SYSTEMATIC REVIEW

Impact of Water, Sanitation and Hygiene Interventions on Growth, Non-diarrheal Morbidity and Mortality in Children Residing in Low- and Middle-income Countries: *A Systematic Review*

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ABSTRACT

Objective: To evaluate the impact of water, sanitation and hygiene (WASH) interventions in children (age <18 y) on growth, non-diarrheal morbidity and mortality in children.

Design: Systematic review of randomized controlled trials, non-randomized controlled trials and controlled before-after studies.

Setting: Low- and middle-income countries.

Participants: 41 trials with WASH intervention, incorporating data on 113055 children.

Intervention: Hygiene promotion and education (15 trials); water intervention (10 trials), sanitation improvement (7 trials), all three components of WASH (4 trials), combined water and sanitation (1 trial) and sanitation and hygiene (1 trial).

Outcome Measures: (*i*) Anthropometry: weight, height, weight-for-height, mid-arm circumference; (*ii*) Prevalence of malnutrition; (*iii*) Non-diarrheal morbidity; and (*iv*) mortality.

Results: There was no effect of hygiene intervention on most anthropometric parameters (low to very low quality evidence). Hygiene intervention reduced the risk of developing Acute respiratory infections by 24% (RR 0.76; 95% CI 0.59, 0.98; moderate quality evidence), cough by 10% (RR 0.90; 95% CI 0.83, 0.97; moderate quality evidence), laboratory-confirmed influenza by 50% (RR 0.5; 95% CI 0.41, 0.62; very low quality evidence), fever by 13% (RR 0.87; 95% CI 0.74, 1.02; moderate quality evidence), and conjunctivitis by 51% (RR 0.49; 95% CI 0.45, 0.55; low quality evidence). There was low quality evidence to suggest no impact of intervention on mortality (RR 0.65; 95% CI 0.25, 1.7). Improvement in water supply and quality was associated with slightly higher weight-for-age Z-score (MD 0.03; 95% CI 0, 0.06; low quality evidence), but no significant impact on other anthropometric parameters or infectious morbidity (low to very low quality evidence). There was very low quality evidence to suggest reduction in mortality (RR 0.45; 95% CI 0.25, 0.81). Improvement in sanitation had a variable effect on the anthropometry and infectious morbidity. Combined water, sanitation and hygiene intervention improved height-for-age z scores (MD 0.22; 95% CI 0.12, 0.32) and decreased the risk of stunting by 13% (RR 0.87; 95% CI 0.81, 0.94) (very low quality of evidence). There was no evidence of significant effect of combined WASH interventions on non-diarrheal morbidity (fever, respiratory infections, intestinal helminth infection and school absenteeism) were not altered by intervention (low to very low quality of evidence). Any WASH intervention (considered together) resulted in lower risk of underweight (RR 0.81; 95% CI 0.69, 0.96), stunting (RR 0.77; 95% CI 0.68, 0.86) and wasting (RR 0.12, 0.85) (low to very low quality of evidence).

Conclusion: Available evidence suggests that there may be little or no effect of WASH interventions on the anthropometric indices in children from low- and middle-income countries. There is low to very low quality of evidence to suggest decrease in prevalence of wasting, stunting and underweight. WASH interventions (especially hygiene intervention) were associated with lower risk of non-diarrheal morbidity (very low to moderate quality evidence). There was very low quality evidence to suggest some decrease to no change in mortality. These potential health benefits lend support to the ongoing efforts for provision of safe and adequate water supply, sanitation and hygiene.

Keywords: *Growth, Morbidity, Mortality, Respiratory infections, WASH intervention*.

Systematic Review Registration: PROSPERO/ CRD42017063779
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INTRODUCTION

The role of water supply and sanitation in controlling enteric infections, malnutrition, as well as their contribution to poverty alleviation is gaining global importance, and coverage targets for both were included in the Millennium Development Goals. Access to potable water supply and proper sanitation facilities still eludes a large part of the global population, particularly in the low- and middle-income (LMIC) countries. Improvements in these aspects, also referred to as WASH (**WA**ter supply, **S**anitation and **H**ygiene) interventions, are generally classified into four categories: (*i*) provision of an improved source of water and/or improved distribution, such as piped water or standpipes, provided either at public (source) or household (point-of-use) levels; (*ii*) sanitation ('hardware') interventions that provide improved means of excreta disposal; (*iii*) hygiene interventions that focus on health and hygiene education; and (*iv*) promotion of specific health behaviors like hand-washing [1].

The vast majority of research data, including systematic reviews, have focused on the impact of WASH interventions on diarrhea [2-4]. The link between WASH interventions and improvement in diarrheal infections has not translated into a demonstrable consistent improvement in other health parameters like child growth in various trials. Nutritional status of children is probably the best indicator of the health of a population, and more objective than historical recalls of diarrhea [5]. There is a paucity of systematic reviews evaluating the effect of WASH interventions on other health indicators, like malnutrition [6], mortality, and non-diarrheal morbidity; and additional trials have also now become available. We conducted this systematic review to evaluate the impact of WASH interventions on growth, non-diarrheal morbidity and mortality in children.

METHODS

Type of Studies

Individual- or cluster-randomized trials, and non-randomized and controlled before-after studies (CBA) from LMIC (individuals, families or communities) reporting outcomes in children (age <18 y) were eligible for inclusion in this review. Non-randomized trials were considered eligible for inclusion only if they had a concurrent comparison group (no WASH intervention) and adjustment for baseline characteristics and confounders. CBA studies were considered eligible for inclusion if allocation to the different comparison groups were not made by the investigators, and outcomes of interest were measured in both intervention and control groups before the WASH intervention was introduced, and again after a reasonable period of the intervention. We included non-randomized cluster trials, and CBA studies only with at least two intervention sites and two control sites.

Type of Intervention

We included studies that compared the provision of an improved source of water and/or improved distribution – such as piped water or standpipes, provided either at public (source) or household (point-of-use) levels; sanitation ('hardware') interventions that provide improved means of excreta disposal; hygiene interventions that focused on health and hygiene education and promotion of specific health behaviors like hand-washing; and various combinations of the above listed interventions by local government, research institutions, or other non-governmental organizations – with no intervention.

Outcomes

The outcomes evaluated were: (*i*) anthropometry: weight, height and weight-for-height (WFH), mid-arm circumference; (*ii*) prevalence of malnutrition [stunting (author defined), wasting (author defined), low weight-for-age or underweight (author defined) or low BMI (author defined)); (*iii*) non-diarrheal morbidity (helminth infestation, dranculiasis, respiratory infections and others); and (*iv*) mortality.

Search Methods

We searched (August 2016) the following electronic databases: Medline, Web of Science, The Cochrane Controlled Trials Register, EMBASE, LILACS, Popline, and Graysource. Reference lists of all included papers and relevant reviews were scanned to identify citations that could have been missed in the primary search. We contacted authors of other relevant reviews in the field, relevant agencies and networks for the identification of ongoing or unpublished studies. The search results from the various databases and other sources were merged using reference management software (Endnote) to remove duplicate records. The title and abstract of the studies identified in the computerized search were scanned in duplicate to exclude references that were obviously irrelevant. In order to determine eligibility for inclusion of the remaining articles, their full texts were reviewed, and multiple reports of the same study were linked together. Two authors independently screened and assessed the eligibility of the studies, extracted relevant data and assessed the risk of bias for all included studies. Any dispute regarding these criteria was resolved among the investigators by mutual consultation.

Data Management

We evaluated the risk of bias for each trial using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions [7]. Plots of 'Risk of bias' assessments were created in Review Manager (RevMan) [8].

Risk ratio (RR) estimates with 95% confidence intervals (CI) were used for binary outcomes; for continuous outcomes mean differences (MD) were used. In order to maximize the data input for the pooled outcome measures, we utilized post-intervention values (means and standard deviations (SDs)) in preference to the changes from baseline [7]. In factorial trials and in multi-arm designs yielding two or more intervention groups (*e.g.*, improved water supply and promotion of hand-washing) and a single control group, the data in the intervention groups was pooled and compared against the single control group to prevent unit-of-analysis error. For cluster-randomized trials, we used the stated cluster-adjusted RR or means and 95% CI, irrespective of the method employed for adjustment. In case of missing data, we contacted trial authors for information wherever possible; and where this could not be done, or the authors did not respond, we imputed the missing values, where feasible. with the help of a statistician. In case any assumptions were made for such imputations, they were recorded, and are detailed in ***Web Appendix* 1**.

