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Hand-washing promotion for preventing diarrhoea (Review)

Ejemot-Nwadiaro RI, Ehiri JE, Arikpo D, Meremikwu MM, Critchley JA

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TABLE OF CONTENTS

[Intervention Review]

Hand-washing promotion for preventing diarrhoea

Regina I Ejemot-Nwadiaro[1], John E Ehiri[2], Dachi Arikpo[3], Martin M Meremikwu[4], Julia A Critchley[5]

[1]Department of Public Health, College of Medical Sciences, University of Calabar, Calabar, Nigeria. [2]Division of Health Promotion Sciences, University of Arizona, Mel & Enid Zuckerman College of Public Health, Tucson, Arizona, USA. [3]Cochrane Nigeria, Institute of Tropical Diseases Research and Prevention, University of Calabar Teaching Hospital, Calabar, Nigeria. [4]Department of Paediatrics, University of Calabar Teaching Hospital, Calabar, Nigeria. [5]Population Health Sciences Institute, St George's, University of London, London, UK

Contact address: Regina I Ejemot-Nwadiaro, reginaejemot@yahoo.com, r.ejemot_nwadiaro@unical.edu.ng.

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ABSTRACT

Background

Diarrhoea accounts for 1.8 million deaths in children in low- and middle-income countries (LMICs). One of the identified strategies to prevent diarrhoea is hand washing.

Objectives

To assess the effects of hand-washing promotion interventions on diarrhoeal episodes in children and adults.

Search methods

We searched CENTRAL, MEDLINE, Embase, nine other databases, the World Health Organization (WHO) International Clinical Trial Registry Platform (ICTRP), and metaRegister of Controlled Trials (mRCT) on 8 January 2020, together with reference checking, citation searching and contact with study authors to identify additional studies.

Selection criteria

Individually-randomized controlled trials (RCTs) and cluster-RCTs that compared the effects of hand-washing interventions on diarrhoea episodes in children and adults with no intervention.

Data collection and analysis

Three review authors independently assessed trial eligibility, extracted data, and assessed risks of bias. We stratified the analyses for child day-care centres or schools, community, and hospital-based settings. Where appropriate, we pooled incidence rate ratios (IRRs) using the generic inverse variance method and a random-effects model with a 95% confidence interval (CI). We used the GRADE approach to assess the certainty of the evidence.

Main results

We included 29 RCTs: 13 trials from child day-care centres or schools in mainly high-income countries (54,471 participants), 15 community-based trials in LMICs (29,347 participants), and one hospital-based trial among people with AIDS in a high-income country (148 participants). All the trials and follow-up assessments were of short-term duration.

Hand-washing promotion (education activities, sometimes with provision of soap) at child day-care facilities or schools prevent around one-third of diarrhoea episodes in high-income countries (incidence rate ratio (IRR) 0.70, 95% CI 0.58 to 0.85; 9 trials, 4664 participants, high-certainty evidence) and may prevent a similar proportion in LMICs, but only two trials from urban Egypt and Kenya have evaluated this (IRR 0.66, 95% CI 0.43 to 0.99; 2 trials, 45,380 participants; low-certainty evidence). Only four trials reported measures of behaviour change, and the methods of data collection were susceptible to bias. In one trial from the USA hand-washing behaviour was reported to improve; and in the trial from Kenya that provided free soap, hand washing did not increase, but soap use did (data not pooled; 3 trials, 1845 participants; low-certainty evidence).

Hand-washing promotion among communities in LMICs probably prevents around one-quarter of diarrhoea episodes (IRR 0.71, 95% CI 0.62 to 0.81; 9 trials, 15,950 participants; moderate-certainty evidence). However, six of these nine trials were from Asian settings, with only one trial from South America and two trials from sub-Saharan Africa. In seven trials, soap was provided free alongside hand-washing education, and the overall average effect size was larger than in the two trials which did not provide soap (soap provided: RR 0.66, 95% CI 0.58 to 0.75; 7 trials, 12,646 participants; education only: RR 0.84, 95% CI 0.67 to 1.05; 2 trials, 3304 participants). There was increased hand washing at major prompts (before eating or cooking, after visiting the toilet, or cleaning the baby's bottom) and increased compliance with hand-hygiene procedure (behavioural outcome) in the intervention groups compared with the control in community trials (data not pooled: 4 trials, 3591 participants; high-certainty evidence).

Hand-washing promotion for the one trial conducted in a hospital among a high-risk population showed significant reduction in mean episodes of diarrhoea (1.68 fewer) in the intervention group (mean difference −1.68, 95% CI −1.93 to −1.43; 1 trial, 148 participants; moderate-certainty evidence). Hand-washing frequency increased to seven times a day in the intervention group versus three times a day in the control arm in this hospital trial (1 trial, 148 participants; moderate-certainty evidence).

We found no trials evaluating the effects of hand-washing promotions on diarrhoea-related deaths or cost effectiveness.

Authors' conclusions

Hand-washing promotion probably reduces diarrhoea episodes in both child day-care centres in high-income countries and among communities living in LMICs by about 30%. The included trials do not provide evidence about the long-term impact of the interventions.

PLAIN LANGUAGE SUMMARY

Does encouraging people to wash their hands stop them having diarrhoea?

Key messages

Encouraging hand washing probably reduces the number of times children have diarrhoea, by around 30%, in communities in low- to middle-income countries and in child-care centres in high-income countries.

We did not find evidence about the long-term effects of hand-washing programmes.

What causes diarrhoea?

‘Diarrhoea’ is the name for frequent bowel movements or the passing of unusually soft or watery faeces. Infections of the gut by bacteria, viruses, or parasites commonly cause diarrhoea, and are mostly spread through water contaminated with faeces.

The symptoms of diarrhoea usually improve in a couple of days. However, in severe or long-lasting diarrhoea, too much water, salts, and nutrients may be lost from the body. This loss can cause dehydration and even death. Diarrhoea is a leading cause of death and sickness among children under five years of age.

Preventing diarrhoea

Most deaths associated with diarrhoea are caused by pathogens acquired as a result of unsafe drinking water, poor sanitary conditions, and lack of hygiene. Washing hands with soap and water removes the bacteria, viruses, and parasites that cause disease. Programmes and activities encouraging people to wash their hands have been developed for use in communities and schools, including hygiene training, posters, leaflets, comic books, songs, and drama.

Why we did this Cochrane Review

We know that hand washing at appropriate times can prevent diarrhoea, but we do not know how best to encourage the practice. We wanted to find out if programmes and activities that had been studied for this purpose were effective at increasing hand washing and reducing diarrhoea.

What did we do?

We searched for studies that investigated the use of programmes to encourage hand washing in communities, day-care centres, schools, hospitals, and households. We were interested in whether taking part in the programmes affected the number of times people in the study reported having diarrhoea.

We looked for studies in which the treatments people received were decided at random. This type of study usually gives the most reliable evidence about the effects of a treatment.

Search date

We included evidence published up to 8 January 2020.

What we found

We found 29 studies:

13 studies (in 54,471 people) took place in child day-care centres or schools in mainly high-income countries;
15 studies (in 29,347 people) were community-based in low- to middle-income countries; and
1 study (in 148 people) was hospital-based.

The studies looked at the effects of hand-washing programmes on the number of times people in the study reported having diarrhoea. The effects of the programmes were followed for four months to one year.

No studies reported the effects of hand-washing programmes on how many people died from diarrhoea, how many children under five years of age died (of any cause), or whether the benefits associated with the programme outweighed any extra costs.

What are the results of our review?

All studies compared the effects of programmes to encourage hand washing with not having any programmes about hand washing.

In child-care centres and schools: in high-income countries, encouraging hand washing reduced the number of times children had diarrhoea (9 studies, 4664 children); and in low- to middle-income countries may have reduced the number of times children had diarrhoea (2 studies, 45,380 children).

In communities in low- to middle-income countries, encouraging hand washing probably reduced the number of times children (up to 15 years of age) had diarrhoea (9 studies,; 15,950 children).

In hospitalized adults with AIDS, encouraging hand washing probably reduced the number of times they had diarrhoea and probably improved hand-washing behaviour (washing hands more often) over one year of follow-up (1 study, 148 people).

How reliable are these results?

We are confident that, in high-income countries, hand-washing programmes in schools and child-care centres reduced the number of times children had diarrhoea. This result is unlikely to change with more evidence. We are less confident about our result for low- to middle-income countries, which is based on a small number of studies and might or might not change with more evidence.

We are moderately confident about our results for children in communities and in hospitalized adults with AIDS. These results might change if more evidence becomes available.

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings table 1

Hand-washing promotion at child care centres and schools compared to no intervention for preventing diarrhoea

Patient or population: children
Setting: child day-care centres or schools
Intervention: hand-washing promotion
Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (trials)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with hand-washing promotion at child care centres and schools				
Episodes of diarrhoea	High-income countries		IRR 0.70 (0.58 to 0.85)	4664 (9 RCTs)	⊕⊕⊕⊕ HIGH[b,c,d,e]	Hand-washing promotion reduces the risk of diarrhoea in high-income countries compared to no hand-washing promotion
	4 episodes per 100 children per year[a]	2 episodes per 100 children per year (2 to 3)				
	Low- or middle-income countries		IRR 0.66 (0.43 to 0.99)	45,380 (2 RCTs)	⊕⊕⊖⊖ LOW[f,g,h]	Hand-washing promotion may reduce the risk of diarrhoea in low- or middle-income countries compared to no hand-washing promotion
	22 episodes per 100 children per year	15 per 1000 (9 to 22)				

*__The risk in the intervention group__ (and its 95% CI) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: Confidence interval; **IRR:** Incidence rate ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a]The median incidence of diarrhoea in the control groups was 4 episodes per 100 children per year.
[b]No serious risk of bias: most trials are at high or unclear risk of detection or reporting bias due to no description of blinding of outcome assessors. Restriction of the analysis to just the blinded trials finds a slightly smaller effect size, but the result remains statistically significant. Not downgraded.
[c]No serious inconsistency: although statistical heterogeneity was high, this heterogeneity was related to the size of the effect, not the direction of effect. The individual effect sizes in trials ranged from a 10% relative reduction in diarrhoea to a 50% reduction.
[d]No serious indirectness: these nine trials were conducted in day-care centres/schools in high-income countries (USA, Denmark, Australia, Netherlands and Canada).

[e]No serious imprecision: the result is statistically significant and the meta-analysis adequately powered to detect this result.
[f]No serious inconsistency: while both trials found reductions in diarrhoea incidence, the reduction was only statistically significant in the trials from Egypt. However, we did not downgrade.
[g]The incidence of diarrhoea in the control group in the trial from Egypt was 22 per 100 children per year. The incidence in the control group in the Kenya trial was not stated.
[h]Downgraded by two levels for serious indirectness: only one trial was conducted in a low-income country (Pickering 2013 KEN). This trial from an urban slum in Nairobi did not find a statistically significant benefit on diarrhoea incidence.

Summary of findings 2. Summary of findings table 2

Hand-washing intervention in the community compared to no intervention for preventing diarrhoea

Patient or population: children up to 15 years of age
Setting: community
Intervention: hand-washing promotion
Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with Hand washing intervention in the community				
Episodes of diarrhoea: rate ratios	Low- or middle-income countries		Incidence rate ratio 0.71 (0.62 to 0.81)	15,950 (9 RCTs)	⊕⊕⊕⊖ MODERATE-b,c,d,e	Hand-washing promotion probably reduces the risk of diarrhoea in low- or middle-income countries compared to no hand-washing promotion
	3 episodes per 100 children per year[a]	2 episodes per 100 children per year[a] (2 to 2)				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **IRR:** Incidence rate ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a]The median incidence of diarrhoea in the control groups was three episodes per 100 children per year.
[b]No serious risk of bias: most trials are at high or unclear risk of detection or reporting bias, due to no description of blinding of outcome assessors. Restriction of the analysis to just the blinded trials finds a slightly smaller effect size, but the result remains statistically significant. Not downgraded.

[c]No serious inconsistency: although statistical heterogeneity was high, this heterogeneity was related to the size of the effect, not the direction of effect. The individual effect sizes in trials ranged from a 6% relative reduction in diarrhoea to a 29% reduction.
[d]No serious imprecision: the result is statistically significant and the meta-analysis adequately powered to detect this result.
[e]Downgraded by one level for serious indirectness: eight trials were conducted in low- and middle-income countries (the Democratic Republic of Congo, Pakistan, Bangladesh, Myanmar, Peru, India, and Nepal), and one trial was conducted in a low-income country (Ethiopia).

Summary of findings 3. Summary of findings table 3

Hand-washing intervention in a hospital setting compared to no intervention for preventing diarrhoea

Patient or population: adults with AIDS
Setting: hospital
Intervention: Hand-washing promotion
Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with hand- washing intervention in hospital setting				
Episodes of diarrhoea assessed with: self-reports collected through home visits; hospital/health centre/clinic records, including admission for diarrhoea-related dehydration follow up: mean 1 year	The mean episodes of diarrhoea was 2.92	The mean episodes of diarrhoea was 1.24	Mean difference 1.68 lower (1.93 lower to 1.43 lower)	148 (1 RCT)	⊕⊕⊕⊖ MODERATE[a,b,c,d]	Hand-washing promotion probably reduces the risk of diarrhoea in adults with AIDS compared to no hand-washing promotion
Hand-washing behavioural changes/ changes in knowledge, attitude and practice assessed with: frequency of hand washing per day follow-up: mean 1 year	4 times daily	7 times daily	-	(1 RCT)	⊕⊕⊕⊖ MODERATE[c,d,e]	Hand-washing promotion probably improves hand-washing behaviour, knowledge, attitude, and practice in adults with AIDS compared to no hand- washing promotion

*__The risk in the intervention group__ (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a]Outcomes assessed in adults in high-risk group (people with AIDS).
[b]The mean episodes in the control groups was 2.92, while that of the intervention group was 1.24 episodes over the 1-year trial period.
[c]Downgraded by one level for serious risk of bias: the trial is at an unclear risk of selection bias due to failure to describe a process of allocation concealment. This trial is also at high risk of detection or reporting bias due to no description of blinding of outcome assessors. Blinding of participants would not have been possible.
[d]Evidence from this setting was very limited, since it is from only one trial (Huang 2007 USA).
[e]Hand-washing rates: intervention: seven times daily from three times at baseline; control: four times daily from three times.

BACKGROUND

Description of the condition

Diarrhoeal disease ranks among the top 1% of causes of death, particularly at the two extremes of life (Mbakaya 2017). Diarrhoea remains a serious global public health problem, accounting for 1.8 million deaths annually, especially among children under five years of age (Walker 2013). The yearly global diarrhoeal disease burden is estimated at 72.8 million disability-adjusted life years lost through incapacitation and premature deaths, mainly in low- and middle-income countries (LMICs) (Murray 2012).

A synergistic relationship exists between diarrhoea and malnutrition, often demonstrated through a combination of forced low-nutrient intake, reduced absorption, and increased nutrient excretion (WHO 2003; Luby 2018 BGD). The malnutrition-infection complex is clearly reinforced during diarrhoea episodes, as poor nutritional status predisposes children to more severe and persistent diarrhoea, impaired growth and development, and higher case fatality rates (UNICEF/WHO 2009; Lee 2012; Luby 2018 BGD).

Diarrhoeal disease pathogens are usually transmitted through the faecal-oral route (Curtis 2000). The pathways include ingestion of food and water contaminated by faecal matter, person-to-person contact, and direct contact with infected faeces (Eisenberg 2012). Some trials estimate that over 75% of all diarrhoea cases can be attributed to contaminated food and water (Curtis 2000; Maxwell 2012). Poor hygiene behaviours and improper handling practices of caregivers are associated with high levels of bacterial contamination of food and water (Iroegbu 2000; Mannan 2010; Pickering 2011).

Behaviours that encourage human contact with faecal matter include the following: improper disposal of faeces; children defaecating on the floor; rags being used to cleanse the child after defaecation; and lack of hand washing after defaecation, handling faeces (including children's faeces), or cleansing the child's perineum before handling food by caregivers and children (Pickering 2011). In particular, hand contact with ready-to-eat food (i.e. food consumed without further washing, cooking, or processing or preparation by the consumer) represents a potentially important mechanism by which diarrhoea-causing pathogens contaminate food and water (UNICEF/WHO 2009). In addition, flies serve as vectors of diarrhoea-causing pathogens to humans. Thus, consumption of food exposed to flies is associated with a high risk of diarrhoea (Marino 2007).

Household economic status is significantly associated with diarrhoea prevalence (Woldemicael 2001), especially in low-income countries. Households may lack basic infrastructure for proper hygiene practices, such as facilities for proper disposal of excreta. In addition, even where available, these may not be adapted for children's use (Tumwine 2002; UNICEF/WHO 2009). This often leads to indiscriminate defaecation in and around the premises and to increased risk of excreta handling by mothers, caregivers, and children (Nielsen 2001). A trial in Eritrea found that the availability of a toilet facility in households was associated with a 27% reduction in the risk of diarrhoea (Woldemicael 2001). The same trial also found associations between the number of children living in the house and diarrhoea morbidity. In some cultures children's faeces are regarded as innocuous. For this reason adults may not wash their hands after handling children's faeces and may cleanse a child with their bare hands (Traoré 1994; Curtis 2000). However, evidence suggests that children's faeces are as hazardous as adult faeces and may contain even higher concentrations of pathogens than those of adults, due to the children's increased interactions with contaminated materials in their surroundings (Oketcho 2012).

Description of the intervention

Hygiene-promotion interventions constitute one of a number of strategies identified by the World Health Organization (WHO) for control of diarrhoea (UNICEF/WHO 2009). These constitute a range of activities aimed at encouraging individuals and communities to adopt safer practices within domestic and community settings to prevent hygiene-related diseases that lead to diarrhoea (WELL 1999; Ehiri 2001); hand washing is one such intervention. The practice of hand washing and the factors that influence hand-washing behaviour among individuals in communities are complex and include psychosocial, contextual, and infrastructural reasons (Whitby 2007; Mbakaya 2017); for example, washing hands with water only or with soap may be influenced both by knowledge of best practice and by the availability of water and soap (Curtis 2011). Also, hand washing may require infrastructural, cultural, and behavioural changes, which take time to develop, as well as substantial resources (e.g. trained personnel, community organization, provision of water supply and soap) (Luby 2001a; UNICEF/WHO 2009). Consideration of the wide applicability and sustainability of hygiene interventions continues to come under critical review (Luby 2006 PAK; Ejemot-Nwadiaro 2008; Gould 2017; Curtis 2011; Huis 2012; Madhu 2012; Ejemot-Nwadiaro 2015; Luby 2018 BGD; Null 2018 KEN). For example, maintenance of the new hand-washing behaviours that result from promotional interventions is vital to maximizing the associated potential health benefits. Apart from the challenges of sustaining new behaviour (hand washing) among the target communities, cost has been identified as a major factor that limits the sustainability of hand-hygiene behaviour (Langford 2007 NPL; Hartinger 2011 PER). For example, to sustain the health benefits of newly-acquired hand-washing behaviours, it is also important that individuals and communities have access to resources that support hand washing, including water and soap. Lack of access to hand-washing resources may therefore limit the potential impact of hand washing on health, particularly for low-income households and communities.

How the intervention might work

Hand washing helps decontaminate the hands and prevent cross-transmission of diarrhoeal-causing pathogens (Ehiri 2001; Gurjeet 2013). Hand-washing promotion uses direct approaches, such as training and educating individuals or groups of individuals about hygiene, diarrhoea transmission, the relationship between germs and health and demonstrating this relationship through leaflets, posters, drama, and songs (Whitby 2007; Curtis 2011). Washing hands with soap and water removes pathogens mechanically and may also chemically kill contaminating and colonizing flora, making hand washing more effective (Hugonnet 2000). Washing hands with soap under running water or large quantities of water with vigorous rubbing was found to be more effective than several members of a household dipping their hands into the same bowl of water (often without soap) (Luby 2005), which is a common practice in many low-income countries, especially before household meals (Ehiri 2001). This may contribute to, rather

than prevent, food contamination, as pathogens present on the contaminated hands of household members can be transferred to those who subsequently dip their hands in the same bowl of water (Prüss 2002).

Why it is important to do this review

Hand washing is an effective intervention in the control of diarrhoeal diseases. It is listed in the UNICEF/WHO 2009 seven-point plan for comprehensive control of diarrhoea. Hand washing requires infrastructural, cultural, and behavioural changes that take time and substantial resources to develop (Cave 1999; Yeager 1999; Luby 2001b). Given that resources spent on interventions to promote hand washing could be invested in other public health programmes, it is important to ascertain whether hand-washing promotion is an efficient use of scarce health resources. In 2008, we published a review that assessed in RCTs the broader question of the effectiveness of hand washing with soap in preventing diarrhoea compared with other interventions, such as provision of water and improvement of water quality (treatment of water) (Ejemot-Nwadiaro 2008). A review by Curtis 2003, which examined the effectiveness of hand washing with soap in community-based trials, estimated that hand washing could reduce diarrhoea risk by up to 47%. Similarly, Fewtrell 2005 examined a range of water, sanitation, and hygiene interventions in LMICs, and estimated that hygiene interventions reduced diarrhoea incidence by 44%. However, both reviews included non-randomized trials. Curtis 2003 included cross-sectional trials, which have inherent limitations on the establishment of causal relationships. Fewtrell 2005 presented evidence of publication bias in included trials. In this Cochrane Review, we assess whether the estimate of effect observed only in RCTs is of similar magnitude to those seen in previous reviews, and the applicability of hand-washing promotion in reducing diarrhoeal diseases across wide population groups. We also include both institution-based and community-based trials in countries of any income level.

In 2015, we published a review update that provided evidence that interventions to promote hand hygiene observed only in RCTs can decrease diarrhoea rates by approximately 30% (Ejemot-Nwadiaro 2015). However, there were few studies of high methodological quality to make a strong statement on the effect of the intervention in each of the identified settings. In addition, it is important to assess the sustainability of hand-washing practices or behaviours and effects on diarrhoeal illness in the long term. Single or multiple hand-washing intervention pathways to reducing diarrhoea still remain a key issue, especially for scaling up (large-scale and long-duration studies) and for cost benefit or cost effectiveness analysis. Evidence on these aspects remains scant (Ejemot-Nwadiaro 2015), with these intricately related to issues of intervention sustainability. Given that diarrhoea remains a significant public health problem in LMICs, there is a need for robust evidence to improve precision in the magnitude of effect obtained and the certainty of the evidence presented in the last update.

OBJECTIVES

To assess the effects of hand-washing promotion interventions on diarrhoeal episodes in children and adults.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs), including cluster-RCTs.

Types of participants

Individuals (adults and children) in day-care centres (DCCs) or schools, communities, or households, and patients in hospitals.

Types of interventions

Intervention

Activities that promoted hand washing after defaecation or after disposal of children's faeces and before eating, preparing, or handling foods; for example, small-group discussions and larger meetings on hygiene education, germs-health awareness interventions, multimedia communication campaigns with posters, radio and TV campaigns, leaflets, comic books, songs, slide shows, use of T-shirts and badges, pictorial stories, dramas, and games. We included trials that focused exclusively on hand washing and those that had hand washing as part of a broader package of hygiene interventions if they undertook analyses of the effects of hand washing on diarrhoea.

Control

No hand-washing promotion.

Types of outcome measures

Primary outcomes

- Episodes of diarrhoea (self-reports collected through home visits; hospital or health-centre or clinic records, including admissions for diarrhoea-related dehydration).

We defined diarrhoea as:

- acute or primary diarrhoea: passage of three or more loose or watery stools in a 24-hour period, a loose stool being one that would take the shape of a container, or definitions used by trial authors consistent with this standard definition;
- persistent diarrhoea: diarrhoea lasting 14 days or more;
- dysentery: stool with blood.

Secondary outcomes

- diarrhoea-related death among children or adults;
- behavioural changes, such as changes in the proportion of people who reported or are observed washing their hands after defaecation, disposal of children's faeces, or before preparing or handling foods;
- changes in knowledge, attitudes, and beliefs about hand washing;
- all-cause under-five mortality;
- cost effectiveness.

Search methods for identification of studies

We attempted to identify all relevant trials regardless of language or publication status (published, unpublished, in press, and in progress) (Lefebvre 2020).

Electronic searches

We searched the following databases using the search terms and strategy described in Appendix 1: Cochrane Infectious Diseases Group Specialized Register (8 January 2020); Cochrane Central Register of Controlled Trials (CENTRAL), published in the Cochrane Library (2020, Issue 1); PubMed (MEDLINE), 1966 to 8 January 2020); Embase (OVID; 1974 to 8 January 2020); PsycINFO (EBSCOHost, 1967 to 8 January 2020); Science Citation Index, Social Sciences Citation Index, SSCI, CPCI-S, CPCI-SSH (1981 to 8 January 2020); ERIC (Educational Resources Information Center; 1966 to 8 January 2020), and LILACS (Bireme; 1982 to 8 January 2020).

We also searched the following databases using a simplified strategy (diarrhea, diarrhoea, handwashing): SPECTR (The Campbell Collaboration's Social, Psychological, Educational, and Criminological Trials Register; 2000 to 8 January 2020); Bibliomap and TRoPHI (The Trials Register of Promoting Health Interventions) maintained by the Evidence for Policy and Practice Information and Co-ordinating Centre www.eppi.ioe.ac.uk) (1990 to 8 January 2020); and The Grey Literature (www.nyam.org/library/grey.shtml; 2002 to 8 January 2020). We also searched the World Health Organization (WHO) International Clinical Trial Registry Platform (ICTRP) and the metaRegister of Controlled Trials (mRCT) for ongoing trials on 8 January 2020 using diarrhoea, diarrhea, and hand washing as search terms. The PRISMA flow diagram is shown in Figure 1 below.

Searching other resources

Researchers and organizations

To obtain further information, we contacted researchers in the field for unpublished and ongoing trials (October 2019).

Reference lists

We also examined the reference lists of articles for relevant trials.

Data collection and analysis

Three review authors (RIE, JAC, and DA) independently screened titles and abstracts of relevant articles to assess their eligibility for inclusion in the review.

Selection of studies

We retrieved full texts of articles that were deemed potentially relevant to the review for further assessment. We decided on inclusion by consensus among all review authors. We scrutinized each trial report to ensure that we included multiple publications from the same trial only once. We listed the excluded trials and the reasons for their exclusion.

