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Review Article

# Hand hygiene to reduce community transmission of influenza and acute respiratory tract infection: a systematic review

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Hand hygiene may be associated with modest protection against some acute respiratory tract infections, but its specific role in influenza transmission in different settings is unclear. We aimed to review evidence that improving hand hygiene reduces primary and secondary transmission of (i) influenza and (ii) acute respiratory tract infections in community settings. We searched Medline, Embase, Global Health and Cochrane databases up to 13 February 2012 for reports in any language of original research investigating the effect of hand hygiene on influenza or acute respiratory tract infection where aetiology was unspecified in community settings including institutions such as schools, and domestic residences. Data were presented and quality rated across outcomes according to the Grading of Recommendations Assessment, Development and Evaluation system. Sixteen articles met inclusion criteria. There was moderate to low-quality evidence of a reduction in both influenza and respiratory tract infection with hand hygiene interventions in schools, greatest in a lower–middle-income setting. There was high-quality evidence of a small reduction in respiratory infection in childcare settings. There was high-quality evidence for a large reduction in respiratory infection with a hand hygiene intervention in squatter settlements in a low-income setting. There was moderate- to high-quality evidence of no effect on secondary transmission of influenza in households that had already experienced an index case. While hand hygiene interventions have potential to reduce transmission of influenza and acute respiratory tract infections, their effectiveness varies depending on setting, context and compliance.

**Keywords** Acute respiratory tract infection, hand hygiene, influenza, systematic review.

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## Introduction

Hand hygiene is a simple, low-cost, non-pharmaceutical intervention that was recommended by local, national and international health agencies to prevent influenza transmission during the 2009 H1N1 influenza pandemic.[1,2] Although evidence suggests that hand hygiene reduces diarrhoea episodes by around a third,[3] the specific effect on influenza transmission is unclear. One previous review suggested that hygienic measures including hand washing,[4] especially around young children, could reduce spread of respiratory tract viruses in general. Two earlier reviews estimated that hand hygiene may reduce transmission of respiratory tract infections by 16%[5] and 21%,[6] although these figures were pooled across studies with different designs, settings and outcome measures. Results may also have been biased by poor quality of included studies.[5]

It is biologically plausible that enhanced hand hygiene would interrupt influenza transmission, predominantly through reducing contact and some droplet spread rather than through effects on aerosol transmission. However, it is unclear whether effects are likely to differ in different community settings, for example, in schools compared with households or in high versus low–middle-income countries. These questions are likely to be of interest to governments and policymakers developing preparedness strategies for the next influenza pandemic and were the focus of our review.

We anticipated that interest in the 2009 pandemic may have stimulated new research into non-pharmaceutical interventions for influenza. We systematically reviewed the latest evidence from both intervention and observational studies to investigate whether hand hygiene practised in the community protected against influenza or acute respiratory

tract infection in children and adults. We included studies based in both institutional non-healthcare settings, for example schools, and in domestic residences. We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to present data and rate quality of evidence.[7]

## Methods

### Search strategy

We sought to identify studies in community settings that examined the effect of a hand hygiene exposure (e.g. hand washing or hand sanitiser) on the risk or rate of developing influenza or an acute respiratory tract infection. Searches were carried out in any language in Medline (1946–), Embase (1974–) and Global Health (1910–) though OvidSP and in the Cochrane Central Register of Controlled Trials on 27 June 2011 and updated on 13 February 2012. Reference lists of relevant review articles were searched by hand. The following search strategy was used:

### Medline

1. exp Handwashing/
2. ('Hand washing' or 'handwashing' or 'hand-washing' or 'Hand hygiene' or 'Hand gel*' or 'Hand sanitizer*').tw.
3. 1 or 2
4. exp Influenza, Human/or exp Respiratory Tract Infections/
5. ('Influenza' or 'Flu' or 'Respiratory tract infection*' or 'Acute respiratory infection*').tw.
6. 4 or 5
7. 3 and 6

### Embase and Global Health

1. exp Hand Washing/
2. (hand washing or handwashing or hand-washing or hand hygiene or hand gel* or hand sanitizer*).tw.
3. 1 or 2
4. exp Influenza/or exp respiratory tract infection/
5. (influenza or flu or acute respiratory infection* or acute respiratory tract infection*).tw.
6. 4 or 5
7. 3 and 6

### Cochrane Central Register of Controlled Trials

#1 MeSH descriptor handwashing explode all trees
#2 (handwashing):ti,ab,kw or (hand washing):ti,ab,kw or (hand-washing):ti,ab,kw or (hand hygiene):ti,ab,kw or (hand gel*):ti,ab,kw or (hand sanitiser*):ti,ab,kw or (hand sanitizer*):ti,ab,kw in Cochrane Reviews, Other Reviews and Clinical Trails
#3 (#1 OR #2)
#4 MeSh descriptor Influenza, Human explode all trees
#5 MeSh descriptor Respiratory Tract Infections explode all trees
#6 (influenza):ti,ab,kw or (flu):ti,ab,kw or (Respiratory tract infection*):ti,ab,kw or (acute respiratory infection*):ti,ab,kw
#7 (#4 OR #5 OR #6)
#8 (#3 AND#7)

### Eligibility

Articles describing original research conducted in community settings were eligible for inclusion if they reported a measure of the effect of hand hygiene on influenza or acute respiratory tract infection or the means to calculate it. Community settings included institutions such as schools, childcare centres and workplaces as well as domestic residences. We did not include research conducted in hospitals or care homes as the focus was on non-healthcare settings. We considered individually or cluster randomised controlled trials, quasi-randomised controlled trials, crossover trials, cohort studies, case–control studies and cross-sectional surveys. We excluded before–after and ecological studies. We also excluded studies that described multicomponent hygiene interventions or that tested large numbers of measures of hand hygiene without adjustment for multiple testing.

