

# Physical interventions to interrupt or reduce the spread of respiratory viruses: a Cochrane review

T Jefferson,<sup>1\*</sup> C Del Mar,<sup>2</sup> L Dooley,<sup>2</sup>  
E Ferroni,<sup>3</sup> LA Al-Ansary,<sup>4</sup> GA Bawazeer,<sup>5</sup>  
ML van Driel,<sup>2</sup> S Nair,<sup>6</sup> R Foxlee<sup>7</sup>  
and A Rivetti<sup>8</sup>

<sup>1</sup>Vaccines Field, The Cochrane Collaboration, Roma, Italy

<sup>2</sup>Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia

<sup>3</sup>Infectious Diseases Unit, Public Health Agency of Lazio Region, Rome, Italy

<sup>4</sup>Department of Family & Community Medicine, Holder of “Shaikh Abdullah S. Bahamdan” Research Chair for Evidence-Based Health Care and Knowledge Translation, College of Medicine, King Saud University, Riyadh, Saudi Arabia

<sup>5</sup>Department of Clinical Pharmacy & KKUH, King Saud University, Riyadh, Saudi Arabia

<sup>6</sup>Department of Statistics, Manipal University, Manipal, India

<sup>7</sup>Department of Health Sciences, University of York, York, UK

<sup>8</sup>Servizio Regionale di Riferimento per l’Epidemiologia, SSEpi – SeREMI – Cochrane Vaccines Field, Azienda, Sanitaria Locale ASL AL, Alessandria, Italy

\*Corresponding author

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## Abstract

T Jefferson,<sup>1\*</sup> C Del Mar,<sup>2</sup> L Dooley,<sup>2</sup> E Ferroni,<sup>3</sup> LA Al-Ansary,<sup>4</sup>  
GA Bawazeer,<sup>5</sup> ML van Driel,<sup>2</sup> S Nair,<sup>6</sup> R Foxlee<sup>7</sup> and A Rivetti<sup>8</sup>

<sup>1</sup>Vaccines Field, The Cochrane Collaboration, Roma, Italy

<sup>2</sup>Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia

<sup>3</sup>Infectious Diseases Unit, Public Health Agency of Lazio Region, Rome, Italy

<sup>4</sup>Department of Family & Community Medicine, Holder of “Shaikh Abdullah S. Bahamdan”  
Research Chair for Evidence-Based Health Care and Knowledge Translation, College of Medicine,  
King Saud University, Riyadh, Saudi Arabia

<sup>5</sup>Department of Clinical Pharmacy & KKUH, King Saud University, Riyadh, Saudi Arabia

<sup>6</sup>Department of Statistics, Manipal University, Manipal, India

<sup>7</sup>Department of Health Sciences, University of York, York, UK

<sup>8</sup>Servizio Regionale di Riferimento per l'Epidemiologia, SSEpi – SeREMI – Cochrane Vaccines Field,  
Azienda, Sanitaria Locale ASL AL, Alessandria, Italy

\*Corresponding author

**Background:** Viral epidemics or pandemics of acute respiratory infections like influenza or severe acute respiratory syndrome pose a world-wide threat. Antiviral drugs and vaccinations may be insufficient to prevent catastrophe.

**Objectives:** To systematically review the effectiveness of physical interventions to interrupt or reduce the spread of respiratory viruses.

**Search strategy:** We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, issue 2); MEDLINE (1966 to May 2009); OLDMEDLINE (1950 to 1965); EMBASE (1990 to May 2009); and CINAHL (1982 to May 2009).

**Selection criteria:** We scanned 2958 titles, excluded 2790 and retrieved the full papers of 168 trials, to include 59 papers of 60 studies. We included any physical interventions (isolation, quarantine, social distancing, barriers, personal protection and hygiene) to prevent transmission of respiratory viruses. We included the following study designs: randomised controlled trials (RCTs), cohorts, case controls, cross-over, before-after, and time series studies.

**Data collection and analysis:** We used a standardised form to assess trial eligibility. RCTs were assessed by: randomisation method; allocation generation; concealment; blinding; and follow up. Non-RCTs were assessed for the presence of potential confounders, and classified into low, medium, and high risks of bias.

**Main results:** The risk of bias for the four RCTs, and most cluster RCTs, was high. The 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. Additional benefit from reduced transmission from children to other household members is broadly supported in results of other study designs, where the potential for confounding is greater. Six case-control studies suggested that implementing barriers to transmission, isolation, and hygienic measures are effective at containing respiratory virus epidemics. We found limited evidence that N95 respirators were superior to simple surgical masks, but were more expensive, uncomfortable, and caused skin irritation. The incremental effect of adding virucidals or antiseptics to normal handwashing to decrease respiratory disease remains uncertain. Global measures, such as screening at entry ports, were not properly evaluated. There was limited evidence that social distancing was effective especially if related to the risk of Physical interventions to interrupt or reduce the spread of respiratory viruses exposure.

**Authors' conclusions:** Many simple and probably low-cost interventions would be useful for reducing the transmission of epidemic respiratory viruses. Routine long-term implementation of some of the measures assessed might be difficult without the threat of a looming epidemic.





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## 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 because of their wide spread. In 2003 the severe acute respiratory syndrome (SARS) epidemic affected ~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 anxiety. Single 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 physical barriers (such as handwashing or wearing masks) in reducing the

spread of respiratory viruses, including influenza viruses.

We found 60 studies including randomised controlled trials (RCTs) and observational studies with a mixed risk of bias.

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. The more expensive, irritating and uncomfortable N95 respirators might be superior to simple 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 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 is underway at the time of writing) (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 4 million deaths worldwide, mostly occurring in low-income countries) ([www.who.int/healthinfo/global\\_burden\\_disease/estimates\\_regional/en/index.html](http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html)). 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](http://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 their 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) 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 aerosol from infected to susceptible people (such as by Physical interventions to interrupt or reduce the spread of respiratory viruses using masks and distancing measures), and by fomites (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 (isolation, quarantine, social distancing, barriers, personal protection and 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 (e.g. clinical symptoms as a proxy for viral illness).

### Search methods for identification of studies

#### Electronic searches

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 ublic 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 4 not 55

The search strategies for, Cochrane Central Register of Controlled Trials (CENTRAL), Ovid EMBASE and EBSCO CINAHL can be found in Appendix 1, Appendix 2 and Appendix 3, respectively.

### 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 no filters were applied 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

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

## Data extraction and management

Two review authors (TOJ, CDM) independently applied inclusion criteria to all identified and retrieved articles. Four review authors (TOJ, EF, BH, AP) extracted data from included studies and checked their accuracy on standard Cochrane Vaccines Field forms. The procedure was supervised and arbitrated by CDM.

For the 2009 update three review authors (EF, LAA, GAA) extracted data independently two review authors (TOJ, CDM) checked the procedure. CDM arbitrated.

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<sup>2</sup> statistic for each pooled estimate to assess the impact on statistical heterogeneity (Higgins 2002; Higgins 2003). Physical interventions to interrupt or reduce the spread of respiratory viruses

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 were not available, relevant P values).

We contacted one trial author (Dr Michael Broderick) to better understand the risk of bias in his study (Broderick 2008).

### Assessment of risk of bias in included studies

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

#### Randomised studies

Three of the four 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 difficult to reconcile (Kitimura 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). This practice 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 other cluster randomised trial (Sandora 2008) is at low risk of bias with careful evaluation of compliance in the intervention arm (hand sanitiser wipes and disinfection of surfaces).

#### **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 seven 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.

#### **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 five retrospective cohort studies had high risk of bias (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**

Outcome measures varied from incidence of experimentally induced rhinovirus infections, to the incidence of naturally occurring undifferentiated 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 ILI. Other included studies focused on SARS specifically, or respiratory syncytial virus (RSV).

Proxy measures of illness included absenteeism.

#### **Subgroup analysis and investigation of heterogeneity**

An a priori subgroup analysis was planned for:

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

We had sufficient data to carry out only the last.