Data extraction and management

Three review authors (RIE, DA, and JAC) independently extracted data on methods, types of participants, interventions, and outcomes from the selected trials using a standardized data extraction form. We resolved any disagreements by discussion and consensus among review authors. We requested unpublished data and additional information from published trials from relevant individuals, groups, and organizations.

We extracted the year of completion of the trial rather than the year of publication for identification of included trials. When such data were not reported, we used the year of publication. This was to give a clear time frame for this Cochrane Review (1977 to 2019). In addition, we used the three-letter international code of the country where the trial was conducted in the study ID. We extracted data on each trial site, including any measures of availability of water and soap, and literacy level of the communities. Where data were available, we extracted the socioeconomic status of trial participants, since resources for effective hand washing (e.g. running water and soap) may be more accessible to higher-income households. We carefully summarized details of the intervention including type of promotional activity, whether soap and water provision was part of the intervention, method of hand washing promoted (washing in a bowl or under running water), and procedure for hand washing.

We had intended to analyze episodes of diarrhoea as a dichotomous outcome, but the data reported by the trials did not permit this type of analysis. We analyzed the outcome as count data, when either the incidence rate ratio (IRR) and its 95% confidence interval (CI) or the number of episodes of diarrhoea and the person-time at risk was reported, or as continuous data when the mean number of diarrhoea episodes and standard deviation (SD) were presented.

For RCTs which randomized individuals, when continuous outcomes data were summarized as arithmetic means we extracted the arithmetic means, SDs, and numbers of participants for the treatment and control groups. For count (rate) outcome data, we extracted the number of episodes, the number of person-years at risk, and the number of participants for each intervention group, or we extracted a rate ratio and measure of variation (e.g. CI) directly from the publication.

Cluster-RCTs required the use of different data extraction methods and analysis methods, because trials with a cluster design require more complex analysis than trials that randomized individuals. Observations on participants in the same cluster tend to be correlated, so the intracluster variation must be accounted for during the analysis. If this correlation is ignored in the analysis and the same techniques are employed as for RCTs that randomized individuals, the resulting measure of effect remains a valid estimate, but the associated variance of the estimate will be underestimated, leading to unduly narrow CIs. For meta-analysis this means that trials analyzed without allowing for this design effect will receive too much weight.

For the cluster-RCTs, we extracted information on the number of clusters, average size of clusters, unit of randomization, whether the trials adjusted for clustering, and the statistical method used to analyze cluster trials. When a trial's analysis had adjusted for clustering, we extracted the point estimate and 95% CI. For count data we extracted the IRR. If a trial had not adjusted for clustering, we extracted the same data as for RCTs that randomized individuals.

Assessment of risk of bias in included studies

Two review authors (RIE and DA) independently assessed the risks of bias in included trials using the Cochrane 'Risk of bias' assessment tool (Higgins 2011). We assessed the risks of bias across the following domains: randomization sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other potential biases. We classified

our judgements as 'high', 'unclear', or 'low' risk of bias using criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

In the blinding domain, we acknowledged that double blinding is not possible in trials of hand-washing interventions since there is no obvious placebo. However, outcome assessors could be blinded, and we assessed whether or not this had occurred. It is also difficult to assess losses to follow-up (incomplete outcome data) in open cluster-RCTs. Some adults and children may leave the trial, but others are born or enter the trial during the follow-up period, hence participant numbers are in constant flux. Inclusion of all randomized participants in the analysis is thus most clearly represented as the person-time at risk accrued as a percentage of maximum possible person-time at risk in each trial arm. We therefore reported on this measure and also on any loss to follow-up of both clusters and participants. We assessed this as low risk if it was at least 90%. We also assessed whether baseline characteristics were comparable across the intervention groups and whether data were collected at similar time points for the intervention and control sites with a view to identifying selective reporting and other possible biases. The details are shown in Figure 2 and Figure 3.

Measures of treatment effect

We qualitatively compared included trials to ascertain the feasibility of pooling them in a meta-analysis. Thus we identified three distinct settings, covering child DCCs, community-based interventions, and hospital-based trials, since the factors that affect hand-washing practice may vary in these settings. We stratified the trials based on these settings for the meta-analysis and calculated incidence rate ratios (IRRs) for dichotomous outcomes, mean differences (MDs) for continuous outcome measures on the same scale, and standardized mean differences (SMDs) for continuous outcomes measured using different scales.

Unit of analysis issues

For all trials that did not adjust for clustering, we made approximate adjustments using estimates of the intra-cluster correlation coefficient (ICC) from other trials that did adjust for clustering and reported this statistic. We did this by multiplying the standard error (SE) for each trial by the square root of the design effect. We estimated the design effect as 1 + (m - 1) * ICC, where 'm' is the average cluster size and 'ICC' is the intra-cluster correlation coefficient (Higgins 2020).

Dealing with missing data

We contacted authors of eligible trials for missing data or for additional information when the trials were less than 15 years old.

Assessment of heterogeneity

We checked for heterogeneity by visually inspecting the forest plots, applying the Chi^2 test, with a P value of 0.10 indicating statistical significance, and also implementing the I^2 statistic with a value of 50% used to denote moderate levels of heterogeneity. We used the random-effects model to pool data if we detected heterogeneity and it was still considered clinically meaningful to combine the trials. Due to the limited number of trials in each setting, we were unable to explore potential sources of heterogeneity in depth. We explored and attempted to explain heterogeneity where possible using a predefined trial characteristic (provision of hand-washing material (soap) as part of intervention and type of promotional activity employed) and quality characteristics (whether or not outcome assessors were blinded and whether or not trials had adjusted for clustering) (Deeks 2020).

Assessment of reporting biases

We planned to assess the possibility of publication bias by producing a funnel plot if at least 10 trials contributed to the treatment comparison. However, we did not undertake this, due to an insufficient number of included trials.

Data synthesis

We analyzed the data using RevMan 5 (Review Manager 2019) and present all results with 95% CIs. We stratified the analysis into three categories of settings: child DCCs and school-based interventions (DCCs or primary schools), community-based interventions, and hospital-based intervention (in persons at high risk of diarrhoea - people with AIDS). Also we stratified the analyses by the income status of the countries where the trials were conducted. Since the outcomes and methods of measuring behaviour changes were too variable to make meta-analysis meaningful, we tabulated the results.

RCTs that randomize individuals

We summarized continuous outcome data from RCTs randomizing individuals using the MD value. We did not undertake meta-analysis of RCTs randomizing individuals, due to their limited number.

Cluster-RCTs that adjusted for clustering

For count outcomes, we pooled the IRR in RevMan 5, using the generic inverse variance method with the random-effects model. We used standard techniques for calculating SEs from 95% CIs (Deeks 2020). When the outcomes and methods of measuring outcomes were too variable to make meta-analysis meaningful (for changes in hand-washing behaviour), we tabulated the results. One trial performed child- and site-level analyses (Haggerty 1988 COD), without providing the 95% CI for the site-level analysis. We therefore estimated the denominator from the number of children by trial arm by assuming that all those who had remained in the trial for at least nine weeks had a total of 12 weeks of follow-up. The numerator (average number of episodes per child) was provided at the cluster level. We classified this trial as cluster-adjusted. Several community studies in LMICs reported changes in diarrhoea as the difference in the 'mean longitudinal prevalence' of diarrhoea episodes over a certain period of time (Luby 2006 PAK; Galiani 2016 PER; Kapoor 2016 IND; Briceno 2017 TZA; Luby 2018 BGD; Null 2018 KEN). Where feasible (i.e. where the period of time was consistently one week and sufficient details were reported to estimate a SE), we combined these in a meta-analysis using the generic inverse variance method.

Cluster-RCTs that did not adjust for clustering

For trials that did not report on or were unclear on the method used to adjust for clustering, we either extracted information on the rate ratio and unadjusted 95% CI or, wherever possible, estimated the unadjusted rate ratios and 95% CIs from the total number of diarrhoea episodes and person-time at risk in each trial arm. Where data on person-time at risk were not directly provided by the trial authors, we estimated this as accurately as possible from

the follow-up duration multiplied by the total number of children as the denominator for both intervention and control groups, respectively. The measures of effect and CIs are presented in tables. One trial adjusted for clustering by comparing the mean incidence rate of intervention and non-intervention classrooms (Kotch 1989 USA), but presented only cluster-adjusted 95% CIs for a different outcome (excess mean episodes) and not a rate ratio. We took the cluster-adjusted estimate of the numerator (the mean incidence rate across the clusters) from the published data and estimated the person-time at risk crudely by multiplying the number of contacts every two weeks by the number of children, assuming this was equally distributed between the intervention and control groups. We classified this trial as not having adjusted for clustering.

For all trials that did not adjust for clustering, we attempted to make an approximate adjustment using estimates of the ICC from one of the trials that did adjust for clustering and reported this statistic. Only two trials reported this statistic: one community-based trial (Luby 2003b PAK), and one trial in a child DCC (Roberts 1996 AUS). We assumed that these ICC estimates could be generalized to other community-based and child DCCs or to school-based trials, respectively. We extracted the number of children and number of clusters from each unadjusted trial to estimate the average cluster size. We then followed standard methods to estimate the design effect for each trial and multiplied the SE for each trial by the square root of this design effect (Higgins 2020). This approximate adjustment increases the SE (and hence the width of the CIs for the unadjusted trials) and appropriately reduces the weight given to such trials in the meta-analysis. We performed meta-analyses by pooling the estimates of the cluster-adjusted and approximately-adjusted trials together.

Certainty of evidence

We assessed the certainty of the evidence using the GRADE approach (Guyatt 2008; Schünemann 2020). We imported data from RevMan 5 to GRADEpro 2014 to create a 'Summary of findings' table containing relevant information on the outcomes of interest. We then appraised the certainty of the evidence for each outcome across the following domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias for each trial that contributed to the outcome. Where we identified deficiencies that were sufficient to decrease our confidence in the estimates of effect, we downgraded the certainty of evidence for RCTs from 'high' to either 'moderate', 'low', or 'very low', and explained our reasons for doing so in footnotes. We have included the prespecified outcomes for the three independent settings in Summary of findings 1; Summary of findings 2; and Summary of findings 3.

Subgroup analysis and investigation of heterogeneity

If we detected any heterogeneity, we planned to explore its possible causes using subgroup analysis. We conducted subgroup analyses for trial setting, provision of hand-washing material (soap) as part of intervention, type of promotional activity employed (focused or multiple hygiene interventions), and quality characteristics (whether outcome assessors were blinded).

Sensitivity analysis

We undertook a sensitivity analysis to explore the robustness of our findings, including the trial size, duration of follow-up, differences in method of assessing the primary outcome, and differences in methodological quality (blinding of outcome assessors) of the included trials.

Summary of findings and assessment of the certainty of the evidence

We assessed the certainty of the evidence using the GRADE approach (Guyatt 2008; Schünemann 2020). We imported data from RevMan 5 to GRADEpro 2014 to create a 'Summary of findings' table containing relevant information on the outcomes of interest. We then appraised the certainty of the evidence for each outcome across the following domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias for each trial that contributed to the outcome. Where we identified deficiencies that were sufficient to decrease our confidence in the estimates of effect, we downgraded the certainty of evidence for RCTs from 'high' to either 'moderate', 'low', or 'very low', and explained our reasons for doing so in footnotes. We have included the prespecified outcomes for the three independent settings in Summary of findings 1; Summary of findings 2; and Summary of findings 3.

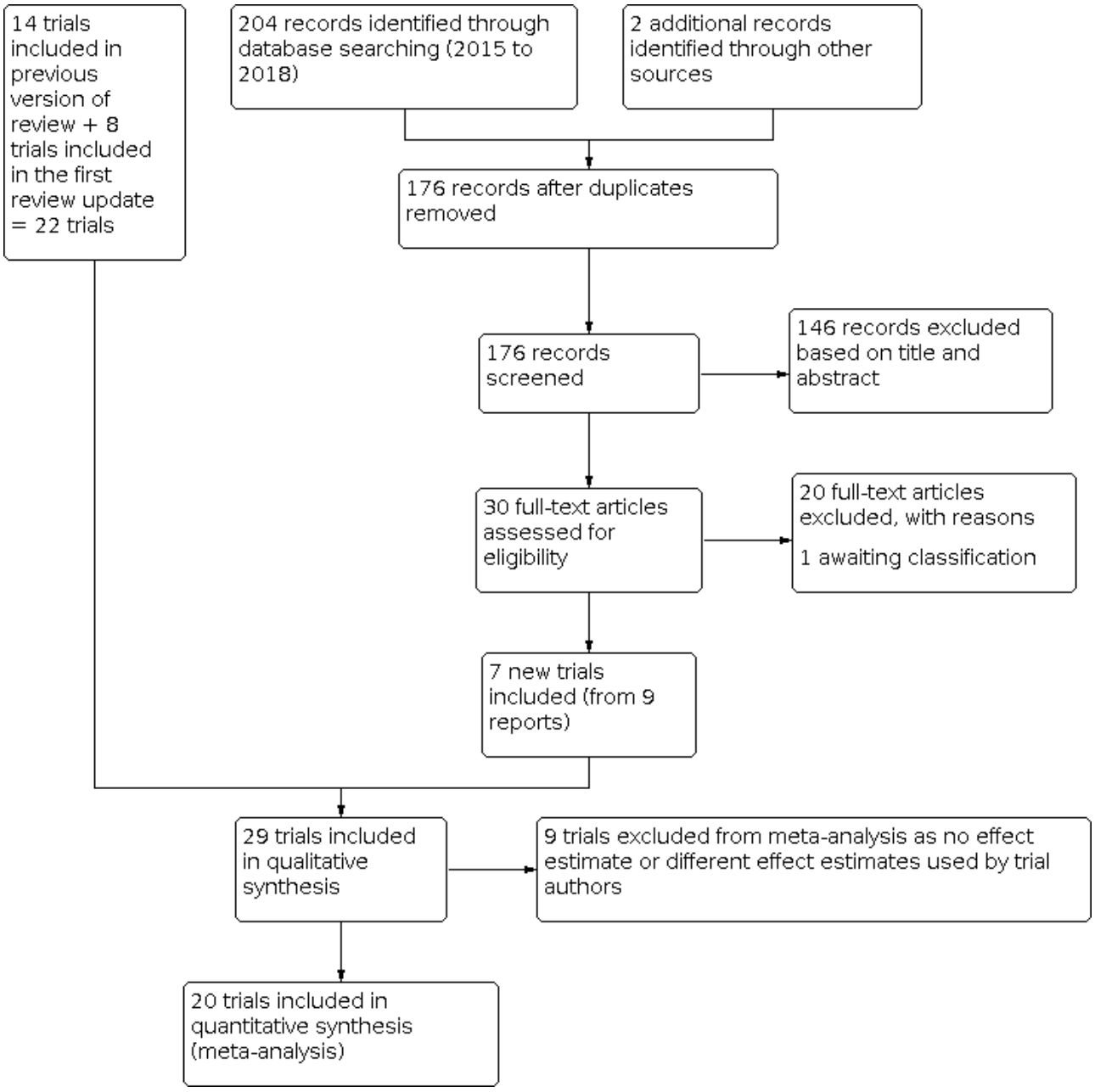
RESULTS

Description of studies

Results of the search

Our search yielded 206 potentially relevant trials, making a total of 290 when combined with the 47 search results of the first review update (Ejemot-Nwadiaro 2015), and the 37 search results of the original review (Ejemot-Nwadiaro 2008). Twenty-nine trials met the inclusion criteria: 14 trials were included in the original version of the review (Ejemot-Nwadiaro 2008), eight new trials were added to the first review update, and we included seven new trials based on our updated search. See Figure 1. We describe them in the Characteristics of included studies tables. One trial was in Danish (Ladegaard 1999 DEN), and the rest were written in English. Thirteen trials were DCC- or school-based, 15 were community-based (one of the trials had both community-based and school-based components, but the community-based component predominated), and one trial (Huang 2007 USA) was in a high-risk group. We have listed reasons for excluding 84 trials in the Characteristics of excluded studies table.

Figure 1. PRISMA flow diagram.



Included studies

Child DCCs or schools

All 13 trials in this group were randomized by cluster using primary schools (Bowen 2004 CHN; Talaat 2008 EGY; Pickering 2013 KEN), DCCs (Black 1977 USA; Bartlett 1984 USA; Butz 1990 USA; Roberts 1996 AUS; Carabin 1997 CAN; Ladegaard 1999 DEN; Kotch 2003 USA; Zomer 2015 NED), or classrooms in DCCs as the unit of randomization (Kotch 1989 USA; Ban 2015 CHN). These trials were all conducted in high-income countries except for two trials conducted in an upper-middle income country (UMIC): Bowen 2004 CHN and Ban 2015 CHN (conducted in Hubei province and Fujian province in China, respectively), and another two conducted in LMICs: Talaat 2008 EGY (conducted in Cairo, Egypt) and Pickering 2013 KEN (conducted in Nairobi, Kenya). The other trials were performed in Australia (Roberts 1996 AUS), Europe (Ladegaard 1999 DEN; Zomer 2015 NED), and North America (Black 1977 USA; Bartlett 1984 USA; Kotch 1989 USA; Butz 1990 USA; Carabin 1997 CAN; Kotch 2003 USA), where resources and materials for hand washing were relatively available and accessible.

Interventions

All trials used multiple hygiene interventions, except for Black 1977 USA, Bowen 2004 CHN, and Pickering 2013 KEN, which used only a hand-washing intervention. Although Pickering 2013 KEN was a three-arm trial that investigated hand sanitizer and hand washing with soap, we considered only the hand-washing arm with soap in this Cochrane Review; it is therefore categorized as a hand

washing-only intervention. Kotch 2003 USA assessed the impact of the provision of hand-washing and diapering equipment on the incidence and duration of infectious illness (including diarrhoea) in both children and staff. We describe the interventions in more detail in Table 1. In addition to instruction on proper hand-hygiene techniques in Ban 2015 CHN, parents or guardians and teachers were given antimicrobial supplies with which to regularly clean hard surfaces and disinfect the classrooms and homes of the participants.

All but one of the included trials based in child DCCs or schools had intervention and control arms (monitoring only). Bowen 2004 CHN had three arms for the standard intervention, expanded intervention (which included the standard intervention and peer monitoring of hand washing), and control. It is important to note that the control group in most cases received quite frequent monitoring (estimating diarrhoea illness episodes typically on a two-week basis). This monitoring itself may have influenced hand-washing behaviour. Carabin 1997 CAN attempted to tease out the effects of the intervention alone from 'monitoring'. The monitoring effect in this trial was estimated as the difference in diarrhoea incidence rates within each arm over one year of the trial (September 1996 to November 1997). The crude effectiveness of intervention was estimated as the difference between the monitoring effect in the intervention group and control group.

Participants

Thirteen trials including 54,471 children met the inclusion criteria. Seven trials included children under three years of age, another trial included children less than five years of age (Ban 2015 CHN), one trial was in children under six years of age (Ladegaard 1999 DEN), and one trial was with children under seven years of age (Butz 1990 USA). Bowen 2004 CHN involved children in the first grade at school in China; Talaat 2008 EGY included children in government elementary schools in Cairo, Egypt; and Pickering 2013 KEN involved children aged five to 10 in primary schools in Nairobi, Kenya. Hand-washing behavioural changes and changes in knowledge, attitude, and beliefs on hygiene were assessed in the day-care providers (number not precisely reported) and children, while the primary outcome measures were assessed in the children.

The number of clusters ranged from 4 to 87 (Black 1977 USA; Bowen 2004 CHN). Primary outcome measures were assessed across 278 DCCs, two kindergartens, and 151 schools. Participants were exposed to mainly small- and large-group training sessions on hygiene education and germs-health theory that used multiple promotional techniques (e.g. audio and video tapes, pamphlets, practical demonstrations, drama, posters, songs, games, or peer monitoring). Kotch 2003 USA used the 'Keep-it-clean' module in training caregivers to standardize the interventions across the trial arms. The aim was to provide education about personal hygiene, diarrhoea transmission, treatment, and prevention, and the importance of techniques for hand washing. Intervention and control groups were generally comparable in important characteristics at baseline (Table 1).

Outcome measures

All included trials measured our primary outcome of episodes of diarrhoea. Three trials reported the proportion of people washing their hands or changes in knowledge, attitude, and beliefs about hand washing, or both (Kotch 1989 USA; Roberts 1996 AUS; Pickering 2013 KEN). No trials reported diarrhoea-related deaths, all-cause under-five mortality, or cost-effectiveness data. However, Kotch 2003 USA reported that the cost of purchasing and installing one unit of the hand-washing and diapering equipment was USD 10,385 (USD 7500 for the equipment and the rest for installation) by classroom. Follow-up periods ranged from two to 12 months.

Adjustment for clustering

Six trials did not appear to have accounted for clustering in the analysis for any outcome measure (Black 1977 USA; Bartlett 1984 USA; Butz 1990 USA; Ladegaard 1999 DEN; Talaat 2008 EGY; Ban 2015 CHN). Kotch 1989 USA adjusted for clustering by comparing the mean incidence rate of intervention and non-intervention classrooms, but only a cluster-adjusted 95% CI for a difference outcome (excess mean episodes) was presented, and not a rate ratio. Kotch 2003 USA reported controlling for clustering by estimating a random effect for the centres, but this does not seem to have been reflected in the results. In the other five cluster-adjusted trials. Bowen 2004 CHN presented only the school-level analysis (mean illness and absence rates by school); Carabin 1997 CAN adjusted for clustering using a Bayesian hierarchical model, while Roberts 1996 AUS, Pickering 2013 KEN, and Zomer 2015 NED estimated robust SEs in a Poisson regression model.

Community-based trials

We included 15 community-based trials. Fourteen were cluster-RCTs that used entire communities (generally villages, squatter settlements, or neighbourhoods, except for Han 1985 MMR and Kapoor 2016 IND, which used households) as units of randomization. These trials were conducted in low- and middle-income countries (LMICs) in Africa (Haggerty 1988 COD; Briceno 2017 TZA; Hashi 2017 ETH; Null 2018 KEN), Asia (Han 1985 MMR; Stanton 1985 BGD; Luby 2003a PAK; Luby 2003b PAK; Luby 2006 PAK; Langford 2007 NPL; Nicholson 2008 IND; Galiani 2016 PER; Kapoor 2016 IND; Luby 2018 BGD), and South America (Hartinger 2011 PER). Galiani 2016 PER was a community-based trial that also had a school component.

Interventions

Five trials evaluated hand-washing-only interventions (Han 1985 MMR; Luby 2003a PAK; Luby 2003b PAK; Langford 2007 NPL; Nicholson 2008 IND). Luby 2003a PAK had two hand-washing arms, one with plain soap and one with antibacterial soap. These two arms had similar results and are combined in this review. Han 1985 MMR used plain soap. Luby 2003b PAK was a five-arm trial that investigated water-quality interventions, hand washing, and a combination of the two; only the arm with antibacterial soap and hand-washing education is considered in this review. Luby 2006 PAK conducted a follow-up trial to the Luby 2003b PAK trial, maintaining the initial randomization process to assess if learned hygiene behaviours could be sustained over time without additional hygiene-promotion intervention. Three other trials used multiple hygiene interventions that included hand washing with soap (the type of soap used is not described) (Stanton 1985 BGD; Haggerty 1988 COD; Hartinger 2011 PER). We have provided more detailed descriptions of the interventions in Table 2.

Participants

We included 15 trials with about 29,347 children. In the community-based trials, seven trials were with very young children (under three years) (Haggerty 1988 COD; Langford 2007 NPL; Hartinger 2011 PER; Galiani 2016 PER; Kapoor 2016 IND; Luby 2018 BGD; Null 2018 KEN);

four trials were with children less than five years of age (Han 1985 MMR; Briceno 2017 TZA; Hashi 2017 ETH), or less than six years of age (Stanton 1985 BGD); and three involved older children, up to 15 years of age (Luby 2003a PAK; Luby 2003b PAK; Luby 2006 PAK). Nicholson 2008 IND had four categories of participants: targeted children five years old, children less than five years old, children 6 to 15 years old, and adults in the families. The primary outcome measure (incidence of diarrhoea) was assessed in each of these categories with their corresponding control groups, except for the adults reported as the 'whole family'. In this review, we considered results only from the target group, as the first three categories had similar effect sizes. Hand-washing behavioural changes and changes in knowledge, attitude, and beliefs about hygiene were assessed in the mothers (number not precisely reported), while the primary outcome measures were assessed in the children.

The number of clusters varied from 18 to 1923 (Haggerty 1988 COD; Stanton 1985 BGD). The participants were provided with hand-washing materials and were involved in large-group hygiene education training, except for Luby 2006 PAK, which was a follow-up trial. The intervention and control groups were socioeconomically comparable at baseline.

Outcome measures

All included trials measured diarrhoea episodes except for Luby 2006 PAK; Galiani 2016 PER; Kapoor 2016 IND; Briceno 2017 TZA; Luby 2018 BGD; Null 2018 KEN, which measured mean longitudinal prevalence of diarrhoea. Some trials also assessed different types of diarrhoea: Han 1985 MMR measured dysentery rates, and Luby 2003a PAK and Luby 2003b PAK also assessed the rate of persistent diarrhoea. Two of the included trials reported all-cause under-five mortality (Luby 2018 BGD; Null 2018 KEN). None of the included trials reported diarrhoea-related deaths or cost-effectiveness data. However, Briceno 2017 TZA also estimated the associated cost-per-household gaining access to improved sanitation to be USD 194. Langford 2007 NPL reported changes in hand washing from baseline to end-line at hand-washing junctures, Stanton 1985 BGD reported on changes in hand-washing behaviour, while Nicholson 2008 IND reported hand washing using soap wrappers collected as an indirect measure of soap consumption. Length of follow-up ranged from 4 to 12 months.

Adjustment for clustering

All trials adjusted for clustering in some way, except for Han 1985 MMR; Langford 2007 NPL; Nicholson 2008 IND; Hartinger 2011 PER; and Kapoor 2016 IND. Stanton 1985 BGD and Luby 2003a PAK adjusted for clustering by estimating rates at the group level; Luby 2003b PAK adjusted for clustering by calculating an ICC based on an analysis of variance level and design effect. Luby 2006 PAK, measuring mean longitudinal prevalence of diarrhoea, accounted for clustering using generalized estimating equations. Luby 2018 BGD and Null 2018 KEN adjusting for covariates using targeted maximum likelihood estimation. Haggerty 1988 COD performed child- and site-level analyses, without providing the 95% CI for the site-level analysis. The numerator (average number of episodes per child) was provided at the cluster level. Galiani 2016 PER and Briceno 2017 TZA used clustered SEs.

