OPEN ACCESS

Effectiveness of hand hygiene interventions in reducing illness absence among children in educational settings: a systematic review and meta-analysis

Micky Willmott, Alexandra Nicholson, Heide Busse, Georgina J MacArthur, Sara Brookes, Rona Campbell

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/archdischild-2015-308875).

School of Social and Community Medicine, University of Bristol, Bristol, UK

Correspondence to
Professor Rona Campbell, School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol BS8 2PS, UK; Rona.Campbell@bristol.ac.uk

Received 28 April 2015
Accepted 14 September 2015
Published Online First 15 October 2015

ABSTRACT

Objective To undertake a systematic review and meta-analysis to establish the effectiveness of handwashing in reducing absence and/or the spread of respiratory tract (RT) and/or gastrointestinal (GI) infection among school-aged children and/or staff in educational settings.

Design Randomised-controlled trials (RCTs).

Setting Schools and other settings with a formal educational component in any country.

Patients Children aged 3–11 years, and/or staff working with them.

Intervention Interventions with a hand hygiene component.

Main outcome measures Incidence of RT or GI infections or symptoms related to such infections; absenteeism; laboratory results of RT and/or GI infections.

Results Eighteen cluster RCTs were identified; 13 school-based, 5 in child day care facilities or preschools. Studies were heterogeneous and had significant quality issues including small numbers of clusters and participants and inadequate randomisation. Individual study results suggest interventions may reduce children's absence, RT infection incidence and symptoms, and laboratory confirmed influenza-like illness. Evidence of impact on GI infection or symptoms was equivocal.

Conclusions Studies are generally not well executed or reported. Despite updating existing systematic reviews and identifying new studies, evidence of the effect of hand hygiene interventions on infection incidence in educational settings is mostly equivocal but they may decrease RT infection among children. These results update and add to knowledge about this crucial public health issue in key settings with a vulnerable population. More robust, well reported cluster RCTs which learn from existing studies, are required.

What is already known on this topic

- As semiclosed settings where large numbers of children with immature immunity regularly congregate, educational establishments are potentially effective places to prevent spread of infection.
- Evidence is equivocal but potentially promising for the effectiveness of hand hygiene interventions in preventing the spread of respiratory tract and gastrointestinal infection.
- Three systematic reviews of studies of hand hygiene interventions to prevent respiratory and/or gastrointestinal infections focus on educational settings; each has significant limitations.

What this study adds

- Eighteen cluster randomised controlled trials of the effectiveness of hand hygiene interventions in educational settings were identified; more than in previous dated reviews.
- Study design and reporting standards are generally low quality, impeding meta-analyses, but recently published studies show signs of improvements.
- Evidence of the impact of hand hygiene interventions among this population remains equivocal: this review makes recommendations for improving future trials to evaluate interventions.

Open Access
Scan to access more free content

To cite: Willmott M, Nicholson A, Busse H, *et al*. *Arch Dis Child* 2016;**101**:42–50.

INTRODUCTION

Young children are particularly susceptible to respiratory tract (RT) and gastrointestinal (GI) infections. While usually self-limiting, these highly infectious illnesses spread quickly in semiclosed settings such as schools. Infections affect child health, causing missed educational opportunities which may have a detrimental effect on educational outcomes,[1 2] lost productivity and days off work for school staff.[3] Educational settings where large numbers of children with immature immunity congregate are promising sites for preventing infection, particularly as outbreaks can affect whole schools and spread to vulnerable populations (eg, younger siblings) in the community.[4 5]

Several systematic reviews (SRs) have evaluated evidence of interventions to prevent RT and GI infections;[6–16] current evidence is equivocal but promising for the effectiveness of hand hygiene interventions in preventing RT and GI infection. Four SRs have included studies evaluating interventions in educational settings alongside other settings;[8 9 11 14] two focus on RT infection,[11 14] two focus on diarrhoea prevention.[8 9] Two of these are Cochrane reviews;[8 11] one recommended that: "effort should be concentrated on reducing

transmission from young children through regular education at school on hygiene" (ref.11, p.9).

Three SRs[12 13 16] focus exclusively on studies among children in educational settings. However, one only included hand sanitiser interventions;[13] another included children 2–11 years old and is over a decade old.[16] The most recent SR focused on the effects of multicomponent interventions (access to safe water, handwashing facilities, hygiene education) but did not assess study quality, included numerous study designs and had limited search parameters (eg, only searched in two databases).[12] None of these SRs included meta-analyses (MAs). This review aimed to update these reviews using thorough methods (eg, searching a range of databases) to identify all relevant studies which apply the most robust study design (randomised controlled trial, RCT) for evaluating interventions.

The objective of this SR was to summarise evidence of the effectiveness of hand hygiene interventions in reducing infectious illness and/or absence in educational settings for children aged 3–11 years and/or staff working with them, and to obtain a quantified estimate of the effect using MAs if possible.

METHODS

This SR is reported in line with current guidance.[17] Review coauthors agreed the review protocol.[18]

Eligibility criteria

This SR included RCTs of interventions with a hand hygiene component (any comparator) in educational settings for children aged 3–11 years in any country. No length of follow-up was defined.

Educational settings were defined as institutions incorporating formal educational activities including day care facilities and nurseries. Other community settings (eg, playschools) and domestic child care settings were excluded. Study populations could include staff and/or children in these settings. The review age range aimed to ensure the inclusion of all studies in formal educational settings for younger (primary or elementary school-aged) children—hereafter referred to as primary school-aged children—where children can be expected to understand hand hygiene, toilet themselves and clean their own hands. Study populations could include children whose age overlapped with the review age range (eg, 2–6-year-old, 5–12 year-old) because school policy and practice varies between countries: children start formal education at different ages; children may repeat a year so may be older than 11 years in primary school; structured nursery facilities for younger children may be integrated in schools.

Hand hygiene interventions were defined as any initiative for children and/or staff working with them undertaken to prevent the spread of infectious illness. Comparators could include placebos or active comparators such as handwashing with soap compared with hand sanitiser use.

Inclusion criteria were piloted on reports known to authors.

Primary review outcomes were: incidence of RT or GI infections or symptoms related to such infections; absenteeism rate; or laboratory results of RT and/or GI infections. Secondary outcomes were: hospital admissions due to such infections; changes in knowledge, attitudes, beliefs or behaviours about hand hygiene among children and/or staff working with them. We intended that outcomes related to children and staff be considered separately: we did not anticipate many studies would report staff outcomes. Studies which presented outcome data for staff and children together would be considered separately from studies which presented data for staff and students.

Information sources and search strategy

The search strategy had three components: handwashing, population and setting and study type. Handwashing, population and setting terms were extensive; handwashing terms used free-text terms as well as available controlled vocabulary terms. Population and setting terms were not used in education databases (Education Resource Information Center, Australian Education Index, British Education Index). The search focused on sources reporting RCTs and excluded unpublished literature as the coauthors agreed this was unlikely to report RCTs. A broad study type filter was used in databases where RCTs were less well indexed (see figure 1 for MEDLINE search strategy). No date or language restrictions were applied.

Eight electronic databases were initially searched from inception to April 2011: MEDLINE (1950 to date), EMBASE (1980–2011, week 15), Social Science & Science Citation Indexes (ISI Web of Knowledge), CINAHL, Cochrane Library, Education Resource Information Center (1966 to date), Australian Education Index (1979 to date) and British Education Index (1975 to date). The search was updated twice using the same strategy, first to cover up to 26 September 2012, then up to 5 September 2014; dates overlapped with previous searches to ensure items were not missed. Results of each search were uploaded to an EndNote database, combined and deduplicated.

Study selection and data collection process

All titles were screened for eligibility by one reviewer; 10% were independently screened by a second reviewer (Cohen's κ statistic=≥0.75). Abstracts were independently screened by two reviewers. Where reviewers did not agree, abstracts were included in full paper screening. Full papers were dual reviewed and reasons for exclusion recorded: coauthors moderated where there was disagreement. Additional studies were identified through references in full papers and citation search facilities in ISI Web of Science, journal websites and Google Scholar.

Two potentially eligible abstracts not in English were reviewed by native speakers. A full translation was obtained for the one study that met review criteria.[19] Protocols for included studies were obtained from trial registers where available.

Data collection and data items

Two reviewers independently extracted study data using a form developed from a template from another SR[16] and piloted on a sample of included studies. Data included were: study details; intervention description; study recruitment; random allocation; study baseline data; follow-up; process evaluation; outcomes and analysis. Reviewers discussed differences and recorded moderated results.

Risk of bias assessment

Study quality was assessed independently by two reviewers using the Cochrane Risk of Bias tool (V.5.1), compliance with reporting guidance[20 21] and good research practice (research governance, process evaluation, outcome measurement methods) pertinent to interventions with this population in these settings.

Summary measures

All effect measures pertaining to review outcomes are reported. Where studies included children under 3 years old and stratified the results they presented by age, we only report results for children over 3 years old. Where possible we present unadjusted results, where adjusted results are stated the variables used for adjustment are described. As a large number of studies reported

Figure 1 Search strategy used for Medline.

1. (handwashing or hand washing).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]
2. ((hand or hands) adj2 wash*).mp.
3. Health Education/
4. 3 and (hand or hands).mp.
5. ((hand or hands) and hygiene).mp.
6. ((hand or hands) and (cleansing or cleaning)).mp.
7. ((hand or hands) and disinfect*).mp.
8. hand antisepsis.mp.
9. 1 or 2 or 4 or 5 or 6 or 7 or 8
10. Communicable Disease Control/
11. 10 and (hand or hands).mp.
12. ((infect* adj2 control*) and (hand or hands)).mp
13. (soap or soaps).mp
14. 13 and (hand or hands).mp.
15. (Alcohol gel? or anti-microbial gel? or disinfectant gel? or antimicrobial gel?).mp.
16. saniti?er*.mp.
17. 11 or 12 or 14 or 15 or 16
18. 9 or 17
19. (school* or child*).mp.
20. (day care or preschool or pre-school).mp
21. (nurser* or kindergarten* or creche*).mp.
22. (reception class* or elementary class*).mp
23. (pupil* or student*).mp.
24. (teacher* or teaching staff).mp
25. 19 or 20 or 21 or 22 or 23 or 24
26. (randomized controlled trial or controlled clinical trial).pt.
27. (randomi?ed or placebo or randomly).mp. or trial.ti. or trial.ab. or groups.ti. or groups.ab.
28. 26 or 27
29. (crossover or cross-over).mp.
30. control*.ti. or control*.ab.
31. (intervention* or experiment*).mp
32. follow-up.mp.
33. (comparison* or comparative).mp. [
34. evaluat*.mp
35. nursing research/ or clinical nursing research/ or nursing evaluation research/ or nursing methodology research/
36. 29 or 30 or 31 or 32 or 33 or 34 or 35
37. 28 or 36
38. 18 and 25 and 37
39. schools, dental/ or schools, medical/ or schools, nursing/ or schools, pharmacy/ or schools, public health/ or schools, veterinary/
40. 38 not 39

absence by reason, three additional sets of outcome data are presented; absence due to any illness, absence due to RT infection, absence due to GI infection.