## Results

### Description of studies

See 'Characteristics of included studies' table.

### Included studies

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

### Excluded studies

See 'Characteristics of excluded studies' table.

### 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 issues' 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. This common problem 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).

We classified four of the six case-control studies as having medium risk of bias (Lau 2004a; Seto 2003; Wu 2004; Yin 2004) 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.

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 high risk of bias.

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 of the reference population, making interpretation and generalisability of their conclusions questionable.

### Effects of interventions

We scanned 2958 titles, excluded 2790 and retrieved the full papers of 168 trials, to include 59 papers of 60 studies.

### Reported results from randomised studies

Three studies tested the effects of cleaning hands 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 RT-PCR-confirmed infection was reduced, an effect attributable to reductions in infection among participants using face masks plus hand hygiene (adjusted odds ratio, 0.33 (95% CI 0.13 to 0.87)) (Cowling 2009).

### Reported results from case-control studies

Seven 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. Binary data were pooled; none of the comparisons showed significant heterogeneity, so we used a fixed-effect model. 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 most cases (OR 0.45, 95% CI 0.36 to 0.57), based on all six studies (Lau 2004a; Nishiura 2005; Seto 2003; Teleman 2004; Wu 2004; Yin 2004); simple mask wearing was highly effective (OR 0.32, 95% CI 0.25 to 0.40), based on five studies (Lau 2004a; Nishiura 2005; Seto 2003; Wu 2004; Yin 2004); two studies found N95 respirator wearing even more effective (OR 0.09, 95% CI 0.03 to 0.30) (Seto 2003; Teleman 2004); glove wearing was effective (OR 0.43, 95% CI 0.29 to 0.65) (Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); gown wearing was also effective (OR 0.23, 95% CI .14 to 0.37) (Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); and all means combined (handwashing, masks, gloves, and gowns) achieved very high effectiveness (OR 0.09, 95% CI 0.02 to 0.35) (Nishiura 2005; Seto 2003). Another study from Hong Kong and Guangzhou hospitals wards reported that a minimum distance between beds of less than one meter was a risk factor for transmission (Yu 2007). Disaggregated data were not reported and therefore this study is not pooled

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.

### 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 reusable 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. Perhaps more than the additional portable virucidal hand foam as an adjunct to handwashing, one staff educational programme on handwashing in a daycare centre for adults was effective over the last four years 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 (Falsey 1999). This confirmed an earlier report of the effectiveness of a handwashing programme in reducing absenteeism for ILI in a primary school (Kimmel 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 were 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 interruption of transmission 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).

### 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 huge 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), intensive care units, and paediatric wards (Gala 1986; Leclair 1987) in high-income countries; slums in low-income countries (Luby 2005); 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 limit generalisability of findings further (Heymann 2004).

The variable quality of the methods of these studies is striking. Hasty design of interventions for public health crises, particularly the six 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), 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 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 to apparently 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.

## 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 from the results of other study designs where the potential for confounding is greater.

The six pooled case-control studies suggest that implementing barriers to transmission, isolation, and hygienic measures are effective with the use of relatively cheap interventions to contain epidemics of respiratory viruses. We found limited evidence of the superior effectiveness of droplet barrier devices such as the N95 respirator over simple surgical masks. N95 respirators have a 95% filtration capability against non-oily particulate aerosols (Teleman 2004). More expensive and uncomfortable (especially if worn for long periods) than simple surgical masks, they may be useful in very high risk 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.



## Summary of main results

	RCT (n = 4)	C-RCT (n = 15)	Casecontrol (n = 7)	Prospective cohort (n = 16)	Retrospective cohort (n = 5)	Before–after (n = 13)
Handwashing	–	3 trials in children effective; 1 trial in households effective if implemented < 36 hours after onset	6 studies OR 0.45 (0.36–0.57)	2 studies found effect and 2 no effect on ARI	–	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	–	–	–	–	–
Virucidal tissues	–	1 trial small effect; 2 trials non-significant	–	1 study effective	–	–
Disinfection of living quarters	–	–	1 study OR 0.30 (0.23–0.39)	–	–	–
Barriers (masks, gloves, gowns combined)	–	–	2 studies OR 0.09 (0.02–0.35)	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 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	5 studies OR 0.32 (0.25–0.40)	3 studies masks effective (with air filter safer)	1 study harm related to mask wearing	1 study in children's hospital effective

	RCT (n = 4)	C-RCT (n = 15)	Casecontrol (n = 7)	Prospective cohort (n = 16)	Retrospective cohort (n = 5)	Before-after (n = 13)
N95 Respirator	-	-	2 studies OR 0.09 (0.03-0.30)	-	1 study harm related to N95 respirator wearing	-
Gloves	-	-	4 studies OR 0.43 (0.29-0.65)	-	1 study harm related to gloves	-
Gowns	-	-	4 studies OR 0.23 (0.14-0.37)	-	1 study harm related to gown wearing	1 study no added effect in neonatal ICU
Distancing	-	-	-	1 study no effect in military recruits; 2 studies cohorting in hosp effective	1 study cohorting in paed wards effective; 1 study in military hosp cohorting with handwashing & 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	-



## 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. 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.





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## Contributions of authors

Ruth Foxlee (RF) and Alex Rivetti (AR) were responsible for constructing the search strategies.

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 this 2009 update, and Mieke van Driel (MvD) assisted in the writing, construction of the summary of results table and updating with the most recent trial.

All 2009 review authors contributed to the final report.







## Differences between protocol and review

### Published 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.





## Characteristics of studies

### Characteristics of included studies

#### Agah 1987

<b>Methods</b>	Prospective cohort study carried out in California hospital during the autumn 1984 to spring 1985 season. The study assessed the efficacy of HCWs 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
<b>Participants</b>	168 healthcare workers (HCW) caring for children < 5 years with differential diagnosis of RSV
<b>Interventions</b>	Mask and goggles (sometimes gowns too) versus normal care
<b>Outcomes</b>	RSV illness reduced from 61% (controls) to 5% (intervention) Laboratory: swabs for RSV diagnosis Effectiveness: RSV illness Safety: N/A
<b>Notes</b>	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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Broderick 2008**

<b>Methods</b>	<p>Prospective cohort study carried out in a military recruit training centre during the first 4 weeks of recruit training. Data was collected between February 2004 and March 2005 (duration of recruit training is not reported).</p> <p>It isn't 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.</p> <p>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.</p> <p>Housing units (<math>n = 196</math> units) were divided into closed units [<math>n = 30</math>] (experiment/intervention) or open units (<math>n = 166</math>) (control). For description of how the closed units were selected and geographical position in the training centre see notes.</p> <p>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</p>
<b>Participants</b>	<p>Male military recruits (<math>n = 13,114</math>), 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.</p> <p>Ten percent of medical convalescent unit (MCU) subjects (762) and 6% of physical conditioning unit (PCU) subjects (395) were positive for adenovirus 4 by PCR</p>
<b>Interventions</b>	<p>To test the effect of social distancing: Subjects were either assigned (allocation process not clear) to closed or open units. The closed units didn't introduce any new subjects once their personnel had been assigned (socially-distant); sick recruits were removed but if their symptoms did not require placement in the MCU, the recruits returned to their units. The open units accepted recovering subjects after being discharged from MCU and PCU.</p> <p>To test an environmental aetiology: Some of the units, which were vacant after 4 weeks of occupation, were swabbed. The MCU was also swabbed. Then samples were tested by PCR and were cultured</p>
<b>Outcomes</b>	<p>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.</p> <p>Effectiveness: Cases of FRI was defined either by a body temperature of <math>&gt;38^{\circ}\text{C}</math> 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.</p> <p>Safety: N/A</p>
<b>Notes</b>	<p>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 'etiological' 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.</p>

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 localized in certain (isolated) area) is lacking. Despite these clear limitations this pragmatic study 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’s 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 not typically interact with each other. They are large permanent buildings each consisting of 12 large rooms and a hallway.

#### Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Carabin 1999

<b>Methods</b>	Cluster randomised controlled trial carried out in day care 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
<b>Participants</b>	1729 children aged 18 to 36 months in 47 DCCs (83 toddler classrooms). 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
<b>Interventions</b>	Training session (1 day) with washing of hands, toy cleaning, window opening, sand pit cleaning and repeated exhortations to hand wash
<b>Outcomes</b>	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
<b>Notes</b>	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 two 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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Cowling 2008**

<b>Methods</b>	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 three interventions carried out. Randomisation was carried out in two different schedules (2:1:1 for the first 100 households and subsequently 8:1:1) but it is unclear why and how
<b>Participants</b>	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 two 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
<b>Interventions</b>	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
<b>Outcomes</b>	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:  Fever more or equal to 38 degrees or at least two of following symptoms, headache, coryza , sore throat, muscle aches and pains  At least two of the following S/S: fever more or equal to 37.8 degrees, cough ,headache ,sore throat, and muscles aches and pains  Fever of more or equal to 37.8 degrees plus cough or sore throat  Safety:  No harms were reported in any of the arms
<b>Notes</b>	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 long 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. The choice of season, change in randomization 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

**Risk of bias table**

<b>Item</b>	<b>Judgement</b>	<b>Description</b>
Adequate sequence generation?	Yes	Randomisation was computer generated by a biostatistician
Allocation concealment?	Yes	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?	No	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 addressed?	Yes	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
Free of selective reporting?	Yes	



**Cowling 2009**

<b>Methods</b>	Cluster randomised controlled trial
<b>Participants</b>	<p>Households in Hong Kong</p> <p>From 45 outpatient clinics in both the private and public sectors across Hong Kong, we 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</p> <p>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</p>
<b>Interventions</b>	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
<b>Outcomes</b>	<p>Influenza virus infection in household contacts, as confirmed by reverse transcription polymerase chain reaction (RT-PCR) or diagnosed clinically after 7 days</p> <p>“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.”</p> <p>Statistical analysis: adjusted for clustering</p> <p>Results:</p> <p>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 inpatient to wearing a face mask between 15 and 49%</p>
<b>Notes</b>	“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 inter-pandemic influenza”

**Risk of bias table**

<b>Item</b>	<b>Judgement</b>	<b>Description</b>
Adequate sequence generation?	Yes	Randomisation was computer generated by a biostatistician
Allocation concealment?	Yes	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?	No	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 addressed?	Yes	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
Free of selective reporting?	Yes	

**Derrick 2005**

<b>Methods</b>	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 then combinations of layers, but this is not further described
<b>Participants</b>	Six volunteers who wore the masks and had their droplet count taken
<b>Interventions</b>	Pleated rectangular three-ply surgical mask
<b>Outcomes</b>	Laboratory
<b>Notes</b>	<p>Risk of bias: high (report too brief to allow assessment)</p> <p>Notes: The authors conclude that the best combination of five 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 single 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 five layers of masks to stop infections such as SARS as the infective count of the SARS-CoV is unknown.</p> <p>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</p>

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Dick 1986

<b>Methods</b>	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. Twenty 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. Eight of them with the most severe colds (donors) played cards with 12 antibodyfree men (recipients) in a experiment room. Four experiments were conducted, in experiments B and C volunteers used CMS tissues to prevent spreading of R16 colds. In the two control experiments (A and D) volunteers were permitted to use cotton handkerchiefs
<b>Participants</b>	Males ~ 18 years of age with a laboratory-induced R 16 cold (donors) and 12 antibody-free men (recipients)
<b>Interventions</b>	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
<b>Outcomes</b>	Laboratory: serological evidence (serum samples or viral isolation) Effectiveness: rhinovirus colds
<b>Notes</b>	Risk of bias: low  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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Doherty 1998**

<b>Methods</b>	Retrospective cohort study carried out in North Staffordshire hospital (UK) during two 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 minimize 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 six bedded bays on the paediatric ward. All carers observed standard routines (handwashing and gown wearing)
<b>Participants</b>	Children less than three 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
<b>Interventions</b>	RSV diagnosis and cohorting versus normal care
<b>Outcomes</b>	Laboratory: aspirates for RSV diagnosis Effectiveness: RSV illness (developed at least five days since admission) Safety: N/A “RSV infection reduced” (but data tabled do not support this conclusion)
<b>Notes</b>	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 controls arms were (i.e. cohorting of RSV infected children to prevent infection in whom?)

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Dyer 2000

<b>Methods</b>	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. Seven classes received the instant sanitiser, while the remaining seven classes were assigned to the control group. Male-to-female ratios and age distributions of the two groups did not differ significantly. Prior to study commencement all students participated in an educational program 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
<b>Participants</b>	420 children in a private elementary school in California aged 5 to 12 years; cluster open-label crossover cohort study over 10 weeks
<b>Interventions</b>	Educational programme plus the SAB (surfactant, allantoin and benzal konium chloride) spray hand sanitiser in 1oz bottles fitted with a pump spray top and with at-will soap-and-water handwashing versus nothing
<b>Outcomes</b>	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%
<b>Notes</b>	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 socio-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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Falsey 1999**

<b>Methods</b>	Prospective cohort study conducted at three adult daycare centers in Rochester, New York. The study assessed the value of a staff educational program 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
<b>Participants</b>	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
<b>Interventions</b>	Addition of virucidal hand foam as a supplement versus normal handwashing and educational programme
<b>Outcomes</b>	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
<b>Notes</b>	Risk of bias: low  Notes: The authors conclude that the educational program 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 four 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 four study years is reflected in the decline in viral isolates, suggesting that aspecific measures such as handwashing are effective against the main respiratory viruses

**Risk of bias table**

<b>Item</b>	<b>Judgement</b>	<b>Description</b>
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Farr 1988a

<b>Methods</b>	<p>The study was a six-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</p> <p>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</p>
<b>Participants</b>	<p>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</p>
<b>Interventions</b>	<p>Use of virucidal tissues versus placebo tissues versus no tissues. The treated tissues were impregnated with malic and citric acids and sodium lauryl sulfate, while placebo tissues contained saccharin</p>
<b>Outcomes</b>	<p>Laboratory: serological evidence: no Effectiveness: respiratory illness Safety: N/A</p>
<b>Notes</b>	<p>Risk of bias: high (failure of blinding)</p> <p>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 two study group, but only the difference between active and placebo groups was statistically significant (3.4 illness per person versus 3.9 for placebo group, <math>p = 0.04</math> and 3.6 for no tissues control group <math>P = 0.2</math>, 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 receiving 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</p>

### Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	



**Farr 1988b**

<b>Methods</b>	The study was a six-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
<b>Participants</b>	98 families, 58 in the active group and 40 in the placebo group. Two-hundred and thirty-one 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
<b>Interventions</b>	Use of virucidal tissues versus placebo tissues. The treated tissues were impregnated with malic and citric acids and sodium lauryl sulfate, while placebo tissues contained succinic acid. Participants in the treated and placebo groups were instructed to use only tissues received through the study
<b>Outcomes</b>	Laboratory: serological evidence: no Effectiveness: respiratory illness Safety: N/A
<b>Notes</b>	Risk of bias: high (failure of blinding)  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 table**

<b>Item</b>	<b>Judgement</b>	<b>Description</b>
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Foo 2006