Hospital-based trial (high-risk group)

We identified only one trial in a high-risk group (Huang 2007 USA). It individually randomized 148 adults with AIDS from one HIV clinic in the USA to receive intensive hand-washing promotion delivered by specialist nurses (Huang 2007 USA). The intervention included hygiene education, hand-washing demonstrations by nurses and participants, and weekly telephone calls to reinforce hand-washing messages (Table 3). The major outcomes reported were mean episodes of diarrhoea in each group and the number of hand-washing episodes per day. They reported the mean hand-washing frequency per day at baseline and at the end of the intervention (Table 4).

Excluded studies

We have listed the excluded trials and the reasons for exclusion in the Characteristics of excluded studies section.

Risk of bias in included studies

See Figure 2 and Figure 3 for a summary of the 'Risk of bias' assessments for all included trials.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included trials.

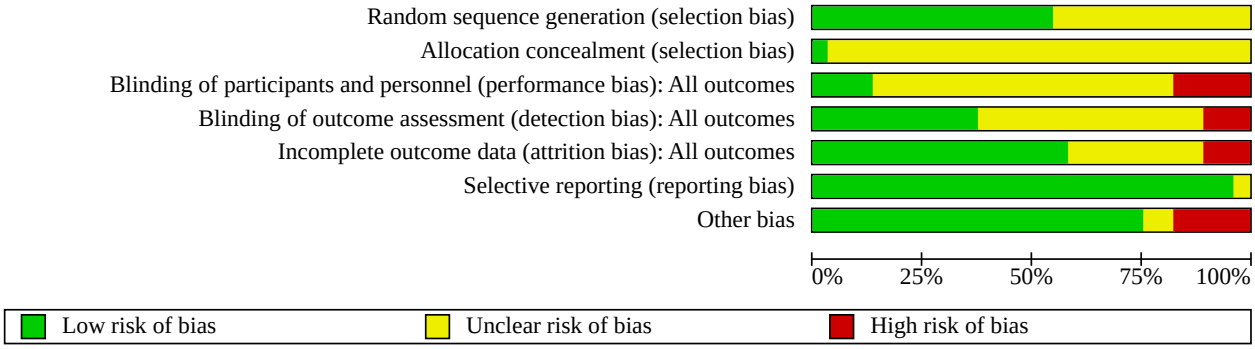


Figure 3.

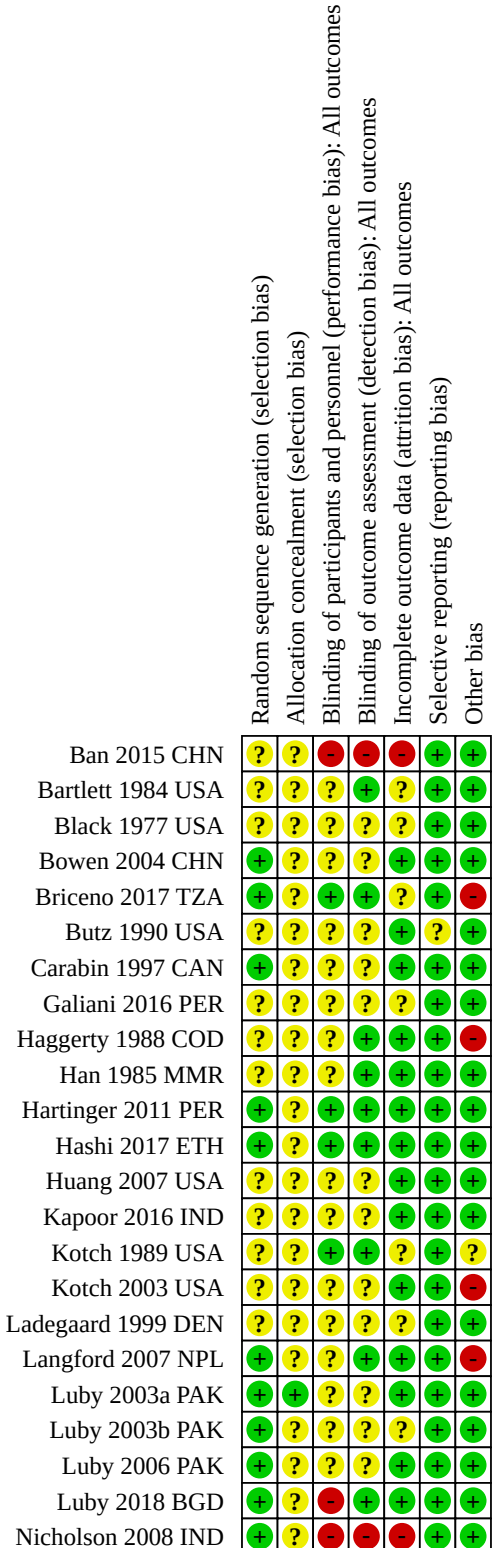
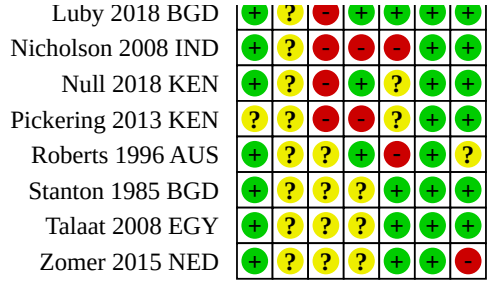


Figure 3. (Continued)



Allocation

Child DCCs or school-based trials

Five of the 13 trials used an adequate method to generate the allocation sequence (Roberts 1996 AUS; Carabin 1997 CAN; Bowen 2004 CHN; Talaat 2008 EGY; Zomer 2015 NED); the method was unclear in the others. The method used to conceal allocation was unclear in all trials. In cluster-RCTs, lack of concealment of allocation is not considered a major risk of bias, since all clusters are usually randomized at the same time (Higgins 2020).

Community-based trials

Eleven of the 15 included community-based trials reported adequate methods for generating allocation sequence (Stanton 1985 BGD; Luby 2003a PAK; Luby 2003b PAK; Luby 2006 PAK; Langford 2007 NPL; Nicholson 2008 IND; Hartinger 2011 PER; Briceno 2017 TZA; Hashi 2017 ETH; Luby 2018 BGD; Null 2018 KEN). Only Luby 2003a PAK reported adequate allocation concealment; it was unclear in the other trials.

Hospital-based trial (high-risk group)

Huang 2007 USA did not clearly report the method of randomization or allocation concealment, and we adjudged this trial as having an unclear risk of selection bias.

Blinding

Child DCCs or school-based trials

Three trials reported blinding of the outcome assessors (Bartlett 1984 USA; Kotch 1989 USA; Roberts 1996 AUS); the rest were open trials.

Community-based trials

Eight trials reported blinding of outcome assessors, and the rest were open trials (Han 1985 MMR; Haggerty 1988 COD; Langford 2007 NPL; Hartinger 2011 PER; Briceno 2017 TZA; Hashi 2017 ETH; Luby 2018 BGD; Null 2018 KEN).

Hospital-based trial (high-risk group)

Huang 2007 USA was at an unclear risk of performance and detection bias, because the trial authors did not provide enough information to make a judgement about the blinding of participants and personnel or of outcome assessors.

Incomplete outcome data

Child DCCs or school-based trials

It was difficult to assess the number of randomized participants included in the analysis, as this was reported at different levels (cluster, child, person-time at risk). However, all trials were able to account for the number of randomized clusters included in the analysis. Six trials were at low risk of attrition bias because they reported outcome data for at least 90% of their participants (Butz 1990 USA; Carabin 1997 CAN; Kotch 2003 USA; Bowen 2004 CHN; Talaat 2008 EGY; Zomer 2015 NED). Roberts 1996 AUS; Ban 2015 CHN and Nicholson 2008 IND were at high risk of attrition bias, as they had attrition rates greater than 10%. The rest of the trials were at unclear risk of attrition bias (Black 1977 USA; Bartlett 1984 USA; Kotch 1989 USA; Ladegaard 1999 DEN; Pickering 2013 KEN). It was also unclear in Kotch 1989 USA why one of the DCCs withdrew from the trial.

Community-based trials

Inclusion of all randomized participants in the analysis was unclear, as it was reported at different levels of analysis (cluster, household, child), except for Nicholson 2008 IND, which reported 18% average attrition bias for all the subgroups in both arms. Luby 2003b PAK and Null 2018 KEN were at unclear risk of attrition bias because the trial authors did not provide sufficient information to make a judgement. Attrition bias was unclear in Galiani 2016 PER and Briceno 2017 TZA because data were collected from a sample, and different participants were surveyed at baseline and follow-up.

Hospital-based trial (high-risk group)

Attrition bias was unclear in Huang 2007 USA.

Selective reporting

Child DCCs or school-based trials

We note that in Butz 1990 USA the intervention arm received combined interventions, including a hand-washing educational programme, use of vinyl gloves, use of disposable diaper-changing pads, and use of alcohol-based hand rinse by the day-care provider. The trials did not measure the relative contribution of each component of intervention, so we adjudged reporting bias in this trial to be unclear. The trial authors, however, reported that to reduce reporting bias, all day-care providers were aware that the intervention programme was being tested in certain homes.

Community-based trials

We did not detect any evidence of selective outcome reporting in any of the included studies.

Other potential sources of bias

Child DCCs or school-based trials

Eight trials reported adequate comparability between the intervention and control groups for diarrhoea incidence and sociodemographic characteristics at baseline (including mean total enrolment; percentage of dropouts; sex, age, and race composition of children enrolled; diapering; and toilet facilities) (Black 1977 USA; Bartlett 1984 USA; Butz 1990 USA; Ladegaard 1999 DEN; Bowen 2004 CHN; Talaat 2008 EGY; Pickering 2013 KEN; Ban 2015 CHN). Investigators in Bowen 2004 CHN were forced to over- or undersample certain regions to obtain more 'control' schools after the original control schools were sent intervention packs by mistake and thus were excluded. This trial reported small differences in household sanitation and piped water at baseline but no differences between schools in the number of students, class size, or hygiene infrastructure. Comparability at baseline was unclear in the two other trials (Kotch 1989 USA; Roberts 1996 AUS), while it was considered inadequate in two trials. Kotch 2003 USA reported baseline differences in total number of children and boys in favour of the intervention, which they believed may have influenced the outcome measure. Zomer 2015 NED acknowledged baseline imbalance in crude incidence of diarrhoeal episodes per child-year of 3.0 for intervention versus 5.1 for the control, but they applied statistical adjustments for this baseline characteristic. All trials reported collecting data at the same time for both the intervention and control groups.

Community-based trials

Eleven trials reported baseline similarity of diarrhoea morbidity and socioeconomic characteristics (including population and household size, socioeconomic status, hand washing and sanitary facilities, and sources of water supply) between the intervention and control groups (Han 1985 MMR; Stanton 1985 BGD; Luby 2003a PAK; Luby 2003b PAK; Luby 2006 PAK; Langford 2007 NPL; Nicholson 2008 IND; Hartinger 2011 PER; Hashi 2017 ETH; Luby 2018 BGD; Null 2018 KEN). There were some differences at baseline in Haggerty 1988 COD (controls had diarrhoea episodes of longer duration than the intervention group), therefore the study was assessed to be at a high risk of other bias. Briceno 2017 TZA and Langford 2007 NPL were also assessed to be at high risk of other bias because of possible cross contamination between the study sites. All the trials reported collecting data at the same period for intervention and control groups.

Hospital-based trial (High-risk group)

All 148 randomized participants (Huang 2007 USA) were followed for the trial's one-year duration. Participants were similar at the start of the trial in terms of age, sex, ethnicity, hand-washing episodes per day, CD4 count, HIV load, and prophylaxis for opportunistic infections. The results were presented as a continuous outcome only (mean and SD of number of diarrhoea episodes in each arm over the year). This should be viewed with caution, as it is likely that the distribution of diarrhoea episodes may be highly skewed (the mean of 1.24 and SD of 0.9 episodes in the intervention arm imply a non-normal distribution of diarrhoea episodes). If so, the mean may not be the most appropriate measure of the 'average number' of episodes per participant. The trial reported collecting data at the same period for intervention and control groups.

Effects of interventions

See: **Summary of findings 1** Summary of findings table 1; **Summary of findings 2** Summary of findings table 2; **Summary of findings 3** Summary of findings table 3

We have presented the results as reported by each trial in Table 4 (behavioural change), Table 5, Table 6, Table 7 (incidence of diarrhoea), Table 8, and Table 9. For trials with cluster-adjusted results and trials that were individually randomized, we summarized the data in forest plots. For trials where this was not possible, we summarized the data in tables in the Data and analyses section.

1. Child DCCs or schools

Primary outcomes

1.1. Incidence of diarrhoea

Overall, hand-washing promotion reduced diarrhoea episodes by about one-third (incident rate ratio (IRR) 0.69, 95% CI 0.59 to 0.81; 11 trials, 50,044 children (Bowen 2004 CHN and Ban 2015 CHN not included in analysis); Analysis 1.1). Most data were from high-income countries (IRR 0.70, 95% CI 0.58 to 0.85; 9 trials, 4664 participants; high-certainty evidence; Analysis 1.1), with only two trials from LMICs (IRR 0.66, 95% CI 0.43 to 0.99; 2 trials, 45,380 participants; low-certainty evidence; Analysis 1.1).

All trials showed a benefit for the intervention, except for Bowen 2004 CHN, which showed no difference between each arm and for which it was not possible to calculate a rate ratio (the median episodes of diarrhoea were 0 per 100 student-weeks in the control group, standard intervention group, and expanded intervention) (Table 5). Roberts 1996 AUS showed greater risk reduction than other trials (IRR 0.50, 95% CI 0.36 to 0.69; 1 trial, 558 participants), possibly due to a more specific technique of hand washing used (an approximate 'count to 10' to wash and 'count to 10' to rinse). Ban 2015 CHN (not included in the analysis) reported an odds ratio of 0.37 (95% CI 0.22 to 0.60) person-months of illness due to diarrhoea.

All participants were monitored at least every two weeks to collect data on diarrhoea episodes, while Ban 2015 CHN reported quarterly home visits. This monitoring itself may have helped to improve compliance with hand washing. Only Carabin 1997 CAN attempted to investigate this effect by assessing rates in both groups compared to the pre-intervention period. They found that monitoring alone appeared to reduce the incidence of diarrhoea (IRR 0.73, 95% CI 0.54 to 0.97; Table 5) and that the intervention effect did not appear to have any benefits beyond this monitoring effect when adjusted for age and gender (IRR 0.77, 95% CI 0.51 to 1.18; Table 5) or when adjusted for age, gender, season, and baseline incidence rate in each cluster (IRR 1.10, 95% CI 0.81 to 1.50; Table 5). However, monitoring was particularly frequent (daily) in this trial. In Bowen 2004 CHN among first-grade students in schools in China, monitoring may have been less intensive, as in-class monitoring was carried out one day a week by teachers; reasons for absenteeism were noted when recorded. As the trial was school-based, no illness information was collected during weekends or school holidays. This design reduced the teachers' burden of data collection, but it may also have reduced the ability of the trial to

detect differences in the incidence of diarrhoea between each trial arm.

Black 1977 USA and Pickering 2013 KEN focused only on a hand-washing intervention, and found no significant difference in the effect estimate (IRR 0.69, 95% CI 0.43 to 1.09; 2 trials, 1045 participants). Nine trials involved multiple hygiene interventions (Bartlett 1984 USA; Kotch 1989 USA; Butz 1990 USA; Roberts 1996 AUS; Carabin 1997 CAN; Ladegaard 1999 DEN; Kotch 2003 USA; Talaat 2008 EGY; Zomer 2015 NED) (IRR 0.69, 95% CI 0.57 to 0.84; 9 trials, 48,999 participants; Analysis 1.2). The implication of this aspect of hand-hygiene interventions should be further investigated, as we had too few trials in each category to make a statement.

Three trials attempted blinding of outcome assessors (Bartlett 1984 USA; Kotch 1989 USA; Roberts 1996 AUS), with the benefit of hand washing seeming to be less in a 26% reduction (rate ratio 0.74, 95% CI 0.56 to 0.98; 3 trials, 1303 participants; Analysis 1.3), than in the trials that did not blind outcome assessors (Black 1977 USA; Butz 1990 USA; Carabin 1997 CAN; Ladegaard 1999 DEN; Kotch 2003 USA; Talaat 2008 EGY; Pickering 2013 KEN; Zomer 2015 NED), a 33% reduction (IRR 0.67, 95% CI 0.56 to 0.80; 8 trials, 48,741 participants; Analysis 1.3).

Secondary outcomes

1.2. Behavioural changes

Four trials reported measures of behavioural change (Kotch 1989 USA; Roberts 1996 AUS; Pickering 2013 KEN; Zomer 2015 NED). As described in Table 8, Kotch 1989 USA reported that hand-washing behaviour based on 'event sampling scores' improved in the intervention classrooms compared with control classrooms. Roberts 1996 AUS reported that the intervention improved compliance with infection-control procedures from 53% at baseline to more than 80% at end-line. Pickering 2013 KEN reported a statistically significant rate of hand washing with soap at intervention schools: 37% against 2% for the control for all toilet events (prevalence ratio 17.2, 95% CI 4.4 to 67.5), while the mean proportion (intervention 0.70, control 0.01) of students hand washing with soap before lunch events was equally significantly different between schools (prevalence ratio 143.0, 95% CI 38.9 to 525.6) (data not pooled; 3 trials, 1845 participants; Table 8). Zomer 2015 NED reported a significant increase in hand-hygiene compliance for caregivers in intervention DCCs than in control groups, but this did not seem to have any effect on the incidence of diarrhoea episodes. Kotch 1989 USA; Roberts 1996 AUS; Pickering 2013 KEN also reported changes in knowledge, attitude, and beliefs about hand washing (Table 8).

1.3. Diarrhoea-related deaths, all-cause under-five mortality

None of the included trials reported diarrhoea-related deaths or all-cause under-five mortality.

1.4 Cost effectiveness

None of the included trials reported cost-effectiveness data. However, Kotch 2003 USA reported that the cost of purchasing and installing one unit of the hand-washing and diapering equipment was high, at USD 10,385 (USD 7500 for the equipment and the rest for installation) per classroom.

2. Community-based trials

Primary outcomes

2.1. Incidence of diarrhoea

Overall, community-based hand-washing promotion reduced the incidence of diarrhoea by around one-quarter (IRR 0.71, 95% CI 0.62 to 0.81; 9 trials, 15,950 participants; moderate-certainty evidence; Analysis 2.1). All the trials were conducted in eight LMICs (six from Asia, one from South America, and one from Africa) and one low-income country (LIC) (Ethiopia).

Three trials assessed the effect of intervention on the incidence rate of different categories of diarrhoea (Han 1985 MMR; Luby 2003a PAK; Luby 2003b PAK). Han 1985 MMR reported on dysentery, and Luby 2003a PAK and Luby 2003b PAK reported on persistent diarrhoea. None of the results were statistically significant (Table 6). Some trials reported the results by participant age (Han 1985 MMR; Stanton 1985 BGD; Luby 2003a PAK; Luby 2003b PAK; Nicholson 2008 IND), with no discernible trend of which age group intervention had greater diarrhoeal reductions (Table 6). Han 1985 MMR and Stanton 1985 BGD reported greater diarrhoeal reduction in children under two years of age, while Luby 2003a PAK and Luby 2003b PAK reported greater reductions in older children. For Nicholson 2008 IND, the effect for the different age groups (five years old, less than five years old, and 6 to 15 years old) were similar.

Five trials promoted hand washing only (Han 1985 MMR; Luby 2003a PAK; Luby 2003b PAK; Langford 2007 NPL; Nicholson 2008 IND), while four trials promoted multiple hygiene interventions (Stanton 1985 BGD; Haggerty 1988 COD; Hartinger 2011 PER; Hashi 2017 ETH). The reduction in the risk of diarrhoea was greater in the trials that promoted hand washing only (IRR 0.63, 95% CI 0.52 to 0.78; 5 trials, 10,888 participants) than in the trials that promoted multiple hygiene interventions (IRR 0.77, 95% CI 0.65 to 0.90; 4 trials, 5062 participants; Analysis 2.3). This aspect of hand-hygiene interventions should be interpreted with caution, as we had too few trials in each category to make a strong statement. Luby 2006 PAK; Galiani 2016 PER; Kapoor 2016 IND; Briceno 2017 TZA; Luby 2018 BGD; and Null 2018 KEN also promoted multiple hygiene interventions, but we did not include them in the analyses because of the way the data were presented. For instance, the outcome measure for Luby 2003b PAK was mean incidence, while Luby 2006 PAK (which was a follow-up to Luby 2003b PAK) reported a different outcome measure of longitudinal prevalence. It is therefore difficult to make meaningful direct comparisons. However, Luby 2006 PAK reported that each arm of their intervention significantly reduced diarrhoea, but that simultaneously combining hand-washing promotion and water treatment had no apparent benefits.

Five trials attempted blinding of outcome assessors, with the benefit of hand washing appearing to be lower than in trials which did not blind outcome assessors (IRR 0.76, 95% CI 0.64 to 0.90; 5 trials, 4294 participants) versus (IRR 0.63, 95% CI 0.48 to 0.83; 4 trials, 11,656 participants; Analysis 2.4).

Seven trials provided soap alongside hand-hygiene promotional activities, and the effect seemed to be larger in these trials than in those which did not provide soap (IRR 0.66, 95% CI 0.58 to 0.75; 7 trials, 12,646 participants) versus (IRR 0.84, 95% CI 0.67 to 1.05; 2 trials, 3304 participants; Analysis 2.5). With only a small number of trials, these differences may be due to chance or, even if real, it is

difficult to discern which components (providing soap or focusing on hand washing only) are most effective.

2.1.1 Mean longitudinal prevalence of diarrhoea

Six studies reported the mean longitudinal prevalence of diarrhoea. All of these showed a reduction in the prevalence of diarrhoea favouring the intervention arm, but not all were statistically significant (Analysis 2.6). One study did not report sufficient information about the method of measuring diarrhoea, time period, or study sample size to extract data for a meta-analysis (Kapoor 2016 IND). The study results showed a reduction in the episodes of diarrhoea from 90% to 52% in the intervention group, and from 88.7% to 83.2% in the control group, as well as a post-intervention prevalence of diarrhoea 3.9 times higher in the control group after adjusting for confounding variables. Similarly, Luby 2006 PAK reported a mean prevalence of 4.73 person-weeks with diarrhoea in the soap and hand-washing promotion arm compared to 8.62 person-weeks with diarrhoea in the control arm following the intervention. The other four studies all reported the mean longitudinal prevalence over a one-week period (Galiani 2016 PER; Briceno 2017 TZA; Luby 2018 BGD; Null 2018 KEN). Overall, the meta-analysis showed a reduction in the prevalence of diarrhoea of over four percentage points (4.60% reduction, 95% CI 1.19 to 8.02; 4 studies, 14,577 participants; Analysis 2.2).

Secondary outcomes

2.2. Behavioural changes

Stanton 1985 BGD adjusted for clustering and reported that the intervention group exhibited a greater increase in hygiene practices (IRR 1.48, 95% CI 1.01 to 2.21), although this increase is of borderline statistical significance (P = 0.056; Table 9). Langford 2007 NPL reports that at the end of the intervention, hand washing after cleaning the baby's bottom or before cooking, eating, or feeding the baby had increased in mothers from the intervention areas (McNemar's test, P < 0.01 for all four junctures), while hand-washing practices remained unchanged in the control areas. Nicholson 2008 IND measured hand-washing behaviour between trial groups indirectly by assessing soap consumption (soap wrapper collection) and reported median soap consumption per household per week of 235 g for intervention households compared with 45 g for the controls. Kapoor 2016 IND reported improvements in the hand-washing practices of mothers in the intervention group. (Data not pooled; 4 trials, 3591 participants; trials reporting mean longitudinal prevalence Galiani 2016 PER and Briceno 2017 TZA are not included; Table 9).

2.3. Diarrhoea-related deaths and all-cause under-five mortality

Two trials assessed all-cause mortality as tertiary outcomes in their trials (Luby 2018 BGD; Null 2018 KEN). All-cause mortality was higher in the intervention arm – hand-washing only (5.3%) than in the active control arm (3.9%). All-cause mortality was lower in the combined water sanitation, hand-washing, and nutrition group (2.8%) than in the control arm.

Luby 2018 BGD showed no difference in all-cause mortality between the hand-washing arm and the control arm, respectively (4.5% vs 4.7%). All-cause mortality was lower in the combined nutrition, water, sanitation, and hygiene arm than the control arm (2.9% versus 4.7%).

None of the included trials reported diarrhoea-related deaths.

2.4 Cost effectiveness

None of the included trials reported cost-effectiveness data.

3. Hospital-based trial (high-risk group)

3.1. Episodes of diarrhoea

In Huang 2007 USA, the intensive hand-washing intervention reduced the mean number of episodes of diarrhoea over the one-year trial period (2.92 in control group, 1.24 in intervention group; a reduction of 1.68 episodes, 95% CI −1.93 to −1.43; 148 participants; moderate-certainty evidence; Analysis 3.1).

3.2. Behavioural changes

At the beginning of the trial, there was no difference in daily hand-washing frequency between intervention and control groups (3.4 ± 1.1 in control group; 3.3 ± 0.98 in intervention group; Table 4), but at the end of the trial the intervention group reported hand washing seven times a day compared with four times daily in the control group (P < 0.05; moderate-certainty evidence).

DISCUSSION

In the original review (Ejemot-Nwadiaro 2008), 14 trials met the inclusion criteria. Eight other trials were included in the first review update (Ejemot-Nwadiaro 2015). We have included seven additional trials in this review update, making a total of 29 included trials. Luby 2006 PAK was a follow-up trial to Luby 2003b PAK. This trial involved no primary interventions, but assessed the sustainability of the Luby 2003b PAK hand-hygiene interventions in preventing diarrhoea. The other trials had primary interventions.

Summary of main results

Hand-washing promotion at child day-care facilities or schools prevents around one-third of diarrhoea episodes in high-income countries (high-certainty evidence; Summary of findings 1). It may prevent a similar proportion in LMICs, but only two trials (from urban Egypt and Kenya) have evaluated this (low-certainty evidence).