Synthesis of results

We aimed to conduct MAs if studies were sufficiently homogenous and data were adequate. Missing and unclear data were identified in the data extraction form. Studies where additional data could not be accessed were excluded from MA and reasons recorded. Authors were only contacted in exceptional circumstances due to the length of time since completion for many studies. No authors provided additional data. This led to the exclusion of several studies. Six studies were excluded due to design flaws (risk of contamination between study arms); cross-over design,[22 23] clusters at class level,[24–26] and clusters at class and school levels.[27 28] Therefore, MAs were not conducted.

Additional analyses

Prespecified subgroup analyses (age, gender, location, setting, intervention and duration) and sensitivity analyses were not possible due to poor reporting and data quality.

RESULTS

Study selection

Of the 5306 titles assessed for eligibility, 18 studies fitted review criteria (figure 2). Protocols for four RCTs with as yet unpublished results were identified.[29–32]

Study characteristics

All included studies were cluster RCTs, including two with a cross-over design[22 23] (table 1).

Study participants

Age of participating children was not always reported. Five of the 13 school-based studies included all children in each school;[26 27 37 39 41] others included one or more age grade. Six studies included children under 3 years.[19 24 37 46 47 53] These were retained because the interventions included hand hygiene for children as well as staff. Four studies included students over the typical maximum primary school age of 11 years.[27 34 36 37] These were retained because students' education level was likely to be equivalent to students in other contexts.

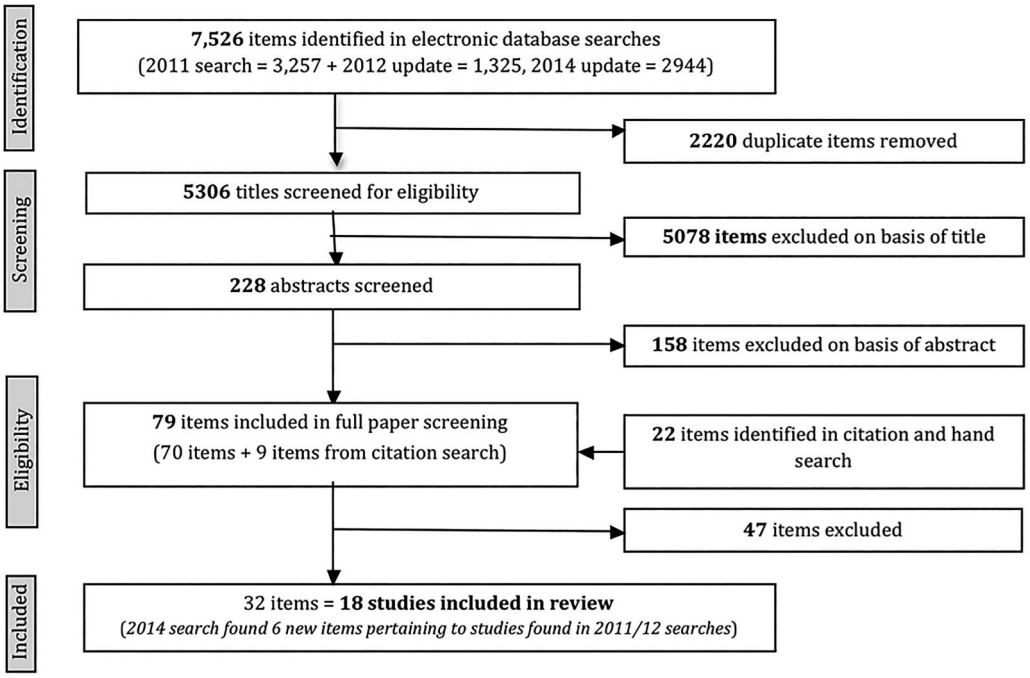

Figure 2 Flow of papers through the review.

Country location and setting

Thirteen studies were school-based; five were in day care facilities or preschools. Institutions were not necessarily representative of settings in that country. For example, one study only included schools with continuous water supply.[45] Eleven studies were in high-income countries (defined using World Bank categories[54]); only two did not involve hand sanitiser.[19 48] Four studies were from middle-income countries;[24 33 45 46] three were from one low-income country (Kenya).[34 36 37]

Interventions and comparators

Twelve interventions included hand sanitiser;[22–27 37 39 41 46 47 53] six focused on handwashing with soap.[19 33 34 36 45 48] Several interventions included additional infection control measures, such as eliminating shared cups,[48] water treatment and building new latrines,[34 36] cleaning toys or equipment.[25 53] Five included a home component such as parental information.[19 33 41 45 48]

Fourteen studies compared interventions with 'standard practice' but this was often unclearly defined. One study was placebo-controlled,[26] three compared an intervention with an alternative intervention.[23 36 39] Four studies compared two interventions and a control.[24 33 34 37] Only two studies adopted a multifactorial design to test the effect of different intervention components.[24 37]

Hand hygiene protocols varied. For example, only 7 of the 12 studies including hand sanitiser described the frequency and/or intensity of use. Nine interventions lasted 10 weeks or less.[19 22 23 25 26 33 34 37 48]

Outcomes

The online supplementary table S2 presents study results according to review outcomes. Only three studies[34 36 46] did not report absence outcomes. Six studies presented results concerning RT infection and/or symptoms;[33 37 41 45 46 53] four presented results concerning GI infection and/or symptoms.[33 37 46 53] Two studies reported laboratory results, both pertaining to influenza-like illness (ILI).[41 45] Six studies presented knowledge, attitude and/or behavioural outcomes.[34 36 37 41 48 53] No study reported hospital admissions due to infection. Four studies presented staff outcomes.[36 37 48 53]

Outcome definitions and summary measures varied. Three reports did not clearly define illnesses or symptoms.[23 47 48] Some only reported adjusted outcomes (variables differed between studies).

Risk of bias within studies

Methodological issues increased risk of bias in most studies (see online supplementary table S1, reviewers' assessment of the quality and risk of bias of included studies). Some issues highlight difficulties in evaluating behaviour change (eg, lack of participant blinding); others indicate study design weaknesses (eg, random sequence generation) and inadequate reporting (eg, only reported statistically significant results).

Five studies described an adequate method of random sequence generation,[39 41 45 46 53] only two adequately described allocation concealment.[39 41] Perhaps unsurprisingly given the nature of the intervention, only the study where a placebo hand sanitiser was the comparator was judged to be at low risk of performance bias.[26] Only one study[39] was assessed as having adequately described all measures to blind outcome assessors. The completeness of data reported for each outcome was assessed as adequate in five studies;[23 25 39 46 48] high risk of selective reporting was identified in four studies.[24 26 37 41]

Four reports did not present baseline data.[19 22 23 26] Despite being concerned with illness outcomes, only eight reported baseline health data.[24 25 27 39 46–48 53]

Six studies[22–28] had clusters at class level (two of these applied a cross-over design), therefore increasing risk of contamination between study arms. Not all investigators took clustering into account in sample size calculation or analysis.

Three studies were funded by companies producing hygiene products,[23 25 33] three used manufacturer-donated products,[22 37 46] one required parents to provide soap and hand

Table 1 Characteristics of included studies

Study author (study name)	Year of study	Population				Intervention (product details provided where reported)	Control (not all authors defined standard practice)	Study design (cluster RCTs)	
		Participants	Age in years (school grade)	Setting	Location			Cluster	Number of clusters
School-based studies									
Azor Martínez *et al*[27 28]	2009–2010	School children (n=1640)	4–12 years	Primary school (n=5)	Spain (Almeria)	Handwashing with soap followed by hand sanitiser (ALCO ALOE GEL)	Standard practice	School and classroom	4 schools, 29 classes from another school
Bowen *et al*[33] (Safeguard Promotion Program)	2003–2004	School children (n=3962)	Median 7.53 years (1st grade)	Primary school (n=90)	China (3 counties in Fujian Province)	(1) Standard programme (teacher training to encourage handwashing with soap, student take home pack) (2) Enhanced programme (standard programme plus supply of safeguard soap, student peer mentors)	Standard practice (Annual statement about Handwashing before eating and after toilet)	School	90 30 intervention (1), 30 intervention (2), 30 controls
Freeman *et al* (WASH programme)[34 35]	2007	School children (n=5989 supplied absence data)	6–16 years; median 13 years (4th–8th grade)	Public primary school (n=135)	Kenya (4 districts in Nyanza Province)	(1) Hygiene promotion (HP) and water treatment (WT) (3 days teacher training, follow-up sessions) (2) HP and WT plus up to 7 new latrines per school	Standard practice	School	135 45 intervention (1) 45 intervention (2) 45 controls
Graves *et al*[36] (substudy of NICHE: Nyando Integrated Child Health and Education)	2008–2009	School children (precise number not reported)	Age not reported (Students in NICHE study were in 4th–8th grade)	Primary school (n=21)	Kenya (rural western area)	NICHE intervention (multiple components including health promotion by teachers, installation of drinking water, handwashing stations) plus a visual aid poster designed by students in intervention schools	NICHE intervention only	School	21 schools 10 intervention 11 control (14 included in analysis)
Morton and Schultz (Healthy hands)[22]	2000–2001	School children (n=253)	Age not reported (Kindergarten–3rd grade)	Elementary school (n=1)	USA (New England)	Handwashing with soap and AlcoSCRUB alcohol gel use (45 min session for students)	Standard practice (handwashing with soap)	Classroom	17 (*cross-over design*)
Pandejpong *et al*[24]	2009–2010	School children (n=1437)	2–3, 3–4, 4–5, 5–6 years	Private school (n=1)	Thailand (suburban Bangkok)	Application of alcohol hand gel: Two intervention groups (1) every 60 min; (2) every 120 min	Standard practice (alcohol gel application once, before lunch)	Classroom	68 (*not clear how many classes in each arm*)
Pickering *et al*[37]	Unclear	School children (n=1364)	5–10 years (preunit to P5). 1 included a nursery (2–4 years), 4 included 10–13-year-olds (P6-8 grades)	Primary school (n=6)	Kenya (Kibera urban community in Nairobi)	(1) Handwashing with soap. Two soap dispensers installed by toilets, eating area (plus water tank with a spigot). (2) Alcohol-based hand sanitiser use (Purell). Two dispensers installed by toilets, eating area	No intervention (standard practice)	School	6 2 intervention (1) 2 intervention (2) 2 controls
Priest *et al*[38–40]	2009	School children (n=16 245)	5–11 years (school years 1–6)	Primary school (n=68)	New Zealand (Dunedin, Christchurch, Invercargill)	30 min inclass hand hygiene education session, instruction on hand sanitiser use, 'no touch' dispensers installed in classrooms	30 min inclass hand hygiene education session only (no instruction on hand sanitiser use)	School	68 schools 34 intervention 34 controls
Sandora *et al*[25]	2006	School children (n=285)	Age not reported (3rd–5th grade)	Elementary school (n=1)	USA (Avon, Ohio)	Handwashing with soap, Aerofirst hand sanitiser use, plus Clorox disinfectant wipes (Student instruction, teachers wiped students' desks once a day, after lunch)	Standard practice (handwashing with soap)	Team	6 teams in 15 classrooms
Stebbins *et al* (Pittsburgh Influenza Prevention Project)[41–44]	2007–2008	School children (n=3360)	Age not reported (Kindergarten—5th grade)	Elementary school (n=10)	USA (Pittsburgh, Pennsylvania)	Handwashing and Purell hand sanitiser use (45 min presentation for students, educational materials for parents)	Standard practice	School	10 5 intervention 5 controls

