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Systematic Review

Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression

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Abstract

OBJECTIVE To assess the impact of inadequate water and sanitation on diarrhoeal disease in low- and middle-income settings.

METHODS The search strategy used Cochrane Library, MEDLINE & PubMed, Global Health, Embase and BIOSIS supplemented by screening of reference lists from previously published systematic reviews, to identify studies reporting on interventions examining the effect of drinking water and sanitation improvements in low- and middle-income settings published between 1970 and May 2013. Studies including randomised controlled trials, quasi-randomised trials with control group, observational studies using matching techniques and observational studies with a control group where the intervention was well defined were eligible. Risk of bias was assessed using a modified Ottawa–Newcastle scale. Study results were combined using meta-analysis and meta-regression to derive overall and intervention-specific risk estimates.

RESULTS Of 6819 records identified for drinking water, 61 studies met the inclusion criteria, and of 12 515 records identified for sanitation, 11 studies were included. Overall, improvements in drinking water and sanitation were associated with decreased risks of diarrhoea. Specific improvements, such as the use of water filters, provision of high-quality piped water and sewer connections, were associated with greater reductions in diarrhoea compared with other interventions.

CONCLUSIONS The results show that inadequate water and sanitation are associated with considerable risks of diarrhoeal disease and that there are notable differences in illness reduction according to the type of improved water and sanitation implemented.

keywords water, sanitation, diarrhoea, global burden of disease, risk estimates

Introduction

Diarrhoea is among the main contributors to global child mortality, causing one in ten child deaths (WHO 2009; Liu *et al.* 2012), and inadequate water and sanitation have long been associated with diarrhoea (Esrey & Habicht 1986; Esrey *et al.* 1991; Clasen *et al.* 2006, 2010; Waddington *et al.* 2009; Cairncross *et al.* 2010). In 2011, 11% of the world population reported using 'unimproved' drinking water supplies (defined as unprotected springs and dug wells, surface water and water stored in a tank) and 36% had 'unimproved' sanitation (defined as flush toilets not connected to a sewer or septic system, pit latrines without slab, bucket latrines or open defecation). 'Improved' and 'unimproved' drinking water and sanitation refer to specific sources and facilities as defined by the WHO/UNICEF Joint Monitoring Programme (JMP 2013) and are often taken as proxy indicators for appropriate and inappropriate water and sanitation. 'Inadequate' water and sanitation, as we define it for the purpose of this manuscript, means any drinking water or sanitation provision whose use poses a risk to health, which cannot be used safely, which is not available in sufficient quality or quantity or which is too distant for convenient access.

The 2010 Global Burden of Disease Study (GBD), by Lim *et al.* (2012), concluded that the impact of water and sanitation on diarrhoea was much smaller than previous GBD estimates (Prüss *et al.* 2002; Clasen *et al.* 2014). Their conclusion, based on a yet-to-be published systematic review, was that there was an increased risk of diarrhoea associated with unimproved water (RR 1.34, 95% CI 1.02–1.72) and unimproved sanitation (RR 1.33, 95% CI 1.02–1.74). They reported no additional benefit, however, from improved water quality or access over other improved water sources (such as public taps, protected springs or dug wells, boreholes and rainwater) after adjusting for potential bias due to lack of blinding (Lim *et al.* 2012; Engell & Lim 2013).

The 2010 GBD conclusions, with respect to the health impact associated with water and sanitation, represent a significant departure from previous estimates. This review was undertaken to update previous research and to explore the impact of other methods to adjust for non-blinding. Meta-regression was used to explore the impact of different types of improvement to drinking water or sanitation, as well as other study characteristics. The methods are described in line with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analysis' (PRISMA) guideline (Moher *et al.* 2009) and include a PRISMA checklist (Online-only Appendix 1).

Methods

The objective of this study was to estimate the effect of different water and sanitation interventions on diarrhoeal disease morbidity, based on pooled estimates from existing studies. The protocol for this study was agreed, in advance, by an expert group convened by the World Health Organization (WHO) before the searches began.

Systematic literature review

Selection criteria and search strategy. Studies were sought that reported the effects on diarrhoea at the individual, household or community level of any drinking water or sanitation intervention providing they could be grouped within our conceptual models for drinking water and sanitation (Figures 1 and 2). Eligible study designs included:

- randomised (including cluster randomised) controlled trials;
- quasi-randomised and non-randomised controlled trials, when baseline data on the main outcome were available before the intervention was conducted (i.e. before and after studies with control group);
- case–control and cohort studies when they were related to an intervention;
- studies using time-series and interrupted time-series design; and
- observational studies using specific matching methods.

Studies were excluded if they mainly targeted institutions such as schools or the work place, or if they used non-representative population groups (e.g. people with HIV). We excluded studies in which the rate of implementation of the intervention was very low and studies that had very low compliance (<20%). A poor implementation rate might be reflected in similar rates of uptake in intervention and control groups: changes in morbidity cannot then confidently be attributed to the water or sanitation source or technology. As an example, Boisson *et al.* (2009) tested a novel portable water filter technology, but it was reportedly used by only 13% of the participants, and the authors themselves conclude that the health effect was likely not be due to the intervention and we excluded the study. Other studies in which interventions did not lead to differences in drinking water or sanitation access between intervention and control groups included Pradhan and Rawlings (2002) for household sanitation and Walker *et al.* (1999) for drinking water.

A wide range of single and combined water and sanitation interventions were eligible. Studies were included

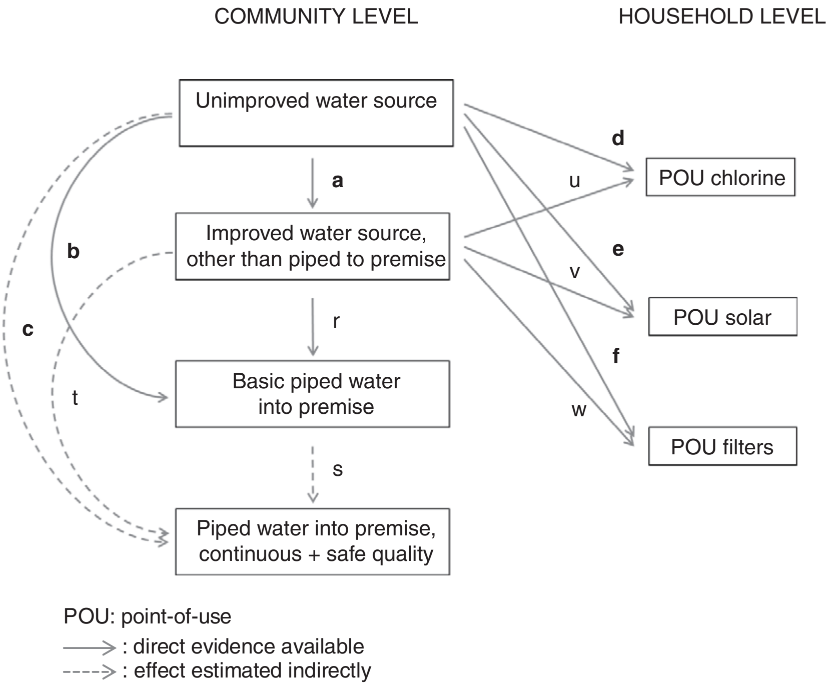

Figure 1 Conceptual framework for analysis of drinking water studies.