Hand-washing promotion among communities in LMICs probably prevents around one-quarter of diarrhoea episodes (moderate-certainty evidence; Summary of findings 2). However, six of these eight trials were from Asian settings, with one trial from South America and two trials (one of them (Ethiopia) a LIC) from sub-Saharan Africa. In seven trials, soap was provided free alongside education and behavioural-change interventions. The overall effect size was larger in the trials that provided soap (34%) than in the two trials that did not provide soap (16%). The influence of this on the intervention effect estimate is not well understood. This underscores the need for data on the long-term sustainability of hand-washing promotion to inform research design and policy decisions, especially for LMICs, which tend to have a higher burden of diarrhoea but lack the resources to address it (Ejemot-Nwadiaro 2015; Luby 2018 BGD).

The effect of hand-washing promotion in a hospital-based setting among a high-risk population had a significant reduction in mean episodes of diarrhoea that favoured the intervention group (moderate-certainty evidence; Summary of findings 3). This is from only one trial.

The effect of the intervention on the hand hygiene-related behavioural outcome in all settings showed an increase in the proportion of hand-washing or hand-hygiene compliance at essential junctures (before eating and cooking and after visiting the toilet or cleaning the baby's bottom), favouring the intervention groups (unpooled data, reflecting a range of low- to high-certainty evidence; Summary of findings 1; Summary of findings 2; Summary of findings 3). The effectiveness of each type of hand-washing promotion or a combination of different types was not assessed and is therefore unknown. We found no trials evaluating or reporting the effects of hand-washing interventions on diarrhoea-related deaths or cost effectiveness. The effect of hand-washing interventions on all-cause under-five mortality in community-based trials in LMICs is unclear. One trial reported no difference between the intervention and control arm, while the other reported a higher all-cause mortality in the intervention arm. In both trials, the cumulative incidence was lower in the combined nutrition, water, sanitation, and hygiene arm than control arm. The results suggest that there may be other modifiers of all-cause mortality than hand-washing interventions alone.

Overall completeness and applicability of evidence

We believe we identified all RCTs that met our inclusion criteria. We further categorized the included trials into three distinct settings: child DCCs or schools, community, and hospital. Although there were only a few trials included in each category, evidence favours hand-washing interventions in preventing diarrhoea in all the settings. This suggests that the intervention exhibits population-wide health gains. However, most included trials in the institution category were from childcare settings in high-income countries. We are therefore not confident that this finding can be applied to schools in LMIC settings or alternative institutions. Also, only one hospital-based trial met the inclusion criteria, so evidence from this setting was limited.

Ninety-five per cent of the participants for whom the primary outcome was measured were below five years of age. Talaat 2008 EGY measured the primary outcome in participants with a mean age of eight years but did not stratify the results by age. Nicholson 2008 IND measured the primary outcome in participants of various ages (target children five years of age, children below five years of age, children between 6 and 15 years of age, and adults) and stratified results by these independent subgroups and reported effect sizes, with no significant trend observed. Although children under five years of age are most at risk of diarrhoeal infection, understanding the effect of this intervention in participants above five years of age and in adults would provide better comparative evidence.

All included trials were relatively small and had short follow-up durations, including intensive monitoring, and they demonstrated significant reductions in the risk of diarrhoea after hand-hygiene intervention. However, in one relatively large trial (Bowen 2004 CHN), and in three with longer follow-up (Luby 2006 PAK; Luby 2018 BGD; Null 2018 KEN), there were no apparent benefits, as no significant differences between the incidence or longitudinal prevalence of diarrhoea were found. We are therefore unclear if the reductions in incidence of diarrhoea would be maintained if these trials had been larger and conducted over a longer period.

The effect size was lower in child DCCs and school-based trials that attempted blinding outcome assessors than in trials that did not (26% versus 33% reduction in the incidence of diarrhoea, respectively). The same trend was observed for community-based trials, with a 24% reduction for five trials that attempted blinding of outcome assessors and a 37% reduction for four trials that did not attempt blinding. This suggests a possible introduction of bias in trials that did not attempt blinding. However, there were too few trials in each category to draw strong conclusions.

Community-based trials that focused only on hand-washing interventions showed a greater effect size than those that involved multiple hygiene interventions (37% versus 23%), whereas in child DCC and school-based trials there was no detectable difference in effect size. Although there were few trials in both settings to suggest direction in intervention designs, Luby 2018 BGD opined that a single intervention may provide greater health benefits than multiple interventions that are likely to reach fewer people. However, a lack of evidence on which to make design decisions or support this assertion remains a challenge, particularly in light of scarce and competing health resources.

Quality of the evidence

We assessed the certainty of the evidence using the GRADE approach (GRADEpro 2014). In general, the evidence that hand washing promotion reduces the incidence of diarrhoea in both child DCCs in high-income countries and community settings in LMICs is considered high-certainty (Summary of findings 1; Summary of findings 2). Most trials were at high or unclear risk of detection or reporting bias because there was no description of outcome assessors blinding. However, this made a negligible difference to our findings, as restriction of the analysis to just the blinded trials found a slightly smaller but statistically significant effect size. In addition, the trials' results showed a lot of statistical heterogeneity. However, these inconsistencies did not affect the certainty of evidence in these settings, since all trials favoured the intervention, albeit with varying effect sizes. We are therefore confident in the estimate of effect, and further research is very unlikely to change our confidence in the estimate.

For the trials conducted in LMIC schools, we considered the certainty of evidence to be low due to indirectness, as this limits our confidence in the effect estimate. Talaat 2008 EGY and Pickering 2013 KEN were conducted under experimentally-controlled conditions. Although they showed benefits in favour of the intervention groups, we are unsure if these benefits would be maintained if trials were longer, with minimal provision of hand-washing materials and less intense follow-up.

Certainty of evidence from unpooled data for the behavioural outcomes ranged from low to high in all settings. These should be interpreted with caution, as there were too few trials in each setting and the methods of assessment were too varied to make strong statements. The benefit of adopting an explicit behavioural change model is still unclear; this may influence the maintenance and sustainability of hand-hygiene behaviour, as Whitby 2007 has opined that the strongest determinant of hand-washing behaviour may be its habituation.The certainty of evidence about the other outcomes (diarrhoea-related deaths, all-cause under-five mortality, and cost effectiveness) were not determined due to a paucity of included trials providing data on which to make such judgements. Further research is therefore necessary to provide a basis for assessment of evidence for these factors critical to hand-washing interventions in preventing diarrhoea.

Potential biases in the review process

We did not identify any potential biases in the review process. We only included peer-reviewed and published randomized controlled trials in this review. We also included a trial published in Danish (Ladegaard 1999 DEN). We also searched grey literature and clinical trials registers to identify eligible ongoing trials. One of the settings (hospital-based) had only one trial (Huang 2007 USA) and small number of participants - 148. This limits our interpretation of the effect of the intervention in this setting.

Agreements and disagreements with other studies or reviews

The magnitude of the intervention effect (≃ 30%) in both child DCCs or schools and community settings that we observed in this review did not differ significantly from that of the original review (Ejemot-Nwadiaro 2008), or the first update (Ejemot-Nwadiaro 2015). The effect size, however, remains lower in magnitude than previous reviews of hand-washing interventions, which was 47% (Curtis 2003), and about 44% in the reviews of Fewtrell 2004 and Fewtrell 2005. These differences may be attributable to the choice of effect measure, mixed trial designs, and a single setting. Curtis 2003 used odds ratios, which are known to inflate effects sizes for conditions such as diarrhoea with common event rates in the analyses. In our review, we reported only rate ratios, which Guevara 2004 opines improves clinical interpretation of pooled effect estimates. Fewtrell 2005 presented evidence of publication bias, while Curtis 2003 included case-control and cross-sectional trials as well as prospective interventions. Both reviews considered only hand-hygiene interventions conducted in LMICs. In our review, we included only RCTs and mixed settings (child DCC- or school-, community-, and hospital-based trials conducted in both developing and developed countries). However, they are all in agreement that hand-hygiene interventions are effective for reducing diarrhoeal diseases.

AUTHORS' CONCLUSIONS

Implications for practice

Hand-washing promotion leads to a reduction in diarrhoea episodes by about 30%, both in child DCCs in high-income countries and among communities in LMICs.
We have little evidence about the sustainability of changes in hand-washing behaviour or how best to promote this over a longer period.

Implications for research

The findings of this Cochrane Review show that further research to determine the efficacy of hand-washing intervention in preventing diarrhoea will be unnecessary in child DCCs in high-income countries and in communities in LMICs, although only one of these trials was conducted in Africa. Most of the included studies were of short duration and follow-up. They could therefore be described as high intensity, since trial participants were contacted at least twice weekly during the intervention. There is a need to assess the effect of the intervention in trials of longer duration and follow-up, and to ascertain the sustainability of hand-washing behaviours. This presents an evidence gap and rationale for further research to guide practice and policy directions. This becomes all the more critical in areas of limited competing resources, particularly in LMICs.

More trials conducted in child DCCs or schools in LMICs are needed to enhance our ability to generalize the intervention effects. The need to conduct research with longer follow-ups that uses a structured method of assessing the primary outcome is pertinent, since it has been observed that an arbitrary use of methods may have a significant effect on the precision of estimates (Morgado 2017). Outcome assessors should be blinded to reduce the bias in estimates of effect size. Evidence of the effects of hand washing interventions on diarrhoea incidence in hospital-based settings is still limited, as we found only one trial that met the inclusion criteria. Further research in this area is therefore warranted.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Ban 2015 CHN

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: 84% included Length of follow-up: 12 months Cluster-adjustment method: not adjusted
Participants	Number: 2 kindergartens, with 465 children (intervention: 221 children from 5 classes; control: 244 children from 6 classes) Inclusion criteria: not stated Exclusion criteria: not stated Age: < 5 years
Interventions	Intervention (see Table 1 for detailed description): • Hygiene education (parents or guardian and teachers were instructed in person on proper hand-hygiene techniques and how to use the antibacterial products they had received • Unscheduled parents' meetings, quarterly home visits, phone interviews, and monthly cell phone messages Control: • No intervention
Outcomes	Illness symptoms for • diarrhoea Not used in this review: • Fever • Cough and expectoration • Runny nose and nasal congestion • Abdominal pain • Compliance with the intervention
Notes	Location: Xianto city, Hubei province, China Duration: October 2010 to September 2011
Risk of bias	

Ban 2015 CHN *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "We did not adopt the use of individual randomized design. Randomization was based on the kindergarten, 221 children from one kindergarten as the intervention group, and 245 children from the other kindergarten as the control group."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Neither the participants nor the investigators were blinded. However, keeping these limitations in mind, we attempted to reduce ascertainment bias through the use of Daily Record Calendars for both the homes and kindergartens while maintaining close contact with the parents, or guardians, and teachers from both groups."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Neither the participants nor the investigators were blinded. However, keeping these limitations in mind we attempted to reduce ascertainment bias through the use of Daily Record Calendars for both the homes and kindergartens while maintaining close contact with the parents, or guardians, and teachers from both groups."
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition more than 10%. 466 enrolled, 72 not analysed (16% attrition)
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Bartlett 1984 USA

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 12 months Cluster-adjustment method: not adjusted
Participants	Number: 26 day-care centres, with 374 children (196 intervention and 178 control) Inclusion criteria: not stated Exclusion criteria: not stated Age: < 3 years
Interventions	Intervention (see Table 1 for detailed description): • Large group meetings (directors and caregivers) • Provision of posters and handouts depicting the procedures taught Control:

Bartlett 1984 USA *(Continued)*

- Visited to review surveillance procedures, but no instruction in disease prevention or management provided.

Outcomes	Diarrhoea rates
Notes	Location: Maricopa County, Arizona, USA Duration: October 1981 to September 1984

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "22 day care centres were randomly selected from the 108 day care centres in Maricopa county licensed to care for infants and toddlers. The 22 trial day care centres were divided into three strata, based on surveillance rates of infant-toddler diarrhoea in the preceding 12 months. Half of the centres in each stratum were then randomly assigned to intervention groups."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Student nurses were blinded in regard to intervention or control status of the day-care centres
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Black 1977 USA

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 6 months Cluster-adjustment method: not adjusted
Participants	Number: 4 day-care centres, with 116 children Inclusion criteria: not stated Exclusion criteria: not stated

Black 1977 USA *(Continued)*

	Age: < 3 years
Interventions	Intervention (see Table 1 for detailed description): • Large-group education Control: • No intervention
Outcomes	• Diarrhoea rates Not used in this review: • Estimate of load of diarrhoea causative agent
Notes	Location: suburban Atlanta, Georgia, USA Duration: June 1976 to April 1977

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Bowen 2004 CHN

Study characteristics

Methods	Cluster-RCT Inclusion of all participants in the analysis: 93% (3962/4256) agreed to participate Length of follow-up: 2003/2004 school year

Bowen 2004 CHN *(Continued)*

	Cluster-adjustment method: adjusted
Participants	Number: 87 schools (57 intervention; 30 control); with 3962 children (2670 intervention; 1292 control) Inclusion criteria: public primary schools; at least 20 students in first-grade year in 2003 to 2004; no overnight boarders; at least 1 running water tap for every 30 first grade students Exclusion criteria: no compulsory hand washing or provision of hand-cleaning products before school lunch; no commercial hand-washing promotion programmes at school during previous 5 years
Interventions	Intervention (see Table 1 for detailed description): • Expanded programme: as standard programme plus continuous supply of Safeguard soap for school sinks; 1 student from each class was recruited to assist peers with hand-washing techniques and reminded them of key hand-washing opportunities; teachers were asked to encourage this student weekly but were not instructed to enforce hand-washing behaviour • Standard programme: Proctor and Gamble's Safeguard promotion programme delivered in Chinese schools since 1999; teachers deliver programme to first-grade children during single 40-minute classroom session; also single 2-hour training session for each first-grade teacher delivered by Proctor and Gamble staff; teacher's pack contains guidebook outlining hand washing, basic information on infectious disease transmission, 5 posters describing hand-washing procedure, videotape, and 5 wall charts for classroom hygiene competition; student take-home pack includes hygiene board game, parent booklet on hand washing, and 50 g bar Safeguard soap Control: • All 3 groups received government hygiene educational programme consisting of a brief statement manual about hand washing after using toilet and before eating
Outcomes	• Diarrhoea rates Not used in this review: • School absences • Rates of other common illnesses
Notes	Location: 3 counties in Fujian province, Southeast China

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Adequate
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	3962 (93%) first grade students from the 4256 first graders attending the enrolled schools agreed to participate and were included in the analysis

Bowen 2004 CHN *(Continued)*

Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Briceno 2017 TZA

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 1 year and 3 months Cluster-adjustment method: adjusted
Participants	Number: 10 districts with 181 wards (44 wards with 88 villages and 1433 children < 5 years assigned to sanitation only treatment, 45 wards with 90 villages and 1452 children < 5 years assigned to hand washing only treatment, 46 wards with 92 villages and 1431 children < 5 years assigned to combined treatment, 46 wards with 92 villages and 1481 children < 5 years assigned to control) Inclusion criteria: largest rural wards Exclusion criteria: not described Age: children < 5
Interventions	Intervention (see Table 2 for detailed description): Intensive social marketing including • Hand-washing promotion events with women on market days, during prenatal clinic visits, and at village meetings • Distribution of promotional materials • Face-to-face interactions • Teaching/helping households build 'tippy' taps • Travelling road shows • Mass media radio campaigns Control: • No intervention

Outcomes	• Diarrhoea
	• Caregiver hand-washing practices
	  * After faecal contact: after defaecating, after toileting, after cleaning child post-toileting
	  * Before handling food: before cutting or preparing food, eating, serving food, or breastfeeding
	• Hand-washing knowledge index
	Not used in this review:
	• Access to an improved latrine
	• Open defaecation
	• Safe disposal of child faeces
	• Open defaecation-free villages
	• Child cleanliness

Briceno 2017 TZA *(Continued)*

- Caregiver hand cleanliness
- Anaemia
- Malnutrition

Notes	Location: rural Tanzania Duration: February 2009 to May 2012 (3 years and 3 months) Data were collected via surveys, with 10 households randomly selected from each village

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The ward-level randomization was stratified by district and population size using Stata."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "It was not possible to blind participants, although they were never told explicitly about the link between the survey and interventions, and any questions on program exposure were included only at the end of the survey."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "To mitigate enumerator bias, survey firms were never provided information on treatment status of participating wards."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data were collected by surveys from 10 randomly-selected households in each village
Selective reporting (reporting bias)	Low risk	None observed
Other bias	High risk	Quote: "These districts were purposively targeted because of operational feasibility for program implementation, taking into account the existence of ongoing MoW and MoHSW projects." Comment: Purposively selecting districts with ongoing related projects may make it difficult to isolate the effects of the intervention. Possible 'contamination'

Butz 1990 USA

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 12 months Cluster-adjustment method: not adjusted
Participants	Number: 24 family day-care centres, with 108 children (58 intervention, 50 control)

Butz 1990 USA *(Continued)*

	Inclusion criteria: not stated Exclusion criteria: unclear Age: 1 month to 7 years
Interventions	Intervention (see Table 1 for detailed description): • Large-group training (in-home instruction to day-care providers) Control: • No intervention
Outcomes	Incidence of infectious disease symptoms (diarrhoea)
Notes	Location: Baltimore, Maryland, USA Duration: 12 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	28 children (114 children were enrolled from the FDCHs but actual number of children used in the analysis is 86).
Selective reporting (reporting bias)	Unclear risk	Did not measure the relative contribution of each component of intervention, but "to reduce reporting bias, all day care providers were aware that the intervention program was being tested in certain homes"
Other bias	Low risk	None observed

Carabin 1997 CAN

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 6 months

Carabin 1997 CAN *(Continued)*

	Cluster-adjustment method: adjusted
Participants	Number: 52 day-care centres, with 1729 children Inclusion criteria: presence of at least 1 sandbox and 1 play area; at least 12 available toddler places Exclusion criteria: not stated Age: 18 months to 3 years
Interventions	Intervention (see Table 1 for detailed description): • Large-group hygiene training (educators) • Handouts Control: • No intervention
Outcomes	Diarrhoea rates
Notes	Location: Quebec, Canada Duration: September 1996 to November 1997

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated block randomized
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	43 children lost to follow-up (5 day-care centres excluded from the analysis)
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Galiani 2016 PER

Study characteristics

Methods	Cluster-RCT

Galiani 2016 PER *(Continued)*

	Inclusion of participants in the analysis: unclear Length of follow-up: 3 years Cluster-adjustment method: adjusted
Participants	Number: 85 districts (intervention: 44; control: 41), 3756 households included in the baseline and end-line survey Inclusion criteria: families that had at least 1 child under 2 years of age Exclusion criteria: not stated Age: children under 5 years
Interventions	Intervention (see Table 2 for detailed description): • A mass media plus a direct consumer contact campaign; • Training of trainers for community-based agents of change, such as teachers, medical professionals, and community leaders • Capacity building and providing educational hand-washing sessions for mothers, caregivers, and children • Hand-washing curricula in selected primary schools Control: • No intervention.
Outcomes	• Exposure to hand-washing promotion • Effects on hand-washing determinants (hand-washing knowledge and beliefs and access to and placement of soap and water) • Hand-washing behavior (self-reported and observed hand washing and hand cleanliness) • Environmental contamination (bacterial prevalence in drinking water) • Child health (prevalence of diarrhoea, ALRI, anaemia, parasites in stools, nutrition, and anthropometric measurements)
Notes	Location: Peru Duration: 2008 - 2011

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	From these provinces, 85 districts (with between 1500 and 100,000 inhabitants) were randomly selected, with 44 randomly assigned to receive the district-level community treatment and the other 41 randomly assigned to serve as the control group
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias)	Unclear risk	Not described

Galiani 2016 PER *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "Our surveys record an overall attrition rate of 20% after 3 years." "To make up for the loss in sample size due to attrition, we included 688 new households in the follow-up survey to replace households that had dropped out."
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Haggerty 1988 COD

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 6 months Cluster-adjustment method: adjusted and unadjusted results given
Participants	Number: 18 sites (intervention: 9; control: 9), with 1954 children (intervention: 977; control: 977) Inclusion criteria: not stated Exclusion criteria: not stated Age: 3 months to 35 months
Interventions	Intervention (see Table 1 for detailed description): • Large-group training Control: • No intervention
Outcomes	Diarrhoeal rates
Notes	Location: Kikwit, Bandundu Province, Zaire (Democratic Republic of Congo) Duration: October 1987 to December 1988

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Unclear risk	Not described

Haggerty 1988 COD *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Observers blind to the diarrhoea histories of families
Incomplete outcome data (attrition bias) All outcomes	Low risk	190 children enrolled in the follow-up were excluded from the analysis due to incomplete data; 1954 children were enrolled in the follow-up trial but 1764 were retained for analysis
Selective reporting (reporting bias)	Low risk	None observed
Other bias	High risk	Reported some baseline differences (control group had diarrhoea episodes of longer duration than the intervention group)

Han 1985 MMR

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 4 months Cluster-adjustment method: not adjusted
Participants	Number: 350 households (intervention: 162 intervention; control: 188) with 494 children (intervention: 236; control: 258) Inclusion criteria: households with 1 or more children between 6 and 59 months; those in which regular follow-up was possible; not allergic to soap; gave informed consent Exclusion criteria: not stated Age: < 5 years
Interventions	Intervention (see Table 1 for detailed description): • Small-group education (households) Control: • No intervention
Outcomes	• Incidence of diarrhoea • Incidence of dysentery
Notes	Location: Nga-Kha ward of Thin-Gun-Kyun township, Rangoon, Burma (now Myanmar) Duration: June to November 1985

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Han 1985 MMR *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "to avoid bias staff were blind to which households were intervention or otherwise"
Incomplete outcome data (attrition bias) All outcomes	Low risk	12 children (7 from intervention, 5 from control households) of the 494 enrolled
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Hartinger 2011 PER

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 12 months Cluster-adjustment method: unclear
Participants	Number: 51 communities, 534 households (intervention: 267; control: 267) with 534 children (intervention: 267; control: 267) Inclusion criteria: • at least 1 child aged 6 to 35 months living in the home • using wood or solid fuel as main energy source for cooking • not being connected to public sewage • tenants planning to stay in their home for the next 12 months Exclusion criteria: • the child had any congenital abnormalities or suffered from a chronic debilitating illness • families that had 2 or more households in different geographical areas with migration within sites that lasted more than 6 months during the year (mainly for migratory agriculture practices) Age: 6 to 35 months
Interventions	Intervention (see Table 1 for detailed description): • Hygiene education with small and large group meetings

Hartinger 2011 PER *(Continued)*

	• 51 community clusters received integrated home-hygiene intervention package Control: • Psychomotor-stimulation package
Outcomes	• Diarrhoeal episodes Not used in this review: • Prevalence of cough and fever • Duration of days spent ill • Average number of days for healthcare seeking • Child growth outcomes (stunting, wasting and underweight)
Notes	Location: San Marcos province, Cajamarca region, Peru Duration of trial: March 2008 to January 2010 (23 months)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomized "...using covariate-based constrained randomisation as proposed by Moulton (2004)". Researchers went to extra lengths to ensure integrity of the randomizations.
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "As a strategy to reduce non-blinding bias, a child psychomotor development intervention was implemented in the control arm as an equivalent to the IHIP in the intervention arm"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...and data collection was done by an independent team of field workers, which was not part of the initial education and re-enforcement of the interventions during the follow-up period". Comment: We consider this an attempt to blinding outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Researchers presented a detailed account of the randomization and follow-up in a PRISMA flow diagram
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Hashi 2017 ETH

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: adequate

Hashi 2017 ETH *(Continued)*

	Length of follow-up: 6 months Cluster-adjustment method: adjusted
Participants	Number: 24 sub-Kebelles districts with 1224 children (12 sub-Kebelles with 612 children < 5 years assigned to the intervention group; 12 sub-Kebelles with 612 children < 5 years assigned to the control group) Inclusion criteria: at least 1 child aged 1 – 59 months living in the home, and not a model health extension household Exclusion criteria: see inclusion criteria above Age: children < 5 years
Interventions	Intervention (see Table 2 for detailed description): • Health education on key water, sanitation and hygiene (WASH) messages • Demonstration of hand washing with soap (how to wet their hands, lather them completely with soap, and rub together for 1 min) • Provision of soap (white bars) • Primary caretakers of children were instructed to keep their water storage container clean and covered, to have a latrine and use properly, and to wash their hands and children's hands ideally with soap after defecation, before meal preparation, and before eating • Provision of other key messages using megaphone at 1 time in each visit • Village meetings mass media radio campaigns Control: • No intervention, treatment as usual
Outcomes	• Longitudinal incidence of diarrhoea Not used in this review: • Bacteriological quality of drinking water
Notes	Location: rural areas of Jigjiga district of Ethiopian-Somali Regional State (ESRS), Eastern Ethiopia Duration: February 1, 2009 to July 30, 2015 (4 years and 5 months)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Sub-Kebelles were then randomly selected from the 56 total sub-Kebelles by using simple randomisation (computer generated numbers)"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Neither the community (both control and intervention group) nor the field workers knew the intervention purpose."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Neither the community (both control and intervention group) nor the field workers knew the intervention purpose."

