This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/ by-nc/2.5/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. Published by Oxford University Press on behalf of the International Epidemiological Association. *International Journal of Epidemiology* 2010;**39**:i193–i205 © The Author 2010; all rights reserved. doi:10.1093/ije/dyq035

# Water, sanitation and hygiene for the prevention of diarrhoea

Sandy Cairncross,<sup>1</sup>\* Caroline Hunt,<sup>1</sup> Sophie Boisson,<sup>1</sup> Kristof Bostoen,<sup>1</sup> Val Curtis,<sup>1</sup> Isaac CH Fung<sup>2</sup> and Wolf-Peter Schmidt<sup>1</sup>

<sup>1</sup>London School of Hygiene & Tropical Medicine, Department of Infectious & Tropical Diseases, London, UK and <sup>2</sup>Department of Epidemiology and Biostatistics, College of Public Health, University of Georgia, Athens, GA, USA.

\*Corresponding author. London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK. E-mail: sandy.cairncross@lshtm.ac.uk

Background	Ever since John Snow's intervention on the Broad St pump, the
	effect of water quality, hygiene and sanitation in preventing
	diarrhoea deaths has always been debated. The evidence identified
	in previous reviews is of variable quality, and mostly relates to
	morbidity rather than mortality.

- **Methods** We drew on three systematic reviews, two of them for the Cochrane Collaboration, focussed on the effect of handwashing with soap on diarrhoea, of water quality improvement and of excreta disposal, respectively. The estimated effect on diarrhoea mortality was determined by applying the rules adopted for this supplement, where appropriate.
- **Results** The striking effect of handwashing with soap is consistent across various study designs and pathogens, though it depends on access to water. The effect of water treatment appears similarly large, but is not found in few blinded studies, suggesting that it may be partly due to the placebo effect. There is very little rigorous evidence for the health benefit of sanitation; four intervention studies were eventually identified, though they were all quasi-randomized, had morbidity as the outcome, and were in Chinese.
- **Conclusion** We propose diarrhoea risk reductions of 48, 17 and 36%, associated respectively, with handwashing with soap, improved water quality and excreta disposal as the estimates of effect for the LiST model. Most of the evidence is of poor quality. More trials are needed, but the evidence is nonetheless strong enough to support the provision of water supply, sanitation and hygiene for all.
- **Keywords** Water, sanitation, hygiene, diarrhoea, mortality

## Background

It has been estimated, at least for Africa, that 85% of the burden of disease preventable by water supply is caused by feco-oral, mainly diarrhoeal diseases, largely due to the substantial child mortality which they cause.<sup>1</sup> In 1854, Dr John Snow famously incriminated the water from the Broad St pump as the vehicle of cholera transmission in London's Soho, but much of the medical establishment continued to uphold the miasma theory for many years thereafter. Ever since then, the role of water in diarrhoea transmission and prevention has been hotly debated. More recently, awareness has also grown about the importance of excreta disposal in preventing diarrhoeal disease, culminating in the recent poll of readers of the *British Medical Journal* in which sanitation was voted the greatest advance in public health in the last century.<sup>2</sup>

There is strong temptation to conduct evaluations of the health impact of water supply, sanitation and hygiene interventions, but the challenges also are many. Often it is difficult or impossible to randomize or to blind the intervention. In practice, most studies do not identify specific aetiologies and so deal with an outcome (diarrhoea) which is caused by various pathogens, transmitted by various routes and associated with various potential confounding factors. The vulnerability of such studies to confounding is compounded by the use of observational study designs and the low relative risks (RRs) involved, which are typically less than two. In developing countries, most episodes of diarrhoea morbidity-even much of the life-threatening morbidity-are not reported to the health system, so that active surveillance involving home visits is used to detect them, often with excessive recall periods. In the circumstances then, it is not surprising that the first methodological review of this literature<sup>3</sup> located some 50 epidemiological studies, but found serious flaws in every one.

A series of literature reviews conducted by Esrey and others<sup>4–7</sup> established a consensus view on the impacts on health of improved water quality, water quantity and sanitation, which was summarized in the relevant chapter of Disease Control in Developing Countries.<sup>8</sup> A more recent review<sup>9</sup> gave prominence to a number of studies of household-based water treatment, and arrived at a greater estimate of the impact of water quality than previous reviews. However, the confidence intervals (CIs) for this and the other such estimates were very wide, so wide as to show that the new figures were not *significantly* different from the corresponding previous estimates.

In this article, drawing on three systematic reviews of the literature, we present the evidence for an impact on diarrhoea mortality from improvements in hygiene (specifically, handwashing with soap),<sup>10</sup> drinking-water quality,<sup>11</sup> and excreta disposal. The reviews of effectiveness of the interventions are shaped in large part by the needs of the LiST model. In that model, increases in coverage of an intervention result in a reduction of deaths due to one or more causes or in the reduction of a risk factor. Therefore, the reviews and the grade process used were designed to develop estimates of the effect of an intervention in reducing either a risk factor or deaths due to a specific cause. For more details of the review methods, the adapted grade approach or the LiST model, see other articles in this supplement.

## Methods

## Handwashing with soap

The original review<sup>10</sup> aimed to identify all studies published in English up to the end of 2002 relating handwashing to the risk of infectious intestinal or diarrhoeal diseases in the community. Medline, CAB Abstracts, Embase, Web of Science and the Cochrane Library were systematically searched for papers related to handwashing, use of soap, as well as disease terms such as diarrhoea, typhoid, enteric, cholera, shigellosis, dysentery, and mortality. Searches were also undertaken by hand with reference lists from these papers, the authors' own collections and review articles. No limitations were placed on date or geographical location. The search was updated in 2008.