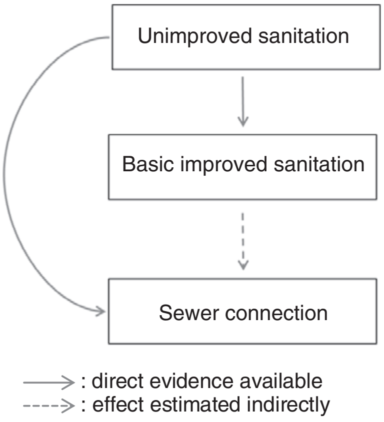

Figure 2 Conceptual framework for analysis of sanitation studies.

with participants of all ages from low- and middle-income settings. Due to the limited number of studies reporting mortality, studies had to report our primary outcome of diarrhoeal disease morbidity, regardless of aetiology and case confirmation. The main definition for diarrhoea was the WHO standard of at least three loose stools passed in the previous twenty-four hours (WHO 2005), but alternative case definitions were permitted providing that they could be assessed for validity. Studies were required to be published in a peer-reviewed journal or to have been assessed according to transparent criteria for methodological quality in a previously published systematic review.

Five databases were searched (Cochrane Library, MEDLINE & PubMed, Global Health, Embase and BIOSIS) in May 2013, using keyword and Medical Search Headings. The search terms and strategy are outlined in Online-only Appendix 2. In addition, reference lists of key articles (previously published systematic reviews and an unpublished literature review conducted by WHO) were examined, and subject experts and study authors were contacted to provide additional information and further relevant references where required. The search strategy was prepared and implemented in English, and only reports in English or French were considered. However, if a study published in a language other than English or French had been included in a previously published English or French language systematic review and the relevant data had been extracted and made available, this study was included in our analysis.

Data extraction and quality assessment. Titles and abstracts were screened by a single reviewer, and data extraction and quality assessment was carried out by two independent reviewers, using a structured and piloted form. Differences between reviewers over data extraction and quality assessment were reconciled with the intervention of a third abstractor, where required. The quality assessment criteria were adapted from the Newcastle–Ottawa scale (Wells *et al.* undated) by Pope *et al.* (2010) for assessing the quality of studies for the health effects of interventions to reduce indoor air pollution. Specific quality criteria were adapted to each study type (intervention, cohort, case–control, cross-sectional) to assess the risk of sampling bias, bias in exposure and outcome measurements, bias in results analysis and reporting. The criteria are included in the data extraction form (Online-only Appendix 3).

The summary effect estimates were calculated as risk ratios (RR) with 95% confidence intervals (95% CI). For studies with multiple intervention arms (including factorial trials), we derived a single pair-wise comparison of the most comprehensive intervention compared with the least comprehensive intervention (or control) among the categories indicated in Figures 1 and 2, subject to availability of results. Where possible, we combined data across intervention arms falling within the same category (e.g. different methods for filtering at point of use). Whenever possible, effect estimates adjusted for clustering at household or community level were extracted.

Statistical analysis

General approach. Random-effects meta-analyses were conducted to examine, separately, the effect of improvements in drinking water or sanitation on diarrhoeal morbidity. Bayesian meta-regression was used to estimate the impact of different intervention types, baseline water and sanitation conditions and additional study characteristics (Thompson 1994). Other pre-specified covariates were retained in the model if the *P*-value was smaller than 0.2 or if they changed effect estimates of other variables by at least 15% (Kirkwood & Sterne 2003; McNamee 2003).

Systems for drinking water and sanitation provision lie on a continuum between poor and good supply/quality/facilities. Studies were grouped into categories according to the nature of the improvement, following conceptual models, as shown in Figures 1 and 2 and described in subsequent sections.

As a sensitivity analysis, 20% of studies with the lowest quality rating were excluded. For community- and household-level water interventions, separate sensitivity analyses were conducted as the studies tend to have different characteristics (with household-level interventions, for example, tending to be randomised controlled trials, while community-level interventions are often of a lower quality design – Clasen *et al.* 2006).

Potential for publication bias was examined with inspection of funnel plots and the use of Begg's and Egger's test. Analyses were performed with Stata 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp. LP). Bayesian meta-regression and bias adjustments were performed using WinBUGS (Lunn *et al.* 2000).

Analysis of drinking water interventions. The conceptual model used for the analysis of drinking water interventions is presented in Figure 1. Interventions were grouped as community-level (structural changes in supply) or household-level interventions (point-of-use treatment). Within point-of-use treatments, chlorine, solar disinfection and filter interventions were analysed separately. Within community-level interventions, studies were grouped according to whether the intervention led to an improved water source other than piped water (piped water means piped into premise throughout the article), a basic piped water source or a piped water source with a continuous supply and safe quality (referred to as higher-quality piped water).

We distinguish between 'basic piped water' and 'piped water, continuous and safe quality'. Practically, in all interventions providing piped water to households or premises, piped water was of non-optimal quality and/or supply was non-continuous requiring water storage in the households. The endpoint of these studies was therefore classified as 'basic piped water'. A 'piped water source, continuous and safe quality' is similar to the standard water supply in high-income countries. Studies of interventions that provide a continuous piped water supply of high water quality are currently not available for low- and middle-income settings besides one study (Hunter *et al.* 2010), which may come closest to the supplies typically encountered in high-income countries. We therefore approximated the transition from 'basic piped water' to 'piped water, continuous and safe quality' by the effect of safe water storage plus the effect of any quality improvements on a piped water system.

In Figure 1, the transitions a to f represent 'basic parameters' in the meta-regression model, each represented by a covariate. All other transitions are coded as combinations of these basic parameters: specifically, $r = b - a$, $s = c - b$, $t = c - a$, $u = d - a$, $v = e - a$ and $w = f - a$. 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 (Salanti *et al.* 2008).

Safe water storage in the household is an important component to prevent contamination and maintain adequate water quality (WHO 2013a). The effect of safe water storage was estimated by including a binary covariate to indicate either:

- when the intervention provided a safe storage container (i.e. a container with a narrow opening that prevents the introduction of objects) or
- when safe storage was an inherent part of the intervention (as with ceramic filters or solar disinfection of water in PET bottles).

The following further study characteristics were explored in meta-regression analyses:

- combined *vs.* single intervention, that is, plus additional hygiene education or sanitation provision;
- intention-to-treat *vs.* treatment-on-the-treated analysis;
- urban *vs.* rural settings;
- length of follow-up;
- sanitation provision at study baseline;
- provision of safe water storage;
- randomisation of study participants to the intervention;
- different interactions (see Online-only Appendix 4);
- type of household water treatment; and
- regional specificity (as dummy variable and according to WHO groupings – WHO 2013b).

Blinding study participants in household-level drinking water interventions. Studies where participants were blinded to point-of-use water quality interventions have consistently failed to show a statistically significant effect on diarrhoeal disease. As there are only three blinded household water interventions in low- and middle-income settings that meet the inclusion criteria (Kirchhoff *et al.* 1985; Jain *et al.* 2010; Boisson *et al.* 2013), it was felt that these were insufficient to define the potential bias associated with non-blinding. As diarrhoea in intervention studies is usually self-reported and non-blinding in subjectively assessed outcomes has been associated with bias (Wood *et al.* 2008; Savović *et al.* 2012), an additional analysis was performed, which incorporated bias adjustments based on empirical evidence (as described by Savović *et al.* (2012) and outlined below).

