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Systematic Review

Impact of drinking water, sanitation and handwashing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression

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Abstract

OBJECTIVES Safe drinking water, sanitation and hygiene are protective against diarrhoeal disease; a leading cause of child mortality. The main objective was an updated assessment of the impact of unsafe water, sanitation and hygiene (WaSH) on childhood diarrhoeal disease.
METHODS We undertook a systematic review of articles published between 1970 and February 2016. Study results were combined and analysed using meta-analysis and meta-regression.
RESULTS A total of 135 studies met the inclusion criteria. Several water, sanitation and hygiene interventions were associated with lower risk of diarrhoeal morbidity. Point-of-use filter interventions with safe storage reduced diarrhoea risk by 61% (RR = 0.39; 95% CI: 0.32, 0.48); piped water to premises of higher quality and continuous availability by 75% and 36% (RR = 0.25 (0.09, 0.67) and 0.64 (0.42, 0.98)), respectively compared to a baseline of unimproved drinking water; sanitation interventions by 25% (RR = 0.75 (0.63, 0.88)) with evidence for greater reductions when high sanitation coverage is reached; and interventions promoting handwashing with soap by 30% (RR = 0.70 (0.64, 0.77)) *vs*. no intervention. Results of the analysis of sanitation and hygiene interventions are sensitive to certain differences in study methods and conditions. Correcting for non-blinding would reduce the associations with diarrhoea to some extent.
CONCLUSIONS Although evidence is limited, results suggest that household connections of water supply and higher levels of community coverage for sanitation appear particularly impactful which is in line with targets of the Sustainable Development Goals.

keywords diarrhoea, hygiene, meta-analysis, sanitation, review, water

Introduction

The Sustainable Development Goals (SDGs) adopted by 193 Member States at the UN General Assembly in 2015 aim to substantially improve water and sanitation globally and include two specific targets within Goal 6 for drinking water, sanitation and hygiene (WaSH) [1]:

- 6.1 By 2030, achieve universal and equitable access to safe and affordable drinking water for all.
- 6.2 By 2030, achieve access to adequate and equitable sanitation and hygiene for all and end open defecation, paying special attention to the needs of women and girls and those in vulnerable situations.

Progress towards the Millennium Development Goals (MDGs) which preceded the SDGs was monitored globally based on the use of improved drinking water supplies and sanitation facilities. The SDGs aim at higher water and sanitation service provision and are being monitored

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Table 1 Global indicators for drinking water, sanitation and hygiene in the MDG and SDG periods

	MDG Indicator	SDG Indicators and further details
Drinking water	Proportion of population using an improved drinking water source*	Proportion of population using safely managed drinking water services† Safely managed drinking water services: Use of an improved drinking water source, which is located on premises, available when needed, and compliant with faecal and priority chemical standards‡ Basic drinking water services: use of an improved drinking water source provided collection time is not more than 30 min for a roundtrip including queuing‡ Limited drinking water services: use of an improved drinking water source where collection time exceeds 30 min for a roundtrip to collect water including queuing‡
Sanitation	Proportion of population using an improved sanitation facility which is not shared with other households*	Proportion of population using safely managed sanitation services, including a handwashing facility with soap and water† Safely managed sanitation services: Use of an improved sanitation facility which is not shared with other households, and where excreta are safely disposed *in situ* or transported and treated offsite‡ Basic sanitation services: Use of an improved sanitation facility which is not shared with other households‡ Limited sanitation services: Use of an improved sanitation facility which is shared between two or more households‡
Hygiene	None	Proportion of population using safely managed sanitation services, including a handwashing facility with soap and water†

MDG, Millennium Development Goal; SDG, Sustainable Development Goal.
*Official list of MDG indicators (United Nations Statistics Division 2008).
†Official list of SDG Indicators (Division 2016).
‡For a listing of improved drinking water sources and sanitation facilities, see https://washdata.org/.

using indicators which include elements of service quality that were not captured by the MDG indicators (Table 1) [2]. Moreover, while the MDGs did not include a hygiene target, SDG 6 specifically includes a place for handwashing with water and soap in the household.

Achieving the SDG WaSH targets will be challenging. In 2015, only 68% of the world population used improved sanitation, meaning that 2.4 billion people still lacked even simple sanitation facilities like pit latrines and septic tanks. Although 91% of the world population used improved drinking water sources in 2015, 663 million people still used unimproved sources such as unprotected springs, wells and surface water [3]. Furthermore, it has been estimated that 10% of improved drinking water sources are heavily contaminated with faecal material, that is, contain at least 100 *Escherichia coli* or thermotolerant coliform bacteria per 100 ml [4], underlining that improved water sources do not guarantee water that is safe for drinking. Estimates suggest that only 19% of the world population washes hands with soap after contact with excreta [5]. Those that lack access are typically the poorest and most marginalised, which adds importantly to the costs and the efforts of reaching universal coverage [3].

Inadequate WaSH is considered as an important risk for diarrhoea [6–8] and has been linked to many other adverse health- and non-health consequences, such as other infectious diseases, poor nutritional status, reduced security and spare time [9–13]. Diarrhoea remains among the most important causes for global child mortality and is estimated to account for approximately 600 000 deaths in children under 5 years annually [14].

This updated systematic review and meta-analysis provide new estimates for the impact of WaSH interventions on childhood diarrhoea. New WaSH studies have been published including studies on continuous water supply and rigorous studies of improved sanitation which permit adaptation and extension of the exposure scenarios previously presented and which better align with the SDG6 targets for water, sanitation and hygiene improvements. Our updated analysis of the latest evidence on water, sanitation and hygiene and diarrhoea is key for guiding the choice of interventions according to their potentially highest health benefits and provides a basis for estimating the global burden of disease from WaSH.

Methods

The protocol for this study was agreed, in advance, by an expert group convened by WHO in 2013. Participating experts who took part in this initial meeting are listed in Appendix S4. The update of this systematic review is registered within PROSPERO [15] under the registration number CRD42016043164. Appendix S1 shows the

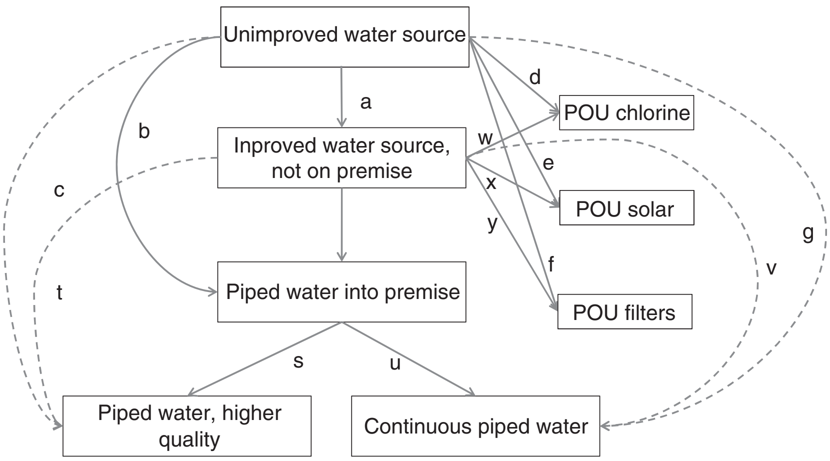

Figure 1 Conceptual framework for the analysis of drinking water studies. POU: point-of-use; ⟶ direct evidence available, – → effect estimated indirectly, 'improved water source' according to the WHO/UNICEF Joint Monitoring Programme (JMP) not including piped water into premises, POU chlorine includes chlorination and flocculation; additional covariates are examined in meta-regression.