Studies were retained for the meta-analysis if they provided point estimates and 95% CIs (or the means to calculate them) of the risk of not washing hands. Intervention trials not solely concerned with handwashing were excluded. Where both crude and adjusted odds ratios were presented, adjusted values were used. The risk values for studies with several measures of handwashing practice were combined by averaging, if they concerned the same sample group. If they concerned different groups, they were treated as if they were separate studies. Similarly, studies with two different outcome measures were entered into the meta-analysis as if they were separate studies.

## Water quality

Following the Cochrane peer-reviewed protocol,<sup>12</sup> we searched the specialized register of the Cochrane Infectious Diseases Group, CENTRAL, Medline, Embase and LILACS for all randomized and quasi-randomized controlled trials of interventions to improve water quality for the prevention of diarrhoeal disease, regardless of language, publication status, or date, up to December 2005. Interventions included any measure to improve the microbial quality of drinking water, unless undertaken in response to epidemic diarrhoea. The primary outcome was diarrhoea in adults or children. We hand searched conference proceedings, contacted researchers and organizations working in the specialty, and checked the references of identified studies. Two reviewers independently examined the electronic records for potentially eligible studies and the full text of potentially eligible reports. Disagreements were resolved by a third reviewer.

Measures of effect reported were risk ratios, rate ratios, odds ratios and longitudinal prevalence ratios (number of days or weeks with diarrhoea divided by number of days or weeks under observation in a person). The results are presented separately by study type and also by type of intervention, whether source- or household-based. A random effects inverse variance method was used on the log scale to calculate pooled estimates.

#### **Excreta** disposal

Again we followed the Cochrane approved protocol<sup>13</sup> to search for interventions to dispose of human excreta so as to reduce direct or indirect human contact. This includes any steps to remove or contain faeces, such as simple pit latrines, bucket latrines, hanging toilets and composting toilets, and should be contrasted with open defecation. Diarrhoea was again the outcome measure, whether or not microbiologically confirmed. We defined diarrhoea and an episode in accordance with the case definitions used in each trial. We excluded trials that had no clinical outcomes; for example, trials that only reported on microbiological pathogens in the stool.

We searched the following databases up to April 2007: Cochrane Infectious Disease Group Specialized Register; CENTRAL; MEDLINE; EMBASE; LILACS, and also Chinese-language databases available under the Wan Fang portal using the Chinese equivalents of our search terms where appropriate. We searched the metaRegister of Controlled Trials (mRCT) using 'diarrhea', 'diarrhoea' and 'sanitation or latrine or toilet or privy or disposal' as search terms, and also a number of relevant conference proceedings. Other researchers and relevant international agencies were also contacted in the search for unpublished and ongoing trials. The reference lists of studies identified as above were also scanned for any further relevant studies.

#### General

All studies which met final inclusion and exclusion criteria were double data abstracted into a standardized form for each outcome of interest.14 We abstracted key variables with regard to the study identifiers and context, study design and limitations, intervention specifics, and outcome effects. Each study was assessed and graded according to the adaptation by the Child Health Epidemiology Reference Group (CHERG) of the GRADE technique.<sup>15</sup> Studies received an initial score of high if a randomized or cluster randomized trial. The grade was decreased one grade for each study design limitation. In addition, studies reporting an intent-to-treat analysis or with statistically significant strong levels of association (>80% reduction) receive 1-2 grade increases. Any study with a final grade of very low was excluded on the basis of inadequate study quality. The process is summarized in Tables 1, 2 and 3. To save space, we have not listed all of the studies in all three reviews with the bibliography of this article; instead, a detailed listing is provided in three corresponding Supplementary Tables 1, 2 and 3 available at IJE online. The numbers in Tables 1, 2 and 3 refer to these supplementary tables.

For the outcome of interest, namely the reduction of diarrhoea mortality, we applied the CHERG Rules

for Evidence Review<sup>14</sup> to the collective diarrhoea morbidity and mortality outcomes to generate a final estimate of effect.

## Results

#### Handwashing with soap

The search identified a total of 38 studies (Figure 1) but 21 were not suitable for data extraction, either because they did not specify whether soap was used, or did not present data permitting a calculation of effect. Of the 17 remaining studies, 7 were intervention trials and 10 were observational (Table 1). All of the interventions or exposure measures related to handwashing before eating or food handling, or after defecation or handling of child stools, or a combination of these.

Only one mortality study was found.<sup>16</sup> The number of events was not stated, but the wide confidence intervals (reduction of +62% to -43%) suggest there were very few, and the study was observational, with weaknesses in the outcome definition (deaths from other infectious diseases besides diarrhoea were included) and ascertainment of compliance.

We therefore turned to morbidity studies. None of the intervention studies gave adequate compliance data, so that the effect reported (a reduction of 47%) is that of handwashing promotion rather than of handwashing itself; i.e. the effect of the intervention, not the individual's response to it. However, this was slightly greater than the pooled effect (a reduction of 43%) of all studies in the review (Figure 2a and b). In other words, the observational studies, which did report the effect of individuals' behaviour, did not find a greater effect. The original review found that the effect was remarkably consistent across studies of higher methodological quality, and studies with severe forms of diarrhoea as an outcome. In each of these categories, the pooled estimate of effect is of a reduction within the range of 42-48% (Table 1). The combined effect of the more severe diarrhoeas was a 48% reduction. Two studies of laboratory confirmed shigellosis,<sup>17,18</sup> a more severe and a 'harder' outcome than self-reported diarrhoea, had a pooled effect of reduction by 59%. On the other hand, three studies were conducted in settings where water use was known to be constrained; (i) a low-income area of Lima, Peru, where vendors sell water expensively from tanker trucks, (ii) a refugee camp in Malawi and (iii) a setting in Burundi where median water usage was only 51 per capita per day. The reductions in risk were 11, 26 and 41%, respectively, all of them less than the combined effect of 43% found in the review as a whole.