As community-level interventions are often less apparent to the recipient (study participant) than household-based interventions, it is likely that community-level interventions will be less prone to bias as a result of non-blinding. This idea is supported by the finding of similar results for community water or sanitation interventions when observational studies (examining survey data) and experimental studies were analysed separately. It is assumed that observational studies, using specific matching methods on survey data, are less prone to bias as a result of non-blinding because there is no single study hypothesis; the hypothesis regarding a potential impact of sanitation or water on diarrhoea would be just one of many possible hypotheses investigated in the survey. Such studies therefore offer an opportunity for limiting bias arising from non-blinding.

Meta-regression was repeated after making a bias adjustment in studies of household-level interventions. The result of each non-blinded study was separately adjusted by introducing bias through a prior distribution in a Bayesian framework (Welton *et al.* 2009). On the basis of the findings of Savović *et al.* (2012), who examined the distribution of bias due to lack of blinding in a large-scale meta-epidemiological study, three different prior distributions on size and direction of this bias were explored (Welton *et al.* 2009). These distributions incorporate variability in bias across studies and across meta-analyses. The prior which best represents the findings of the meta-epidemiological study (Savović *et al.* 2012) is based on the mean bias and the sum of all variance components. This is the preferred approach for the current analysis, as it will adjust the biased studies and should appropriately down-weight them. More information on bias adjustment for non-blinding and results with the other two prior distributions on size and direction of this bias are outlined in Online-only Appendix 4.

Analysis of sanitation interventions. Sanitation studies were grouped and analysed according to the conceptual model in Figure 2. We examined, in particular, the possibility of a differential effect of sewer connections over basic household improved sanitation (defined here as all other improved sanitation besides sewer connection). The following study characteristics were explored:

- combined *vs.* single intervention (i.e. plus additional hygiene education or water provision);
- urban *vs.* rural; and
- water provision at study baseline.

Results

Systematic search and quality grading

For water, of 6751 records identified through database searches and a further 68 identified through other sources, 3672 records were screened (after de-duplication) and 110 full-text articles were assessed for inclusion of which 61 were included for the meta-regression analysis.

For sanitation, of 12 502 records identified through database searches and a further 13 identified through other sources, 10 057 records were screened (after de-duplication) and 34 full-text articles were assessed for inclusion of which 11 were included for the meta-regression analysis. Figures 3 and 4 provide study flow

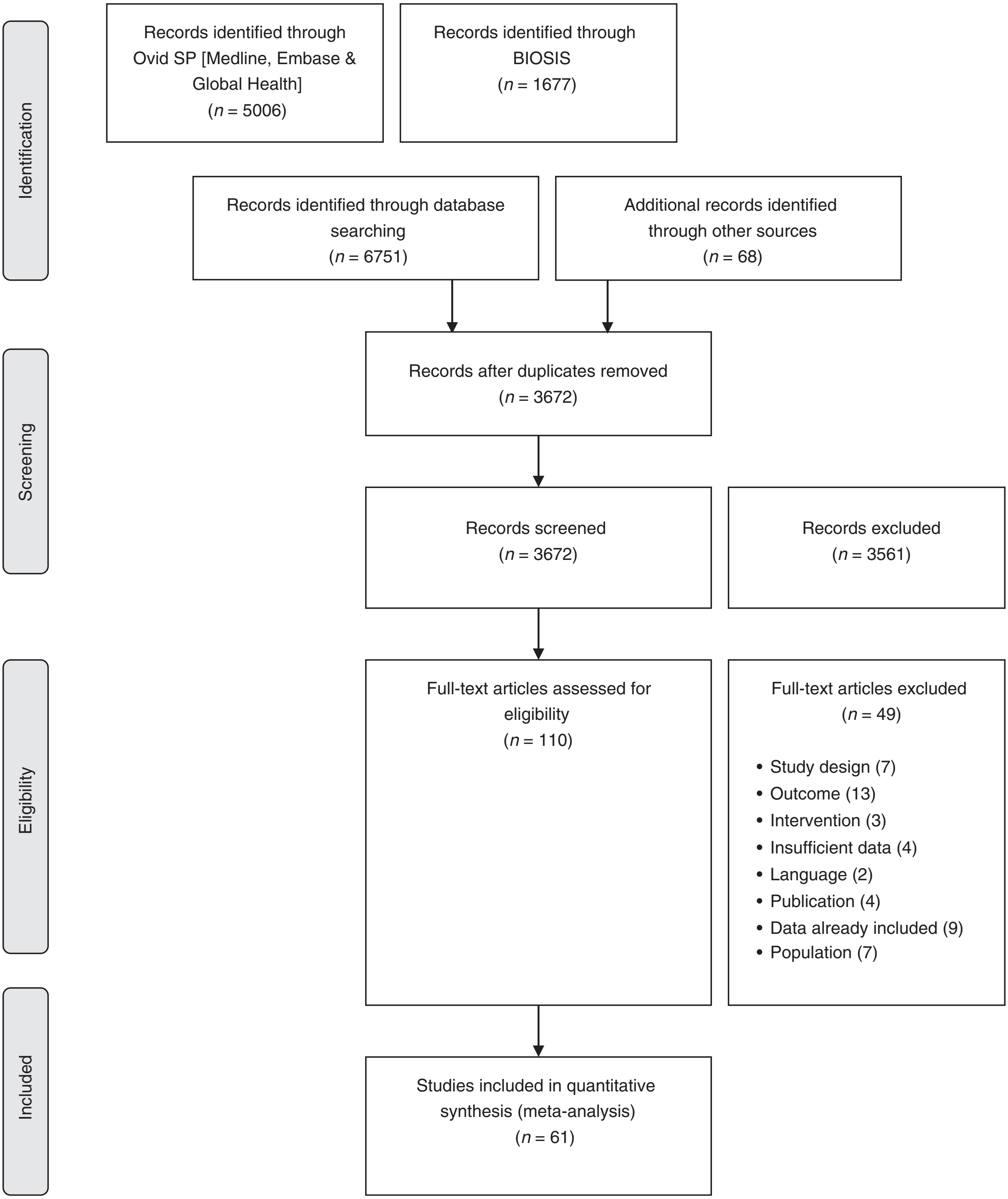

Figure 3 Flow chart of the selection process of drinking water studies.