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.

Systematic literature review

Selection criteria and search strategy. We included any study reporting the effect on diarrhoea morbidity in children less than 5 years of age of any WaSH intervention providing they reported sufficient data to allow for characterisation in accordance with the conceptual models for WaSH that were generated by mapping the available evidence (Figures 1 and 2) [16]. More information on the conceptual framework is given in the paper on the initial systematic review [16]. If data on children under five were not available, we included estimates for all ages or older children. Only studies with a clearly specified intervention matching our pre-defined exposure scenarios (Figures 1 and 2) that provided improved household or community water supply or sanitation facilities or promoted handwashing with soap were included in this review. Interventions needed to be tested against a control group that did not receive the respective intervention (s) or that received a control or placebo intervention. Eligible study designs included

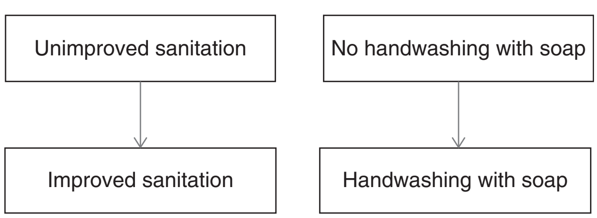

Figure 2 Conceptual frameworks for the analysis of sanitation and hygiene studies. Additional covariates are examined in meta-regression.

- randomised (including individual and cluster randomised) controlled trials;
- quasi-randomised and non-randomised controlled trials, the latter when baseline data on the main outcome were available before the intervention was conducted (i.e. before and after studies with a concurrent control group);
- case–control and cohort studies when they were related to a clearly specified intervention;
- studies using time-series and interrupted time-series design; and
- studies without a clearly specified intervention analysing cross-sectional household survey data but with appropriate matching methods to permit causal inference [17].

For the purpose of this analysis, we will refer to studies listed under 1. to 4. as 'studies evaluating specific interventions' and studies listed under 5. 'survey data analyses'.

We included single and combined water and sanitation interventions that reported relative risk estimates or the relevant data for their calculations. For water and sanitation, we restricted study location to households in low- and middle-income settings, that is low- and middle-income countries according to the World Bank classification [18] and interventions in low-income settings in high-income countries, whereas for hygiene, we also included studies performed in institutions such as daycare centres/homes and primary schools from high-income settings because we assume these settings represent the high potential for faecal pathogen transmission. We only included hygiene interventions that included a handwashing component and excluded interventions concerning hand sanitisers such as alcohol-based handrubs in Correa *et al.* [19]. For the water and sanitation analysis, we excluded studies that mainly targeted institutions like schools or the work place and, in general, we excluded studies where the study population was considered to be non-representative with regard to the exposure–outcome relationship of interest (e.g. interventions targeting HIV+ population). Included effect estimates were usually based on intention-to-treat analyses rather than estimates in those who actually adopted the intervention, despite often low compliance levels.

Interventions including both a drinking water and a sanitation component were included in both water and sanitation analysis. As hygiene interventions are often added as an additional component to water and sanitation interventions, studies included in the hygiene analysis needed to report effect estimates separately for the hygiene component, needed to be exclusive hygiene interventions or to clearly have the hygiene intervention as the main component.

Studies were included in the review only if they were published in a peer-reviewed scientific journal in English or French or to have been assessed according to transparent criteria for methodological quality in a previously conducted systematic review. Studies published in languages other than English or French were included provided the relevant data were available in a previous systematic review published in English or French.

Non-randomised studies with baseline differences in diarrhoea occurrence that were not accounted for in the analysis were not included in the analyses as the effect estimate related to the intervention could not reasonably be estimated.

We systematically searched Pubmed, Embase, Scopus and Cochrane Library using both keywords and MeSH terms to identify WASH studies and their impact on diarrhoeal disease. The update covered the search between 1 January 2012 and early 2016 (February for the search on water and sanitation interventions and May for hygiene). As such the systematic review now covers studies published from 1970 until early 2016 [16]. The search strategy and search terms for the four databases are detailed in Appendix S2. The reference sections of systematic reviews on WaSH were also searched. References were also provided from subject-matter experts, including co-authors of this study and those included in the acknowledgements section.

Data extraction and quality assessment. Study title and abstract screening, data extraction and quality assessment were primarily performed by a single reviewer. A second reviewer subsequently checked inclusion of studies and data extraction. Data extraction was carried out using a structured and piloted form [16]. Differences between reviewers over data extraction were reconciled with a third reviewer, where required. Authors were contacted for additional details when required for extraction or calculation of effect estimates or classification of the studies.

Study quality was assessed using a revised and previously published version [20] of the Newcastle-Ottawa scale [21] that we used in our previous reviews for WaSH interventions [5, 16]. Quality criteria were adapted for studies evaluating specific interventions and survey data analyses (Appendix S5). Study quality scores were used to identify and exclude the lowest-rated studies for sensitivity analyses.

Where possible we extracted the adjusted relative risk from the paper in the following order of preference:

1. longitudinal prevalence ratio, that is the proportion of time ill,
2. prevalence ratio/risk ratio,
3. rate ratio,
4. odds ratio.

When these values were not given in the paper, we calculated relative risks and confidence intervals from data presented in the paper. Where confidence intervals could not be calculated, the study was excluded from meta-analysis. Standard errors of the log relative risk were calculated using standard formulae [22]. Odds ratios can overstate the estimated intervention effect especially when the respective disease is frequent and effect estimates are large (further away from 1) [23]. Therefore, odds ratios were converted to risk ratios using the control group risk as given in the respective paper [22, 24]. Risk ratios, prevalence ratios, rate ratios and means ratios were combined without any conversion.

For one study presenting adjusted odds ratios [25], the control group risk was not given. Effect estimates of this study were included as odds ratio. We, however, performed a sensitivity analysis converting the odds ratios of this study to risk ratios with a – conservatively high – assumed control group diarrhoea prevalence of 30% over the preceding week.

Where possible, we combined effect estimates across intervention arms falling within the same category (e.g. different methods for filtering drinking water at point of use). When multiple relevant effect estimates were given within a study, we included independent subgroups (separate intervention and separate control group in different settings) from a single study separately. In the case of multiple comparisons within a study (e.g. effect estimates for different POU water interventions) but with the same control group or different effect sizes across relevant age groups or for the same individuals over time, effect estimates were combined using methods described in

Borenstein *et al.* [26]. In brief, effect estimates from different participants, for example from different relevant age groups, were combined as independent subgroups, whereas different effect estimates on the same participants, for example collected at different time points, were combined taking into account the correlation between the effect estimates. In the case of water interventions, multiple comparisons were often not combined if the groups were not sufficiently similar (e.g. water intervention separately and water intervention plus hygiene education). In these cases, including factorial designs, we derived a single pairwise comparison of the most comprehensive intervention compared with the least comprehensive intervention (or control; comprehensive according to Figure 1 with, e.g. a piped water intervention being more comprehensive than an improved, not on premises water source). We, however, chose preferably intervention arms that did not combine different components of WaSH (e.g. water interventions without an additional hygiene or sanitation component).

