in the RSV cohort
Participants	All hospitalised paediatric patients regarded as potentially infected with RSV
Interventions	RSV screening cohorting and service education programme versus do nothing
Outcomes	The authors concluded that screening and subsequent cohorting reduced RSV infections (from 5.33 infections per 1000/patient days of care to 1.23 infections per 1000/patient days after introduction of screening). There was an attempt at correlation between RSV admissions and RSV community circulation
Notes	Risk of bias: medium Notes: the authors concluded that screening and subsequent cohorting reduced RSV infections (from 5.33 infections per 1000/patient days of care to 1.23 infections per 1000/patient days after introduction of screening). There was an attempt at correlation between RSV admissions and RSV community circulation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Krilov 1996

Methods	Controlled before and after study carried out in a 16 classrooms of special needs school for Down Syndrome children in New York State. The study took place between November 1991 and November 1993. The 'before' period between November 1991 and October 1992, followed by a 1-month washout period during which the intervention was introduced, followed by 12 months of 'after' period (December 1992 to November 1993)
Participants	33 children aged 6 weeks to 5 years took part in the 'before' and 38 in year 2 ('after' period). During the study period there were about 110 children in the school but the parents of the majority did not agree to replying to 2-weekly questionnaires, so their children were not entered in the study. In addition 5 sets of questionnaires in the 'before' and 2 in the 'after' periods did not contain sufficient data (6 months' worth) and were excluded. Despite this there were no significant differences between 'before' and 'after' children. The authors also describe viral circulation during the study periods from isolates in

Krilov 1996 *(Continued)*

	the local hospital. All community isolates were constant with the exception of adenovirus which doubled in the 'after' period of the study
Interventions	Training and sanitary programme with handwashing, disinfection of school buses, appliances and toys. In addition a person designated a study monitor carried out intensive monitoring of classroom behaviour and reinforced messages. Disinfection took place with Reckitt & Colman products (sponsors of the study)
Outcomes	Laboratory: viral isolates from surrounding community (non-random samples) Effectiveness: ARI (cough, runny nose, sore throat, wheezing or rattling in the chest, ear ache). Vomiting and diarrhoea (data not extracted). Follow up was carried out on the basis of parents' questionnaire Safety: N/A
Notes	Risk of bias: high (disinfectants provided and study sponsored by manufacturer) Notes: the authors concluded that respiratory illnesses decreased from a median of 0.67 to 0.42 per child per month (P < 0.07), physician visits, 0.50 versus 0.33 (P < 0.05), mean course of antibiotics prescribed 0.33 versus 0.28 (P < 0.05) and days of school missed because of respiratory infections 0.75 versus 0.40 (P < 0.05). Respiratory illnesses decreased from a median of 0.67 to 0.42 per child per month. Small study with a serious selection bias and generalisability problems

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Ladegaard 1999

Methods	RCT with cluster-randomisation to intervention or control. Out of 10 institutions they excluded 2 because they wanted institutions to be comparable in uptake area (that means housing and income). Interventions were given to children, parents and teachers at the institutions
Participants	Children 0 to 6 years old
Interventions	Multifaceted: information, t-shirts to the children with: "Clean hands - yes, thank you", performance of a fairytale "The princess who did not want to wash her hands", exercise in handwashing, importance of clean and fresh air. The aims of the intervention were: - to increase the hygiene education of the daycare teachers - to motivate the children by practical learning to have a better hand hygiene - to inform the parents about better hand hygiene

Ladegaard 1999 *(Continued)*

Outcomes	34% decrease in 'sickness' (probably mostly gastroenteritis)
Notes	Risk of bias: limited data only available Notes: the authors conclude that there was a 34% decrease in sickness in the intervention arm, this is probably overall sickness as gastroenteritis is part of the outcomes (data no extracted). Limited data only available from translation by Jørgen Lous

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Randomisation by "lottery", the same as "flip the coin" Concealment not reported
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	High risk	No total numbers of children included in each arm reported
Selective reporting (reporting bias)	High risk	Limited data reported, especially denominators missing

Larson 2010

Methods	Cluster block-randomised, controlled trial carried out between 20 November 2006 and 20 June 2008 in an upper Manhattan immigrant Latino neighbourhood ("19 month data collection period"). The study aimed at assessing the effects of eduction versus education and hand sanitiser use versus education and hand sanitiser use and common mask use against upper respiratory infections over a period of under 2 years. Follow up was though an automated telephone system with a small financial incentive (USD 20) for those with 75% or more compliance. Those reporting an ILI received a visit within 48 hours for swabbing An index case was someone who at the "onset day of illness nobody else in the household had been symptomatic within the previous five days" A secondary case for each episode "was any member of the household who developed symptoms within five days following the index case", "The secondary attack rate was defined as the number of secondary cases recorded within 5 days of the onset of symptoms in the index case divided by the number of household members minus one" The text implies that the unit of observation was the episode ("study subjects contributed more than one episode in which they were considered to be the index case")
Participants	Recruitment and allocation were carried out by household. These had to have at least 3 people living in the household, with at least 1 being a preschool or elementary school child, speaking English or Spanish, having a telephone willingness to complete symptom assessments and having bimonthly home visits and not using alcohol-based hand sanitiser routinely 617 households were randomised, 211 to the education, 205 to the hand sanitiser and 201 to the hand sanitiser and mask groups. The participants were 2708, mostly adult Latino immigrants to the USA

Larson 2010 *(Continued)*

	Intracluster correlation coefficients are reported on page 179 of the manuscript
Interventions	Written Spanish or English language educational materials regarding the prevention and treatment of URTIs and influenza or the same educational materials and hand sanitiser (Purell, J&J), in large (8- and 4-ounce) and small (1-ounce) containers to be carried by individual household members to work or school or the same interventions as well as regular surgical face masks (Procedure Face Masks for adults and children, Kimberly-Clark) with instructions for both the caretaker and the ill person to wear them when an ILI occurred in any household member. Replenishment of intervention stocks was done at the bimonthly home visit Caretakers had to wear a mask for 7 days when within 3 feet of a symptomatic case. These were also encouraged to wear masks within 3 feet of any household member. Reinforcing phone calls were made 3 times in 6 days The text clearly reports active influenza vaccine promotion during the bi-monthly visits (“The home visit to each household was made every 2 months to minimise study dropout, reinforce adherence to the assigned intervention, replenish product supplies and record use of supplies, answer questions, and correct ongoing misconceptions. At each visit, new educational materials regarding URTI prevention and treatment and influenza vaccination were distributed.” (PDF page 3). Also just before the Discussion as follows: “Influenza vaccination rates: There was an increase between the baseline and exit interview in all three groups that reported 50% of more of members receiving influenza vaccine (pre- versus post-intervention for each group: 21.1% and 40.8% in the Education group, 19.0% and 57.1% in the hand sanitiser group, and 22.4% and 43.5% in the hand sanitiser and face mask group (P = 0.001). Additionally, those in the hand sanitiser group reported a significantly greater increase than the other 2 groups, controlling for baseline rates (P = 0.002)” Coverage was unequal across groups, no information on the progressive impact of the vaccine, or indeed the nature of the vaccine(s) is reported. Apparently the first season was mild and the vaccine mismatched, compliance with the trial interventions was low in Arm 3 and a local epidemic of *S. aureus* meant that the control group started washing hands The authors report no effect on reporting rates of vaccine coverage by arms but with so many confounders who knows?
Outcomes	Laboratory: PCR carried out on samples from deep nasal swabs for influenza and the most common other pathogens (RSV, rhinovirus, enterovirus, parainfluenza viruses etc.). The text describing the results of the swabbing is confusing but in general appears to be non-random “Households reported 669 episodes of ILI (0 to 5 per individual)". Of the 234 deep nasal swabs obtained, 33.3% (n = 78) tested positive for influenza; 43.6% (n = 34) were influenza A and 56.4% (n = 44) were influenza B. Among the 66.7% who tested negative for influenza, 30.8% (48/156) tested positive for other viruses: 7 for respiratory syncytial virus, 9 for parainfluenza, 11 for enterovirus, 10 for rhinovirus, 6 for adenovirus, and 5 for metapneumovirus. Swabs were not obtained from the remaining 435 reported ILI episodes for the following reasons: 72.0% (n = 313) did not meet the CDC definition of an ILI and were therefore included in the URTI symptom count, 21.4% of episodes (n = 93) were reported after 48 hours of ILI onset or the participant refused to be swabbed, and the research staff were unable to reach the participant in 6.7% of episodes (n = 29) As no definition of URTI is given it is unclear what kind of biases are introduced by the non-swabbing of the 313/435 “not meeting CDC definition”. Effectiveness: ILI (CDC definition): “temperature of 37.8°C or more and cough and/or sore throat in the absence of a known cause other than influenza” URTI only referred to as “Viral upper respiratory infections (URTIs)” Safety: N/A
Notes	The authors conclude that “the Hand Sanitizer group was significantly more likely to report that no household member had symptoms (P,0.01), but there were no significant differences in rates of infection by intervention group in multivariate analyses. Knowledge improved significantly more in the Hand Sanitizer group (P,0.0001). The proportion of households that reported >50% of members receiving influenza vaccine increased during the study (P,0.001). Despite the fact that compliance with mask wearing was poor, mask wearing as well as increased crowding, lower education levels of caretakers,

Larson 2010 *(Continued)*

and index cases 0–5 years of age (compared with adults) were associated with significantly lower secondary transmission rates (all P,0.02). In this population, there was no detectable additional benefit of hand sanitiser or face masks over targeted education on overall rates of URTIs, but mask wearing was associated with reduced secondary transmission and should be encouraged during outbreak situations. During the study period, community concern about methicillin-resistant *Staphylococcus aureus* was occurring, perhaps contributing to the use of hand sanitiser in the Education control group, and diluting the intervention's measurable impact".

The study is at high risk of bias. Randomisation and reasons for dropout are not described. Differentials in cluster characteristics across arms point to randomisation not having worked and the confounding effects of a post-randomisation staphylococcal scare is difficult to judge. Symptom-driven follow up gives no idea of the effects on asymptomatic ILI/influenza. Poor definitions (URTI?). There are unexplained dropouts and the analysis plan is unclear. Finally the very small number of cases of influenza and an unclear swabbing attrition may introduce further elements of confounding

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Cluster block randomised, controlled trial", but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	"Households were block randomised into one of three groups:" Allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	High risk	In 211 control group HH 26 dropped out and 37 did not consent In 205 hand sanitiser group HH 21 dropped out and 36 did not consent In 201 hand sanitiser and face mask group HH 19 dropped out and 35 did not consent Reasons for dropout not described
Selective reporting (reporting bias)	Unclear risk	617 of 772 eligible households were randomised HH in groups comparable

Lau 2004a

Methods	Case-control study carried out in Hong Kong, SARS of China during 4 April to 10 June 2003, at the height of the SARS outbreak. The aim was to describe the defined and undefined sources of SARS cases groups and assess the protective effects of various public health measures Defined sources were classified as being a healthcare worker in a hospital, living in Amoy Gardens (a known focus of infection) having had a contact with a member of the household with SARS of earlier onset, hospital in patients infected with SARS by other hospital inpatients and contacts of SARS cases before the onset of their own symptoms The undefined sources group of cases were all the other categories Cases in general were identified and interviewed on the phone. Households with more than 1 index case were considered as having 2 index cases. Of the 1690 identified cases, 1214 from 996 households were enrolled in the study. 140 cases could not be contacted as they had a wrong phone number, 163 were uncontactable after at least 5 attempts, 163 refused to take part and 10 did not speak either Chinese or English. 17 were further excluded because they were aged less than 16. 22 questionnaires were

Lau 2004a *(Continued)*

	unusable. (This makes 1175, obviously the 17 minors are included in the case-control study, as adding them makes a total of 1192)
Participants	Description of cases: 330 probable cases of SARS selected as follows. From 1192 people with probable SARS reported to the Department of Health in the territory of HK up to 16 May 2003, 1175 were entered in the case-control analysis. SARS cases were defined as Xray evidence of pulmonary infiltration consistent with pneumonia with a temperature of > 38°C or a history of such in the previous 2 days and at least 2 of the following: history of chills in the previous 2 days new or increased cough, breathing difficulty, general malaise of myalgia, typical signs of consolidation and known exposure to SARS. The authors say that this definition is the same the WHO's case definition of probable SARS. At interview, risk factors were elicited and identified. There were 727 cases in the defined source category and 347 in the undefined sources category (330 after exclusion of 17 minors) Description of controls: 660 controls of undefined origin and with no description of selection
Interventions	Natural exposure to SARS during a serious epidemic
Outcomes	Community transmission of SARS reduced OR 0.30 (95% CI 0.23 to 0.39)
Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls) Notes: the authors conclude that community transmission was of less importance than previously thought and public health measures worked. The following risk factors were significantly associated with SARS (matched multivariate analysis OR with 95% CIs): - Visit to mainland China 1.95 (1.11 to 3.42) - Visited Prince of Wales Hospital 7.07 (1.62 to 30.75) - Visited other hospitals 3.70 (2.54 to 5.39) - Visited Amoy Gardens 7.63 (3.77 to 15.43) The following activities/interventions had a significant protective function: - Thorough disinfection of living quarters 0.41 (0.29 to 0.58) - Wore a mask in public places frequently 0.36 (0.25 to 0.52) - Washed hands 11 or more times a day 0.58 (0.38 to 0.87) Potentially a very interesting study possibly rigorously conducted let down by a very confusingly written text. The biggest problem is lack of clarity as to who the controls were. This may be a reflection of the pressure of carrying out a study in the midst of a serious epidemic

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Leclair 1987

Methods	Controlled before and after study conducted in children's hospital of Boston, USA, to determine whether increased compliance with a policy of glove and gown isolation precautions could reduce the high rate of nosocomial RSV infection on an infant and toddler ward. All patients admitted to the 28-bed infant and toddler medical ward during 3 consecutive RSV seasons (1982 to 1985) were included in the study. When patients with known or suspected RSV infection were admitted, an attempt was made to place them in single rooms or to group them together, but infected patients were frequently required to share rooms with susceptible patients during the winter months, when the prevalence of RSV on the wards is highest. The RSV season was defined as the 24 weeks each year starting at the beginning of November and continuing through the end of April. All the documented cases of RSV infection occurred during that period, and all the patients and patient-days during that interval on the study ward were recorded. RSV infections were classified as nosocomial if symptoms developed 5 or more days after the patient's admission to the hospital. All cases of RSV infection were confirmed virologically. During the first half of the study nursing staff wore both gloves and gowns for only 20 of 52 observed contacts. During and after the second compliance survey, compliance rapidly increased: nursing staff wore both gloves and gowns for 73 of 90 of their contacts
Participants	695 patients aged from 5 days to 4 years and 11 months. The distribution of ages was similar in the 2 periods. 37 acquired nosocomial RSV infections
Interventions	Infection-control intervention to increase use of gloves and gowns versus no intervention
Outcomes	Laboratory: yes Effectiveness: RSV infection Safety: N/A
Notes	Risk of bias: low Notes: the authors concluded that the incidence of nosocomial RSV infection rose with the intensity of hospital exposure and that this rise was markedly different in the periods before and after intervention. The use of gloves and gowns can reduce the nosocomial transmission of RSV, particularly with increasing exposure to patients shedding the virus (RR for pre and post-intervention periods infection rates 2.9, 1.5 to 5.7). Compliance by the staff improved dramatically after the intervention and it continued even after the end of the study, probably because the favourable results of the intervention were well-publicised, the head nurse introduced an educational programme emphasising the appropriate application of isolation precautions, and gowns and gloves became more accessible to care givers. The study, although prone to selection bias, is better designed than some of it peers as there is an attempt at adjusting for different levels of RSV circulation by sub-analysis by virus shedding days by the infected participants

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Leung 2004

Methods	Prospective cohort study conducted during 13 March to 29 June 2003 in the paediatric department of the Prince of Wales Hospital at the height of the SARS epidemic in Hong Kong, China. The aim of the study was to test the effectiveness of procedures to stop transmission of SARS from infected children to carers and visitors
Participants	26 HCWs in close contact with probable or suspected SARS and 88 HCWs in contact with patients in other study areas during the study period
Interventions	Triage and UHR-S isolation and strict infection control procedures versus triage and UHR-S isolation and less strict infection control procedures Healthcare workers were exposed to 9 children with probable SARS and 29 with suspected SARS admitted into the Ultra High Risk SARS (UHR-S) areas with a mean age of 8.9 years, 88 children with pneumonia but no SARS contact with a mean age of 8.2 admitted to the isolation cubicle of the Ultra High Risk Infection (UHR-I) area, 227 with febrile illness and normal chest radiograph aged 4.9 years treated in an open cubicle in the UHR-I area and 274 non-febrile children with a mean age of 7.5 years admitted into the High Risk (HR) area. The study tested the effectiveness of triage and UHR-S isolation + strict infection control procedures versus triage and UHR-S isolation + less strict infection control procedures Triage at admission aimed at identifying children aged less than 18 who: - were febrile or afebrile with a known SARS contact who were admitted to the UHR-S area - with a positive CXR and a SARS contact who were admitted to the UHR-S area - with CXR changes but no SARS contact who were admitted to the UHR-I area - were febrile or afebrile but no SARS contact who were admitted to the HR area Very strict infection control measures were implemented on entry and exit from the UHR-S area (handwashing, gown, caps, goggles, mask, upper and trousers of cloth operating theatre garments and N95 face respirator for HCWs, all measures but no goggles or undergarments for visitors and handwashing and mask for patients) Less strict infection control measures were implemented on entry and exit from the UHR-I area (handwashing, gown, goggles, mask, upper and trousers of cloth operating theatre garments and N95 face respirator for HCWs, and handwashing and mask for visitors and patients), Even less strict infection control measures were implemented on entry and exit from the HR area (handwashing, gown, caps, goggles, mask, upper and trousers of cloth operating theatre garments and mask of N95 face respirator for HCWs and handwashing and paper mask for visitors and patients) Enforcement was directed by a police nurse in the UHR areas
Outcomes	Laboratory: laboratory confirmation of SARS Effectiveness: probable or suspected SARS according to WHO definitions Safety: N/A
Notes	Risk of bias: low Note: the authors conclude that the measures worked well as no HCW or visitor became ill. This is a remarkably well-conducted and clearly reported study in the midst of a major infectious disease outbreak with a previously unknown agent. The Prince of Wales Hospital had previously witnessed an outbreak in which an index patient had infected 138 healthcare workers. All the more remarkable as the paediatric department had not been built as isolation facility and had to be rapidly reorganised