We intended to assess contextual and clinical heterogeneity, but this was not done because of only a few studies available for quantitative synthesis. Statistical heterogeneity was identified and measured as recommended [7]. A *P* value of 0.05 from the Chi^2 test was used to determine statistical significance with regard to heterogeneity. Assessment for the reporting bias using the funnel plot was also not done in view of insufficient number of trials. Subgroup analysis and sensitivity analysis were also not performed because of only a few studies available for quantitative synthesis.

We performed statistical analysis using the Revman software [8]. In concordance with the current recommendations [7], we conducted the meta-analysis of included randomized controlled trials and observational studies separately. In view of variation in studies with respect to populations, interventions, comparators, outcome and settings, the pooled effects were computed by random effects model. If it was not possible to amalgamate the data from the included studies, we provided a narrative synthesis of the results. For each primary outcome, quality assessment of the results was carried out using the GRADE approach [9].

RESULTS

The search strategy for various databases is detailed in ***Web Appendix* 2**, and the results are summarized in ***Fig.* 1**. We screened 24258 records, of which 177 were potentially eligible. Of these 107 references were excluded and 62 publications (41 studies) were included in the final analyses [10-71]. Six studies (8 publications) were ongoing [72-79].

The 41 included studies (***Web Table* I**) reported data on 113055 children. Thirty-three trials were cluster randomized controlled trials, four were CBA studies, and the remaining four were cluster non-randomized controlled trials. Twenty trials were conducted in Africa, 17 in Asia and 4 in Latin America. Twenty-three trials included infants or preschool children (age <5 years), while the remaining included older children as well. The intervention was hygiene promotion and education in 15 trials, improvement in water supply, quality and storage in 10 trials, and improvement in sanitation in 7 trials. All three components of WASH intervention (water, sanitation and hygiene) were studied in 4 trials. Water and sanitation improvement was studied in one trial and sanitation and hygiene in one study. Three trials had multiple comparison groups and yielded different combinations of interventions for analysis.

***Web Fig.* 1** and ***Web Fig.* 2** summarize the Risk of Bias for the included studies. The risk of bias for random sequence generation was low for the 33 cluster randomized controlled trials, unclear or high for two non-randomized controlled trials, and high for the remaining six studies. The risk of bias for allocation concealment was judged to be low in six, unclear in eight and high in the remaining studies. Attrition was high or unequal in the intervention and the control groups in eleven trials (high risk of bias), unclear for two trials, and low for the remaining 28 trials. Four trials were considered to be at high risk of bias on account of baseline imbalance of clusters, whereas the risk of bias was unclear for three trials, and low for remaining 34 trials. The cluster effect was not taken into account while doing the statistical analyses in six trials and these were considered to be at high risk of bias for unit of analysis error.

Effects of Interventions

Comparison 1: Hygiene versus No Intervention (17 Trials; 82456 participants) (***Table*** **I**)

For anthropometry, one trial [66) enrolling 1272 participants showed no evidence of difference (very low quality evidence) in the change in anthropometry (weight, height, Z scores) between intervention and control groups (***Table*** **I**). Two studies [16,66) evaluated the weight-for-age after long-term follow-up. Pooled analyses (no significant heterogeneity; I^2=0%, *P*=0.9) showed no difference (very low quality evidence) in weight-for-age or height-for-age. One trial [16] studied the impact of hygiene on BMI Z-score on follow-up and reported no change (very low quality evidence). The impact of hygiene interventions on other outcomes are also presented in ***Table*** **I**. The number of episodes of ARI were 24% lower in the hygiene intervention group (*P*=0.03; 6 trials, moderate quality evidence) (***Fig.*** **2**) [26,44, 50,63,65,70]. Similar benefits were also observed for cough (*P*=0.006; low quality evidence) [63], and laboratory confirmed influenza (*P*<0.001; very low quality evidence) [70]. Meta-analyses of data from four trials [50,54,58,70] showed that hygiene intervention reduced absence from school in children by 22% (*P*<0.001; moderate quality evidence). There was no evidence of any effect of hygiene intervention on mortality in children (*P*=0.38; low quality evidence).

Comparison 2: Water (Quality and Supply Improvement) vs. No Intervention

Table **II** presents the results of the effect of improvement in water quality and supply on various outcomes in children. Limited data from individual studies indicated marginal improvement in anthropometry, but no evidence of any significant benefit in reduction of morbidities or school absenteeism. Five trials with water intervention reported on mortality data, showing a reduction in mortality by more than 50% (*P*=0.007; very low quality of evidence) (***Fig*. 3**) [25,27,29,32,53].

Comparison 3: Improvement in Sanitation vs. No Intervention

Table **III** presents the effect of improvement in sanitation on various outcomes. Data from individual studies did not show any significant positive effect of sanitation related interventions on anthropometry of children, but there was a marginal benefit in terms of reduction of prevalence of underweight, wasting and stunting [13,56). There was no evidence of significant effect on morbidity or mortality (***Fig.* 4**) [23,56,69].

Comparison 4: Combined Interventions

Tables* IV** shows the magnitude of the effect in studies where more than one WASH interventions were delivered. Data on two of the WASH interventions were available only from individual studies [16,28,33,36,37,60], which did not document any significant impact on anthropometry or morbidity. ***Table* V** compares the effect of any of the WASH intervention (in comparison to no intervention) on child health outcomes. There was no evidence of any significant difference in the anthropometry (weight, height, BMI, Z scores) between the intervention and control groups, but the prevalence of underweight (Fig.* 5**), wasting and stunting (***Fig.* 6**) was significantly less in intervention group [11,13,56,60].

DISCUSSION

In this systematic review of 41 trials with WASH interventions, incorporating data on 113055 children, there was no evidence of effect of hygiene intervention on anthropometry. However, hygiene intervention reduced the risk of developing acute respiratory infections by 24%, cough by 10%, laboratory confirmed influenza by 50%, and conjunctivitis by 51%. There was low quality evidence to suggest no impact of intervention on mortality. Improvement in water supply and quality was associated with slightly higher weight-for-age Z-score without any evidence of impact on other anthropometric measures, non-diarrheal morbidity or school absenteeism. There was very low quality evidence to suggest about 55% reduction in mortality. Improvement in sanitation had a variable effect on the anthropometry in children; no positive effect on anthropometric measures but there was a reduction in risk of wasting, stunting and underweight. Individual studies on combination of two WASH interventions did not document any significant benefit in terms of child anthropometry or morbidity. Combined water, sanitation and hygiene intervention improved height-for-age Z-scores and decreased the risk of stunting. Any WASH intervention (considered together) resulted in lower prevalence of malnutrition (underweight, stunting and wasting).

Most studies in this review involved study populations from LMIC with high prevalence of malnutrition and infectious morbidities; these settings are expected to benefit from WASH interventions in case of a true effect. Although the nature of interventions under each heading varied among trials, control groups in most trials were comparable with intervention groups at baseline. Thus any observed effects in the intervention groups are more likely to be attributable to the WASH strategy than to spontaneous improvements noted over time. Evidence from these trials is largely applicable to real-life situations among populations in LMIC.

Most of the studies included in this review did not have good methodological quality on some criteria. WASH is a complex intervention, and conducting field trials to evaluate its impact is challenging. By its very nature, allocation concealment and blinding of participants and observers to the intervention are very tough to execute (although a couple of trials managed to do that). Of the included trials, most were carefully conducted cluster randomized controlled trials with low risk of recruitment bias, baseline comparability of clusters, no loss of clusters and appropriate analysis. Owing to the widely varying nature of interventions, we evaluated the impact of individual group of interventions separately. This also restricted the availability of studies available for quantitative synthesis for most of the outcomes, thus downgrading the certainty of evidence for some of them.