Statistical analysis

General approach. Random effects meta-analysis was conducted separately by WaSH component to examine the association with diarrhoeal morbidity. Random effects meta-regression was used to examine drinking water interventions according to our conceptual framework (Figure 1) and to examine further pre-specified covariates as indicated below. Bayesian meta-regression was used to adjust study results of point-of-use drinking water treatment and hygiene interventions for non-blinding bias (described in more detail below). Following our previous approach [16], we adjusted only point-of-use and hygiene interventions for non-blinding bias as these interventions usually aim exclusively to improve health which is apparent to the recipient, whereas water and sanitation interventions that improve supply are often less apparent to the recipient and have aims beyond health such as community development, environmental hygiene benefits and time savings of water collection.

Possible publication bias was examined with inspection of funnel plots and the use of Egger's test. Analyses were performed with Stata 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Bayesian meta-regression and bias adjustments were performed using WinBUGS version 1.4 [27].

Analysis of drinking water interventions. The conceptual model for the analysis of drinking water interventions is shown in Figure 1. Interventions were grouped as structural changes in supply, for example, from unimproved over improved towards different levels of piped water to premises, and point-of-use treatment in the household, for example, chlorine, solar and filter treatment. As more studies have been published, our conceptual framework for the drinking water analysis has been adjusted to include two additional categories of piped water to premises services (Figure 1): treatment of piped water to improve its quality and a continuous supply of piped water (vs. an intermittent supply).

In Figure 1, transitions a to g present basic parameters in the meta-regression model, each represented by a covariate. All other transitions are coded as combinations of these parameters, specifically: $r = b - a$, $s = c - b$, $t = c - a$, $u = g - b$, $v = g - a$, $w = d - a$, $x = e - a$, $y = f - a$. The model allows the indirect estimation of transitions that have not been directly observed (including those representing basic parameters), following ideas of network meta-analysis [28]. The adapted exposure scenario aligns more closely with the SDGs which aim at higher water service provision than just improved water supply.

The *a priori* model for the meta-regression of drinking water interventions included seven binary variables presenting the basic parameters outlined in Figure 1 plus two additional variables, that is, whether safe water storage was provided and whether the intervention included also hygiene education and/or a sanitation intervention (from now called 'combined intervention'). The association of safe water storage and diarrhoea was estimated by including a binary covariate that was coded one for interventions providing a safe storage container (i.e. a container with a narrow opening that prevents the introduction of objects either separately or inherently in ceramic filter interventions). Additional assessed covariates included access to improved or unimproved sanitation in the study population, interventions in rural compared to urban or mixed areas, survey data analysis *vs.* studies evaluating specific interventions and time of follow-up in studies evaluating specific interventions. The covariates were examined as indicator variables and time of follow-up as indicator and as continuous variable. As sensitivity analyses, we excluded cross-sectional, non-intervention studies, non-randomised studies, the quintile of studies evaluating specific interventions with the lowest quality rating, studies that did not report on diarrhoea in children <5 years and studies published before 2012.

Blinding study participants in point-of-use drinking water interventions. Most WaSH interventions are unblinded and diarrhoea is self-reported in most intervention evaluation studies which may lead to biased reports of diarrhoea [29, 30]. We performed an additional analysis that incorporates bias adjustments for the POU water quality interventions based on empirical evidence [29]. This Bayesian meta-regression analysis was performed by subtracting a bias factor from the log risk ratio from each non-blinded study. This bias factor is based on 234 meta-analyses including a total of 1970 trials across a broad range of clinical areas, settings and types of experimental interventions including curative and preventive interventions [29]. The bias factor was given a prior distribution in the shape of a normal distribution with mean 0.25 and variance 0.2, reflecting findings from the BRANDO meta-epidemiological study [29]. Further descriptions of this approach can be found in Appendix S4.

Analysis of sanitation interventions. We examined the overall association between sanitation interventions and diarrhoea morbidity with random effects meta-analysis. We also examined the association of sewer connections and diarrhoea as compared to improved sanitation at the household-level alone using meta-regression with two binary variables to describe the transitions from unimproved to improved sanitation other than sewer and to sewer connections plus a binary variable indicating a combined intervention. We also examined a disaggregation of unimproved sanitation into open defecation and use of unimproved sanitation facilities in studies that disaggregated accordingly.

Other examined covariates were access to improved or unimproved drinking water in the study population at baseline, the level of community sanitation coverage reached after the intervention, whether the sanitation intervention provided sanitation promotion only as compared to interventions that provided also sanitation hardware (e.g. latrine construction or material), survey data analyses *vs.* studies evaluating specific interventions, time of follow-up in studies evaluating specific interventions and whether the intervention was a combined intervention, that is, aiming also at water or hygiene improvements. Community coverage was examined as indicator variable with two categories ≤75% and >75% sanitation coverage after the intervention and as a continuous variable (percentage with access to sanitation in the intervention group after the intervention). The choice of the categories was informed by a recent study that found changes in the relationship between sanitation and diarrhoea prevalence at about 75% [31]. Other covariates were examined as indicator variables and time of follow-up as indicator and as continuous variable. Time of follow-up as indicator variable in the analysis of sanitation studies was examined with a cut-off of 24 months as compared to the analysis of water and hygiene studies with a cut-off of 12 months to reflect the generally longer duration of sanitation studies (median duration of sanitation, water and hygiene interventions was 24, 8 and 8 months, respectively).

As sensitivity analyses, we excluded survey data analyses, non-randomised studies, the quintile of studies evaluating specific interventions with the lowest quality rating, studies that did not report on diarrhoea in children <5 years and studies published before 2012.

Analysis of hygiene interventions. The overall association between hygiene interventions and diarrhoea morbidity was examined using random effects meta-analysis, as were the following covariates using meta-regression: exclusive promotion of handwashing with soap *vs.* broader hygiene education, provision of soap, high-income *vs.* low- and middle-income countries, community *vs.* institutional (e.g. day-care, schools) interventions and time of follow-up in studies evaluating specific interventions. These were examined as indicator variables and time of follow-up as indicator and as continuous variable.

As sensitivity analyses, survey data analyses, non-randomised studies, the quintile of studies evaluating specific interventions with the lowest quality rating, studies that did not report on diarrhoea in children <5 years, studies published before 2012, studies in institutional settings, studies in household setting and studies from high-income countries were excluded.

An additional analysis was performed to adjust effect estimates of unblinded studies for the assumed effect of non-blinding bias as described before.

Results

Systematic literature search

Studies on water and sanitation were searched simultaneously, hygiene studies in a separate literature search. The electronic searches of four databases yielded 11 723 water and sanitation studies, along with a further 120 identified through scanning the reference sections of previous systematic reviews or provided from subject-matter experts, which was then reduced to 8700 after de-duplication. Separate electronic searches of the same four databases yielded 363 hygiene studies, along with a further nine identified through scanning the reference sections of previous systematic reviews, which was then reduced to 308 after de-duplication. Hence, 8779 and 308 titles and abstracts were screened respectively for water and sanitation, and hygiene, from which 80 full water and sanitation texts and 11 full hygiene texts were assessed for inclusion. Finally, 14 new water studies, eight new sanitation studies (Figure 3) and eight new hygiene studies (Figure 4) were included for quantitative meta-analysis alongside those studies identified in our previous water and sanitation [16] and hygiene [5] reviews. The complete databases therefore comprise 73 studies providing 80 observations for drinking water, 19 studies providing 22 observations for sanitation and 33 studies providing 33 observations for hygiene. Appendix S3 presents citations and characteristics for all WASH studies included in the analysis.