Hashi 2017 ETH *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Study accounted for all the participants included in the study and attrition was < 10%
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Huang 2007 USA

Study characteristics	
Methods	RCT with individual randomization Inclusion of participants in the analysis: 100% Length of follow-up: 1 year
Participants	Number: intervention: 73; control: 75 Inclusion criteria: people with AIDS at local HIV clinic; HIV-1 infection verified by both ELISA and Western blot; AIDS by CD4 counts and plasma HIV RNA; been on highly active anti-retroviral therapy (HAART) for at least 6 weeks and without diarrhoea for at least 3 months
Interventions	Both groups: 3 dedicated trial nurses educated participants on health problem associated with contaminated hands and provided specific hand-washing instructions at enrolment; hand-washing technique demonstrated by nurses, including wetting hands, lathering completely with soap, rubbing together for at least 15 seconds, and drying hands with towels; all 148 participants then demonstrated adequate hand-washing technique intervention (see Table 1 for detailed description): • Weekly telephone call from nurses to determine number of hand-washing episodes per day, ensure compliance, answer questions, re-educate participants on importance, and go over instructions. Control: • Weekly telephone calls but only to ascertain diarrhoea episodes.
Outcomes	• Incidence of diarrhoea • Hand-washing behaviour Not used in this review: • Microbiological diagnosis of diarrhoea episodes
Notes	Location: USA (location unclear) Duration: 1 year (exact dates unclear)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described

Huang 2007 USA *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants were accounted for
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Kapoor 2016 IND

Study characteristics	
Methods	RCT Inclusion of participants in the analysis: 100% Length of follow-up: 6 months
Participants	Number: 101 mothers with children below 2 years (50 mothers assigned to the intervention group, 51 mothers assigned to the control group) Inclusion criteria: not explicitly stated Exclusion criteria: not explicitly stated Age: children < 2 years
Interventions	Intervention (see Table 2 for detailed description): • Hygiene education using flip books and pamphlets Control: • No intervention
Outcomes	• Episodes of diarrhoea • Hand-washing practices • Behaviour change
Notes	Location: a resettlement colony, northwest of Chandiagrh, India Duration: July to November 2014 (6 months)
Risk of bias	

Kapoor 2016 IND *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "3 strata were randomly allocated to intervention and control group"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants were accounted for and included in the analysis
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Kotch 1989 USA

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 7 months Cluster-adjustment method: adjusted
Participants	Number: 24 day-care centres, with 389 children Inclusion criteria: children < 3 years; present in the day care at least 20 hours per week; absence of chronic illness or medication that would predispose to infection; youngest of potentially eligible children in the same family; consenting English-speaking parents with access to a telephone; intending to remain in day-care centre throughout trial Exclusion criteria: not stated Age: < 3 years
Interventions	Intervention (see Table 1 for detailed description): • Large-group training • Curriculum for caregivers Control: • No intervention

Kotch 1989 USA *(Continued)*

Outcomes	Diarrhoeal rates
Notes	Location: Cumberland County, North Carolina, USA Duration: October 1988 to May 1989

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: " specifically, parental illness reports were blind to the intervention status of their children's DCCs, potential confounders were controlled for and effect modifiers were examined"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	18 children out of the 389 enrolled were lost to follow-up. 1 day-care centre withdrew from the trial
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Unclear risk	Comparability at baseline is unclear

Kotch 2003 USA

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 7 months (November 2002 to May 2003) Cluster-adjustment method: unclear
Participants	Number: 46 child-care centres (intervention: 23; control: 23) with 388 infants and toddlers Inclusion criteria: Child expected to remain in the child-care centre for the duration of trial and < 36 months of age at the end of data collection; at least 1 family member contact could participate in a telephone survey in English Exclusion criteria: not stated Age: Infants and toddlers < 36 months
Interventions	Intervention (see Table 1 for detailed description):

Kotch 2003 USA *(Continued)*

	• Larger training staff of centres were trained using the *Keep it clean* training module Control: • No intervention but received the same equipment at the completion of the trial
Outcomes	• Diarrhoeal rates Not used in this review: • Days child absent from child-care centre per 100 child days • Percentage of days child ill per 100 child-days • Percentage of days caregiver absent from work as a result of illness
Notes	Location: North Carolina, USA Duration: September 2002 to May 2003

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Applied different statistical tests for different nature of variables: Quote: "No control variables are included in these descriptive comparisons".
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Attrition form the intervention and control groups during the course of the trial was comparable"
Selective reporting (reporting bias)	Low risk	None observed
Other bias	High risk	Quote: "Two significant differences between the 2 trial groups were noted. The total number of children and the number of boys were larger in the intervention classrooms. These differences may have reduced the overall effect of the intervention, because number of children per classroom is a risk factor, and boys tend to stay in diapers longer. In addition, control centres were working hard to get their perceived reward (the free equipment that they were promised at the end of the trial). These 3 factors should have reduced the difference in outcomes between the intervention and control groups, suggesting that the significant differences in illnesses and absences that were found favouring the intervention group are all the more impressive"

Ladegaard 1999 DEN

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 4 months Cluster-adjustment method: not adjusted
Participants	Number: 8 day-care centres, with 475 children (intervention: 212; control: 263) Inclusion criteria: not stated Exclusion criteria: not stated Age: < 6 years
Interventions	Intervention (see Table 1 for detailed description): • Small-group practical demonstration Control: • No intervention
Outcomes	Diarrhoeal rates
Notes	Location: Odense, Denmark Duration: 6 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear whether they were divided in 2 groups manually and then randomized or randomized stratified. Quote: "The 8 institutions were allocated based on likeliness and randomized to intervention or control with 4 institutions in each"
Allocation concealment (selection bias)	Unclear risk	Randomization not described in detail
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	One institution had not written down attendance for the children 0 - 2 years. There were 212 children in the intervention group and 263 in the control group but no account of what happened to the children over time
Selective reporting (reporting bias)	Low risk	No evidence of outcomes not presented

Ladegaard 1999 DEN *(Continued)*

Other bias	Low risk	None observed

Langford 2007 NPL

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: adequate (11 of 99 lost) Length of follow-up: 6 months Cluster-adjustment method: unclear
Participants	Number: 88 children (intervention: 45; control: 43) Inclusion criteria: not stated Exclusion criteria: not stated Age: 3 to 12 months old
Interventions	Intervention (see Table 1 for detailed description): • Larger meetings of educational interactive sessions • Posters • Dramas Control: • No intervention
Outcomes	• Impact of intervention on morbidity (diarrhoeal rates) • Impact of intervention on hand-washing practices Not used in this review: • Impact of intervention on growth • Impact of intervention on biochemical markers (subclinical rates of infection) • Associations between biochemical markers and growth variables
Notes	Location: Kathmandu, Nepal Duration: May to November 2007

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Groups were randomly allocated by flipping a coin to intervention or control groups
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Unclear risk	Not described

Langford 2007 NPL *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "To prevent bias in data collection, these field workers were never involved in any aspect of the program to promote hand washing".
Incomplete outcome data (attrition bias) All outcomes	Low risk	11 children from 99 originally recruited were not included in the analysis
Selective reporting (reporting bias)	Low risk	None observed
Other bias	High risk	Quote: "It was not possible to randomly allocate each separate settlement to control/intervention conditions as many sites were situated very close to one another (e.g. separated just by road or stream) such that the intervention message could easily have crossed over into control settlements." Comment: cross-contamination possible

Luby 2003a PAK

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 12 months Cluster-adjustment method: adjusted
Participants	Number: 36 neighbourhoods (intervention: 25; control: 11), with 4691 children (intervention: 3163; control: 1528) Inclusion criteria: household located in the trial area; have at least 2 children < 5 years; intention to reside in the house for the duration of trial Exclusion criteria: not stated Age: < 15 years
Interventions	Intervention (see Table 1 for detailed description): • Large-group training using slide shows, pamphlets, and video tapes Control: • No intervention
Outcomes	Diarrhoeal rates
Notes	Location: low-income squatter settlements, Karachi, Pakistan Duration: April 2002 to April 2003

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Luby 2003a PAK *(Continued)*

Random sequence generation (selection bias)	Low risk	Adequate
Allocation concealment (selection bias)	Low risk	Adequate
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	139 children from the intervention arm and 85 from the control arm of the 4691 children originally enrolled were lost to follow-up
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Luby 2003b PAK

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 9 months Cluster-adjustment method: adjusted
Participants	Number: 18 clusters, with 544 households (intervention: 262; control: 282) Inclusion criteria: households with at least 1 child < 5 years; provided informed consent Exclusion criteria: not stated Age range: < 15 years
Interventions	Intervention (see Table 1 for detailed description): • Large-group training using slide shows, pamphlets, and video tapes. Control: • No receipt of products expected to change risk of diarrhoea but provided them with regular supply of children's books, note books, etc
Outcomes	• Primary diarrhoea rates • Persistent diarrhoea rates
Notes	Location: Multi-ethnic squatter settlements in Central Karachi, Pakistan

Luby 2003b PAK *(Continued)*

	Duration: April 2003 to December 2003

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The 5 trial groups were assigned a random number generated by a computer spreadsheet.
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described (open trial)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described (open trial)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not clearly stated
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Luby 2006 PAK

Study characteristics	
Methods	Cluster-RCT Length of follow-up: 14 months (63 weeks) Cluster-adjustment method: adjusted
Participants	Number: 577 households: hand-washing promotion (195 households), hand-washing promotion plus water treatment (187 households) and control arm (195 households) Inclusion criteria: same used in Luby 2003b PAK Exclusion criteria: same used in Luby 2003b PAK Age: children under 5 years
Interventions	Intervention (see Table 1 for detailed description): • Follow-up of 2003 trial • See Luby 2003b PAK.
Outcomes	• Longitudinal prevalence of diarrhoea • Sustainability of hand washing behaviour

Luby 2006 PAK *(Continued)*

Notes	Location: Karachi, Pakistan Duration: 63 weeks

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Adequate
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	None. Trial is a follow-up to Luby 2003a PAK
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 household was not accounted for in the analysis
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Luby 2018 BGD

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: 100% Length of follow-up: 2 years Cluster-adjustment method: adjusted
Participants	Number: 5551 pregnant women in 720 clusters were randomly allocated to 1 of 7 groups. 1382 women were assigned to the control group; 698 to water; 696 to sanitation; 688 to hand washing; 702 to water, sanitation, and hand washing; 699 to nutrition; and 686 to water, sanitation, hand washing, and nutrition Inclusion criteria: in utero children of enrolled pregnant women (index children) were eligible for inclusion if their mother was planning to live in the study village for the next 2 years, regardless of where she gave birth. Only 1 pregnant woman was enrolled per compound, but if she gave birth to twins, both children were enrolled. Children who were younger than 3 years at enrolment and lived in the compound were included in diarrhoea measurements Exclusion criteria: not described

Luby 2018 BGD *(Continued)*

	Age: unclear

Interventions	Hand-washing interventions, sanitation intervention, drinking water interventions, nutrition intervention
	
	hand-washing intervention (see Table 2 for detailed description):
	
	• Hygiene education;
	• Households with index children received:
	  • 2 hand-washing stations
	  • 1 with a 40 L water reservoir placed near the latrine
	  • 16 L reservoir for the kitchen
	
	Each hand-washing station included:
	
	• a basin to collect rinse water
	• a soapy water bottle
	• promoters also provided a regular supply of detergent sachets for making soapy water
	
	Control:
	
	• No intervention

Outcomes	• Caregiver reported diarrhoea in the past 7 days Not used in this review: • Length-for-age Z score
Notes	Location: Bangladesh Duration: February 2009 to May 2012 (3 years and 3 months) Data were collected via surveys, with 10 households randomly selected from each village

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Clusters were randomly allocated to treatment using a random number generator"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Interventions included distinct visible components so neither participants nor data collectors were masked to intervention assignment, although the data collection and intervention teams were different individuals. Two investigators (BFA and JBC) did independent, masked statistical analyses from raw data sets to generate final estimates, with the true group assignment variable replaced with a re-randomised uninformative assignment variable. The results were unmasked after all analyses were replicated"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Interventions included distinct visible components so neither participants nor data collectors were masked to intervention assignment, although the data collection and intervention teams were different individuals. Two investigators (BFA and JBC) did independent, masked statistical analyses from raw data sets to generate final estimates, with the true group assignment variable replaced with a re-randomised uninformative assignment variable. The results were unmasked after all analyses were replicated".

Luby 2018 BGD *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "331 (6%) women were lost to follow-up"
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Nicholson 2008 IND

Study characteristics	
Methods	Cluster-RCT Length of follow-up: 41 weeks Cluster-adjustment method: not adjusted
Participants	35 matched pairs communities (70 in total for intervention and control); 30 households from each of the communities. Target children: 2052 (intervention: 1026; control: 1026); < 5 years of age: 2469 (intervention: 1190; control: 1279); 6 - 15 years: 3519 (Intervention: 1784; control: 1735); adults: 3685 (intervention: 1892; control: 1793) All participants: 11,725 (intervention: 5892; control: 5833) Inclusion criteria: informed consent Exclusion criteria: not stated Age: 5 years (target); < 5 years, children 6 - 15 years, and adults (non-targets)
Interventions	Intervention (see Table 1 for detailed description): • Large-group education training of the connection between germs and illnesses; establishment of a 'Good Mum's' club Control: • No intervention
Outcomes	• Episodes of diarrhoea • Soap consumption as indirect measure of hand-washing behaviour Not used in this review: • Episodes of Acute Respiratory Infections (ARI) • School absences among the target children • Episodes of other illness (eye infection, ear aches, etc) except diarrhoea and ARI
Notes	Location: West and South Mumbai, India Duration: 22 October, 2007 to 2 August 2008 (41 weeks)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Nicholson 2008 IND *(Continued)*

Random sequence generation (selection bias)	Low risk	Repeated coin-tossing
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "It was impossible to 'blind' either the participants or those responsible for data collection." Comment: None (open trial)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "It was impossible to 'blind' either the participants or those responsible for data collection." Comment: None (open trial)
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up in both arms and for all the subgroups were more than 10% (average attrition in all groups 18%)
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Null 2018 KEN

Study characteristics	
Methods	Cluster-RCT Length of follow-up: 2 years Cluster-adjustment method: adjusted
Participants	Number: 702 village clusters with 158 clusters assigned to the active control arm; 80 clusters assigned to the passive control arm; 77 clusters assigned to the water arm; 77 assigned to the sanitation arm; 77 clusters assigned to the hand-washing arm; 76 clusters assigned to the combined water, sanitation, and hand-washing arm; 78 clusters assigned to the nutrition arm; and 79 clusters assigned to the combined water, sanitation, hand-washing, and nutrition arm Inclusion criteria: villages were eligible for selection into the study if they were rural, most of the population relied on communal water sources and had unimproved sanitation facilities, and there were no other ongoing water, sanitation, hand-washing, or nutrition programmes. Within selected villages, women were eligible to participate if they reported that they were in their second or third trimester of pregnancy, planned to continue to live at their current residence for the next 2 years, and could speak Kiswahili, Luhya, or English well enough to respond to an interviewer-administered survey Exclusion criteria: see inclusion criteria above Age: 0-2 years
Interventions	Hand-washing interventions, sanitation intervention, drinking water interventions, nutrition intervention Hand-washing intervention (see Table 2 for detailed description): • Hygiene education

Null 2018 KEN *(Continued)*

	• Study compounds were given:
	  • 2 permanent, water-frugal hand-washing stations intended to be installed near the food preparation area and the latrine
	  • quarterly supply of bar soap
	
	Control:
	
	• No intervention

Outcomes	Outcomes were assessed in the children of the enrolled pregnant women (index children), including twins. Primary outcomes: • Caregiver-reported diarrhoea in the past 7 days (based on all data from year 1 and year 2) • All-cause mortality Not used in this review: • Length-for-age Z score at year 2 in index children Secondary and tertiary outcomes: • Length-for-age Z score at year 1 • Weight-for-length Z score • Weight-for-age Z score • Head circumference-for-age Z score at year 1 and year 2 • Prevalence of stunting (length-for-age Z score < −2), severe stunting (length-for-age Z score < −3) • wasting (weight-for-length Z score < −2), and underweight (weight-for-age Z score < −2)
Notes	Location: rural villages in Bungoma, Kakamega, and Vihiga counties in Kenya's western region Duration: November 2012 to May 2014

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Clusters were randomly allocated to treatment using a random number generator with reproducible seed"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "investigators remained blinded to treatment assignments. Blinding of participants was not possible. Participants were informed of their treatment assignment after baseline data collection and might have known the treatment assignment of nearby villages. The health promoters and staff who delivered the interventions were not involved in data collection, but the data collection team could have inferred treatment status if they saw intervention materials in study communities."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "investigators remained blinded to treatment assignments. Blinding of participants was not possible. Participants were informed of their treatment assignment after baseline data collection and might have known the treatment assignment of nearby villages. The health promoters and staff who delivered the interventions were not involved in data collection, but the data collection team could have inferred treatment status if they saw intervention materials in study communities."

Null 2018 KEN *(Continued)*

		Comment: 2 biostatisticians, blinded to treatment assignment, independently replicated the analyses following the prespecified analysis plan with minor updates
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear. Not explicitly reported
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Pickering 2013 KEN

Study characteristics	
Methods	Cluster-RCT Length of follow-up: 2 months (8 weeks) Cluster-adjustment method: adjusted
Participants	Number: 6 schools (2 hand sanitizer; 2 hand washing with soap; 2 control). Student numbers: hand washing with soap: 460; hand sanitizer: 435; control: 469 Inclusion criteria: schools with > 100 student population; written consent from parents/teachers Exclusion criteria: schools that shared latrines with community members Age: 5- to 10-year-old-schoolchildren
Interventions	Intervention (see Table 1 for detailed description): • Large-group education training on germ theory and hygiene; installation of soap dispensers. Control: • No intervention.
Outcomes	• Diarrhoeal rates • Students' hand-washing rates Not used in this review: • Respiratory infection rates • Student and teacher perception of waterless hand sanitizer versus hand washing with soap
Notes	Location: Kibera, Nairobi, Kenya Duration: 2 months

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "schools randomly assigned to receive"

Pickering 2013 KEN *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open trial. Quote: "Treatment assignment was not blinded".
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open trial. Quote: "Treatment assignment was not blinded".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not clearly stated, as the trial authors only reported total observations
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Roberts 1996 AUS

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 9 months Cluster-adjustment method: adjusted
Participants	Number: 23 day-care centres, with 558 children Inclusion criteria: Day-care centres licensed in the Australian Capital Territory; children < 3 years as at January 1996; attendance for at least 3 days per week; have no underlying chronic illness that predisposes to infection Exclusion criteria: not stated Age: < 3 years
Interventions	Intervention (see Table 1 for detailed description): • Large group training • Booklets/newsletters • Songs about hand washing for children Control: • No intervention
Outcomes	• Diarrhoeal rate • Knowledge, attitude, and practice of hand washing
Notes	Location: Australian Capital Territory, Australia

Roberts 1996 AUS *(Continued)*

Duration: March to November 1996

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used a random-number table generated using EpiInfo
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	None described
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The observer was not informed of the content of the training sessions or the intervention status of the centres". "The staff members in the centres were aware the observer was watching hygiene practices but not which specific practices were being recorded".
Incomplete outcome data (attrition bias) All outcomes	High risk	22% (123 children) from 558 children enrolled were lost to follow-up
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Unclear risk	Baseline comparable data not given

Stanton 1985 BGD

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: unclear Length of follow-up: 6 months Cluster-adjustment method: adjusted
Participants	Number: 1923 families (intervention: 937; control: 986) with 1350 children (intervention: 675; control: 675) Inclusion criteria: not stated Exclusion criteria: not stated Age: < 6 years
Interventions	Intervention (see Table 1 for detailed description): • Small-group discussion (only women or children) • Larger demonstrations (mixed audience) • Posters, games, pictorial stories, and 'flexiflans' for illustrations

Stanton 1985 BGD *(Continued)*

	Control: • No intervention
Outcomes	• Diarrhoeal rates • Change in knowledge, attitude, and practice of water sanitation behaviours
Notes	Location: Urban Dhaka, Bangladesh Duration: October 1984 to May 1985

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified randomized allocation
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Equal number of emigrant and immigrant included in effectiveness analyses but not in behavioral assessment
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	None observed

Talaat 2008 EGY

Study characteristics

Methods	Cluster-RCT Inclusion of participants in the analysis: adequate Length of follow-up: 12 weeks (February to May 2008) Cluster-adjustment method: adjusted
Participants	Number: 60 government elementary schools (intervention: 30; control: 30), with 44,451 children (intervention: 20,882; control: 23,569) Inclusion criteria: not stated Exclusion criteria: not stated

Talaat 2008 EGY *(Continued)*

	Age: children in elementary schools (median age 8 years)
Interventions	Intervention (see Table 1 for detailed description): • Larger-group meetings (mixed audience nurses and teachers) • Grade-specific student booklets • Posters, fliers, games, songs about hand washing • Other fun activities that promoted hand washing School's contribution: • Selecting a weekly hand hygiene champion, launching school contest for drawing, songs, and dramas that promote hygiene Control: • No intervention
Outcomes	• Diarrhoeal rate Not used in this review: • Rates of absenteeism caused by influenza-like illness (ILI) • Rates of absenteeism caused by conjunctivitis • Rates of absenteeism caused by laboratory-confirmed influenza
Notes	Location: Cairo, Eygpt Duration: February to May 2008 (12 weeks)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	60 elementary schools were randomly selected by using a computer-generated random-number table
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Accounted for number enrolled for the trial in the analysis
Selective reporting (reporting bias)	Low risk	None observed
Other bias	Low risk	Quote: "No significant differences were found for the 2 groups in median (8 years), sex distribution (51% male) or the median number of students per school (635 [interquartile range 394-978])"

Zomer 2015 NED

Study characteristics	
Methods	Cluster-RCT Inclusion of participants in the analysis: adequate Length of follow-up: November 2011 to March 2012 Cluster-adjustment method: adjusted
Participants	Number: 71 day-care centres (DCC) (intervention: 36; control: 35) with 545 children (278 from 34 intervention DCCs and 267 from 35 control DCCs) Inclusion criteria: children attended the DCC at least 2 days a week; aged between 6 months and 3 - 5 years; intended to attend the DCC throughout the trial period; parents consented; Dutch-speaking and had access to e-mail or regular post Exclusion criteria: child had chronic illness; child was on medication that predisposed him/her to infection and sibling is taking part in the trial (1 per child per family participant) Age: children between 6 months and 60 months
Interventions	Intervention (see Table 1 for detailed description): • Hand-hygiene products provided free of charge • Training on Dutch Hand Hygiene guidelines with booklet on its content distributed • Training sessions aimed at goal setting and formulating specific hand-hygiene improvement activities • Provision of posters and stickers to children and caregivers as reminders and cue to action Control: • No intervention (continued their usual hand hygiene practice)
Outcomes	• Incidence of gastrointestinal infections (incidence of diarrhoea specifically) • Caregivers hand-hygiene compliance Not used in this review: • incidence of respiratory infections.
Notes	Location: Rotterdam-Rijnmond, Gouda, and Leiden regions of Netherlands Duration: September 2011 to April 2012 (7 months)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Stratified randomized allocation
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described

Zomer 2015 NED *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	553 children included in the trial; 545 included in the analysis
Selective reporting (reporting bias)	Low risk	None observed
Other bias	High risk	Quote: "...the crude incidence of diarrhoeal episodes differed between intervention and control DCCs at baseline..." Comment: There were some differences in baseline characteristics between intervention and control groups.

[a]See Table 1; Table 2; and Table 3 for a detailed description of the interventions.