Continued

Table 1 Continued

Study author (study name)	Year of study	Population				Intervention (product details provided where reported)	Control (not all authors defined standard practice)	Study design (cluster RCTs)	
		Participants	Age in years (school grade)	Setting	Location			Cluster	Number of clusters
Talaat *et al*[45]	2008	School children (n=44 451)	Median 8 years (1st–3rd grade)	Elementary school (n=60)	Egypt (Cairo)	Handwashing with soap (school-specific activities, coordinated by teachers, school nurse; pupils provided soap, drying materials)	Standard practice	School	60 30 intervention 30 controls
Vessey *et al*[23]	Not known	School children (n=383)	Age not reported (2nd and 3rd grades)	Elementary school (n=4)	USA (Butte, Montana)	Hand sanitiser use (one educational session for students)	Handwashing with soap	Classroom	18 (*cross-over design*)
White *et al*[26]	1999	School children (n=769)	5–12 years (Kindergarten—6th grade)	Elementary school (n=3)	USA (California)	Handwashing and alcohol-free hand sanitiser use (all students attended 22-min assembly)	Handwashing and placebo sanitiser use (all students had 22-min assembly)	Classroom	72 32 retained for analysis: 16 intervention, 16 controls
Non-school based studies									
Correa *et al*[46]	2008	Children (n=1727)	1–5-years	Child care centre (n=42)	Colombia (6 urban settings)	Purell alcohol-based hand sanitiser use (training workshop for staff and children, monthly refresher workshops)	Standard practice (handwashing with soap)	Child care centre	42 (32 community, 10 preschool)
Ladegaard and Stage[19]	Not known	Children (n=399 aged 3–6 years)	0–2 years and 3–6 years	Nursery (n=8)	Denmark (Borough of Odense)	Handwashing with soap (staff training, take home book, 1 h education session for children)	Standard practice	Nursery	8 4 intervention, 4 controls
Lennell *et al*[47]	2004–2005	Children (n=1477)	0–5 years. Mean: 3.2 years (intervention), 3.1 years (control). Circa 30% <3 years	Day care centre (n=60)	Sweden (10 counties, south and mid-Sweden)	Handwashing with soap and alcohol-based oily disinfectant gel use (instruction, demonstration to staff and children)	Standard practice (handwashing with soap)	Day care centre	60 30 intervention, 30 controls (matched pairs)
Rosen *et al* (Jerusalem handwashing study)[48–52]	2001	Children (n=1029)	3 years and 4 years	Preschool (n=40)	Israel (Jerusalem)	Handwashing with soap (2 3-h staff training sessions, child education programme, take home pack)	Standard practice and alternative take-home pack (about oral hygiene)	Preschool	40 20 intervention 20 controls
Uhari and Möttönen[53]	1991–1992	Children (n=1522)	861 >3 years 661 <3 years Mean: 3.6 years (intervention), 3.5 years (control)	Child day care centre (n=20)	Finland (Oulu city)	Handwashing with soap and alcohol-based oily disinfectant use, plus cleaning environment (staff lecture on infection prevention; cleaning toys; staff encouraged to take sick leave at first sign of symptoms)	Standard practice	Day care centre	20 10 intervention 10 controls (matched pairs)

RCT, randomised controlled trial; WASH, Water, Sanitation and Hygiene.

drying materials.[45] It is unclear whether the way in which these interventions were resourced affected their acceptability, sustainability or study outcomes: only two study reports state the role of these companies in the study, analysis and report. [25 33]

Most reports described the intervention protocol and monitoring, three noted intervention costs[24 28 46] but few presented process evaluation data.

Most outcome measurement methods could have introduced bias due to poor case definition, use of non-validated tools or self-report (including routine school absence reporting data). Some studies which attempted to validate outcomes (eg, illness) experienced attrition due to the complexity of the process (ref. 41, p.3).

Individual study results

Five of the six studies reporting children's absence and 8 of the 13 studies measuring children's illness absence reported an intervention effect (see online supplementary table S2 for study results according to review outcomes). The one study reporting staff illness absence found it was higher among the intervention group[53] which may be because the intervention included asking staff not to attend work if they had infection symptoms.

All five studies reporting RT infection incidence showed a reduction, but each applied different outcome definitions. Three reported RT infection symptoms (rhinitis, cough); one[53] found a reduction in both, one[37] only identified a reduction in observed rhinorrhoea and another[33] found no change in cough and a 12% increase in rhinorrhoea episodes ('standard' intervention vs control).

Two studies reported GI incidence; one reported a reduction,[46] the other did not.[53] Only one of three studies recording diarrhoeal symptoms found any effect.[37] Two studies reported vomiting outcomes,[37 53] only one found an effect.[53]

Two studies[41 45] collecting laboratory results found some evidence of decreased ILI, although in one study this only related to influenza A (ref. [41], Supplemental Digital Content (SDC) 2).

Four of five studies reporting children's behaviour change identified a positive intervention effect.[34 37 41 48] All five studies reporting changes in children's and/or staff hand hygiene knowledge, attitudes and/or beliefs found an intervention effect.[34 37 41 51 53]

Synthesis of results

Due to study heterogeneity and the generally low quality of study design and of study reporting, coauthors agreed that it could be misleading to present pooled estimates of the effect of interventions using MAs.

DISCUSSION

Main findings

We found 18 cluster RCTs investigating the effect of interventions with a hand hygiene component on absence and infection among 3–11-year-old children in educational settings. Individual study results suggest interventions may reduce children's absence, RT infection incidence and symptoms, and laboratory-confirmed ILI. They may also improve children's and staff hand hygiene attitudes, knowledge and behaviour. Evidence of impact on GI infection or symptoms was equivocal. Despite updating existing SRs and identifying new studies, individual study results appear to show that there remains equipoise about the effectiveness of hand hygiene in preventing RT and GI infection.

Strengths and limitations of this review

Much has been made of the potential of hand hygiene interventions for reducing infection in this population.[11] This review provides a more detailed assessment of such interventions and how promising they might be based on studies which apply the most rigorous, RCT evidence. This review updates existing SRs focused on this population, and our comprehensive search strategy resulted in finding more studies than previous SRs. Findings of this review corroborate existing SRs; that studies have significant design limitations and poor quality reporting. The quality of reporting in more recently published studies[27 28 39] seems to have improved which perhaps indicates the impact of guidance on the reporting of cluster RCTs.[20 21] This may result in improved evidence, capable of demonstrating the effectiveness of this important public health issue. Despite identifying new studies, it was not possible to produce meaningful MAs (as earlier SRs have found) due to study heterogeneity, study design limitations and poor quality reporting.

Limitations of this SR include that: we assumed that report titles or abstracts would contain 'handwashing' or 'hand/s' but they did not; unpublished literature was excluded; some included studies had study populations which included children younger and older than the prespecified review age range; RT and GI infection incidence can vary within the age range included in the review, as can the potential effectiveness of interventions (due to children's developmental stage); risk of bias assessment was impeded by inadequate reporting. Furthermore, all interventions with a hand hygiene component were included so the impact of hand hygiene cannot be isolated. This review does not distinguish between handwashing with soap or hand sanitiser use even though these methods may have different resource implications and be differentially effective in eliminating certain pathogens.[55]

What this study adds

While studies are heterogeneous, there is evidence that hand hygiene interventions among primary school-aged children in educational settings may be beneficial, particularly in reducing RT infection incidence. However, this SR highlights limitations of evidence on this crucial public health issue in a key setting with a vulnerable population and the need for improved studies to enable more definitive assessment (eg, MA) of the effectiveness of simple public health interventions to inform practice. We have four recommendations for future research and which may enable future estimates of the pooled effects of such interventions using MA.

First, better designed and reported cluster RCTs are required. Investigators should apply guidance[20 21] and learn from robust studies[39] in order to avoid design flaws (eg, clusters at classroom level) and improve reporting (eg, children's age, control group conditions). Second, studies should incorporate technical advances for outcome measurement, such as the use of environmental swabs to detect the level of viral and/or bacterial contamination in schools[56] which may enable robust, standardised outcome measures instead of using self-report and observations. Third, research should include process evaluation to refine interventions and establish intervention acceptability and fidelity. Studies which have done process evaluations[40 57] have identified barriers to hand hygiene including access to adequate sanitary facilities (even in high-income countries), suggesting that provision of hygiene products and education may be insufficient to achieve effective infection prevention and control and more robust studies of complex, multicomponent interventions are required. Fourth, studies should evaluate cost, cost-effectiveness and intervention sustainability in educational settings.

CONCLUSION

Interventions to improve hand hygiene in educational settings may reduce RT infection incidence among younger children. More robust, well reported studies are required, especially of multicomponent interventions.

Acknowledgements The authors thank Val Hamilton for constructing the search strategy and doing the database search in 2011 and 2012; Dagmar Luettel, Lone Gale and Julianna Photopoulos for their translations. Beki Langford advised on the review process; Kate Tilling, Deborah Caldwell and Hayley Jones provided statistical advice.

Contributors The manuscript has been read and approved by all authors. RC, SB, AN conceived and instigated the study. RC, SB, AN and MW drafted the protocol. MW conducted the 2014 search and all citation searches. MW, GJM and AN screened the results. MW, AN and HB extracted the data and assessed the quality of studies. RC and SB were moderators. MW and RC analysed the data. MW drafted the manuscript for publication. All authors contributed to this report and subsequent revisions. Each author believes that the manuscript represents honest work.

Funding This work was undertaken with the support of NIHR Research for Patient Benefit Grant (PB-PG-1207-15212) and of The Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement (DECIPHer), a UKCRC Public Health Research Centre of Excellence. Joint funding (MR/KO232331/1) from the British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council, the Welsh Government and the Wellcome Trust, under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged. Views expressed in this paper do not represent those of the funders. The funders had no role in study design, data collection and analysis, decision to publish or manuscript preparation.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Additional unpublished data from the study (data extraction forms, attempted meta-analyses) are available on request from the corresponding author.