Analysis of drinking water interventions

We included 80 observations from 73 individual studies, with 14 additional observations from 14 studies not included in our previous review [16]. The number of observations describing each link between study baseline and outcome is listed in Table 2. Effect estimates of individual observations are listed in Appendix S3. Forest plots separated by type of drinking water intervention are shown in Appendix S4.

Random effects meta-analysis of all 80 observations yielded a pooled effect estimate of 0.67 (0.62, 0.73) with an I^2 of 92% indicating considerable heterogeneity of effect estimates between studies. Results of random effects meta-regression according to Figure 1 (without bias adjustment for non-blinding) are presented in Table 3a with the effect estimates of provision of safe water storage and combined interventions in the table footnote. The meta-regression model explained 39% of the between-study variance. Further covariates, examined in the full meta-regression model, included access to improved *vs.* unimproved sanitation (RR 0.98 (0.80, 1.21)), interventions in rural *vs.* urban or mixed areas (RR 1.00 (0.87, 1.17)), survey data analyses *vs.* studies evaluating specific interventions (RR 1.00 (0.74, 1.34)) and time of follow-up in studies evaluating specific interventions as continuous (in months: RR 1.00 (0.99, 1.00) and as indicator variable ≥12 months *vs.* <12 months: RR 1.02 (0.86, 1.21)) showed no association with diarrhoea and did not considerably change effect estimates of the other variables in the model (i.e. no confounding, all effect estimates changed less than 5%). There were no missing values for any of these covariates. Results of the analysis adjusting for bias due to lack of blinding are presented in Table 3b. After adjusting for bias, there was no evidence that POU chlorine treatment or POU solar treatment was beneficial (confidence intervals widely cross

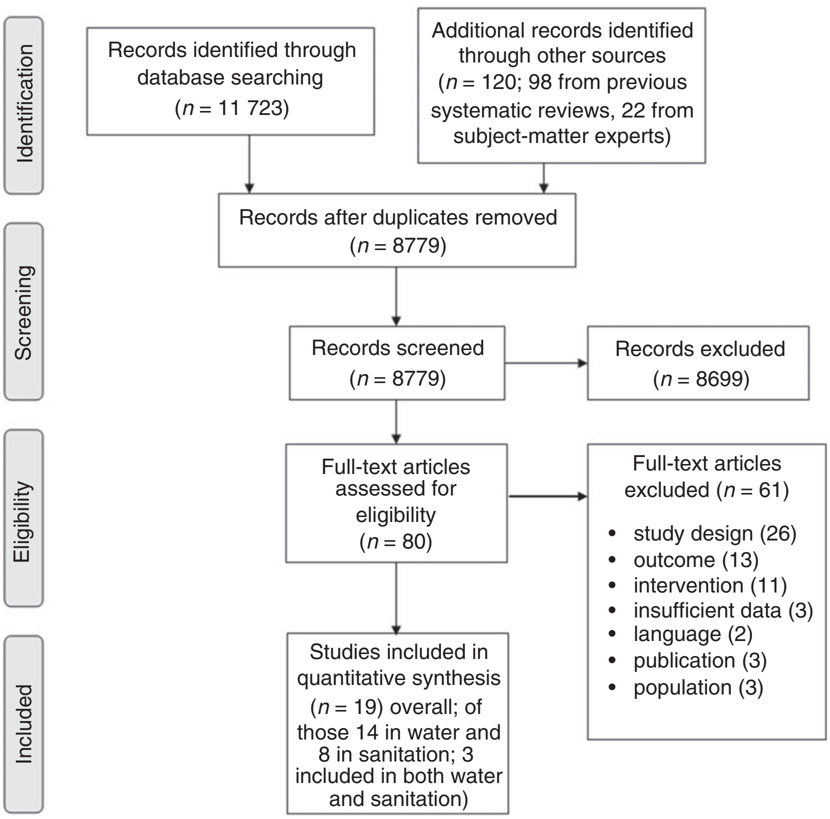

Figure 3 PRISMA Flow chart [75] of the selection process of drinking water and sanitation studies (update only).

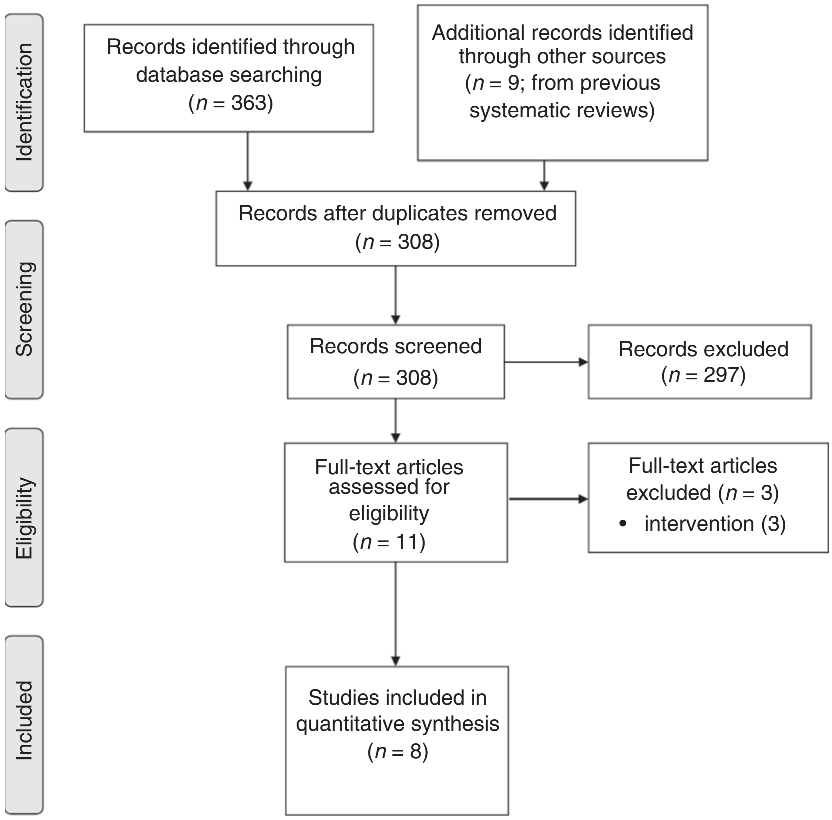

Figure 4 PRISMA Flow chart [75] of the selection process of hygiene studies (update only).