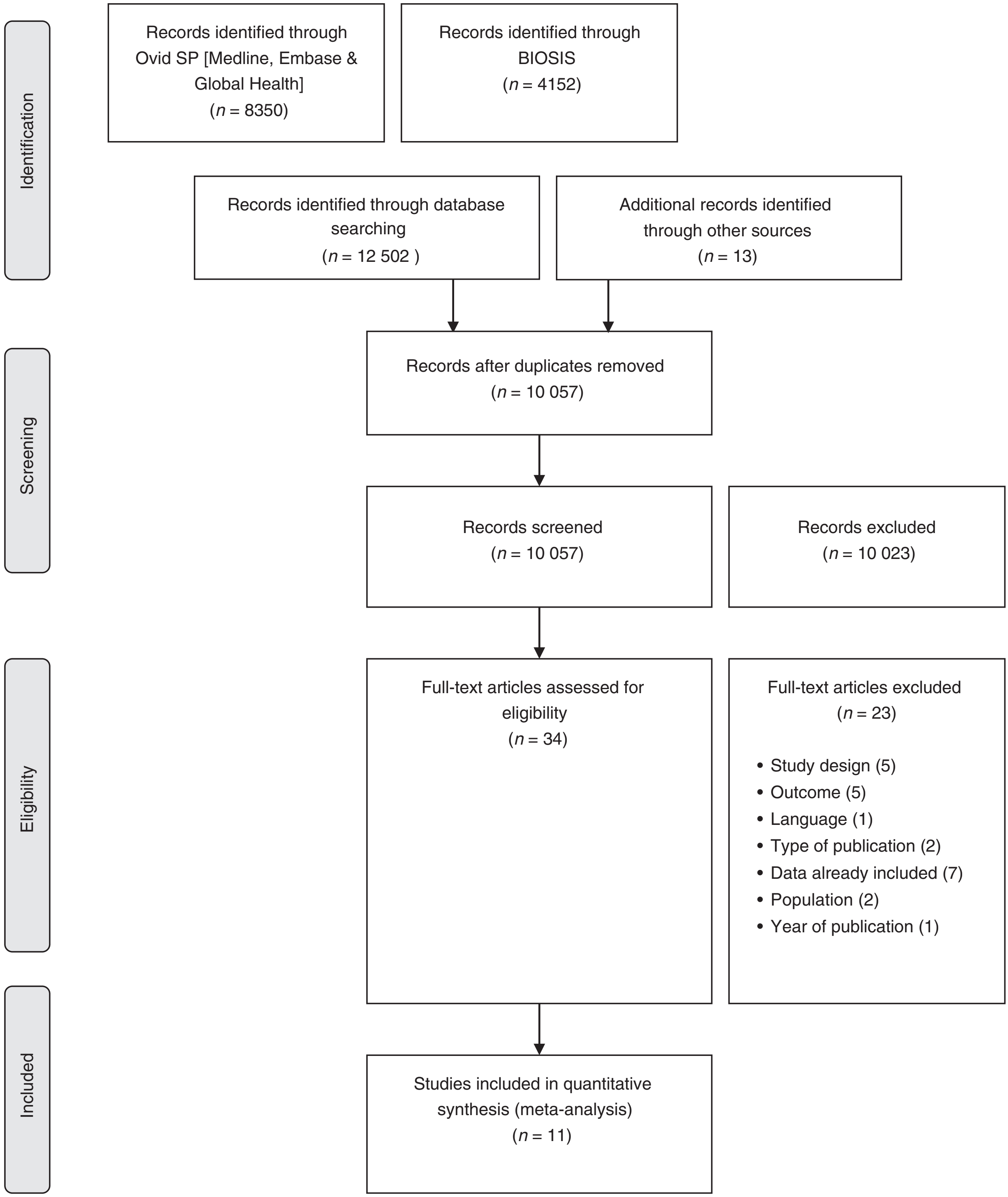

Figure 4 Flow chart of the selection process of sanitation studies.

Table 1 Included drinking water interventions according to study baseline and outcome

Baseline water	Outcome water	Comparisons	Transition (Figure 1)
Unimproved source	Improved community source	8	a
Unimproved source	Piped water	4	b
Improved community source	Piped water	7	r
Piped water	Higher-quality piped water	1	s
Unimproved source	POU chlorine treatment	16	d
Unimproved source	POU solar treatment	6	e
Unimproved source	POU filter treatment	14	f
Improved community source	POU chlorine treatment	4	u
Improved community source	POU solar treatment	5	v
Improved community source	POU filter treatment	3	w

POU = point-of-use, higher-quality piped water means quality improvements and safe storage of piped water.

diagrams of the number of studies screened and assessed for eligibility and included in the review. The Online-only Appendix 5 presents the citation, definitions and characteristics for all studies included in this analysis.

Analysis of water interventions

We included 68 comparisons of 61 individual studies from low- and middle-income settings. The number of observations describing each link between study baseline and outcome is listed in Table 1.

The summary risk ratio of all observations from the water interventions (all transitions), in a random-effects meta-analysis of the data, is 0.66 (0.60–0.71). Tables 2 and 3 show the results for individual transitions from the meta-regression analysis without and with bias adjustment for non-blinding.

The results from multivariable meta-regression before adjusting for non-blinding were nearly identical between Stata and WinBUGS. The results for chlorine and solar interventions were very similar and so, for convenience, they were combined in all analyses (in the context of Figure 1, this corresponds to setting d = e and hence u = v). Covariates retained in the model were provision of safe water storage and whether the intervention was a combined intervention.

Bias adjustment for non-blinding down weighs mainly estimates for point-of-use water treatment, higher-quality piped water and provision of safe water storage (Table 3).

The multivariable meta-regression model explained 53% of the between-study variance. Improved over unimproved sources are associated with only small reductions in diarrhoea, with a larger effect for piped water compared with other improved sources. The biggest protective effect on diarrhoeal disease was found for higher-quality (i.e. continuous and safe quality) piped water. Among household-level studies, filter interventions that also provided safe storage (for example, ceramic filters) were associated with a large reduction in diarrhoeal dis-

Table 2 Meta-regression results for water interventions, not adjusted for non-blinding

	Outcome water				
Baseline water	Improved community source	Basic piped water	Piped water, higher quality*	Chlorine/solar+*safe storage*	Filter+*safe storage*
Unimproved source	0.89 (0.78, 1.01)	0.77 (0.64, 0.92)	0.19 (0.07, 0.50)	0.82 (0.69, 0.96) *0.63 (0.55, 0.72)*	0.53 (0.41, 0.67) *0.41 (0.33, 0.50)*
Improved community source		0.86 (0.72, 1.03)	0.21 (0.08, 0.56)	0.92 (0.76, 1.10) *0.71 (0.61, 0.82)*	0.59 (0.45, 0.78) *0.46 (0.36, 0.58)*
Basic piped water			0.25 (0.09, 0.65)	1.07 (0.84, 1.34) *0.82 (0.67, 1.01)*	0.69 (0.51, 0.93) *0.53 (0.40, 0.69)*

*Continuous and safe water quality, based on limited evidence (Hunter *et al.* 2010) for quality improvements on basic piped water and should therefore be considered with caution.

Figures are relative risks (and 95% confidence intervals) and those in italics relate to additional safe storage.

Posterior estimates and credible interval limits were extracted as the median, 2.5% percentile and 97.5% percentile.

Results are adjusted for provision of safe water storage (RR 0.77 (0.64, 0.93)) and combined intervention (RR 0.84 (0.71, 0.99)).

Table 3 Meta-regression results for water interventions, adjusted for non-blinding

	Outcome water				
Baseline water	Improved community source	Basic piped water	Piped water, higher quality*	Chlorine/solar+*safe storage*	Filter+*safe storage*
Unimproved source	0.89 (0.78, 1.01)	0.77 (0.64, 0.92)	0.21 (0.08, 0.55)	0.99 (0.76, 1.27) *0.84 (0.61, 1.16)*	0.66 (0.47, 0.92) *0.55 (0.38, 0.81)*
Improved community source		0.86 (0.72, 1.03)	0.23 (0.09, 0.62)	1.11 (0.85, 1.44) *0.94 (0.68, 1.30)*	0.74 (0.52, 1.05) *0.62 (0.42, 0.93)*
Basic piped water			0.27 (0.10, 0.71)	1.29 (0.95, 1.74) *1.09 (0.76, 1.56)*	0.85 (0.58, 1.25) *0.72 (0.47, 1.11)*

*Continuous and safe water quality, based on limited evidence (Hunter *et al.* 2010) for quality improvements on basic piped water and should therefore be considered with caution.