### Study selection and data extraction

Two authors (EF and CWG) independently read all titles and relevant abstracts to determine eligibility for full-text review. Reference lists of relevant articles were hand searched for further references. EF and CWG independently read all articles included in the full-text review, determined which met inclusion criteria and extracted relevant data. Any discrepancies were discussed and if necessary referred to a 3rd author (ACH). Data were extracted on definitions of outcome, descriptions of exposure or intervention, study size, design, population, setting, for example, institutional versus domestic, high versus low or middle-income, duration and effect sizes, for example, risk, rate or odds ratio with 95% confidence intervals. Where possible, the main reported multivariable measures of effect were presented for each study with 95% confidence intervals. If no effect measure was reported but raw figures were given, the most appropriate ratio measure of effect was calculated along with 95% confidence intervals (according to formulae in Appendix S1[8]) by two authors independently. For cluster intervention studies where it was necessary to calculate an effect measure, if possible a design effect was also calculated[9] (see Appendix S1). The square root of the design effect was then multiplied by the standard error, and 95% confidence intervals were recalculated using the generic inverse variance method in RevMan software to account for the effect of clustering[9] (see Appendix S1 for further details). This is denoted by the symbol[†] in the tables. Where this was not possible, for example, if no intracluster

correlation coefficient was reported and none was available from similar studies, 95% confidence intervals were calculated but without adjustment for clustering. This would result in artificially narrowed confidence intervals which are denoted by italics in tables.

### Data presentation

Results were presented in Tables 1 (laboratory-confirmed influenza) and Table 2 (acute respiratory tract infection including influenza-like illness). These were adapted from GRADE 'Summary of Findings' tables.[10] It was not feasible to meta-analyse these data due to heterogeneity, in particular variable reporting of intracluster correlation coefficients, design effect and adjustment for clustering in cluster intervention trials. Instead, we plotted the effect size against the log of the sample size to compare the effects of hand hygiene on (i) influenza and (ii) acute respiratory tract infection in different settings. Where results were presented by setting income, the World Bank classification of countries as 'low', 'lower–middle', 'upper–middle' and 'high'-income economies was used. An exception to this was a study in Pakistan (a lower–middle-income economy) that was conducted in squatter settlements; this was described as a 'low-income' setting.

### Quality assessment

A key feature of the GRADE method is that quality is assessed across outcomes rather than by individual study.[11] There are four categories of quality ratings in GRADE – 'high', 'moderate', 'low' and 'very low'. Briefly, the default quality rating is 'high' for evidence from randomised controlled (including cluster) trials and 'low' for evidence from observational studies. Evidence for each outcome is examined for risks of bias, inconsistency, indirectness, imprecision and publication bias. Quality may be rated down if there is evidence of any of these five factors, for example, a randomised controlled trial where risk of bias is judged to be serious would be rated down by 1 point from 'high' to 'moderate'. Conversely, quality may be modified upward if there is a large magnitude of effect, a dose response observed or if any plausible confounders are likely to minimise the observed effect. Quality was assessed independently by two authors for each outcome following GRADE guidance. Overall quality ratings are shown in Tables 1 and 2 (with 'low' and 'very low' categories combined). Further information on how ratings were determined for each outcome is given in the table footnotes.

## Results

### Included studies

Eight hundred and seventy-five citations were found from searches of electronic databases, of which 96 were retrieved for full-text review and 13 met inclusion criteria. Three additional references were found through hand searches – see Figure 1.

Intervention studies were carried out in various community settings including institutions: schools (5), childcare centres (2), an elderly day care centre (1), an office (1) and student halls of residence (1) as well as domestic settings: households (4) and squatter settlements (1). Interventions included hand hygiene education along with provision of either soap (3), hand sanitiser (7) or both (1), education and required washing or sanitising of children's hands (3), education and training of children, teachers and parents (1). Further details of interventions are given in Table S1. The one included observational study was a matched case–control study in healthy clinic attendees in which usual hand hygiene practices were surveyed.

### Hand hygiene and laboratory-confirmed influenza – institutional settings

In two cluster randomised trials of a hand hygiene intervention in schools,[12,13] rates of laboratory-confirmed influenza were lower in those receiving a hand hygiene intervention compared with controls – rate ratio (RR) 0·50 (95% confidence interval 0·38–0·66)[13] and RR 0·81 (0·54–1·23)[12] – although this was only significant for one study in a lower–middle-income setting. In the second study, there was a significant reduction in incidence of influenza A [RR 0·48 (0·26–0·87)] but not influenza B [RR 1·45 (0·79–2·67)] in subgroup analysis.[12] Overall, this evidence was rated moderate quality.