Subsequent to our initial review,<sup>10</sup> a Cochrane review of the effect of handwashing on diarrhoea was published.<sup>19</sup> Most of the studies included were in institutional settings, but five were conducted in the community. In two of those, the intervention

7 ~		0	т т					
No of studies		Q	ality assessment			No of e	vents	Effect
(supplementary table ref.)	Design	Limitations	Consistency (based on the heterogeneity of the meta)	Generalizability to population of interest	Generalizabi- lity of intervention	Intervention	Control	RR (95% CI)
Outcome 1: Diarrhoeá 1 <sup>15</sup>	n mortality; Quality Observational (case control)	:: very low Not randomized, no placebo, unreliable exposure measure (-2)	Not applicable	Only one study (–0.5)		Not given	Not given	0.97 (0.38–1.43) <sup>a</sup>
Outcome 2: Diarrhoeá 7 <sup>1–7</sup>	ı morbidity; Qualit RCT/quasi-RCT	y: very low Inadequate randomization, no placebo, compliance not measured, no	Tests for heterogeneity gave significant result (-0.5)	1 study in USA, 1 Australia; 3 studies are all	Moderate and severe morbidity	739 <sup>b</sup>	1157 <sup>b</sup>	0.53 (0.37–0.76) <sup>c</sup>
31.2.10	High methodo- logical quality (trials & observational studies) <sup>d</sup>	1 of 3 randomized, no placebo, 1 high loss to follow-up, 1 compliance not assessed (-0.5)	Heterogeneity not significant. Random effects modes used for pooled estimates. Both fixed and random effect models gave the same pooled estimate	ages (-0.5) 1 study in USA, 1 Asia, 1 Latin Am, 1 study is all ages (-0.5)	(c.u-) Moderate and severe morbidity (-0.5)	55 <sup>b</sup>	109 <sup>b</sup>	0.58 (0.49–0.69) <sup>c</sup>
Outcome 3: Severe of 924.6.11.12.14,15.16.18	ttcomes (hospitaliz RCT/quasi-RCT/ observational	ed enteric infection cases, cho Inadequate randomization, no placebo, compliance not assessed, no baseline incidence (-1)	lera, shigellosis, typhoid and Tests for heterogeneity gave significant result(-0.5)	deaths); Quality: ve Mostly Asia; most studies are all ages(-0.5)	ry low Severe morbidity and cause- specific mortality (-0.5)	492 <sup>b</sup>	798 <sup>b</sup>	0.52 (0.34–0.65) <sup>c</sup>
Outcome 4: Shigellosi 2 <sup>2,6</sup>	.s; Quality: low RCT/quasi-RCT	Inadequate randomization, no placebo, compliance not measured, no baseline incidence (-1)	Heterogeneity not significant. Random effects model used for pooled estimates (Fixed effect model gave the same pooled estimate)	Both studies in Asia, both all ages (-0.5)	Severe morbidity	17	51	0.41 (0.27–0.62) <sup>c</sup>
Source of systematic <sup>a</sup> Effect comes from 1	review and measunadiusted odds r	sures of effect: Ref. <sup>10</sup> ratio of 0.97 reported in Hoc	nue <i>et al</i> . <sup>16</sup>					

 Table 1
 Quality assessment of trials of handwashing with soap for the prevention of diarrhoea

<sup>b</sup>Number of events not available for all studies. <sup>c</sup>Random effect meta-analysis. <sup>d</sup>Includes trials with baselines and concurrent control groups and observational studies with adequate control for confounding.