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A

Leung 2004 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Liu 2009

Methods	The paper is a re-analysis and publication in English of Ma 2004, a case-control study carried out shortly after the SARS outbreak at the Armed Forces Hospital (AFH) in Beijing in which 16 HCW died. The data from Ma 2004 had been published in Chinese only. The paper assesses relationships between protective and risk factors in cases and controls using a 2-step analysis procedure: univariate analysis and then multivariate analysis for those associations found significant up to the 10% level
Participants	Description of cases - 51 HCW (age mean 29.5 years) who were admitted to AFH during 5 March to 17 May 2003 with clinical features fitting WHO's SARS criteria. All enrolled analysed cases subsequently proved to be IgG SARS positive (1 case was excluded because he/she was negative). Probable cases of SARS are defined as: documented fever (temperature > 38°C), presence of cough, shortness of breath or breathing difficulty, and a significant history of exposure to a SARS patient not more than 10 days prior to onset of symptoms, plus radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR) (World Health Organization criteria, 2003). The text mentions that cases were 76% (51 of the 67) "survived" staff in the AFH Description of controls; 426 HCW (age mean 31.4 years) working in AFH during the same period as cases with self-reported exposure to SARS but had no symptoms (the text says "uninfected"). All enrolled analysed controls subsequently proved to be IgG SARS negative and their exposure within 1 month of a SARS case was confirmed. These are 90% of AFH employees exposed to SARS.
Interventions	Exposure and risk or protective factors were subsequently elicited by questionnaire and interviews in June to July 2003: gender, age, ethnic group, educational level, co-morbidity, smoking status, alcohol intake, contact date, occupation, department, contacts with SARS and exposure time. None of these factors proved to be significant in a multivariate analysis. At univariate analysis 17 variables were significantly associated with SARS, 10 of which were protective (i.e. negative association): - wearing a 12-layer cotton surgical mask - wearing 16-layer cotton surgical mask (and wearing layers of mask) - wearing glasses - wearing gloves - wearing goggles - wearing multiple layers of protective clothing - taking "prophylactic medicine" (such as "antivirals" and vitamin supplements), performing nose washes after contact and having training prior to exposure N95 mask use was non-significant probably because of the rarity of its use At multivariate analysis level, 12 and 16-layer mask non-use and not undergoing training, not taking medicine and not wearing multiple layers of masks were found to be associated with SARS onset
Outcomes	Laboratory: all clinically diagnosed hospital-acquired SARS cases confirmed by + SARS-CoV IgG ELISA and all controls confirmed by a - SARS-CoV IgG ELISA Effectiveness: univariate and multivariate analysis among the 28 variables elicited in questionnaires and by interview

Liu 2009 *(Continued)*

Notes	The authors conclude that "this study identified exposure to high-risk procedures (such as chest compression), and contact with respiratory secretions to be significant risk factors for SARS infection among HCWs in a hospital in Beijing. These results also provide confirmation that personal protective measures against droplet spread, such as wearing multiple layers of mask, are effective against the nosocomial spread of SARS" The main points to bear in mind when interpreting this study are: - the possibility of selection bias in cases (only living cases were recruited whereas we know that 16 HCWs in AFH died) - protective variables are not well-defined (i.e. the make or type of masks used, whether fitted or not) - information on the 10 protective interventions (variables) was elicited post hoc with a possibility of recall bias (mentioned by the authors in their Discussion) - the lack of reporting of numerator and denominator data for cases and controls - the apparent lack of mention of data assessment and analysis blinded to case or control status - failure to attempt matching between cases and controls and the partly prospective nature of the study design

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Loeb 2009

Methods	Open non-inferiority randomised, controlled trial carried out to compare the surgical mask with the N95 respirator in protecting healthcare workers against influenza. The trial was carried out between 2008 (enrolment started in September and follow up on 12 January 2009) and 23 April 2009 (when all HCWs were told to wear a N95 respirator for all HCWs caring for febrile patients because of the appearance of novel A/H1N1). The trial trigger was the beginning of the influenza season defined as isolation of 2 or more viruses in a district in the same week. Following the 2003 SARS outbreak all Ontario nurses caring for febrile patients (38 °C or more and new onset cough or SOB) had to wear surgical masks. The randomisation (carried out in blocks of 4 by centre) then consisted of either confirmation to same-maker surgical mask wear or N95 respirator wear. Investigators and laboratory staff were blind to allocation status, but for obvious reasons (the visible difference in interventions), participants were unblinded. "The criterion for non-inferiority was met if the lower limit of the 95% confidence interval (CI) for the reduction in incidence (N95 respirator minus surgical group) was greater than -9%". So this is the non-inferiority margin. It is assumed that the "minus surgical group" means minus surgical mask group.
Participants	Consenting nurses (n = 446 randomised) aged a mean of 36.2 years working full time (≥ 37 hours/week) in 23 acute units (a mix of paediatric, A&E and acute medical units) in 8 hospitals in Ontario, Canada. 225 were randomised to the surgical mask and 221 to the N95 respirator. There were 13 and 11

Loeb 2009 *(Continued)*

	dropouts respectively from each arm (all accounted for) plus 21 and 19 lost to follow up. 11 in each arm gave no reason, the others are accounted for. There were no deaths. The final total of 212 and 210 was included in the analysis. Table 1 reports the demographic data of participants by arm, which appear comparable
Interventions	Surgical masks (as standard wear by the standard distributor) or fit–tested N95 respirator. All nurses wore gloves or gowns in the presence of a febrile patient
Outcomes	Laboratory RT-PCR paired sera with 4-fold antibody rise from baseline (only for unvaccinated) nurses Effectiveness: follow up (lasting a mean of around 97 days for both arms) was carried out twice-weekly on a web-based instrument. Nurses with new symptoms were asked to swab a nostril if any of the following signs or symptoms had developed: fever (temperature ≥ 38°C), cough, nasal congestion, sore throat, headache, sinus problems, muscle aches, fatigue, earache, ear infection or chills The text defines influenza with laboratory-confirmation and separately reports criteria for swab triggering and a definition of ILI ("Influenza-like illness was defined as the presence of cough and fever: a temperature ≥ 38°C"). But this is not formally linked to influenza in the text as it appears that primary focus was the detection of laboratory-confirmed influenza (either by RT-PCR or serology) Additional outcome data sought were work-related absenteeism and physician visits for respiratory illness Secondary outcomes included detection of the following non-influenza viruses by PCR: parainfluenza virus types 1, 2, 3 and 4; respiratory syncytial virus types A and B; adenovirus; metapneumovirus; rhinovirus-enterovirus; and coronaviruses OC43, 229E, SARS, NL63 and HKU1 Audits to assess nurse compliance with the interventions were carried out in the room of each patient cared for. The text reports that 50 and 48 nurses in the surgical mask and N95 groups respectively had laboratory confirmation of influenza infection, indicating non-inferiority. Interestingly non-inferiority seemed to be applicable both to seasonal viruses and nH1N1 viruses (as 8% and 11.9% were serologically positive to nH1N1). This finding is explained either by seeding or cross reaction with seasonal H1N1. Equivalent conclusions could be drawn for nurses with complete follow up. Non-inferiority was applicable also to other ILI agents identified. None of the 52 persons with positive isolates met the criteria for ILI All cases of ILI were confirmed as having influenza (9 and 2 respectively). This means that all the 11 cases of ILI had influenza but that most of those with a laboratory diagnosis of influenza did not have cough and fever. For example the text reports that "Of the 44 nurses in each group who had influenza diagnosed by serology, 29 (65.9%) in the surgical mask group and 31 (70.5%) in the N95 respirator group had no symptoms". By implication of the 88 nurses with antibody rises 28 had symptoms of some kind, i.e. two-thirds were asymptomatic. Absenteeism was 1 versus 39 episodes in the mask versus respirator arms. No episodes of LRTI were recorded. The number of family contacts with ILI were the same for each arm (45 versus 47). Physician visits were similar in both groups Safety: no AEs are reported
Notes	The authors conclude that "Among nurses in Ontario tertiary care hospitals, use of a surgical mask compared with a N95 respirator resulted in non-inferior rates of laboratory-confirmed influenza" This a well-designed and conducted trial with credible conclusions. The only comment is that the focus in the analysis on influenza (symptomatic and asymptomatic) is not well-described, although the rationale is clear (interruption of transmission)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was performed centrally ...."

Loeb 2009 *(Continued)*

Allocation concealment (selection bias)	Low risk	"...by an independent clinical trials coordinating group such that investigators were blind to the randomisation procedure and group assignment and was stratified by centre in permuted blocks of 4 participants."
Blinding (performance bias and detection bias) All outcomes	Low risk	Outcome assessment blinded: "It was not possible to conceal the identity of the N95 respirator or the surgical mask since manipulating these devices would interfere with their function. Laboratory personnel conducting hemagglutinin inhibition assays, polymerase chain reaction (PCR), and viral culture for influenza were blinded to allocation."
Incomplete outcome data (attrition bias) All outcomes	Low risk	21 of 225 randomised in mask group and 19 of 221 randomised in N95 group were lost to follow up, reasons reported Study stopped early: "We had planned to stop the study at the end of influenza season. However, because of the 2009 influenza A(H1N1) pandemic, the study was stopped on April 23, 2009, when the Ontario Ministry of Health and Long-Term Care recommended N95 respirators for all healthcare workers taking care of patients with febrile respiratory illness."
Selective reporting (reporting bias)	Low risk	All outcomes reported

Longini 1988

Methods	Cluster-controlled, double-blind, randomised trial to assess the efficacy of virucidal tissues in interrupting family transmission of rhinovirus and influenza virus. The study was carried out in the community of Tecumseh, Michigan, USA during the period 25 November 1984 to 28 April 1985. However, the authors only report results for the period 13 January to 23 March 1985, when a high circulation of influenza A H3N2 and rhinovirus was detected
Participants	296 households were enrolled but for "technical reasons" 5 household were eliminated from the analysis. The analysis was carried out in households with 3 to 5 members. The authors report data on 143 households randomised to virucidal tissues and 148 to placebo tissue. Average age in households was around 22 and the difference between arms was not significant. Randomisation was carried out by the sponsor and tissues were pre-packed in coded boxes with no other identifying features and delivered to households at the beginning of the study period
Interventions	Disposable 3-layered virucidal tissues (citric and malic acids with sodium lauryl sulphate in the middle layer) or placebo (succinic acid in the middle layer) tissues. They were used to blow the nose and for coughing or sneezing into Households were also stratified by level of tissue use. Tissue use was significantly higher in the intervention arm (82% versus 71%)
Outcomes	Laboratory: yes - viral culture from nasal and throat swabs from symptomatic participants Effectiveness: ARI (with a proportion of laboratory-confirmed diagnosis in non-randomly chosen participants with symptoms lasting 2 days or more) Follow up and surveillance was carried out using a telephone questionnaire Safety: N/A
Notes	Risk of bias: high (inappropriate choice of placebo) Notes: the authors conclude that virucidal tissues were up to 36.9% effective in preventing transmission of ARIs as measured by secondary attack rates (18.7% versus 11.8%). This was not significant but may well have been affected by the lack of do-nothing community controls. This a well-designed, well-written study despite the unexplained attrition of 5 families, the lack of reporting of cluster coefficients and the differential in tissue use between the 2 arms which raises questions about the robustness of double-blinding. Particularly notable is the discussion on the low generalisability of results from the study from the placebo arm given that even the inert barrier of the tissues is a likely to have limited

Longini 1988 *(Continued)*

	spread. Also the lengths to which the authors went to obtain allocation concealment and maintenance of double-blind conditions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Treated and placebo tissues were randomly assigned ..." Sequence generation not reported
Allocation concealment (selection bias)	Low risk	"Treated and placebo tissues were randomly assigned by the sponsor to 296 participating households stratified by household size, such that roughly half the households would receive treated tissues. Thus, the investigators were unaware of the assignment of treated tissues."
Blinding (performance bias and detection bias) All outcomes	Low risk	"The type of tissue was identified by code, and the boxes in which tissues were contained were not marked with any specific identifiers. Therefore, the study was double-blinded."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	296 HH eligible. "The final sample used for analysis consisted of 143 households in the treatment group and 148 households in the placebo group."
Selective reporting (reporting bias)	High risk	"The analysis of secondary spread was restricted to households of three to five members for technical reasons, which eliminated five households." "The two groups were almost identical in composition."

Luby 2005

Methods	Partly double-blind, cluster-randomised controlled trial carried out during 15 April 2002 to 5 April 2003 in Karachi, Pakistan. The trial assessed the effects of mother and child handwashing on the incidence of respiratory infections, impetigo (data not extracted) and diarrhoea (data not extracted) Randomisation took place by computer-generated random numbers in 3 phases: - 25 neighbourhoods were assigned to handwashing and 11 to standard practice - 300 households assigned to using antiseptic soap - 300 households assigned to using plain soap - 306 households assigned to standard practice - 1523 children younger than 15 years assigned to using antiseptic soap - 1640 children younger than 15 years assigned to using plain soap - 1528 children younger than 15 years assigned to standard practice Soaps were identical weight, colour and smell and were packed centrally with a coded packing case matched to households containing 96 bars. Neither field workers not participants were aware of the content. Control arm households were visited with the same frequency as intervention household but were given books and pens. Codes were held centrally by the manufacturer and broken after the end of the trial to allow analysis
Participants	Householders of slums in Karachi. Of the 1523 children younger then 15 years assigned to using antiseptic soap 117 dropped out (1 died, 51 were born in and 65 aged out) = 1406; 504 were aged less than 5 Of 1640 children younger then 15 years assigned to using plain soap 117 dropped out (3 died, 44 were born in and 70 aged out) = 1523; 517 were aged less than 5 1528 children younger then 15 years assigned to standard practice 125 dropped out (3 died, 40 were born in and 82 aged out) = 1403; 489 were aged less than 5

Luby 2005 *(Continued)*

Interventions	Instruction programme and antibacterial soap containing 1.2% triclocarban, or ordinary soap to be used throughout the day by householders or standard procedure
Outcomes	Laboratory: N/A Effectiveness: - Number of new respiratory illness per person per week - Pneumonia (cough or difficulty in breathing with a respiratory rate of > 60 min in children less than 60 days old, > 50 min in those less than 1 year old and > 40 min for those aged 1 to 5 years) Follow up was weekly with household interview and direct observation. Children aged less than 5 were weighed and the report presents stratification of results by child weight Safety: N/A
Notes	Risk of bias: low (cluster coefficients and analysis by unit of randomisation provided) Notes: the authors conclude that "handwashing" neighbourhoods has significantly less episodes of respiratory disease than controls (e.g. 50% less cough). "Handwashing" children aged less than 5 had 50% less episodes of pneumonia than controls (-65% to -35%). However there was no difference in respiratory illness between types of soap. The report is confusing, with a shifting focus between children age groups. The impression reading is of an often re-written manuscript. There is some loss of data (for example in the results by weight, i.e. risk group) because of lack of clarity on denominators. Despite this, the trial is a landmark.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation took place by computer-generated random numbers in 3 phases:
Allocation concealment (selection bias)	Low risk	"One of the investigators (SL) who did not participate in recruiting neighbourhoods or households programmed a spreadsheet to randomly generate the integers of a 1 or a 2. He applied the random numbers sequentially to the list of neighbourhoods. Neighbourhoods with a 1 were assigned to control, and those with a 2 were assigned to handwashing promotion. Random assignment continued until neighbourhoods consisted of at least 600 handwashing promotion households and 300 control households were assigned."
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	89% of the study population followed up, but no data on the clusters
Selective reporting (reporting bias)	Low risk	"At baseline, households in the three intervention groups were similar."

Macartney 2000

Methods	Controlled before and after study with economic evaluation (data not extracted) carried out over 8 RSV seasons in 1988 to 1996. The study assessed the impact of a programme for the interruption of transmission of RSV in a children hospital in Philadelphia, USA. Analyses are presented both by risk group (exposure to patients by days of viral shedding) and as aggregate. Only for the latter numerators and denominators are provided, whereas for the former figures are presented in bar chart format

Macartney 2000 *(Continued)*

Participants	Children with community-acquired RSV infection and the inpatient children exposed to them (1604 in 4 seasons before and 2065 in the "after the intervention" seasons. Children were aged around 1 year and those with risk factors were equally spread (51% versus 54%) in the 2 periods
Interventions	Education with high index of suspicion for case-finding with barriers (but no goggles or masks) and handwashing for patients and staff with contact precautions for RSV + patients for 2 weeks with isolation (when possible) with cohorting of patients and staff with enhanced surveillance with restriction of visits with discouragement of staff with ARIs from working unprotected in SCBU
Outcomes	Laboratory: ELISA confirmation of RSV infection on all children admitted with respiratory symptoms. In a proportion of cases RSV culture was undertaken, although this had a minimal practical impact as any child with respiratory symptoms was considered as a RSV case Effectiveness: clinically-defined RSV cases contracted nosocomially (with symptoms appearing after at least 6 days from admission) Safety: N/A
Notes	Risk of bias: low Notes: the authors conclude that 10 RSV infections were prevented per season (RR for post-intervention compared to pre-intervention periods 0.61, 95% CI 0.53 to 0.69). The study is well-reported and the conclusions appear reasonable, but no information is given on the background rate of infection and the impact of the intervention on HCW morbidity is not analysed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

MacIntyre 2009

Methods	Prospective cluster-randomised trial carried out in Sydney, Australia, to assess the use of surgical masks, P2 masks and no masks in preventing influenza-like illness (ILI) in households. The study was carried out during the 2 winter seasons of 2006 and 2007 (August to the end of October 2006 and June to the end of October 2007). “Gaussian random effects were incorporated in the model to account for the natural clustering of persons in households"
Participants	290 adults from 145 families; 47 households (94 enrolled adults and 180 children) were randomised to the surgical mask group, 46 (92 enrolled adults and 172 children) to the P2 mask group, and 52 (104 enrolled adults and 192 children) to the no-mask (control) group
Interventions	Use of surgical masks and P2 mask versus no mask. The P2 mask is described as very cumbersome

MacIntyre 2009 *(Continued)*

Outcomes	Laboratory: serological evidence Effectiveness: Influenza-like illness (ILI) (described as fever, history of fever or feeling feverish in the past week, myalgia, arthralgia, sore throat, cough, sneezing, runny nose, nasal congestion, headache) However, a positive laboratory finding for influenza converts the ILI definition into one of influenza Safety:N/A
Notes	The authors conclude that adherence to mask use significantly reduced the risk for ILI-associated infection, but < 50% of participants wore masks most of the time. We concluded that household use of face masks is associated with low adherence and is ineffective for controlling seasonal respiratory disease. Compliance was by self-report – therefore likely to be an underestimate The primary outcome was ILI or lab-positive illness. This showed no effect Sensitivity analysis by adherence showed that under the assumption that the incubation period is equal to 1 day (the most probable value for the 2 most common viruses isolated, influenza (21) and rhinovirus (26)), adherent use of P2 or surgical masks significantly reduces the risk for ILI infection, with a hazard ratio equal to 0.26 (95% CI 0.09 to 0.77; P = 0.015). No other covariate was significant. Under the less likely assumption that the incubation period is equal to 2 days, the quantified effect of complying with P2 or surgical mask use remains strong, although borderline significant; hazard ratio was 0.32 (95% CI 0.11 to 0.98; P = 0.046). The study was underpowered to determine if there was a difference in efficacy between P2 and surgical masks (Table 5). The study conclusion appears to be a post-hoc data exploration. Regardless of this the study message is that respirator use in a family setting is unlikely to be effective as compliance is difficult unless there is a situation of real impending risk