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

Study	Reason for exclusion
Ahmed 1993	Observational trial examining risk factors for diarrhoeal infections
Aiello 2008	Combined both randomized and quasi-experimental trials in the analysis. Outcome measure was on general GIT illnesses including diarrhoea
Alam 1989	Main intervention was provision of water supply through hand pumps
Andrade 2017	Quasi-RCT and Incidence of diarrhoea was not assessed
Arnold 2009	Cross-sectional cohort intervention trial (non-randomized study)
Arnold 2013	Description of planned intervention trial design and rationale
Azor-Martinez 2014	Acute gastroenteritis (AGE) outcome assessed, not specific to diarrhoea
Barros 1999	Observational trial examining risk factors for diarrhoeal infections
Benjamin-Chung 2017	Hand-washing promotion was part of a group of interventions administered. No handwashing-only arm
Bieri 2013	Hand washing not an intervention and diarrhoea not an outcome
Biran 2009	Hand washing an outcome not an intervention
Biran 2014	Diarrhoea not an outcome, assessed emotional drivers of behaviour for improving hand-washing behaviours
Boubacar Maïnassara 2014	Mixed hygiene interventions not specific to hand washing
Bowen 2012	Diarrhoea not an outcome, assessed child growth and development

Study	Reason for exclusion
Bowen 2013	Did not assess diarrhoeal outcomes but assessed hand-washing behaviours – 1 of our secondary outcome measures
Burns 2018	Diarrhoea not an outcome
Burton 2011	Measures effect on hand contamination not diarrhoeal rates
Caruso 2014	Diarrhoea not an outcome; assessed the effect of latrine cleaning and hand washing with soap intervention on school absenteeism
Chard 2018	Diarrhoea not an outcome
Chard 2019	Hand-washing promotion was part of a group of interventions administered including drinking water filters. No handwashing-only arm
Clasen 2014a	Hand-washing promotion not an intervention
Clasen 2014b	Hand-washing promotion not specific intervention but latrine use/coverage
Clemens 1987	Observational trial examining risk factors for diarrhoeal infections
Contzen 2015	Non-randomized trial. Diarrhoea incidence not assessed
Correa 2012	Trial did not promote handwashing but alcohol-based hand rubs as complement to handwashing; control continued existing handwashing practices
Curtis 2001	No concurrent control
Doebbeling 1992	Outcome measure (incidence of nosocomial infection) not specific to diarrhoea episodes but to incidence of gastrointestinal infections in general
Dreibelbis 2014	Mixed hygiene intervention, not specific to hand washing
Dreibelbis 2016	Not an RCT and Incidence of diarrhoea was not assessed
Duijster 2017	Not an RCT and Incidence of diarrhoea was not assessed
Dyer 2000	Intervention was instant hand sanitizer
Ecrumen 2018	Incidence of diarrhoea not assessed
Ecrumen 2019	Incidence of diarrhoea not assessed
Enebeli 2017	Not an RCT
Erismann 2017	Incidence of diarrhoea not assessed
Fan 2011	Non-randomized study
Freeman 2014	Mixed water, sanitation and hygiene intervention, not specific to hand washing
Greene 2012	Measured exposure to faecal pathogen (risk of *Escherichia coli*). Hand contamination of *E. coli*
Greenland 2016	Incidence of diarrhoea was not assessed. The trial assessed use of zinc and ORS to treat diarrhoea, and reported incidence of diarrhoea in children that were treated with zinc

Study	Reason for exclusion
Guinan 2002	Observational study
Hammond 2000	Intervention did not involve hand washing
Hovi 2017	Incidence of diarrhoea not assessed. Trial reports the effect of the intervention on weekly prevalence of reported symptoms of gastrointestinal infection in general
Hübner 2010	Hand washing not an intervention (but measured the effectiveness of hand disinfection with alcoholic rubs)
Huda 2012	Assessed observed hand-washing hygiene behaviours
Jinadu 2007	Diarrhoea episodes not assessed, but rather hygiene behavioural change.
Johansen 2015	Outcome measure not directly on diarrhoea but on infectious illness and school absenteeism. Paper describes the design of the RCT
Kamm 2016	Incidence of diarrhoea was not assessed
Kang 2017	Incidence of diarrhoea not assessed
Khan 1982	Case-control study
Larson 2003	No relevant outcome measures. Assessed colony-forming units of bacteria
Larson 2004	Outcome measure not specific to incidence of diarrhoea
Lee 1991	Controlled before-and-after study
Luby 2001b	Observational trial
Luby 2004	Non-randomized trial
Luby 2007	Diarrhoea episodes not assessed. Measured hand contamination
Luby 2008	Hand washing not an intervention but use of flocculant-disinfectant for treating drinking water
Luby 2010	Diarrhoea episodes not assessed. Measured hand contamination
Manjang 2018	Incidence of diarhoea not assessed. Study reports baseline characteristics only
Master 1997	Outcome measure not specific on diarrhoeal episodes
Morton 2004	Outcome measure not specific on diarrhoeal episodes
Najnin 2017	None of the arms received hand-washing promotion only
Naluonde 2018	Incidence of diarrhoea not assessed
Oncu 2018	Incidence of diarrhoea not assessed
Oughton 2009	Diarrhoea episodes not assessed but removal of *Clostridium difficile*
Overgaard 2016	Incidence of diarrhoea not assessed. Study reports incidence of episodes of school absence ascribed to diarrhoea per school year

Study	Reason for exclusion
Patel 2012	Non-randomized trial
Peterson 1998	Observational trial examining risk factors for diarrhoeal infections
Pinfold 1996	No comparable baseline information on diarrhoeal episodes provided
Priest 2014	Diarrhoea episodes not the outcome, but illness absence including general GIT infection
Rosen 2009	Diarrhoea episodes not assessed. Tested effect of hand-washing intervention on psychosocial measures
Saboori 2013	Diarrhoea episodes not assessed. Assessed hand-washing episodes and *E. coli* hand contamination
Savolainen-Kopra 2012	Outcome measure not specific to diarrhoeal morbidity but to incidence of GIT infection
Shafique 2013	Hand sanitizer not hand washing the intervention. Mean duration of diarrhoea and not diarrhoea episodes the main outcome measure
Shahid 1996	No comparable baseline information provided
Sinharoy 2017	Hand washing was part of a group of interventions administered to the 2 intervention arms in the trial
Sircar 1987	No comparable baseline information on diarrhoea episodes provided
Slayton 2013	Hand towels the main intervention, not hand washing
Vally 2019	Mixed water, sanitation and hygiene intervention, not specific to hand washing
Vindigni 2011	Combined both randomized and quasi-experimental trials in the analysis. Measured hand washing adherence
White 2003	Outcome measure not specific to diarrhoeal morbidity
Wilson 1991	Controlled before-and-after study
Zhang 2013	Diarrhoea not the direct outcome; Proxy data of 'stomach pain' was reported

GIT: gastro-intestinal tract

Characteristics of studies awaiting classification *[ordered by study ID]*

Denbaek 2018

Methods	3-armed cluster-randomized controlled trial using school-based multicomponent interventions to improve hand washing among schoolchildren
Participants	Schoolchildren in Danish schools; 2 intervention arms involving 14 schools each and 15 control schools
Interventions	A curriculum component addressing knowledge and skills, daily hand washing before lunch, extra cleaning of school toilets during the school day
Outcomes	Infectious illness days, infectious illness episodes, and illness-related absenteeism

Denbaek 2018 *(Continued)*

Notes

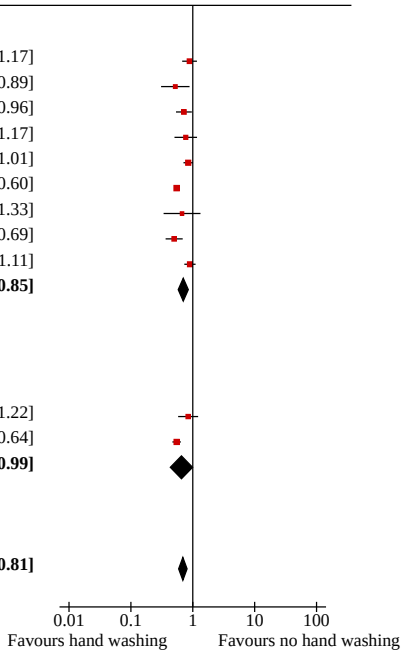
DATA AND ANALYSES

Comparison 1. Hand washing intervention at child care centres and schools versus no intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Incidence of diarrhoea; subgrouped by country income strata	11	50044	Rate Ratio (IV, Random, 95% CI)	0.69 [0.59, 0.81]
1.1.1 High-income countries	9	4664	Rate Ratio (IV, Random, 95% CI)	0.70 [0.58, 0.85]
1.1.2 Low- or middle-income countries	2	45380	Rate Ratio (IV, Random, 95% CI)	0.66 [0.43, 0.99]
1.2 Incidence of diarrhoea; subgrouped by co-interventions	11		Rate Ratio (IV, Random, 95% CI)	Subtotals only
1.2.1 Focused: hand washing only	2	1045	Rate Ratio (IV, Random, 95% CI)	0.69 [0.43, 1.09]
1.2.2 Multiple hygiene interventions	9	48999	Rate Ratio (IV, Random, 95% CI)	0.69 [0.57, 0.84]
1.3 Incidence of diarrhoea; subgrouped by blinding	11		Rate Ratio (IV, Random, 95% CI)	Subtotals only
1.3.1 Blinding of outcome assessors	3	1303	Rate Ratio (IV, Random, 95% CI)	0.74 [0.56, 0.98]
1.3.2 No blinding of outcome assessors	8	48741	Rate Ratio (IV, Random, 95% CI)	0.67 [0.56, 0.80]

Analysis 1.1. Comparison 1: Hand washing intervention at child care centres and schools versus no intervention, Outcome 1: Incidence of diarrhoea; subgrouped by country income strata

Study or Subgroup	log[Rate Ratio]	SE	Handwashing Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
1.1.1 High-income countries						
Bartlett 1984 USA	-0.12	0.14	196	178	9.7%	0.89 [0.67 , 1.17]
Black 1977 USA	-0.65	0.27	62	54	5.4%	0.52 [0.31 , 0.89]
Butz 1990 USA	-0.33	0.15	58	50	9.3%	0.72 [0.54 , 0.96]
Carabin 1997 CAN (1)	-0.2613	0.214	865	864	7.0%	0.77 [0.51 , 1.17]
Kotch 1989 USA (2)	-0.17	0.09	185	186	11.8%	0.84 [0.71 , 1.01]
Kotch 2003 USA (3)	-0.601	0.05	194	194	13.1%	0.55 [0.50 , 0.60]
Ladegaard 1999 DEN	-0.4	0.35	212	263	3.8%	0.67 [0.34 , 1.33]
Roberts 1996 AUS	-0.6931	0.1622	299	259	8.8%	0.50 [0.36 , 0.69]
Zomer 2015 NED	-0.1054	0.1068	278	267	11.1%	0.90 [0.73 , 1.11]
Subtotal (95% CI)			**2349**	**2315**	**80.0%**	**0.70 [0.58 , 0.85]**
Heterogeneity: Tau² = 0.06; Chi² = 38.54, df = 8 (P < 0.00001); I² = 79%						
Test for overall effect: Z = 3.70 (P = 0.0002)						
1.1.2 Low- or middle-income countries						
Pickering 2013 KEN	-0.1729	0.1897	460	469	7.8%	0.84 [0.58 , 1.22]
Talaat 2008 EGY	-0.601	0.08	20882	23569	12.2%	0.55 [0.47 , 0.64]
Subtotal (95% CI)			**21342**	**24038**	**20.0%**	**0.66 [0.43 , 0.99]**
Heterogeneity: Tau² = 0.07; Chi² = 4.32, df = 1 (P = 0.04); I² = 77%						
Test for overall effect: Z = 2.00 (P = 0.05)						
Total (95% CI)			**23691**	**26353**	**100.0%**	**0.69 [0.59 , 0.81]**
Heterogeneity: Tau² = 0.05; Chi² = 44.69, df = 10 (P < 0.00001); I² = 78%						
Test for overall effect: Z = 4.62 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.08, df = 1 (P = 0.77), I² = 0%						

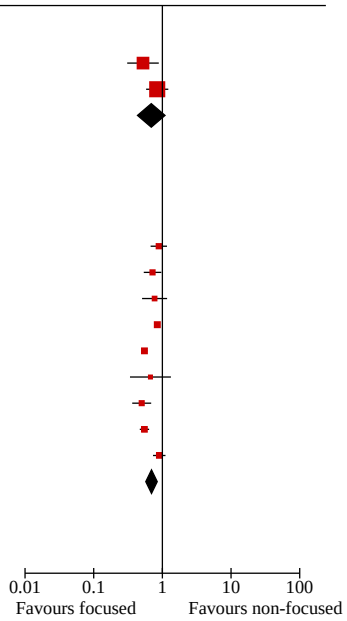


Footnotes

(1) Carabin 1997 CAN: The exact number of children per study arm was not provided. We simply divided the total by two
(2) Kotch 1989 USA: The exact number of children per study arm was not provided. We simply divided the total by two
(3) Kotch 2003 USA: The exact number of children per study arm was not provided. We simply divided the total by two

Analysis 1.2. Comparison 1: Hand washing intervention at child care centres and schools versus no intervention, Outcome 2: Incidence of diarrhoea; subgrouped by co-interventions

Study or Subgroup	log[Rate Ratio]	SE	Handwashing Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
1.2.1 Focused: hand washing only						
Black 1977 USA	-0.65	0.27	62	54	41.9%	0.52 [0.31 , 0.89]
Pickering 2013 KEN	-0.1729	0.1897	460	469	58.1%	0.84 [0.58 , 1.22]
Subtotal (95% CI)			**522**	**523**	**100.0%**	**0.69 [0.43 , 1.09]**
Heterogeneity: Tau² = 0.06; Chi² = 2.09, df = 1 (P = 0.15); I² = 52%						
Test for overall effect: Z = 1.58 (P = 0.11)						
1.2.2 Multiple hygiene interventions						
Bartlett 1984 USA (1)	-0.12	0.14	196	178	11.2%	0.89 [0.67 , 1.17]
Butz 1990 USA	-0.33	0.15	58	50	10.8%	0.72 [0.54 , 0.96]
Carabin 1997 CAN (2)	-0.2613	0.214	865	864	8.6%	0.77 [0.51 , 1.17]
Kotch 1989 USA (3)	-0.17	0.01	185	186	14.5%	0.84 [0.83 , 0.86]
Kotch 2003 USA (4)	-0.601	0.05	194	194	14.0%	0.55 [0.50 , 0.60]
Ladegaard 1999 DEN	-0.4	0.35	212	263	5.1%	0.67 [0.34 , 1.33]
Roberts 1996 AUS	-0.6931	0.1622	299	259	10.4%	0.50 [0.36 , 0.69]
Talaat 2008 EGY	-0.601	0.08	20882	23569	13.2%	0.55 [0.47 , 0.64]
Zomer 2015 NED	-0.1054	0.1068	278	267	12.4%	0.90 [0.73 , 1.11]
Subtotal (95% CI)			**23169**	**25830**	**100.0%**	**0.69 [0.57 , 0.84]**
Heterogeneity: Tau² = 0.07; Chi² = 109.60, df = 8 (P < 0.00001); I² = 93%						
Test for overall effect: Z = 3.72 (P = 0.0002)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.97), I² = 0%						

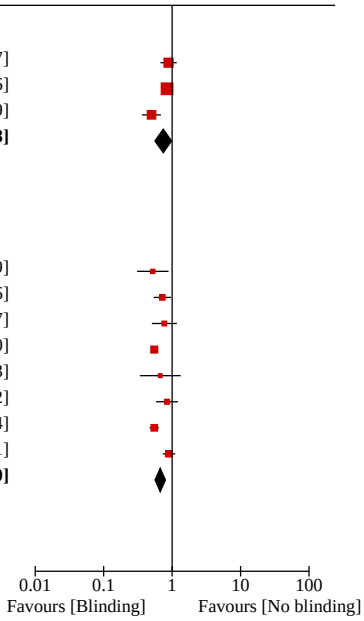


Footnotes

(1) Bartlett 1984 USA: The exact number of children per study arm was not provided. We simply divided the total by two.
(2) Carabin 1997 CAN: The exact number of children per study arm was not provided. We simply divided the total by two.
(3) Kotch 1989 USA: The exact number of children per study arm was not provided. We simply divided the total by two.
(4) Kotch 2003 USA: The exact number of children per study arm was not provided. We simply divided the total by two.

Analysis 1.3. Comparison 1: Hand washing intervention at child care centres and schools versus no intervention, Outcome 3: Incidence of diarrhoea; subgrouped by blinding

Study or Subgroup	log[Rate Ratio]	SE	Handwashing Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
1.3.1 Blinding of outcome assessors						
Bartlett 1984 USA	-0.12	0.14	196	178	30.2%	0.89 [0.67 , 1.17]
Kotch 1989 USA (1)	-0.17	0.01	185	186	42.4%	0.84 [0.83 , 0.86]
Roberts 1996 AUS	-0.6931	0.1622	299	259	27.4%	0.50 [0.36 , 0.69]
Subtotal (95% CI)			**680**	**623**	**100.0%**	**0.74 [0.56 , 0.98]**
Heterogeneity: Tau² = 0.05; Chi² = 10.50, df = 2 (P = 0.005); I² = 81%						
Test for overall effect: Z = 2.09 (P = 0.04)						
1.3.2 No blinding of outcome assessors						
Black 1977 USA	-0.65	0.27	62	54	7.1%	0.52 [0.31 , 0.89]
Butz 1990 USA	-0.33	0.15	58	50	13.2%	0.72 [0.54 , 0.96]
Carabin 1997 CAN (2)	-0.2613	0.214	865	864	9.5%	0.77 [0.51 , 1.17]
Kotch 2003 USA (3)	-0.601	0.05	194	194	20.0%	0.55 [0.50 , 0.60]
Ladegaard 1999 DEN	-0.4	0.35	212	263	4.9%	0.67 [0.34 , 1.33]
Pickering 2013 KEN	-0.1729	0.1897	460	469	10.8%	0.84 [0.58 , 1.22]
Talaat 2008 EGY	-0.601	0.08	20882	23569	18.2%	0.55 [0.47 , 0.64]
Zomer 2015 NED	-0.1054	0.1068	278	267	16.3%	0.90 [0.73 , 1.11]
Subtotal (95% CI)			**23011**	**25730**	**100.0%**	**0.67 [0.56 , 0.80]**
Heterogeneity: Tau² = 0.04; Chi² = 25.22, df = 7 (P = 0.0007); I² = 72%						
Test for overall effect: Z = 4.54 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.36, df = 1 (P = 0.55), I² = 0%						



Footnotes

(1) Kotch 1989 USA: The exact number of chidlren per study arm was not provided. We simply divided the total by two.
(2) Carabin 1997 CAN: The exact number of chidlren per study arm was not provided. We simply divided the total by two.
(3) Kotch 2003 USA: The exact number of chidlren per study arm was not provided. We simply divided the total by two.

Comparison 2. Hand washing intervention in the community versus no intervention

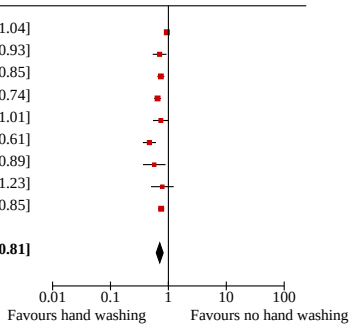
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Incidence of diarrhoea: rate ratios	9	15950	Incidence rate ratio (IV, Random, 95% CI)	0.71 [0.62, 0.81]
2.2 Mean longitudinal prevalence (pooled)	4	14577	Mean Difference (IV, Random, 95% CI)	-4.60 [-8.02, -1.19]
2.3 Incidence of diarrhoea; subgrouped by co-interventions	9	15950	Rate Ratio (IV, Random, 95% CI)	0.71 [0.62, 0.81]
2.3.1 Focused: hand washing only	5	10888	Rate Ratio (IV, Random, 95% CI)	0.63 [0.52, 0.78]
2.3.2 Multiple hand hygiene interventions	4	5062	Rate Ratio (IV, Random, 95% CI)	0.77 [0.65, 0.90]
2.4 Incidence of diarrhoea; subgrouped by blinding	9		Rate Ratio (IV, Random, 95% CI)	Subtotals only
2.4.1 Blinding of outcome assessors	5	4294	Rate Ratio (IV, Random, 95% CI)	0.76 [0.64, 0.90]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4.2 No blinding of outcome assessors	4	11656	Rate Ratio (IV, Random, 95% CI)	0.63 [0.48, 0.83]
2.5 Incidence of diarrhoea; subgrouped by provision of soap	9		Rate Ratio (IV, Random, 95% CI)	Subtotals only
2.5.1 Soap provided	7	12646	Rate Ratio (IV, Random, 95% CI)	0.66 [0.58, 0.75]
2.5.2 No soap provided	2	3304	Rate Ratio (IV, Random, 95% CI)	0.84 [0.67, 1.05]
2.6 Mean longitudinal prevalence	6		Other data	No numeric data

Analysis 2.1. Comparison 2: Hand washing intervention in the community versus no intervention, Outcome 1: Incidence of diarrhoea: rate ratios

Study or Subgroup	log[Incidence rate ratio]	SE	Intervention Total	Control Total	Weight	Incidence rate ratio IV, Random, 95% CI
Haggerty 1988 COD (1)	-0.061799999999999994	0.051399999999999994	977	977	15.3%	0.94 [0.85 , 1.04]
Han 1985 MMR	-0.35	0.14	236	258	10.0%	0.70 [0.54 , 0.93]
Hartinger 2011 PER	-0.3	0.07	267	267	14.3%	0.74 [0.65 , 0.85]
Hashi 2017 ETH	-0.4308	0.067	612	612	14.4%	0.65 [0.57 , 0.74]
Langford 2007 NPL	-0.3	0.16	45	43	8.9%	0.74 [0.54 , 1.01]
Luby 2003a PAK	-0.755	0.1332	3163	1528	10.4%	0.47 [0.36 , 0.61]
Luby 2003b PAK	-0.5621	0.2293	1711	1852	6.0%	0.57 [0.36 , 0.89]
Nicholson 2008 IND	-0.24	0.23	1026	1026	6.0%	0.79 [0.50 , 1.23]
Stanton 1985 BGD (2)	-0.2876	0.061500000000000006	675	675	14.8%	0.75 [0.66 , 0.85]
Total (95% CI)			**8712**	**7238**	**100.0%**	**0.71 [0.62 , 0.81]**

Heterogeneity: Tau² = 0.03; Chi² = 37.67, df = 8 (P < 0.00001); I² = 79%
Test for overall effect: Z = 4.92 (P < 0.00001)
Test for subgroup differences: Not applicable

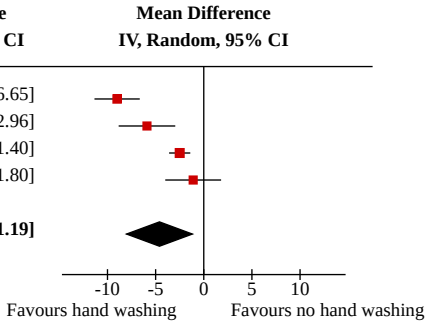


Footnotes
(1) Haggerty 1988 COD: The exact number of children per study arm was not provided. We simply divided the total by two.
(2) Stanton 1985 BDG: The exact number of children per study arm was not provided. We simply divided the total by two.

Analysis 2.2. Comparison 2: Hand washing intervention in the community versus no intervention, Outcome 2: Mean longitudinal prevalence (pooled)

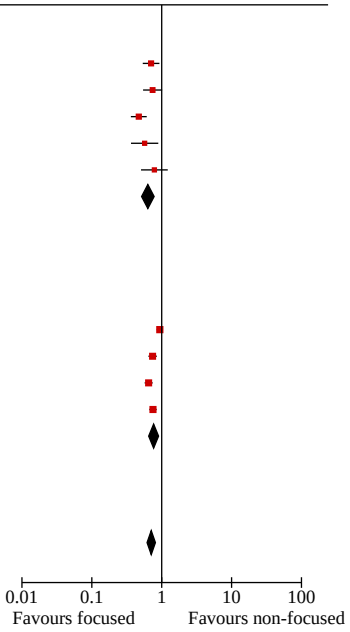
Study or Subgroup	MD	SE	Experimental Total	Control Total	Weight	Mean Difference IV, Random, 95% CI
Briceno 2017 TZA	-9	1.2	1452	1481	25.1%	-9.00 [-11.35 , -6.65]
Galiani 2016 PER	-5.9	1.5	1788	1788	23.5%	-5.90 [-8.84 , -2.96]
Luby 2018 BGD	-2.5	0.5612	1795	3517	27.7%	-2.50 [-3.60 , -1.40]
Null 2018 KEN	-1.1	1.4796	1352	1404	23.6%	-1.10 [-4.00 , 1.80]
Total (95% CI)			**6387**	**8190**	**100.0%**	**-4.60 [-8.02 , -1.19]**

Heterogeneity: Tau² = 10.64; Chi² = 29.29, df = 3 (P < 0.00001); I² = 90%
Test for overall effect: Z = 2.64 (P = 0.008)
Test for subgroup differences: Not applicable



Analysis 2.3. Comparison 2: Hand washing intervention in the community versus no intervention, Outcome 3: Incidence of diarrhoea; subgrouped by co-interventions

Study or Subgroup	log[Rate Ratio]	SE	Intervention Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
2.3.1 Focused: hand washing only						
Han 1985 MMR	-0.35	0.14	236	258	10.0%	0.70 [0.54 , 0.93]
Langford 2007 NPL	-0.3	0.16	45	43	8.9%	0.74 [0.54 , 1.01]
Luby 2003a PAK	-0.755	0.1332	3163	1528	10.4%	0.47 [0.36 , 0.61]
Luby 2003b PAK	-0.5621	0.2293	1711	1852	6.0%	0.57 [0.36 , 0.89]
Nicholson 2008 IND	-0.2411	0.2246	1026	1026	6.1%	0.79 [0.51 , 1.22]
Subtotal (95% CI)			**6181**	**4707**	**41.4%**	**0.63 [0.52 , 0.78]**
Heterogeneity: Tau² = 0.03; Chi² = 7.64, df = 4 (P = 0.11); I² = 48%						
Test for overall effect: Z = 4.34 (P < 0.0001)						
2.3.2 Multiple hand hygiene interventions						
Haggerty 1988 COD (1)	-0.0618	0.0514	977	977	15.3%	0.94 [0.85 , 1.04]
Hartinger 2011 PER	-0.3	0.07	267	267	14.2%	0.74 [0.65 , 0.85]
Hashi 2017 ETH	-0.4308	0.067	612	612	14.4%	0.65 [0.57 , 0.74]
Stanton 1985 BGD (2)	-0.2876	0.0615	675	675	14.7%	0.75 [0.66 , 0.85]
Subtotal (95% CI)			**2531**	**2531**	**58.6%**	**0.77 [0.65 , 0.90]**
Heterogeneity: Tau² = 0.02; Chi² = 21.46, df = 3 (P < 0.0001); I² = 86%						
Test for overall effect: Z = 3.22 (P = 0.001)						
Total (95% CI)			**8712**	**7238**	**100.0%**	**0.71 [0.62 , 0.81]**
Heterogeneity: Tau² = 0.03; Chi² = 37.67, df = 8 (P < 0.00001); I² = 79%						
Test for overall effect: Z = 4.93 (P < 0.00001)						
Test for subgroup differences: Chi² = 2.01, df = 1 (P = 0.16), I² = 50.4%						

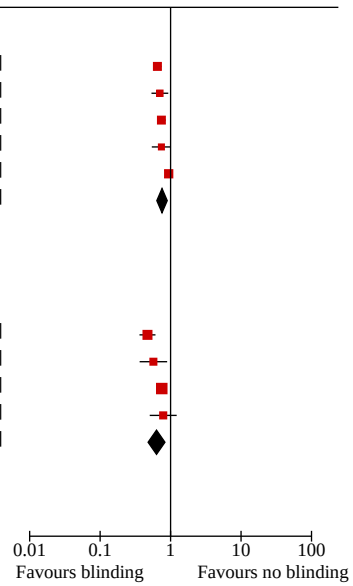


Footnotes

(1) Haggerty 1988 COD: The exact number of children per study arm was not provided. We simply divided the total by two.
(2) Stanton 1985 BGD: The exact number of children per study arm was not provided. We simply divided the total by two.