No of studies		Quality	/ assessment			No of ev	vents	Effect
(supplemen- tary table ref.)	Design	Limitations	Consistency (based on the heterogeneity of the meta)	Generalizability to population of interest	Generalizability of intervention	Intervention	Control	RR (95% CI)
Outcome 1: Diarrl 2 <sup>8,27</sup>	noeal mortality for all RCT and quasi-RCT	ages; Quality: very low No placebo, not blinded, one randomized, self-reported and self-defined diarrhoea (-1.5)	NA	Both Africa, 1 is all ages, 1 under 5s (-0.5)	l all-cause mortal- ity, 1 diarrhoeal mortality	34	55	Ranging from 0.61 to 0.15 <sup>a</sup>
Outcome 2: Diarri 38 (30 studies, 5 with multiple arms; arms counted as additional	noeal morbidity for al RCT and quasi-RCT	l ages; Quality: very low Only three blinded and placebo, few adequately randomized, most self-reported diarrhoea with excessive recall period. (-1.5)	Test for hetero- geneity gave significant result (-0.5)	Mostly Africa, Latin America and Asia, all ages (–0.5)	Moderate and severe morbidity (-0.5)	41 485 <sup>b</sup>	64 224 <sup>b</sup>	0.58 (0.46–0.72) <sup>c</sup>
27 (19 studies, 5 with multiple	RCT	Only three blinded and with pla- cebo, few adequately rando-	Significant heterogeneity	Mostly Africa and Latin America, all	Moderate and severe morbidity	23 151	45 098	0.54 (0.38–0.88) <sup>c</sup>
4 <sup>1,5,12</sup>	Double blind studies	Indequate (-1) Inadequate randomization, high loss to follow-up, coverage not	Heterogeneity not significant	ages (-0.2) 1 Lat Am, 1 Africa, 1 USA, all ages	Moderate and severe morbidity	1912	1987	0.93 (0.70–1.33) <sup>c</sup>
11 <sup>20–30</sup>	Quasi-RCT	Intersured (-0.) Inadequately randomized, no placebo, mostly self-reported with excessive recall period	r = 0.00 Significant heterogeneity (-0.5)	(-0.5) Mostly Asia and Africa, all ages (-0.5)	Moderate and severe morbidity (-0.5)	18 334 <sup>b</sup>	19 125 <sup>b</sup>	0.62 (0.48–0.89) <sup>c</sup>
620,21,23,24,27,30	Quasi-RCT source-based	(2) Inadequately randomized, no placebo, mostly self-reported,	Significant heterogeneity	4 Asia, 2 Africa, all ages (–0.5)	Moderate and severe morbidity	18 164	18723	0.73 (0.53–1.01) <sup>c</sup>
321-19,22,25,26,28,29	interventions RCT and quasi-RCT house-hold-based interventions	excessive recall period (-2) Only three blinded and placebo, few adequately randomized, most self-reported diarrhoea with excessive recall period. (-1.5)	(-0.5) Significant heterogeneity (-0.5)	Mostly Africa and Latin America, all ages (–0.5)	(-0.5) Moderate and severe morbidity (-0.5)	23 321 <sup>b</sup>	45 500 <sup>b</sup>	0.57 (0.46–0.70) <sup>c</sup>
Outcome 3: Diarrl 29 <sup>1-4,8-13,15-20,</sup> 22-24,26,27	noeal morbidity for ch RCTs and quasi-RCTs	uldren <5 years; Quality: very low Only three blinded and placebo, few adequately randomized, most self-reported diarrhoea with excessive recall period	Significant heterogeneity (-0.5)	Mostly Latin America and Africa, under 5s	Moderate and severe morbidity (-0.5)	17 687 <sup>b</sup>	39165 <sup>b</sup>	0.60 (0.44–0.81) <sup>c</sup>
4 <sup>20,23,24,27</sup>	Quasi-RCT source-based	Inadequately randomized, no placebo, most self-reported,	Test for hetero- geneity gave	2 Africa, 2 Asia, under 5s	Moderate and severe morbidity	1603	1924	0.85 (0.71–1.02) <sup>c</sup>
25 <sup>1-4,8,11-13,</sup> 15-19,26,27	RCT and quasi-RCT household-based interventions	Only three blinded and placebo, few adequately randomized, most self-reported diarrhoea with excessive recall period. (-1.5)	Significant heterogeneity (-0.5)	Mostly Latin America and Africa, under 5s	Moderate and severe morbidity (-0.5)	16 084 <sup>b</sup>	37241 <sup>b</sup>	0.56 (0.39–0.81) <sup>c</sup>
Source: Clasen T,	2006, PhD Dissertati	on, University of London. <sup>11</sup>						

Table 2 Quality assessment of trials of water quality improvement for the prevention of diarrhoea

<sup>a</sup>We did not calculate pooled estimates for the studies on water quality reporting mortality. <sup>b</sup>Number of events not available for one or more studies. <sup>c</sup>Random effects inverse variance method on the log scale was used to calculate pooled estimates. Heterogeneity was examined using the  $\chi^2$  test with a 10% level of statistical significance and the  $\Gamma^2$  test for consistency.

Downloaded from http://ije.oxfordjournals.org/ by guest on December 9, 2015

PREVENTION OF DIARRHOEA i197

<b>Table 3</b> Quality assessme	ent of trials of excreta disposal for the	prevention of dis	arrhoea				
No of studies	Quality a	assessment			No of e	vents	Effect
(supplementary Design table ref.)	Limitations	Consistency (based on the heterogeneity of the meta)	Generaliz- ability to population of interest	Generaliz- ability of intervention	Intervention	Control	RR (95% CI)
Outcome 1: Diarrhoeal moi 4 <sup>1-4</sup> Quasi-R	<ul> <li>cr all ages; Quality: very low</li> <li>cr Inadequate randomization, no placebo, no baseline, compliance not assessed, long recall for self-reported diarrhoea (-1.5)</li> </ul>	Not applicable	All China, all ages (–0.5). Limited relevance outside China	Severe to moderate morbidity (-0.5)	2471	3925	Ranging from 0.92 to 0.37; median 0.49 to 0.80 <sup>a</sup>
Outcome 2: Diarrhoeal moi Before/ study	chidity, ages 0–3 years Quality: low after Inadequate randomization, and no placebo	Not applicable	Urban, high coverage of on-plot water	Sewerage, not on-site low-cost systems	Not given; 24 sentinel areas studied	Not given	City-wide reduction of 21% (19%, 26%), and 43% (39%, 46%) in the high risk areas



Figure 1 Synthesis of study identification in review of the effect of handwashing with soap on diarrhoea mortality and morbidity<sup>10</sup>

did not involve soap and was not focussed on handwashing. Pooling the other three<sup>20-22</sup> gave a reduction in diarrhoea by 43% (95% CI 25-56%).

#### Water quality interventions

preventing diarrhoea. Cochrane Database Syst Rev DRAFT (April 2009)

for

excreta disposal

improve

Interventions to

et al.

W-P

Schmidt

Bostoen K,

Source: Clasen TF,

<sup>a</sup>We did not calculate pooled estimates for the sanitation trials.