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Participating households were randomised to 1 of 3 arms by a secure computerised randomisation process:"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"Study participants and trial staff were not blinded, as it is not technically possible to blind the mask type to which participants were randomised. However, laboratory staff were blinded to the arm of randomisation."
Incomplete outcome data (attrition bias) All outcomes	Low risk	143 families of 145 randomised were analysed; 2 families in the control group were lost to follow up during the study. No reason was given for this
Selective reporting (reporting bias)	Low risk	No differences between groups at baseline

Madge 1992

Methods	Prospective cohort study conducted in 4 medical wards of the Royal Hospital for Sick Children in Glasgow, UK, to evaluate the effectiveness of 4 infection control procedures in preventing nosocomial infection with RSV. This is an interruption of transmission study. Every child up to 2, irrespective of clinical presentation, had respiratory secretions tested for RSV antigen within 18 hours of admission. Nosocomial infection was assumed if a child become RSV positive 7 days or more after admission. Children after discharge from hospital were not studied

Madge 1992 *(Continued)*

Participants	No special precaution group 152 (winter 1); gowns/gloves 337 (winter 1 and 2); cohort nursing 265 (winter 1 and 2); cohort nursing and gowns/gloves 310 (winter 1 and 2); 1001 (winter 3)
Interventions	Stepwise intervention programmes: gowns/gloves; cohort nursing + gowns/gloves; cohort nursing, versus no special precautions. The procedures evaluated in the 2 winter periods were gowns/gloves; cohort nursing + gowns/gloves; cohort nursing, versus no special precautions. In the third year the most effective strategy was introduced into all ward areas and its efficacy in clinical practice was assessed. There was not separate area for managing children with infections
Outcomes	Laboratory: yes - culture, antibodies titres, serological studies Effectiveness: RSV infections (seroconversion within 7 days of admission) Safety: N/A
Notes	Risk of bias: low Notes: the authors conclude that combined with rapid laboratory diagnosis, cohort nursing and the wearing of gowns and gloves for all contacts with RSV-infected children can significantly reduce the risk of nosocomial RSV infection (odds reduced to between 1.27% to 75.6%). One confounding effect that was not accounted for in the study design was a possible "ward effect". For practical reasons, 2 wards (3 and 4) continued with the same policy over the first 2 years of the study. Since it was also necessary apply policies to whole wards there is a possibility that ward 4 might have been especially effective at implementing their assigned policy

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Makris 2000

Methods	Prospective cohort study carried out in 8 private, freestanding long-term care facilities located in New Jersey and Delaware, to determine the impact of an ongoing infection control intervention programme in reducing the incidence of nosocomial infections. The 8 facilities were selected on the basis of similarity with respect to admission rate, size, acuity levels, availability of services, overall infection rates, in-house environmental service departments. Resident populations were comparable in terms of age, sex and underlying disease. The 8 facilities were grouped into 4 sets of matched pairs. Within each pair, each home was designated at random as either a test site or a control site. The results was that 4 facilities (2 urban and 2 suburban, with a total of 443 beds), were selected as test sites and another 4 facilities, 2 urban and 2 suburban, with a total of 447 beds, were selected as control sites

Makris 2000 *(Continued)*

Participants	443 beds (patients) in the test group, 447 beds (patients) in the control group. We assumed number of beds as number of participants.
Interventions	Infection-control education programme reinforcing handwashing and other hygienic measures versus normal care
Outcomes	Laboratory: no Effectiveness: upper respiratory infections Safety: N/A
Notes	Risk of bias: high (internal inconsistencies) Notes: the authors conclude that infection control education measures that reinforce handwashing and other hygienic measures helps reduce the number of organisms present on hands and surfaces and may have contributed to the non-significant reduction of URTIs (the opposite is reported in the paper: incidence density rate of 4.15/1000 patient days in the test homes versus 3.15/1000 patient days in the control homes) showed in this study. We assumed number of beds as number of participants to the study, but we do not know the characteristics of the patients (age, sex, underlying conditions, etc.). The authors confuse a cohort design with a before and after design and in the report they confusingly use both terms and reach conclusions not supported by the evidence presented

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Master 1997

Methods	Prospective cohort study conducted in an elementary school, Detroit, to evaluate the effect of a mandatory scheduled handwashing programme on absenteeism due to acute communicable illness (including upper respiratory disease). Classrooms were divided into either control or experimental groups without formal randomisation. Six classrooms were assigned to the handwashing group and 8 classrooms were assigned to the control group. Data were collected for 37 school days. Information about absent children was recorded daily by the school secretary. Symptoms were used to classify students as having respiratory or gastrointestinal illness. Upper respiratory infections and gastrointestinal symptoms (data not extracted) were not considered mutually exclusive
Participants	14 classrooms including 305 healthy, predominantly upper middle-class children ranging from ages 5 to 12. All grade levels from kindergarten through fifth grade were included. Six classrooms (143 students) were the handwashing group and 8 classrooms (162 students) were the control group

Master 1997 *(Continued)*

Interventions	Handwashing programme versus usual practice. Children in the handwashing group were asked to wash their hands after arrival at school, before eating lunch, after lunch recess, and before going home. Children in the control group washed at their normal frequency. All children in both groups washed with the school soap, which was not antibacterial
Outcomes	Laboratory: no Effectiveness: upper respiratory infections (URTI) - cough sneeze, pink eye, headache, mononucleosis, acute exacerbation of asthma, sinus trouble, fever alone, bronchitis Safety: N/A
Notes	Risk of bias: high Notes: the authors conclude that handwashing among children can be effective in preventing transmission of disease, but the difference in days of absence is statistically significant only for gastrointestinal symptoms (RR for ARIs 0.79, P = 0.756). Limitations in the study design are: use of a discrete population without socio-economically diverse backgrounds, use of a single institution, lack of blind assessment, low specificity of symptoms, and lack of accurate symptom definition

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Morton 2004

Methods	Cross-over study to evaluate the effectiveness of an alcohol gel as an adjunct to regular handwashing for decreasing absenteeism among elementary children by reducing specific communicable diseases such cold, flu and conjunctivitis. The study was conducted in an elementary school in New England, US. In the cross-over design classrooms in each grade level were randomised to begin as the experimental group (alcohol gel) or the control group (regular handwashing). A study protocol for hand hygiene was introduced following the germ unit education. The handwashing product was a soap and water alternative that is approximately 60% ethyl alcohol. In phase 1 (46 days) children in 9 classrooms were in the experimental group, and children in 8 classrooms were in the control group. After a 1 week washout period when no children had access to the alcohol gel, Phase 2 (47 days) started, and the classroom that had participated before as an experimental group passed in the control group and vice versa. Data were collected by the parents that informed the secretary or the school nurse of the reasons for a child's absence, including symptoms of any illness. Respiratory illnesses were defined by symptoms of URTI
Participants	253 children, 120 girls and 133 boys, from kindergarten to 3rd grade. 32 children dropped out (10 due to skin irritation and 22 because of lack of parental consent)

Morton 2004 *(Continued)*

Interventions	Use of an alcohol gel as an adjunct to regular handwashing and educational programme versus regular handwashing and educational program
Outcomes	Laboratory: no Effectiveness: days of absences from school for respiratory illness Safety: N/A
Notes	Risk of bias: high (no description of randomisation; partial reporting of outcomes, numerators and denominators) Notes: the authors conclude that significantly fewer children became ill while using the alcohol gel as an adjunct to regular handwashing than when using regular handwashing only (decreased school absenteeism of 43% with the use of alcohol gel on top of handwashing). The authors also described, as a limitation of the study, the fact that the school nurse served as the data collector, and this could be perceived as bias in measurement of the outcome variable Randomisation and allocation are not described, there are no cluster coefficients reported and attrition is not taken into consideration during the analysis. Unit of randomisation and analysis are different. No reporting by arm. No ORs, no CIs reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Murphy 1981

Methods	Prospective cohort study carried out in the Children's Hospital, Denver, to examine the effect of using gowns, masks and handwashing on the acquisition of symptomatic respiratory infections by medical personnel caring for infants with respiratory disease
Participants	58 people of nursing, medical, respiratory therapy personnel; 30 in the handwashing group, 28 in the handwashing, masks and gowns. Seventy HCWs initially were available for enrolment, 9 refused to take part and 3 withdrew
Interventions	Handwashing versus handwashing, masks and gowns
Outcomes	Laboratory: yes Effectiveness: viral infections (including RSV) Safety: N/A
Notes	Risk of bias: medium

Murphy 1981 *(Continued)*

	Notes: the authors conclude that there was no difference between the 2 groups with respect to number of viral infections (i.e. 4/30 in the handwashing group versus 5/28 in the handwashing gown and masking group (P > 0.20). The findings cannot demonstrate any effect of adding the use of both gown and mask to the usual handwashing routine on the development of illness in personnel caring for infants with respiratory disease. Possible reasons for lack of effect are: the heavy exposure all adults have to respiratory viral illness in the community at large; poor compliance to the study protocol, modes of virus spread which would not be blocked by the use of mask and gown

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Niffenegger 1997

Methods	Prospective 2-centre cohort study assessing the effects of a handwashing programme in Indiana, USA. Two centres were enrolled for the August to December 1994 (21 weeks) study: a test and a control centre
Participants	Eight teachers and 26 children (aged 3 to 5) in the test group and 12 children and 8 teachers in the control group. According to the authors, age, experience gender and socioeconomic variables were equally distributed between the 2 groups, but data are not shown. No attrition is mentioned
Interventions	Three weekly cycles of teachings, handwashing routine encouragement for children, parents and staff and correct sneezing and coughing procedure. Follow up was weekly filling in of a teacher report. It is unclear from the text what happened in the control site, or indeed if they were fully aware of the project
Outcomes	Laboratory: N/A Effectiveness: colds and ARIs no better defined Safety: N/A
Notes	Risk of bias: high (wide range of incidence of infections) Notes: the authors conclude that during the first 11 weeks of the study the test centre had double the incidence of colds compared to the control centre this is explained by the author as caused by the influx of new children bringing in new viruses in the test centre. In the second period the reverse was true, explained as the stabilising of the population and the taking effect of the programme. The list of potential confounders and biases is countless. For example there is only a very cursory description of participants in both arms and the role of teachers especially in the control centre is not explained

Niffenegger 1997 *(Continued)*

	The test group had significantly fewer colds than the control group (P < 0.05)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Nishiura 2005

Methods	Case-control study carried out during the SARS outbreak (26 February 2003 to 28 April 2003) in Hanoi, Vietnam. The study aimed at assessing the relationship between SARS infection and behaviour. The study population was based at the Hanoi French Hospital (HFH) and followed the outbreak during 3 phases. The first phase (26 February to 4 March 2006) in which an index case and 9 suspected secondary cases were admitted/cared for. The second phase (8 March to 11 March 2003) in which outpatients were closed and staff no longer returned home as the outbreak spread and the third phase (11 March 2003 to 28 April 2003) in which the HFH was closed to all other then SARS cases who were isolated
Participants	Description of cases: 29 surviving people with laboratory confirmed SARS cases either admitted and retained or transferred to other hospitals. Nine cases did not take part (5 died, 1 refused and 3 had relocated). Twenty-eight were HCWs employees of the HFH and 1 a relative of a patient. Substantial exposure and behaviour were documented through observation and questionnaires Description of controls: 90 people aged > 20 who provided written consent with substantial SARS exposure, 57 of whom were HFH employees
Interventions	Handwashing before contact with SARS patient Handwashing after contact with SARS patient Masks Gloves Gowns All measures combined Analysis by epidemic stage is reported
Outcomes	SARS infection
Notes	Risk of bias: low Notes: the authors conclude that masks (OR 0.3, 95% CI 0.1 to 0.7) and gowns (OR 0.2, 95% CI 0.0 to 0.8) were significantly associated with protection during phase 1 but in Phase 2 masks (OR 0.1, 95% CI 0.0 to 0.3) and all measures (OR 0.1, 95% CI 0.0 to 0.3) were associated with protection probably because of

Nishiura 2005 *(Continued)*

	the increased awareness of the danger of the outbreak and increase us of measures - this is confirmed by the results of the mathematical model in the second part of the study. A well-written and reported study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Ou 2003

Methods	Retrospective cohort study carried out in selected precincts of Haidian district of Beijing, People's Republic of China between March and May 2003 during the epidemic of SARS (attack rate 19/100,000 population in the period March to July). Precincts were chosen on the basis of the highest number of quarantinees. The study aimed at assessing the risk of acquiring SARS among quarantinees. A better definition of the risk would help in future to identify better candidates for quarantine and target resources accordingly. The study was based on a questionnaire-based survey on the reasons for quarantine. SARS diagnosis for contacts was independently carried out from lists
Participants	171 SARS cases (29% of total) were identified in the precincts and 1210 persons (23%) quarantined from the selected districts (contacts). These were sampled from a total population of 2.24 million, with 5.186 quarantinees. Response rate was 85% (1.028 quarantinees who completed the questionnaire, of which 232 developed probable SARS while in quarantine)
Interventions	Quarantine at home or hospital for 14 days post-exposure (reduced to 10 and then to 3). Quarantine is defined as the separation and or restriction of movement of persons who due to recent exposure to a communicable disease risk acquiring the disease and transmitting to third parties. A contact was defined as: - Healthcare worker not using personal protective equipment (PPE) when caring for/assessing a SARS case: - other persons caring for a SARS case - persons sharing accommodation with a SARS case - persons visiting a SARS case - persons working with a SARS case - classmates or teachers of a SARS case - persons sharing the same means of public transport with a SARS case All quarantinees were followed up daily and were admitted to hospital if they developed fever (38 °C or more)
Outcomes	Laboratory: no

Ou 2003 *(Continued)*

	Effectiveness: definition of SARS was based on criteria of Chinese Ministry of Health. Definition was clinical and not based on laboratory isolation of the SARS-CoV Safety: N/A
Notes	Risk of bias: high Notes: the authors conclude that only those quarantinees who actually had home or hospital contact with a symptomatic SARS patient developed the illness (attack rate 31.1, 95% CI 20.2 to 44.4 for carers, 8.9%, 95% CI 2.9 to 22.1 for visitors, 4.6%, 95% CI 2.3 to 8.9 for those who lived with a SARS case) but not those living in the same building or working with them and not contacts of any SARS case during the incubation period. Fever was also not a good reason to quarantine people (attack rate nil). Quarantine also appeared to prevent transmission, although there were numerous cases in which quarantine was not required. There are several limitations to the conclusion of the study Non-random basis for the sample, selection bias of the sample and responders, recall bias of responders and the absence of a laboratory-confirmed diagnosis may have affected the conclusion one way or another Overall, not enough denominator data, non-exposed data are given to allow data extraction or calculate OR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Pang 2003

Methods	Ecological study describing and analysing the effects of public health measures on the SARS epidemic between 5 March and 29 May 2003 in Beijing, China. Data were collected from centralised notification and close contact databases
Participants	2521 probable SARS cases mostly hospitalised aged around 33 (407 or 16% were HCWs) and 192 of these who died out of a total population of 13.6 million people. The peak took place on 25 April with 173 hospitalised cases
Interventions	SARS was made notifiable on 9 April and contact tracing commenced a day later. On 18 April 62,363 of the estimated 85,000 Beijing HCWs received training in the management of SARS cases and were issued gowns, gloves, masks. By 17 April, 123 fever clinics were opened, however these were contiguous to hospitals and it is thought that some transmission occurred By 21 April quarantine of close contacts was underway (these were only allowed to leave quarantine in exceptional circumstances and only wearing a mask) and fever check at airports were begun the day after. By 24 April all schools and universities closed. Two days later public meeting places (bars, libraries etc) were closed. From 27 April all SARS cases were placed in designated hospital wards and by 8 May SARS cases were only sent to designated hospitals. By 1 May a SARS hospital of 1000 beds built in 1

Pang 2003 *(Continued)*

	week was opened and received only SARS cases (40% of total cases). The last cases were registered on 26 May. The highest attack rate (14.5%) of quarantined people was those of spouses of SARS cases
Outcomes	Laboratory: laboratory testing for the presence of SARS-CoV was not part of the case definition Effectiveness: probable SARS cases (close contact of a SARS sufferer with signs and symptoms of febrile respiratory disease and chest X-ray changes, or person visiting of residing in an area with recent SARS activity and with signs and symptoms of febrile respiratory disease and chest X-ray changes and lack of response to antibiotics or person visiting of residing in an area with recent SARS activity and with signs and symptoms of febrile respiratory disease and chest X-ray changes and normal or decreased WBC count) Safety: N/A
Notes	Risk of bias: low Notes: the authors conclude that in virtue of the shape of the epidemic curve it is likely that the combination of measures taken before the 25 April helped contain the spread of SARS. Although there may be alternative explanations this appears to be the most likely explanation of the facts. Hospitals were seen early on as sources of transmission of the SARS Co-V. The authors seem to doubt the direct effectiveness of entry port (for example, airports, stations, etc.) checks (12 cases identified out of over 13 million people screened). They think screening was more useful to keep away sick people

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Pelke 1994

Methods	Controlled before and after study conducted in a neonatal intensive care unit (NICU) of Kapiolani medical centre, Honolulu, Hawaii, to assess the effect of gowning on RSV and other infections, on traffic and handwashing patterns. Alternate 2-month gowning and no-gowning cycles were established in a 24-bed NICU for 8 months. One entire 4-month cycle was repeated to eliminate the potential for seasonal variables and outbreaks. All the people entering into the NICU (physicians, nursing staff, ward clerks, families and visitors) wore gowns. During the no-gowning periods nursing staff wore hospital-issued pantsuit, washed at home through ordinary methods and worn from home. Ward clerks, physicians, hospital staff, families and visitors wore street clothes without gowns. Throughout the entire 8-month period, there was the recommendation for all staff and visitors to enforce initial 2-minute hand-scrub. Nails were cleaned before scrubbing, and a minimum 15-second handwash between infants or equipment was expected. Surveillance cultures were done weekly on all patients. Without the knowledge of the NICU staff, a neonatal research nurse scheduled observations of traffic patterns, while ostensibly reviewing charts, to determine if a lack of gowning procedures encourage more traffic. Handwashing