Analysis 2.4. Comparison 2: Hand washing intervention in the community versus no intervention, Outcome 4: Incidence of diarrhoea; subgrouped by blinding

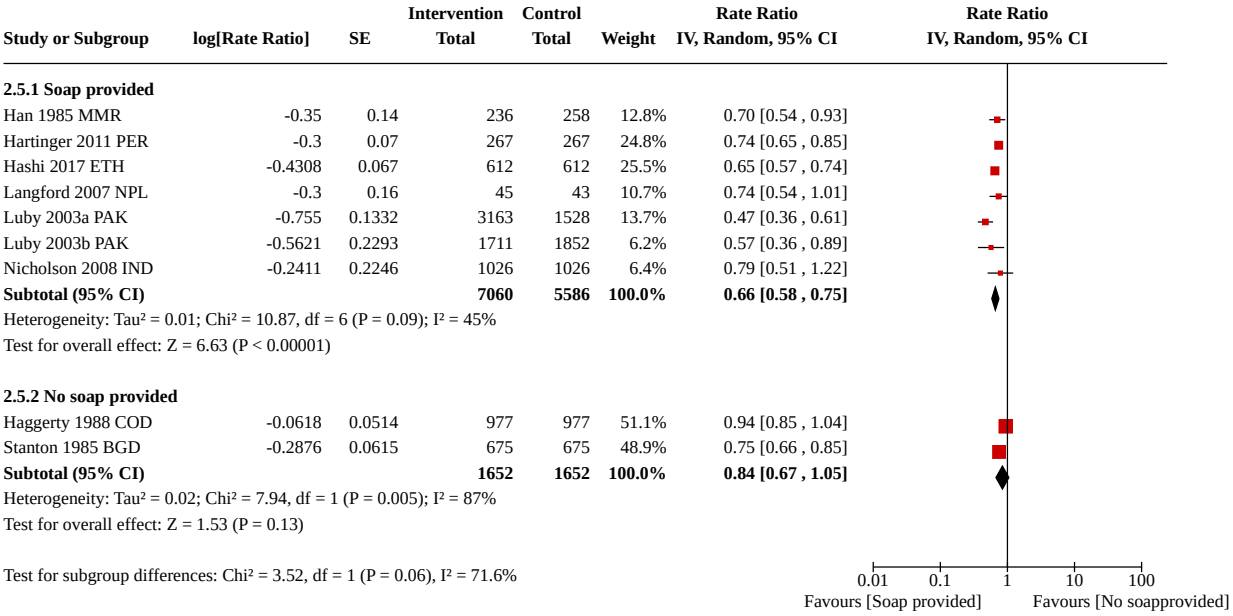
Study or Subgroup	log[Rate Ratio]	SE	Intervention Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
2.4.1 Blinding of outcome assessors						
Hashi 2017 ETH	-0.4308	0.067	612	612	23.1%	0.65 [0.57 , 0.74]
Han 1985 MMR	-0.35	0.14	236	258	15.7%	0.70 [0.54 , 0.93]
Hartinger 2011 PER	-0.3	0.07	267	267	22.8%	0.74 [0.65 , 0.85]
Langford 2007 NPL	-0.3	0.16	45	43	14.0%	0.74 [0.54 , 1.01]
Haggerty 1988 COD (1)	-0.0618	0.0514	977	977	24.5%	0.94 [0.85 , 1.04]
Subtotal (95% CI)			**2137**	**2157**	**100.0%**	**0.76 [0.64 , 0.90]**
Heterogeneity: Tau² = 0.03; Chi² = 21.60, df = 4 (P = 0.0002); I² = 81%						
Test for overall effect: Z = 3.23 (P = 0.001)						
2.4.2 No blinding of outcome assessors						
Luby 2003a PAK	-0.755	0.1332	3163	1528	27.8%	0.47 [0.36 , 0.61]
Luby 2003b PAK	-0.5621	0.2293	1711	1852	18.6%	0.57 [0.36 , 0.89]
Stanton 1985 BGD (1)	-0.2876	0.0615	675	675	34.6%	0.75 [0.66 , 0.85]
Nicholson 2008 IND	-0.2411	0.2246	1026	1026	19.0%	0.79 [0.51 , 1.22]
Subtotal (95% CI)			**6575**	**5081**	**100.0%**	**0.63 [0.48 , 0.83]**
Heterogeneity: Tau² = 0.05; Chi² = 11.18, df = 3 (P = 0.01); I² = 73%						
Test for overall effect: Z = 3.28 (P = 0.001)						
Test for subgroup differences: Chi² = 1.19, df = 1 (P = 0.27), I² = 16.1%						



Footnotes

(1) The exact number of children per study arm was not provided. We simply divided the total by two.

Analysis 2.5. Comparison 2: Hand washing intervention in the community versus no intervention, Outcome 5: Incidence of diarrhoea; subgrouped by provision of soap



Analysis 2.6. Comparison 2: Hand washing intervention in the community versus no intervention, Outcome 6: Mean longitudinal prevalence

Mean longitudinal prevalence

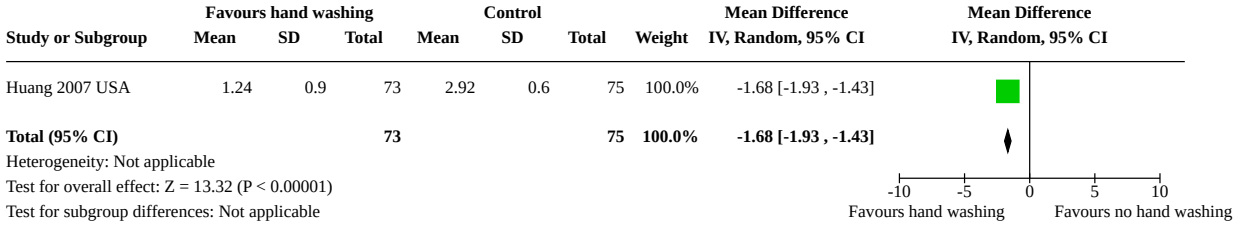
Study	Mean longitudinal prevalence of diarrhoea for all children under observation (Hand washing promotion)	Control	Standard error	Adjusted prevalence difference (study Author reported)	Time period of measurement	How the measurement was made
Briceno 2017 TZA	-0.004 (-0.4%)	0.086 (8.6%)	0.012	-	Diarrhoeal symptoms in the past 7 days	Caregiver-reported diarrhoea
Galiani 2016 PER	0.001 (0.1%)	0.060 (6%)	0.015	-	Diarrhoeal symptoms in the past 7 days	Caregiver-reported diarrhoea
Kapoor 2016 IND	38%	5.5%	-	"After controlling the confounding variables the prevalence of diarrhoea was 3.9 times higher in control group as compared to intervention group (adjusted odds ratio)"	"End line survey in both groups was carried after 3 months to record mothers' behaviour and number of episodes of diarrhoea among children." There were also five visits where the episodes of diarrhoea where recorded	Caregiver-reported
Luby 2006 PAK	4.73%	8.62%	1.232	-	7 days (weekly longitudinal prevalence of diarrhoea)	Person-weeks with diarrhoea/Person-weeks of observation
Luby 2018 BGD	3.5%	5.7%	0.561	Adjusted prevalence difference (95% CI) -2.5 (-3.6 to -1.3)	Diarrhoeal symptoms in the past 7 days	Caregiver-reported diarrhoea

				Prevalence ratio (95%CI) 0.60(0.45 to 0.80)		
Null 2018 KEN	26.1%	27.1%	1.479	Adjusted prevalence difference (95% CI) -1.1 (-4.0 to -1.8) Prevalence ratio (95%CI) 0.98 (0.87 to 1.09)	Diarrhoeal symptoms in the past 7 days	Caregiver-reported diarrhoea

Comparison 3. Hand washing intervention in hospital setting versus no intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Episodes of diarrhoea	1	148	Mean Difference (IV, Random, 95% CI)	-1.68 [-1.93, -1.43]

Analysis 3.1. Comparison 3: Hand washing intervention in hospital setting versus no intervention, Outcome 1: Episodes of diarrhoea



ADDITIONAL TABLES

Table 1. Description of hand-washing interventions at child day-care centres and schools

Trial	Promotional activity	Classification[a]	Message content	Hand- washing method	Hand- washing style[b]	Material provision	Water availability
Ban 2015 CHN	Parents or guardians and teachers in the intervention group were instructed, in person, on: 1. proper hand-hygiene techniques 2. how to use all of the antibacterial products which were distributed 3. Hard surfaces in kindergartens were to be cleaned or disinfected every day using antiseptic-germicide or bleach 4. hard surfaces in homes were to be cleaned or disinfected at least twice every week. Items such as children's toys, house furnishings, frequently-touched objects (doorknobs, tables or desks), kitchen surfaces (utensils, cutlery, countertops, chopping boards, sinks, floors, etc.), bathroom surfaces (toilet, sink, floor, etc.) were also included in the weekly cleaning or disinfecting practices	1. Provision of hand-hygiene products 2. Hand-hygiene education	Children, their family members and teachers were advised to wash their hands daily using liquid antimicrobial soap, especially 1. before eating 2. after using the bathroom 3. after blowing their nose 4. after outdoor activities. Instant hand sanitizer was to be carried daily and used without running water	1. water with liquid antimicrobial soap 2. hand sanitizers used without running water	Not specified	Families and kindergartens in the intervention group were provided with antibacterial products for hand hygiene and surface cleaning or disinfection produced by the Whealthfields Lohmann (Guangzhou) Company Ltd. Items distributed included liquid antimicrobial soap for hand washing, instant hand sanitizer for hand-disinfecting antiseptic-germicide and bleach for surface disinfecting.	Unknown
Bartlett 1984 USA	1. Group meetings (directors and caregivers) 2. Posters and handouts	1. Hygiene education 2. Participatory learning[c]	Staff and child hand washing, diapering, food handling, and environmental cleaning	Unclear	Not specified	Not specified	Adequate
Black 1977 USA	Large-group education	Hygiene education	Staff and child hand-washing before handling food and after defaecation	Water with bar soap and paper towels	Unclear	By the day-care centres' management	Adequate

Table 1. Description of hand-washing interventions at child day-care centres and schools *(Continued)*

Bowen 2004 CHN	1. Large-group training 2. Posters, videotape, wall charts, games 3. Take-home packs 4. Peer trainers and peer monitoring	1. Hygiene education 2. Behaviour modification	Hand washing before eating and after toileting	Water with soap	Under running water	Supplies of soap to schools in 'expanded Intervention'; 1 bar of soap to homes in both expanded and standard intervention	Adequate (criteria for taking part in trial)
Butz 1990 USA	Large-group training (in-home instruction to day-care providers)	1. Hygiene education 2. Provision of soap/ hand rinse material	1. Modes of transmission of pathogens in the home 2. Indications of hand washing 3. Use of vinyl gloves and disposable diaper changing pad 4. Use of an alcohol-based hand rinse (if unable to wash hands with water plus soap)	Water with soap	Not specified	All supplies provided by researchers	Adequate
Carabin 1997 CAN	1. Large-group hygiene training (educators) 2. Handouts	Hygiene education	1. Wash hands before lunch and after using the toilets 2. Clean toys with bleach 3. Use of reminder cues for hand washing 4. Clean the sandbox with bleach 5. Open windows at least 30 mins every day	Unclear	Not specified	Unclear	Adequate
Kotch 1989 USA	1. Large-group training 2. Curriculum for caregivers	Hygiene education	1. Hand washing of children and staff 2. Disinfection of diapering areas and toilet 3. Physical separation of diapering areas from food preparation and serving areas 4. Hygienic diaper disposal	Water with soap plus disposable towel	Under running water	Unclear	Adequate

Table 1. Description of hand-washing interventions at child day-care centres and schools *(Continued)*

Kotch 2003 USA	1. Large-group training using the Keep it clean module for caregivers	1. Hygiene education 2. Provision of equipment for food preparation, diaper changing and hand washing	Training to improve and standardize the hand-washing, sanitation, diapering, and food preparation procedures in both intervention and control centres by addressing knowledge, attitudes, and behaviours of child-care providers and promoting use of the equipment	Not described	Not described	Diapering, hand-washing, and food preparation equipment was provided by the researchers	Adequate
Ladegaard 1999 DEN	Small-group practical demonstration	1. Hygiene education 2. Participatory learning[c]	1. Hand washing after stool contact 2. Information on disease spread and when to wash hands to prevent diarrhoea	Water with soap	Under running water	Unclear	Adequate
Pickering 2013 KEN	1. Participatory discussion with teachers on germ theory and hygiene 2. UNICEF in Kenyan-designed hygiene promotion kit (including posters, stickers, a classroom activity, etc.)	1. Hygiene education 2. Installation of soap wall dispenser	1. Hand washing before eating 2. After using the toilet	Water with soap	Not described	Researchers provided liquid soap and water tank	Adequate
Roberts 1996 AUS	1. Large-group training 2. Booklets/newsletters 3. Songs about hand washing for children	1. Hygiene education 2. Behaviour modification	1. Hand washing before eating and after toileting or changing a diaper (staff and child) 2. Wash toys daily in dishwashers	Water with soap	Under running water	Unclear	Adequate
Talaat 2008 EGY	1. Larger-group training sessions 2. Posters 3. Informational fliers were distributed to parents to reinforce the messages delivered at the schools	Hygiene education	1. Hand washing with soap and water upon arriving at school 2. Hand washing after coughing or sneezing 3. Hand washing after using the bathroom, stool contact/defaecation	Water with soap	Under running water	1. School administration 2. Parents of trial participants	Adequate (Cairo governate was chosen because of the continuous availability of water in school settings)

Table 1. Description of hand-washing interventions at child day-care centres and schools *(Continued)*

	4. A special song to promote hand hygiene was developed and played regularly at schools 5. Grade-specific students booklets were developed: each included a set of 12 games and fun activities that promoted hand washing 6. The school contributes to promoting hand washing by selecting a weekly hand-hygiene champion, launching school contest for drawing, songs, and drama		4. Hand washing before and after meals				
Zomer 2015 NED	1. Hand hygiene products provided free of charge 2. Training on Dutch Hand Hygiene guidelines with booklet on its content distributed 3. Training sessions aimed at goal setting and formulating specific hand hygiene improvement activities. 4. Provision of posters and stickers to children and caregivers as reminders and cue to action	1. Provision of hand-hygiene products 2. Hand-hygiene education 3. Compliance with hand-hygiene guidelines	1. Hand hygiene before touching/preparing food, eating or assist children to eat, and wound care 2. Hand hygiene after diapering, toilet use/wiping buttocks, coughed/sneezed/wiped their own nose, contact with body fluids, wound care and after hands were visibly soiled	Water with soap	Not described	Trial investigators provided hand-hygiene products free of charge (dispenser for paper towels, soap, alcohol-based hand sanitizer and hand cream, with refills for 6 months)	Adequate

[a]Message classification.
[b]Whether done under running water; in a bowl, by an individual, or by several people.
[c]Participatory learning involves a process that helps engage learners in an active role of inquiry in which they share experiences and reflect critically on practice in a context that many group members find stimulating and relatively safe (Martin 1997).

Table 2. Description of hand-washing intervention in communities

Trial	Promotional activity	Classification[a]	Message content	Hand- washing method	Hand-washing style[b]	Material provision	Water availability
Briceno 2017 TZA	Intensive social marketing, including:	1. Hygiene education	1. importance of hand washing	Water with soap	Under running water ('tippy' taps)	Not specified	Unknown

Table 2. Description of hand-washing intervention in communities *(Continued)*

	1. hand-washing promotion events with women on market days, during prenatal clinic visits, and village meetings 2. Distribution of promotional materials 3. face-to-face interactions 4. Helping households build 'tippy' taps 5. Travelling road shows 6. Mass media radio campaigns	2. Behaviour modification	2. hand washing after faecal contact: after defaecating, after toileting, after cleaning child post-toileting 3. hand washing before handling food: before cutting or preparing food, before eating, before serving food, before breastfeeding				
Galiani 2016 PER	hand-washing promotion through: 1. radio 2. printed materials 3. promotional events 4. educational sessions	1. Hygiene education 2. Behaviour modification	1. hand washing with soap	Water with soap	Unclear	Adequate	Unknown
Haggerty 1988 COD	Large-group training	Hygiene education	1. Hand washing before meal preparation and eating 2. Hand washing after defaecation (wash both hand and buttocks for children) 3. Proper disposal of children's faeces 4. Disposal of animal faeces from yard	Unclear	Not specified	Unclear	Unknown

Table 2. Description of hand-washing intervention in communities *(Continued)*

Han 1985 MMR	Small-group education (households)	1. Hygiene education 2. Provision of hand-washing material	Hand washing: 1. after defaecation; 2. before preparing or eating food.	Water with bar soap	Not specified	Plain bar soap provided by researcher	Unknown
Hartinger 2011 PER	1. Hygiene education 2. Provision of an Integrated home-based intervention package (IHIP)	1. Hygiene education 2. Home-hygiene intervention package including OPTIMA-improved stove, kitchen sink, hand washing, and solar drinking water disinfection (SODIS) household water treatment	Hand washing: 1. After stool contact/ defaecation 2. Before food preparation/ handling 3. Before eating and feeding infants and small children 4. After changing diapers 5. Correct use of improved stoves, including clearing and removing ashes and wood residues that could obstruct ventilation 6. Correct application of the solar drinking water disinfection (SODIS) method 7. Elimination of animal excreta and isolation of animals from the kitchen environment	Water with soap	Not specified	IHIP provided by researchers	Unknown
Hashi 2017 ETH	1. Sessions on health education 2. Provision of soap 3. community meetings 4. Distribution of pamphlets 5. Hygiene education 6. Demonstration	1. Hygiene education 2. Behaviour modification	1. hand washing messages · wash your hands before meal preparation · wash your hands before eating food · wash your children's hands with the soap (provided) after defaecation, before meal preparation, and before eating 2. Water storage behaviour messages: · cover your water storage container properly	Water with soap	Not specified	Saop provided by the researchers	Unknown

Table 2. Description of hand-washing intervention in communities *(Continued)*

			· use narrow-mouthed storage container · Clean your water storage container regularly · have a latrine 3. Latrine availability messages - If you don't have a latrine, share with the nearest neighbourhood and build a latrine · use your latrine properly · make a hand-washing site with soap, and use properly regularly by washing your hands every time you use 4. Safe waste disposal messages · dispose of liquid waste properly · dispose of solid waste properly · dispose of your children's waste properly				
Kapoor 2016 IND	1. Hygiene education 2. Flip books 3. Distribution of pamphlets	1. Hygiene education 2. Behaviour modification	1. hand washing 2. personal hygiene of mother and child 3. clean storage of drinking water 4. food hygiene 5. sanitation	Not specified	Key observations reported: 1. wet hands under running water 2. apply soap/ sanitizer; 3. rub hands together for 15 - 30 seconds	Not reported	Unknown
Langford 2007 NPL	1. Larger meetings	1. Behaviour modification	Hand washing:	Water with soap	Not specified	Soap provided by researcher (com-	Adequate (water for hy-

Table 2. Description of hand-washing intervention in communities *(Continued)*

	2. Small group meetings: focus group discussion of 6 to 8 women 3. Posters 4. Dramas	2. Hygiene education	1. After stool contact/defaecation including wiping bottoms of babies 2. After refuse disposal 3. Before food preparation/ handling 4. Before eating			munity motivators distributed a new bar of soap to each mother at these meetings)	gienic purposes, but was always available from these tubes and deep wells)
Luby 2003a PAK	1. Large group training using slide shows, pamphlets, and video tapes 2. Education at weekly field visits	Hygiene education	Hand washing: 1. Before preparing food 2. Before eating food	Water with plain or antibacterial soap	Water from a pitcher (though not clearly stated)	Soap provided by researchers	Unknown
Luby 2003b PAK	1. Large group training using slide shows, pamphlets, and video tapes 2. Education at twice-weekly visits	1. Hygiene education 2. Provision of hand washing material	Hand washing: 1. After stool contact/ defaecation 2. Before food preparation/handling/eating 3. Before feeding infants	Water with antibacterial soap	Not specified	Soap provided by researchers	Unknown
Luby 2006 PAK	Follow-up trial of Luby 2003b PAK	No intervention was conducted	Follow-up trial of Luby 2003b PAK above	No intervention	No intervention	No intervention	Follow-up trial
Luby 2018 BGD	1. Discussions 2. video dramas 3. storytelling 4. games 5. songs 6. training on hardware maintenance	1. Hygiene education 2. Behaviour modification	Wash hands with soapy water 1. before preparing food 2. before eating or feeding a child 3. after defaecating 4. after cleaning a child who has defaecated.	Water with soap	Not specified	Promoters also provided a regular supply of detergent sachets for making soapy water. Intervention households received 2 hand-washing stations, 1 with a 40 L water reservoir placed near the latrine and a 16 L reservoir for the kitchen.	Unknown

Table 2. Description of hand-washing intervention in communities *(Continued)*

						Each hand-washing station included a basin to collect rinse water and a soapy water bottle.16 Promoters also provided a regular supply of detergent sachets for making soapy water	
Nicholson 2008 IND	1. Large group training 2. Establishment of a 'Good Mums' Club 3. Environmental cues (wall hangers, danglers, etc) 4. Reward system from mothers to children (stickers, toy animals, coins, etc)	1. Hygiene education 2. Behaviour modification (intervention designed according to behaviour change principles of (Claessen 2008)	1. Hand washing after stool contact/defaecation 2. Hand washing before eating 3. Hand washing during bathing	Water with soap	Not specified	Soap provided by researchers	Unknown
Null 2018 KEN	1. Guided discussions 2. using visual aids 3. song 4. storytelling 5. resupply of consumable intervention materials;	1. Hygiene education 2. Behaviour modification	Hand washing with soap 1. before handling food 2. after defaecation (including assisting a child)	Water with soap	Not specified	Soap provided by researchers. Study compounds were given 2 permanent, water-frugal hand-washing stations intended to be installed near the food preparation area and the latrine. Hand-washing stations were constructed of painted metal, with 2 foot-ped-	Unknown

Table 2. Description of hand-washing intervention in communities *(Continued)*

						al-operated jerry-cans that dispensed a light flow of rinse water and soapy water. Promoters added chunks of bar soap to the soapy water container quarterly	
Stanton 1985 BGD	1. Small group discussion (only women or children) 2. Larger demonstrations (mixed audience) 3. Posters, games, pictorial stories, and 'flexiflans' for illustrations	Hygiene education	1. Hand washing before food preparation 2. Defaecation away from the house and in a proper site 3. Suitable disposal of waste and faeces	Unclear	Not specified	Unclear	Inadequate

[a]Message classification.
[b]Whether done under running water; in a bowl by an individual, or by several people.

Table 3. Description of hand-washing intervention among high-risk group (AIDS patients)

Trial	Promotional activity	Classification[a]	Message content	Hand washing method	Hand washing style[b]	Material provision	Water availability
Huang 2007 USA	Demonstration by nurses and patients	Hygiene education	1. Hand washing after toileting, before food preparation/handling, eating 2. After cleaning infants who had defaecated 3. Before and after sex	Water with soap	Under running water	Unclear (probably not relevant in this population)	Adequate

[a]Message classification.
[b]Whether done under running water; in a bowl by an individual or by several people.

Table 4. Hand washing in high-risk group (AIDS patients): behavioural change outcomes and KAB

Trial	Cluster adjusted?	KAP[a] changes	Outcome	Intervention	Control	Effect size/P value
Huang 2007 USA	Individual randomization	Frequency of hand washing per day	Mean hand-washing frequency per day at baseline	3.3	3.4	P value not significant
			Mean hand washing frequency per day at end-line	7	4	P value not provided[a]

Abbreviations; KAB = knowledge, attitude, and beliefs.
[a]Percentage change in the mean frequency of hand washing in the intervention arm is 109% versus 18% in the control arm.

Table 5. Incidence of diarrhoea in child day-care centres and schools

Trial	Cluster- adjusted?	Outcome and result	Method of assessment	Sample size
Ban 2015 CHN	No	Number of person-months for diarrhoea OR = 0.37 (95% CI 0.22 to 0.60). Protective effect of the intervention on diarrhoea Intervention −0.11, control −0.11, protection rate 60.83 (95% CI 42.73 to 78.94)	1. A 'Children's Daily Health Calendar' was sent to families of both groups to collect daily data on illness symptoms. All of the symptoms of illness were diagnosed and filled out by the parents or guardians based on the stated definitions. Every month upon completion, the Calendars were collected by the teachers of each classroom. The teachers checked the completeness and accuracy of the Calendars and made corrections with the parents or guardians according to the children's morning checking and medicine taking log 2. A Children's Daily Sick Leave Calendar was sent to the classroom teachers of both groups to collect daily data on sick leave, and were filled out by the teachers	221 children from 1 kindergarten as the intervention group, and 245 children from the other kindergarten as the control group
Bartlett 1984 USA	No	Diarrhoea rate per child-year of observation Intervention: 0.71 (95% CI 0.65 to 0.77) Control: 0.81 (95% CI 0.75 to 0.87)	1. Active day-care centre-based surveillance (weekly visits plus daily telephone calls to identify diarrhoeal illness 2. Family-based surveys (questionnaire every 2 weeks)	26 day-care centres with 374 children (196 intervention, 178 control) aged 0 to 3 years
Black 1977 USA	No	Diarrhoea incidence/100/child-weeks of observation Intervention: 4.2/100/child-week Control: 8.1/100/child-week	Daily record of attendance plus diarrhoea occurrence for each child by day-care personnel	4 day-care centres (2 intervention, 2 control) with 116 children < 3 years

Table 5. Incidence of diarrhoea in child day-care centres and schools *(Continued)*

Bowen 2004 CHN	Yes	Median episodes of diarrhoea per 100 student weeks Expanded intervention: 0 per 100 student-weeks Standard intervention: 0 per 100 student-weeks Control: 0 per 100 student-weeks	Teachers trained using standardized case definitions to identify 10 symptoms or signs of illness and record these among students in class, 1 day per week; if parent's reported infection as cause of absence, teachers recorded name of syndrome and asked parent if child suffered any of 10 individual symptoms; verified verbally that reports of diarrhoea met case definition	3962 children within 87 primary schools
Butz 1990 USA	No	Proportion of diarrhoea days per month Diarrhoea episodes/child-days Intervention: 93/10,159 Control: 133/10,424	Daily symptom record for each child by care providers	24 family day-care homes with 108 children (58 intervention, 50 control) aged 1 month to 7 years
Carabin 1997 CAN	Yes	Diarrhoea incidence: episodes/100 child-days at risk Incidence rate ratio (95% Bayesian credible interval) 1.10 (0.81 to 1.50), adjusted for age and gender Intervention alone: 0.77 (0.51 to 1.18) Monitoring alone: 0.73 (0.54 to 0.97)	Daily record of diarrhoea episodes on calendar by educators	52 day-care centres with 1729 children aged 18 months to 3 years
Kotch 1989 USA	Yes	Diarrhoea rates: incidence density (episodes/child-year) Intervention (< 2 years): 4.54 Intervention (> 2 years): 2.85 Control (< 2 years): 5.12 Control (> 2 years): 2.79 All: RR 1.19, 95% CI −0.48 to 1.96	1. Telephone interview methodology (calls to families every 2 weeks) 2. 5-week interval visits to day-care centres	24 day-care centres with 389 children < 3 years
Kotch 2003 USA	No	Intervention group experienced significantly lower episodes of diarrhoea Incidence density score: Intervention: 0.90 diarrhoea illness per 100 child-days. P < 0.001 Control: 1.58 diarrhoea illness per 100 child-days. P < 0.001 Children in the intervention group sick with diarrhoea a lower proportion of days than children in the control group:	1. Field data collectors recorded baseline and monthly observations during school visits using a standard event-sampling form 2. Telephone interviews to parents of children to ascertain frequency and severity of diarrhoea every 2 weeks	46 child-care centres (23 child-care centres in the intervention arm and 23 child-care centres in the control arm) with 388 children (infants and toddlers < 36 months)

Table 5. Incidence of diarrhoea in child day-care centres and schools *(Continued)*

		Days ill with diarrhoea: Intervention: 4.0% Control: 5.0% P < 0.001		
Ladegaard 1999 DEN	No	Diarrhoea episodes/child-month Intervention: 33/848 Control: 61/1052 (34% reduction from 3.25 days per child in favour of children 3 years or more)	Information on absenteeism recorded on a form by child-care provider	8 day-care centres with 475 children (212 intervention, 263 control) aged 6 years and below
Pickering 2013 KEN	Yes	Hierarchical (Poisson) model result soap versus control; Diarrhoea (defined as 3 or more loose/watery stool in 24 hours): RR 0.84, 95% CI 0.58 to 1.22; P = 0.36 Any loose/watery stool in 24 hours: RR 1.09 (95% CI 0.92 to 1.30). P = 0.33 Loose/watery stool identified on Bristol stool Chart: RR 1.04 (95% CI (0.85 to 1.29); P = 0.69	1. Structured observation, health and survey data were collected with personal digital assistant (PDA) 2. Daily rotated visits to schools by enumerators (Structured observation of hand-cleansing behaviour) 3. Students interviewed weekly (self-reported illness symptoms/events)	6 primary schools (2 each for Hand washing with soap (HWWS), Hand sanitizer and control) with a total of 1364 children participants. However, the intervention of interest (HWWS = 460; control = 469) therefore total = 929). aged between 5 and 10 years.
Roberts 1996 AUS	Yes	Diarrhoeal rates: episodes/child-year Intervention: 1.9 episodes/child-year Control: 2.7 episodes/child-year All: RR 0.50, 95% CI 0.36 to 0.68 < 2 years: RR 0.90, 95% CI, 0.67 to 1.19 > 2 years: RR 0.48, 95% CI 0.29 to 0.78 (Adjusted for clustering by centre, confounding variables (age, sex, weight at birth, breastfeeding status, child care history, and home factors), and interactions between age and intervention status, and between having a sibling who attends child care and intervention status)	1. Telephone interviews (parents' reports of symptoms) every 2 weeks 2. Observation for compliance with recommended practices every 6 weeks	23 day-care centres (11 intervention, 12 control) with 558 children under 3 years
Talaat 2008 EGY	No	Diarrhoea episodes Intervention: 639 episodes Median IQR: 0.2 (0.0 to 0.5) Control: 1316 episodes Median IQR: 0.3 (0.1 to 0.6)	1. School interviews by school nurse, teachers and surveillance officer to complete data collection forms 2. Telephone interviews to parents of children absent due to illness to complete an absenteeism data collection form	60 elementary schools (30 intervention, 30 control) with 44,451 children (20,882 intervention; 23,569 control)

Table 5. Incidence of diarrhoea in child day-care centres and schools *(Continued)*

		33% reduction P < 0.0001 Incidence of absenteeism caused by diarrhoea was 33% lower in school children in the intervention schools	3. School absenteeism records	Median age: 8 years
Zomer 2015 NED	Yes	Diarrhoeal rates: episodes/child-year (7 symptom-free days between episodes) Intervention: 3.0 episodes/child-year Control: 3.4 episodes/child-year IRR 0.90, 95% CI 0.73 to 1.11 P value: 0.32	1. Parents monitored child disease incidence using infection calendar and reported this every 2 weeks onto an online version of the calender or sent in by post 2. Observation for hand-hygiene compliance at 6 months follow-up	71 day-care centres (36 intervention; 35 control 35) with 545 children (278 from 34 intervention DCC and 267 from 35 control DCC)

Abbreviations: CI: confidence interval; IQR: interquartile range.