<b>Methods</b>	<p>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&amp;E) and the intensive care unit (ICU)</p> <p>Control group: unclear</p> <p>Control group: none</p>
<b>Participants</b>	<p>Three hundred and forty healthcare staff were surveyed, 322 responded (60 from the NSC, 77 from the TTSH A&amp;E, and 185 from the TTSH ICU)</p>
<b>Interventions</b>	<p>Use of personal protective equipment (PPE), namely, masks, gloves and gowns. Adverse skin reactions to PPE</p>
<b>Outcomes</b>	<p>Laboratory: None</p> <p>Effectiveness: Not applicable</p> <p>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)</p>
<b>Notes</b>	<p>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:</p> <p>Those who developed acne with masks were younger (mean of 29.5 years) compared with those who didn't (mean of 33.2; <math>p &lt; 0.001</math>).</p> <p>Those who developed dry skin with gloves were younger (mean of 28.7 years) compared with those who didn't (mean of 33.2; <math>p &lt; 0.002</math>).</p> <p>Those who developed itch with gloves were younger (mean of 29.5 years) compared with those who didn't (mean of 33.2; <math>p &lt; 0.001</math>).</p> <p>Survey results show that acne, itach and rash are the most common harms reported after wearing a N95 respirator (59.6%, 51.4% and 35.8%) and that drynskin, 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</p>

### Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Gala 1986**

<b>Methods</b>	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. Two 3 week study periods were compared: period 1, during which all staff members used the goggles, and period 2, where 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 two studies. The first is a non-concurrent cohort study, in which two different population of children are assessed separated by a 1 week "washout" 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
<b>Participants</b>	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 one 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, two of the ward staff were acquired RSV infection and were not considered susceptible
<b>Interventions</b>	Use of a disposable plastic eye-nose goggle and respiratory infection control procedures versus only respiratory infection control procedures (cohorting, isolation and handwashing)
<b>Outcomes</b>	Laboratory: serological evidence Effectiveness: RSV infection (symptoms and laboratory confirmation) Safety: N/A
<b>Notes</b>	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 table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Gwaltney 1980

<b>Methods</b>	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 experiments were conducted to evaluate the virucidal activity of aqueous iodine applied to the fingers immediately before viral contamination. Other two 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 three 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 sec. Donors and recipients wore masks during the exposure period
<b>Participants</b>	15 and 20 volunteers in two experiments
<b>Interventions</b>	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
<b>Outcomes</b>	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
<b>Notes</b>	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 of 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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Hall 1981a**

<b>Methods</b>	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 three groups: “cuddlers”, exposed to an infected infant over two to four hours by caring the baby in the usual manner, wearing gowns, but no mask or gloves; “touchers”, exposed with the infant out of the 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 three 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
<b>Participants</b>	31 Volunteers: seven in the cuddler group, 10 in toucher group and 14 in the sitter group
<b>Interventions</b>	Exposure to infants admitted with bronchiolitis or pneumonia during a community outbreak of RSV isolation
<b>Outcomes</b>	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
<b>Notes</b>	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. Infections 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 table**

<b>Item</b>	<b>Judgement</b>	<b>Description</b>
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Hall 1981b

<b>Methods</b>	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 two months. All patients and staff on the ward for children less than three years of age were included. During the first four weeks (period 1) of the study the infectioncontrol 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 four week the wearing of gowns and masks was discontinued and handwashing alone was used for the final five weeks of the study. Throughout the study handwashing, cohorting and isolation were employed and emphasized. The number of nosocomial infections in patients and staff for period 1 were compared with the period 2 (last four weeks of the study). Infections occurred in the interval week were not counted
<b>Participants</b>	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
<b>Interventions</b>	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
<b>Outcomes</b>	Laboratory: serological evidence Effectiveness: RSV infection demonstrated by symptoms, viral isolation and serology Safety: N/A
<b>Notes</b>	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 two 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 two 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 table

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Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Heymann 2004**

<b>Methods</b>	Controlled before and after study to evaluate the effect of school closure on the occurrence of respiratory infection among children ages 6-12 years and its impact on health care 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-weeks 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
<b>Participants</b>	186,094 children aged 6 to 12 years
<b>Interventions</b>	Effect of a school closure on the occurrence of respiratory infection during an "influenza" outbreak
<b>Outcomes</b>	Laboratory: no Effectiveness: respiratory tract infections Safety: N/A
<b>Notes</b>	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 per centage of children. In addition there may be a difference in parental attitudes toward respiratory illness symptoms in other cultures that affect health care utilization. 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 Dec 1999  Observed effect may be due to school closure or they may be due to lower circulation of the viruses

**Risk of bias table**

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## Isaacs 1991

<b>Methods</b>	<p>Retrospective and prospective cohort study was conducted to evaluate the effectiveness of cohorting and educational program (handwashing) in reducing the incidence of nosocomial respiratory syncytial virus infections</p> <p>Data on all children with RSV infection on any of the paediatric wards in winter of 1986-7 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 two paediatric wards and the paediatric intensive care unit and the number they spent in hospital. For the next two 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</p>
<b>Participants</b>	Children < 2 years of age: 425 in period 1; 840 in period 2; 552 in period 3
<b>Interventions</b>	Isolation and handwashing versus normal care
<b>Outcomes</b>	<p>Laboratory: indirect immunofluorescence on nasopharyngeal secretions or by culture of secretions</p> <p>Effectiveness: RSV infection</p> <p>Safety: N/A</p>
<b>Notes</b>	<p>Risk of bias: high (poor descriptions)</p> <p>Notes: the authors concluded that handwashing and cohorting reduced at least 66% in the number of hospital acquired infections due to RSV in the two 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</p>

### Risk of bias table

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**Kimel 1996**

<b>Methods</b>	Prospective cohort study conducted in a school of Chicago, USA, to evaluate the effectiveness of a handwashing program in reducing the absenteeism caused by flu-like illness. The school was located in a predominantly white, middle to upper middle class suburb. All four kindergarten and five 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 program was planned for presentation just prior to this time. The effectiveness of the program was determined by comparing absentee rates among participants and non-participating classes (the control group). Absentee rates were determined by reviewing the computerized 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
<b>Participants</b>	199 children of kindergarten and first grade schools
<b>Interventions</b>	Handwashing and educational program versus no intervention
<b>Outcomes</b>	Laboratory: no Effectiveness: flu-like illness Safety: N/A Absenteeism from influenza-like illness was approximately double in the control arm ( $p = 0.01$ )
<b>Notes</b>	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 flu-like illness 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 flu season was later than usual (February), and this represented a confounding variable. The teacher surveys indicated problems with handwashing facilities

**Risk of bias table**

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Free of selective reporting?	Unclear	

## Kotch 1994

<b>Methods</b>	Pair-matched cluster randomised controlled trial conducted in the period 19 October 1988 to 23 May 1989 in 24 child care centres in North Carolina, USA. The trial tested the effects of a handwashing and environment sterilizing programme on diarrhoea (data not extracted) and ARIs. Child day care 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 coefficient reported. Centre were matched in pairs and then randomly allocated to either intervention or control programmes
<b>Participants</b>	389 children aged 3 years or less in day care 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
<b>Interventions</b>	Structured handwashing and environment (including surfaces, sinks, toilets and toys) disinfecting programme with waterless disinfectant scrub
<b>Outcomes</b>	Laboratory: N/A Effectiveness: ARI (coughing, runny nose, wheezing, sore throat or earache) Safety: N/A
<b>Notes</b>	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 table

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**Krasinski 1990**

<b>Methods</b>	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 four children shared a room. All paediatric patients hospitalised on or before Dec 31 1986 were 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
<b>Participants</b>	All hospitalised paediatric patients regarded as potentially infected with RSV
<b>Interventions</b>	RSV screening cohorting and service education programme versus do nothing
<b>Outcomes</b>	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
<b>Notes</b>	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 table**

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## Krilov 1996

<b>Methods</b>	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 to November 1993. The before between Nov 1991 and Oct 1992, followed by a one month washout period during which the intervention was introduced, followed by 12 months of after period (Dec 1992 to Nov 1993)
<b>Participants</b>	Thirty three 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 the local hospital. All community isolates were constant with the exception of adenovirus which doubled in the after period of the study
<b>Interventions</b>	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)
<b>Outcomes</b>	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
<b>Notes</b>	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 table