Figures are relative risks (and 95% confidence intervals) and those in italics relate to additional safe storage.

Posterior estimates and credible interval limits were extracted as the median, 2.5% percentile and 97.5% percentile.

Results are adjusted for provision of safe water storage (RR 0.85 (0.69, 1.04)) and combined intervention (RR 0.83 (0.73, 1.01)).

ease. After taking account of safe water storage, the effects of ceramic and biosand filters were not significantly different from each other and so are grouped for further analysis. Chlorine and solar interventions did not appear to reduce diarrhoeal disease risk (applied to either unimproved or improved sources) after results were adjusted for non-blinding. There was some evidence of a greater diarrhoea risk reduction from improving household water storage and combining the water intervention with hygiene education and/or improved sanitation than through the water intervention alone (see footnotes of Table 2 and 3).

Analysis of sanitation interventions

We included 14 comparisons from low- and middle-income settings. Twelve observations compared improved sanitation facilities (other than sewer connections) with unimproved sanitation, and two observations had sewer connections as their outcome.

Table 4 Meta-regression results for sanitation interventions

	Outcome sanitation	
Baseline sanitation	Improved sanitation, no sewer	Sewer connection*
Unimproved sanitation	0.84 (0.77, 0.91)	0.31 (0.27, 0.36)
Improved sanitation, no sewer connection		0.37 (0.31, 0.44)

*Based on limited evidence (Pradhan & Rawlings 2002; Moraes *et al.* 2003) and should therefore be considered with caution.

Figures are relative risks (and 95% confidence intervals).

Results are adjusted for combined intervention (RR 0.88 (0.77, 1.01)).

The final model explained 97% of the between-study variance. The overall relative risk for improved over unimproved sanitation on diarrhoea, based on meta-analysis, was 0.72 (0.59, 0.88). The results of multivariable meta-regression are shown in Table 4. A larger association between sewer interventions and reduction in diarrhoea was observed compared with other improved sanitation.

Excluding 20% of studies with the lowest quality rating did not significantly change estimates, either for the water or the sanitation analysis. Funnel plot asymmetry was observed among the studies of household-level water quality interventions, which may be due to publication bias. There was no evidence of funnel plot asymmetry in studies of community-level water or sanitation improvements with or without sewer interventions. Funnel plots and results of statistical tests examining evidence for publication bias are shown in the Online-only Appendix 4.

Water and sanitation intervention studies typically report diarrhoeal levels in children up to 5 years of age, with impacts in other age groups less frequently reported. Data on other age groups were extracted wherever possible, and the results for all ages compared with children under five. The effect estimates were found to be very similar and mostly within the confidence interval of the under-five age group. It has therefore been assumed that the estimates derived here can be used for all ages.

Discussion

Results

The results show that there are large potential reductions in diarrhoeal disease risk through improvements to both water and sanitation in low- and middle-income settings.

For water, the most effective household-level intervention was found to be a point-of-use filter in combination with safe water storage. At the community level, introduction of high-quality piped water (i.e. water supplied continuously to the household of good microbial water quality) was found to be most effective. There were also differences in the impact of sanitation interventions, and there is evidence that sewer interventions are associated with a greater reduction in diarrhoea than basic household sanitation. These results are largely consistent with previously published reviews, where provision of improved community water supply was associated with a limited reduction in diarrhoeal illness (Waddington *et al.* 2009), and some water quality interventions (especially water filters) had a significant impact on reducing illness (Clasen *et al.* 2006; Hunter 2009; Waddington *et al.* 2009; Cairncross *et al.* 2010). This is also true for sanitation, as sanitation interventions in previous analyses have been shown to reduce diarrhoea by 30–40% (Waddington *et al.* 2009; Cairncross *et al.* 2010), with a larger effect observed for sewer connection (Norman *et al.* 2010).

The effect estimates for higher-quality piped drinking water and sewer connection should, however, be treated with caution. We approximated the transition from 'basic piped water' to 'piped water, continuous and safe quality' by the effect of safe water storage plus the effect of any quality improvements on a piped water system. We acknowledge that this is likely an underestimate as it accounts for the quality aspect but not any benefits derived through greater water access and its impact on, for example, personal hygiene. Source water quality improvement on piped water was estimated from one single study (Hunter *et al.* 2010), although the results are consistent with evidence from high-income countries (Payment *et al.* 1991; Colford *et al.* 2009). The effect of a sewered system was derived from two observations (Pradhan & Rawlings 2002; Moraes *et al.* 2003). Given the small number of observations used to derive these results, generalisation should be made only with caution. For example, in the intervention study that provided source water quality improvements on a piped water supply (Hunter *et al.* 2010), it is possible that the baseline piped water may have been of poorer quality than 'typical' piped water in low- and middle-income settings. However, reclassifying the baseline water in this study as unimproved in the analysis barely changed the diarrhoeal effect estimates. Given the limited evidence base, it is likely that these estimates may change considerably as additional evidence becomes available. They do, however, indicate the large potential benefits of improving water and sanitation and call for a disaggregation of the 'improved' levels defined by JMP (JMP 2013).

The finding of potentially important disease reduction beyond improved non-piped and also basic piped water sources is eminently plausible. Water from those improved sources is frequently contaminated during collection, transport and household storage (Wright *et al.* 2004; Rufener *et al.* 2010). Household piped water in low- and middle-income settings is frequently non-continuous (e.g. Brown *et al.* 2013) which presents two microbial risks, namely infiltration into non-pressurised distribution systems and recontamination or growth during household storage. In addition, community and non-continuous household water supply may reduce the amount of water available for hygiene purposes. Water availability and distance to the water source are both associated with risk of diarrhoea (Wang & Hunter 2010; RSS 2011; Pickering & Davis 2012). Reliable at-home water supplies were shown to increase water availability and key hygiene practices (Evans *et al.* 2013). The current analysis further suggests that improved water storage is associated with decreased risk of diarrhoea; a finding which has been previously described (Roberts *et al.* 2001; Günther & Schipper 2013). The beneficial effect of filters over both unimproved and improved sources remained significant and substantial after bias adjustment for non-blinding. This may reflect the fact that even water from improved sources is frequently of poor quality (Bain *et al.* 2012, 2014; Wolf *et al.* 2013). The smaller effect seen from chlorine and solar treatments could be explained if a significant proportion of diarrhoea episodes was caused by agents that are less susceptible to those treatments, non-exclusive use (Mäusezahl *et al.* 2009), and/or there is low uptake (compliance) of the intervention (as the need for adequate compliance has been shown in previous epidemiological modelling – Hunter *et al.* 2009; Brown & Clasen 2012; Enger *et al.* 2013).