Dangour, *et al*. [6] assessed the effect of WASH interventions on weight for age, weight for height and height for age z scores. The studies included in this review were different from ours. Few studies included in this review were excluded for various reasons from the present review. In addition, we included some additional studies. The results were however similar in both the reviews, with no to minimal effect on these indices. Cumming, *et al*. [80] reviewed the effect of WASH interventions on stunting. However, it was more of a qualitative review, which focused more on observational data, and on the data from an earlier systematic review [6]. The authors suggested that WASH interventions may be effective if introduced before the onset of growth faltering. Diarrheal morbidity and mortality and onset of stunting are more concentrated before two years, and it might be important to focus on this age group to make WASH interventions more effective. A meta-analysis of the effect of hand hygiene on infectious disease risk in the community setting reported a reduction in respiratory illness of 21% (95% CI 5% to 34%) [81]. Rabie, *et al*. [82] studied the effect of handwashing on respiratory infections. All eight eligible studies reported that handwashing lowered risks of respiratory infection, with risk reductions ranging from 6% to 44% (pooled value 24%). Though none of the studies included in the review by Rabie, *et al*. [82] were included in the present systematic review because all of these included participants from high-income countries (Australia, Denmark, USA), these estimates are similar to our review. Pruss, *et al*. [83] reviewed the impact of the various environmental interventions on trachoma reduction. However, this again was a qualitative review with bulk of the evidence emerging from observational studies, and the conclusions cannot be compared with this review.

Evidence from this review suggests that though there is little or no effect of WASH interventions on the anthropometric indices in children from LMIC, they may result in reduction in prevalence of wasting, stunting and underweight. Moreover, WASH interventions (especially hygiene intervention) are probably associated with lower risk of non-diarrheal morbidity. There are several ongoing trials on these interventions, which may alter the conclusions and improve the quality of evidence available till date.

Nevertheless, these potential health benefits lend support to the ongoing efforts for provision of safe and adequate water supply, sanitation and hygiene. Future studies from varied settings need to focus on long-term benefits and other important outcomes necessary for decision-making, including the effect on micronutrient status, equity aspects and cost effectiveness.

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WHAT IS ALREADY KNOWN?

- Interventions focusing on Water, Sanitation and Hygiene (WASH) result in reduction in incidence and risk of diarrhea.

WHAT THIS REVIEW ADDS?

- WASH interventions may lead to reduction in prevalence of wasting, stunting and underweight in low- and middle-income countries.
- WASH interventions (especially hygiene intervention) probably lowers risk of non-diarrheal morbidity.

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TABLE I EFFECT OF HYGIENE INTERVENTIONS (*VS* NO INTERVENTION) ON ANTHROPOMETRY, NUTRITIONAL STATUS, AND NON-DIARRHEAL MORBIDITY AND MORTALITY

Outcome	*Studies*	*N*	*Effect estimate (95% CI)*
Weight (kg)	1	1272	0.20 (-0.12, 0.52)*
Weight (Follow up)	1	1390	-0.20 (-0.53, 0.13)*
Height (mm)	1	1272	10.00 (-5.39, 25.39) *
Height (Follow-up) (mm)	1	1390	-10.00 (-24.77, 4.77) *
Weight for age	1	1272	0.00 (-1.26, 1.26) *
WAZ (Follow-up)	2	1691	0.00 (-0.09, 0.10) *
Height for age	1	1272	0.00 (-0.66, 0.66) *
HAZ (Follow-up)	2	1691	-0.00 (-0.10, 0.09)#
Weight for Height	1	1272	0.00 (-0.99, 0.99) *
WFH (Follow-up)	1	1390	-1.00 (-1.95, -0.05) *
BMI Z-score (Follow-up)	1	301	0.10 (-0.20, 0.40) *
Low WAZ	1	168	0.85 (0.46, 1.58)$
ARI (ep/person-week)	6	894427	0.76 (0.59, 0.98) $
Cough (episodes/ person-week)	1	20980	0.90 (0.83, 0.97) $
URI (episodes/ person-week)	2	231113	0.67 (0.35, 1.28) $
Laboratory-confirmed Influenza	1	44451	0.50 (0.41, 0.62) $
Fever	2	25140	0.87 (0.74, 1.02) $
Skin Infection	2	214293	0.80 (0.51, 1.25) $
Conjunctivitis (episodes/person-week)	1	533416	0.49 (0.45, 0.55) $
Intestinal parasite infection	2	1456	0.65 (0.31, 1.37) $
School absence (episodes/person-week)	4	587825	0.78 (0.76, 0.80) $
School absence (mean)	1	10792	0.00 (-0.01, 0.01) *
Mortality	2	5158	0.65 (0.25, 1.70) $

Mean difference (95% CI); #Standardized mean difference (95% CI); $Risk ratio (95% CI)

WAZ: Weight-for-age Z score; HAZ: Height-for-age Z score; WFH: Weight-for-height; ARI: Acute respiratory infection; UI: Upper respiratory infection

TABLE II EFFECT OF INTERVENTIONS FOCUSING ON IMPROVEMENT IN WATER SUPPLY OR DISTRIBUTION (*VS* NO INTERVENTION) ON ANTHROPOMETRY, AND NON-DIARRHEAL MORBIDITY AND MORTALITY

Outcome	*Studies*	*Participants*	*Effect Estimate (95% CI)*
WAZ	1	121	0.03 (0.00, 0.06)*
Cough	1	5518	0.97 (0.84, 1.12)#
Fever (episodes/person-weeks)	1	5518	1.02 (0.89, 1.18) #
Ocular chlamydia	1	557	1.35 (0.87, 2.09) #
Active trachoma	1	557	1.10 (0.93, 1.29) #
School absenteeism (days absent/total child-school days)	1	91946	0.99 (0.96, 1.02) #
Mortality	5	4088	0.45 (0.25, 0.81) #
RCT	4	3739	0.45 (0.25, 0.82) #
Non RCT	1	349	0.50 (0.05, 5.43) #

**Mean difference (95% CI);* #*Risk ratio (95% CI)*

WAZ: Weight-for-age Z score; RCT: Randomized controlled trial

TABLE III EFFECT OF SANITATION INTERVENTIONS (*VS* NO INTERVENTION) ON ANTHROPOMETRY, NUTRITIONAL STATUS, AND NON-DIARRHEAL MORBIDITY AND MORTALITY

Outcome	*Studies*	*Participants*	*Effect Estimate (95% CI)*
Weight	1	4315	-0.21 (-0.42, 0.01)*
Height	1	4360	-0.63 (-1.18, -0.08) *
WAZ	3	9719	-0.01 (-0.12, 0.10) *
HAZ	3	7462	-0.02 (-0.28, 0.23) *
WHZ	1	4108	-0.01 (-0.18, 0.16) *
MUAC	1	4388	-0.02 (-0.17, 0.12) *
MUAC Z-score	1	4388	0.00 (-0.13, 0.13) *
BMI Z-score	1	4104	-0.06 (-0.23, 0.11) *
Stunting	2	2791	0.88 (0.78, 0.99) #
Cluster RCT	1	2415	0.85 (0.77, 0.95) #
CBA	1	376	1.01 (0.76, 1.34) #
Underweight	2	2708	0.86 (0.76, 0.98) #
Cluster RCT	1	2452	0.85 (0.74, 0.98) #
CBA	1	256	0.98 (0.68, 1.42) #
Wasting	1	120	0.12 (0.02, 0.85) #
RTI (number of episodes)	1	5209	1.27 (1.12, 1.45) #
RTI	1	6017	0.01 (-0.02, 0.03) *
Fever	1	6015	-0.00 (-0.03, 0.02) *
Helminth Infection	3	5326	0.74 (0.41, 1.33) #
Cluster RCT	2	4985	0.98 (0.86, 1.13) #
CBA	1	341	0.40 (0.28, 0.58) #
C. trachomatis infection	1	1211	1.01 (0.77, 1.33) #
Clinically active trachoma	2	1390	0.94 (0.83, 1.06) #
School absence (mean)	1	12262	-0.00 (-0.01, 0.01) *
Mortality (<10 years)	3	20086	1.03 (0.77, 1.39) #

**Mean difference (95% CI); #Risk ratio (95% CI)*

WAZ: Weight-for-age Z score; HAZ: Height-for-age Z score; WHZ: Weight-for-height Z score; MUAC: Mid upper arm circumference; RCT: Randomized controlled trial; CBA: Controlled before-after study; RTI: Respiratory tract infection.