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**Ladegaard 1999**

<b>Methods</b>	RCT with cluster randomisation (they called it “lottery”, the same as “clip the coin”) to intervention or control. Out of 10 institutions they excluded two because they want institutions comparable in uptake area (that means housing and income). Interventions were given to children, parents and teachers at the institutions
<b>Participants</b>	Children 0 to 6 years old
<b>Interventions</b>	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 day care teachers to motivate the children by practical learning to have a better hand hygiene to inform the parents about better hand hygiene
<b>Outcomes</b>	34% decrease in ‘sickness’, (probably mostly gastroenteritis)
<b>Notes</b>	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 not extracted). Limited data only available from translation by Jørgen Lous

**Risk of bias table**

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## Lau 2004a

<b>Methods</b>	<p>Case-control study carried out in Hong Kong, SAR 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</p> <p>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</p> <p>The undefined sources group of cases were all the other categories</p> <p>Cases in general were identified and interviewed on the phone. Households with more than one index case were considered as having two index cases. Of the 1690 identified cases, 1214 from 996 households were enrolled in the study. One hundred and forty cases could not be contacted as they had a wrong phone number, 163 were uncontactable after at least five attempts, 163 refused to take part and 10 did not speak either Chinese or English. Seventeen were further excluded because they were aged less than 16. Twenty two questionnaires were unusable. (This makes 1175, obviously the 17 minors are included in the case-control study, as adding them makes a total of 1192)</p>
<b>Participants</b>	<p>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 RX evidence of pulmonary infiltration consistent with pneumonia with a temperature of &gt; 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)</p> <p>Description of controls: 660 controls of undefined origin and with no description of selection</p>
<b>Interventions</b>	Natural exposure to SARS during a serious epidemic
<b>Outcomes</b>	Community transmission of SARS reduced OR 0.30 (95% CI 0.23 to 0.39)
<b>Notes</b>	<p>Risk of bias: medium (inconsistencies in the text: lack of description of controls)</p> <p>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):</p> <p>Visit to mainland China 1.95 (1.11 to 3.42)</p> <p>Visited Price of Wales Hospital 7.07 (1.62 to 30.75)</p> <p>Visited other hospitals 3.70 (2.54 to 5.39)</p> <p>Visited Amoy Gardens 7.63 (3.77 to 15.43)</p> <p>The following activities/interventions had a significant protective function:</p> <p>Thorough disinfection of living quarters 0.41 (0.29 to 0.58)</p> <p>Wore a mask in public places frequently 0.36 (0.25 to 0.52)</p> <p>Washed hands 11 or more times a day 0.58 (0.38 to 0.87)</p> <p>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</p>

### Risk of bias table

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**Leclair 1987**

<b>Methods</b>	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 three 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 five 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
<b>Participants</b>	695 patients aged from 5 days to 4 years and 11 months. The distribution of ages was similar in the two periods. Thirty-seven acquired nosocomial RSV infections
<b>Interventions</b>	Infection-control intervention to increase use of gloves and gowns versus no intervention
<b>Outcomes</b>	Laboratory: yes Effectiveness: RSV infection Safety: N/A
<b>Notes</b>	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 publicized, the head nurse introduced an educational program 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 its 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 table**

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## Leung 2004

<b>Methods</b>	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
<b>Participants</b>	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
<b>Interventions</b>	<p>Triage and UHR-S isolation &amp; strict infection control procedures versus triage and UHR-S isolation and less strict infection control procedures. Healthcare workers were exposed to nine 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</p> <p>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</p> <p>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)</p> <p>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)</p> <p>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</p>
<b>Outcomes</b>	<p>Laboratory: laboratory confirmation of SARS</p> <p>Effectiveness: probable or suspected SARS according to WHO definitions</p> <p>Safety: N/A</p>
<b>Notes</b>	<p>Risk of bias: low</p> <p>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 health care workers. All the more remarkable as the paediatric department had not been built as isolation facility and had to be rapidly reorganised</p>

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**Longini 1988**

<b>Methods</b>	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
<b>Participants</b>	296 households were enrolled but for “technical reasons” five 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
<b>Interventions</b>	Disposable three-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, 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%)
<b>Outcomes</b>	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
<b>Notes</b>	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 two 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 spread. Also the lengths to which the authors went to obtain allocation concealment and maintenance of double-blind conditions

**Risk of bias table**

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Free of selective reporting?	Unclear	

## Luby 2005

<b>Methods</b>	<p>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 three phases:</p> <p>25 neighbourhoods were assigned to handwashing and 11 to standard practice</p> <p>300 households assigned to using antiseptic soap</p> <p>300 households assigned to using plain soap</p> <p>306 households assigned to standard practice</p> <p>1523 children younger than 15 years assigned to using antiseptic soap</p> <p>1640 children younger than 15 years assigned to using plain soap</p> <p>1528 children younger than 15 years assigned to standard practice</p> <p>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 nor 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</p>
<b>Participants</b>	<p>Householders of slums in Karachi. Of the 1523 children younger than 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</p> <p>Of 1640 children younger than 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</p> <p>1528 children younger than 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</p>
<b>Interventions</b>	<p>Instruction programme and antibacterial soap containing 1.2% triclocarban, or ordinary soap to be used throughout the day by householders or standard procedure</p>
<b>Outcomes</b>	<p>Laboratory: N/A</p> <p>Effectiveness:</p> <p>Number of new respiratory illness per person per week</p> <p>Pneumonia (cough or difficulty in breathing with a respiratory rate of &gt; 60 min in children less than 60 days old, &gt; 50 min in those less than 1 year old and &gt; 40 min for those aged 1 to 5 years)</p> <p>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</p> <p>Safety: N/A</p>
<b>Notes</b>	<p>Risk of bias: low (cluster coefficients and analysis by unit of randomization provided)</p> <p>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</p>

### Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Macartney 2000**

<b>Methods</b>	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
<b>Participants</b>	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 two periods
<b>Interventions</b>	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
<b>Outcomes</b>	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 from admission  Safety: N/A
<b>Notes</b>	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 table**

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## MacIntyre 2009

<b>Methods</b>	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 two 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"
<b>Participants</b>	Two hundred and ninety 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. Two families in the control group were lost to follow-up during the study. No reason was given for this
<b>Interventions</b>	Use of surgical masks and P2 mask versus no mask. The P2 mask is described as very cumbersome
<b>Outcomes</b>	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
<b>Notes</b>	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 [confidence interval] 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 0.11–0.98; $p = 0.046$ ). The study was underpowered to determine if there was a difference in efficacy between P2 and surgical masks (Table 5). The study conclusion appear to be a posthoc 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

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**Madge 1992**

<b>Methods</b>	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
<b>Participants</b>	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)
<b>Interventions</b>	Stepwise intervention programmes: gowns/gloves; cohort nursing + gowns/gloves; cohort nursing, versus no special precautions. The procedures evaluated in the two 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
<b>Outcomes</b>	Laboratory: yes - culture, antibodies titres, serological studies Effectiveness: RSV infections (seroconversion within 7 days of admission) Safety: N/A
<b>Notes</b>	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, two 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

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## Makris 2000

<b>Methods</b>	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 program 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
<b>Participants</b>	443 beds (patients) in the test group, 447 beds (patients) in the control group. We assumed number of beds as number of participants
<b>Interventions</b>	Infection-control education programme reinforcing handwashing and other hygienic measures versus normal care
<b>Outcomes</b>	Laboratory: no Effectiveness: upper respiratory infections Safety: N/A
<b>Notes</b>	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 don't 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 table

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**Master 1997**

<b>Methods</b>	Prospective cohort study conducted in an elementary school, Detroit, to evaluate the effect of a mandatory scheduled handwashing program 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 eight 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
<b>Participants</b>	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 eight classrooms (162 students) were the control group
<b>Interventions</b>	Handwashing program 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
<b>Outcomes</b>	Laboratory: no Effectiveness: upper respiratory infections (URI) - cough sneeze, pink eye, headache, mononucleosis, acute exacerbation of asthma, sinus trouble, fever alone, bronchitis Safety: N/A
<b>Notes</b>	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 table**