Household members with improved sanitation may still be exposed to high levels of pathogens from faecal material if their neighbours have no improved sanitation (Root 2011; Baker & Ensink 2012), or when on-site sanitation is not managed hygienically. In urban areas, especially, latrines have been observed to fill and overflow, which can lead to major contamination of the surrounding area (Carter 2013). Introduction of sewered sanitation at large scale in urban areas in low- and middle-income settings would be expected to have a positive impact on health, although care must be taken that sewage is appropriately treated to avoid the diarrhoeal disease burden being shifted 'downstream' to the receiving communities (Baum *et al.* 2013). As such, it is acknowledged that sewered systems with appropriate sewage treatment are costly, and in some settings, decentralised systems for managing on-site sanitation may be more cost-effective and appropriate (Norman *et al.* 2010).

Limitations

Effect estimates are from heterogeneous interventions and therefore only approximate the impact of improving water and sanitation on diarrhoea. Study quality is generally low which confirm previous analyses (Waddington *et al.* 2009; Cairncross *et al.* 2010; Clasen *et al.* 2010). Blinding and randomisation of study participants in water and sanitation interventions is often not possible and sometimes may not be desirable as blinding could negatively influence compliance and community dynamics which are important components for the adoption of interventions (Hartinger *et al.* 2011). Sanitation studies especially are often quasi-randomised (Capuno *et al.* 2011; Kumar & Vollmer 2013) which can introduce bias. Additionally, some point-of-use interventions have been shown to have low acceptability to the population (Boisson *et al.* 2009; Luoto *et al.* 2012) leading to poor adoption, and even an effective point-of-use treatment will have little impact on health if it is not consistently applied (Enger *et al.* 2013). In addition, few point-of-use interventions are effective against all typical classes of pathogens, and post-treatment contamination is frequent (Wright *et al.* 2004; Stauber *et al.* 2012). Even piped water interventions frequently provide low-quality non-continuous water which therefore requires storage, point-of-use treatment or the use of alternative water sources (Wang *et al.* 1989; Brown *et al.* 2013). Better quality water and sanitation interventions showed greater effectiveness in reducing diarrhoeal disease (Clasen *et al.* 2006). An attempt was made to account for some of these limitations by exploring health impacts beyond basic improved water and sanitation, by the use of specific bias adjustments and different sensitivity analyses.

We applied a bias adjustment to account for non-blinding, based on the findings of Savović *et al.* (2012). These, however, are based on clinical interventions, and there is little evidence that the pooled estimated bias is representative for the type of interventions covered in this article. The estimate is, however, specific to subjectively assessed outcomes (such as self-reported diarrhoea), and we believe that it represents the best currently available evidence on the effect of bias due to non-blinding.

Currently, only the impact of water and sanitation on diarrhoeal morbidity has been considered. Many other health effects (such as intestinal parasite infections, impaired nutritional status and possibly environmental enteropathy) have been associated with inadequate water and sanitation (Korpe & Petri 2012; Ziegelbauer *et al.* 2012; Dangour *et al.* 2013; Lin *et al.* 2013). Furthermore, inadequate water and sanitation have been associated with reduced school attendance (Freeman *et al.* 2012) and personal security issues, especially for women (Bapat & Agarwal 2003; Talaat *et al.* 2011). Unfortunately, quantitative evidence on these effects is currently very limited.

Meta-regression yields observational associations between variables, and is therefore prone to bias (Thompson & Higgins 2002). Use of water sources and sanitation facilities was defined at study level, although it may vary within the community. This can underestimate the true baseline or outcome effect. To include access as a continuous variable is currently not possible as many studies omit this information.

General discussion

The choice of what level of water and sanitation to consider as representing the highest attainable degree of safety (i.e. the counterfactual) has major implications in terms of the burden of disease that is attributable to inadequate water and sanitation. The analysis demonstrates health benefits beyond those achievable with basic improved water and sanitation, and it seems that health gains can be maximised when high-quality drinking water is available in sufficient quantities in the home and the sanitation system effectively prevents exposure to faecal material (through isolation and/or appropriate treatment). Thus, the results suggest that use of facilities defined as 'improved', as used in the 2010 GBD study (Lim *et al.* 2012), should not be construed as use of fully safe and adequate water and sanitation, devoid of an associated disease burden.

Service levels are frequently lower in low- and middle-income countries than those in high-income countries, but it is suggested that high-level services could represent a reference against which the risk for lower levels of water and sanitation could be estimated. Even defining high-level water services (i.e. high-quality water piped continuously to the home) as the counterfactual may lead to underestimates of the burden of disease. In Iceland, for example, the introduction of water safety plans was associated with a significant reduction of diarrhoea in the population (Gunnarsdottir *et al.* 2012). Also, tap water in California, USA, meeting all the required quality standards, was still associated with gastrointestinal illness (Colford *et al.* 2009). However, at present, data limitations preclude the setting of even higher counterfactuals for water and sanitation.

The systematic literature reviews and analyses reported in this paper have led to the identification of areas where evidence is missing on the linkages between water, sanitation and health. It is believed that effect estimates from meta-analyses would greatly benefit from more well-conducted and reported water and sanitation intervention studies complying to, for example, the CONSORT Statement for randomised controlled trials (Schulz *et al.* 2010) or the STROBE Statement for observational studies (Von Elm *et al.* 2007). Studies applying a factorial design might be a promising approach to assess different interventions simultaneously and, given a sufficiently large sample size, interactions between different WASH interventions (Montgomery *et al.* 2003). Studies reporting consistently not only on health outcome but also on implementation and compliance would enable inclusion of this information in future analyses. Additionally, research on underlying factors that strengthen intervention implementation and increase people's acceptance, adoption and sustained use is still rare. Improved methods for using natural experiments or pre-existing development interventions, in which exposure is not artificially manipulated, also seem to be a promising way forward (Arnold *et al.* 2009; Craig *et al.* 2012). Furthermore, impacts resulting from inadequate water and sanitation other than diarrhoea morbidity are currently under-researched. More evidence on these topics would enable more meaningful estimates of the potential health benefits of improving water and sanitation to be made.

Conclusions

Inadequate drinking water and sanitation are associated with considerable risks for diarrhoeal disease. The choice of a suitable approach that can differentiate health effects between different improvements in water and sanitation relative to the baseline is crucial for meaningful estimates. However, evidence from well-conducted intervention studies assessing exclusive use of adequate access and supply of safe water or universal use of effective sanitation is still very limited.

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References

Arnold B, Arana B, Mäusezahl D, Hubbard A & Colford JM Jr (2009) Evaluation of a pre-existing, 3-year household water treatment and handwashing intervention in rural Guatemala. *International Journal of Epidemiology* **38**, 1651–1661.

Bain R, Gundry S, Wright J, Yang H, Pedley S & Bartram J (2012) Accounting for water quality in monitoring access to safe drinking-water as part of the Millennium Development Goals: lessons from five countries. *Bulletin of the World Health Organization* **90**, 228–235.

Bain R, Cronk R, Hossain R *et al.* (2014) Assessment of the level of exposure to fecally contaminated drinking water in developing countries. *Tropical Medicine and International Health* **19** [Epub ahead of print]

Baker SM & Ensink J (2012) Helminth transmission in simple pit latrines. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **106**, 709–710.

Bapat M & Agarwal I (2003) Our needs, our priorities; women and men from the slums in Mumbai and Pune talk about their needs for water and sanitation. *Environment & Urbanization* **15**, 71–86.

Baum R, Luh J & Bartram J (2013) Sanitation: a global estimate of sewerage connections without treatment and the resulting impact on MDG progress. *Environmental Science & Technology* **47**, 1994–2000.