TABLE IV EFFECT OF COMBINED (WATER, SANITATION OR HYGIENE) INTERVENTIONS (*VS* NO INTERVENTION) ON ANTHROPOMETRY, NUTRITIONAL STATUS, NON-DIARRHEAL MORBIDITY AND MORTALITY

Outcome	*Studies*	*Participants*	*Effect Estimate (95% CI)*
Sanitation and Hygiene			
STH	1	727	1.14 (0.87, 1.50)#
School absence (mean)	2	14337	-0.01 (-0.05, 0.02)*
Water and Hygiene			
WAZ (Follow-up)	1	320	-0.14 (-0.50, 0.22) *
HAZ (Follow-up)	1	320	-0.13 (-0.55, 0.29) *
BMI Z-score (Follow-up)	1	320	-0.05 (-0.39, 0.29) *
Water and Sanitation			
Low weight-for-age	1	197	0.77 (0.50, 1.19) #
Water, Sanitation and Hygiene			
HAZ	1	1899	0.22 (0.12, 0.32) *
Stunting	1	1899	0.87 (0.81, 0.94) #
STH Prevalence	2	1291	0.88 (0.60, 1.29) #
Cluster RCT	1	1113	1.06 (0.83, 1.36) #
Cluster Non-RCT	1	178	0.73 (0.57, 0.94) #
School absence (mean)	1	2263	-0.02 (-0.07, 0.02) *

**Mean difference (95% CI);* #*Risk ratio (95% CI)*

STH: Soil transmitted helminthes; WAZ: Weight-for-age Z score; HAZ: Height-for-age Z score; BMI: Body mass index; RCT: Randomized controlled trial

TABLE V EFFECT OF ANY (WATER, SANITATION OR HYGIENE) INTERVENTION (*VS* NO INTERVENTION) ON ANTHROPOMETRY AND NUTRITIONAL STATUS OF CHILDREN

Outcome	*Studies*	*Participants*	*Effect Estimate (95% CI)*
Weight (kg)	2	5587	-0.02 (-0.42, 0.38)*
Weight (Follow-up)	1	1390	-0.20 (-0.53, 0.13) *
Height (mm)	2	5632	1.79 (-6.95, 10.53) *
Height (Follow-up) (mm)	1	1390	-10.00 (-24.77, 4.77) *
WAZ/WFA	5	11112	0.01 (-0.06, 0.09)#
WAZ (Follow-up)	2	2011	-0.01 (-0.10, 0.08) #
HAZ/HFA	5	10633	0.01 (-0.11, 0.14) #
HAZ (Follow-up)	2	2011	-0.01 (-0.10, 0.07) #
WFH	2	5380	-0.00 (-0.06, 0.05) #
WFH (Follow-up)	1	1390	-1.00 (-1.95, -0.05) *
MUAC	1	4388	-0.02 (-0.17, 0.12) *
MUAC Z-score	1	4388	0.00 (-0.13, 0.13) *
BMI Z-score	1	4104	-0.06 (-0.23, 0.11) *
BMI Z-score (Follow-up)	1	320	-0.05 (-0.39, 0.29) *
Underweight/ Low WAZ	4	3073	0.85 (0.76, 0.97)$
Stunting	3	4690	0.87 (0.82, 0.93) $
Wasting	1	120	0.12 (0.02, 0.85) $

**Mean difference (95% CI); #Standardized mean difference (95% CI); $Risk ratio (95% CI)*

WAZ: Weight-for-age Z score; HAZ: Height-for-age Z score; WFH: Weight-for-height; MUAC: Mid upper arm circumference; BMI: Body mass index.