REFERENCES

1 DfE. The link between absence and attainment at KS2 and KS4. 2012/13 Academic Year. Research Report. London: Department for Education, 2015.
2 PHE. *The link between pupil health and wellbeing and attainment: A briefing for head teachers, governors and staff in education settings*. London: Public Health England, 2014.
3 Bowers T. Teacher absenteeism and ill health retirement: a review. *Cambridge J Educ* 2001;31:135–57.
4 Monto AS. Studies of the community and family: acute respiratory illness and infection. *Epidemiol Rev* 1994;16:351–73.
5 Nafstad P, Hagen JA, Botten G, *et al*. Lower respiratory tract infections among Norwegian infants with siblings in day care. *Am J Public Health* 1996;86:1456–9.
6 Aiello A, Coulborn R, Perez V, *et al*. Effect of hand hygiene on infectious disease risk in the community setting: a meta-analysis. *Am J Public Health* 2008;98:1372–81.
7 Curtis V, Cairncross S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *Lancet Infect Dis* 2003;3:275–81.
8 Ejemot RI, Ehiri JE, Meremikwu MM, *et al*. Hand washing for preventing diarrhoea. *Cochrane Database Syst Rev* 2008;(1):CD004265.
9 Freeman MC, Stocks ME, Cumming O, *et al*. Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. *Trop Med Int Health* 2014;19:906–16.
10 Jasper C, Le TT, Bartram J. Water and sanitation in schools: a systematic review of the health and educational outcomes. *Int J Environ Res Public Health* 2012;9:2772–87.
11 Jefferson T, Del Mar C, Dooley L, *et al*. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. *BMJ* 2009;339:b3675.
12 Joshi A, Amadi C. Impact of water, sanitation, and hygiene interventions on improving health outcomes among school children. *J Environ Public Health* 2013;2013:984626.
13 Meadows E, Le Saux N. A systematic review of the effectiveness of antimicrobial rinse-free hand sanitizers for prevention of illness-related absenteeism in elementary school children. *BMC Public Health* 2004;4:50.
14 Rabie T, Curtis V. Handwashing and risk of respiratory infections: a quantitative systematic review. *Trop Med Int Health* 2006;11:258–67.
15 Warren-Gash C, Fragaszy E, Hayward AC. Hand hygiene to reduce community transmission of influenza and acute respiratory tract infection: a systematic review. *Influenza Other Respir Viruses* 2013;7:738–49.
16 Wilson J, Wang D, Meads C. *Simple interventions to prevent respiratory and gastrointestinal infection in children in day care and school settings—a systematic review and economic evaluation*. Birmingham: West Midlands Health Technology Assessment Collaboration, 2006.
17 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 2009;6:e1000097.
18 Nicholson A, Willmott M, Brookes S, *et al*. *A systematic review to evaluate the evidence of the effectiveness of hand washing in reducing the spread of infectious illness in primary schools. Protocol*. Bristol: DECIPHer, University of Bristol, 2012. http://decipher.uk.net/research-page/handwashing-absenteeism/ (accessed 27 Apr 2015).
19 Ladegaard MB, Stage V. Hand-hygiene and sickness among small children attending day care centers. An intervention study. *Ugeskr Laeger* 1999;161:4396–400.
20 Schulz K, Altman D, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
21 Campbell MK, Piaggio G, Elbourne DR, *et al*. Consort 2010 statement: extension to cluster randomised trials. *BMJ* 2012;345:e5661.
22 Morton JL, Schultz AA. Healthy Hands: use of alcohol gel as an adjunct to handwashing in elementary school children. *J Sch Nurs* 2004;20:161–7.
23 Vessey JA, Sherwood JJ, Warner D, *et al*. Comparing hand washing to hand sanitizers in reducing elementary school students' absenteeism. *Pediatr Nurs* 2007;33:368–72.
24 Pandejpong D, Danchaivijitr S, Vanprapa N, *et al*. Appropriate time-interval application of alcohol hand gel on reducing influenza-like illness among preschool children: A randomized, controlled trial. *Am J Infect Control* 2012;40:507–11.
25 Sandora TJ, Shih MC, Goldmann DA. Reducing absenteeism from gastrointestinal and respiratory illness in elementary school students: a randomized, controlled trial of an infection-control intervention. *Pediatrics* 2008;121:e1555–62.
26 White CG, Shinder FS, Shinder AL, *et al*. Reduction of illness absenteeism in elementary schools using an alcohol-free instant hand sanitizer. *J Sch Nurs* 2001;17:258–65.
27 Azor-Martínez E, Cobos-Carrascosa E, Gimenez-Sanchez F, *et al*. Effectiveness of a multifactorial handwashing program to reduce school absenteeism due to acute gastroenteritis. *Pediatr Infect Dis J* 2014;33:e34–9.
28 Azor-Martínez E, Gonzalez-Jimenez Y, Seijas-Vazquez ML, *et al*. The impact of common infections on school absenteeism during an academic year. *Am J Infect Control* 2014;42:632–7.
29 Johansen A, Denbæk AM, Thørring Bonnesen C, *et al*. The Hi Five study: design of a school-based randomized trial to reduce infections and improve hygiene and well-being among 6-15 year olds in Denmark. *BMC Public Health* 2015;15:207.
30 Overgaard HJ, Alexander N, Mátiz MI, *et al*. Diarrhea and dengue control in rural primary schools in Colombia: Study protocol for a randomized controlled trial. *Trials* 2012;13:182.
31 Zomer TP, Erasmus V, Vlaar N, *et al*. A hand hygiene intervention to decrease infections among children attending day care centers: design of a cluster randomized controlled trial. *BMC Infect Dis* 2013;13:259.
32 Bowen A. Evaluation of a school-based handwashing promotion program in three countries. Clinical Trials identifier: NCT010438092010. http://clinicaltrials.gov/show/NCT01043809 (accessed 27 Apr 2015).
33 Bowen A, Ma H, Ou J, *et al*. A cluster-randomized controlled trial evaluating the effect of a handwashing-promotion program in Chinese primary schools. *Am J Trop Med Hyg* 2007;76:1166–73.
34 Freeman MC, Clasen T, Dreibelbis R, *et al*. The impact of a school-based water supply and treatment, hygiene, and sanitation programme on pupil diarrhoea: a cluster-randomized trial. *Epidemiol Infect* 2014;142:340–51.
35 Greene LE, Freeman MC, Akoko D, *et al*. Impact of a school-based hygiene promotion and sanitation intervention on pupil hand contamination in Western Kenya: a cluster randomized trial. *Am J Trop Med Hyg* 2012;87:385–93.
36 Graves JM, Daniell WE, Harris JR, *et al*. Enhancing a safe water intervention with student-created visual aids to promote handwashing behavior in Kenyan primary schools. *Int Q Community Health Educ* 2011;32:307–23.
37 Pickering AJ, Davis J, Blum AG, *et al*. Access to waterless hand sanitizer improves student hand hygiene behavior in primary schools in Nairobi, Kenya. *Am J Trop Med Hyg* 2013;89:411–18.
38 McKenzie JE, Priest P, Audas R, *et al*. Hand sanitisers for reducing illness absences in primary school children in New Zealand: a cluster randomised controlled trial study protocol. *Trials* 2010;11:7.
39 Priest P, McKenzie JE, Audas R, *et al*. Hand sanitiser provision for reducing illness absences in primary school children: a cluster randomised trial. *PLoS Med* 2014;11:e1001700.
40 Reeves LM, Priest PC, Poore MR. School toilets: facilitating hand hygiene? A review of primary school hygiene facilities in a developed country. *J Public Health* 2012;34:483–8.

41 Stebbins S, Cummings DA, Stark JH, *et al*. Reduction in the incidence of influenza A but not influenza B associated with use of hand sanitizer and cough hygiene in schools: a randomized controlled trial. *Pediatr Infect Dis J* 2011;30:921–6.
42 Stebbins S, Downs JS, Vukotich CJ Jr. Using nonpharmaceutical interventions to prevent influenza transmission in elementary school children: parent and teacher perspectives. *J Public Health Manag Pract* 2009;15:112–17.
43 Stebbins S, Downs JS, Vukotich CJ. The effect of grade on compliance using nonpharmaceutical interventions to reduce influenza in an urban elementary school setting. *J Public Health Manag Pract* 2011;17:65–71.
44 Stebbins S, Stark JH, Vukotich CJ. Compliance with a multilayered nonpharmaceutical intervention in an urban elementary school setting. *J Public Health Manag Pract* 2010;16:316–24.
45 Talaat M, Afifi S, Dueger E, *et al*. Effects of hand hygiene campaigns on incidence of laboratory-confirmed influenza and absenteeism in schoolchildren, Cairo, Egypt. *Emerg Infect Dis* 2011;17:619–25.
46 Correa JC, Pinto D, Salas LA, *et al*. A cluster-randomized controlled trial of handrubs for prevention of infectious diseases among children in Colombia. *Rev Panam Salud Publica* 2012;31:476–84.
47 Lennell A, Kühlmann-Berenzon S, Geli P, *et al*. Alcohol-based hand-disinfection reduced children's absence from Swedish day care centers. *Acta Paediatr* 2008;97:1672–80.
48 Rosen L, Manor O, Engelhard D, *et al*. Can a handwashing intervention make a difference? Results from a randomized controlled trial in Jerusalem preschools. *Prev Med* 2006;42:27–32.
49 Rosen L, Manor O, Engelhard D, *et al*. Design of the Jerusalem Handwashing Study: meeting the challenges of a preschool-based public health intervention trial. *Clin Trials* 2006;3:376–84.
50 Rosen L, Manor O, Engelhard D, *et al*. Erratum: Design of the Jerusalem Handwashing Study: Meeting the challenges of a preschool-based public health intervention trial (Clinical Trials (2006) 3, (376–384)). *Clin Trials* 2007;4:475.
51 Rosen L, Zucker D, Brody D, *et al*. The effect of a handwashing intervention on preschool educator beliefs, attitudes, knowledge and self-efficacy. *Health Educ Res* 2009;24:686–98.
52 Rosen L, Zucker D, Brody D, *et al*. Enabling hygienic behavior among preschoolers: improving environmental conditions through a multifaceted intervention. *Am J Health Promot* 2010;25:248–56.
53 Uhari M, Möttönen M. An open randomized controlled trial of infection prevention in child day-care centers. *Pediatr Infect Dis J* 1999;18:672–7.
54 World Bank. Data: Country and Lending Groups. 2015. http://data.worldbank.org/about/country-and-lending-groups (accessed 1 Sep 2015).
55 Bloomfield SF, Aiello AE, Cookson B, *et al*. The effectiveness of hand hygiene procedures in reducing the risks of infections in home and community settings including handwashing and alcohol-based hand sanitizers. *Am J Infect Control* 2007;35:S27–64.
56 Boxman IL, Dijkman R, te Loeke NAJM, *et al*. Environmental swabs as a tool in norovirus outbreak investigation, including outbreaks on cruise ships. *J Food Prot* 2009;72:111–19.
57 Chittleborough CR, Nicholson AL, Young E, *et al*. Implementation of an educational intervention to improve hand washing in primary schools: process evaluation within a randomised controlled trial. *BMC Public Health* 2013;13:757.