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## Morton 2004

<b>Methods</b>	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 crossover 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
<b>Participants</b>	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)
<b>Interventions</b>	Use of an alcohol gel as an adjunct to regular handwashing and educational program versus regular handwashing and educational program
<b>Outcomes</b>	Laboratory: no Effectiveness: days of absences from school for respiratory illness Safety: N/A
<b>Notes</b>	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 table

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**Murphy 1981**

<b>Methods</b>	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
<b>Participants</b>	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
<b>Interventions</b>	Handwashing versus handwashing, masks and gowns
<b>Outcomes</b>	Laboratory: yes Effectiveness: viral infections (including RSV) Safety: N/A
<b>Notes</b>	Risk of bias: medium  Notes: the authors conclude that there was no difference between the two 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

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## Niffenegger 1997

<b>Methods</b>	Prospective two-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
<b>Participants</b>	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 two groups, but data are not shown. No attrition is mentioned
<b>Interventions</b>	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
<b>Outcomes</b>	Laboratory: N/A Effectiveness: colds and ARIs no better defined Safety: N/A
<b>Notes</b>	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. The test group had significantly less colds than the control group ( $p < 0.05$ )

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**Nishiura 2005**

<b>Methods</b>	Case-control study carried out during the SARS outbreak (26 Feb 03 to 28 Apr 03) 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 three phases. The first phase (26 Feb to 4 Mar 06) in which an index case and 9 suspected secondary cases were admitted/cared for. The second phase (8 Mar to 11 Mar 03) in which outpatients were closed and staff no longer returned home as the outbreak spread and the third phase (11 Mar 03 to 28 April 03) in which the HFH was closed to all other than SARS cases who were isolated
<b>Participants</b>	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
<b>Interventions</b>	Handwashing before contact with SARS patient Handwashing after contact with SARS patient Masks Gloves Gowns All measures combined Analysis by epidemic stage is reported
<b>Outcomes</b>	SARS infection
<b>Notes</b>	Risk of bias: low  Notes: the authors conclude that masks (OR 0.3, 95% 0.1 to 0.7) and gowns (OR 0.2, 95% 0.0 to 0.8) were significantly associated with protection (OR, 95% to) during phase 1 but in Phase 2 masks (OR 0.1, 95% 0.0 to 0.3) and all measures (OR 0.1, 95% 0.0 to 0.3) were associated with protection probably because of 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

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## Ou 2003

<b>Methods</b>	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 Severe Acute Respiratory Syndrome (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
<b>Participants</b>	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)
<b>Interventions</b>	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: Health care 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)
<b>Outcomes</b>	Laboratory: no 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
<b>Notes</b>	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

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**Pang 2003**

<b>Methods</b>	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
<b>Participants</b>	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
<b>Interventions</b>	SARS was made notifiable on 9th of 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 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
<b>Outcomes</b>	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
<b>Notes</b>	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 25th of 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 table**

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## Pelke 1994

<b>Methods</b>	Controlled before and after study conducted in a neonatal intensive care unit (NICU) of Kapiolani medical center, Honolulu, Hawaii, to assess the effect of gowning on RSV and other infections, on traffic and handwashing patterns. Alternate 2- months 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 hand wash 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 compliance was studied, again without staff awareness, by 30 minutes direct observation. Follow-up of infection rates was planned through standard infection control surveillance
<b>Participants</b>	230 infants, aged 22 to 42 weeks, with birth a weight of 464-6195 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)
<b>Interventions</b>	Use of gowns and standard procedures (handwashing) versus standard procedures
<b>Outcomes</b>	Laboratory: serological evidence: yes Effectiveness: RSV infection Safety: N/A
<b>Notes</b>	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

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**Roberts 2000**

<b>Methods</b>	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
<b>Participants</b>	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
<b>Interventions</b>	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
<b>Outcomes</b>	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
<b>Notes</b>	Risk of bias: low (cluster coefficients and analysis by unit of randomization) Notes: The authors conclude that although there was no overall decrease in respiratory illness (RR 0.95 95% CI 0.89 to 1.01), but 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 three compliance levels are also reported. A so-so reported and well conducted trial

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Ryan 2001

<b>Methods</b>	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 two years of the study
<b>Participants</b>	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
<b>Interventions</b>	Structured top-down programme of handwashing at least 5 times daily
<b>Outcomes</b>	Laboratory: N/A Effectiveness: respiratory illness detected from sick parade records and outgoing recruits questionnaire on a sample survey Safety: N/A
<b>Notes</b>	Risk of bias: low Notes: the authors conclude that implementation of the control programme has seen near-halving of incidence of ARIs (based on three stratified samples of recruits infrequent hand washers 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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	



**Sandora 2005**

<b>Methods</b>	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 child care 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
<b>Participants</b>	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
<b>Interventions</b>	Alcohol-based hand sanitiser with bi-weekly hand-hygiene educational materials over 5 months versus bi-weekly educational material on healthy diet
<b>Outcomes</b>	Effectiveness: ARI (two 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)
<b>Notes</b>	Risk of bias: low 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 table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Sandora 2008

<b>Methods</b>	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'
<b>Participants</b>	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
<b>Interventions</b>	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
<b>Outcomes</b>	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 record reason for absenteeism either for gastrointestinal or respiratory causes Safety: N/A
<b>Notes</b>	The authors conclude that multifaceted intervention that included alcoholbased 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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**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 one study physician who was not informed of the results of assignment. Analysis was done based on the intention-to-treat. The study targeted community healthcare all over Japan and was conducted between Dec 2002 and Mar 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 one of the following: water gargling,  $n = 122$  (20 mL of water for about 15 seconds three times consecutively, at least three 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).

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 one symptom increased by two grades or more, and (3) worsening of a symptom of one 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 38C 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 (analyzed 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 two 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 table**

<b>Item</b>	<b>Judgement</b>	<b>Description</b>
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Seto 2003**

<b>Methods</b>	Case-control study Hong Kong, China, conducted during the period 15 March to 24 March 2003 in five hospitals. The study aims were to assess the effectiveness of protective procedures for contracting SARS in HCWs exposed to 11 index cases in three of the five hospitals during the SARS epidemic
<b>Participants</b>	<p>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.</p> <p>A SARS cases was defined as having fever of 38 C or more, radiological infiltrates, and two of either: new cough, malaise, signs of consolidation</p> <p>Description of controls: 241 staff from the five 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</p>
<b>Interventions</b>	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
<b>Outcomes</b>	SARS
<b>Notes</b>	<p>Risk of bias: medium (inconsistencies in the text: lack of description of controls)</p> <p>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</p>

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Simon 2006

<b>Methods</b>	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
<b>Participants</b>	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
<b>Interventions</b>	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
<b>Outcomes</b>	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
<b>Notes</b>	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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Snydman 1988**

<b>Methods</b>	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 two seasons following the introduction of infection control measures
<b>Participants</b>	HCW and patients in the special care baby unit
<b>Interventions</b>	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
<b>Outcomes</b>	Laboratory: RSV culture Effectiveness: RSV cases with symptoms and laboratory confirmation Safety: N/A
<b>Notes</b>	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 table**

<b>Item</b>	<b>Judgement</b>	<b>Description</b>
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Somogyi 2004

<b>Methods</b>	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
<b>Participants</b>	1 volunteer
<b>Interventions</b>	Three masks, two without air filter and allowing external exhalation, one with manifold and air filter
<b>Outcomes</b>	Effectiveness: plume of droplets as observed and photographed: masks were poor at preventing droplet spread
<b>Notes</b>	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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	



**Teleman 2004**

<b>Methods</b>	Case-control study assessing risk and protective factors in HCWs during the SARS outbreak in Singapore (1 to 22 March 2003)
<b>Participants</b>	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
<b>Interventions</b>	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 meter 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 Performed or assisted in intubation Performed suction of body fluids Administered oxygen Handwashing after each patient
<b>Outcomes</b>	SARS
<b>Notes</b>	Risk of bias: low Notes: The authors conclude that three 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. I wonder how much of the non-significance for certain factors is due to lack of statistical power