Two studies with a mortality outcome were found and following the Cochrane protocol<sup>12</sup> included. (see Figure 3 and Table 2). One of these<sup>23</sup> had ascertained diarrhoea mortality, but the intervention included health education about oral rehydration therapy for diarrhoea, which alone could explain the 85% reduction in diarrhoea mortality that was observed. Moreover, only two villages had been ran-domized. The other trial,<sup>24</sup> whose authors admit that it was not designed to detect a mortality outcome, found a significant reduction (RR of death = 0.58, P < 0.036) only for all causes and all ages by pooling two intervention arms (total 59 events). Pooling the studies would be questionable, as the interventions were very different.

The serious limitations of the mortality studies led us to consider the morbidity studies. All took selfreported diarrhoea as the outcome; the Cochrane protocol had excluded trials that had no clinical outcomes, such as trials that report only on microbiological pathogens in the stool. Similar results were obtained for diarrhoea in all age groups and with the outcome limited to children aged <5 years. The type of study seemed to have little bearing on the measure of effect, which ranged from 46% in randomized controlled trials (RCTs) to 38% of quasi-RCTs. The review protocol approved by the Cochrane Collaboration had limited its scope to trials, so that no observational studies were included. Interventions based at the water source had less effect (27% for all ages, 15% for young children) than household-based ones, with an effect of 43-44%, depending on the age range. Two studies implemented in settings where the water before treatment had <10 faecal coliforms/100 ml (a concentration classified by WHO as



**Figure 2** Forest plots of (**a**) all studies in handwashing review, and (**b**) intervention studies only. Numbers on *y*-axis are references to studies in Supplementary Table 1. The diamond represents the combined relative risk and 95% CI from random effects model<sup>10</sup>



**Figure 3** Synthesis of study identification in review of the effect of water quality interventions on diarrhoea mortality and morbidity<sup>11</sup>

'low risk') had a combined effect of reducing risk by 61% (95% CI 30–67%) with insignificant heterogeneity. The greatest difference of all was between the 31 unblinded and the 4 blinded trials,  $^{25-28}$  with the latter giving a reduction of only 7% in diarrhoea risk, which was not statistically significant (Figure 4).

#### Excreta disposal

Our initial attempt at this review nearly foundered. The initial search<sup>13</sup> produced seven quasi-randomized intervention studies with diarrhoea morbidity as the outcome measure, and one with diarrhoea mortality (Figure 5, Table 4). The mortality study has already been mentioned;<sup>23</sup> the intervention included water supply and education about oral rehydration therapy, which could explain the observed reduction in mortality. All eight studies involved an intervention to improve water supply as well as excreta disposal, so that in none of them is it possible to assess the impact of sanitation as an intervention *per se*.

A renewed effort to locate suitable studies produced a further four,  $^{29-32}$  in which the intervention involved excreta disposal alone. All four were conducted in China (see the following URL http://maps.google .com/maps/ms?ie=UTF8&hl=en&msa=0&msid=109 120590372693546058.000465c8157b73053ba7f&z=6 for a map of the study sites), and published in Chinese (Table 3). The reductions in diarrhoea morbidity in the four studies were 63, 51, 20 and 8%, respectively. In all but the last, the confidence interval did not include zero reduction. We did not calculate pooled estimates for the sanitation trials, because



**Figure 4** Forest plots of (a) all 35 studies in water quality review, and (b) the four blinded studies  $\text{only}^{35}$ 

most studies randomized a very small number of villages, which makes calculation of confidence intervals impossible. Also, the interventions tested were very different from one another, which also makes pooling questionable.

These four studies are hardly ideal; they are quasi-randomized, not full RCTs; the control groups did not lack sanitation altogether, but mainly used some sort of pit latrine; and third, the published studies are not available for scrutiny except by those able to read Chinese. We therefore widened our scope further to include before/after studies. The unit of intervention is effectively the community, neighbourhood or village, but only one such study considered enough such units for statistical tests to be applied at this level. This recent study<sup>33</sup> is, strictly speaking, a before/after design, but is in many ways akin to a



**Figure 5** Synthesis of study identification in review of the effect of excreta disposal on diarrhoea morbidity

quasi-randomized trial in 24 neighbourhoods of the City of Salvador, Brazil. It found a city-wide reduction of 21% (95% CI 19–26%), and 43% (CI 39–46%) in the high risk areas.

### Discussion

### Handwashing with soap

Once the nature of the studies has been consistently defined (in the present case, community-based studies with an intervention focussed on handwashing and involving soap), the studies in the literature are remarkably consistent, showing a reduction in diarrhoea by 42–48%. We took 48%, the reduction found for the more severe diarrhoeas, as the figure to propose for LiST.

Results of initial search for evidence of the effect of sanitation in diarrhoea control

4

Table .

Au

Dut

Dut

The problem encountered with water quality interventions, that the blinded studies do not support the positive picture drawn by the others, raises the question of whether this problem applies to handwashing with soap. After all, one cannot persuade people to wash their hands without their knowledge! The differing results of the blinded and unblinded studies suggest that much of the apparent impact of water treatment is attributable to bias, but by the same token that possibility cannot be ignored in the case of handwashing.