Pelke 1994 *(Continued)*

	compliance was studied, again without staff awareness, by 30 minutes direct observation. Follow up of infection rates was planned through standard infection control surveillance
Participants	230 infants, aged 22 to 42 weeks, with birth a weight of 464 to 6195 grams. Overall there were 330 infants admitted to NICU during the study period. Thus 17% of participants had no RSV cultures taken. The reasons given are vague (transfer or death)
Interventions	Use of gowns and standard procedures (handwashing) versus standard procedures
Outcomes	Laboratory: serological evidence: yes Effectiveness: RSV infection Safety: N/A
Notes	Risk of bias: medium (17% loss to follow up) Notes: the authors conclude that gowning did not protect NICU infants from any type of infection or affect mortality (1.21 versus 1.38/100 patient-days of gowning and no-gowning periods respectively). Gowning procedures did not deter staff or visitors from entering the unit, since traffic was also unchanged between periods. Finally the results showed no change in handwashing patterns between periods. Besides the advantage of eliminating a potentially unnecessary ritual that may be perceived as a psychological barrier to families visiting their infants, other benefits to discontinuing gowning include saving staff time involved in various gowning procedures and costs. If gowns are eliminated, it is recommended to perform careful follow up. The study conclusions must be taken with caution given the likely selection bias introduced by the missing 17% of children

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Roberts 2000

Methods	Open cluster-RCT carried out between March and November 1996 (the southern hemisphere winter season) in 23 child care centres caring for a minimum of 50 children 10 hours a day, 5 days a week in Australia. The study assessed the effects of an Australian national handwashing programme compared to standard procedure. Randomisation was according to a random number table and cluster coefficients are reported
Participants	Children (299 in the intervention arm and 259 in the control arm) aged 3 or younger attending the centres at least 3 days a week. Attrition was 51 children in the intervention arm and 72 children in the control arm due mainly to staff leaving the centres

Roberts 2000 *(Continued)*

Interventions	Handwashing programme with training for staff and children. It is unclear whether any extra hand cleansing agents were used, as GloGerm (?) is mentioned when it was used in a preliminary study
Outcomes	Laboratory: N/A Effectiveness: ARI (runny nose, cough and blocked nose) Follow up was via a parental phone interview every 2 weeks Safety: N/A
Notes	Risk of bias: low (cluster coefficients and analysis by unit of randomisation) Notes: the authors conclude that although there was no overall decrease in respiratory illness (RR 0.95, 95% CI 0.89 to 1.01), in children up to 24 months the decrease was significant (RR 0.90, 95% CI 0.83 to 0.97). The authors speculated that this was because maximum benefits are likely from this age group because of their limited ability to wipe their nose and hands without a structured programme. Analyses by 3 compliance levels are also reported. A so-so reported and well-conducted trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was according to a random number table
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind the intervention
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Recruitment rate 88% (23 of 26 CCCs); loss to follow up not clear as no denominator given
Selective reporting (reporting bias)	Low risk	Centres comparable at baseline

Ryan 2001

Methods	Retrospective and prospective, controlled, before and after study carried out at the US Navy's Great Lakes recruit training centre in Illinois. Rates of respiratory disease were retrospectively calculated for recruits undergoing training for 3 periods: 1996, before the implementation of "Operation Stop Cough" and 1997 and 1998. To compare rates of respiratory illness with a similar community the authors also looked at the incidence of respiratory illness in a population of phase II sailors undergoing the second part of their training in the same camp. In addition a compliance questionnaire was also carried out during the latter 2 years of the study
Participants	Recruits undergoing training (44,797 in 1996; 47,300 in 1997; and 44,128 in 1998) mainly men, aged around 19 to 20 and a control population of phase II training sailors (no precise denominators given but around 10,000 yearly) who did not have a programme of handwashing
Interventions	Structured top-down programme of handwashing at least 5 times daily
Outcomes	Laboratory: N/A Effectiveness: respiratory illness detected from sick parade records and outgoing recruits questionnaire on a sample survey Safety: N/A

Ryan 2001 *(Continued)*

Notes	Risk of bias: low Notes: the authors conclude that implementation of the control programme has seen near-halving of incidence of ARIs (based on 3 stratified samples of recruits infrequent handwashers had more self-reported episodes of ARIs (4.7 versus 3.2 per recruit, OR 1.5, 95% CI 1.2 to 1.8) and reported more hospitalisations (OR 10.9, 95% CI 2.7 to 46.2). Despite dramatic results, implementation was and continues to be difficult

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Sandora 2005

Methods	Single-blind, cluster-randomised controlled trial carried around the Boston area, USA, in the period November 2002 to April 2003. The trial tested the effects of using a hand sanitiser and a programme of instruction on the transmissions of GI infections (data not extracted) and ARIs in families. Units of randomisation were childcare centres and were carried out on enrolment by an investigator using random block size generated by computer. Assignment was single-blind (i.e. investigator blinded to the status of the centre). Cluster correlation was 0.01
Participants	292 families with 1 or more children aged 6 months to 5 years who were in child care for 10 or more hours a week. There were 155 children in 14 centres allocated to the intervention arm and 137 children in 12 centres allocated to the control arm. The mean age was 3 to 2.7 years. Attrition was respectively 15 (3 lost to follow up and 12 who discontinued the intervention) and 19 (8 lost to follow up and 11 who discontinued the intervention). ITT analysis was carried out
Interventions	Alcohol-based hand sanitiser with bi-weekly hand hygiene educational materials over 5 months versus bi-weekly educational material on healthy diet
Outcomes	Effectiveness: ARI (2 of the following symptoms for 1 day or 1 of the following symptoms for 2 days: runny nose, cough, sneezing, stuffy or blocked nose, fever, sore throat). An illness episode had to be separated by 2 symptom-free days from a previous episode. A secondary illness was when it followed a similar illness in another family member by 2 to 7 days Follow up was by means of bi-weekly phone calls to care givers Safety: dry skin (71 reports), stinging (11 reports), bad smell (7 reports), dislike (2 reports), allergic reaction (2 reports), slippery feel (1 report) and irritation (20 reports)
Notes	Risk of bias: low

Sandora 2005 *(Continued)*

	Notes: the authors conclude that although the rate of GI illnesses was significantly lower in the intervention group, the incidence rate ratio - IRR was not significantly different for ARIs (0.97, 95% CI 0.72 to 1.30). Compliance and droplet route spread may account for this apparent lack of effect. A well-reported trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Random assignments were generated by computer using a permuted-blocks design with random block sizes."
Allocation concealment (selection bias)	Low risk	"Assignments were concealed in opaque envelopes, and centers were assigned to control or intervention groups by a study investigator as they were enrolled."
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition was 15 in intervention arm (3 lost to follow up and 12 who discontinued the intervention) and 19 in the control arm (8 lost to follow up and 11 who discontinued the intervention). ITT analysis was carried out
Selective reporting (reporting bias)	Unclear risk	Well-reported

Sandora 2008

Methods	Cluster-randomised, controlled trial carried out in a single elementary school system located in Avon, Ohio, USA to assess the effectiveness of a multifactorial infection-control intervention, including alcohol-based hand sanitiser and surface disinfection, in reducing absenteeism caused by gastrointestinal and respiratory illnesses among elementary school students. The study also aimed to describe the viral and bacterial contamination of common surfaces in the school classroom and to assess the impact of an environmental disinfectant on the presence of selected viruses and bacteria on these surfaces. Clustering was described as "teams of 3-4 classes depending on the class year"
Participants	A total of 363 students in 15 different classrooms were eligible to participate and received letters about the study. A total of 285 of these students provided written informed consent and were randomly assigned to the intervention group (146) or to the control group (139). No students were lost to follow up or discontinued the intervention during the study period. Baseline demographic characteristics were similar in the intervention and control groups. Most families were white and non-Hispanic and in excellent or very good health at baseline
Interventions	Alcohol-based hand sanitiser to use at school and quaternary ammonium wipes to disinfect classroom surfaces daily for 8 weeks versus usual handwashing and cleaning practices
Outcomes	Laboratory: Serological evidence: no Swabs for bacteria and viruses from 3 types of classroom surfaces were taken Effectiveness: Respiratory illness defined as days absent as measured by a (blinded) school worker who routinely recorded reason for absenteeism either for gastrointestinal or respiratory causes Safety: N/A

Sandora 2008 *(Continued)*

Notes	The authors conclude that multifaceted intervention that included alcohol-based hand sanitiser use and disinfection of common classroom surfaces reduced absenteeism from gastrointestinal illness among elementary school students. The intervention did not impact on absenteeism from respiratory illness. In addition, norovirus was detected less frequently on classroom surfaces in the group receiving the intervention. The study is good quality with low risk of bias. The authors checked compliance by counting discarded wipes. Reasons given for the apparent lack of effect against ARIs but good effect on GI illness are that disinfecting the classroom surfaces (daily at lunchtime with alkali) was important – as well as the alcohol wipes. The authors measured the norovirus concentration on surfaces and found this reduced. Other reasons may be that droplets are not affected by this method or that contamination of hands by respiratory infections is likely to be continuous (in orofaecal transmission is mostly at the time of defecation)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The allocation sequence was generated by computer ..."
Allocation concealment (selection bias)	Unclear risk	"...and teams were assigned to study groups by a study investigator (Dr Shih)." Blinding of allocation cannot be guaranteed
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	No students were lost to follow up or discontinued the intervention during the study period
Selective reporting (reporting bias)	Unclear risk	Well-reported

Satomura 2005

Methods	Randomised controlled trial, randomisation was achieved by simple computer-generated random digit. Allocation was concealed using sealed opaque envelopes. Not clear if there was a central randomisation centre. Post hoc exchange of envelopes was prevented by writing both the name of each subject and the number on the envelope he/she drew before breaking the seal. Participants were not blinded to the intervention, however, disease incidence was determined by 1 study physician who was not informed of the results of assignment. Analysis was done based on the intention-to-treat principle. The study targeted community healthcare all over Japan and was conducted between December 2002 and March 2003 for a follow-up period of 60 days
Participants	Three hundred and eighty-seven participants at 18 sites were recruited. Included in the analysis 384, follow up was completed on 338 participants. Attrition was fully explained for URTI analysis, however, 2 subjects were not accounted for in the ILI analysis. Forty-six participants did not complete the follow up due to either discontinuation of diary use (n = 9) or contracting influenza-like illness (ILI) (n = 37) Of the 37 participants with ILI, 11 were in povidone-iodine group, 12 in water group and 14 in control. Analysis was performed on 35 participants (Kitamura 2007)
Interventions	Participants were randomised to 1 of the following: water gargling, n = 122 (20 mL of water for about 15 seconds 3 times consecutively, at least 3 times a day); povidone-iodine gargling, n = 133 (20 mL of 15 to 30 times diluted 7% povidone-iodine (as indicated by the manufacturer) in the same way as water gargling); and control, n = 132 (retain their previous gargling habits)

Satomura 2005 *(Continued)*

	All groups were asked to fill a daily gargling diary (standardised form to record: gargling habits, handwashing and influenza complaints) The frequency of gargling in the water group was higher (3.6), frequency of handwashing was similar between the 3 groups URTI symptom was classified according to Jackson methods. Diary recording was continued throughout the follow-up period and for 1 week after the onset of URTI. ILI were reported separately
Outcomes	Laboratory: none Effectiveness: primary outcome: incidence of first URTI. Index cases were defined as all of the following conditions: (1) both nasal and pharyngeal symptoms, (2) severity of at least 1 symptom increased by 2 grades or more, and (3) worsening of a symptom of 1 increment or more for > 3 days Secondary outcome: severity of URTI of the incident cases was assessed by grading each symptom during the initial 7 days after the onset of URTI in numeric scores: none = 0, mild = 1, moderate = 2 and severe = 3 ILI was defined as both developing a fever of 38 °C or higher, and worsening arthralgia in addition to some respiratory symptoms (Kitamura 2007) Safety: no harm was reported. However, 2 patients in the povidone group switched to water gargling (analysed in their assignment group)
Notes	The authors conclude that simple water gargling is effective to prevent URTIs among healthy people. However, no significant difference was observed against ILIs Study was well-conducted, blinding would have added to the validity of the results. In addition, the study was not powered enough to detect significant preventative effect against ILI The study demonstrated that in addition to handwashing, simple gargling even with simple water can reduce URTI but not ILI. However, during periods of endemic influenza, multiple inexpensive and simple modalities (handwashing, masks, gargling) can be utilised together to reduce infection and transmission. Overall, the reporting of the 2 combined studies together is highly confusing. In the first study (Satomura 2005) the main outcome is URTI defined as fever and arthralgia. The second study (which is a presentation of further data from the 2005 publication in the guise of a short report) introduces the outcome ILI with a definition similar to that of URTI in the first study but referring to the earlier outcome as common cold. Also of note is reporting of significance without confidence intervals. Overall this potentially important study should be repeated with a larger denominator Medium risk of bias because of confused reporting and absence of double-blinding

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Group assignment was based on simple computer-generated random digits..."
Allocation concealment (selection bias)	Low risk	"By an individual drawing of sealed opaque envelopes, subjects were randomly assigned to the following three groups" "allocation was completely concealed from study administrators"
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	338 of 385 randomised followed up; reasons reported

Satomura 2005 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Confusing reporting

Seto 2003

Methods	Case-control study Hong Kong, China, conducted during the period 15 March to 24 March 2003 in 5 hospitals. The study aims were to assess the effectiveness of protective procedures for contracting SARS in HCWs exposed to 11 index cases in 3 of the 5 hospitals during the SARS epidemic
Participants	Description of cases: 13 HCWs infected with confirmed SARS within 2 to 7 days of exposure with no community exposure, 4 males and 9 females 2 doctors, 6 nurses, 4 healthcare assistants and 1 domestic staff who came into contact with SARS index cases. Only one used no protection measures and all omitted at least one of the protective measures required (handwashing, masks, gloves, gowns). Cases were identified through notification, which has been active since early February A SARS cases was defined as having fever of 38 °C or more, radiological infiltrates, and 2 of either: new cough, malaise, signs of consolidation Description of controls: 241 staff from the 5 hospitals who were not infected. The authors report that use of measures was elicited using questionnaires, 365 of which were returned (85% response rate). Non-responders were likely to be on leave or night shift. Data for 102 staff were excluded because they had no exposure to SARS
Interventions	Exposure was defined as coming within 0 to 91 metres (3 feet) of an index case with SARS symptoms when providing care. Recommended measures were handwashing, masks, gloves and gowns
Outcomes	SARS
Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls) Notes: the authors conclude that the 69 staff reporting use of all 4 measures were not infected, whereas all infected staff had omitted at least one measure. Simple analysis showed that masks, gowns and handwashing (OR 5, 95% CI 1 to 19) were effective but only masks (OR 13, 95% CI 3 to 60) were significant at logistic regression, possibly through lack of power. No blind assessment of cases and control data was carried out and 15% attrition of questionnaires may have introduced bias. The study was published as research letter in the Lancet, so possible lack of space may have affected reporting clarity

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Simon 2006

Methods	Prospective cohort surveillance study conducted in the University Children's Hospital in Bonn, Germany, to assess the global efficacy of a complex intervention programme to contain nosocomial transmission of RSV infections. This is a before-after design, with a multifactorial intervention carried out in one hospital
Participants	6548 paediatric patients admitted at the University Children's Hospital in the period of study (2200 in 1999 to 2000; 2298 in 2000 to 2001; 1959 in 2001 to 2002). 283 RSV infections were documented in 278 hospitalised paediatric patients: 138 in 1999 to 2000, 89 in 2000 to 2001, 56 in 2001 to 2002. Of the general population 244 events were ambulatory RSV infections and 39 nosocomial RSV infections
Interventions	Intervention strategy aimed at increasing vigilance to identify and isolate RSV-infected patients together with enforced contact precautions versus standard procedures. Interventions are not described very well: vigilance + cohorting versus vigilance versus standard practice
Outcomes	Laboratory: All RSV infections were confirmed by antigen detection or cell culture using MS cells Effectiveness: RSV infections no better defined clinically Safety: N/A
Notes	Risk of bias: low The authors conclude that the multi-factorial prevention strategy (early diagnosis, a strict cohorting and contact isolation policy, and prospective surveillance) probably contributed significantly to the reduced risk of nosocomial RSV infections in the hospital. In the pre-intervention period there were 39 cases (13.8%) nosocomial infections with an incidence density of 0.99/1000 patient-days; following the introduction of the surveillance and prevention policy there was a 9-fold decrease of the incidence (1.67 versus 0.18/1000 patient-days)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Snydman 1988

Methods	Controlled before and after study conducted during the winters of 1983-84 (retrospectively), 1984 to 1985 and 1985 to 1986 (prospectively) to assess whether the introduction of infection control measures halted transmission of RSV in a special nursery in Boston, USA. Record review for the retrospective part and prospective study for the 2 seasons following the introduction of infection control measures
Participants	HCW and patients in the special care baby unit
Interventions	From the 1984 to 1985 season the following were introduced: Active surveillance Extensive cohorting of patients and staff Respiratory precautions on suspicion of respiratory case Gown, mask and gloves used on contact Restricted visiting policy Segregation of cases
Outcomes	Laboratory: RSV culture Effectiveness: RSV cases with symptoms and laboratory confirmation Safety: N/A
Notes	Risk of bias: high Notes: the authors conclude that there were 7 cases in the season "before" and no cases in the following seasons (no transmission per 1000 patient days in the post-intervention period compared 8 per 1000 patient-days in the pre-intervention period). No denominators are provided (hence no data can be extracted) and exposure is generically quantified by aggregate patient-days of exposure. It is unclear how the circulation of RSV outside related to the claimed success of the measures, as no information is provided

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Somogyi 2004

Methods	Prospective cohort study of 9 observations (3 each when using 3 different masks). The authors observed and photographed droplet dispersal while a volunteer breathed out 3 times in 3 different types of mask
Participants	1 volunteer

Somogyi 2004 *(Continued)*

Interventions	Three masks, 2 without air filter and allowing external exhalation, 1 with manifold and air filter
Outcomes	Effectiveness: plume of droplets as observed and photographed: masks were poor at preventing droplet spread
Notes	Risk of bias: low Notes: the authors conclude that the mask with manifold and air filter did not allow dispersal of droplets and was far safer in an epidemic such as SARS to contain the spread. Simple, safe and effective study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Teleman 2004

Methods	Case-control study assessing risk and protective factors in HCWs during the SARS outbreak in Singapore (1 to 22 March 2003)
Participants	Description of cases: 36 HCWs admitted with probable SARS (according to WHO definition) during 1 to 31 March 2003. Six others were too ill to speak and 2 others died Description of controls: 50 HCWs working on the same wards who had definite exposure to SARS (physical proximity of 1 metre or less of a patient subsequently diagnosed as having SARS) but did not develop SARS
Interventions	Data on personal details and symptoms and exposure were gathered via a closed phone questionnaire. The 2 groups were comparable for demographic and epidemiological characteristics except that non-Chinese ethnic groups were twice as common among controls The following risk factors were assessed: Distance from source of infection < 1 metre Duration of exposure 60 or more minutes Wearing N95 respirator Wearing gloves Wearing gown Touched patients Touched patients' personal belongings Contact with respiratory secretions Performed venepuncture