A small matched case–control study[14] provided low-quality evidence of a protective effect in healthy clinic attendees in an upper–middle-income setting: participants reporting frequent hand washing were significantly less likely to be seropositive to influenza A H1N1 pandemic strain – odds ratio 0·21 (0·06–0·74) – than those who washed their hands less often.

### Hand hygiene and laboratory-confirmed influenza – domestic settings

In one household study,[15] there was no evidence of a protective effect of hand hygiene on rates of laboratory-confirmed influenza [RR 1·15 (0·57–2·32)]. The quality of this evidence was low. Two household studies of the effect of implementing a hand hygiene intervention to prevent secondary influenza transmission after a case in the household[16,17] provided moderate-quality evidence of no effect on secondary transmission. See Table 1.

### Hand hygiene and influenza-like illness or acute respiratory tract infection – institutional settings

In the same two cluster randomised studies in schools reported above,[12,13] hand hygiene interventions were

**Table 1.** Effect of hand hygiene on laboratory-confirmed influenza

| Description | | | Risk or rate of illness | | Relative effect (95% CI) | Quality of evidence |
|---|---|---|---|---|---|---|
| No. of studies | Design | Setting | Hand hygiene | Control | | |
| Influenza attack rate in schools [follow-up mean 131 days; assessed with: RT-PCR (1 study) or QuickVue antigen detection test (1 study)] | | | | | | |
| 2 | Randomised cluster trials | Schools<br>Egypt[13]<br>USA[12] | Influenza rate<br>=125/250 584 child weeks<br>=51/42 375 child weeks<br>*n* = 22 577 | Influenza rate<br>=281/282 832 child weeks<br>=53/41 625 child weeks<br>*n* = 25 234 | RR 0·50 (0·38–0·66†)<br>RR 0·81 (0·54–1·23)[a] | ⊕⊕⊕O<br>Moderate-quality[b] evidence of effect in lower–middle-income setting |
| Influenza H1N1 seropositivity in community (assessed with: Haemagglutinin inhibition assay titre ≥40) | | | | | | |
| 1 | Case–control study | Serological survey, various settings<br>China[14] | Raw data not shown<br>*n* = 65 | Raw data not shown<br>*n* = 65 | OR 0·21 (0·06–0·74) | ⊕⊕OO<br>Low-quality[c] evidence of effect |
| Influenza attack rate in households (follow-up 19 months; assessed with: RT-PCR) | | | | | | |
| 1 | Randomised cluster trial | Households<br>USA[15] | Influenza rate<br>=0·60/1000 person weeks<br>*n* = 946 | Influenza rate<br>=0·52/1000 person weeks<br>*n* = 904 | RR 1·15 (0·57–2·32†) | ⊕⊕OO<br>Low-quality[d] evidence of no effect |
| Risk of secondary influenza transmission in households (follow-up mean 381·5 days; assessed with: RT-PCR or serology (4-fold rise in HI titre in paired samples)[e] | | | | | | |
| 2 | Randomised cluster trials | Households<br>Hong Kong[16]<br>Thailand[17] | Secondary influenza risk<br>=14/257 (5·4%)<br>=66/292 (22·6%)<br>*n* = 549 | Secondary influenza risk<br>=28/279 (10·0%)<br>=58/302 (19·2%)<br>*n* = 581 | OR 0·57 (0·26–1·22)[f]<br>OR 1·20 (0·76–1·88) | ⊕⊕⊕O<br>Moderate-quality[g] evidence of no effect on secondary transmission |

RR (95% confidence intervals†) denotes confidence intervals calculated according to formulae in Appendix S1 and adjusted for clustering by multiplying standard error by square root of design effect.

[a]In subgroup analysis in one study, there was a significantly lower incidence of influenza A in the intervention group: adjusted IRR = 0·48 (95% CI 0·26–0·87) but not for influenza B: adjusted IRR = 1·45 (95% CI 0·79–2·67).[12]

[b]Outcome rated 'moderate quality' due to serious risk of bias associated with low rates of influenza testing which may have been differential across intervention and control groups: in one study, only 34% of school absences had a reason given (so many ILIs may have been missed) and up to 24% of ILIs identified were not tested for influenza.[12] In a second study, only 33% and 47% of ILIs in the control and intervention groups, respectively were tested for influenza.[13] Also despite randomisation, there were significant differences in baseline characteristics between groups in one study.[12]

[c]Outcome rated 'low quality' as evidence is from an observational study with a risk of selection bias as only half of potential cases were included due to lack of contact information. Also the exposure 'frequent hand washing' was not defined, and there was little description of control for confounding.

[d]Outcome rated 'low quality' due to imprecision (small number of cases) and serious risk of bias. Risk of bias was due to loss to follow-up: 17·5% of households were not contactable after randomisation, some baseline imbalances between groups, differential reporting of weekly illnesses between intervention and control groups and recording of outcomes was sometimes unclear, for example, groups combined for influenza/ILI/ARI in some analyses.