Blinding can be applied to two groups; the subjects, and those who assess their status. It can refer to each subject's exposure allocation, or to the nature of the exposure or the disease outcome. Indeed, the Cochrane review of handwashing<sup>19</sup> noted that one

reduction	th education about diar-	giene education 25% pusehold chlorination, 29%	inproved water storage health & hygiene education –3% th education about 30% DRT	902 9 VU	ote boiling of water, 55% of livestock, fly control,	nts, etc 50%
	Public taps, 2 h/week healt rhoea prevention & ORT	Improved water supply, hy Improved water supply; ho	nygiene equication and in Boreholes & handpumps, h Public taps, 2 h/week healt diarrhoea prevention & C	Household water connectio	Health education to promo handwashing, corralling (	road & drain improvemer Piped water supply
	Unclear	N0 N0	No Unclear	No	No	No, but the two
	rural	rural rural	rural rural	rural	rural	rural
	Ivory Coast	Bangladesh Kenya	Nigeria Ivory Coast	USA	China	China
	mortality Quasi-RCT	morbidity Quasi-RCT Quasi-RCT	Quasi-RCT Quasi-RCT Messou (b)	morbidity Quasi-RCT	Quasi-RCT	Quasi-RCT
	arrhoea 1997	arrhoea 1990 2008	1990 1997	1969	1997	2000
	ttcome 1: Dia Messou <i>et al</i> .	ttcome 2: Diá Aziz <i>et al.</i> Garrett <i>et al.</i>	Huttly <i>et al.</i> Messou <i>et al.</i>	Rubenstein	ti ui. Xiao et al.	Zhang <i>et al</i> .

study<sup>34</sup> had used a placebo intervention to conceal from the subjects and assessors which was the intervention group and which the control, and had found a smaller effect than the other community-based trials. An alternative explanation is that this study did not focus on handwashing or provide soap. All of the community-based trials which did not focus on handwashing or provide soap found smaller reductions in diarrhoea than either of those which did those things. Of the less focussed group, the partially blinded study<sup>34</sup> found a reduction of 6% (95% CI: -44-15%) while the other, open trial of this kind<sup>35</sup> found 25% (95% CI 15–34 $\overline{$ ) so the lack of blinding seems to explain at least part of the difference. Of course, such non-focussed trials were excluded from our earlier review,<sup>10</sup> and none of the intervention studies focussed on handwashing (Figure 2a) used a placebo intervention. The consistency of effect between observational and intervention studies led us to judge that the effect is probably genuine, but more research is needed to clarify this point.

#### Water quality interventions

Enthusiasts for point-of-use household-based water treatment argue that the smaller effect of source-based interventions is due to subsequent contamination of the water on its way to, or during storage in the household. Sceptics point to the lack of significant effect found in the blinded studies, attributing the difference to courtesy bias or placebo effect. They suggest that consumers are less conscious of treatment administered centrally, and so less likely to show these forms of bias in their self-reporting of diarrhoea.

These findings have given rise to a lively debate about the desirability of scaling-up household-based water treatment.<sup>36,37</sup> The only certain conclusion is that the implications are uncertain, and it is unlikely that a Delphi process would arrive at an amicable consensus.

There are several reasons to believe that the bias may apply to water quality but which are less applicable to handwashing. First, there is biological plausibility; in many settings, a subject would have to ingest very large amounts of water in order to consume an infectious dose of a bacterial pathogen. Second, the anomaly that the reduction in diarrhoea seems to be independent of the quality of the ambient water before it is treated. Third, the observational studies of drinking-water quality (e.g. see ref.<sup>38</sup>) do not show such large effects as the point-of-use intervention trials. And fourth, most of these trials were funded by manufacturers of water treatment chemicals or equipment.

In these circumstances the data from the recent spate of trials-and hence, any systematic review based on them-do not offer a firm basis for judging the effect of water quality improvements. The options include adopting the effect of the four blinded trials (no significant reduction in any trial), adopting the pooled effect of the source-based intervention studies (three trials among children under five gave a 7% reduction), or keeping the pre-existing consensus view arrived at two decades ago in reviews of observational and source-based intervention studies,<sup>4,7</sup> that water quality improvements can be expected to be associated with a reduction of some 17% in diarrhoea risk. This latter figure was proposed for LiST as associated with use of an improved water supply, which is available within a reasonable distance, requiring a return journey of 30 min or less.

One theme which emerged from the debate was that 'harder' outcomes such as care-seeking for diarrhoea would be more objective and less prone to bias than a relatively 'softer' outcome such as self-reported diarrhoea. One well-known water quality trial,<sup>39</sup> excluded from our review because the outcome included gastroenteritis without diarrhoea, found that during the study period 'the number of visits to physicians for gastrointestinal symptoms and of hospitalizations was similar in both groups.' In this context, one recent trial with both handwashing and water quality arms<sup>40</sup> is of particular interest, as the authors documented the effect of each arm both in terms of self-reported diarrhoea and of care-seeking (see Table 5). The effect of each intervention is very similar, whichever the outcome. This suggests, either that any bias affecting the former outcome also affected the latter; or that the former was not susceptible to bias as the blinded studies suggest.

**Table 5** Comparison of effects of (i) promotion of hand washing with soap, and (ii) household water treatment, measured in terms of weekly prevalence of diarrhoea, and of frequency of consulting a practitioner for treatment for diarrhoea<sup>22</sup>

Intervention group	Reduction in weekly self-reported diarrhoea prevalence (95% CI)	Reduction in care-seeking for diarrhoea in children <5 years (95% CI)
Soap and hand washing promotion	45% (12-68%)	48% (15-71%)
Bleach water treatment	53% (22-75%)	54% (22-77%)
Flocculant-disinfectant water treatment	59% (29-82%)	61% (31-84%)
Flocculant-disinfectant plus hand washing with soap	50% (18–72%)	55% (23–77%)

#### Excreta disposal

It is in this area that the evidence is weakest. It is not surprising that trials are few, as provision of hundreds of latrines is expensive. Observational studies cannot be trusted, in view of evidence that people in latrine-owning households (a self-selected group) behave more hygienically than others, even in respects which have nothing to do with excreta disposal.<sup>41,42</sup> This is not to say that excreta disposal has no effect on diarrhoea. Indeed, there is a striking consistency between the reductions found in various reviews of 36%,<sup>7</sup> 32%,<sup>9</sup> 20-51% (the four Chinese studies) and 22-43%.<sup>33</sup> That being so, there is not enough evidence to justify a departure from the prevailing consensus, published nearly two decades ago<sup>7</sup> and widely cited with approval since then, that sanitation reduces diarrhoea risk by about 36%. This then is the strength of effect proposed for the LiST model.