Table 2 Included drinking water interventions according to study baseline and outcome

Baseline water	Outcome water	Comparisons	Transition (Figure 1)
Unimproved source	Improved source, not on premises	11	a
Unimproved source	Piped water	6	b
Improved source, not on premises	Piped water	7	r
Piped water	Piped water, higher quality	1	s
Piped water	Continuous piped water	2	u
Unimproved source	POU chlorine treatment	18	d
Unimproved source	POU solar treatment	5	e
Unimproved source	POU filter treatment	15	f
Improved source, not on premises	POU chlorine treatment	5	w
Improved source, not on premises	POU solar treatment	6	x
Improved source, not on premises	POU filter treatment	3	y
Total		79*	

POU, point-of-use; 'piped water' means piped to premises.
*Comparisons add up to 79 observations (as compared to 80 included observations) as one study provided improved water storage only [74].

one, columns 6 and 7 of Table 3b) whereas filtering of unimproved and improved sources, excluding piped water to premises, remains significantly beneficial (column 8 of Table 3b).

Sensitivity analyses. Excluding survey data analyses (eight observations from five individual studies) yielded a pooled estimate of 0.65 (0.60, 0.71), I^2: 92% in meta-analysis. Effect estimates for individual transitions

Table 3 (a) Risk ratios for drinking water interventions, not adjusted for non-blinding. (b) Risk ratios for drinking water interventions, adjusted for non-blinding in point-of-use water interventions

Baseline water	Outcome water: Improved source, not on premises	Piped water	Piped water, higher quality*	Continuous piped water*	POU chlorine treatment	POU solar treatment	POU filter treatment filter + *safe storage*†
(a)							
Unimproved source	0.89 (0.77, 1.02)	0.77 (0.64, 0.93)	0.25 (0.09, 0.67)	0.64 (0.42, 0.98)	0.76 (0.64, 0.91)	0.67 (0.54, 0.84)	0.49 (0.38, 0.64) *0.39 (0.32, 0.48)*
Improved source, not on premises		0.87 (0.72, 1.04)	0.28 (0.10, 0.76)	0.73 (0.48, 1.10)	0.86 (0.71, 1.04)	0.76 (0.62, 0.92)	0.55 (0.41, 0.74) *0.44 (0.34, 0.56)*
Piped water			0.32 (0.12, 0.86)	0.84 (0.57, 1.22)	0.99 (0.78, 1.26)	0.87 (0.67, 1.13)	0.64 (0.46, 0.88) *0.50 (0.38, 0.66)*
(b)							
Unimproved source	0.89 (0.77, 1.02)	0.77 (0.64, 0.92)	0.25 (0.09, 0.66)	0.64 (0.42, 0.97)	0.91 (0.70, 1.18)	0.88 (0.60, 1.27)	0.60 (0.42, 0.84) *0.52 (0.35, 0.77)*
Improved source, not on premises		0.87 (0.72, 1.04)	0.28 (0.10, 0.75)	0.72 (0.47, 1.10)	1.02 (0.78, 1.35)	0.99 (0.68, 1.42)	0.67 (0.46, 0.97) *0.59 (0.39, 0.88)*
Piped water			0.32 (0.12, 0.84)	0.83 (0.57, 1.21)	1.18 (0.86, 1.60)	1.14 (0.76, 1.70)	0.77 (0.53, 1.14) *0.68 (0.44, 1.04)*

(a) Results are adjusted for provision of safe water storage (0.79 (0.64, 0.98)) and combined intervention (0.84 (0.70, 1.00)).
(b) Results are adjusted for provision of safe water storage (0.87 (0.69, 1.11)) and combined intervention (0.85 (0.72, 1.01)).
*Based on limited evidence, one observation with 'piped water, higher quality' as outcome [34] and two observations with 'continuous piped water' as outcome [32, 33].
†Some point-of-use filter treatments include safe drinking water storage as an integrated component, such as ceramic filter interventions that filter the water in a closed water container with a tap.

between exposure scenarios did not change besides the transition to continuous piped water (one of two studies describing this transition analysed survey data, e.g. from unimproved to continuous piped: 0.71 (0.39, 1.27) instead of 0.65 (0.42, 0.98), from improved community source to continuous piped: 0.81 (0.45, 1.46) instead of 0.73 (0.48, 1.10) and from piped to continuous piped: 0.93 (0.55, 1.58) instead of 0.84 (0.57, 1.22)).

Excluding the eleven studies evaluating specific interventions with the lowest quality rating yielded a pooled effect estimate of 0.67 (0.62, 0.73), excluding non-randomised studies a pooled effect estimate of 0.62 (0.56, 0.68), excluding studies that did not report diarrhoea in children <5 years a pooled effect estimate of 0.69 (0.65, 0.75) and excluding studies published before 2012 a pooled effect estimate of 0.69 (0.59, 0.81) in meta-analysis as compared to the pooled estimate of the whole dataset of 0.67 (0.62, 0.73).

Converting the odds ratios of Clasen *et al.* [25] to risk ratios with the assumed control group risk of 30% only slightly reduced the estimates for filter interventions (e.g. from unimproved source to filter: 0.51 (0.39, 0.66) instead of 0.49 (0.38, 0.64) and from improved community source to filter: 0.57 (0.42, 0.76) instead of 0.55 (0.41, 0.74)).

Analysis of sanitation interventions

We included 22 observations from 19 individual studies, eight additional observations from eight studies compared to the previous review. Random effects meta-analysis of all 22 observations yielded an effect estimate of 0.75 (0.63, 0.88), I^2: 95% (Figure 5). Effect estimates of individual observations are listed in Appendix S3.

Eighteen observations reported the association between improved household sanitation facilities and diarrhoea compared to unimproved sanitation and two observations respectively of sewer connection compared to unimproved and improved sanitation facilities. From 12 of the 13 intervention studies, a measure of sanitation coverage after the intervention could be extracted (Appendix S3).

Examining improved household sanitation and sewer connection separately in meta-regression resulted in an effect estimate of 0.84 (0.73, 0.98) for improved household sanitation and 0.60 (0.39, 0.92) for sewer connection compared to a baseline of unimproved sanitation and 0.71 (0.47, 1.07) of sewer connection compared to a baseline of improved household sanitation (adjusted for combined interventions: RR 0.65 (0.48, 0.89)). This model explained 59% of the between-study variance. When disaggregating unimproved sanitation into open defecation and unimproved sanitation facilities (16 of the 22 observations allowed this disaggregation), there was no difference in diarrhoea risk between open defecation and unimproved sanitation facilities (RR 1.00 (0.71, 1.42)) and hence no difference in effect estimates for improved household sanitation and sewer connection *vs.* a baseline of either open defecation or unimproved sanitation facilities.

Meta-regression results of the further examined covariates were 1.19 (0.79, 1.79) for baseline access to an improved *vs.* unimproved water source, 0.96 (0.64, 1.44) for latrine promotion only *vs.* also provision of latrine hardware, 1.26 (0.90, 1.78) for survey data analyses *vs.* studies evaluating specific interventions, 1.32 (0.72, 2.43) for studies evaluating specific interventions with a follow-up time of more than 24 months *vs.* those up to 24 months and 1.01 (0.99, 1.04) for each one month increase in follow-up time, and 0.59 (0.43, 0.81) for combined *vs.* single interventions. Studies evaluating specific interventions that led to a sanitation coverage up to 75% reduced diarrhoea on average by 24% (RR 0.76 (0.51, 1.13)) in the intervention compared to the control group, and those with sanitation coverage above 75% after the intervention by 45% (RR 0.55 (0.34, 0.91) in the intervention compared to the control group. There were no missing values for any of these covariates besides one missing observation for community coverage in one intervention study. Here, we used listwise deletion, that is the record was excluded from the respective analysis.