Supplementary Data 1: Summary of reviewers' assessment of the quality and risk of bias of included studies

Study	Risk of bias (according to Cochrane Risk of Bias tool)							Additional issues (Cluster RCT method, research governance and ethics, process evaluation, measurement)
	Random sequence generation	Allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Justification of bias identified	
School-based studies								
Azor Martinez *et al* 2014(a), 2014(b)	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	A random number table was used to allocate schools/ classes to each arm but schools were selected because they had previously been involved in a study. Personnel were unlikely to be blind to allocation because they did data collection, visited classrooms and delivered hand hygiene activities. Parents (who reported absence and illness) may not have been blinded. Paediatricians who reviewed medical records of absent pupils and made final diagnosis were not blinded. Diagrams of participant flow in the two study papers show different numbers of participants. A protocol is available; not clear if all outcomes are reported.	Clusters are at two different levels; school and classes. The authors state that they did not adjust for clustering. Observer effect; behaviour might have changed due to presence of researcher/field workers at site. No information on fidelity or adherence to intervention. Authors acknowledge an adverse reaction to the hand sanitizer. There was some baseline information about the use of hand sanitizer at home but only 83% of parents provided this information. Authors state that baseline socio-demographic characteristics of participants were similar.
Bowen *et al*. 2007 (Safeguard Promotion Program)	High risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Allocation sequence generation was adequately described, but 24 control schools were excluded post randomisation and replaced with non-stratified schools because they distributed the wrong take-home packs. Participants and outcome assessors (teachers) were not blinded but some attempt was made to conceal the aim of the intervention by telling teachers It was a health intervention looking at illness rates among students. It is unclear if outcome data reported (table 4, 5) is complete. A protocol is available; all outcomes are reported.	Adjustment was made for clustering in the sample size calculation and in analysis. Study funders had input into the study protocol but the authors state that they "*were not involved in the study implementation or data analysis*" (p.1168). There are questions about potential contamination and intervention fidelity as the authors reported that some students brought soap from the home pack to use in school. Authors note that there was a lack of sensitivity in the 'health surveillance system' used and there may have been over-reporting of illness (e.g. where the same student was absent twice in one week).
Freeman *et al*. 2012 (WASH programme)	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	Schools were "*randomly selected and randomly assigned*" (p.382) but it is not clear how. Participants and personnel were not blinded (students reported their own absence) although researchers "*conducted a roll-call assessment of absence for all registered students the day of the field visit to assess the validity of our primary absence measure*" (p.383) a high risk of bias is likely. The flow of participants through the study is unclear. It is unclear whether all outcomes are presented.	Adjustment was made for clustering in the sample size calculation and analysis; ICC is reported. Teachers consented on behalf of students. Absence measure is subject to recall bias (incidence extrapolated from 2-week report given by a sample of students) and "*follow-up data were collected at a time when pupils may have been more likely to attend for test preparation*." (p.389). Also deworming was done in all schools that may have impacted intervention effect. Fewer than 40% of students from intervention arms reported soap was always available for hand washing, suggesting sustainability issues.
Graves *et al* 2011	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	No description random sequence generation or method of concealment. Not clear whether participants or personnel were blinded. Four trained personnel observed hand	No adjustment for clustering in design or analysis, no ICC reported. Potential for observer effect (behaviour might have changed due to observations). Subjective outcome measures applied (observations

Study	Risk of bias (according to Cochrane Risk of Bias tool)							Additional issues (Cluster RCT method, research governance and ethics, process evaluation, measurement)
	Random sequence generation	Allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Justification of bias identified	
							hygiene behaviours; they would not have been blind to the presence of the intervention posters. The flow of participants through the study is not clear. This is a sub-study of a larger (NICHE) study; it is not clear whether the outcomes were planned in advance and that all outcomes are reported.	only carried out for two hours in the morning). Possibility of measurement bias - observers estimated some outcomes (e.g. distance between handwashing station and latrine). Authors accept that "*it is not possible to assess the impact of the intervention independent of the physical and educational resources provided by NICHE*" (p.318). Little information on fidelity or adherence but authors report limited access to soap and/or water some sites.
Morton and Schultz 2004 (Healthy hands)	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	The randomisation method was not clear. This was a crossover study with clusters at the classroom level in the same school, leading to high risk of contamination and performance bias; it would not be possible to conceal the allocation because of the design. The study nurses noted outcome data but were also delivering part of the intervention. There was a higher attrition rate in the 2nd phase; authors suggested this was due to weather changes which may have made children susceptible to dry skin which was exacerbated by the sanitizer. No protocol was identified so it is unclear whether all outcomes are reported.	It is not clear whether adjustment was made for clustering in the sample size calculation and no ICC is reported. McNewar's test for dichotomous variables with paired subjects was used for analysis (p.165). The acceptability of the intervention is questionable during the Winter-time (flu season) as more children experienced dry skin in cold weather. Also, one child felt that the intervention was making her sick.
Pandejpong *et al*. 2012	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	Authors state they used; "*cluster randomisation to assign the school's classrooms to intervention or control groups*" but do not describe how they did this (p.508); insufficient details about allocation concealment are provided. The study design (clusters at classroom level) introduces potential contamination and performance bias; authors attempted to control for this by having fieldworkers observe compliance with the different time schedules for using the hand gel. It is not clear whether all outcome data are presented; a protocol was not found. It appears that authors only report statistically significant results (p.510).	It is not clear whether adjustment was made for clustering in the sample size calculation, no ICC are reported, but the analysis accounts for clustering. Illness could have been misclassified by parents/guardians. Adherence to the intervention protocol (sanitizer application every 60 or 120 minutes) was monitored and the authors do not explore whether this was sustainable or if the frequency of the application was acceptable to teachers and/or students.
Pickering *et al* 2013	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias	High risk of bias	Random sequence generation and allocation concealment are not described. Participants were not blind to allocation as "*the consenting process informed parents of the assignment*" (p.412) and parents could have told children of their allocation. Field researchers were not blinded and it is not clear the outcome assessors were blinded. The flow of	It is not clear whether adjustment was made for clustering in sample size calculation. Analysis methods take clustering into account; ICC are reported. Authors acknowledge that: "*the study was not designed to have sufficient power to detect significant impacts on health*" (p.412). Authors state that "*sanitizer was well-accepted by teachers and students*" but that teachers and students disliked the product odour

Study	Risk of bias (according to Cochrane Risk of Bias tool)							Additional issues (Cluster RCT method, research governance and ethics, process evaluation, measurement)
	Random sequence generation	Allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Justification of bias identified	
							participants through the study is not clear (no diagram presented). Authors clearly state the primary and secondary outcomes and present results for each of these.	before eating (p.416) Authors report there were no adverse events but table 2 presents data suggesting that some participants experienced a skin rash and that "*teachers did report that some students attempted to lick or eat both the sanitizer and liquid soap*" (p.417). Health status and compliance was self-reported.
Priest *et al* (2014)	Low risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Process of randomisation, allocation concealment and reasons for this are clearly provided by authors. The extent of blinding of participants and researchers is clearly described: participants were not blinded due to the nature of the intervention but investigators not involved in running the trial, outcome assessors and statistician were blind to the group allocation until after the analysis was complete. The flow of schools and individual participants is clearly presented. The trial was registered with a clinical trials registry. Deviations from the planned process and outcomes are set out and explained.	Adjustment was made for clustering in sample size calculation and analysis; ICC are reported. Product formulation is noted. Intervention acceptability, fidelity, adherence and number of skin reactions are reported. Authors report limitations of the study, including that follow up children (for whom reasons for absence were collected) were recruited after clusters were randomised and caregivers knew the allocation. Rate of consent to follow up was low (36.4%) and lower amongst disadvantaged schools. Authors acknowledge potential measurement and recall bias as outcomes were based on caregiver reports. The H1N1 pandemic occurred during the study; some control schools introduced hand sanitizers and all schools may have taken additional preventive steps so there could have been some contamination effect.
Sandora *et al*. 2008	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	The authors describe the randomisation process but it is not clear how teams were assigned and the study was only in one school so participants may have known their allocation although "*the allocation sequence was generated by computer, and teams were assigned to study groups by a study investigator*." (e1556). Due to the nature of the intervention and study design, teachers were likely to know to which study arm they were assigned, although the person receiving parental reports of illness was blind to allocation. A protocol was identified and authors explain missing data and report all pre-specified outcomes.	It is not clear whether adjustment was made for clustering in the sample size calculation, but an ICC is reported. The analysis accounts for clustering but no ICC is reported. The Clorox Company provided the products used in the study. The baseline level of hand sanitizer use in the home was almost 50% (intervention and control groups) suggesting that the intervention was acceptable. Authors note that 63 children refused to participate but it is not clear why. Authors note that they did not observe use of the hand sanitizer so cannot "*address timing of usage in relation to specific exposures*" (e1561), neither can issues of the acceptability of the intervention be ascertained.
Stebbins *et al*. 2011 (Pittsburgh Influenza Prevention Project)	Low risk of bias	Low risk of bias	High risk of bias	High risk of bias	High risk of bias	High risk of bias	Schools were allocated to study arms "*by a constrained randomisation algorithm*" and allocation concealment is described (p.2). Participants were not blinded and not all outcome assessors (teachers) were blinded either. As Stebbins et al note, teachers may have felt pressure to provide "*right*" answers (p.323) in reporting behavioural outcomes. The authors acknowledge high loss to follow up	Adjustment was made for clustering in sample size calculation and analysis, and ICC are reported. The authors indicate that 2 schools used hand sanitizer before which may have affected the outcomes observed. Influenza testing of absent students was only carried out during the flu season that may have distorted results. Authors note adherence to the intervention. However, only results from teachers who responded to all three behavioural outcome surveys were

Study	Risk of bias (according to Cochrane Risk of Bias tool)							Additional issues (Cluster RCT method, research governance and ethics, process evaluation, measurement)
	Random sequence generation	Allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Justification of bias identified	
							and account for this. A protocol is available, but it is not clear if all outcomes are reported.	analysed and the survey may have been subject to reporting and recall bias. The study was underpowered for most outcomes.
Talaat *et al.* 2011	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	Random sequence generation described but it is not clear whether allocation was concealed. Participants and outcome assessors (included teachers) were not blinded; authors note underreporting of illness as a cause for absenteeism in intervention schools. Lack of precise description of outcomes means it is difficult to assess level of reporting bias. Authors do not reflect on the loss of data caused by parents declining consent for their children's swab specimens to be taken. No protocol identified.	Adjustment was made for clustering in the sample size calculation and analysis; no ICC were reported. Absence incidence may have been overestimated if a child were ill at the end of 1 week and at the beginning of the next, although this is could have been the same in intervention and control schools. Also, the rapid test used for influenza diagnosis had low sensitivity and there was a low rate of testing in students absent due to ILI in control schools compared to intervention schools. Monitoring teams found that approximately 93% of students were observed to have soap and drying material available.
Vessey *et al.* 2007	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias	Low risk of bias	Unclear risk of bias	Insufficient information on randomisation was provided. This was a crossover study with clusters at the classroom level in the same school so there is high risk of performance bias and it would difficult to conceal allocation. Authors note teachers were more critical about reporting children to the school nurse during the study because they were not blinded. School secretaries collected absence information but are likely to have known the classes receiving the intervention. Authors report loss to follow-up. No protocol was identified so it is unclear whether all pre-specified outcomes are reported.	It is not clear whether adjustment was made for clustering in the sample size calculation or analysis. No ICC are reported. A hand sanitizer manufacturer funded the study and whilst it was not found to be more effective than normal practice in preventing illness absence, the authors present data showing teachers preferred the sanitizer and perceived "*improved adherence*" to hand sanitizer than hand washing, although teachers also noted when the sanitizer dripped it "*removed the wax from the tile*" (p.371). Authors noted it might be difficult to maintain supplies of soap, towels and hand sanitizer, and limitations of absenteeism as a proxy measure and parent reports (p.371).
White *et al*. 2001	Unclear risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias	High risk of bias	High risk of bias	Randomisation and allocation concealment processes are unclear. There is low risk of performance bias as this was a placebo-controlled trial. Teachers assessed outcomes and were blind to allocation but the measure used was subjective. Authors report a large loss to follow up due to lack of compliance with the intervention (classes which did not comply with minimum product use of ≥3 times per day were excluded from analysis). No protocol was identified; pre-specified outcomes are not clearly presented.	It is unclear whether adjustment was made for clustering in the sample size calculation, no adjustment was made in analysis; no ICC are reported. Intervention acceptability is questionable because authors admit that teachers were "*tired of the study*" and not all complied with the intervention – 40 classes did not meet the 'minimum' required product use of ≥3 times per day (p.262-3).
Non-school based studies								
Correa *et al*. 2012	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Random sequence generation was thoroughly described (p.478); allocation concealment was not. Participants, study personnel (teachers) and outcome assessors were not blinded (p.478). Authors account for attrition and state how	Adjustment was made for clustering in the sample size calculation and analysis; ICC are reported. Authors attempted to reduce ascertainment bias by not providing teachers with case definitions and case registry were reviewed by project coordinator who was blinded