#### General

The lack of conclusive evidence of the effect on diarrhoea of improvements in water, hygiene and sanitation in developing countries is not an excuse for inaction.<sup>43</sup> We know enough to do a lot of good. In spite of doubts about the detail, it is clear that such environmental interventions can have a substantial effect on diarrhoea morbidity, and the very few relevant studies<sup>44</sup> confirm that they have a similar effect upon diarrhoea mortality. Moreover, water, hygiene and sanitation have other important benefits, including the emancipation of women from drudgery and the enhancement of human dignity, and even other health benefits such as the control of trachoma and of intestinal helminths.

It is not entirely surprising that the evidence is weak; studies of mortality are fraught with ethical and logistic problems; water supplies and sanitation are expensive interventions to trial; and the engineers who install them are not accustomed to trials as an important part of their professional culture. Moreover, it is particularly difficult to blind a trial of an intervention involving the provision of hardware or the promotion of behaviour change, and as we have seen, it appears that the lack of blinding can lead to substantial bias if the outcome is 'soft'.

In the context of a literature of uneven quality such as this, these reviews can also teach us that there is no definitive systematic review, or objective set of rules for conducting one. The examples here show how the result of a systematic review depends upon a number of questions, such as the definition of the outcome (should only diarrhoea be accepted, and vomiting rejected?), of the intervention (is sewerage in Brazil different from pit latrines in Africa?), on the range of languages accepted (in several recent reviews,<sup>13,45</sup> more than a third of useful studies were in Chinese) and on which are regarded as the gravest methodological deficiencies. Each of those questions has more than one reasonable answer. Judgement-free data are a myth.

## Supplementary data

Supplementary data are available at *IJE* online.

## Funding

The US Fund for UNICEF from the Bill & Melinda Gates Foundation (grant 43386, partially) to 'Promote evidence-based decision making in designing maternal, neonatal and child health interventions in low- and middle-income countries' and UNICEF, Unilever research and WaterAid.

## Acknowledgements

Stimulating discussions with colleagues in the CHERG have helped to improve this article; their input is gratefully acknowledged. So are the major contributions of Tom Clasen as principal author of the reviews on water and on sanitation, the patient and constructive support of Therese Dooley and the administrative wizardry of Eileen Chappell.

Conflict of interest: None declared.

#### **KEY MESSAGES**

- Effect of handwashing with soap is most consistent at roughly 48% reduction in diarrhoea.
- Effect of water quality improvements found in RCTs seems to be affected by bias not seen in blinded studies.
- Evidence for effect of sanitation is weakest randomized trials are needed but may be 36% reduction.
- Though evidence is weak compared with clinical RCTs, it is enough for action.
- Analysing such evidence needs more than algorithms it requires judgement.

## References

- <sup>1</sup> Rosen S, Vincent JR. African Economic Policy Discussion Paper 69. 2001. *Household Water Resources and Rural Productivity in Sub-Saharan Africa: A Review of the Evidence*.Cambridge, MA: John F. Kennedy School of Government, Harvard University.
- <sup>2</sup> Mozynski P. BMA says inadequate sanitation is a global crisis. *BMJ* 2008;**336**:117.
- <sup>3</sup> Blum D, Feachem RG. Measuring the impact of water supply and sanitation investments on diarrhoeal diseases: problems of methodology. *Int J Epidemiol* 1983;12:357–65.
- <sup>4</sup> Esrey SA, Feachem RG, Hughes JM. Interventions for the control of diarrheal diseases among young children: improving water supplies and excreta disposal facilities. *Bull WHO* 1985;**63**:757–72.
- <sup>5</sup> Esrey SA, Habicht J-P. Cornell International Nutrition Monograph Series 15. *The Impact of Improved Water Supplies and Excreta Disposal Facilities on Diarrheal Morbidity, Growth, and Mortality among Children*. Ithaca, NY: Division of Nutritional Sciences, Cornell University, 1985.
- <sup>6</sup> Esrey SA, Potash JB, RobertsL, Shiff C. Health Benefits from Improvements in Water Supply and Sanitation: Survey and Analysis of the Literature on Selected Diseases. WASH Technical Report 66. Rosslyn, VA: Environmental Health Project, for USAID, 1990.
- <sup>7</sup> Esrey SA, Potash JB, Roberts L, Shiff C. Effects of improved water supply and sanitation on ascariasis, diarrhea, dracunculiasis, hookworm infection, schistosomiasis, and trachoma. *Bull WHO* 1991;69:609–21.
- <sup>8</sup> Cairncross S, Valdmanis V. Water supply, sanitation and hygiene promotion. In: Jamison DT, Breman JG, Measham AR *et al.* (eds). *Disease Control Priorities in Developing Countries.* 2nd edn. Washington DC: The World Bank, 2006, pp. 771–92.
- <sup>9</sup> Fewtrell L, Kaufmann RB, Kay D, Enanoria W, Haller L, Colford JM Jr. Water, sanitation, and hygiene interventions to reduce diarrhoea in less developed countries: a systematic review and meta-analysis. *Lancet Infect Dis* 2005;**5**:42–52.
- <sup>10</sup> Curtis V, Cairncross S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *Lancet Infect Dis* 2003;**3**:275–81.
- <sup>11</sup> Clasen T, Schmidt W-P, Rabie T, Roberts I, Cairncross S. Interventions to improve water quality for preventing diarrhoea: a systematic review and meta-analysis. *BMJ* 2007;**334:**782(Evid Based Med 2007;12;127–28).
- <sup>12</sup> Clasen T, Roberts I, Rabie T, Cairncross S. Interventions to improve water quality for preventing diarrhoea (Protocol for a Cochrane Review). *The Cochrane Library, Issue 2*. Oxford: Update Software, 2004.
- <sup>13</sup> Clasen T, Bostoen K, Schmidt W-P *et al.* Interventions to improve excreta disposal for preventing diarrhoea (Protocol for a Cochrane Review). *The Cochrane Library, Issue 2.* Oxford: Update Software, 2008.
- <sup>14</sup> Walker N, Fischer CL, Bahl R *et al.* The CHERG methods and procedures for estimating effectiveness of interventions on cause-specific mortality. *Int J Epidemiol* 2010;**39** (Suppl 1):i88–101.
- <sup>15</sup> Atkins D, Best D, Briss PA *et al.* Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**: 1490.