Teleman 2004 *(Continued)*

	Performed or assisted in intubation Performed suction of body fluids Administered oxygen Handwashing after each patient
Outcomes	SARS
Notes	Risk of bias: low Notes: the authors conclude that 3 factors were associated with significant risks or protection: Wearing N95 respirator OR 0.1 (95% CI 0.02 to 0.86) Contact with respiratory secretions OR 21.8 (95% CI 1.7 to 274.8) Handwashing after each patient OR 0.07 (95% CI 0.008 to 0.66) A well-reported study, let down by the failure to indicate whether assessment of risk factors had been carried out blindly to cases or control status. We wonder how much of the non-significance for certain factors is due to lack of statistical power

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Turner 2004a

Methods	Double-blind randomised controlled trial conducted by Hill Top Research, Inc. Winnipeg, Canada, to assess the efficacy of acids with virucidal activity for the inactivation of virus and prevention of experimental rhinovirus colds. Subjects in good health, aged 18 to 60, were recruited from Winnipeg and surrounding communities for participation. Qualified subjects were randomised to treatment with vehicle (62% ethanol, 1% ammonium lauryl sulfate and 1% Klucel), vehicle containing 3.5% salicylic acid or vehicle containing 1% salicylic acid and 3.5% pyroglutamic acid. The volunteers' hands were disinfected and then test product was applied to both hands of each subject. Fifteen minutes after application, the fingerprints of each hand were contaminated with Rhinovirus type 39. The volunteers touched conjunctiva and the nasal mucosa only with the right hand. Viral contamination of the fingers was assessed in the left hands of the volunteers, and viral infection was assessed by culture of nasal lavage specimens and blood samples
Participants	85 volunteers, 31 control group, 27 used vehicle with 3.5% salicylic acid, 27 used vehicle with 1% salicylic acid and 3.5% pyroglutamic acid
Interventions	Use of salicylic acid versus salicylic acid and pyroglutamic acid versus "placebo" substance

Turner 2004a *(Continued)*

Outcomes	Laboratory: yes Effectiveness: rhinovirus type 39 infection Safety: N/A
Notes	Risk of bias: unclear (no description of randomisation process, concealment or allocation) Notes: the authors concluded that organic acids commonly used in over-the-counter skin care and cosmetic products have substantial virucidal activity against rhinovirus. These preparations provided effective residual antiviral activity on the hands. The virucidal effect of these hand treatments resulted in a reduction in the incidence of rhinovirus infection in the treated volunteers (P = 0.025). The utility of this observation in the natural setting remains to be determined. The volunteers were not allowed to use their hands in the interval between the hand treatment and the virus challenge, so the effect of normal use of the hands on the virucidal activity of these organic acids is not known. Similarly, the virus challenge method used in these experiments may not simulate the natural setting in all aspects. The effect of nasal secretions that would be transferred with the virus in the natural setting on the activity of the acids or on the transmission of virus was not tested in the model We are unsure as to the practical significance of this study and the generalisability of its results to the real world. Poorly-reported study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised" Sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"double blind" but no description
Incomplete outcome data (attrition bias) All outcomes	Low risk	All accounted for (short study)
Selective reporting (reporting bias)	High risk	Poorly reported

Turner 2004b

Methods	Double-blind, randomised controlled trial conducted by Hill Top Research, Inc. Winnipeg, Canada, to assess the residual virucidal activity of a skin cleanser wipe and its effectiveness in preventing experimental rhinovirus colds. Subjects in good health and from 18 to 60 were recruited from Winnipeg and surrounding communities for participation The residual activity of a skin cleanser wipe containing 4% pyroglutamic acid formulated with 0.1% benzalkonium chloride was tested. The negative control treatment was 62% ethanol. Benzalkonium chloride had been previously tested and was found to have no virucidal activity. Volunteers were randomly assigned to use the control preparation or the active preparation. The study material was applied to hands with a towelette. Fifteen minutes later, when the fingers were completely dry, the fingertips of each hand of the control subjects and the volunteers in the active treatment group were contaminated with rhinovirus type 39. An additional volunteer in the active group were challenged with virus 1 hour after application and the final group of volunteers was challenged 3 hours after application. Viral infection was assessed by culture of nasal lavage specimens and blood samples

Turner 2004b *(Continued)*

Participants	122 volunteers, 30 control group, 92 active group (30 tested after 15 minutes, 30 after 1 hour, 32 after 2 hours)
Interventions	Use of a skin cleanser wipe containing 4% pyroglutamic acid formulated with 0.1% benzalkonium chloride versus skin cleanser wipe containing ethanol
Outcomes	Laboratory: yes Effectiveness: rhinovirus type 39 infection Safety: N/A
Notes	Risk of bias: unclear (no description of randomisation process, concealment or allocation)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised" Sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"double blind" but no description given
Incomplete outcome data (attrition bias) All outcomes	Low risk	All accounted for (short study)
Selective reporting (reporting bias)	High risk	Poorly reported

Wang 2007

Methods	Prospective cohort, surveillance study carried out to identify risk factors for development of SARS among quarantined persons in Taiwan. Two types of quarantine were implemented during the SARS outbreak in Taiwan: level A and level B quarantine. Level A quarantine was designed for persons who had known and, at times, had close exposure to persons infected with SARS in healthcare facilities and other community and domestic areas. Level B quarantine was designed for travellers who sat on the same flight within 3 rows of a person infected with SARS or were returning from World Health Organization–designated SARS-affected areas
Participants	During the study period 52,255 persons were placed under level A quarantine and 95,271 persons were placed under level B quarantine
Interventions	Exposure to level A quarantine versus level B
Outcomes	Laboratory: Serological evidence: yes Effectiveness: SARS (definition not reported) Safety: N/A

Wang 2007 *(Continued)*

Notes	The authors conclude that focusing quarantine efforts on persons with known or suspected exposure can greatly decrease the number of persons placed under quarantine, without substantially compromising its yield and effectiveness. This is an important study, as it implies that risk banding can increase effectiveness and efficiency of quarantine procedures. The risk of bias is high as most of the answers to the NOS items are clearly no, however it is very difficult to get answers to a question such as the effectiveness of quarantine using any other design

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

White 2001

Methods	Double-blind, placebo-controlled, cluster-randomised trial that took place in 3 schools in California during March to April 1999. The study assessed the incremental value of using an alcohol hand rub together with water and soap handwashing. Both arms had been given an educational programme starting 2 weeks prior to the beginning of the trial. Randomisation was by classroom and the placebo hand rub was indistinguishable from the active ingredient. Details of randomisation are not given
Participants	Of the 72 classes originally recruited, lack of compliance (use of supplementary product at least 3 times a day), reduced the classes to 32 (16 in both arms) with 769 participants aged 5 to 12
Interventions	Pump-activated antiseptic hand rub with benzalkonium chloride (SAB) (Woodward Laboratories) or inert placebo that "virtually" looked the same in batches of 4 colour-coded bottles containing both. School staff, parents and participants were blinded
Outcomes	Laboratory: testing of virucidal and bactericidal activity of the active compound Effectiveness: ARI (cough, sneezing, sinus trouble, bronchitis, fever, red eye, headache, mononucleosis, acute exacerbations of asthma) Gastrointestinal and other illnesses (data not extracted) Follow up and observation was carried out by classroom staff and illnesses were described by parents Safety: 7 students dropped out because of mild sensitivity to the rub
Notes	Risk of bias: high (no description of randomisation; partial reporting of outcomes, numerators and denominators) Notes: the authors conclude that addition of the rub led to a 30% to 38% decrease of illness and absenteeism (RR for illness absence incidence 0.69, RR for absence duration 0.71). Very high attrition, unclear randomisation procedure, educational programme and use of placebo hand rub make generalisability of the results debatable. No confidence intervals reported

White 2001 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised trial", but sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blind, placebo-controlled, cluster-randomised trial. Randomisation was by classroom and the placebo hand rub was indistinguishable from the active ingredient
Incomplete outcome data (attrition bias) All outcomes	High risk	Partial reporting of outcomes, numerators and denominators
Selective reporting (reporting bias)	High risk	Poor reporting

White 2003

Methods	Prospective, open, cohort study carried out at the University of Colorado, Boulder campus during 8 weeks in the autumn-winter of 2002. The study aimed at assessing the effects of hand hygiene on URTIs and absenteeism. Allocation was by residence hall with 2 halls doing "knowledge studies" being allocated, one to each arm
Participants	430 students aged around 18 mainly females were recruited but only 188 in the intervention cluster and 203 in the control cluster completed at least 3 weeks' follow up. Students were recruited with cash incentives. No reasons for attrition are given
Interventions	Education programme and alcohol gel adjunct to handwashing in residence halls versus standard hygiene
Outcomes	Laboratory: in vitro testing of the antibacterial and antiviral properties of the hand rub Effectiveness: URTI (at least 2 symptoms with one of them lasting at least 2 to 3 days. List of symptoms as follows: sore throat, stuffy nose, ear pain, painful/swollen neck, cough, chest congestion, sinus pain, fever, working days lost). Weekly surveys were carried out before during and after the study Safety: N/A
Notes	Risk of bias: medium Notes: the authors conclude that the intervention resulted in significantly fewer symptoms (reductions of 14.8% to 39.9 %) and absenteeism (40% reduction). Unexplained attrition and unknown effect of cash incentives. Relatively unclear definition of illness with a hint of a sensitivity analysis in the footer to a table

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A

White 2003 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Wu 2004

Methods	Case-control study carried out on the Beijing SARS outbreak to assess the reasons for the insurgence of SARS cases in people who had no apparent contact with a SARS case
Participants	Description of cases: 94 probable or suspected SARS cases (Ministry of Health of China definitions) hospitalised during the period 28 April 2003 to 9 June 2003, aged 14 or more and non-HCWs with no known or reported no close contact with probably or suspected SARS cases. Fifty percent of cases were males with a median age of 29 years. The definition changed after 3 May to include those with symptoms who travelled to or resided in areas with known recent SARS activity but did not necessarily have contact with an index case. No laboratory confirmation of SARS was included in the definition which was purely practical (i.e. clinical-anamnestic). However antibody titres were taken several weeks after symptoms had abated. Close contacts (which played a part in the earlier case definition) were defined as persons who shared utensils, meals, residence hospital room or transportation vehicle with a suspected SARS or those who visited or came into contact with body fluids up to 14 days prior to the development of the index case's symptoms. Cases and controls were interviewed during the period 3 to 16 June Description of controls: 281 controls selected each by telephone random number change of last digits of the cases' phone numbers. This was aimed at providing neighbouring matching. Controls were interviewed by 4 July 2003 Seven controls (2 matched sets) were excluded because they were aged less than 14 and 7 matched sets were excluded because the case was reclassified as a HCW Cases and controls were interviewed for the 2 weeks preceding symptoms
Interventions	Always wearing a mask Intermittently wearing a mask Washing hands Owning a pet Visiting a farmer's market Visited clinics, eaten out or taken taxis
Outcomes	SARS
Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls) Notes: the authors conclude that cases were more likely than controls to have chronic pathologies (OR 4.1, 95% CI 1.8 to 9.3) or have visited fever clinics (OR 13.4, 95% CI 3.8 to 46.7), eaten out (OR 2.3, 95% CI 1.2 to 4.5) or taken taxis more than once a week (OR 3.2, 95% CI 1.3 to 8.0). In other words, unrecognised sources of transmission were present in the community. Always wearing a mask use was strongly protective (70% reduction in risk OR 0.3, 95% CI 0.2 to 0.7) and even wearing one intermittently with a smaller significant reduction in risk (OR 0.5, 95% CI 0.2 to 0.9) and so was always washing hands after returning home (OR 0.3, 95% CI 0.2 to 0.7) and owning a pet (OR 0.4, 95% CI 0.2 to 0.9) and visiting a

Wu 2004 *(Continued)*

farmer's market (OR 0.4, 95% CI 0.2 to 0.8). Of great interest is the role of fever clinics in spreading the disease, probably because of poorly-implemented isolation and triage procedures. A fascinating study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Yen 2006

Methods	Prospective cohort study performed in a 67-bed military hospital in Taiwan to assess the effectiveness of the integrated infection control strategy by comparing the rate of SARS transmission in HCWs in the study hospital with that in other major hospitals in Taiwan without the integrated infection control strategy
Participants	Healthcare workers (HCWs) of a 67-bed military hospital, that was the study hospital. Eighty-six hospitals were used as comparison hospitals with a total of 746 negative pressure isolation rooms (NPIR beds), caring for SARS patients without the integrated infection control strategy. All HCWs in this group were trained before the SARS epidemic in Taiwan through a national regulation for a standard nosocomial infection control programme, with infectious diseases physicians/infection control nurses available in each regional and tertiary hospital
Interventions	Integrated infection control strategy (consisting of patient traffic into hospital, zone of risks and extensive installation of alcohol dispensers for glove-on hand-rubbing) versus standard nosocomial infection control programme
Outcomes	Serological evidence: yes Effectiveness: SARS (definition?) Safety: N/A
Notes	Risk of bias: high The authors conclude that the integrated infection control strategy appeared to be effective in reducing the incidence of HCWs contracting SARS. Point estimates? 95% CIs. The advantages included rapid implementation without negative pressure isolation rooms, flexibility to transfer patients, and re-enforcement for HCWs to comply with infection control procedures, especially handwashing. The efficacy and low cost are major advantages, especially in countries with large populations at risk and fewer economic resources

Yen 2006 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Yin 2004

Methods	Case-control study carried out in 10 hospitals of Guangdong province, China, comparing the rate of usage of protective measures in HCWs with SARS and without SARS. The rate of exposure to SARS between 2 groups was similar. The data were obtained by questionnaire. Limited information is available from the abstract and from partial translation of the original text in Chinese
Participants	Description of cases: 77 HCWs who had contracted SARS Description of controls: 180 HCWs who had not contracted SARS Both cases and controls had been working in isolation units and took part in delivering first aid and caring for SARS patients. No significant differences were noted between cases and controls for a series of variables
Interventions	Mouth mask Thick mouth mask (more than 12 layers of cloths) Use one-off paper mouth mask Never use mouth mask Wear eye mask if necessary Protecting for nose and eyes mucosa Wear shoe gloves Wear barrier gown Wear hand gloves Rinse out mouth Take bath and change clothes before home Check mouth mask Intake oseltamivir phosphate orally Never eating and smoking in the ward Handwashing and disinfection Using nose clamp Intake herbal Banlangen (Indigowoad Root) orally
Outcomes	SARS
Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls)

Yin 2004 *(Continued)*

	Notes: the authors conclude that the combination of mouth mask, barrier gown, gloves, goggles, footwear, rinse out mouth and take bath and change clothes before provided significant protection and that there was a dose-response relation with the more interventions used in combination the better the protection. Single measures such as wearing of a mask (OR 0.78, 95% CI 0.60 to 0.99), goggles (OR 0.20, 95% CI 0.10 to 0.41) and footwear (OR, 0.58 95% CI 0.39 to 0.86) were effective Limited information is available from the abstract and from partial translation of the original text in Chinese

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Yu 2007

Methods	Case-control study to analyse the risk factors associated with nosocomial outbreaks of SARS in hospital wards in Guangzhou and Hong Kong, China. The study was designed with the individual hospital wards as the units for data collection and analysis. Case wards were hospital wards in which super spreading events of SARS occurred, and control wards were hospital wards in which patient(s) with SARS were admitted, but no super spreading events occurred. A super spreading event is defined as the development of ≥ 3 new cases of SARS in a ward during the period from 2 to 10 days after the admission of an identifiable index patient or as the development of a cluster of ≥ 3 new cases of SARS in a ward during a period of 8 days but without any known sources of SARS
Participants	Eighty-six wards in 21 hospitals in Guangzhou and 38 wards in 5 hospitals in Hong Kong were included in the study. One ward in Guangzhou and 2 wards in Hong Kong did not participate and they were excluded from the analysis
Interventions	Information related to 2 factors was collected: (1) environmental and administrative factors and (2) host factors. Environmental and administrative factors included physical factors, procedural or situational factors, and administrative factors pertaining to each ward. Host factors included symptoms, severity or dependency (for activities of daily living and behaviour changes), treatment or intervention, and comorbidity of the identified index patient in a case ward or in the first patient with SARS admitted in a control ward
Outcomes	Laboratory: serological evidence: no Effectiveness: SARS (no definition) Safety: N/A

Yu 2007 *(Continued)*

Notes	The authors conclude that environmental risk factors were significantly associated with the occurrence of a super spreading event (clustering of ≥ 3 cases) included minimum distance between beds of ≤ 1 m and performance of resuscitation in the ward. Use of BIPAP ventilation and use of oxygen were the significant risk factors associated with the host patient. Of the administrative factors, allowing staff with symptoms to work also increased the risk. Providing adequate washing or changing facilities for staff was protective As disaggregate data are not reported we did not extract numerator/denominator data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

AEs: adverse events
AFH: Armed Forces Hospital
ARI: acute respiratory infection
ASR: adverse skin reactions
A&E: accident and emergency
BIPAP: Bilevel Positive Airway Pressure
CCC: Child Care Centre
CIs: confidence intervals
CDC: Centers for Disease Control and Prevention
CMF:citric acid: malic acid: sodium lauryl sulfate (a virucidal mixture added to tissue paper)
CoV: coronavirus
C-RCT: cluster-randomised controlled trial
CXR: chest X-ray
DCC: daycare centre
FRI: febrile respiratory illness
GI: gastro-intestinal
HCW: healthcare worker
HFH: Hanoi French Hospital
HH: hand hygiene
HR: high risk
ICU: intensive care unit
ILI: influenza-like illness
IRR: incident rate ratio
ITT: intention-to-treat
LRTI: lower respiratory tract infection
m: metre
MCU: medical convalescent unit
MDCK: Madin Darby canine kidney cell line
MS: monkey-derived cell line

N/A: not applicable
NICU: neonatal intensive care unit
NOS: Newcastle-Ottawa Scales
NTS: National Skin Centre
OR: odds ratio
PCR: polymerase chain reaction
PCU: physical conditioning unit
PPE: personal protective equipment
RCT: randomised controlled trial
RDS: respiratory distress syndrome
RR: risk ratio
RTI: respiratory tract infection
RT-PCR: reverse-transcriptase polymerase chain reaction
RSV: respiratory syncytial virus
SAB: surfactant, allantoin and benzalkonium chloride
SARS: severe acute respiratory syndrome
SD: standard deviation
SOPs: standard operating procedures
S/S: signs/symptoms
SOB: shortness of breath
SCBU: special care baby unit
UHR-I: ultra high-risk infection
UHR-S: ultra high-risk SARS
URTI: upper respiratory tract infection
WBC: white blood cell
WHO: World Health Organization

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abou El Hassan 2004	Topic completely extraneous
Amirav 2005	Randomised controlled trial of aerosol treatment
Anderson 2004	Mathematical model with interesting discussion of interaction between public health measures
Anonymous 2002	News item
Anonymous 2003	No data presented
Anonymous 2004	News item
Anonymous 2005a	News item
Anonymous 2005b	News item
Anonymous 2005c	News item
Apisarnthanarak 2009	Intervention bundle not broken down
Apisarnthanarak 2010	Participants took antivirals
Aragon 2005	Descriptive paper (non-comparative). Has no viral outcomes
Barros 1999	Correlational study between incidence of upper respiratory tract infection (URTI) and factors such as overcrowding