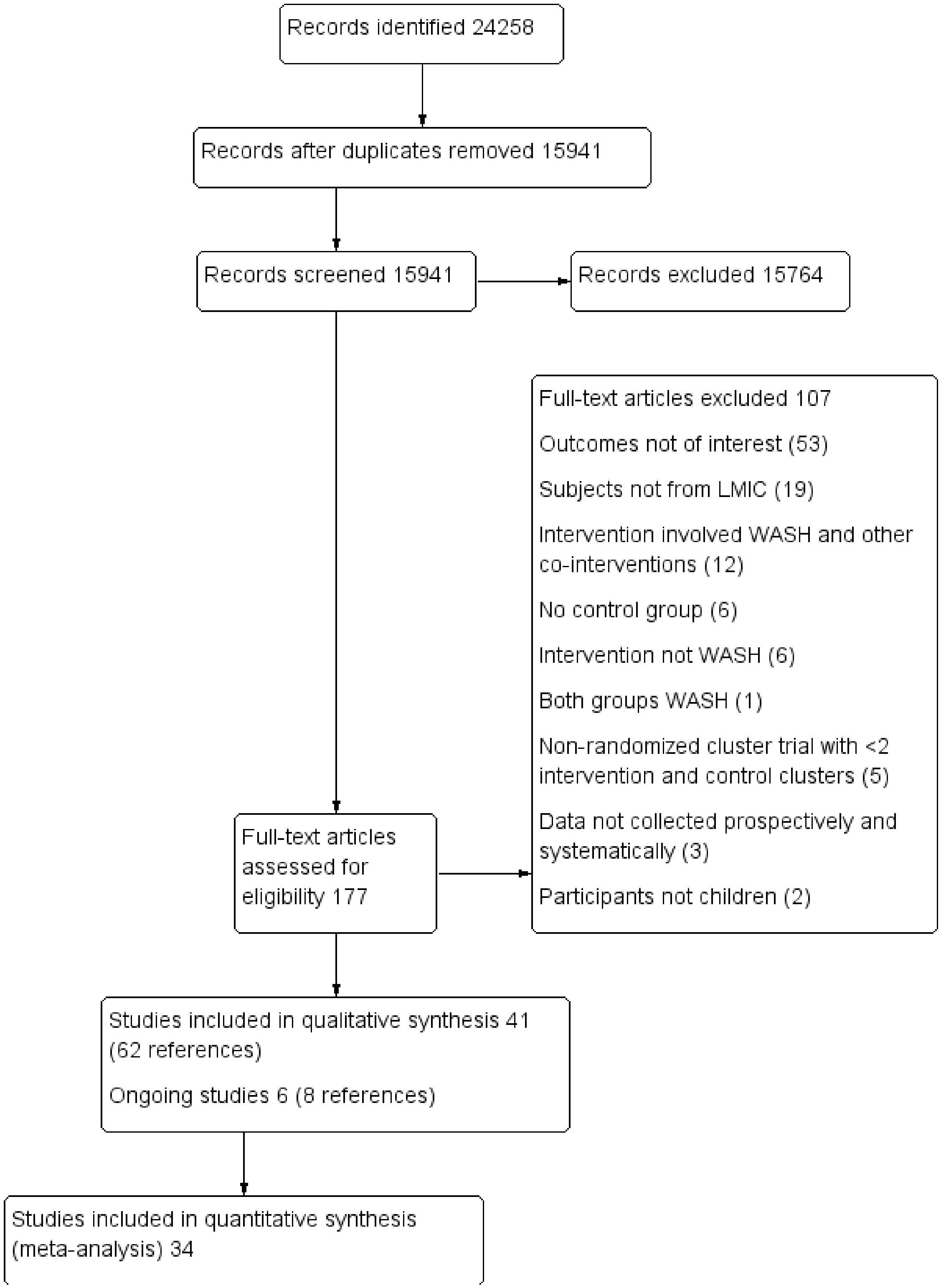


***Fig.* 1** *The PRISMA flow chart.*

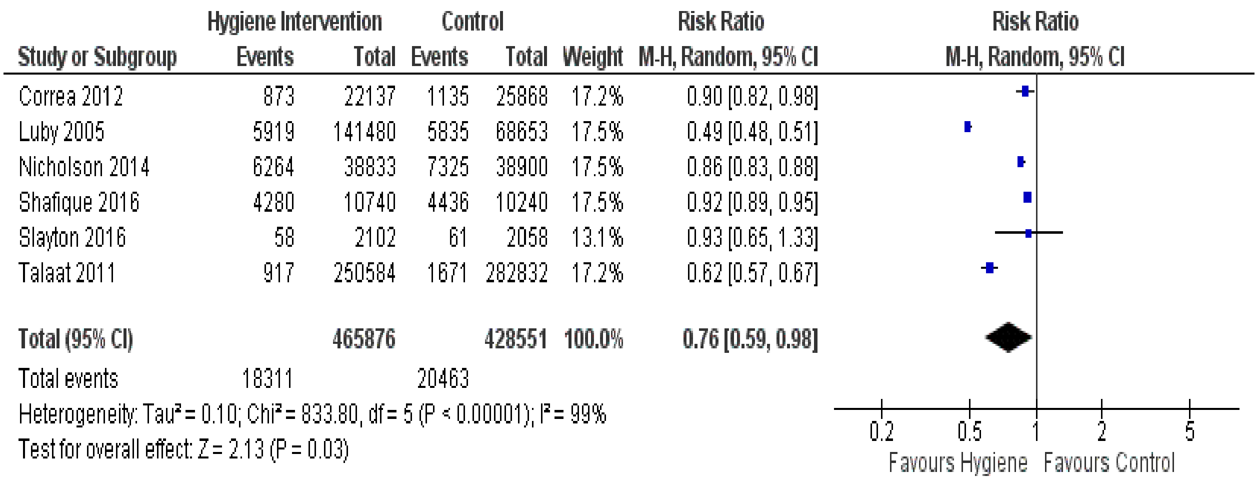


Fig. 2 Forest plot of effect of Hygiene intervention versus no Intervention on incidence of acute respiratory infections (episodes/person-week).

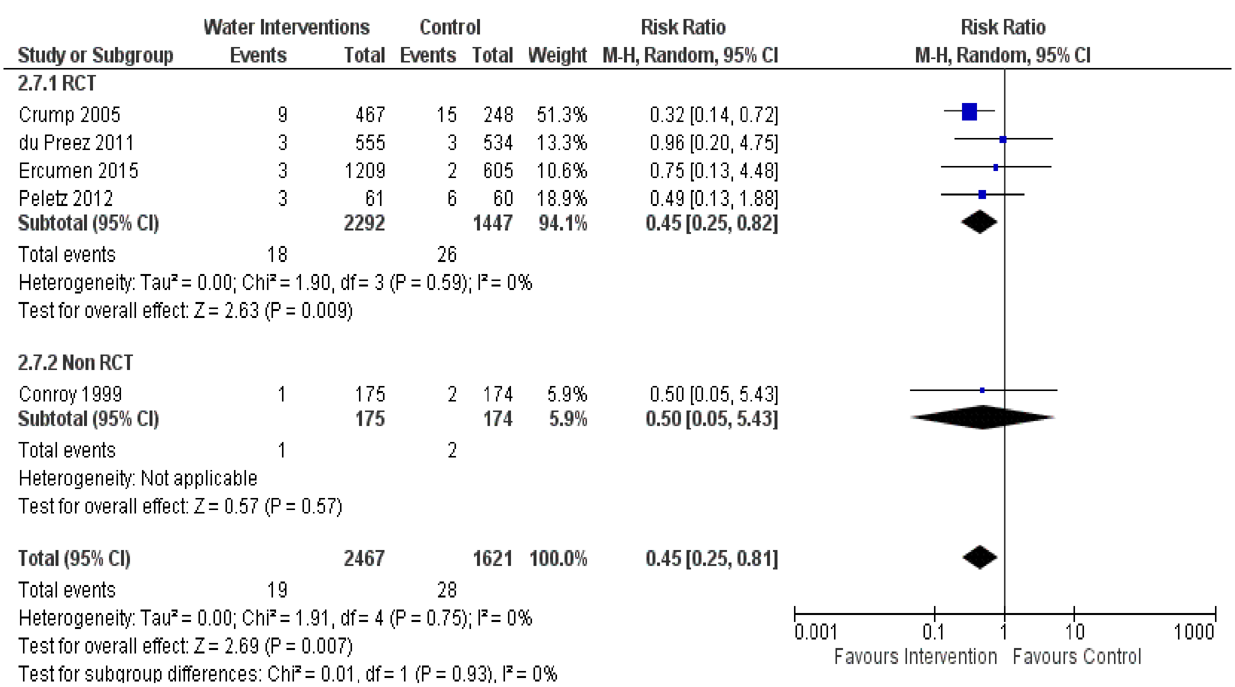


Fig. 3 Forest plot of effect of Water intervention on mortality.