Sensitivity analyses. Excluding survey data analyses yielded a pooled effect estimate of 0.68 (0.50, 0.91), excluding the study with the lowest quality rating a pooled effect estimate of 0.75 (0.63, 0.89), excluding non-randomised studies a pooled effect estimate of 0.96 (0.87, 1.06), excluding studies that did not report diarrhoea in children <5 years a pooled effect estimate of 0.76 (0.64, 0.91) and excluding studies published before 2012 a pooled effect estimate of 0.88 (0.81, 0.94) in meta-analysis as compared to the pooled estimate of the whole dataset of 0.75 (0.63, 0.88). Forest plots by intervention type (improved household sanitation and sewer), community coverage (up to and above 75%) and for randomised studies are shown in Appendix S4.

Analysis of hygiene interventions

We included 33 observations from 33 individual studies, eight additional observations compared to the previous review. Random effects meta-analysis of all 33 observations yielded an effect estimate of 0.70 (0.64, 0.77), I^2: 89% (Figure 6). A Bayesian bias-adjusted analysis to account for lack of blinding in all of the studies changed

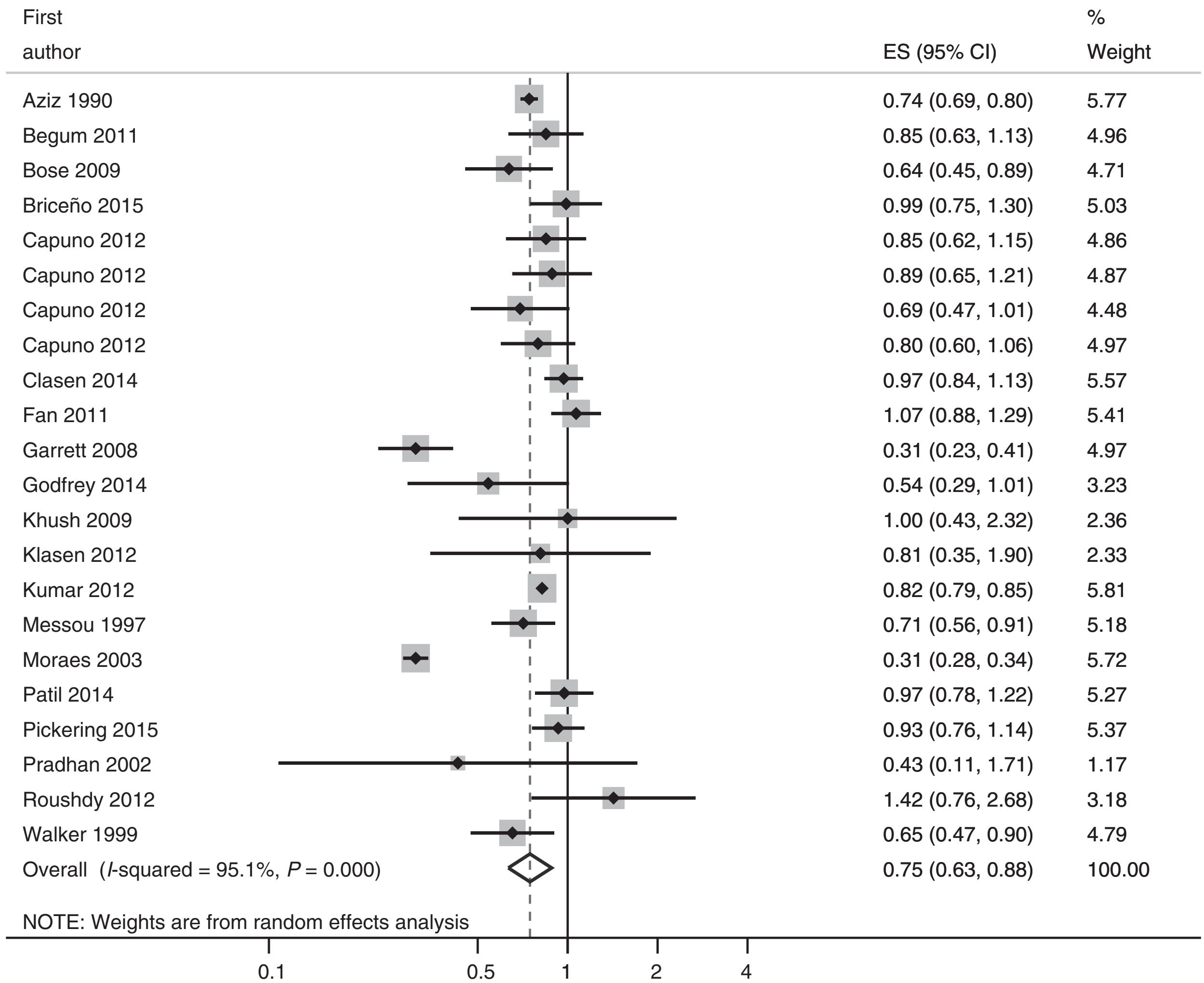

Figure 5 Forest plot of included sanitation interventions.

the effect estimate to 0.90 and introduced considerable uncertainty (95% confidence interval from 0.37 to 2.17) (Table 3). Effect estimates of individual observations are listed in Appendix S3.

In meta-regression, there was no evidence for an association of exclusive promotion of handwashing *vs.* broader hygiene education (RR 0.91 (0.76, 1.09)), the provision of soap (RR 0.88 (0.73, 1.05)), high-income *vs.* low- and middle-income countries (RR 1.01 (0.82, 1.24)), community *vs.* institutional interventions (RR 1.02 (0.83, 1.24)) and time of follow-up in studies evaluating specific interventions as continuous (in months: RR 1.01 (1.00, 1.02) and as indicator variable ≥12 months *vs.* <12 months: RR 1.12 (0.93, 1.36) and diarrhoea. There were no missing values for any of these covariates.

Sensitivity analyses. Excluding one survey data analysis yielded a pooled effect estimate of 0.71 (0.64, 0.78), excluding the five studies evaluating specific interventions with the lowest quality rating yielded a pooled effect estimate of 0.68 (0.62, 0.74), excluding non-randomised studies a pooled effect estimate of 0.74 (0.65, 0.83), excluding studies that did not report diarrhoea in children <5 years a pooled effect estimate of 0.70 (0.64, 0.78), excluding studies published before 2012 a pooled effect estimate of 0.92 (0.84, 1.02), excluding institutional-level studies a pooled effect estimate of 0.70 (0.62, 0.79), excluding household-level studies a pooled effect estimate of 0.69 (0.59, 0.81) and excluding studies conducted in high-income countries a pooled effect estimate of 0.70 (0.62, 0.78) in meta-analysis as compared to the pooled estimate of the whole dataset of 0.70 (0.64, 0.77).