Study	Reason for exclusion
Bauer 2009	Historical comparison with RSV gammaglobulin among interventions
Bell 2004	Has unpublished entry exit screening data and extensive references but no comparative data
Bellissimo-Rodrigues 2009	Intervention is chlorexidine
Ben-Abraham 2002	Exclude - bacterial illness only
Black 1981	Diarrhoea only outcome
Borkow 2010	No human beings involved
Bouadma 2010	Hospital based ventilator routine
Breugelmans 2004	Description of risk factors in aircraft
Cai 2009	Compliance study
Cantagalli 2010	Outcome outside inclusion criteria
Carbonell-Estrany 2008	Immunoglobulin intervention and descriptive review
Carter 2002	News item
Castillo-Chavez 2003	Editorial
Cava 2005a	Survey of quarantinees' views
Cava 2005b	Personal experiences of quarantine
CDC 2003	Case reports
Chai 2005	Letter - about MRSA
Chaovavanich 2004	Case report
Chau 2003	No original retrievable data. Mathematical model fitting expected to observed cases with quarantine in the SARS of Hong Kong
Chau 2008	Audit of infection control procedures and compliance with guidelines
Chen 2007	An assessment of the impact of different handwashing teaching methods. No clinical outcomes
Cheng 2010	Confounded by antiviral use for post-exposure prophylaxis
Chia 2005	Knowledge survey
Clynes 2010	Letters
Cowling 2007	Epidemiology, non-comparative, non-interventions study
Daniels 2010	Commentary
Daugherty 2008	No free data presented

Study	Reason for exclusion
Davies 1994	Antibody titres as outcomes with so many biases that interpretation of study is problematic
Day 1993	No acute respiratory infection outcome data
Day 2006	Mathematical model; no new data
Dell'Omodarme 2005	Probabilistic and Bayesian mathematical model of screening at entry
Desenclos 2004	Description of transmission
DiGiovanni 2004	Qualitative study of compliance factors in quarantine
Doebbeling 1992	RCT respiratory data not present. Only 3 viruses isolated in total with no viral typing available
Dwosh 2003	Case series
Edmonds 2010	Lab study
Fendler 2002	Cohort study badly biased with differential health profiles and healthcare workers dependency in intervention and control semi-cohorts. No attempt at adjusting for confounders was made. No denominators available
Flint 2003	Description of spread in aircraft and non-comparative data
Fung 2004	Non-comparative
Garcia 2010	Commentary
Gaydos 2001	Editorial linked to Ryan 2001
Gensini 2004	Interesting historical review
Giroud 2002	Non-clinical outcomes
Glass 2006	Mathematical model - no original data presented
Goel 2007	Non-comparative study
Gomersall 2006	Non-comparative study
Gore 2001	Summary of Dyer 2000 (already included)
Gostin 2003	Not an analytical study
Gralton 2010	Review
Guinan 2002	It would appear that 9 classes took part and "acted as their own controls", but it is not clear if there was cross-over of classes or not. In addition the outcome is combined gastrointestinal/respiratory. The clue lies in the presence of a nested economic analysis which shows considerable savings in time for staff and pupils if the soap is used: in other words this is a (covert) publicity study
Gupta 2005	Economic model - no new data
Gwaltney 1982	No breakdown of cases by arm given

Study	Reason for exclusion
Han 2003	Non-comparative
Hayden 1985	This is a RCT with laboratory-induced colds, small numbers and uncertain numerators but almost certainly because of the unique laboratory conditions (placebo tissues not being a placebo at all) of impossible generalisation. It was a pilot to the far bigger trial by Farr 1988a; Farr 1988b
Hendley 1988	Inappropriate intervention
Hens 2009	Model
Heymann 2009	Already in review as Heymann 2004
Hilburn 2003	No ARI/viral outcomes (e.g. URTIs)
Hilmarsson 2007	Animal study
Hirsch 2006	Study tested pharmacological interventions
Ho 2003	Descriptive review
Hsieh 2007	Mathematical model
Hugonnet 2007	Letter without any data
Jiang 2003	Two papers probably the same paper in different versions: Jiang SP, Huang LW, Wang JF, Wu W, Yin SM, Chen WX, et al. [A study of the architectural factors and the infection rates of healthcare workers in isolation units for severe acute respiratory syndrome]. [Chinese] Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih [Chinese Journal of Tuberculosis & Respiratory Diseases]. 26(10):594-7, 2003 Oct
Johnson 2009	Outcomes are non-clinical
Jones 2005	Historical account
Kaydos-Daniels 2004	Not an analytical study
Kelso 2009	Model
Khaw 2008	Assessing the efficacy of O_2 delivery
Kilabuko 2007	Aetiological study
Kosugi 2004	Non-comparative study
Lam 2004	Outcomes were generic (infection rates). No laboratory data available for viral diagnosis
Lange 2004	No data presented
Larson 2004	Inappropriate outcomes
Larson 2005	Cluster-RCT comparing the effects of 2 hand hygiene regimens on infection rates and skin condition and microbial counts of nurses' hands in neonatal intensive care units. Outcomes were generic (for example, pneumonia and microbial counts of participants' skin). No laboratory data available for viral diagnosis
Lau 2004b	Attitude survey

Study	Reason for exclusion
Lau 2005	Herbal remedy effectiveness assessment
Lee 2005	Descriptive study of risk and protective factors of transmission in households. No assignment took place
Lee 2010	Cohort study; unclear numbers were vaccinated against influenza
Lipsitch 2003	Mathematical model fit to evidence
Luckingham 1984	Historical report on Tucson experience during Spanish flu pandemic
Ma 2004	Case-control study of risk factors for SARS
MacIntyre 2010	Commentary on Cowling 2009
Malone 2009	Model
Marin 1991	Viral resistance study
McSweeny 2007	Historical description
Mielke 2009	Review
Mikolajczyk 2008	No intervention
Monsma 1992	Non-comparative study
Nishiura 2009	Model
O'Callaghan 1993	Letter linked to Isaacs 1991
Olsen 2003	Description of transmission
Ooi 2005	Descriptive study but with interesting organisational chart
Orellano 2010	Confounded by antiviral use
Panchabhai 2009	Pharma intervention
Pang 2004	Descriptive study of Beijing outbreak. Some duplicate data in common with Pang 2003
Pittet 2000	Analysis of relationship between handwashing compliance campaign and nosocomial bacterial infections (e.g. MRSA)
Prasad 2004	Letter about retrospective cohort - behavioural
Rabenau 2005	In vitro test of several disinfectants
Reynolds 2008	Describes the psychological effects of quarantine
Richardson 2010	Non-clinical study
Riley 2003	Mathematical model fit to evidence
Rodriguez 2009	A “reasonable attempt at minimizing bias” (see inclusion criteria) does not include absenteeism

Study	Reason for exclusion
Rosenthal 2005	Outcomes were generic (for example, pneumonia, URTIs). No laboratory data available for viral diagnosis
Safiulin 1972	Non-comparative set of studies with no clinical outcomes
Sandrock 2008	Review
Satter 2000	Experiment assessing virucidal activity of finger tip surface - no clinical outcome data
Schull 2007	Describes the impact of SARS in a Toronto study
Seal 2010	Lab study
Seale 2009	Study looking at whether using respirators in A&E department is feasible
Sizun 1996	This is a review, with no original data presented
Stebbins 2009	Attitude survey
Stoner 2007	No study data available
Stukel 2008	Impact of the SARS disruption on care/mortality for other pathologies (for example, acute myocardial infarction). There are no interventions and outcomes are unrelated to acute respiratory infections
Svoboda 2004	Descriptive study with before and after data but shifting denominators
Tracht 2010	Model
Ueno 1990	Experimental study. No clinical intervention
van der Sande 2008	Laboratory study without any clinical outcomes
Viscusi 2009a	Lab study
Viscusi 2009b	Lab study
Wang 2003	Descriptive study
Wang 2005	Case-control study of susceptibility factors
Weber 2004	Editorial linked to Larson 2004
Wen 2010	Lab study
White 2005	Redundant publication of White 2003
Wilczynski 1997	Clinical trial of the effects of breast feeding
Wilder-Smith 2003	Description of risk factors in aircraft
Wilder-Smith 2005	Descriptive review
Wong 2005	Attitude survey

Study	Reason for exclusion
Yen 2010	Model
Yu 2004	Description of transmission
Zamora 2006	Head-to-head comparison of two sets of PPEs with no controls and no clinical outcomes
Zhai 2007	Non-comparative study
Zhao 2003	CCT of SARS treatment

A&E: accident and emergency
ARI: acute respiratory infection
CCT: controlled clinical trial
MRSA: methicillin-resistant *Staphylococcus aureus*
RCT: randomized controlled trial
RSV: respiratory syncytial virus
PPE: personal protective equipment
PEP: post-exposure prophylaxis
SARS: severe acute respiratory syndrome
URTI: upper respiratory tract infection

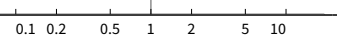
DATA AND ANALYSES

Comparison 1. Case-control studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Thorough disinfection of living quarters	1	990	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.23, 0.39]
2 Frequent handwashing	7	2825	Odds Ratio (M-H, Fixed, 95% CI)	0.54 [0.44, 0.67]
3 Wearing mask	7	3216	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.26, 0.39]
4 Wearing N95 respirator	3	817	Odds Ratio (M-H, Fixed, 95% CI)	0.17 [0.07, 0.43]
5 Wearing gloves	6	1836	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.23, 0.45]
6 Wearing gowns	5	1460	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.24, 0.45]
7 All interventions	2	369	Odds Ratio (M-H, Fixed, 95% CI)	0.09 [0.02, 0.35]
8 Use of eye protection (mask/goggles)	3	1482	Odds Ratio (M-H, Fixed, 95% CI)	0.10 [0.05, 0.17]
9 Nose wash	2	1225	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.16, 0.57]

Analysis 1.1. Comparison 1 Case-control studies, Outcome 1 Thorough disinfection of living quarters.

Study or subgroup	Cases n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Lau 2004a	154/330	492/660		100%	0.3[0.23,0.39]
Total (95% CI)	**330**	**660**		**100%**	**0.3[0.23,0.39]**
Total events: 154 (Cases), 492 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=8.51(P<0.0001)					



Favours disinfection — Favours control

Analysis 1.2. Comparison 1 Case-control studies, Outcome 2 Frequent handwashing.

Study or subgroup	Cases n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen 2009	45/91	323/657		15.86%	1.01[0.65,1.57]
Lau 2004a	61/330	222/660		48.18%	0.45[0.32,0.62]
Nishiura 2005	15/25	56/90		3.89%	0.91[0.37,2.25]
Seto 2003	10/13	227/241		2.14%	0.21[0.05,0.83]
Teleman 2004	27/36	46/50		3.84%	0.26[0.07,0.93]
Wu 2004	73/94	253/281		11.32%	0.38[0.21,0.72]
Yin 2004	28/77	97/180		14.77%	0.49[0.28,0.85]
Total (95% CI)	**666**	**2159**		**100%**	**0.54[0.44,0.67]**
Total events: 259 (Cases), 1224 (Control)					
Heterogeneity: Tau^2=0; Chi^2=14.82, df=6(P=0.02); I^2=59.52%					
Test for overall effect: Z=5.83(P<0.0001)					

Favours handwashing — Favours control

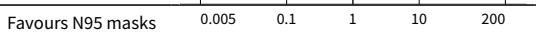
Analysis 1.3. Comparison 1 Case-control studies, Outcome 3 Wearing mask.

Study or subgroup	Cases n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen 2009	59/91	541/657		13.46%	0.4[0.25,0.64]
Lau 2004a	93/330	388/660		54.01%	0.28[0.21,0.37]
Liu 2009	15/51	259/426		11.37%	0.27[0.14,0.51]
Nishiura 2005	8/25	35/90		3.01%	0.74[0.29,1.9]
Seto 2003	0/13	51/241		1.58%	0.14[0.01,2.34]
Wu 2004	25/94	121/281		12.95%	0.48[0.29,0.8]
Yin 2004	68/77	178/180		3.62%	0.08[0.02,0.4]
Total (95% CI)	**681**	**2535**		**100%**	**0.32[0.26,0.39]**
Total events: 268 (Cases), 1573 (Control)					
Heterogeneity: Tau^2=0; Chi^2=10.65, df=6(P=0.1); I^2=43.66%					
Test for overall effect: Z=11.07(P<0.0001)					

Favours masks — Favours control

Analysis 1.4. Comparison 1 Case-control studies, Outcome 4 Wearing N95 respirator.

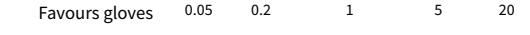
Study or subgroup	Cases n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Liu 2009	2/51	31/426		18.86%	0.52[0.12,2.24]
Seto 2003	0/13	92/241		28.88%	0.06[0,1.02]
Teleman 2004	3/36	23/50		52.26%	0.11[0.03,0.39]
Total (95% CI)	**100**	**717**		**100%**	**0.17[0.07,0.43]**
Total events: 5 (Cases), 146 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.26, df=2(P=0.2); I^2=38.56%					
Test for overall effect: Z=3.72(P=0)					



Favours N95 masks | Favours control

Analysis 1.5. Comparison 1 Case-control studies, Outcome 5 Wearing gloves.

Study or subgroup	Cases n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen 2009	10/91	257/657		41.59%	0.19[0.1,0.38]
Liu 2009	27/30	337/346		4.02%	0.24[0.06,0.94]
Nishiura 2005	8/25	30/90		6.63%	0.94[0.36,2.43]
Seto 2003	4/13	117/241		6.2%	0.47[0.14,1.57]
Teleman 2004	10/36	22/50		9.94%	0.49[0.2,1.23]
Yin 2004	37/77	136/180		31.63%	0.3[0.17,0.52]
Total (95% CI)	**272**	**1564**		**100%**	**0.32[0.23,0.45]**
Total events: 96 (Cases), 899 (Control)					
Heterogeneity: Tau^2=0; Chi^2=8.57, df=5(P=0.13); I^2=41.63%					
Test for overall effect: Z=6.61(P<0.0001)					



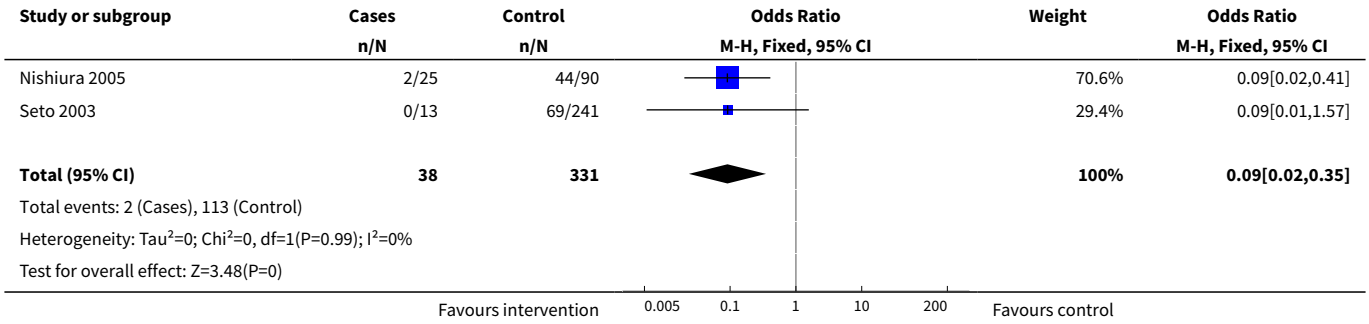
Favours gloves | Favours control

Analysis 1.6. Comparison 1 Case-control studies, Outcome 6 Wearing gowns.

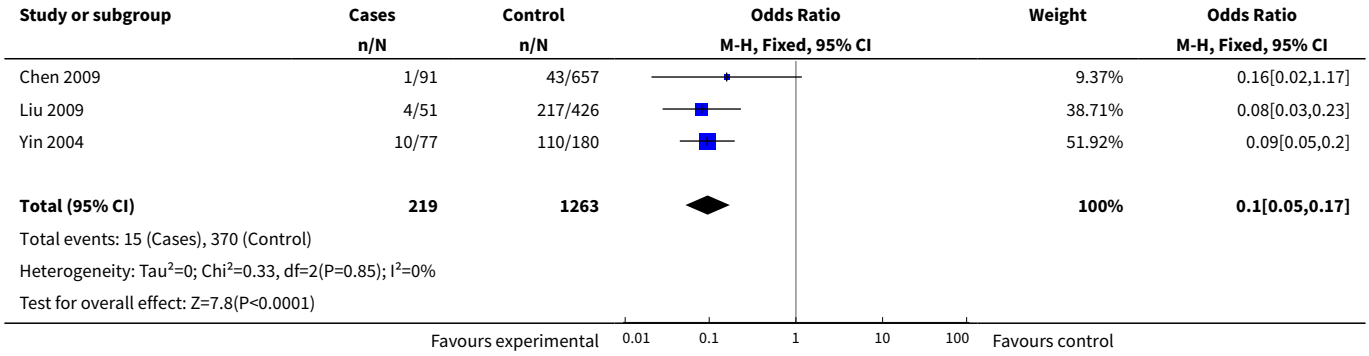
Study or subgroup	Cases n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen 2009	49/91	468/657		40.26%	0.47[0.3,0.74]
Nishiura 2005	2/25	25/90		7.66%	0.23[0.05,1.03]
Seto 2003	0/13	83/241		6.75%	0.07[0,1.2]
Teleman 2004	5/36	13/50		7.18%	0.46[0.15,1.43]
Yin 2004	27/77	128/180		38.15%	0.22[0.12,0.39]
Total (95% CI)	**242**	**1218**		**100%**	**0.33[0.24,0.45]**
Total events: 83 (Cases), 717 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.16, df=4(P=0.19); I^2=35.07%					
Test for overall effect: Z=6.83(P<0.0001)					

Favours gowns | Favours control

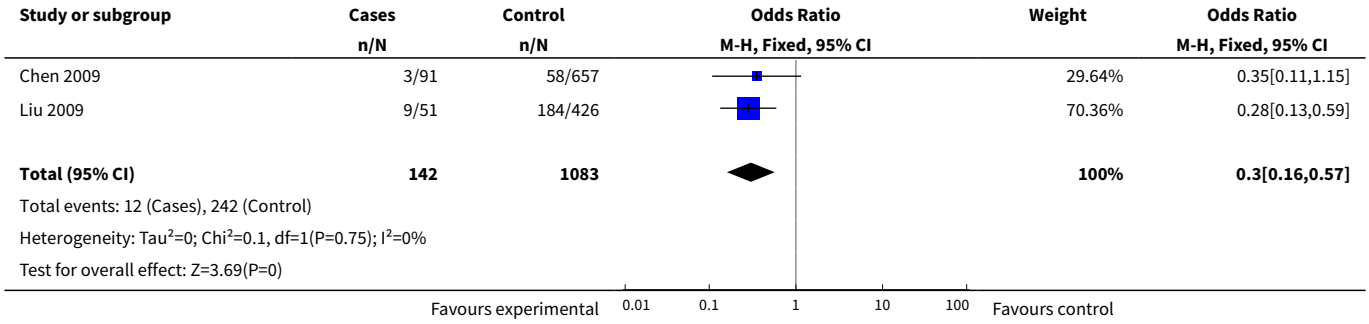
Analysis 1.7. Comparison 1 Case-control studies, Outcome 7 All interventions.