[e]One study used RT-PCR alone for influenza diagnosis.[16] The other study which used both RT-PCR and paired serum samples to detect a fourfold rise in HI titre identified 309 cases (90%) by RT-PCR and an additional 34 (10%) by serology testing.[17]

[f]In Subgroup analysis in one study, where the intervention was applied within 36 hours of diagnosis of the index case, the odds ratio for influenza among contacts was 0·46 (95% CI 0·15–1·43).[16] In the other study, where the intervention was applied within 48 hours of diagnosis of the index case, the odds ratio for influenza among contacts was 1·06 (95% CI 0·62–1·82).[17]

[g]Outcome rated 'moderate quality' due to imprecision (both studies underpowered as did not reach recruitment goals).[16,17]

RR, rate ratio. OR, odds ratio.

**Table 2.** Effect of hand hygiene on acute respiratory tract infection including influenza-like illness

| Description | | | Risk or rate of illness | | Relative effect (95% CI) | Quality of evidence |
|---|---|---|---|---|---|---|
| **No. of studies** | **Design** | **Setting** | **Hand hygiene** | **Control** | | |
| ILI absence rate in schools [follow-up mean 131 days; assessed with CDC definition (fever plus either cough or sore throat)] | | | | | | |
| 2 | Randomised cluster trials | Schools<br>Egypt[13]<br>USA[12] | ILI absence rate<br>=917/250 584 child weeks<br>=171/42 375 child weeks<br>*n* = 22 577 | ILI absence rate<br>=1671/282 832 child weeks<br>=190/41 625 child weeks<br>*n* = 25 234 | <br>RR 0·62 (0·49–0·78[†])<br>RR 0·86 (0·60–1·22) | ⊕⊕⊕O<br>Moderate-quality[a] evidence of effect in lower–middle-income setting |
| Respiratory absence in schools (follow-up mean 47 days; assessed with reason for absence given as symptoms including cough, sneeze, sinus trouble, bronchitis, fever alone, pink eye, headache, mononucleosis and acute exacerbation of asthma) | | | | | | |
| 3 | 2 Non-randomised cluster trials<br>1 non-randomised crossover trial | Schools<br>USA (i)[20]<br>USA (ii)[19]<br>USA (iii)[18] | Respiratory absence rate<br>=69/9615 child days<br>=64/5172 child days<br>=31/8292 child days<br>*n* = 741 | Respiratory absence rate<br>=101/9459 child days<br>=70/5836 child days<br>=62/8260 child days<br>*n* = 753 | <br>*RR 0·67 (0·49–0·91)*<br>*RR 1·03 (0·74–1·45)*<br>*RR 0·50 (0·32–0·77)* | ⊕⊕OO<br>Low-quality[b] evidence of effect |
| Upper respiratory tract infection rate in childcare centres [follow-up 275 days; assessed with two of the following symptoms for 1 day or one symptom (excluding cough) for 2 days: runny nose, blocked nose, cough] | | | | | | |
| 1 | Randomised cluster trial | Child care centres<br>Australia[21] | URI incidence rate<br>=1716/62 159 child days<br>*n* = 299 | URI incidence rate<br>=1547/51 518 child days<br>*n* = 259 | <br>RR 0·95 (0·89–1·01) | ⊕⊕⊕⊕<br>High-quality evidence of marginal effect[c] |
| Sore throat or cold in childcare centres (follow-up 2 months post-intervention; assessed with symptoms reported by parent or teacher but no definition given) | | | | | | |
| 1 | Randomised cluster trial | Child care centres<br>Denmark[22] | Illness risk<br>=29/212 children (13·7%)<br>*n* = 212 | Illness risk<br>=45/263 children (17·1%)<br>*n* = 263 | <br>*RR 0·80 (0·52–1·23)* | ⊕⊕OO<br>Low-quality[d] evidence of no effect |
| Upper respiratory tract infection rate in elderly day care centres (follow-up 4 months; assessed with nasal congestion, sore throat, new or increased cough, wheeze, sputum production or respiratory difficulty with or without fever) | | | | | | |
| 1 | Non-randomised crossover trial | Elderly day care centres<br>USA[23] | Illness rate<br>=8·27/100 person months<br>*n* = 104 (mean across participating months) | Illness rate<br>=7·04/100 person months<br>*n* = 101 (mean across participating months) | <br>*RR 1·28 (0·70–2·32)* | ⊕⊕OO<br>Low-quality[e] evidence of no effect |