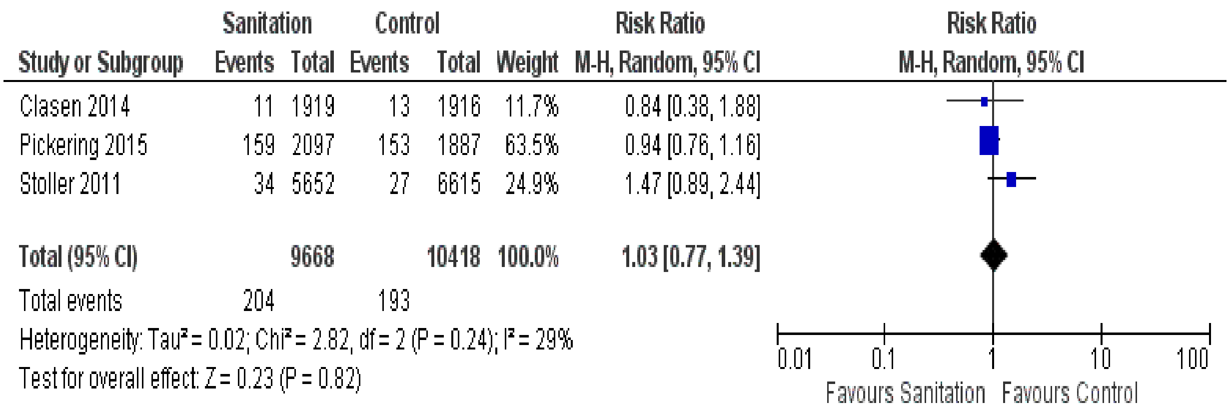


***Fig.* 4** *Forest plot of effect of Sanitation versus no intervention on mortality (<10 years).*

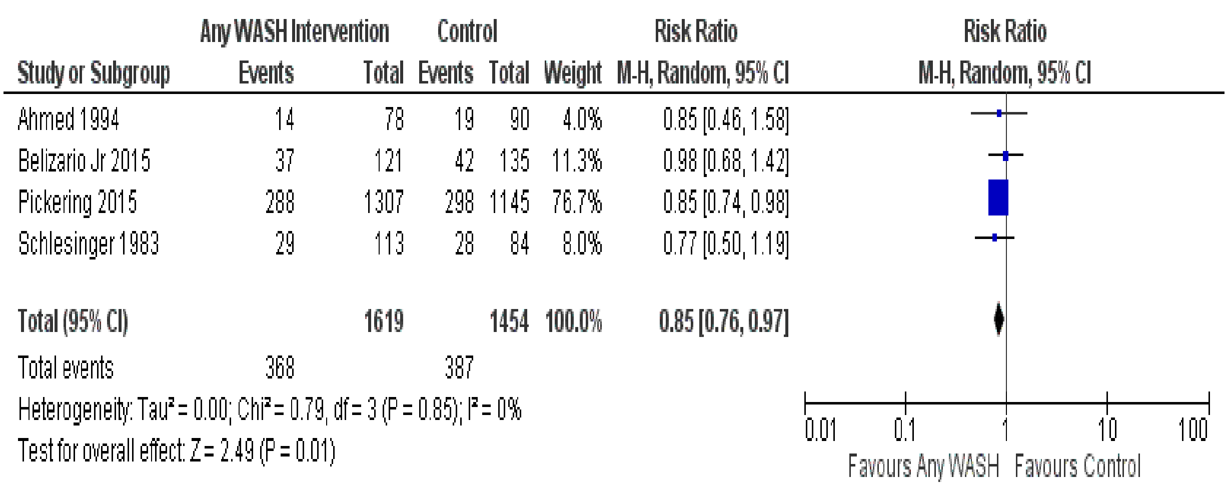


***Fig.* 5** Forest plot of effect of any WASH Intervention on risk of underweight (low weight-for-age).

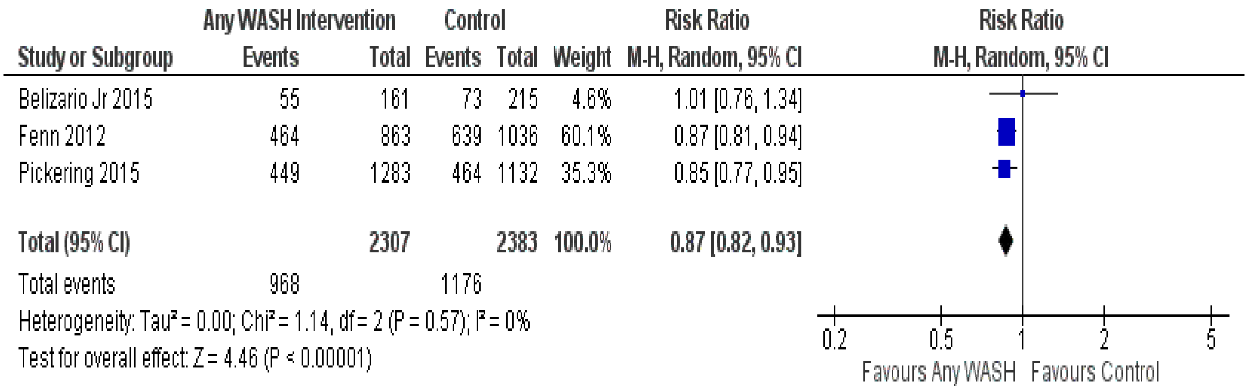
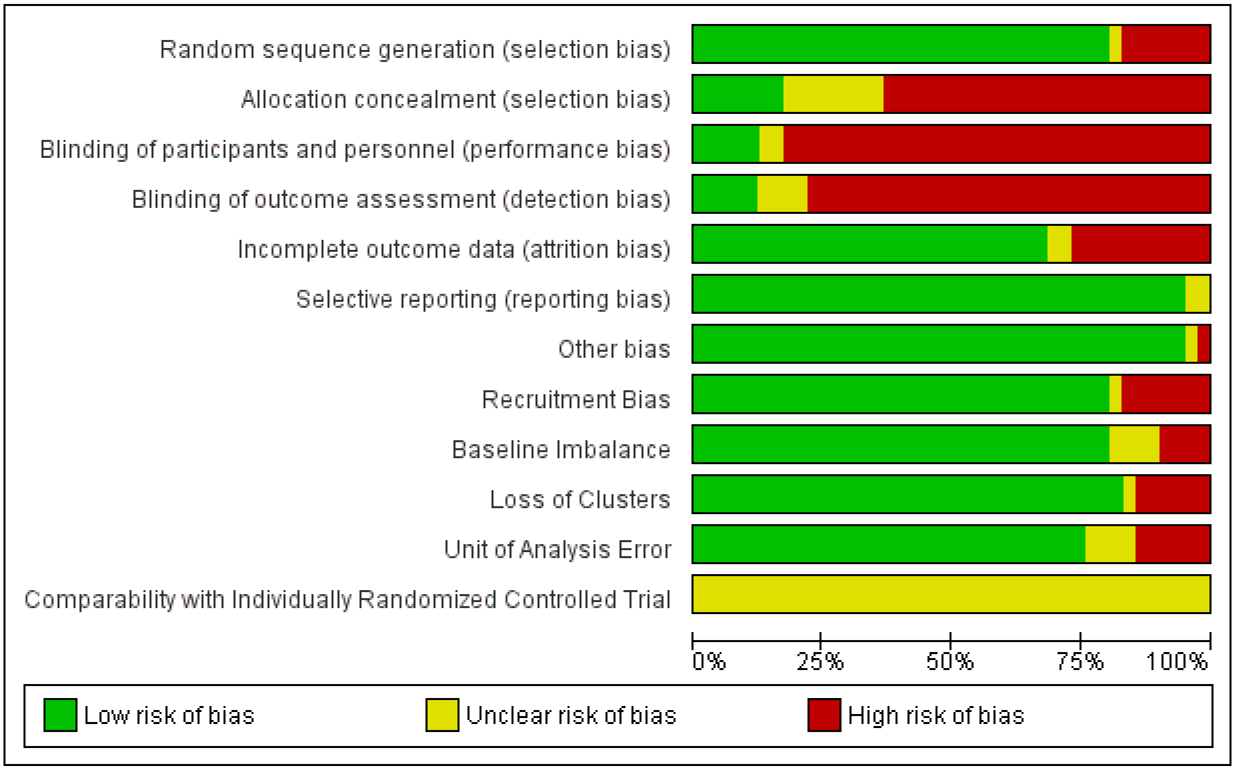
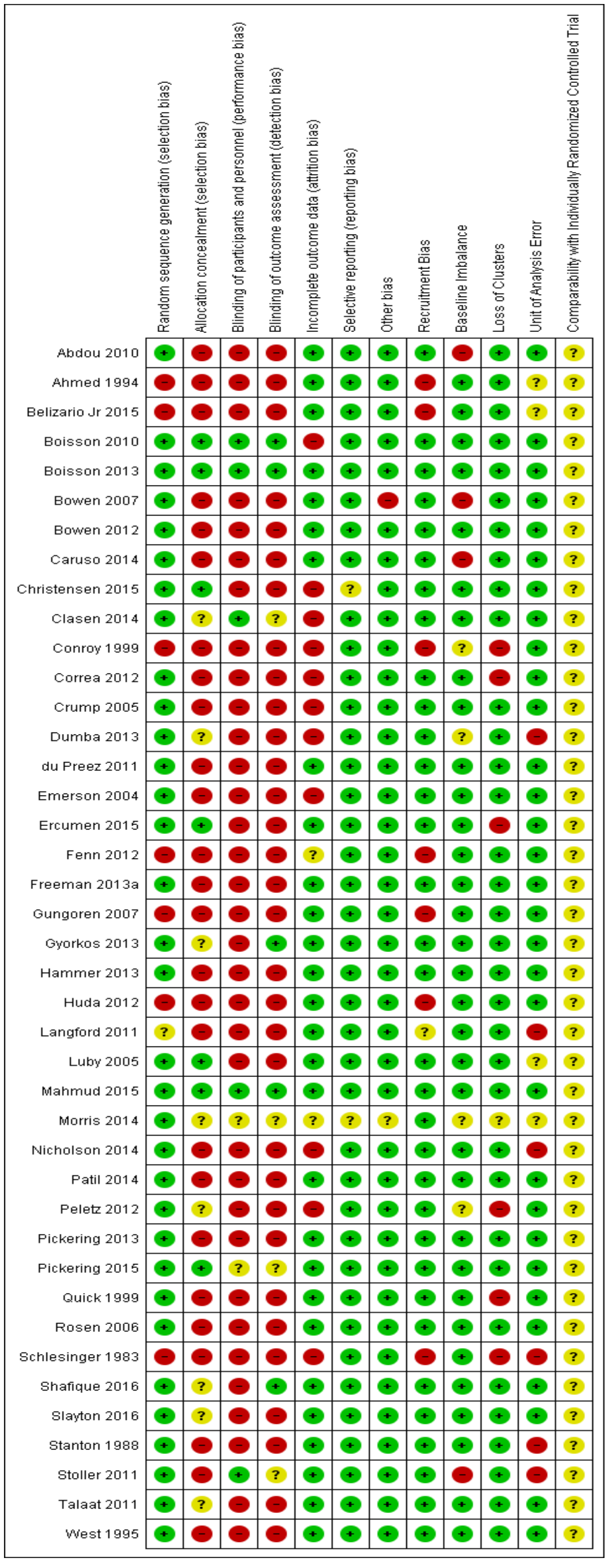


***Fig.* 6** *Forest plot of effect of any WASH Intervention on risk of stunting (low height-for-age).*



***Web Fig.* 1** *Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.*



Web Fig. 2 Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

WEB APPENDIX 1 ASSUMPTIONS AND CALCULATIONS FOR IMPUTATION/INTERPRETATION OF DATA FROM STUDIES INCLUDED IN THE SYSTEMATIC REVIEW

Slayton 2016

1. The total number of participants is not provided in the published paper. The number is assumed from the total number of households and the median number of two children per household.
2. The number of episodes of infection are the reported episodes of illness in the 'past' 48 hours during biweekly visits to the households.
3. The denominator of person weeks calculated by dividing the number of biweekly visits by half.