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Turner 2004a

<b>Methods</b>	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
<b>Participants</b>	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
<b>Interventions</b>	Use of salicylic acid versus salicylic acid and pyroglutamic acid versus "placebo" substance
<b>Outcomes</b>	Laboratory: yes Effectiveness: rhinovirus type 39 infection Safety: N/A
<b>Notes</b>	Risk of bias: high (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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Turner 2004b**

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

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Wang 2007

<b>Methods</b>	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 health care 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
<b>Participants</b>	During the study period 52,255 persons were placed under level A quarantine and 95,271 persons were placed under level B quarantine
<b>Interventions</b>	Exposure to level A quarantine versus level B
<b>Outcomes</b>	Laboratory: Serological evidence: yes Effectiveness: SARS (definition not reported) Safety: N/A
<b>Notes</b>	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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**White 2001**

<b>Methods</b>	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 & 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
<b>Participants</b>	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
<b>Interventions</b>	Pump activated antiseptic hand rub with benzalkonium chloride (SAB) (Woodward Laboratories) or inert placebo that “virtually” looked the same in batches of four colour coded bottles containing both. School staff, parents and participants were blinded
<b>Outcomes</b>	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
<b>Notes</b>	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 randomization procedure, educational programme and use of placebo hand rub make generalisability of the results debatable. No confidence intervals reported

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## White 2003

<b>Methods</b>	Prospective open cohort study carried out at the university of Colorado Boulder campus during eight 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
<b>Participants</b>	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
<b>Interventions</b>	Education programme and alcohol gel adjunct to handwashing in residence halls versus standard hygiene
<b>Outcomes</b>	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
<b>Notes</b>	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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

**Wu 2004**

<b>Methods</b>	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
<b>Participants</b>	<p>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</p> <p>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 (two matched sets) were excluded because they were aged less than 14 and seven matched sets were excluded because the case was reclassified as a HCW</p> <p>Cases and controls were interviewed for the 2 weeks preceding symptoms</p>
<b>Interventions</b>	<p>Always wearing a mask</p> <p>Intermittently wearing a mask</p> <p>Washing hands</p> <p>Owning a pet</p> <p>Visiting a farmer's market</p> <p>Visited clinics, eaten out, or taken taxis</p>
<b>Outcomes</b>	SARS
<b>Notes</b>	<p>Risk of bias: medium (inconsistencies in the text: lack of description of controls)</p> <p>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 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</p>

**Risk of bias table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Yen 2006

<b>Methods</b>	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
<b>Participants</b>	Health care 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
<b>Interventions</b>	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
<b>Outcomes</b>	Serological evidence: yes Effectiveness SARS (definition?) Safety N/A
<b>Notes</b>	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 reinforcement 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

### Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	



**Yin 2004**

<b>Methods</b>	Case-control study carried out in ten hospitals of Gunandong province, China, comparing the rate of usage of protective measures in HCWs with SARS and without SARS. The rate of exposure to SARS between two 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
<b>Participants</b>	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
<b>Interventions</b>	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
<b>Outcomes</b>	SARS
<b>Notes</b>	Risk of bias: medium (inconsistencies in the text: lack of description of controls) 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 doseresponse 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 table**

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

## Yu 2007

<b>Methods</b>	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 superspreading events of SARS occurred, and control wards were hospital wards in which patient(s) with SARS were admitted, but no superspreading events occurred. A superspreading event is defined as the development of $\geq 3$ 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 $\geq 3$ new cases of SARS in a ward during a period of 8 days but without any known sources of SARS
<b>Participants</b>	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
<b>Interventions</b>	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 behavior 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
<b>Outcomes</b>	Laboratory: Serological evidence: no Effectiveness: SARS (no definition) Safety: N/A
<b>Notes</b>	The authors conclude that environmental risk factors were significantly associated with the occurrence of a superspreading event (clustering of $\geq 3$ cases) included minimum distance between beds of $\leq 1$ 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 table

Item	Judgement	Description
Adequate sequence generation?	Unclear	
Allocation concealment?	Unclear	
Blinding?	Unclear	
Incomplete outcome data addressed?	Unclear	
Free of selective reporting?	Unclear	

### Table footnotes

CXR, chest X-ray; GI, gastro-intestinal; HCW, health care worker; HFH, Hanoi French Hospital; ITT, intention-to-treat; MCU, medical convalescent unit; NICU, neonatal intensive care unit; OR, odds ratio; PCU, physical conditioning unit; RSV, respiratory syncytial virus; SCBU, special care baby unit; URTI, upper respiratory tract infection; WBC, white blood cell.

## Characteristics of excluded studies

### Abou El Hassan 2004

Reason for exclusion	Topic completely extraneous
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### Amirav 2005

Reason for exclusion	Randomised controlled trial of aerosol treatment
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### Anderson 2004

Reason for exclusion	Mathematical model with interesting discussion of interaction between public health measures
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### Anonymous 2002

Reason for exclusion	News item
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### Anonymous 2003

Reason for exclusion	No data presented
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### Anonymous 2004

Reason for exclusion	News item
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### Anonymous 2005a

Reason for exclusion	News item
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### Anonymous 2005b

Reason for exclusion	News item
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### Anonymous 2005c

Reason for exclusion	News item
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### Aragon 2005

Reason for exclusion	Descriptive paper (non-comparative). Has no viral outcomes
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### Barros 1999

Reason for exclusion	Correlational study between incidence of upper respiratory tract infection (URTI) and factors such as overcrowding
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### Bell 2004

Reason for exclusion	Has unpublished entry exit screening data and extensive references but no comparative data
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### Ben-Abraham 2002

Reason for exclusion	Exclude - bacterial illness only
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### Black 1981

Reason for exclusion	Diarrhoea only outcome
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### Breugelmans 2004

Reason for exclusion	Description of risk factors in aircraft
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### Carbonell-Estrany 2008

Reason for exclusion	Immunoglobulin intervention and descriptive review
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### Carter 2002

Reason for exclusion	News item
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### Castillo-Chavez 2003

Reason for exclusion	Editorial
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### Cava 2005a

Reason for exclusion	Survey of quarantinees' views
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### Cava 2005b

Reason for exclusion	Personal experiences of quarantine
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### CDC 2003

Reason for exclusion	Case reports
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### Chai 2005

Reason for exclusion	Letter - about MRSA
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### Chaovavanich 2004

Reason for exclusion	Case report
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### Chau 2003

**Reason for exclusion** No original retrievable data. Mathematical model fitting expected to observed cases with quarantine in the SAR of Hong Kong

### Chen 2007

**Reason for exclusion** An assessment of the impact of different handwashing teaching methods. No clinical outcomes

### Chia 2005

**Reason for exclusion** Knowledge survey

### Cowling 2007

**Reason for exclusion** Epidemiology, non-comparative non-interventions study

### Daugherty 2008

**Reason for exclusion** No data free presented

### Davies 1994

**Reason for exclusion** Antibody titres as outcomes with so many biases that interpretation of study is problematic

### Day 1993

**Reason for exclusion** No acute respiratory infection outcome data

### Day 2006

**Reason for exclusion** Mathematical model no new data

### Dell'Omodarme 2005

**Reason for exclusion** Probabilistic and Bayesian mathematical model of screening at entry

### Desenclos 2004

**Reason for exclusion** Description of transmission

### DiGiovanni 2004

**Reason for exclusion** Qualitative study of compliance factors in quarantine

### Doebbeling 1992

**Reason for exclusion** RCT respiratory data not present. Only 3 viruses isolated in total with no viral typing available