**Table 2.** (Continued)

| Description | | | Risk or rate of illness | | Relative effect (95% CI) | Quality of evidence |
|---|---|---|---|---|---|---|
| **No. of studies** | **Design** | **Setting** | **Hand hygiene** | **Control** | | |
| Risk of common cold in the workplace (follow-up 426 days; assessed with reporting of 'cold' but no definition given) | | | | | | |
| 1 | Randomised controlled trial | Office Germany[24] | Cold risk =27/64 participants (42·2%) *n* = 64 | Cold risk =44/65 participants (67·7%) *n* = 65 | OR 0·35 (0·17–0·71) | ⊕⊕OO Low-quality[f] evidence of effect |
| Upper respiratory tract infection risk in student halls of residence (follow-up 8 weeks; assessed with two or more of the following, one of which must last at least 2–3 days: sore throat, stuffy nose, ear pain, painful/swollen neck, cough, chest congestion, sinus pain, fever) | | | | | | |
| 1 | Non-randomised cluster trial | Student halls of residence USA[25] | Illness risk =70/188 participants (37·2%) *n* = 188 | Illness risk =94/203 participants (46·5%) *n* = 203 | *RR 0·80 (0·63–1·01)* | ⊕⊕OO Low-quality[g] evidence of no effect |
| Rates of cough or difficulty breathing in under 15s in squatter settlements [follow-up 355 days; assessed with parent-reported cough or difficulty breathing in the last week. For under 5s, pneumonia diagnosed if raised respiratory rate present above WHO thresholds (>60 if under 60 days old, >50 if aged 60–364 days, >40 if aged 1–5 years)] | | | | | | |
| 1 | Randomised cluster trial | Households in squatter settlements Pakistan[26] | Illness incidence rate = 4·16/100 person weeks *n* = 1640 children <15 years at baseline | Illness incidence rate = 8·50/100 person weeks *n* = 1528 children <15 years at baseline | RR 0·49 (0·35–0·63) | ⊕⊕⊕⊕ High-quality evidence of effect in low-income setting |
| ILI attack rate in households [follow-up 19 months; assessed with CDC definition (fever plus either cough or sore throat)] | | | | | | |
| 1 | Randomised cluster trial | Households USA[15] | ILI rate = 2·52/1000 person weeks *n* = 946 | ILI rate = 2·77/1000 person weeks *n* = 904 | RR 0·91 (0·69–1·20[†]) | ⊕⊕OO Low-quality[h] evidence of no effect |
| Risk of secondary ILI transmission in households [follow-up mean 381·5 days; assessed with CDC definition (fever plus either cough or sore throat) for all except children under 2 years in one study for whom definition was fever plus one of nasal discharge/congestion, cough, conjunctivitis, respiratory distress, sore throat and new seizure] | | | | | | |
| 2 | Randomised cluster trials | Households Hong Kong[16] Thailand[17] | Secondary ILI risk =9/257 participants (3·5%) =50/292 participants (17·1%) *n* = 549 | Secondary ILI risk =14/279 participants (5·0%) =26/302 participants (8·6%) *n* = 581 | OR 0·81 (0·33–2·00) OR 2·09 (1·25–3·50) | ⊕⊕⊕O Moderate-quality[i] evidence of no effect on secondary transmission |

**Table 2.** (Continued)

| Description | | | Risk or rate of illness | | Relative effect (95% CI) | Quality of evidence |
|---|---|---|---|---|---|---|
| **No. of studies** | **Design** | **Setting** | **Hand hygiene** | **Control** | | |
| Upper respiratory tract infection secondary transmission rate in households [follow-up 181 days; assessed with two of the following symptoms for 1 day or one symptom (excluding cough) for 2 days: runny nose, stuffy/blocked nose, cough, fever/chills, sore throat, sneezing] | | | | | | |
| 1 | Randomised cluster trial | Households USA[27] | Secondary URI rate =241/9648 person days *n* = 551 | Secondary URI rate =202/8525 person days *n* = 502 | RR 0·97 (0·72–1·30) | ⊕⊕⊕⊕ High-quality evidence of no effect on secondary transmission |

RR (95% confidence intervals[†]) denotes confidence intervals calculated according to formulae in Appendix S1 and adjusted for clustering by multiplying standard error by square root of design effect.

*RR (95% confidence intervals)* denotes confidence intervals calculated according to formulae in Appendix S1 but unadjusted for clustering.

[a]Outcome rated 'moderate quality' due to serious risk of bias from incomplete ascertainment of outcome (reasons for absence given for only 34% of illnesses in one study[12] and proportion not reported – but appears low – in the other study[13]).

[b]Outcome rated 'low quality' due to very serious risks of bias across all studies from lack of randomisation, loose-case definition, lack of intention to treat analysis (one study[20]), lack of control for clustering, risk of contamination of the intervention across groups in the crossover study[18] and no assessment of compliance with intervention.

[c]Effect described as 'marginal' because although only a small effect that just failed to reach statistical significance in multivariable analysis was seen, significant results were presented for various subgroups including children aged under 24 months [RR 0·90 (0·83–0·97)] and those who complied best with the hand hygiene intervention [RR 0·89 (0·82–0·97)].

[d]Outcome rated 'low quality' due to imprecision (small numbers of illnesses) and serious risk of bias. Risk of bias was due to unclear reporting of loss to follow-up, lack of case definition, absence of statistical analysis, no control for clustering or repeated episodes of illness.

[e]Outcome rated 'low quality' due to imprecision (small number of illnesses) and very serious risks of bias from insufficient number of clusters, lack of randomisation, lack of control for clustering, risk of contamination between periods on and off the intervention, unclear reporting of outcomes and loss to follow-up. NB Rate ratio and confidence intervals calculated from numbers in this table of publication, not rates given in text.

[f]Outcome rated 'low quality' due to imprecision (small number of participants) and serious risk of bias. Risk of bias was due to low initial response rate (15·8%), baseline imbalance between groups (more females in intervention group) and no accounting for multiple episodes of illness in analysis.

[g]Outcome rated 'low quality' due to very serious risks of bias from lack of randomisation, insufficient number of clusters, loss to follow-up, unclear reporting of outcomes, lack of control for clustering or repeated episodes of illness.

[h]Outcome rated 'low quality' due to imprecision (sample size calculation assumes much larger rate of illness than found) and serious risk of bias. Risk of bias was due to differential completing of illness surveys in intervention and control groups, some baseline imbalances between groups, loss to follow-up and unclear reporting of outcomes.