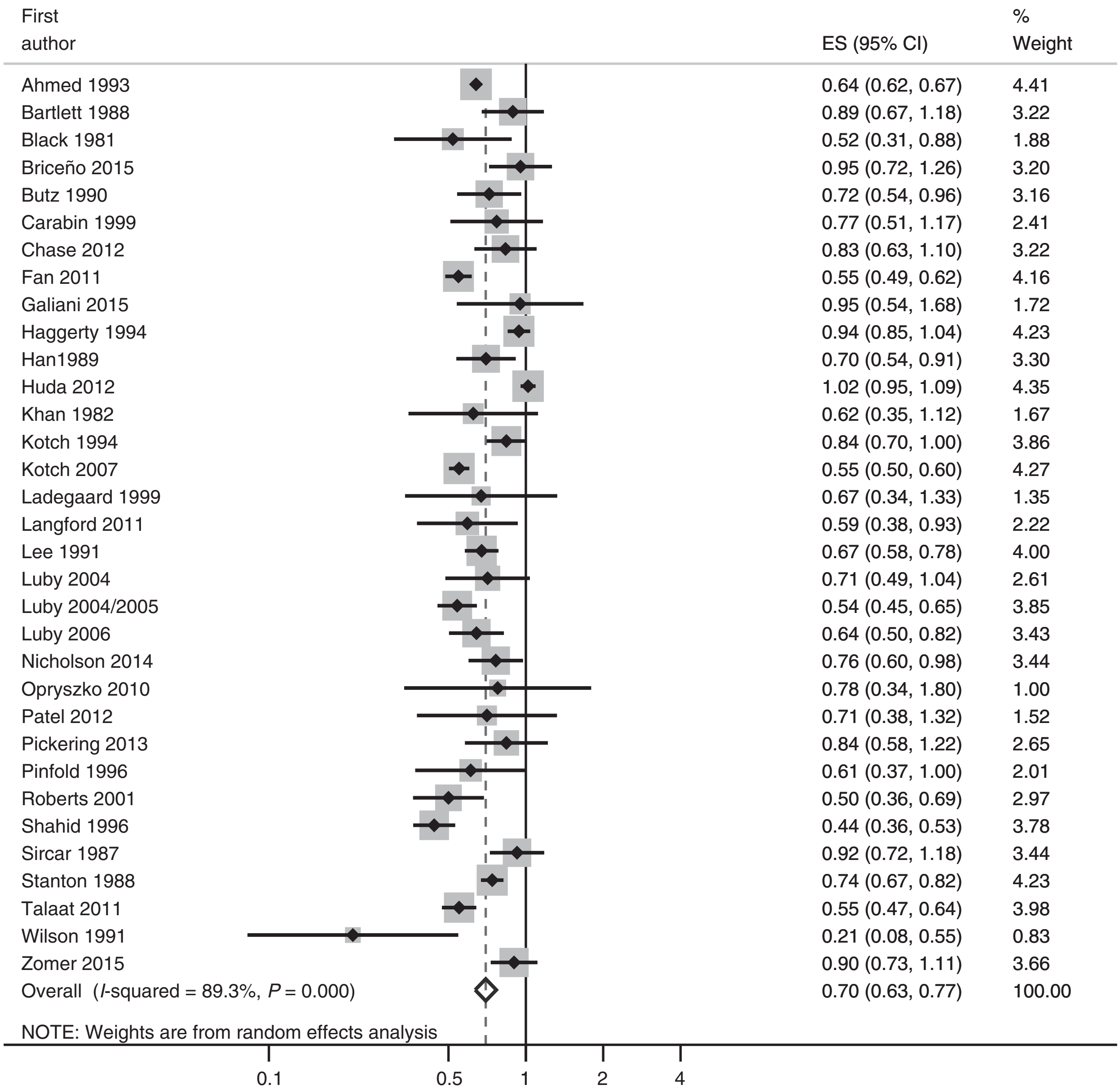

Figure 6 Forest plot of included hygiene interventions.

There was no evidence of funnel-plot asymmetry and small study effects in any of the WaSH meta-analyses (Appendix S4).

Discussion

Main findings

Our results show large potential reductions in the risk of diarrhoeal disease through the delivery of interventions aiming at improvements in drinking water, sanitation and hygiene. For water, the greatest reductions are for a piped water to premises supply that has been treated to improve its quality (75% based on limited evidence) and for POU-filtered water that is safely stored in the household (61% or 48% reduction before and after adjustment for non-blinding) compared to a baseline of unimproved drinking water.

For sanitation, our overall estimates show a 25% mean diarrhoea risk reduction compared to no intervention.

Interventions reaching high sanitation coverage, that is above 75%, in the community were associated with a diarrhoea risk reduction of 45%. Also, sewer connections were associated with larger diarrhoea risk reduction than improved household sanitation (40% *vs.* 16%). In both water and sanitation analyses, diarrhoea morbidity is reduced further when the intervention is combined with other components of WaSH.

Hygiene interventions reduce diarrhoea compared to no intervention (30% reduction before adjustment for non-blinding), but the 10% reduction found after adjustment for non-blinding is not statistically significant.

Limitations

Study limitations. We conducted systematic searches across multiple databases for published literature but relevant grey literature was only identified from the review of historic systematic reviews or when supplied by subject-matter experts. There is a risk therefore that relevant studies may have been missed although comparison with previous systematic reviews suggests that our searches were comprehensive.

Some of the meta-regression effect estimates – indicated above (Table 3a and b) – are based on a small number of studies and should be interpreted with caution. Effect estimates for the transition from piped water to a continuous piped supply are based on only two studies which evaluated this change [32, 33] and the transition from piped water to treated piped water is based on only one study [34]. Of the two studies comparing continuous piped to intermittent piped water, one is a cross-sectional, non-intervention study [33]. We excluded this study in a sensitivity analysis which led to a considerable change in the effect estimate for this transition. Also, the results of the sanitation and hygiene meta-analysis were sensitive to excluding studies published before 2012 (hygiene and sanitation) and excluding non-randomised studies (sanitation). Sanitation coverage of 75% was reached in only five studies [35–39]. These five studies are heterogeneous and include one combined water and sanitation intervention and three sewered sanitation interventions. Larger effect estimates might therefore also be due to study characteristics other than community coverage. As the evidence is scarce, the analysis of sanitation coverage also does not take into account baseline sanitation coverage or coverage in the control group – factors that could substantially impact intervention effects. Effect estimates for these transitions are likely to change as new evidence emerges.

Usually, WaSH interventions are unblinded and often rely on self-reported diarrhoea, which is likely to present a high risk of biased reports of diarrhoea that can lead to over-estimation of effect estimates [29, 30]. We attempt to adjust for this limitation by adjusting point-of-use drinking water and hygiene interventions for the assumed effect of non-blinding bias. WaSH exposure classification is often poor. We could not, for example, always differentiate between several types of unimproved sanitation such as shared sanitation (of an otherwise acceptable type), unimproved facilities and open defecation [3] as this information is not clearly reported in many sanitation studies and, indeed, comparison groups may be using a broad range of facilities within a single study. It is possible that these different unimproved sanitation categories exhibit different impacts on health [40–43]. Some studies reported open defecation separately from other unimproved facilities and our analysis found no differential impact on diarrhoea morbidity. This one-time binary measure of mainly practising open defecation or mainly using unimproved sanitation facilities is a simplification and might therefore be subject to fluctuation and measurement error. A community might have high access to unimproved household sanitation but still many community members might practise open defecation [44]. Similarly, unsafe containment, emptying, transport and treatment of faecal waste from improved facilities may discharge excreta back into the environment.