Study	Risk of bias (according to Cochrane Risk of Bias tool)							Additional issues (Cluster RCT method, research governance and ethics, process evaluation, measurement)
	Random sequence generation	Allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Justification of bias identified	
							many children and centres were lost to follow up. However "*after trial onset, 372 new children entered trial centers*" (p.478-9). A protocol is published and stated outcomes were reported.	to study arms. Intervention adherence was not reported, but authors suggest it was acceptable as in 7 centres, hand sanitizer use amongst teachers almost replaced hand washing when hands were not soiled.
Ladegaard and Stage 2009	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Authors describe a random component to the sequence generation (drawing lots) but it is not clear who did this and whether allocation was concealed. There is little discussion of participant blinding or outcome assessment, but it is likely that participants were not blinded due to the nature of the intervention. Insufficient information was provided to assess attrition or reporting bias.	It is unclear whether adjustment was made for clustering in the sample size calculation and analysis; no ICC are reported. Authors note that staff found it difficult to refuse entry to children who were unwell at arrival and during observation, it was noted that hygiene guidelines and hand washing facilities were not always maintained, suggesting issues of intervention acceptability.
Lennell *et al*. 2008	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Insufficient information to judge randomisation or allocation concealment. Participants and study nurses were not blind to allocation: "*because it was not possible to produce a control gel with the same characteristic smell of the disinfectant gel*" (p.1674). Outcome data were sent away for processing but nurses collected sickness absence data and sought missing data. Centres that did not provide adequate attendance information were excluded from analysis (31/60 centres); children in excluded centres differed from those that were retained (p.1678). Authors state that they will measure the outcome using parental data on attendance but results presented use staff data.	Adjustment was made for clustering in the sample size calculation and may have been carried out for analysis; no ICC are reported. There were issues concerning intervention adherence as some children followed the hand washing protocol but did not apply the alcohol gel. It is likely that there was reporting bias as "*parents alone made the decision whether their child was absent from DCC due to* illness" (p.1673). There is also the possibility of recall bias as reason(s) for absence were collected monthly. The method for outcome measurement changed from parent report to use of routine data.
Rosen *et al*. 2006 (Jerusalem hand washing study)	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Random sequence generation is described but allocation concealment is not adequately described. "*educators, parents and field research staff were… not told that the study included 'intervention' and 'control' groups and that they were being compared with respect to hand washing behaviour and absenteeism*" but risk of bias is unclear because field staff who assessed outcomes may have broken this blinding, as they: "*sometimes became aware that the program was being run in a certain preschool*" (p.28). Explanations for missing data are provided. There is a published protocol; authors report on all outcomes stated in the protocol.	Adjustment was made for clustering in the sample size calculation and analysis; an ICC is reported. Authors indicate that participants were not told that they were being assigned to an intervention and control group which raises ethical issues about informed consent. Authors note that there may have been contamination due to proximity of preschools. Educators were accepted on a '*first to agree, first to be accepted'* basis (p.379) which may have introduced selection bias. There is likely to have been contamination as only 82% of participants received the correct take-home pack and the authors state that they "*received reports of some children exchanging videos, and of other inviting friends and relatives to view the video in their homes*" (p.383).

Study	Risk of bias (according to Cochrane Risk of Bias tool)							Additional issues (Cluster RCT method, research governance and ethics, process evaluation, measurement)
	Random sequence generation	Allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Justification of bias identified	
Uhari and Möttönen 1999	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	Authors report random sequence generation but not how allocation concealment was achieved. Participants, study personnel and parents were not blinded. No protocol was identified; there was insufficient description of pre-specified outcomes or participant flow to assess risk of bias.	It is not clear whether adjustment was made for clustering in sample size calculation or analysis (no ICC are reported). Authors note potential for contamination as; "*some families* [had] *one child at an intervention CDCC and another at a control CDCCs, and some of the personnel changed their working place between intervention and control CDCCs during the trial*". Study nurses estimated intervention compliance which may have introduced bias.

Supplementary Data 2: Summary of study outcomes corresponding to review outcomes

- Outcomes presented are selected from study reports to best fit the review outcomes; study authors may present other results, too.
- Results relate to children, not staff in educational settings or family members/caregivers unless otherwise stated.
- Where authors present them separately, only results pertaining to children > 3 years old are presented here.
- * denotes a school-based study
- ILI - Influenza-like Illness

Study	Study outcome(s) presented	Results (effect of the intervention) and author conclusions
Review outcome (a) reduction in rate or change in respiratory infection		
Bowen *et al* 2007*	In-class illness incidence due to upper respiratory tract infection (URTI)	Standard program: Median average of 0.38 episodes per 100 student weeks in the intervention group, a 21% decline compared to the control group (0.48 episodes per 100 student weeks), p>0.4 (table 4, p.1169) Enhanced program: Median average of 0 episodes per 100 student weeks in the intervention group, a 100% decline compared to the control group (0.48 episodes per 100 student weeks), p=0.21 (table 4, p.1169)
Correa *et al* 2012[1]	New cases of acute respiratory infection	Unadjusted incidence density: 2.18 per child-year; 2.06 per child-year (intervention) vs 2.28 per child-year (control) p = 0.0163. (ICC 0.01). (p.480)
Stebbins *et al* 2011*	Total ILI during intervention	Unadjusted incidence rate ratio 0.86 (95% CI 0.57, 1.28) p = 0.45 (ICC 0.01). Adjusted IRR 0.86 (95% CI 0.60,1.22), p = 0.41 (Table SDC 2 – adjusted for percent students receiving subsidized lunch, student race, grade, class size)
Talaat *et al* 2011*	Laboratory-confirmed in-class influenza episodes	The rate of lab-confirmed influenza was higher among students who reported their illness in control schools (35%) than the rate in intervention schools (18%) (p<0.01).
Uhari and Möttönen 1999[2]	Episodes of infection due to rhinitis (children >3 years) Episodes of infection due to cough (children >3 years)	2.7 episodes per person year at risk (intervention), vs 3.1 per person year at risk (control); a 13% (95% CI 3, 23) difference (p = 0.003). 2.5 episodes per person year at risk (intervention), vs 2.6 per person year at risk (control); a 4% (95% CI -8, 15) difference (p = 0.49). (Table 3)[*translated*]
Review outcome (b) reduction in rate or change in signs and symptoms of respiratory infection		
Bowen *et al* 2007*	Rates of in-class illness (rhinorrhoea) Rates of in-class illness (cough)	Standard program: Median average 0.19 episodes per 100 student weeks in intervention group, a 12% increase compared to the control group (median 0.17 episodes per 100 student weeks), p>0.4 (table 4, p.1169). Enhanced program: Median average 0 episodes per 100 student weeks in intervention group, a 100% decrease compared to the control group (median 0.17 episodes per 100 student weeks), p=0.30 (table 4, p.1169). Standard program: Median average of 0.08 episodes per 100 student weeks in intervention group, a 0% difference compared to the control group (0.08 episodes per 100 student weeks), p>0.4 (table 4, p.1169). Enhanced program: Median average of 0 episodes per 100 student weeks in intervention group, a 100% decline compared to the control group (0.08 episodes per 100 student weeks), p=0.25 (table 4, p.1169)
Pickering *et al* 2013*	Self-reported cough Observed rhinorrhoea	Sanitizer vs. control, Risk ratio (RR) =0.89 (95% CI 0.775-1.05, p=0.16) Soap vs. control, RR=1.03 (95% CI 0.88-1.21, p=0.73) Sanitizer vs. soap, RR=0.86 (95% CI 0.73-1.01, p=0.07) Sanitizer vs. control, RR=0.77 (95% CI 0.62-0.95, p=0.02) Soap vs. control, RR=0.77 (95% CI 0.62-0.95, p=0.01) Sanitizer vs. soap, RR=1.00 (95% CI 0.84-1.18, p=0.99) (table 3, p.415)
Uhari and Möttönen 1999	Rhinitis (children >3 years) Cough (children >3 years)	28.1 events per person year at risk (intervention), compared to 35.3 per person year at risk (control); a 20% (95% CI 18, 23) difference between the two groups (p = 0.001).

[1] The study authors state that: "Incidence densities… were calculated as number of new cases divided by number of susceptible child-days at risk" (Correa et al 2012, p.479). Incidence density can be defined as: "the ratio of incident cases to the population at risk in the course of a time period" (Philippe 2000) and differs from cumulative incidence in that it measures the intensity of a behaviour in a setting whereas cumulative incidence measures the frequency of people doing that behaviour in a setting. Reference: Philippe, P (2000) *Density Incidence And Cumulative Incidence: A Fundamental Difference*. The Internet Journal of Internal Medicine 2(2).

[2] Uhari and Möttönen also report episodes of infection amongst personnel by infection type.