Shafique 2016

1. The data from ‘Hand Sanitiser Only’ and ‘Hand Sanitiser and Micronutrient’ groups combined as intervention and Control, and ‘Micronutrient Only’ groups combined as control.
2. The episodes of cough were diagnosed if the child reported to have any sort of cough or difficulty breathing. An upper respiratory tract infection was diagnosed if the mother reported symptoms of a stuffy or runny nose in her child. Both the episodes are presented separately, and combined under the section 'ARI'.

Pickering 2015

1. The infection episodes are mean proportions expressed by respondents in a 2-week recall period.
2. Respiratory infections were described under three headings: congestion, cough and difficulty breathing. Here cough is included assuming it would be a common symptom for upper and lower respiratory infections.

Patil 2014

The confidence intervals for the change in means is given. The SD is calculated with the assumption that they are the same for both the groups as calculated for Clasen 2014.

Clasen 2014

1. The individual SDs for weight-for-age and length-for-age Z-scores for the control and intervention groups was not available from the intervention data. However, the effect size (difference in mean) and its 95% CI was available. The SD for the two groups was calculated from 95% CI or SE as per standard statistical recommendations.
2. For Soil Transmitted Helmenthiasis, the mean prevalence of the entire population is given. The prevalence was assumed to be the same for children and numbers calculated from there.

Pickering 2013

The number of school absence was calculated from the percentages given. Only one week data was given and this is represented as such in the calculations.

Freeman 2013a

1. A total of 1113 students were assessed at follow up. The split numbers of intervention and control groups were not provided. However, the median populations at the time of second follow up were given as 302 for intervention and 275 for control group. The total population was split in the same proportion.

For intervention, *n* = (302/577)*1113=583

For control, *n* = 530

2. Only the percentage prevalence of helminth infection was mentioned. The individual numbers were calculated from percentages.

3. The same procedure was followed for school absence
4. SE converted to SD. Pupil reported absence used for quantitative analyses

<u>Peletz 2012</u>

For weight-for-age Z scores, the mean scores at the end and P value were mentioned.

Mean intervention=-1.21; Mean control = -1.24; *P*=0.92

n for intervention=61; *n* for control =60

From p to t: Degree of freedom 61+60-2 =119

t=2.358 (from table)

SE=MD/t = -1.21+1.24/2.358 = 0.03/2.358 = 0.0127

SD = 0.0127/0.178 = 0.071

<u>Bowen 2012</u>

SD derived from 95% CI using SD=sqrtn(UL-LL)

<u>Rosen 2006</u>

1. Absenteeism was analyzed in terms of the percentage of days the child was absent; number of days calculated from percentage and n.
2. There were a total of 66 days of study period. Person-weeks of exposure calculated from *n* and this figure.

<u>Crump 2005</u>

This study provided the number of deaths in children less than 5 years of age but not the total number of children. Based on the inclusion criteria, the total number of children less than 2 years is provided. We have this number as the denominator while analyzing the mortality data assuming that the proportion of children between 2-5 years would be the same in the intervention and control groups.

<u>Emerson 2004</u>

The number of children less than 9 years and number with trachoma calculated from percentage figures.

WEB APPENDIX 2 DETAILS OF DATABASE SEARCH

Database	*Date*	*Search Strategy*	*Number of references*
Medline	August 26, 2016	Water (Mesh Terms) OR Drinking Water (Mesh Terms)OR Water Quality (Mesh Terms) OR Water Purification (Mesh Terms) OR Water Supply (Mesh Terms) OR Sanitation (Mesh Terms) OR Environmental Health (Mesh Terms) OR Sanitary Engineering (Mesh Terms) OR Waste Disposal (Mesh Terms) OR Refuse Disposal (Mesh Terms) OR Drainage, Sanitary (Mesh Terms) OR Waste Management (Mesh Terms) OR Toilet Facilities (Mesh Terms) OR Hygiene (Mesh Terms) OR Hygiene, hand (Mesh Terms) OR Hand disinfection (Mesh Terms) Filters: Clinical Trial	4888
Web of Science (including Biosis Previews)	August 26, 2016	TOPIC: ('Water or Drinking Water or Water Quality or Water Purification or Water Supply or Sanitation or Environmental Health or Sanitary Engineering or Waste Disposal or Refuse Disposal or Drainage, Sanitary or Waste Management or Toilet Facilities or Hygiene or Hygiene, hand or Hand disinfection) Refined by: TOPIC: (child) AND TOPIC: (Clinical Trial)	4035
Cochrane Controlled Trials Register	August 26, 2016	'Water OR Drinking Water OR Water Quality OR Water Purification OR Water Supply OR Sanitation OR Environmental Health OR Sanitary Engineering OR Waste Disposal OR Refuse Disposal OR Drainage, Sanitary OR Waste Management OR Toilet Facilities OR Hygiene OR Hygiene, hand OR Hand disinfection in Keywords in Trials'	7900
Embase	August 27, 2016	'Water or Drinking Water or Water Quality or Water Purification or Water Supply or Sanitation or Environmental Health or Sanitary Engineering or Waste Disposal or Refuse Disposal or Drainage, Sanitary or Waste Management or Toilet Facilities or Hygiene or Hygiene, hand or Hand disinfection).mp. (mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword) limit 1 to (human and clinical trial and child <unspecified age>)	1182
LILACS	August 28, 2016	Water OR Drinking Water OR Water Quality OR Water Purification OR Water Supply OR Sanitation OR Environmental Health OR Sanitary Engineering OR Waste Disposal OR Refuse Disposal OR Drainage, Sanitary OR Waste Management OR Toilet Facilities OR Hygiene OR Hygiene, hand OR Hand disinfection as Subject Descriptor	564
Popline	August 29, 2016	Searched under Popline Topic ‘Population Health and Environment’ the subtopics Sanitation and Water Quality and Hygiene. It included keywords:Sanitation or Water Supply or Hygiene or Health Education or Water Quality or Disease Prevention and Control or Delivery of Health Care or Education or Slums or Community Development or Waste Management	3608
Greysource (Open Grey)	August 29, 2016	Water OR Sanitation OR Hygiene discipline:(06E - Medicine)	2081

WEB TABLE I CHARACTERISTICS OF INCLUDED STUDIES

Study	*Design*	*Country*	*Continent*	*Age group*	*N*			*Intervention category*	*Intervention details*	*Outcome of interest*
					Total	*Intervention*	*Control*			
Slayton 2016	Cluster RCT	Kenya	Africa	< 2 y	738			Hygiene	Antimicrobial Hand Towel	Acute respiratory infections, self-reported fever, and skin infections in children
Shafique 2016	Cluster RCT	Banglad esh	Asia	0-12 mo	467	236	231	Hygiene	Hand Sanitiser	Stunting, Infections
Pickering 2015	Cluster RCT	Mali	Africa	< 5 y	6012	3140	2872	Sanitation	Community-led total sanitation (CLTS) uses participatory methods to eliminate the practise of open defecation in rural communities and promote building of toilets.	Respiratory Tract Infections, Anthropometry, Mortality
Patil 2014	Cluster RCT	India	Asia	< 5 y	5209	2600	2609	Sanitation	Subsidies for and promotion of individual household latrines that can safely confine feces (similar to Joint Monitoring Programme defined improved sanitation facilities), school sanitation and hygiene education, Anganwadi (preschool) toilets, and community sanitation complexes.	Respiratory tract infections, Anthropometry, Worm infestation
Mahmud 2015	Cluster RCT	Ethiopia	Africa	6-15 y	367	185	182	Hygiene	Handwashing, Nail Clipping	Worm Infestation
Ercumen 2015	Cluster RCT	Banglad esh	Asia	6 mo-5 y	1814	1209	605	Water	Safe storage and/or water treatment	Mortality
Christensen	Cluster	Kenya	Africa	4-16	432	198	234	Water,	Water treatment, sanitation	Respiratory Tract