Analysis 1.8. Comparison 1 Case-control studies, Outcome 8 Use of eye protection (mask/goggles).



Analysis 1.9. Comparison 1 Case-control studies, Outcome 9 Nose wash.



ADDITIONAL TABLES

Table 1. Significance in multivariable analysis of interventions to prevent SARS

Outcome or subgroup	Studies	How many statistically significant on multivariable analysis

Table 1. Significance in multivariable analysis of interventions to prevent SARS *(Continued)*

1.1 Thorough disinfection of living quarters	1	1
1.2 Frequent handwashing	7	4
1.3 Wearing mask	7	6
1.4 Wearing N95 respirator	3	2
1.5 Wearing gloves	6	2
1.6 Wearing gowns	5	2
1.7 All interventions	2	1
1.8 Use of eye protection (mask/goggles)	3	1
1.9 Nose wash	2	1

Table 2. Summary of main results

	RCT (N = 6)	C-RCT (N = 17)	Case-control (N = 9)	Prospective cohort (N = 16)	Retrospective cohort (N = 6)	Before-after (N = 13)
Handwashing	-	3 trials in children effective 1 trial in households effective if implemented < 36 hours after onset	7 studies OR 0.54 (95% CI 0.44 to 0.67)	2 studies found effect, 2 no effect on ARIs	-	1 study in military recruits: > 5 times per day effective
Handwashing with antiseptic	-	3 trials in children: 2 antiseptic more effective 1 antiseptic = soap	-	2 studies added effect of antiseptic 1 study: no difference	-	-
Handwashing and surface disinfection	-	4 trials in children and families: 2 studies effective	-	-	-	1 study in school effective
Hand disinfection	3 trials effective	-	-	-	-	-
Gargling with iodine	1 trial effective	-	-	-	-	-
Nose wash	-	-	2 studies OR 0.30 (95% CI 0.16 to 0.57)	-	-	-
Virucidal tissues	-	1 trial: small effect 2 trials: non-significant	-	1 study effective	-	-

Table 2. Summary of main results *(Continued)*

Disinfection of living quarters	-	-	1 study OR 0.30 (95% CI 0.23 to 0.39)	-	-	-
Use of eye protection			3 studies OR 0.10 (95% CI 0.05 to 0.17)			
Barriers (masks, gloves, gowns combined)	-	-	2 studies OR 0.09 (95% CI 0.02 to 0.35)	1 study: masks + gowns no added effect to handwashing	-	3 studies: combined with isolation effective 1 study: mask and gown added to isolation not effective 1 study: gowns and gloves effective in paediatric ward
Mask	1 trial: surgical masks no effect	1 trial: no effect added to handwashing 1 trial: no effect of P2 mask 1 trial: added to handwashing effective if implemented < 36 hours after onset of illness 1 trial: added to handwashing effective during weeks 4 to 6 1 trial: no effect added to handwashing	7 studies OR 0.32 (95% CI 0.26 to 0.39)	3 studies: masks effective (with air filter safer)	1 study: harm related to mask wearing	1 study in children's hospital effective
N95 respirator	1 trial: surgical masks non-inferior to N95 respirators	-	3 studies OR 0.17 (95% CI 0.07 to 0.43)	-	1 study: harm related to N95 respirator wearing	-
Gloves	-	-	6 studies OR 0.32 (95% CI 0.23 to 0.45)	-	1 study: harm related to gloves	-
Gowns	-	-	5 studies OR 0.33 (95% CI 0.24 to 0.45)	-	1 study: harm related to gown wearing	1 study: no added effect in neonatal ICU

Table 2. Summary of main results *(Continued)*

Distancing	-	-	-	1 study: no effect in military recruits 2 studies: cohorting in hospitals effective	1 study: cohorting in paediatric wards effective 1 study in military hospital cohorting with handwashing and gowns effective	6 studies: early identification of cases and isolation effective
Quarantine	-	-	-	1 study: isolation of close contacts effective	1 study: isolation of close contacts effective 1 study: marginal non-significant benefit of border entry screening	-

ARI: acute respiratory infection
C-RCT: cluster-randomised controlled trial
ICU: intensive care unit
OR: odds ratio
RCT: randomised controlled trial

APPENDICES

Appendix 1. Previous search strategy

(Details of the search strategy used in the original review and the 2009 search strategy updates for MEDLINE, CENTRAL, EMBASE and CINAHL)

In the first publication of this review we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2006, issue 4); MEDLINE (1966 to November 2006); OLDMEDLINE (1950 to 1965); EMBASE (1990 to November 2006) and CINAHL (1982 to November 2006). The MEDLINE search terms were modified for OLDMEDLINE, EMBASE and CINAHL.

In this 2009 update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, issue 2); Ovid MEDLINE (2006 to May Week 1 2009); OLDMEDLINE (1950 to 1965); Ovid EMBASE (2006 to Week 18, 2009) and Ovid CINAHL (2006 to May Week 1 2009).

Ovid MEDLINE
1 exp Influenza/
2 influenza.tw.
3 flu.tw.
4 exp Common Cold/
5 common cold.tw.
6 exp Rhinovirus/
7 rhinovirus*.tw.
8 exp Adenoviridae/
9 adenovirus*.tw.
10 exp Coronavirus/
11 exp Coronavirus Infections/
12 coronavirus*.tw.
13 exp Respiratory Syncytial Viruses/
14 exp Respiratory Syncytial Virus Infections/
15 respiratory syncytial virus*.tw.
16 respiratory syncythial virus.tw.
17 exp Parainfluenza Virus 1, Human/
18 exp Parainfluenza Virus 2, Human/
19 exp Parainfluenza Virus 3, Human/
20 exp Parainfluenza Virus 4, Human/

21 (parainfluenza or para-influenza or para influenza).tw.
22 exp Severe Acute Respiratory Syndrome/
23 (severe acute respiratory syndrome or SARS).tw.
24 acute respiratory infection*.tw.
25 acute respiratory tract infection*.tw.
26 or/1-25 (59810)
27 exp Hand Washing/
28 (handwashing or hand washing or hand-washing).tw.
29 hand hygiene.tw.
30 (sanitizer* or sanitiser*).tw.
31 (cleanser* or disinfectant*).tw.
32 exp Gloves, Protective/
33 exp Gloves, Surgical/
34 glov*.tw.
35 exp Masks/
36 mask*1.tw.
37 exp Patient Isolators/
38 exp Patient Isolation/
39 patient isolat*.tw.
40 (barrier* or curtain* or partition*).tw.
41 negative pressure room*.tw.
42 reverse barrier nursing.tw.
43 Cross Infection/pc [Prevention]
44 school closure*.tw.
45 (clos* adj3 school*).tw.
46 mass gathering*.tw.
47 public gathering*.tw.
48 (ban or bans or banned or banning).tw.
49 (outbreak* adj3 control*).tw.
50 distancing.tw.
51 exp Quarantine/
52 quarantine*.tw.
53 or/27-49
54 26 and 53
55 (animals not (humans and animals)).sh.
56 54 not 55

CENTRAL search strategy

#1 MeSH descriptor Influenza, Human explode all trees
#2 influenza:ti,ab,kw
#3 flu:ti,ab,kw
#4 MeSH descriptor Common Cold explode all trees
#5 "common cold":ti,ab,kw
#6 MeSH descriptor Rhinovirus explode all trees
#7 rhinovirus*:ti,ab,kw
#8 MeSH descriptor Adenoviridae explode all trees
#9 adenovirus*:ti,ab,kw
#10 MeSH descriptor Coronavirus explode all trees
#11 MeSH descriptor Coronavirus Infections explode all trees
#12 coronavirus*:ti,ab,kw
#13 MeSH descriptor Respiratory Syncytial Viruses explode all trees
#14 MeSH descriptor Respiratory Syncytial Virus Infections explode all trees
#15 respiratory syncytial virus*:ti,ab,kw
#16 respiratory syncythial virus*:ti,ab,kw
#17 MeSH descriptor Parainfluenza Virus 1, Human explode all trees
#18 MeSH descriptor Parainfluenza Virus 2, Human explode all trees
#19 MeSH descriptor Parainfluenza Virus 3, Human explode all trees
#20 MeSH descriptor Parainfluenza Virus 4, Human explode all trees
#21 (parainfluenza or para-influenza or para influenza):ti,ab,kw
#22 MeSH descriptor Severe Acute Respiratory Syndrome explode all trees
#23 (severe acute respiratory syndrome or SARS):ti,ab,kw

#24 acute respiratory infection*:ti,ab,kw
#25 acute respiratory tract infection*:ti,ab,kw
#26 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25)
#27 MeSH descriptor Handwashing explode all trees
#28 (handwashing or hand washing or hand-washing):ti,ab,kw
#29 hand hygiene:ti,ab,kw
#30 (sanitizer* or sanitiser*):ti,ab,kw
#31 (cleanser* or disinfectant*):ti,ab,kw
#32 MeSH descriptor Gloves, Protective explode all trees
#33 MeSH descriptor Gloves, Surgical explode all trees
#34 glov*:ti,ab,kw
#35 MeSH descriptor Masks explode all trees
#36 mask*:ti,ab,kw
#37 MeSH descriptor Patient Isolators explode all trees
#38 MeSH descriptor Patient Isolation explode all trees
#39 (barrier* or curtain* or partition*):ti,ab,kw
#40 negative NEXT pressure NEXT room*:ti,ab,kw
#41 "reverse barrier nursing":ti,ab,kw
#42 MeSH descriptor Cross Infection explode all trees with qualifier: PC
#43 school NEXT closure*:ti,ab,kw
#44 (clos* NEAR/3 school*):ti,ab,kw
#45 mass NEXT gathering*:ti,ab,kw
#46 public NEXT gathering*:ti,ab,kw
#47 ("ban" or "bans" or banned or banning):ti,ab,kw
#48 (outbreak* NEAR/3 control*):ti,ab,kw
#49 distancing:ti,ab,kw
#50 MeSH descriptor Quarantine explode all trees
#51 quarantine*:ti,ab,kw
#52 (#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51)
#53 (#26 AND #52)

Ovid EMBASE search strategy

1 exp Influenza/
2 influenza.tw.
3 flu.tw.
4 exp Common Cold/
5 common cold.tw.
6 exp Human Rhinovirus/
7 rhinovirus*.tw.
8 exp Adenovirus/
9 adenovirus*.tw.
10 exp Coronavirus/
11 coronavirus*.tw.
12 exp Respiratory Syncytial Pneumovirus/
13 respiratory syncytial virus*.tw.
14 respiratory syncythial virus.tw.
15 (parainfluenza or para-influenza or para influenza).tw.
16 exp Severe Acute Respiratory Syndrome/
17 (severe acute respiratory syndrome or SARS).tw.
18 acute respiratory infection*.tw.
19 acute respiratory tract infection*.tw.
20 or/1-19
21 exp Hand Washing/
22 (handwashing or hand washing or hand-washing).tw.
23 hand hygiene.tw.
24 (sanitizer$ or sanitiser$).tw.
25 (cleanser$ or disinfectant$).tw.
26 exp Glove/
27 exp Surgical Glove/

28 glov*.tw.
29 exp Mask/
30 mask*1.tw.
31 patient isolat*.tw.
32 (barrier* or curtain* or partition*).tw.
33 negative pressure room*.tw.
34 reverse barrier nursing.tw.
35 Cross Infection/pc [Prevention]
36 school closure*.tw.
37 (clos* adj3 school*).tw.
38 mass gathering*.tw.
39 public gathering*.tw. (5)
40 (ban or bans or banned or banning).tw.
41 (outbreak* adj3 control*).tw.
42 distancing.tw.
43 quarantine*.tw.
44 or/21-43
45 20 and 44

EBSCO CINAHL search strategy

S26 S10 and S24
S25 S10 and S24
S24 S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or 23 or S24
S23 TI outbreak* N3 control* or AB outbreak* N3 control*
S22 TI (school closure* or mass gathering* or public gathering* or ban or bans or banned or banning or distancing or quarantine*) or AB (school closure* or mass gathering* or public gathering* or ban or bans or banned or banning or distancing or quarantine*)
S21 TI (patient isolat* or barrier* or curtain* or partition* or negative pressure room* or reverse barrier nursing) or AB (patient isolat* or barrier* or curtain* or partition* or negative pressure room* or reverse barrier nursing)
S20 TI (glov* or mask*) or AB (glov* or mask*)
S19 TI (handwashing or hand washing or hand-washing or hand hygiene) or AB (handwashing or hand washing or hand-washing or hand hygiene)
S18 (MH "Quarantine")
S17 (MM "Cross Infection")
S16 (MH "Isolation, Reverse")
S15 (MH "Patient Isolation+")
S14 (MH "Respiratory Protective Devices")
S13 (MH "Masks")
S12 (MH "Gloves")
S11 (MH "Handwashing+")
S10 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9
S9 TI (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythial virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory syndrome or SARS or respiratory viral infection* or viral respiratory infection*) or AB (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythial virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory syndrome or SARS or respiratory viral infection* or viral respiratory
infection*)TI (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythial virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory (syndrome or SARS or respiratory viral infection* or viral respiratory infection*) or AB (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythial virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory syndrome or SARS or respiratory viral infection* or viral
respiratory infection*)
S8 (MH "SARS Virus")
S7 (MH "Severe Acute Respiratory Syndrome")
S6 (MH "Respiratory Syncytial Virus Infections")
S5 (MH "Respiratory Syncytial Viruses")
S4 (MH "Coronavirus+")
S3 (MH "Coronavirus Infections+")
S2 (MH "Common Cold")
S1 (MH "Influenza+")

Appendix 2. Embase.com search strategy, October 2010

The search strategy was broadened in 2010 to be more inclusive of new and emerging viruses.

'influenza'/exp AND [embase]/lim OR ('influenza virus a'/exp OR 'influenza virus b'/de OR 'influenza virus c'/de AND [embase]/lim) OR (influenza*:ab,ti OR flu:ab,ti AND [embase]/lim) OR ('common cold'/de AND [embase]/lim) OR ('common cold':ab,ti OR 'common colds':ab,ti AND [embase]/lim) OR ('human rhinovirus'/de AND [embase]/lim) OR (rhinovir*:ab,ti AND [embase]/lim) OR ('rhinovirus infection'/de AND [embase]/lim) OR ('adenovirus'/de OR 'human adenovirus'/exp AND [embase]/lim) OR ('human adenovirus infection'/exp AND [embase]/lim) OR (adenovir*:ab,ti AND [embase]/lim) OR ('coronavirus'/de OR 'sars coronavirus'/de AND [embase]/lim) OR (coronavir*:ab,ti AND [embase]/lim) OR ('coronavirus infection'/de AND [embase]/lim) OR ('severe acute respiratory syndrome'/de AND [embase]/lim) OR ('severe acute respiratory syndrome':ab,ti OR sars:ab,ti AND [embase]/lim) OR ('respiratory syncytial pneumovirus'/de AND [embase]/lim) OR ('respiratory syncytial virus infection'/de AND [embase]/lim) OR ('respiratory syncytial virus':ab,ti OR 'respiratory syncytial viruses':ab,ti OR rsv:ab,ti OR 'respiratory syncytial pneumovirus':ab,ti OR 'respiratory syncytial pneumoviruses':ab,ti AND [embase]/lim) OR ('parainfluenza virus'/exp AND [embase]/lim) OR (parainfluenza*:ab,ti OR 'para influenza':ab,ti OR 'para-influenza':ab,ti AND [embase]/lim) OR ('enterovirus'/de OR 'enterovirus infection'/de AND [embase]/lim) OR (enterovir*:ab,ti AND [embase]/lim) OR ('human parvovirus b19'/de OR 'bocavirus'/de AND [embase]/lim) OR (parvovirus*:ab,ti OR bocavirus*:ab,ti AND [embase]/lim) OR ('human metapneumovirus'/de AND [embase]/lim) OR (metapneumovir*:ab,ti AND [embase]/lim) OR ('parechovirus'/de AND [embase]/lim) OR (parechovirus*:ab,ti AND [embase]/lim) OR ('acute respiratory infection':ab,ti OR 'acute respiratory infections':ab,ti OR 'acute respiratory tract infection':ab,ti OR 'acute respiratory tract infections':ab,ti AND [embase]/lim) AND ('hand washing'/de AND [embase]/lim OR (handwashing:ab,ti OR 'hand washing':ab,ti OR 'hand-washing':ab,ti AND [embase]/lim) OR ('hand hygiene':ab,ti AND [embase]/lim) OR (sanitiser*:ab,ti OR sanitizer*:ab,ti OR cleanser*:ab,ti OR disinfectant*:ab,ti AND [embase]/lim) OR ('glove'/de OR 'surgical glove'/de AND [embase]/lim) OR (glov*:ab,ti AND [embase]/lim) OR ('mask'/de OR 'face mask'/de OR 'surgical mask'/de AND [embase]/lim) OR (mask:ab,ti OR masks:ab,ti OR respirator:ab,ti OR respirators:ab,ti AND [embase]/lim) OR ('protective clothing'/de OR 'protective equipment'/de AND [embase]/lim) OR ('patient isolator':ab,ti OR 'patient isolators':ab,ti OR 'patient isolation':ab,ti AND [embase]/lim) OR (cohorting:ab,ti OR 'cohort isolation':ab,ti AND [embase]/lim) OR (barrier*:ab,ti OR curtain*:ab,ti OR partition*:ab,ti AND [embase]/lim) OR ('negative pressure room':ab,ti OR 'negative pressure rooms':ab,ti AND [embase]/lim) OR ('reverse barrier nursing':ab,ti OR 'reverse-barrier nursing':ab,ti OR 'reverse barrier unit':ab,ti OR 'reverse-barrier unit':ab,ti AND [embase]/lim) OR (('cross infection' NEAR/2 prevent*):ab,ti AND [embase]/lim) OR ('infection control'/de AND [embase]/lim) OR ((school* NEAR/3 (clos* OR dismissal*)):ab,ti AND [embase]/lim) OR ('temporary closure':ab,ti OR 'temporary closures':ab,ti AND [embase]/lim) OR ('mass gathering':ab,ti OR 'mass gatherings':ab,ti AND [embase]/lim) OR ((public NEAR/2 (gathering* OR event*)):ab,ti AND [embase]/lim) OR (bans:ab,ti OR banning:ab,ti OR banned:ab,ti OR ban:ab,ti AND [embase]/lim) OR ((outbreak* NEAR/3 control*):ab,ti AND [embase]/lim) OR (distancing*:ab,ti AND [embase]/lim) OR (quarantine*:ab,ti AND [embase]/lim) OR ((protective NEAR/2 (cloth* OR garment* OR gown* OR device* OR equipment)):ab,ti AND [embase]/lim) OR (((protective OR preventive) NEAR/2 (procedure* OR behavior* OR behaviour*)):ab,ti AND [embase]/lim) OR ('personal protective':ab,ti OR 'personal protection':ab,ti AND [embase]/lim) OR ('isolation room':ab,ti OR 'isolation rooms':ab,ti OR 'isolation strategy':ab,ti OR 'isolation strategies':ab,ti AND [embase]/lim) OR ((distance NEAR/2 patient*):ab,ti AND [embase]/lim) OR (((spatial OR patient) NEAR/1 separation):ab,ti AND [embase]/lim)) AND ('randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp AND [embase]/lim OR (random*:ab,ti OR placebo*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR 'cross over':ab,ti OR 'cross-over':ab,ti OR volunteer*:ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR ((singl* OR doubl*) NEAR/2 (blind* OR mask*)):ab,ti AND [embase]/lim) OR ('controlled study'/de OR 'treatment outcome'/de OR 'major clinical study'/de OR 'clinical trial'/de AND [embase]/lim) OR (chang*:ab,ti OR evaluat*:ab,ti OR reviewed:ab,ti OR baseline:ab,ti OR compare*:ab,ti OR compara*:ab,ti OR consecutive:ab,ti OR retrospective:ab,ti AND [embase]/lim))

Appendix 3. CINAHL (EBSCO) search strategy, October 2010

The search strategy was broadened in 2010 to be more inclusive of new and emerging viruses.