Study	Study outcome(s) presented	Results (effect of the intervention) and author conclusions
		25.0 events per person year at risk (intervention), compared to 26.9 per person year at risk (control); a 7% (95% CI 4, 10) difference between the two groups (p = 0.001). (table 2) [*translated*]
Review outcome (c) reduction in rate or change in GI infection		
Correa *et al* 2012[1]	New cases of acute diarrheal diseases	Unadjusted incidence density: 0.75 per child-year; 0.61 per child-year (intervention) vs 0.88 per child-year (control) p < 0.0001 (ICC 0.004) (p.480)
Uhari and Möttönen 1999	Episodes of infection due to diarrhoea (children >3 years)	0.4 episodes per person years at risk (intervention) vs. 0.4 per person year at risk (control); 0% difference (95% CI 18, 25) p = 0.59.
	Episodes of infection due to vomiting (children >3 years)	0.7 episodes per person years at risk (intervention) vs. 0.9 per person year at risk (control); 22% difference (95% CI 6, 33) p = 0.008.(table 3)[*translated*]
Review outcome (d) reduction in rate or change in signs and symptoms of GI infection		
Bowen *et al* 2007*	In-class illness incidence due to diarrhoea	Standard program: Median average 0 episodes per 100 student weeks (intervention) vs. 0 episodes per 100 student weeks (control), p>0.4 (table 4, p.1169). Enhanced program: Median average 0 episodes per 100 student weeks (intervention) vs. 0 episodes per 100 student weeks (control), p>0.4 (table 4, p.1169).
Pickering *et al* 2013*	Diarrhoea symptoms (3+ loose/watery stools in 24 hours)	Sanitizer vs. control, Risk Ratio (RR)=0.75 (95% CI 0.52-1.10, p=0.14). Soap vs. control, RR=0.84 (95% CI 0.58-1.22, p=0.36). Sanitizer vs. soap, RR=0.89 (95% CI 0.61-1.30, p=0.56)
	Diarrhoea (any loose/ watery stool in 24 hours)	Sanitizer vs. control, RR=0.87 (95% CI 0.72-1.04, p=0.12). Soap vs. control, RR=1.09 (95% CI 0.92-1.30, p=0.33). Sanitizer vs. soap, RR=0.80 (95% CI 0.67-0.95, p=0.01)
	Diarrhoea (loose/ watery stool identified on stool chart)	Sanitizer vs. control, RR=0.87 (95% CI 0.70-1.08, p=0.19). Soap vs. control, RR=1.04 (95% CI 0.85-1.29, p=0.69). Sanitizer vs. soap, RR=0.83 (95% CI 0.67-1.03, p=0.09)
	Vomiting	Sanitizer vs. control, RR=0.69 (95% CI 0.44-1.09, p=0.11). Soap vs. control, RR=0.95 (95% CI 0.62-1.46, p=0.81). Sanitizer vs. soap, RR=0.93 (95% CI 0.53-1.63, p=0.80)
Uhari and Möttönen 1999	Diarrhoea (children >3 years)	1.1 events per person year at risk (intervention) compared to 1.1 per person year at risk (control); 0% difference (95% CI -17, 18) between intervention and control group (p = 0.86).
	Vomiting (children >3 years)	1.1 events per person year at risk (intervention), compared to 1.5 per person year at risk (control); 27% difference (95% CI 20, 40) between the two groups (p = 0.001). (table 2) [translated]
Review outcome (e) reduction in rate or change in absence		
Absence only[3]		
Azor Martinez *et al* 2014*	Absence (any reason)	Academic year 2009-10: Incidence of episodes/100 children/day Relative Risk (RR) = 1.115 (95% CI 1.105-1.2, p<0.001). Percent total absent days RR = 1.06 (95% CI 1.03-1.10, p<0.001). During influenza season: Incidence of episodes/100 children/day RR = 1.22 (95% CI 1.13-1.32, p<0.001). Percent total absent days RR = 1.08 (95% CI 1.01-1.14, p<0.015) (table 2, p.635)
Freeman *et al* 2012*	Pupil-reported school absence	Adjusted odds ratio (standard intervention vs. control): 0.81 (95% CI 0.50,1.35), p = 0.43 (standard intervention + sanitation vs. control: OR 0.97 95% CI 0.55,1.69, p = 0.90) (2012, p.386, table 4, p.387) (adjusted to account for clustering of students within schools and stratification of geographical districts, p.383).
Priest *et al* 2014*	Number of absence episodes for any reason - all children	Incidence Rate Ratio (hand sanitizer vs. control) = 0.94 (95% CI 0.84,1.05; p=0.283) (table 4, p.11)
Rosen *et al* 2006	Overall absenteeism for any reason	Adjusted relative risk 1.00 (CI 0.90, 1.14), p = 0.97 (2006, table 3, p.30) (adjusted for baseline value, educational sector; Rosen et al. 2006, p.381)
Stebbins *et al.* 2011*	Total absences during intervention	Unadjusted Incidence Rate Ratio 0.81 (95% CI 0.60, 1.10), p = 0.18. ICC 0.02 (Adjusted IRR 0.74 [95% CI 0.56, 0.97], p= 0.03) (table SDC2 – adjusted for percent students receiving subsidized lunch, student race, grade, class size)
White *et al*. 2001*	Absence incidence	"*Absence incidence in the study group was approximately 33.8% (p <.01) lower than the control group*" (p.262)

[3] Uhari and Möttönen also report parental absence from work due to child's illness.

Study	Study outcome(s) presented	Results (effect of the intervention) and author conclusions
Absence due to any illness		
Azor Martinez *et al* 2014*	Absence due to respiratory illness, GI or ILI	Academic year 2009-10: Episodes/100 children/day Relative Risk (RR)= 1.59 (95% CI 1.46-1.74, p<0.001). Percent total absent days RR = 1.46 (95% CI 1.37-1.55, p<0.001). During influenza season: Episodes/100 children/day RR = 1.49 (95% CI 1.29-1.71, p<0.001). Percent total absent days RR = 1.35 (95% CI 1.23-1.48, p<0.001)
Bowen *et al* 2007*	Absence incidence	Standard program: Median average 1.15 episodes per 100 student weeks (p=0.08, 44% decline) in intervention vs. 2.04 episodes per 100 student weeks in control (table 5, p.1170). Enhanced program: Median average 1.19 episodes per 100 student weeks (p=0.03, 42% decline) in intervention vs. 2.04 episodes per 100 student weeks in control (table 5, p.1170).
Ladegaard and Stage 1999	Average number of days absent due to illness (3-6 year olds)	Intervention group: average number days absent due to illness fell from 3.06 days (observation period) to 2.53 (intervention period) and 1.90 days (outcome period). Control group: average number days absent fell from 2.94 days (observation period) to 2.20 days (intervention period) then rose to 2.71 (outcome period). (table 2).
Lennell *et al* 2008	Rate of absenteeism due to infections	Unadjusted Incidence Rate Ratio: 0.86 (95% CI 0.78,0.94) (p.1678) Adjusted IRR 0.88 (95% CI 0.80, 0.96) (table 2, p.1678 – adjusted for age, number of hours/week at day care centres, asthma or allergies)
Morton and Schultz 2004*	Number of absences due to infectious illness	"*Using McNewar's test for dichotomous variables with paired subjects, significantly fewer children became ill while using alcohol gel as an adjunct to regular hand washing than when using regular hand washing only (chi square = 7.787; p = .0053). The odds of being absent due to infectious illness were reduced by 43% with adjunct use of alcohol gel*." (p.165)
Pickering *et al* 2013*	School absence due to illness	Fewer students (11%) in sanitizer intervention schools reported missing at least 1 day of school because of illness in the prior week compared with students at control schools (OR = 0.51, SE = 0.1, P < 0.01). Students in hand washing intervention schools also reported lower rates (14%) of illness-related absenteeism at follow-up than students at control schools, but the difference was not significant (OR = 0.66, SE = 0.3, P = 0.37). (p.416)
Priest *et al* 2014*	Number of absence episodes due to any illness	Incidence rate ratio (hand sanitizer vs. control) = 1.06 (95% CI 0.94,1.18; p=0.346) ICC 0.018 (95% CI 0.012,0.043) (Table 4, p.11)
Rosen *et al* 2006	Illness absenteeism	Adjusted Relative Risk 1.00 (CI 0.81,1.32), p = 0.97 (2006, p.30 and table 3). (Adjusted for baseline value, educational sector; Rosen et al. 2006, p.381)
Stebbins *et al* 2011*	Absence due to any illness during intervention	Unadjusted Incidence Rate Ratio 0.77 (95% CI 0.41, 1.45), p=0.42 Adjusted IRR 0.75 (95% CI 0.49, 1.16), p=0.20 (adjusted for percent students receiving subsidized lunch, student race, grade, class size)
Talaat *et al* 2011*	Absence caused by overall illness	Number of episodes: 13,247 (intervention), 19,094 (control); a 21% reduction in illness absence (p<0.0001) (table 2)
Uhari and Möttönen 1999	Child absence due to illness Personnel absence due to illness	"*In 8 of the 10 pairs of Child Day Care Centres, the proportion of days that children were absent because of illness was less in intervention centres, this difference being statistically significant [p< 0.03(fig 1)]*." "Despite the reduced number of infections, *the personnel of the intervention day care centres had more days of absence due to infections than personnel in the control centres, 5.3 vs. 4.6 per PYR, a 15% increase (95% CI 7%,26%, p < 0.001)*." [translated]
Vessey *et al* 2007*	Illness-related absenteeism	Two-tailed t-test of mean differences of number of days absent between intervention (mean average number days absent: 26.77 days, SD 7) and control (mean average number days absent: 25.44 days, SD 10.27) = 0.664 (df 34), showing no significant difference between groups (table 1, p.371).
White *et al*. 2001*	Illness absence incidence	Relative risk 0.67 (CI not reported). (p.263, table 4). "*Absence incidence in the study group was approximately 33.8% (p< .001) lower than in the control group*" (p.262)
Absence due to respiratory infection		
Azor Martinez *et al* 2014*	Absence due to ILI	During influenza season: Incidence of episodes/100 children/day Relative Risk (RR): 2.50 (95% CI 1.73-3.62, p<0.001). Percent total absent days RR: 2.64 (95% CI 2.16-3.21, p<0.001) (table 3, p.635)

Study	Study outcome(s) presented	Results (effect of the intervention) and author conclusions
Bowen *et al* 2007*	Absence due to URTI (upper respiratory tract infection)	Standard program: Median average of 0.43 episodes per 100 student weeks (intervention); a 39% decline compared to control (0.70 episodes per 100 student weeks), p = 0.34 (table 5, p.1170). Enhanced program: Median average of 0.48 episodes per 100 student weeks (intervention); a 31% decline compared to control (0.70 episodes per 100 student weeks), p = 0.33 (table 5, p.1170).
Ladegaard and Stage 1999	Number of days absent due to bronchitis/pneumonia (3-6 year olds)	Intervention: number of days absent fell from 7 days (observation period) to 2 days in the intervention and outcome periods. In the control group, number of days absent declined from 9 days (observation period) to 5 days (intervention period) to 2 days in the outcome period. (table 3).
Morton and Schultz 2004*	Number of absences due to respiratory or GI infection	"*Significantly fewer children in the alcohol gel group (n=39) contracted a respiratory or GI illness than in the control group (n=69)*." (p.166) [*Note: results not separately presented for RT and GI illness*]
Pandejpong *et al* 2012*	Change in the rate of absence caused by physician-confirmed ILI	"*absenteeism rate due to confirmed ILI was significantly higher in the control group (0.026) compared with intervention (1) (0.017) (rate difference 0.0096; 95% CI, 0.004-0.016; P= .002) and also in the intervention (2) (0.026) compared with intervention (1) (rate difference 0.009; 95% CI, 0.002-0.015; P= .008). No significant difference was found between intervention (2) group and the control group (rate difference, 0.001; 95% CI, 0.005-0.007; P=0.743).*"(p.509).
	Change in the rate of absence caused by total reported ILI (with and without physician confirmation)	"*rates of absenteeism from ILI both with and without a doctor's confirmation were 0.069 in the intervention (1) group, 0.065 in the intervention (2) group and 0.070 in the control groups. No significant effect was found across rates*." (p.509)
Priest *et al* 2014*	Number of absence episodes due to respiratory illness - follow up children only	Incidence Rate Ratio (hand sanitizer vs. control) = 1.05 (95% CI 0.92,1.20; p=0.439) ICC 0.015 (95% CI 0.011,0.037) (Table 4, p.11)
Sandora *et al.* 2008	Rate of absence caused by respiratory infection	Unadjusted rate ratio was 1.07 (95% CI: 0.92, 1.24, p=0.39). Adjusted rate ratio was 1.10 (95% CI: 0.97,1.24, p=0.12) (p.e1559 – adjusted for race, health status, family size, current hand sanitiser use in the home)
Stebbins *et al* 2011*	Cumulative incidence of absence episodes associated with influenza B	Adjusted Incidence Rate Ratio: 0.81 (95% CI: 0.54, 1.23), P = 0.33
	Cumulative incidence of absence episodes associated with influenza A	Adjusted Incidence Rate Ratio: 0.48 (95% CI: 0.26, 0.87), P < 0.02
	Cumulative incidence of absence episodes associated with influenza B.	Adjusted Incidence Rate Ratio: 1.45 (95% CI: 0.79, 2.67), P = 0.23 (p.4) (Adjusted for percent students receiving subsidized lunch, student race, grade, class size)
Talaat *et al* 2011*	Incidence of absence due to ILI	"*In control schools, 65.5% (n=1,671) of students were absent caused by ILI… In the intervention schools, ILI was responsible for 53.7% (n=917) of absenteeism*" A reduction of 40%, p=<0.0001 (table 2, table 2).
White *et al*. 2001*	Total respiratory-related absence Respiratory illness absence incidence	"*Total respiratory-related absences decreased by 30.3% (p<.001) in the study group, compared with control* [placebo] *group. Similar decreases in respiratory-related absence-incidences were observed in the study group by 31.7% (p<.01) as compared with the placebo group*." (p.262)
Absence due to GI		
Azor Martinez *et al* 2014*	Absence due to Acute Gastroenteritis	Bivariate analysis: Incidence Rate Ratio (IRR): 0.65 (95% CI 0.54-0.79, p< 0.001). Multiple regression analysis: Adjusted IRR: 0.64 (95% CI: 0.52-0.78, p<0.001) (e36) (Adjusted by sex, immigrant, age, father's/mother's profession, family size, dwelling type, previous hand sanitiser use in the home, correct handwashing, acute-gastroenteritis preventive behaviours, table 2, e38)
Bowen *et al* 2007*	Absence due to diarrhoea	Median 0 episodes per 100 student weeks in standard intervention group, expanded intervention group and control group (table 5, p.1170)
Ladegaard and Stage 1999	Number of days absent due to diarrhoea	Among 3-6 year olds in intervention group, the number of days absent increased from 15 days (observation period) to 23 (intervention period) then fell to 7 days (outcome period). The number of days absent in the control group increased from 21 days (observation period) to 23 days (intervention period) to 16 days in the outcome period. (table 3).