[i]Outcome rated 'moderate quality' due to imprecision (both studies had small numbers of illnesses and neither reached recruitment goals).

RR, rate ratio or risk ratio depending on effect measure presented. OR, odds ratio.

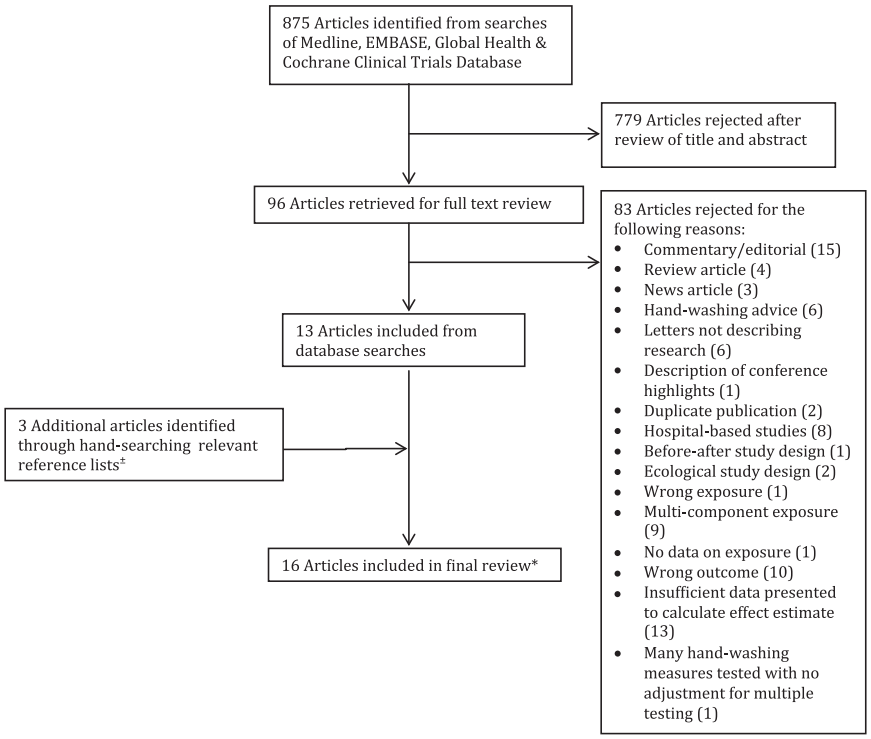


**Figure 1.** Flowchart of studies. *Studies were published between 1997 and 2011 and included nine cluster randomized trials, four non-randomized cluster trials, one crossover intervention trial, one individually randomised controlled trial and one matched case control study. ‡Of the three articles not identified through database searches, two had a main outcome of 'illness absenteeism',[18,20] with respiratory illness as a subgroup and the third was a Danish article with the outcome described as 'sickness' in the limited English translation available online.[22]

associated with a reduction in rates of absenteeism due to clinically defined influenza-like illness (a moderate-quality outcome), which was significant in a lower–middle-income setting – RR 0·62 (0·49–0·78). In three non-randomised cluster intervention studies in elementary schools,[18–20] there was low-quality evidence of a trend towards lower rates of absence due to respiratory tract illness in those receiving the hand hygiene intervention, significant for two of three studies.[18,20] One cluster randomised trial of a hand hygiene intervention in childcare centres[21] found high-quality evidence of a marginal effect – RR 0·95 (0·89–1·01), which was significant for those aged under 24 months [RR 0·90 (0·83–0·97)] and for children who complied best with the hand hygiene intervention [RR 0·89 (0·82–0·97)]. In another cluster intervention study in childcare centres[22] where the outcome was rated 'low quality', no significant protective effect was seen – risk ratio 0·80 (0·52–1·23).

In an elderly day care centre,[23] providing staff with alcohol hand gel resulted in no change to respiratory tract illness rates in elderly attendees over the winter – RR 1·28 (0·70–2·32). A small individually randomised trial in the workplace[24] found a significantly lower risk of a 'cold' in those receiving an alcohol hand gel intervention – odds ratio 0·35 (0·17–0·71). In a study in student halls of residence,[25] although risk of respiratory tract illness was lower in those receiving a hand hygiene intervention, the effect was not significant – risk ratio 0·80 (0·63–1·01). All evidence for these outcomes was rated 'low quality'.

## Hand hygiene and influenza-like illness or acute respiratory tract infection – domestic settings

A cluster randomised trial of a soap and hand hygiene education intervention in squatter settlements in a low-income setting[26] provided high-quality evidence of a significant reduction in rates of cough and difficulty breathing in children aged under 15 – RR 0·49 (0·35–0·63). A household study in the USA[15] provided low-quality evidence of no effect – RR 0·91 (0·69–1·20).

Finally, several cluster randomised studies investigated whether hand hygiene interventions reduced secondary transmission of influenza-like illness (ILI) in households. Two studies from Hong Kong[16] and Thailand[17] provided moderate-quality evidence of no significant reduction in secondary household transmission of ILI when hand hygiene interventions were implemented after identification of a laboratory-confirmed index case. However, in a subgroup analysis in one study, there was a significant reduction in ILI rates in the hand hygiene group when the intervention was implemented within 36 hours of symptom onset in the index case – odds ratio 0·46 (0·22–0·96).[16] There was high-quality evidence of no effect on secondary household transmission of respiratory tract illnesses from a North American study where the intervention was implemented prior to any index case[27] – RR 0·97 (0·72–1·30). See Table 2.