### Dwosh 2003

**Reason for exclusion** Case series

### Fendler 2002

**Reason for exclusion** 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

**Reason for exclusion** Description of spread in aircraft and non-comparative data

### Fung 2004

**Reason for exclusion** Non-comparative

### Gaydos 2001

**Reason for exclusion** Editorial linked to Ryan

### Gensini 2004

**Reason for exclusion** Interesting historical review

### Giroud 2002

**Reason for exclusion** Non clinical outcomes

### Glass 2006

**Reason for exclusion** Mathematical model - no original data presented

### Goel 2007

**Reason for exclusion** Non-comparative study

**Gomersall 2006**

<b>Reason for exclusion</b>	Non-comparative study
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**Gore 2001**

<b>Reason for exclusion</b>	Summary of Dyer 2000 (already included)
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**Gostin 2003**

<b>Reason for exclusion</b>	Not an analytical study
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**Guinan 2002**

<b>Reason for exclusion</b>	It would appear that nine classes took part and “acted as their own controls”, but it is not clear if there was crossover 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 is the soap is used: in other words this is a (covert) publicity study
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**Gupta 2005**

<b>Reason for exclusion</b>	Economic model - no new data
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**Gwaltney 1982**

<b>Reason for exclusion</b>	No breakdown of cases by arm given
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**Han 2003**

<b>Reason for exclusion</b>	Non-comparative
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**Hayden 1985**

<b>Reason for exclusion</b>	This is an RCT with laboratory induced colds, small numbers 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 et al (included)
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**Hendley 1988**

<b>Reason for exclusion</b>	Inappropriate intervention
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**Hilburn 2003**

<b>Reason for exclusion</b>	No ARI/viral outcomes (e.g. URTIs)
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**Hilmarsson 2007**

<b>Reason for exclusion</b>	Animal study
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**Hirsch 2006**

<b>Reason for exclusion</b>	Study tested pharmacological interventions
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**Ho 2003**

<b>Reason for exclusion</b>	Descriptive review
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**Hsieh 2007**

<b>Reason for exclusion</b>	Mathematical model
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**Hugonnet 2007**

<b>Reason for exclusion</b>	Letter without any data
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**Jiang 2003**

<b>Reason for exclusion</b>	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] <i>Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih [Chinese Journal of Tuberculosis &amp; Respiratory Diseases]</i> . 26(10):594-7, 2003 Oct
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**Jones 2005**

<b>Reason for exclusion</b>	Historical account
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**Kaydos-Daniels 2004**

<b>Reason for exclusion</b>	Not an analytical study
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### Khaw 2008

**Reason for exclusion** Assessing the efficacy of O<sub>2</sub> delivery

### Kilabuko 2007

**Reason for exclusion** Aetiological study

### Kosugi 2004

**Reason for exclusion** Non-comparative study

### Lam 2004

**Reason for exclusion** Outcomes were generic (infection rates). No laboratory data available for viral diagnosis

### Lange 2004

**Reason for exclusion** No data presented

### Larson 2004

**Reason for exclusion** Inappropriate outcomes

### Larson 2005

**Reason for exclusion** 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

**Reason for exclusion** Attitude survey

### Lau 2005

**Reason for exclusion** Herbal remedy effectiveness assessment

### Lee 2005

**Reason for exclusion** Descriptive study of risk and protective factors of transmission in households. No assignment took place

### Lipsitch 2003

**Reason for exclusion** Mathematical model fit to evidence

### Luckingham 1984

**Reason for exclusion** Historical report on Tucson experience during Spanish flu pandemic

### Ma 2004

**Reason for exclusion** Case-control study of risk factors for SARS

### Marin 1991

**Reason for exclusion** Viral resistance study

### McSweeny 2007

**Reason for exclusion** Historical description

### Mikolajczyk 2008

**Reason for exclusion** No intervention

### Monsma 1992

**Reason for exclusion** Non-comparative study

### O'Callaghan 1993

**Reason for exclusion** Letter linked to Isaacs 1991

### Olsen 2003

**Reason for exclusion** Description of transmission

### Ooi 2005

**Reason for exclusion** Descriptive study but with interesting organisational chart

### Pang 2004

**Reason for exclusion** Descriptive study of Beijing outbreak. Some duplicate data in common with Pang 2004

**Pittet 2000**

<b>Reason for exclusion</b>	Analysis of relationship between handwashing compliance campaign and nosocomial bacterial infections (e.g. MRSA)
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**Prasad 2004**

<b>Reason for exclusion</b>	Letter of retrospective cohort - behavioural
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**Rabenau 2005**

<b>Reason for exclusion</b>	In vitro test of several disinfectants
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**Reynolds 2008**

<b>Reason for exclusion</b>	Describes the psychological effects of quarantine
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**Riley 2003**

<b>Reason for exclusion</b>	Mathematical model fit to evidence
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**Rosenthal 2005**

<b>Reason for exclusion</b>	Outcomes were generic (for example, pneumonia, URTIs). No laboratory data available for viral diagnosis
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**Safiulin 1972**

<b>Reason for exclusion</b>	Non-comparative set of studies with no clinical outcomes
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**Sandrock 2008**

<b>Reason for exclusion</b>	Review
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**Satter 2000**

<b>Reason for exclusion</b>	Experiment assessing virucidal activity of finger tip surface - no clinical outcome data
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**Schull 2007**

<b>Reason for exclusion</b>	Describes the impact of SARS in a Toronto study
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**Sizun 1996**

<b>Reason for exclusion</b>	This is a review, with no original data presented
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**Stoner 2007**

<b>Reason for exclusion</b>	No study data available
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**Stukel 2008**

<b>Reason for exclusion</b>	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
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**Svoboda 2004**

<b>Reason for exclusion</b>	Descriptive study with before and after data but shifting denominators
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**Ueno 1990**

<b>Reason for exclusion</b>	Experimental study. No clinical intervention
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**van der Sande 2008**

<b>Reason for exclusion</b>	Laboratory study without any clinical outcomes
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**Wang 2003**

<b>Reason for exclusion</b>	Descriptive study
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**Wang 2005**

<b>Reason for exclusion</b>	Case-control study of susceptibility factors
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**Weber 2004**

<b>Reason for exclusion</b>	Editorial linked to Larson 2004
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**White 2005**

<b>Reason for exclusion</b>	Redundant publication of White 2003
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### Wilczynski 1997

Reason for exclusion	Clinical trial of the effects of breast feeding
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### Wilder-Smith 2003

Reason for exclusion	Description of risk factors in aircraft
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### Wilder-Smith 2005

Reason for exclusion	Descriptive review
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### Wong 2005

Reason for exclusion	Attitude survey
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### Yu 2004

Reason for exclusion	Description of transmission
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### Zamora 2006

Reason for exclusion	Head-to-head comparison of two sets of PPEs with no controls and no clinical outcomes
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### Zhai 2007

Reason for exclusion	Non-comparative study
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### Zhao 2003

Reason for exclusion	CCT of SARS treatment
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## References to studies

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## Data and analyses

### Case control studies

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
I.1 Thorough disinfection of living quarters	1	990	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.23, 0.39]
I.2 Frequent handwashing	6	2077	Odds Ratio (M-H, Fixed, 95% CI)	0.45 [0.36, 0.57]
I.3 Wearing mask	5	1991	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.25, 0.40]
I.4 Wearing N95 respirator	2	340	Odds Ratio (M-H, Fixed, 95% CI)	0.09 [0.03, 0.30]
I.5 Wearing gloves	4	712	Odds Ratio (M-H, Fixed, 95% CI)	0.43 [0.29, 0.65]
I.6 Wearing gowns	4	712	Odds Ratio (M-H, Fixed, 95% CI)	0.23 [0.14, 0.37]
I.7 All interventions	2	369	Odds Ratio (M-H, Fixed, 95% CI)	0.09 [0.02, 0.35]







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### Internal sources

- The Cochrane Collaboration Steering Group, UK

### External sources

- NHS R&D programme, UK
- NHMRC, Australia competitive funding 2009





## Appendices

### 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 syncytial 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 syncytial 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 syncytial 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 syncytial 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+”)





## Graphs