Study	Study outcome(s) presented	Results (effect of the intervention) and author conclusions
Morton and Schultz 2004*	Number of absences due to GI infection	"*Significantly fewer children in the alcohol gel group (n=39) contracted a respiratory or GI illness than in the control group (n=69)*." (p.166) [*Note: results not separately presented for RT and GI illness*]
Priest *et al* 2014*	Number of absence episodes due to GI - follow up children only	Incidence Rate Ratio (hand sanitizer vs. control) = 1.11 (95% CI 0.82,1.52; p=0.490) ICC 0.027 (95% CI 0.023,0.066) (Table 4, p.11)
Sandora *et al.* 2009	Rate of absence caused by GI illness	Unadjusted rate ratio: 0.86 (95% CI: 0.79, 0.94, p<.01). Adjusted rate ratio: 0.91 (95% CI 0.87,0.94, p < .01) (p.e1559 – adjusted for race, health status, family size, current hand sanitiser use in the home)
Talaat *et al*. 2011*	Incidence of absences due to diarrhoea	639 episodes in intervention, compared to 1,316 in control; a 33% reduction in absences due to diarrhoea, p=< 0.0001 (table 2)
White *et al*. 2001*	Total GI-related absence GI illness absence incidence	"T*otal GI-related absences were decreased by 32.8% (p<.01) in the study group, compared with the control* [placebo] *group. Similar decreases in gastrointestinal absence-incidences were observed in the study group by 38.6% (p<.01) as compared with the placebo group*." (p.262)
Review outcome (f) Laboratory results of respiratory and/or GI infection		
Stebbins *et al* 2011*	Absence due to episodes of laboratory confirmed influenza (A and/or B) Absence due to episodes of laboratory confirmed influenza A Absence due to episodes of laboratory confirmed influenza B	Unadjusted Incidence Rate Ratio: 0.94 (95% CI 0.59, 1.52), p = 0.81 (ICC 0.001). Adjusted Incidence Rate Ratio: 0.81 (95% CI 0.51, 1.23), p = 0.33. Unadjusted Incidence Rate Ratio 0.58 (95% CI 0.31, 1.10), p = 0.10 (ICC 0.002). Adjusted Incidence Rate Ratio 0.48 (95% CI 0.26, 0.87), p = 0.02 Unadjusted Incidence Rate Ratio 1.60 (95% CI 0.91, 2.84), p = 0.11 (ICC <0.001). Adjusted Incidence Rate Ratio 1.45 (95% CI 0.79, 2.67), p = 0.23 (All adjusted for percent students receiving subsidized lunch, student race, grade, class size, SDC 2)
Talaat *et al**	Incidence of laboratory-confirmed influenza (in-class and absence).	Intervention group: 125/808 cases tested (in-class and absent) were positive for influenza; compared to 795/1075 cases tested (in-class and absent) from control. "*laboratory confirmed influenza reduced 50% (p<0.0001)*" (p.1)
Review outcome (g) Behaviour change related to hand hygiene		
Graves *et al* 2011*	Proportion of students washing hands after latrine use	Difference in proportion of students washing hands was not significant; 0.06 (95% CI -0.27, 0.38). Comparing baseline to follow-up the proportion of students washing hands increased by 2.7% in control schools and decreased by 2.7% in intervention schools (p.314) Hand washing behaviour was not significantly associated with distance of the hand washing station from the latrine, visibility from the classroom or visibility from the latrine (p.314).
Freeman *et al* 2012*	Student WASH practices	Percent of students who reported washing hands after using a latrine: Intervention (1) 78% (SE=5) at baseline, 87% (SE=2) at follow up (p=0.11); Intervention (2) 83% (SE=5) at baseline, 89% (SE=5) at follow up (p=0.18); Control 82% (SE=3) at baseline, 81% (SE=3) at follow up. Percent of students who used soap in the hand washing demonstration: Intervention (1) 71% (SE=5) at baseline, 78% (SE=7) at follow up (p=0.75); Intervention (2) 85% (SE=3) at baseline, 81% (SE=8) (p=0.62) at follow up; Control 82% (SE=5) at baseline and 84% (SE=3) at follow up. (Greene *et al* 2012, p.387-388, table 1).
Pickering *et al* 2013*	Student hand cleaning after toilet use Student hand cleaning rate before lunch	"*Students at sanitizer intervention schools were over twofold more likely to clean their hands after toilet use than control school students (prevalence ratio = 2.2, 95% CI 1.2, 4.3), whereas students at soap intervention schools were not significantly more likely to clean their hands compared with students in control schools (prevalence ratio 1.0, 95% CI 0.3–3.8)*" (p.414) "*Among all toileting events, the rate of hand cleaning with product (soap or sanitizer) was 82% at sanitizer schools (prevalence ratio 38.5, 95% CI 18.1–81.5), 37% at soap intervention schools (prevalence ratio 17.2, 95% CI 4.4–67.5), and 2% at control schools*" (p.414) Mean proportion of students was not significantly different between schools: 0.90 at sanitizer schools (prevalence ratio 1.3, 95% CI 0.8–2.2), 0.82 at soap intervention schools (prevalence ratio 1.2, 95% CI 0.7–2.0), 0.69 at controls schools (p.414).

Study	Study outcome(s) presented	Results (effect of the intervention) and author conclusions
		"*mean proportion of students cleaning hands with product before lunch was 0.61 at sanitizer schools (prevalence ratio 126.8, 95% CI 31.9–503.8), 0.70 at soap intervention schools (prevalence ratio 143.0, 95% CI 38.9–525.6), 0.01 at control schools*" (p.415)
Rosen *et al.* 2006	Children washing hands with soap before lunch Children washing hands with soap after bathroom use	Medium-term adjusted relative risk (RR) was 2.77 (CI: 1.70, 7.46, p < 0.01), long-term adjusted RR was 2.93 (CI 1.86, 6.97, p < 0.01). (p.30) Medium-term adjusted RR was 2.90 (CI: 1.69, 10.06, p < 0.01), long-term adjusted RR = 3.30 (CI: 1.83, 16.67, p < 0.01) (p.30) (Medium-term effect compares results 3 months after program launch in intervention with results before the end of the study period in the control. Long term effects compare results 6 months after program launch in intervention with results just before the end of study period in the control. Effect sizes were adjusted for religious sector and baseline handwashing levels, Rosen et al. 2006, p.28).
Stebbins *et al* 2011*	Behaviour change (students)	"*Students were observed to persist in meaningful and statistically significant improvements in their hand-washing frequency and in using hand sanitizer at least twice per day. The number of students using hand sanitizer four times per day significantly increased during flu season but did appear to drop off somewhat after flu season.*" (p.318-20) *"Students were observed to make and persist in meaningful and statistically significant improvements in covering coughs and sneezes, increasing their frequency of coughing into their elbow or shirt…. All responses were significantly higher in intervention than control schools"* (Stebbins *et al* 2010, p.320).
Review outcome (h) Change in knowledge, attitudes or belief about hand hygiene		
Freeman *et al* 2012*	Changes in pupil knowledge	"*We found significant and substantial differences in pupil knowledge between intervention and control groups after the intervention. Knowledge of key hand washing times and scores on a hand washing demonstration in intervention schools significantly increased."* (p.384, also table 2) Mean number of students who mentioned two key hand washing times (before eating, after defecation): Intervention (1): 72 (SD=15) at baseline, 83 (SD=10) at follow up (p=0.09). Control: 75 (SD=14) at baseline, 78 (SD=12) at follow up. (table 2, p.385)
Pickering *et al* 2013*	Student perceptions of waterless hand sanitizer as an alternative to hand washing with soap and water Teacher perceptions of waterless hand sanitizer as an alternative to hand washing with soap and water	"*91% of students at sanitizer schools stated that they would choose sanitizer to clean their hands over soap and water… they perceived cleaning hands with sanitizer to take a shorter time than hand washing with soap and water*." (p.415) All teachers interviewed at sanitizer schools stated they would prefer provision of sanitizer over provision of soap at their school. (p.415)
Rosen *et al.* 2006	Pre-school educator beliefs Pre-school educator attitudes Pre-school educator knowledge	"*Beliefs about outcomes were positive toward hand washing in both groups (intervention: mean = 5.736, SD = 0.95; control: mean = 5.29, SD = 1.12). The effect of the intervention on beliefs about outcomes was borderline significant [least squares means (LSMeans) intervention 5.82, LSMeans control: 5.22, p = 0.0875, mixed models ANOVA].*" (p.692) "*The effect of the interventions on attitudes was not significant (LSMeans intervention: 5.72, LSMeans group: 5.77, p = 0.9187, mixed models ANOVA).*" (p.692) "*The score for the knowledge scale was 6.24 for the intervention group (SD = 0.73) and 5.81 for the control group (SD = 0.79). Knowledge was significantly higher in the intervention (LSMeans intervention group: 6.22, LSMeans control: 5.66, p = 0.0343"* (Rosen *et al* 2009, p.692)
Stebbins *et al* 2011*	Student knowledge	"*Intervention school students were observed to be more knowledgeable than control school counterparts*." (Stebbins *et* al. 2010, p.320 and table 4)
Uhari and Möttönen 1999	Knowledge of personnel	"*knowledge of infections… at the end of the trial was statistically significantly better at intervention centres in 3 of the 19 statements on the questionnaire, with no difference in the 16 other statements*." [*translated*]