S54 S32 and S53
S53 S44 or S52
S52 S45 or S46 or S47 or S48 or S49 or S50 or S51
S51 TI observational stud* or AB observational stud*
S50 TI cohort stud* or AB cohort stud*
S49 (MH "Cross Sectional Studies")
S48 (MH "Nonconcurrent Prospective Studies")
S47 (MH "Correlational Studies")
S46 (MH "Case Control Studies+")
S45 (MH "Prospective Studies")
S44 S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43
S43 TI allocat* N1 random* or AB allocat* N1 random*
S42 (MH "Quantitative Studies")
S41 TI placebo* or AB placebo*
S40 (MH "Placebos")
S39 TI random* allocation* or AB random* allocation*
S38 (MH "Random Assignment")

S37 TI (randomised control* trial* or randomized control* trial*) or AB (randomised control* trial* or randomized control* trial*)
S36 TI ((singl* W1 blind*) or (singl* W1 mask*) or (doubl* W1 blind*) or (doubl* W1 mask*) or (trebl* W1 blind*) or (trebl* W1 mask*) or (tripl* W1 blind*) or (tripl* W1 mask*)) or AB ((singl* W1 blind*) or (singl* W1 mask*) or (doubl* W1 blind*) or (doubl* W1 mask*) or (trebl* W1 blind*) or (trebl* W1 mask*) or (tripl* W1 blind*) or (tripl* W1 mask*))
S35 TI clinic* W1 trial* or AB clinic* W1 trial*
S34 PT clinical trial
S33 (MH "Clinical Trials+")
S32 S15 and S31
S31 S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30
S30 TI (bans or banning or banned or ban or "outbreak control" or "outbreak controls" or distancing* or quarantine* or "protective clothing" or "protective garment" or "protective garments" or "protective gown" or "protective gowns" or "protective device" or "protective devices" or "protective equipment" or "protective behaviour" or "protective behavior" or "protective behaviours" or "protective behaviors" or "protective procedure" or "protective procedures" or "preventive behaviours" or "preventive behaviour" or "preventive behavior" or "preventive behaviors" or "preventive procedure" or "preventive procedures" or "personal protective" or "isolation room" or "isolation rooms" or "isolation strategy" or "isolation strategies" or "patient distance" or "patient distancing" or "patient separation" or "spatial separation") or AB (handwashing or "hand washing" or hand-washing or "hand hygiene" or sanitiser or sanitizer or cleanser* or disinfectant* or glov* or mask or masks or respirator or respirators or "patient isolation" or "patient isolators" or barrier* or curtain* or partition* or "negative pressure room" or "negative pressure rooms" or "reverse barrier nursing" or "reverse barrier unit" or "reverse barrier isolation" or "cross infection" or "infection control" or "disease control" or "school closure" or "school closures" or "school dismissal" or "school dismissals" or "temporary closure" or "temporary closures" or "mass gathering" or "mass gatherings" or "public gathering" or "public gatherings" or "public event" or "public events")
S29 TI (handwashing or "hand washing" or hand-washing or "hand hygiene" or sanitiser or sanitizer or cleanser* or disinfectant* or glov* or mask or masks or respirator or respirators or "patient isolation" or "patient isolators" or barrier* or curtain* or partition* or "negative pressure room" or "negative pressure rooms" or "reverse barrier nursing" or "reverse barrier unit" or "reverse barrier isolation" or "cross infection" or "infection control" or "disease control" or "school closure" or "school closures" or "school dismissal" or "school dismissals" or "temporary closure" or "temporary closures" or "mass gathering" or "mass gatherings" or "public gathering" or "public gatherings" or "public event" or "public events") or AB (handwashing or "hand washing" or hand-washing or "hand hygiene" or sanitiser or sanitizer or cleanser* or disinfectant* or glov* or mask or masks or respirator or respirators or "patient isolation" or "patient isolators" or barrier* or curtain* or partition* or "negative pressure room" or "negative pressure rooms" or "reverse barrier nursing" or "reverse barrier unit" or "reverse barrier isolation" or "cross infection" or "infection control" or "disease control" or "school closure" or "school closures" or "school dismissal" or "school dismissals" or "temporary closure" or "temporary closures" or "mass gathering" or "mass gatherings" or "public gathering" or "public gatherings" or "public event" or "public events")
S28 (MH "Sterilization and Disinfection")
S27 (MH "Quarantine")
S26 (MH "Area Restriction (Iowa NIC)") OR (MH "Infection Protection (IowaNIC)")
S25 (MH "Infection Control")
S24 (MH "Cross Infection/PC")
S23 (MH "Isolation, Reverse")
S22 (MH "Patient Isolation")
S21 (MH "Protective Devices")
S20 (MH "Protective Clothing")
S19 (MH "Respiratory Protective Devices")
S18 (MH "Masks")
S17 (MH "Gloves")
S16 (MH "Handwashing+")
S15 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14
S14 TI ("acute respiratory tract infection" or "acute respiratory tract infections" or "acute respiratory infection" or "acute respiratory infections") or AB (influenza* or flu or "common cold" or "common colds" or rhinovir* or adenovir* or coronavir* or sars or "severe acute respiratory syndrome" or "respiratory syncytial virus" or "respiratory syncytial viruses" or rsv or pneumovir* or parainfluenza* or "para influenza" or para-influenza or enterovir* or bocavir* or metapneumovir* or parvovir* or parechovir*)
S13 TI (influenza* or flu or "common cold" or "common colds" or rhinovir* or adenovir* or coronavir* or sars or "severe acute respiratory syndrome" or "respiratory syncytial virus" or "respiratory syncytial viruses" or rsv or pneumovir* or parainfluenza* or "para influenza" or para-influenza or enterovir* or bocavir* or metapneumovir* or parvovir* or parechovir*) or AB (influenza* or flu or "common cold" or "common colds" or rhinovir* or adenovir* or coronavir* or sars or "severe acute respiratory syndrome" or "respiratory syncytial virus" or "respiratory syncytial viruses" or rsv or pneumovir* or parainfluenza* or "para influenza" or para-influenza or enterovir* or bocavir* or metapneumovir* or parvovir* or parechovir*)
S12 (MH "Respiratory Tract Infections+")
S11 (MH "Parvovirus Infections+")
S10 (MH "Enterovirus Infections+")
S9 (MH "Enteroviruses+")
S8 (MH "Respiratory Syncytial Virus Infections")
S7 (MH "Respiratory Syncytial Viruses")

S6 (MH "SARS Virus")
S5 (MH "Severe Acute Respiratory Syndrome")
S4 (MH "Coronavirus Infections+")
S3 (MH "Coronavirus+") OR (MH "Coronavirus Infections")
S2 (MH "Common Cold")
S1 (MH "Influenza+") OR (MH "Influenza A H5N1") OR (MH "Influenza A

Appendix 4. LILACS (Latin America and Caribbean) search strategy

Tw acute respiratory tract infection$ or Tw acute respiratory infection$ or Mh human influenza or Mh influenza a virus or Mh influenza a virus, h1n1 subtype or Mh influenza a virus, h3n2 subtype or Mh influenza a virus, h3n8 subtype or Mh influenza a virus, h5n1 subtype or Mh influenza b virus or Mh influenza c virus or Mh influenza in humans or Mh influenza viruses type a or Mh influenza viruses type b or Mh influenza viruses type c or Mh influenza, human or Tw influenza$ or Tw flu or Mh influenzavirus a or Mh influenzavirus b or Mh influenzavirus c or Mh adenoviridae or Mh adenoviridae infections or Mh adenovirus infections or Mh adenovirus infections, human or Mh adenoviruses, human or Tw rhinovir$ or Tw adenovir$ or Tw common cold$ or Tw resfriado comum or Tw resfriado comun or Mh coronavirus or Mh sars-associated coronavirus or Mh human coronavirus 229e or Mh coronavirus 229e, human or Mh coronavirus infections or Tw coronavir$ or Mh severe acute respiratory syndrome or Mh severe acute respiratory syndrome virus or Tw severe acute respiratory syndrome or Tw sars or Tw sindrome respirat$ agudo grave or Mh human respiratory syncytial virus or Mh respiratory syncytial virus infections or Mh respiratory syncytial virus, human or Mh respiratory syncytial viruses or Tw respiratory syncytial virus$ or Tw rsv or Tw virus sincitiales respiratorios or Tw virus sinciciais respiratorios or Mh pneumovirus or Tw pneumovir$ or Mh human parainfluenza virus 1 or Mh parainfluenza virus 1, human or Mh human parainfluenza virus 2 or Mh parainfluenza virus 2, human or Mh human parainfluenza virus 3 or Mh parainfluenza virus 3, human or Mh parainfluenza virus infections Tw parainfluenza$ or Tw para influenza or Tw para-influenza or Mh enterovirus or Mh human enterovirus b or Mh enterovirus b, human or Mh enterovirus infections or Tw enterovir$ or Mh bocavirus or Tw bocavir$ or Mh metapneumovirus or Mh human metapneumovirus or Mh metapneumovirus, human or Tw metapneumovir$ or Mh parvovirus or Mh human parvovirus b19 or Mh parvovirus b19, human or Mh parvovirus infections or Tw parvovir$ or Mh parvoviridae or Mh parvoviridae infections or Tw parechovir$ [Words]

and

Mh Handwashing or Tw handwashing or Tw hand washing or Tw hand-washing or Tw lavado de manos or Tw lavagem de maos or Tw hand hygiene or Tw higiene or Tw sanitiser$ or Tw sanitizer or Tw cleanser$ or Tw disinfectant$ or Tw esteriliza$ or Tw desinfectar$ or Mh protective gloves or Mh surgical gloves or Mh gloves, protective or Mh gloves, surgical or Tw glov$ or Tw guantes or Tw luvas or Mh masks or Mh facial masks or Tw mask or Tw masks or Tw mascaras or Mh respiratory protective devices or Tw respirator or Tw respirators or Mh protective clothing or Mh protective devices or Mh patient isolation or Tw patient isolat$ or Tw aisladores de pacientes or Tw aislamiento de pacientes or Tw isoladores de pacientes or Tw isolamento de pacientes or Tw barrier$ or Tw curtain$ or Tw partition$ or Tw barrera or Tw barreira or Tw cortina or Tw tabique or Tw protective clothing or Tw protective devices or Tw ropa de protec$ or Tw equipos de seguridad or Tw roupa de prote$ or Tw equipamentos de prote$ or Mh cross infection or Tw cross infection or Tw infec$ hospital$ or Tw infection control$ or Tw control$ de infec$ or Mh communicable disease control or Tw communicable disease control or Tw control de enfermedades transmisibles or Tw controle de doen$ transmiss$ or Mh infection control or Mh quarantine Tw quarantine$ or Tw cuarentena or Tw quarentena or Tw protective devices or Tw dispositivos de prtoecc$ or Tw personal protect$ or Tw equipamentos de protec$ or Tw equipo de protecc$ or Tw isolation room or Tw sala de aislamiento or Tw quarto de isolamento or Tw patient distance or Tw distancia del paciente or Tw spatial separation or Tw separa$ especial or Tw cohort isolation or Tw cohort$ or Tw ban or Tw bans or Tw banning or Tw banned or Tw prohibici$ or Tw proibi$ or Tw outbreak control or Tw distanc$ or Tw school closure or Tw temporary closure or Tw cierre de la escuela or Tw fechamento da escola or Tw public gathering or Tw reunion publica or Tw reuni$ publica or Tw reverse barrier nursing or Tw reverse barrier unit or Tw reverse barrier isolation or Tw negative pressure room$ or Tw patient separation [Words]

Appendix 5. Indian MEDLARS search strategy

(influenza$ or flu or common cold$ or rhinovir$ or coronavir$ or adenovir$ or severe acute respiratory syndrome$ or sars or respiratory syncytial virus$ or rsv or parainfluenza$ or enterovir$ or metapneumovir$ or parvovir$ or bocavir$ or parechovir$) and (handwashing or hand washing or mask$ or glov$ or protect$ or isolat$ or barrier$ or curtain$ or partition$ or cross infection$ or infection control$ or disease control$ or school$ or quarantine$ or ban$ or cohort$ or distanc$ or spatial separation$)

Appendix 6. IMSEAR (Index Medicus for the South East Asia Region) search strategy

(influenza or flu or common cold or rhinovirus or coronavirus or adenovirus or severe acute respiratory syndrome or sars or respiratory syncytial virus or rsv or parainfluenza or enterovirus or bocavirus or metapneumovirus or parvovirus or parechovirus) and (handwashing or hand washing or hand hygiene or sanitiser or sanitizer or cleanser or disinfectant or gloves or masks or mask or protective clothing or protective devices or patient isolation or barrier or curtain or partition or cross infection or disease control or infection control or school or schools or bans or banning or banned or ban or distancing or quarantine or isolation or spatial separation or cohorting or cohort isolation)

WHAT'S NEW

Date	Event	Description
1 April 2020	Amended	We deleted the table 'GRADE evidence profiles physical barriers/handwashing and related interventions in hospital and community settings' because the table is not rendering correctly when downloading the PDF.

HISTORY

Protocol first published: Issue 4, 2006
Review first published: Issue 4, 2007

Date	Event	Description
22 October 2010	New citation required but conclusions have not changed	We updated the review again at the behest of the World Health Organization (WHO). External sources of support amended. External support from the WHO. The WHO interim guidelines document on 'Infection Prevention and Control of Epidemic and Pandemic Prone Acute Respiratory Diseases in Health Care' was published in 2007 to provide infection control guidance to help prevent the transmission of acute respiratory diseases (ARD) in health care. The update of these guidelines will be evidence-based and an update of this review was requested to assist in informing the evidence base for the revision of the WHO guidelines. Dr John Conly, Dr Mark Jones and Sarah Thorning joined the review team.
22 October 2010	New search has been performed	Searches conducted. We included seven new trials; four randomised controlled trials and three non-randomised comparative studies. We excluded 36 new trials.
7 May 2009	New search has been performed	For the 2009 update we included three cluster-randomised controlled trials (Sandora 2008; Cowling 2009; MacIntyre 2009) and one individual randomised controlled trial (Satomura 2005, with its linked publication Kitamura 2007). We also included one retrospective cohort study (Foo 2006), one case-control study (Yu 2007) and two prospective cohort studies (Wang 2007; Broderick 2008). The content and conclusions of the 2007 review changed little, but the additional eight studies add more information and certainty. Our meta-analysis remains unchanged as there were no new studies for pooling.
30 April 2009	New citation required but conclusions have not changed	New author joined the review team.
8 July 2008	Amended	Converted to new review format.
20 August 2007	Amended	Review first published Issue 4, 2007.

CONTRIBUTIONS OF AUTHORS

Tom Jefferson (TOJ), Chris Del Mar (CDM) and Liz Dooley (LD) were responsible for drafting the protocol.

TOJ, Eliana Ferroni (EF), Bill Hewak (BH) and Adi Prabhala (AP) extracted study data and Sree Nair (SN) performed the analyses in the original review.

TOJ, EF, Lubna A Al-Ansary (LA), Ghada A Bawazeer (GB) and CDM adjudicated in data extraction in the 2009 update, and Mieke van Driel (MvD) assisted in the writing, construction of the summary of results table and updating with the most recent studies. All 2009 review authors contributed to the final report.

For the 2010 update TOJ and John Conly (JMC) extracted data and CDM checked extractions and arbitrated. All three checked the search strategy terms. Sarah Thorning designed and carried out the searches. All 2010 review authors contributed to the final report.

DECLARATIONS OF INTEREST

Chris Del Mar provided expert advice to GlaxoSmithKline about vaccination against acute otitis media in 2008-2009. He receives royalties from books published through Blackwell, BMJ Books and Elsevier.

SOURCES OF SUPPORT

Internal sources

- The Cochrane Collaboration Steering Group, UK.

External sources

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- National Health and Medical Research Council (NHMRC), Australia.

  Competitive grant to Chris Del Mar and Tom Jefferson, 2009
- Sabbatical year for John Conly while at the WHO in Geneva, Switzerland was supported by the University of Calgary, Calgary, Canada.
- World Health Organization, Geneva, Switzerland.

  Requested and provided support to the Cochrane Collaboration for current update

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None, apart from the change in the title (see Published notes, below).

NOTES

In Issue 1, 2010, the title was changed from *Interventions for the interruption or reduction of the spread of respiratory viruses* to *Physical interventions to interrupt or reduce the spread of respiratory viruses.*

The original review was subsequently published as Jefferson T, Foxlee R, Del Mar C, Dooley L, Ferroni E, Hewak B, Prabhala A, Nair S, Rivetti A. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ 2008;336:77-80 and Jefferson T, Del Mar C, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, van Driel ML, Foxlee R, Rivetti A. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ 2009 Sep 21;339:b3675. doi: 10.1136/bmj.b3675.

INDEX TERMS

Medical Subject Headings (MeSH)

*Virus Shedding; Case-Control Studies; Influenza, Human [transmission] [virology]; Randomized Controlled Trials as Topic; Respiratory Tract Infections [*prevention & control] [transmission] [virology]; Virus Diseases [*prevention & control] [transmission]

MeSH check words

Humans