Results for both influenza and acute respiratory tract infection outcomes are summarised graphically in Figure 2

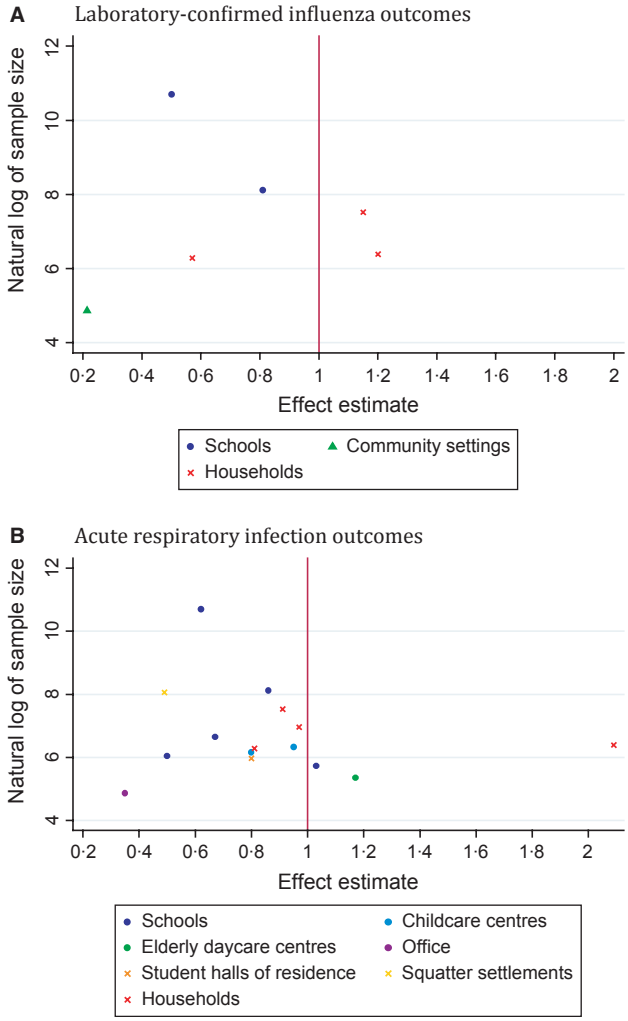


**Figure 2.** Effect of hand hygiene on influenza and acute respiratory infection in different settings. (A) Laboratory-confirmed influenza outcomes. (B) Acute respiratory infection outcomes.

where effect sizes follow a similar distribution across both types of outcome.

## Discussion

### Summary of findings

There was moderate–high-quality evidence that hand hygiene was associated with a large reduction in influenza and acute respiratory tract infections in institutional settings (schools) and a domestic setting (squatter settlements) in two studies in low to middle-income countries. In higher-income countries, one study provided high-quality evidence of a small reduction in acute respiratory tract infections in childcare centres, and there was lower-quality evidence of a protective effect in schools and workplaces. For domestic settings, there was moderate–high-quality evidence that a hand hygiene intervention alone did not prevent secondary influenza transmission in households with an index case.

### Strengths and limitations

Our review was carried out systematically with a comprehensive search strategy that identified all studies included in previous similar reviews along with several new studies published after the 2009 H1N1 influenza pandemic. We clearly defined outcomes and separated results by laboratory-confirmed influenza and clinically defined acute respiratory tract infection or influenza-like illness. We also reviewed quality of evidence by outcome according to GRADE criteria[11] and gave greater weight in our synthesis to outcomes rated 'moderate' or 'high' quality. We attempted to present results by setting (institutional versus domestic and high income versus low to middle income), as knowledge of effects expected in different settings would help to inform policymakers, although this approach was limited both by lack of studies and by the poor quality of studies in certain settings.

We decided not to generate a pooled estimate of effect due to heterogeneity of settings, hand hygiene interventions and outcomes across studies. Synthesising evidence was also made more difficult by poor methodology and reporting of some cluster intervention trials. Several studies had design flaws including insufficient numbers of clusters, no formal randomisation of clusters, no control for clustering in the analysis and no reporting of an intracluster correlation coefficient,[28] so it was not possible to calculate cluster-adjusted confidence intervals. However, outcome quality from any study with these issues was rated 'low' according to the GRADE system and evidence weighted accordingly. Heterogeneity of hand hygiene interventions may have affected results if some interventions were more effective than others. However, evidence suggests that both soap and water and various preparations of alcohol-based hand rub are effective in inactivating H1N1 pandemic strain influenza on human hands.[29] Assessing compliance with hand hygiene interventions was not carried out in a consistent way across studies, so apparent lack of effect may have been due to poor compliance rather than lack of effectiveness. In studies where compliance data were used to inform analyses, greater protective effects were seen in those with the best compliance. [21,27]