Table 6. Incidence of diarrhoea in communities

Trial	Cluster-adjusted?	Outcome and result	Method of assessment	Sample size
Briceno 2017 TZA	Yes	Health indices Diarrhoea in the past 7 days = −0.004 (SE 0.012), control mean = 0.086 Diarrhoea in the past 14 days (listing data) = −0.013 (SE 0.011), control mean = 0.168	1. Caregiver-reported diarrhoea during household surveys 2. Structured observations	10 districts with 181 wards (44 wards with 88 villages and 1433 children < 5 assigned to sanitation-only treatment, 45 wards with 90 villages and 1452 children < 5 assigned to hand washing-only treatment, 46 wards with 92 villages and 1431 children < 5 assigned to combined treatment, 46 wards with 92 villages and 1481 children < 5 assigned to control)
Galiani 2016 PER	Yes	Diarrhoea prevalence in 48 hours A. Community treatment sample Effect of treatment −0.002 (SE 0.011), control mean = 0.040 B. School component sample Effect of treatment 0.001 (SE 0.009), control mean = 0.033 Diarrhoea prevalence in 7 days A. Community treatment sample	1. Caregiver-reported diarrhoea during household surveys 2. Structured observations 3. Self-reported hand-hygiene behaviour	85 districts (44 intervention, 41 control)

Table 6. Incidence of diarrhoea in communities *(Continued)*

		0.001 (SE 0.015), control mean = 0.060 B. School component sample Effect of treatment −0.005 (SE 0.014), control mean = 0.069		
Haggerty 1988 COD	Yes	Diarrhoea rates (mean episodes of diarrhoea) Intervention site: 0.071 Control site: 0.075 (RR 0.94, 95% CI 0.85 to 1.05; P = 0.3)	1. Observation recording form 2. Diarrhoeal morbidity form	18 sites (9 intervention, 9 control) with 1954 children aged 3 months to 35 months
Han 1985 MMR	No	Incidence rate per 1000 child days of observation Intervention: 3.5 Control: 4.9 Incidence density ratio 1. Diarrhoea < 2 years: 0.69 (95% CI 0.48 to 1.10) > 2 years: 0.67 (95% CI 0.45 to 0.98) All: 0.70 (95% CI 0.54 to 0.92) 2. Dysentery < 2 years: 0.59 (95% CI 0.22 to 1.55) > 2 years: 1.21 (95% CI 0.52 to 2.80) All: 0.93 (95% CI 0.39 to 2.23)	Daily surveillance (24-hour recall) for diarrhoea and dysentery	350 households (162 intervention, 188 control) with 494 children (236 intervention; 258 control) under 5 years
Hashi 2017 ETH	Yes	Longitudinal adjusted incidence rate ratio (IRR) 0.65 (95% CI 0.57, 0.73) Episodes of diarrhoea per 100 person-weeks of observation Intervention: 594 episodes (4.1 episodes per 100 person-weeks observation) Control: 905 episodes (6.3 episodes per 100 person-weeks observation)	2-weekly data collection. Data collectors recorded episodes of diarrhoea over the previous 2 weeks based on primary care takers report	24 sub-Kebelles districts with 1224 children (12 sub-Kebelles with 612 children < 5 assigned to the intervention group, 12 sub-Kebelles with 612 children < 5 assigned to the control group) Follow-up: intervention: 603 children, control: 596 children
Hartinger 2011 PER	Unclear	Diarrhoea episodes: Intervention: 287 diarrhoea episodes or a mean of 1.7 episodes per child-year at risk Control: 365 diarrhoea episodes or a mean of 2.3 episodes per child-year at risk	Records and observations through monthly home visits	534 children (267 intervention, 267 control)
Kapoor 2016 IND	No	Episodes of diarrhoea Intervention: reduced from 90% to 52% Control: reduced from 88.7% to 83.2%	Self-reporting/ records collected by health workers during home visits	101 mothers with children below 2 years (50 intervention, 51 control)

Table 6. Incidence of diarrhoea in communities *(Continued)*

		Post-intervention prevalence of diarrhoea was 4.3 times higher in control group compared to intervention group (non-adjusted odds ratio). After controlling the confounding variables the prevalence of diarrhoea was 3.9 times higher in the control group compared to intervention group (adjusted odds ratio)		
Langford 2007 NPL	No	Diarrhoea episodes: children from intervention areas experienced on average 31% fewer episodes of diarrhoea than control counterparts Intervention: 3.0 episodes Control: 4.33 episodes P = 0.049 Intervention children also experienced 41% fewer days of diarrhoea than children in control areas Diarrhoea incidence: Intervention: 9.67 person-days Control: 16.33 person-days P = 0.023	1. Self-reporting/records collected by health workers during home visits using a symptom checklist 2. Observations during home visits	88 children (45 intervention, 43 control) aged 3 to 12 months old had complete data sets
Luby 2003a PAK	Yes	Incidence density of diarrhoea (number of new episodes of diarrhoea divided by the at-risk person-weeks of observation) Mean incidence 1. Primary diarrhoea Intervention: Antibacterial soap: 2.02 Plain soap: 1.91 Control: 4.06 2. Persistent diarrhoea Intervention: Antibacterial soap: 0.14 Plain soap: 0.12 Control: 0.17	Weekly observational visits to households	36 neighbourhoods (25 intervention, 11 control) with 4691 children (3163 intervention, 1528 control) aged < 15 years
Luby 2003b PAK	Yes	Diarrhoea episodes/100 child-weeks: for diarrhoea and persistent diarrhoea Intervention: 3.71 Control: 6.56 RR 0.57, 95% CI 0.35 to 0.86 Diarrhoea, mean incidence: 3.71 Persistent diarrhoea, mean incidence: 0.09	Weekly observational visits to households	18 clusters (544 households; 262 intervention; 282 control) with children < 15 years

Table 6. Incidence of diarrhoea in communities *(Continued)*

		−52% (−100% to 100%)		
Luby 2006 PAK	Yes	Crude diarrhoea longitudinal prevalence (%) 1.58 Modeled risk difference (%) vs. control −0.16 (95% CI −0.92 to 0.60)	Weekly observational visits to household/self-reports	577 households including the hand-washing promotion (195 households), hand-washing promotion plus water treatment (186 households) and control arm (195 households)
Luby 2018 BGD	Yes	Diarrhoea prevalence Mean prevalence - intervention 3.5%, control 5.7% Unadjusted prevalence difference intervention = −2.3 (−3.4 to −1.1) Adjusted prevalence difference intervention = −2.5 (−3.6 to −1.3)	1. Caregiver-reported diarrhoea during caregiver interview	5551 pregnant women in 720 clusters (Control: 1382, water: 698, sanitation: 696, hand washing: 688; water, sanitation, and hand washing: 702, nutrition: 699; and water, sanitation, hand washing, and nutrition: 686)
Nicholson 2008 IND	No	Per protocol analyses for diarrhoea incidence; episodes per 100 person-weeks 1. Target children: intervention 1.70; control 2.28; Observed relative risk reduction (ORRR) 25.3%; Predicted relative risk reduction (PRRR) 21.3% (95% CI −36.6% to −2.3%); P = 0.30 2. Children < 5 years: intervention 2.22; control 3.30; ORRR = 32.5%; PRRR = 24.7% (95% CI −41.1% to −3.8%); P = 0.023 3. Children 6 to 15 years: intervention 1.13; control 1.62; ORRR = 30.0%; PRRR = 24.3% (95% CI −38.7% to −6.6%); P = 0.010 4. Whole families: intervention 1.14; Control 1.64; ORRR = 30.7%; PRRR = 23.1% (95% CI −37.5% to −5.5%); P = 0.013	1. Case record forms (CRFs) covering illness and school absences solely through interviews 2. Households were visited twice week	35 matched pairs communities (70 in total for intervention and control); 30 households from each of the communities. Target children (5 year olds) = 2052 (intervention: 1026; control: 1026); < 5 years of age = 2469 (intervention: 1190; Control: 1279); 6 to 15 years = 3519 (intervention: 1784; control: 1735); adults = 3685 (intervention: 1892; control: 1793) All participants = 11,725 (intervention: 5892; control: 5833) Age: 5 year old children (Target); under-5 years of age, children 6 to15 years and adults (non-targets)
Null 2018 KEN	Yes	Diarrhoea prevalence Mean prevalence: intervention 26.1%, control 27.1% Unadjusted prevalence difference intervention = −0.6 (−3.5 to −2.3) Adjusted prevalence difference intervention = −1.1 (−4.0 to −1.8)	1. Caregiver-reported diarrhoea during end-line survey	702 village clusters (active control arm: 158 clusters; passive control arm: 80 clusters; water arm: 77 clusters; sanitation arm: 77 clusters; hand-washing arm: 77 clusters; combined water, sanitation, and hand-washing arm: 76 clusters; nutrition arm: 78 clusters; and the combined water, sanitation, hand-washing, and nutrition arm: 79 clusters

Table 6. Incidence of diarrhoea in communities *(Continued)*

Stanton 1985 BGD	Yes	Rate of diarrhoea per 100 person-weeks of observation Intervention: 4.29 Control: 5.78 Incidence density ratio 0.75 (95% CI 0.66 to 0.84; P < 0.0001) < 2 years: 0.54 (95% CI 0.43 to 0.66) > 2 years: 0.68 (95% CI 0.54 to 0.85)	1. Histories of diarrhoea for children of all households assessed every 2 weeks 2. Single prolonged on-site visit to each sentinel family for hand washing-related behaviour observation	1923 families (937 intervention, 986 control) with children aged < 6 years

Abbreviations: CI: confidence interval.

Table 7. Incidence of diarrhoea in high-risk group (AIDS patients)

Trial	Cluster adjusted?	Outcome and result	Method of assessment	Sample size
Huang 2007 USA	Not applicable	Mean episodes of diarrhoea over trial period (1 year) Intervention group: 1.24 (± 0.9) Control group: 2.92 (± 0.6)	Daily hand-washing diary to record number of hand-washing episodes per day and diarrhoea diary to record stool frequency and characteristics; weekly telephone calls from trial nurse to ascertain episodes of these outcomes	75 in hand-washing group, 73 controls

Abbreviations: CI: confidence interval.

Table 8. Hand washing in child day-care centres and schools: behavioural change outcomes and KAB

Trial	Cluster-adjusted?	Measured by	Outcome	Intervention	Control	Effect size or P value
Galiani 2016 PER	Yes	Self-reported hand-washing behaviour for hand washing with soap and water before eating, food preparation, feeding child/baby, and after faecal contact	Behaviour index	0.0694	0.000	-
		Structured observations for hand washing with soap and water before eating, food preparation, feeding child/baby, and after faecal contact	Structured observations index	0.0643	0.000	-

Table 8. Hand washing in child day-care centres and schools: behavioural change outcomes and KAB *(Continued)*

Kotch 1989 USA	Yes	Recorded observations at 5-week intervals	Mean hand-washing behaviour score after changing a diaper (0 = none, 0.5 = partial, 1 = correct)	0.75	0.37	P < 0.01
			Mean hand-washing behaviour score after contact with child's mucus, saliva, vomit, etc. (0 = none, 0.5 = partial, 1 = correct)	0.66	0.21	P < 0.01
Pickering 2013 KEN	Yes	Hand-washing events observed 2 to 4 days per week per school	Proportion of people washing hands after toilet use	38%	37%	P > 0.05
			Proportion of people washing hands with soap after toilet use	37%	2%	P < 0.05
			Proportion of people washing hands before lunch	82%	69%	P > 0.05
			Proportion of students washing hands with soap before lunch	70%	1%	P < 0.05
Roberts 1996 AUS	Yes	Observation for compliance of recommended practices every 6 weeks	Compliance of children washing their hands	53% to > 80%	Not reported	Not reported
Zomer 2015 NED	Yes	Observation for hand hygiene compliance at 6 months follow-up	Compliance of caregivers with hand-hygiene guidelines	59%	44%	OR 4.13, 95% CI 2.33 to 7.32

Abbreviations: KAB = knowledge, attitude, and beliefs; OR = odds ratio

Table 9. Hand washing in communities: behavioural change outcomes and KAB

Trial	Cluster-adjusted?	Measured by	Outcome	Intervention	Control	Effect size/ P value
Briceno 2017 TZA	Yes	Structure observations of hand-washing behaviour at critical junctures	Hygiene index	0.096	0.010	P < 0.01
		Observation and caregiver reported information	Sanitation index	0.029	−0.001	-
Galiani 2016 PER	Yes	Self-reported hand-washing behaviour for hand washing with soap and water before eating, food preparation,	Behaviour index	0.0454	0.000	-

Table 9. Hand washing in communities: behavioural change outcomes and KAB *(Continued)*

		feeding child/baby, and after faecal contact				
Kapoor 2016 IND	Unclear	Observations recorded using an observation checklist	Hand-washing practices pre-intervention assessment Median score (IQR)	47.0 (44.0 to 51.0)	48.0 (43.0 to 51.0)	P 0.086
			Hand-washing practices post-intervention assessment Median score (IQR)	51.0 (46.0 to 52.0)	48.0 (43.0 to 50.0)	P < 0.001
Langford 2007 NPL	Approximately adjusted	Trial staff completed questionnaires with mothers' self-reporting their handwashing behaviour	Proportion washing hands after visiting the toilet	100%	90.7%	0.500
			Proportion washing hands after cleaning baby's bottom	100%	83.7%	0.031
			Proportion washing hands before cooking	71.1%	2.3%	< 0.001
			Proportion washing hands before feeding the baby	62.2%	18.6%	0.004
			Proportion washing hands before eating	60%	0%	0.003
Nicholson 2008 IND	Approximately adjusted	Hand-washing behaviour indirectly assessed using soap consumption (soap wrapper collection)	Median soap consumption per household per week	235 g	45 g	-
Stanton 1985 BGD	Yes	Comparison of hygienic practices after intervention	Proportion of mothers who wash their hands before preparing food	39/79 (49%)	25/75 (33%)	RR 1.48, 95% CI 1.01 to 2.21; P = 0.056

Abbreviations; KAB = knowledge, attitude, and beliefs

APPENDICES

Appendix 1. Detailed search strategies

MEDLINE (PubMed)

Search	Query
#1	Search hand AND (wash* or disifect* or clean* or hygiene) Field: Title/Abstract
#2	Search "Hand Disinfection"[Mesh]
#3	Search handwashing Field: Title/Abstract

(Continued)

#4	Search ((#3) OR #2) OR #1
#5	Search diarrh* Field: Title/Abstract
#6	Search "Diarrhea, Infantile"[Mesh]
#7	Search "Diarrhea"[Mesh]
#8	Search gastroenteritis Field: Title/Abstract
#9	Search dysenter* Field: Title/Abstract
#10	Search (((#9) OR #8) OR #7) OR #6 OR #5
#11	Search "Randomized Controlled Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type]
#12	Search random* Filters: Field: Title/Abstract
#13	Search randomized controlled trial Field: Title/Abstract
#14	Search (((#13) OR #12) OR #11) OR (placebo [Title/Abstract] OR double-blind*[Title/Abstract] OR single-blind*[Title/Abstract])
#15	Search (#10) AND #4
#16	Search (#15) AND #14

Search Name: Cochrane Central Register of Controlled Trials

#1 handwash*

#2 hand wash*

#3 hand-wash*

#4 hand and (sanitation or cleaning or cleansing or hygiene or disinfect*)

#5 #1 or #2 or #3 or #4

#6 diarrh*

#7 gastroenteritis

#8 dysenter*

#9 #6 or #7 or #8

#10 #9 and #5, in Trials

Database: Embase

Search Strategy:

---

1 handwashing.mp. or hand washing/

2 ((Hygiene or handwash* or " hand wash*") adj2 (educat* or promot* or communicat* or behavior)).mp.

3 (hand adj2 (wash* or hygiene or disinfect* or clean* or sanit*)).mp.

4 1 or 2 or 3

5 diarrhea/ or acute diarrhea/ or diarrhea.mp.

6 acute gastroenteritis/ or gastroenteritis.mp. or gastroenteritis/

7 5 or 6

8 4 and 7

9 (randomized or randomised or placebo or double-blind* or single-blind*).ti. or (randomized or randomised or placebo or double-blind* or single-blind*).ab.

10 randomized controlled trial/ or controlled clinical trial/

11 9 or 10

12 8 and 11

PsycINFO, ERIC (EBSCOhost)

S1	TX (handwashing or hand washing or hand hygiene) AND TX diarrhea*

SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH (Web of Science Core Collection)

TOPIC: (handwashing or hand hygiene or hand sanitation) AND TOPIC: (diarrhea or gastroenteritis) AND TOPIC: (randomized or trial or double-blind*)

Appendix 2. Prespecified changes for review update

Protocol section	Refreshed protocol
Background and research question	• We have updated information in the Background to follow the advised Cochrane/MECIR subheading structure • We have updated information on why it is important to do this review • The main review question remains relevant
Inclusion criteria	• The existing PICO remains relevant • We have not identified changes in usual-care standards or in standardized core-outcome sets • We are aware of no patient-reported outcomes • We do not think that any changes to studies may warrant stricter inclusion criteria
Methods	• The methods used in the review remain relevant • We have updated the 'Summary of findings' tables with the newly-included studies • We have not identified a need for a new subgroup analysis • We have not made any substantive change to the review structure
Detailed search strategies	The search strategies have been moved from a table to Appendix 1, to accurately report the format search terms are used in different databases

FEEDBACK

Search strategy, December 2011

Summary

I have read the interesting Cochrane Review 'Hand washing for preventing diarrhoea' conducted by you and your colleagues, published in The Cochrane Library 2009, issue 3. I would like to take the liberty to comment on the search strategies shown in Table 1:

- Search set 8 and 9 are identical for MEDLINE and EMBASE – I assume one of them should be upper case to indicate MeSH/EMTREE, or? (The correct MeSH/EMTREE is DIARRHEA, not DIARRHOEA – but either maps to the correct term, and thus gives the same result)
- I suggest you include hand washing$, diarrhoea$ and diarrhoea$ as free text terms.

From the attached search sets it appears that you may have missed 98 and 61 potentially relevant records in MEDLINE and EMBASE respectively. Of course, this does not mean that you have not identified all relevant and available trials but it still poses a risk which I suggest you address in your next update of the review. How I searched MEDLINE and EMBASE, via Ovid (other databases were not searched):

Set 1-11: Identical to the search shown in Table 1 (I assumed set 9 should be in upper case)

Set 12-16: I added hand washing$ as free text term and show how many records are missed (set 16: records published before 2008)

Set 17-22: Same as above, but added diarrhoea$ and diarrhoea$ to the search (set 22: records published before 2008)

Also, it would be helpful to know how many records your retrieved in your initial searches, how many were excluded due to lack of relevance, methodological flaws etc., i.e. presented in a flowchart.

Best regards,

Ole Nørgaard

Reply

We agree with the contributor that there was an error in Table 1. We have corrected this. We do not believe that we have missed any relevant records, but as this review is due to be updated, we will investigate this further during the updating process. With regard to presenting the results in a flowchart, PRISMA diagrams were not expected in Cochrane Reviews at the time this review was initially produced. This will again be dealt with during the updating process.

Contributors

Ole Frandsen Nørgaard of the Department of Computer Science, Faculty of Health Sciences, University of Copenhagen, Denmark identified slight anomalies in the search strategy used in preparing the original review (Ejemot-Nwadiaro 2008). We have incorporated his suggestions appropriately into this review update.

WHAT'S NEW

Date	Event	Description
5 January 2021	New search has been performed	Review updated and 7 new trials included.
5 January 2021	New citation required but conclusions have not changed	No change to conclusions.

HISTORY

Protocol first published: Issue 2, 2003
Review first published: Issue 1, 2008

Date	Event	Description
26 August 2015	New citation required but conclusions have not changed	Review updated and eight new trials included.
26 August 2015	New search has been performed	We updated the literature search and eight new trials met the inclusion criteria. We used GRADEpro 2014 to assess the certainty of the evidence and have included 'Summary of findings' tables in this review update. Also, we have introduced the term 'promotion' into the review title.
17 January 2012	Feedback has been incorporated	We are grateful to an observant reader who identified an error in the search strategy. We have now corrected this.
8 August 2008	Amended	We converted to new review format with minor editing.
2 July 2008	Amended	We removed trials that did not adjust for clustering from the meta-analysis and presented the data in tables. Trials that did not adjust for clustering are clearly labelled in the Results, tables, and 'Characteristics of included studies' sections. We amended the Methods and Results to reflect these changes.

CONTRIBUTIONS OF AUTHORS

Regina Ejemot-Nwadiaro and Dachi Arikpo extracted and analysed data and drafted the review.
John Ehiri developed the protocol and drafted and commented on the review.
Julia Critchley extracted and analyzed data and edited the review.
Martin Meremikwu helped finalize the data extraction form and drafted and commented on the review.

DECLARATIONS OF INTEREST

Regina Ejemot-Nwadiaro: none known.
John Ehiri: none known.
Dachi Arikpo: none known.
Martin Meremikwu: none known.
Julia Critchley: none known.

SOURCES OF SUPPORT

Internal sources

- University of Calabar, Nigeria
- Institute of Tropical Diseases Research and Prevention (ITDR&P), Calabar, Nigeria
- Liverpool School of Tropical Medicine (LSTM), UK
- Division of Health Promotion Sciences, University of Arizona, Mel & Enid Zuckerman College of Public Health, Tucson, Arizona, USA
- Higher Education Funding Council for England, UK
- Cochrane Nigeria, Nigeria

External sources

- Foreign, Commonwealth and Development Office (FCDO), UK

  Project number 300342-104

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We introduced the term 'promotion' into the title of the first review update, and we retain it in this current review update.

We added methods for assessing blinding and changed our primary outcome measure in the protocol from the relative risk of at least one diarrhoea episode to the incidence rate ratio for diarrhoea episodes. We pooled rate ratios in our analyses rather than relative risks, since

all trials presented diarrhoea as episodes, and we removed 'or standard hygiene promotion' as a control because it is included in the 'no hand-washing promotion' control group.

We added all-cause under-five mortality and cost effectiveness as secondary outcome measures for this review update.
We used GRADEpro 2014 to assess the certainty of the evidence. We have also included Summary of findings 1; Summary of findings 2; and Summary of findings 3 in this update.

Henry Ejere, a co-author on the protocol, did not participate in preparing the original review or this review update. Dachi Arikpo joined as a co-author in the first review update published in 2015.

Differences between review update (2015) and review update (2021)

We have updated the literature search methods, changed some of the terms used, and reported the search strategies in Appendix 1. The prespecified changes to the protocol for this review update (2021) are given in Appendix 2.

INDEX TERMS

Medical Subject Headings (MeSH)

Bias; Child Day Care Centers [statistics & numerical data]; Community-Acquired Infections [prevention & control]; Cross Infection [prevention & control]; Developed Countries [statistics & numerical data]; Developing Countries [statistics & numerical data]; Diarrhea [*prevention & control]; Hand Disinfection [*methods]; Randomized Controlled Trials as Topic; Schools [statistics & numerical data]; Soaps

MeSH check words

Adult; Child; Humans