Boisson S, Schmidt W-P, Berhanu T, Gezahegn H & Clasen T (2009) Randomized controlled trial in rural Ethiopia to assess a portable water treatment device. *Environmental Science & Technology* **43**, 5934–5939.

Boisson S, Stevenson M, Shapiro L *et al.* (2013) Effect of household-based drinking water chlorination on diarrhoea among children under five in Orissa, India: a double-blind randomised placebo-controlled trial. *PLoS Medicine* **10**, e1001497.

Brown J & Clasen T (2012) High adherence is necessary to realize health gains from water quality interventions. *PLoS One* **7**, e36735.

Brown J, Hien VH, McMahan L *et al.* (2013) Relative benefits of on-plot water supply over other "improved"sources in rural Vietnam. *Tropical Medicine & International Health* **18**, 65–74.

Cairncross S, Hunt C, Boisson S *et al.* (2010) Water, sanitation and hygiene for the prevention of diarrhoea. *International Journal of Epidemiology* **39**(suppl 1), i193–i205.

Capuno J, Tan CAR & Fabella VM (2011) Do piped water and flush toilets prevent child diarrhea in rural Philippines?

Asia-Pacific Journal of Public Health. Retrieved. September 18, 2013. from http://aph.sagepub.com/content/early/2011/12/08/1010539511430996.abstract.

Carter RC (2013) Editorial: What happens when the pit latrine is full? *Waterlines* **32**, 185–186.

Clasen T, Schmidt WP, Rabie T, Roberts I & Cairncross S (2006) Interventions to improve water quality for preventing diarrhoea (Review). *Cochrane Database of Systematic Reviews* **3**, 1–52.

Clasen TF, Bostoen K, Schmidt WP *et al.* (2010) Interventions to improve disposal of human excreta for preventing diarrhoea. *Cochrane Database of Systematic Reviews* **6**, 1–30.

Clasen T, Pruss-Ustun A, Mathers C, Cumming O, Cairncross S & Colford JM Jr. (2014) Estimating the impact of inadequate water, sanitation and hygiene on the global burden of disease: evolving and alternative methods. *Tropical Medicine and International Health* **19** [Epub ahead of print]

Colford JM Jr, Hilton JF, Wright CC *et al.* (2009) The Sonoma water evaluation trial: a randomized drinking water intervention trial to reduce gastrointestinal illness in older adults. *American Journal of Public Health* **99**, 1988–1995.

Craig P, Cooper C, Gunnell D *et al.* (2012) Using natural experiments to evaluate population health interventions: new Medical Research Council guidance. *Journal of Epidemiology and Community Health* **66**, 1182–1186.

Dangour AD, Watson L, Cumming O *et al.* (2013) Interventions to improve water quality and supply, sanitation and hygiene practices, and their effects on the nutritional status of children. *Cochrane Database of Systematic Reviews* **8** CD009382

Engell RE & Lim SS (2013) Does clean water matter? An updated meta-analysis of water supply and sanitation interventions and diarrhoeal diseases. *Lancet* **381**, S44.

Enger KS, Nelson KL, Rose JB & Eisenberg JNS (2013) The joint effects of efficacy and compliance: a study of household water treatment effectiveness against childhood diarrhea. *Water Research* **47**, 1181–1190.

Esrey SA & Habicht J-P (1986) Epidemiologic evidence for health benefits from improved water and sanitation in developing countries. *Epidemiologic Reviews* **8**, 117–128.

Esrey SA, Potash JB, Roberts L & Shiff C (1991) Effects of improved water supply and sanitation on ascariasis, diarrhoea, dracunculiasis, hookworm infection, schistosomiasis, and trachoma. *Bulletin of the World Health Organization* **69**, 609.

Evans B, Bartram J, Hunter P *et al.* (2013) *Public Health and Social Benefits of at-House Water Supplies*. University of Leeds, UK.

Freeman MC, Greene LE, Dreibelbis R *et al.* (2012) Assessing the impact of a school-based water treatment, hygiene and sanitation programme on pupil absence in Nyanza Province, Kenya: a cluster-randomized trial. *Tropical Medicine & International Health* **17**, 380–391.

Gunnarsdottir MJ, Gardarsson SM, Elliott M, Sigmundsdottir G & Bartram J (2012) Benefits of water safety plans: microbiology, compliance, and public health. *Environmental Science & Technology* **46**, 7782–7789.

Günther I & Schipper Y (2013) Pumps, germs and storage: The impact of improved water containers on water quality and health. *Health Economics* **22**, 757–774.

Hartinger SM, Lanata CF, Hattendorf J *et al.* (2011) A community randomised controlled trial evaluating a home-based environmental intervention package of improved stoves, solar water disinfection and kitchen sinks in rural Peru: Rationale, trial design and baseline findings. *Contemporary Clinical Trials* **32**, 864–873.

Hunter PR (2009) Household water treatment in developing countries: comparing different intervention types using meta-regression. *Environmental Science & Technology* **43**, 8991–8997.

Hunter PR, Zmirou-Navier D & Hartemann P (2009) Estimating the impact on health of poor reliability of drinking water interventions in developing countries. *Science of The Total Environment* **407**, 2621–2624.

Hunter PR, Ramírez Toro GI & Minnigh HA (2010) Impact on diarrhoeal illness of a community educational intervention to improve drinking water quality in rural communities in Puerto Rico. *BMC Public Health* **10**, 219.

Jain S, Sahanoon OK, Blanton E *et al.* (2010) Sodium dichloroisocyanurate tablets for routine treatment of household drinking water in periurban Ghana: a randomized controlled trial. *American Journal of Tropical Medicine and Hygiene* **82**, 16–22.

JMP (2013) *Progress on Sanitation and Drinking-Water. 2013 Update*. World Health Organization, UNICEF, Geneva, Switzerland.

Kirchhoff LV, McClelland KE, Pinho MDC, Araujo JG, De Sousa MA & Guerrant RL (1985) Feasibility and efficacy of in-home water chlorination in rural North-eastern Brazil. *Journal of Hygiene* **94**, 173–180.

Kirkwood B & Sterne JAC (2003) Chapter 29: Regression modelling. In: *Essential Medical Statistics*, 2nd edn Blackwell Science, Oxford, UK, pp. 315–342.

Korpe PS & Petri WA Jr (2012) Environmental enteropathy: critical implications of a poorly understood condition. *Trends in Molecular Medicine* **18**, 328–336.

Kumar S & Vollmer S (2013) Does access to improved sanitation reduce childhood diarrhea in rural India? *Health Economics* **22**, 410–427.

Lim SS, Vos T, Flaxman AD *et al.* (2012) A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **380**, 2224–2260.

Lin A, Arnold BF, Afreen S *et al.* (2013) Household environmental conditions are associated with enteropathy and impaired growth in rural Bangladesh. *American Journal of Tropical Medicine and Hygiene* **89**, 130–137.

Liu L, Johnson HL, Cousens S *et al.* (2012) Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* **379**, 2151–2161.

Lunn DJ, Thomas A, Best N & Spiegelhalter D (2000) WinBUGS: a Bayesian modelling framework: concepts, structure, and extensibility. *Statistics and Computing* **10**, 325–337.