2015	RCT			mo				Sanitation and Hygiene	improvement, health education	Infections, Fever, Growth studied (data not provided)
Belizario 2015	CBA study	Philipin es	Asia	2-15 y	341	150	191	Sanitation	Community-led total sanitation (CLTS) uses participatory methods to eliminate the practise of open defecation in rural communities and promote building of toilets.	Worm Infestation, Anthropometry
Nicholson 2014	Cluster RCT	India	Asia	< 5 y	1680	847	833	Hygiene	Handwashing promotion and provision of free soap	Respiratory Infections, School Absence
Morris 2014	Cluster RCT	Kenya	Africa	4-10 mo	240			Water	Ceramic water filters (CWFs) remove or inactivate waterborne diarrheal pathogens in drinking water through size exclusion and silver exposure.	Respiratory Infections, Febrile Illness
Clasen 2014	Cluster RCT	India	Asia	0-5 y	3835	1919	1916	Sanitation	Latrine promotion and construction by combining social mobilisation with a post-hoc subsidy.	Helminth Infection, Weight, Height, Mortality
Caruso 2014	Cluster RCT	Kenya	Africa	School childre n	17564	12262	5302	1. Sanitation and Handwashin g vs Control; Handwashin g vs Control; Sanitation and Handwashin	Sanitation: Schools received reusable hardware (buckets, brooms, hand brushes, plastic scoop), consumables (bleach, powdered soap), toilet tissue, handwashing materials, sheets for pupils to monitor latrines conditions daily and training for two	School Absence

								g vs Handwashin g	teachers – the head teacher and health patron. Handwashing: Received powdered soap and instructions on how to make soapy water	
Pickering 2013	Cluster RCT	Nairobi	Africa	School childre n	1364	895	469	Hygiene	Provision of soap and water or hand sanitizers for hand hygiene	Vomiting, cough, difficulty breathing, skin rash, rhinorrhea, school absence
Hammer 2013	Cluster RCT	India	Asia	Under 5 years				Sanitation	Latrine promotion and construction by combining social mobilisation with a subsidy.	Height
Gyorkos 2013	Cluster RCT	Peru	South America	10 y	1089	518	571	Hygiene	Hygiene Education	Soil Transmitted Helminthiasis prevalence
Freeman 2013a	Cluster RCT	Kenya	Africa	School childre n	915	470	445	Water, Sanitation and Hygiene; Water and Hygiene	Hygiene promotion, water treatment technology, and sanitation infrastructure, which included commercially manufactured hand washing and drinking water storage containers and a 1-year supply of point-of-use water treatment product distributed by Population Services International with the brand name WaterGuard.	Soil Transmitted Helminthiasis prevalence
Dumba 2013	Cluster RCT	Uganda	Africa	Under 5 years	727	357	370	Sanitation and Hygiene	PHAST means Participatory Hygiene and Sanitation Transformation; a participatory approach	Soil Transmitted Helminthiasis prevalence

									that uses visual tools to stimulate the participation of people in promotion of improved hygiene and sanitation.	
Boisson 2013	Cluster RCT	India	Asia	All children	2986	1504	1482	Water	Intensive promotion campaign and free distribution of sodium dichloroisocyanurate (NaDCC) tablets	Weight-for-age Z score; school absenteeism
Peletz 2012	Cluster RCT	Zambia	Africa	<2 y	121	61	60	Water	LifeStraw Family filter and two 5-L safe storage containers.	Weight-for-age Z score, Mortality
Huda 2012	CBA study	Bangladesh	Asia	< 5 y	1000	500	500	Water, Sanitation and Hygiene	Improvements in latrine coverage and usage; access to and use of arsenic-free water; and improved hygiene practices, especially handwashing with soap.	Acute Respiratory Infections
Correa 2012	Cluster RCT	Colombia	South America	1-5 y	1682	749	933	Hygiene	Alcohol based hand sanitiser	Acute Respiratory Infections
Bowen 2012	Cluster RCT	Pakistan	Asia	< 8 y	461	301	160	1. Hygiene; 2. Water and Hygiene	10 clusters received sodium hypochlorite solution for drinking water treatment; 9 received a flocculent-disinfectant product for drinking water treatment; 10 received soap, handwashing promotion, and flocculent disinfectant for drinking water treatment; 9 received soap and handwashing promotion; and 9 served as the control group.	Weight for age z score, Height for age Z score, Body Mass Index z score on long term follow up

Fenn 2012	CBA study	Ethiopia	Africa	6 mo-3 y	1899	863	1036	Water, sanitation and hygiene	Hygiene education, pit latrines, treated water	Height for age Z score, Stunting
Talaat 2011	Cluster RCT	Egypt	Africa	Median 8 y	44451	20882	23569	Hygiene	Provision of soap and water and education	Acute Respiratory Infection, Influenza, Conjunctivitis, School absenteeism
Stoller 2011	Cluster RCT	Ethiopia	Africa	0-9 y	1211	608	603	Sanitation	Latrine construction	Ocular chlamydia infection; Trachoma
du Preez 2011	Cluster RCT	Kenya	Africa	6 mo - 5 y	1089	555	534	Water	Solar disinfection of water	Mortality, weight for age, height for age, weight for height
Langford 2011	Cluster non-RCT	Nepal	Asia	3-12 mo	88	45	43	Hygiene	Handwashing promotion	Weight for age z score, Height for age Z score, Weight for Height z score, cough, cold, fever
Bosisson 2010	Cluster RCT	Congo	Africa	0-15 y	190	85	105	Water	Lifestraw Family filter for water treatment	Fever, Cough
Abdou 2010	Cluster RCT	Niger	Africa	< 5 y	557	284	273	Water	Wells and Handpump	Ocular chlamydia infection; Trachoma
Gungoren 2007	Cluster non-RCT	Uzbekistan	Asia	2-14 y	178	95	83	Water, Sanitaion and Hygiene	Hand washing with soap, safe disposal of feces and boiling of drinking water.	Soil Transmitted Helminthiasis prevalence
Bowen 2007	Cluster RCT	China	Asia	School children	3810	2545	1265	Hygiene	Handwashing promotion, soap provision	School Absence, Fever, Headache, Otalgia, Rhinnorhea, Conjunctivitis, Sore Throat, Cough, Vomiting
Rosen 2006	Cluster RCT	Israel	Asia	Pre - school children	1029	489	540	Hygiene	Handwashign promotion, eliminating shared cups and towels	School absence
Luby 2005	Cluster RCT	Pakistan	Asia	< 15 y	4691	3163	1528	Hygiene	Handwashing promotion, soap provision	Acute Respiratory Infection, Pneumonia,

										Impetigo, Mortality
Crump 2005	Cluster RCT	Kenya	Africa	< 5 y	715	467	248	Water	Flocullent disinfectant and sodium hypochlorite	Mortality
Emerson 2004	Cluster RCT	Gambia	Africa	<9 y	179	83	96	Sanitation	Latrine construction	Trachoma
Quick 1999	Cluster RCT	Bolivia	South America	< 14 y	403	199	204	Water	Point of use water chlorination and safe storage	Soil Transmitted Helminthiasis prevalence
Conroy 1999	Cluster non-RCT	Kenya	Africa	< 6 y	349	175	174	Water	Solar disinfection of water	Mortality
West 1995	Cluster RCT	Tanzania	Africa	1-7 y	1417	680	737	Hygiene	Facewashing	Trachoma
Ahmed 1994	Cluster non-RCT	Pakistan	Asia	0-18 mo	168	78	90	Hygiene	Hygiene education focusing on ground sanitation, personal hygiene and food hygiene	Weight for age z score
Stanton 1988	Cluster RCT	Bangladesh	Asia	< 6 y	1390	636	754	Hygiene	Education regarding handwashing, defecation away from house and suitable disposal of waste and faeces	Weight, Height, Weight for age z score, Height for age Z score, Weight for Height z score
Schlesinger 1983	CBA study	Chile	South America	0-4 y	197	113	84	Water and Sanitation	Construction of a sanitary unit consisting of a kitchen, sink and lavatory with water supply	Low weight for age

CBA: Controlled before-after; RCT: Randomized controlled trial