### Comparison with previous reviews

Our results were consistent with earlier findings from a previous review of hand washing with water (±soap) in 2006 that found an overall 16% reduction in respiratory tract infections based on seven intervention studies.[5] None of these studies examined influenza specifically, and overall quality of included studies was judged to be poor. Another meta-analysis of the effect of various hand hygiene interventions on respiratory tract infection across 13 studies,

published in 2008[6], estimated a pooled reduction of 21% for respiratory tract illness across multiple settings. Again, no study was specific to influenza, and individual studies had many methodological limitations. A Cochrane review of physical interventions to reduce respiratory tract virus transmission[4] concluded that 'the highest-quality cluster RCTs suggest respiratory tract virus spread can be prevented by hygienic measures, such as hand washing, especially around younger children'. A final review of the effect of hand gel on elementary school absenteeism did not provide a pooled effect estimate and concluded that studies were of poor quality with high-potential risk of bias.[30] We included several newer studies that were not found in any of these reviews,[12–14,17,24] four of which incorporated the outcome laboratory-confirmed influenza.[12–14,17] We excluded several studies that were included in previous reviews because of (i) use of a before–after study design,[31] where lack of accounting for seasonal variability of influenza and other external factors could introduce serious risks of bias and confounding and (ii) insufficient data reported on respiratory tract outcomes to calculate an appropriate effect measure.[32,33] In previous reviews, these studies were generally described as having major methodological limitations.

We also excluded studies that examined the effect of multicomponent hygiene interventions, for example, disinfecting surfaces as well as hands and toys[34–37] as it was difficult to isolate the relative effect of hand hygiene from among these interventions. None of these earlier studies examined the effect of influenza specifically. Three newer cluster randomised trials with influenza and influenza-like illness as outcomes were not eligible for inclusion as they examined the effect of hand hygiene only in combination with facemask use. All three studies (two in university halls of residence in the USA[38,39] and one of secondary transmission in German households[40]) suggested a reduction in influenza and/or ILI in groups receiving hand hygiene and facemasks compared with controls but results were generally not statistically significant. A recently published cluster randomised trial[41] of regular hand sanitiser use on ILI absence in Thai pre-schools was not eligible for inclusion because insufficient data were presented on ILI episodes to allow an effect measure to be calculated.

### Interpretation and implications

The greatest effect of hand hygiene was seen in two studies in low to middle-income settings, which may partly be explained by differences in access to soap and hand-washing equipment. In higher-income settings, smaller effects were seen, which tended to be in institutions such as childcare centres and schools. This may be unsurprising as young children are both less likely to practise good hand hygiene and more prone to experience a relatively heavy burden of influenza-related morbidity.[42] There is good biological plausibility for an effect[43]: improving hand hygiene is likely to reduce transmission of influenza and other respiratory tract viruses by interrupting fomite and to some extent droplet spread,[29,44,45] although it is unlikely to affect aerosol transmission. The likely impact of hand hygiene depends on the relative importance of these different modes of influenza transmission and is likely to be situation-specific, for example, it may be less effective for repeated exposures. Nonetheless, in most domestic and institutional settings such as schools, hand hygiene would be expected to be a safe, acceptable intervention,[43] although evidence from schools suggests acceptability is greater if hand hygiene is used as a temporary measure to prevent ongoing disruption to lessons.[46] Finding interventions that successfully improve hand hygiene remains a challenge; several studies in this review suggested that there was little difference in hand hygiene behaviours between intervention and control groups. In general, interventions designed to improve health that are informed by behavioural change theory are more likely to succeed than others.[47] Compliance with hand hygiene interventions in particular is likely to depend on context, for example, fear generated during a pandemic situation might drive higher compliance,[43] especially if the perceived severity of threat is high. In such a situation, hand hygiene messages might help to promote general awareness of influenza-avoidance strategies such as social distancing and other respiratory tract hygiene behaviours.[43] In household settings, it will be important to intervene early either through efforts to improve general hand hygiene behaviour or advice to implement enhanced hand hygiene immediately after development of an index case (rather than waiting for physician confirmation of diagnosis). Taken together, these findings suggest that the effectiveness of hand hygiene at reducing transmission of influenza and acute respiratory tract infections is dependent on various factors including setting, context and compliance.

### Future directions

Although hand hygiene has the potential to reduce transmission of influenza and acute respiratory tract infections, good compliance with interventions is essential. Improved understanding of the barriers to hand hygiene in community settings will help to inform development of context-specific interventions based on theories of behaviour change. Future research should seek to develop and evaluate such interventions, recognising that it may be difficult to generalise findings from studies carried out in non-pandemic years to pandemic situations.

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## Contributions

CWG conceptualised the study, assisted with design of the search strategy, managed EndNote databases, reviewed titles, relevant abstracts and full-text articles, extracted data, performed quality ratings, generated figures and tables and cowrote the article. EF assisted with search strategy design, performed searches, independently read all titles, relevant abstracts and full-text articles, extracted data, performed quality ratings and cowrote the article. ACH provided supervision, adjudicated on inclusion or exclusion of articles under dispute, advised on design of figures and tables and helped revise drafts of the article. All authors approved the final version. CWG is the guarantor.

## Ethical approval

Not needed.

## Conflicts of interest

All authors declare that they have no conflicts of interest.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Description of hand hygiene interventions and compliance measures for included studies.

**Appendix S1.** Formulae and calculations.