Luoto J, Mahmud M, Albert J *et al.* (2012) Learning to dislike safe water products: results from a randomized controlled trial of the effects of direct and peer experience on willingness to pay. *Environmental Science & Technology* 46, 6244–6251.

Mäusezahl D, Christen A, Pacheco GD *et al.* (2009) Solar drinking water disinfection (SODIS) to reduce childhood diarrhoea in rural Bolivia: a cluster-randomized, controlled trial. *PLoS Medicine* 6, e1000125.

McNamee R (2003) Confounding and confounders. *Occupational and Environmental Medicine* 60, 227–234.

Moher D, Liberati A, Tetzlaff J & Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine* 151, 264–269.

Montgomery AA, Peters TJ & Little P (2003) Design, analysis and presentation of factorial randomised controlled trials. *BMC Medical Research Methodology* 3, 26. doi:10.1186/1471-2288-3-26.

Moraes LRS, Azevedo Cancio J, Cairncross S & Huttly S (2003) Impact of drainage and sewerage on diarrhoea in poor urban areas in Salvador, Brazil. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 97, 153–158.

Norman G, Pedley S & Takkouche B (2010) Effects of sewerage on diarrhoea and enteric infections: a systematic review and meta-analysis. *Lancet Infectious Diseases* 10, 536–544.

Payment P, Richardson L, Siemiatycki J, Dewar R, Edwardes M & Franco E (1991) A randomized trial to evaluate the risk of gastrointestinal disease due to consumption of drinking water meeting current microbiological standards. *American Journal of Public Health* 81, 703–708.

Pickering AJ & Davis J (2012) Freshwater availability and water fetching distance affect child health in sub-Saharan Africa. *Environmental Science & Technology* 46, 2391–2397.

Pope DP, Mishra V, Thompson L *et al.* (2010) Risk of low birth weight and stillbirth associated with indoor air pollution from solid fuel use in developing countries. *Epidemiologic Reviews* 32, 70–81.

Pradhan M & Rawlings LB (2002) The impact and targeting of social infrastructure investments: lessons from the Nicaraguan Social Fund. *World Bank Economic Review* 16, 275–295. World Bank

Prüss A, Kay D, Fewtrell L & Bartram J (2002) Estimating the burden of disease from water, sanitation, and hygiene at a global level. *Environmental Health Perspectives* 110, 537–542.

Roberts L, Chartier Y, Chartier O, Malenga G, Toole M & Rodka H (2001) Keeping clean water clean in a Malawi refugee camp: a randomized intervention trial. *Bulletin of the World Health Organization* 79, 280–287.

Root GPM (2011) Sanitation, community environments, and childhood diarrhoea in rural Zimbabwe. *Journal of Health, Population and Nutrition* 19, 73–82.

RSS (2011) Review evidence on minimum household water security requirements for health protection. Research Division, Royal Scientific Society Amman-Jordon. http://www.mdgfund.org/sites/default/files/ENV_STUDY_Jordan_Minimum%20hosehole%20water%20security.pdf

Rufener S, Mäusezahl D, Mosler H-J & Weingartner R (2010) Quality of drinking-water at source and point-of-consumption—drinking cup as a high potential recontamination risk: A field study in Bolivia. *Journal of Health & Population Nutrition* 28, 34–41.

Salanti G, Higgins JPT, Ades AE & Ioannidis JPA (2008) Evaluation of networks of randomized trials. *Statistical Methods in Medical Research* 17, 279–301.

Savović J, Jones HE, Altman DG *et al.* (2012) Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Annals of Internal Medicine* 157, 429–438.

Schulz KF, Altman DG & Moher D & For the CONSORT Group (2010) CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 340: c332–c332.

Stauber CE, Kominek B, Liang KR, Osman MK & Sobsey MD (2012) Evaluation of the impact of the plastic BioSand filter on health and drinking water quality in rural Tamale, Ghana. *International Journal of Environmental Research and Public Health* 9, 3806–3823.

Talaat M, Afifi S, Dueger E *et al.* (2011) Effects of hand hygiene campaigns on incidence of laboratory-confirmed influenza and absenteeism in schoolchildren, Cairo. *Egypt. Emerging Infectious Diseases* 17, 619–625.

Thompson SG (1994) Systematic review: why sources of heterogeneity in meta-analysis should be investigated. *British Medical Journal* 309, 1351–1355.

Thompson SG & Higgins J (2002) How should meta-regression analyses be undertaken and interpreted? *Statistics in Medicine* 21, 1559–1573.

Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC & Vandenbroucke JP (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Preventive Medicine* 45, 247–251.

Waddington H, Snilstveit B, White H & Fewtrell L (2009). *Water, Sanitation and Hygiene Interventions to Combat Childhood Diarrhoea in Developing Countries*. International Initiative for Impact Evaluation, New Delhi, India.

Walker I, del Cid R, Ordoñez F & Rodríguez F (1999). *Ex-Post Evaluation of the Honduran Social Investment Fund (FHIS 2)*. World Bank, Washington, DC. http://www.esa.hn/pub/FHIS%20Expost%20Evaluation.pdf.

Wang X & Hunter PR (2010) A systematic review and meta-analysis of the association between self-reported diarrheal disease and distance from home to water source. *American Journal of Tropical Medicine and Hygiene* 83, 582–584.

Wang ZS, Shepard DS, Zhu YC *et al.* (1989) Reduction of enteric infectious disease in rural China by providing deep-well tap water. *Bulletin of the World Health Organization* 67, 171.

Wells GA, Shea B, O'Connell D *et al.* (undated) *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-analyses*. Ottawa Hospital. Research Institute. Retrieved. from http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Welton NJ, Ades AE, Carlin JB, Altman DG & Sterne JAC (2009) Models for potentially biased evidence in meta-analysis using empirically based priors. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* **172**, 119–136.

WHO (2005). *The treatment of Diarrhoea. A Manual for Physicians and Other Senior Health Workers*, 4th edn. WHO, Geneva, Switzerland.

WHO (2009) *Global health risks, Mortality and Burden of Disease Attributable to Selected Major Risks*. WHO, Geneva, Switzerland. Retrieved. April 30, 2012. from http://www.who.int/healthinfo/global_burden_disease/global_health_risks/en/index.html.

WHO (2013a) *Safe Household Water Storage*. WHO. Retrieved. December 5, 2013. from http://www.who.int/household_water/research/safe_storage/en/.

WHO (2013b) *World Health Statistics 2013*. World Health Organization, Geneva, Switzerland

Wolf J, Bonjour S & Prüss-Ustün A (2013) An exploration of multilevel modeling for estimating access to drinking-water and sanitation. *Journal of Water and Health* **11**, 64–77.

Wood L, Egger M, Gluud LL *et al.* (2008) Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *British Medical Journal* **336**, 601.

Wright J, Gundry S & Conroy R (2004) Household drinking water in developing countries: a systematic review of microbiological contamination between source and point-of-use. *Tropical Medicine & International Health* **9**, 106–117.

Ziegelbauer K, Speich B, Mäusezahl D, Bos R, Keiser J & Utzinger J (2012) Effect of sanitation on soil-transmitted helminth infection: systematic review and meta-analysis. *PLoS Medicine* **9**, e1001162.

Supporting Information

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

Appendix S1. PRISMA checklist.
Appendix S2. Literature search strategy.
Appendix S3. Data extraction form.
Appendix S4. General extra information.
Appendix S5. List of included intervention studies.

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