Effectiveness trials of WaSH interventions have typically not achieved high coverage or high compliance [45]. This is particularly the case for recent studies of rural onsite sanitation interventions: in Tanzania, latrine construction rates increased only from 39% to 51% [46]; in India, only around 40% of intervention households had a functional or improved toilet post-intervention and use of these facilities remained limited [47, 48]; and in Mali, latrine coverage was 65% in the intervention arm *vs.* 35% in control households while open defecation remained common [44]. None of the included studies analyses a fully safely managed chain of excreta management. Our effect estimates therefore remain a conservative estimate of the potential impact on diarrhoea through interventions reaching high coverage and compliance.

Limitations of the analysis. Results from meta-regression are observational associations between variables and are therefore prone to bias [49]. WaSH at baseline and outcome was defined at study level, although may vary within the community. This can underestimate the true baseline or outcome effect.

The I^2 statistic, a measure of inconsistency across study findings, was high in the water, sanitation and hygiene analysis [50]. This is consistent with the substantial differences among the studies in terms of intervention type and uptake, study methods, settings, populations, pathogens present and transmission pathways dynamics. We applied meta-regression techniques to explore the reasons for this variance. Results suggest that only part of the variance can be explained and that effect estimates might vary substantially depending on study, intervention and implementation characteristics.

Effect estimates included in this review are usually based on intention-to-treat analysis which might again underestimate the true health impact of WaSH interventions which usually achieve low coverage and lower compliance [45, 51]. Exposure reductions are influenced by many factors such as baseline WaSH and changes in supply, use and maintenance. We tried to account for some of these by examining baseline WaSH, time of follow-up and further covariates. We did not, however, adjust effect estimates for compliance which is crucially important for any health impact. A modelling study on household water treatment concluded that diarrhoea risk decreased proportionally with pathogen removal only when compliance was almost 100% [52, 53]. Assuming a compliance of 80–90%, which is seldom reached in WaSH interventions, diarrhoeal disease was much less reduced [52, 53]. However, compliance is often poorly measured or not measured at all in WaSH intervention evaluations [4] and can be assessed by self-report, observations or measurements (e.g. chlorine in drinking water). Results will differ according to which method is chosen and whether compliance is assessed at a single time point or continuously over time. Self-reported household water treatment users in Zambia reported inconsistently on compliance to household water treatment at two different time points [54].

Our exposure scenarios for drinking water do not include bottled or packaged water. Bottled water consumption is estimated to have increased to 391 billion litres in 2017 compared to 212 billion litres in 2007 [55]. Bottled water can show very small levels of faecal contamination [3, 56–59] and was associated with decreased risk for diarrhoea compared to piped water [60]. Research also showed that different kinds of bottled water can exhibit very different diarrhoea disease risks [61]. We did not include bottled water into our exposure scenarios as there is little evidence from interventions of its effect on diarrhoeal disease. The issue should, however, be given further attention and taken into account in future estimates if evidence permits.

Our assessment is limited to diarrhoeal disease, although systematic reviews have assessed the impact of inadequate WaSH on many other health outcomes such as soil-transmitted helminth infections [13], trachoma [12] and schistosomiasis [62]. Additional benefits, such as livelihood impacts, impacts on well-being and environmental consequences, are likely [2]. Furthermore, our water and sanitation and, partially, hygiene analysis are limited to household access and does not include health impact from access to WaSH in institutions such as schools and healthcare facilities.

We limited our search to studies on diarrhoea morbidity rather than diarrhoea mortality as outcome in our search strategy even though mortality studies can be considered a higher level of evidence, one reason being the greater robustness of the outcome. However, the current evidence base from mortality studies is weak, with very scarce studies of generally limited quality. We are only aware of three WaSH studies which report mortality from diarrhoeal disease ([63, 64] and one unpublished study described in Wagner and Lanoix [65]). None of these studies would have met our inclusion criteria: two studies were observational (one case–control study without relation to a clearly specified intervention [63] and one analysing cross-sectional data [64]) and for the unpublished study not enough data were available to judge eligibility.

General interpretation

Our results are broadly consistent with previous evidence. A Cochrane review on interventions to improve water quality for preventing diarrhoea found insufficient evidence for improved community water sources and included no evidence of reliable piped water to households [7]. The same review found that POU water quality interventions reduced diarrhoea by an average of 23% for chlorination, 31% for flocculation and disinfection, 38% for solar water treatment, 53% for biosand filters and 61% for ceramic filters, all prior to adjustment for non-blinding. Previous reviews on sanitation and diarrhoea estimated somewhat larger associations between interventions aiming at improvements in sanitation and diarrhoea [6, 8]. This might be partially due to a number of recent effectiveness trials that did not significantly reduce diarrhoea [44, 46–48]. Our hygiene effect estimate (not adjusted for non-blinding bias) is consistent with unadjusted pooled estimates from a recent update of a Cochrane review on hygiene interventions [66]. An analysis of Demographic and Health Survey (DHS) data found similar results of increased diarrhoea reduction of combined WaSH interventions [67]. These estimates, consistent with protective effects, are comparable to other published estimates but are drawn from unblinded studies relying on subjective outcomes and may therefore be exaggerated due to biased reports of diarrhoea. We add to the available evidence as we present effect estimates conditional on baseline access and adjusted for further covariates and have moreover adjusted selected effect estimates for potential bias arising from non-blinding.

We find evidence for larger diarrhoea reduction for interventions reaching high sanitation coverage in the community compared to those reaching low coverage. In previous research [31, 68, 69], full community coverage was associated consistently with large diarrhoea reductions: a simulation study estimated nearly 60% diarrhoea reduction for a village with full sanitation coverage compared to a village where everybody practices open defecation [68]. Similarly, an analysis of Indian national data concluded a 47% diarrhoea reduction could be expected in children living in a village with complete sanitation coverage compared to children in villages without sanitation [31]. In both studies, 75% of the diarrhoea reduction was attributed to the indirect or community effect that adequate sanitation has on members of other households in the community. An analysis of 29 Demographic and Health Surveys across sub-Saharan Africa and South Asia found that below 60% coverage, improved sanitation was associated with 18% and at 100% coverage with 56% of diarrhoea reduction [69]. Sanitation coverage was also associated with improvements in children's anthropometric status [70, 71] and reduced child mortality [72]. Introducing sewered sanitation in low- and middle-income settings would be expected to have positive health impacts, although care must be taken that sewage is appropriately treated to avoid the diarrhoeal disease burden being shifted 'downstream' to the receiving communities [73].

We identified important evidence gaps while working on this review and analysis. Impact evaluations should report both diarrhoea mortality and morbidity and the exact WaSH exposure both at baseline and follow-up in terms of access and behaviour (e.g. access to facilities and use). Sanitation interventions should aim to yield high community coverage which is crucial for maximum health gains and is important for adding evidence on the direct and indirect health effects of sanitation. Studies providing microbiologically high-quality piped drinking water continuously to households are needed to estimate which effect of safe drinking water on diarrhoea could be maximally achievable. Studies achieving high compliance and considering non-household exposures would be very important to truly disentangle the effect of WaSH interventions on diarrhoea morbidity.

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Supporting Information

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

Appendix S1 PRISMA checklist
Appendix S2 Search Strategy
Appendix S3 Included WaSH studies
Appendix S4 General further information
Appendix S5 Quality ratings

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