- <sup>16</sup> Hoque B, Chakraborty J, Chowdhury J *et al.* Effects of environmental factors on child survival in Bangladesh: a case control study. *Public Health* 1999; 113:57–64.
- <sup>17</sup> Khan M. Interruption of shigellosis by handwashing. *Trans R Soc Trop Med Hyg* 1982;**76:**164–68.
- <sup>18</sup> Shahid N, Greenough W, Samadi A, Huq M, Rahaman N. Hand washing with soap reduces diarrhoea and spread of bacterial pathogens in a Bangladesh village. *J Diarrhoeal Dis Res* 1996;14:85–89.
- <sup>19</sup> Ejemot RI, Ehiri JE, Meremikwu MM, Critchley JA. Hand washing for preventing diarrhoea. *Cochrane Database of Syst Rev.* (Issue 1). Art. No.: CD004265.
- <sup>20</sup> Han AM, Hlaing T. Prevention of diarrhoea and dysentery by hand washing. *Trans R Soc Trop Med Hyg* 1989;**83**: 128–31.
- <sup>21</sup> Luby SP, Agboatwalla M, Painter J, Altaf A, Billhimer WL, Hoekstra RM. Effect of intensive handwashing promotion on childhood diarrhea in high-risk communities in Pakistan: a randomized controlled trial. *JAMA* 2004;**291**:2547–54.
- <sup>22</sup> Luby SP, Agboatwalla M, Painter J *et al.* Combining drinking water treatment and hand washing for diarrhea prevention, a cluster randomised control trial. *Trop Med Int Health* 2006;**11:**479–89.
- <sup>23</sup> Messou E, Sangaré SV, Josseran R, Le Corre C, Guélain J. Effect of hygiene measures, water sanitation and oral rehydration therapy on diarrhea in children less than five years old in the south of Ivory Coast. *Bull Soc Pathol Exot* 1997;**90**:44–47.
- <sup>24</sup> Crump JA, Otieno PO, Slutsker L *et al.* Household based treatment of drinking water with flocculant-disinfectant for preventing diarrhoea in areas with turbid source water in rural western Kenya: cluster randomised controlled trial. *BMJ* 2005;**331:**478.
- <sup>25</sup> Kirchhoff LV, McClelland KE, Do Carmo PM, Araujo JG, De Sousa MA, Guerrant RL. Feasibility and efficacy of in-home water chlorination in rural North-eastern Brazil. J Hyg (*Lond*) 1985;**94:**173–80.
- <sup>26</sup> Austin CJ. Investigation of in-house water chlorination and its effectiveness for rural areas of the Gambia [dissertation]. New Orleans: Tulane University School of Public Health and Tropical Medicine, 1993.
- <sup>27</sup> Colford JM Jr, Rees JR, Wade TJ *et al.* Participant blinding and gastrointestinal illness in a randomized, controlled trial of an in-home drinking water intervention. *Emerg Infect Dis* 2002;**8**:29–36.
- <sup>28</sup> Colford JM Jr, Wade TJ, Sandhu SK *et al.* A randomized, controlled trial of in-home drinking water intervention to reduce gastrointestinal illness. *Am J Epidemiol* 2005;**161**: 472–82.
- <sup>29</sup> Yan Z-S, Wang G-F, Cui C *et al.* An observation of the effect on reducing the fly density and diarrhoea of the use of double urn funnel lavatory in faeces management. *Henan Yu Fang Yi Xue Za Zhi [Henan J Prev Med]* 1986; **1986**:73–76.
- <sup>30</sup> Hu X-R, Liu G, Liu S-P *et al.* [Field evaluation of the effect of diarrhoea control of methanogenesis treatment of human and animal faeces and rubbish of cellulose nature in the rural areas of Xiang Cheng. *Henan Yu Fang Yi Xue Za Zhi [Henan J Prev Med]* 1988; **1988**:11–13.

- <sup>31</sup> Xu J-Z. Observation on the efficacy of three squares septic tank lavatory for disease prevention. *Huan Jing Yu Jian Kang Za Zhi [J Environ Health]* 1990;**1990:**250–52.
- <sup>32</sup> Xu G-X, Zhu X-L. The assessment of the effects for prevention of diseases by non-hazardous treatment of night soil at experimental spots in rural areas. *Wei Sheng Yan Jiu* [*Wei Sheng Yan Jiu*] 1994;**23**:23–37).
- <sup>33</sup> Barreto ML, Genser B, Strina A *et al.* Prado MS, Matos SMA, dos Santos LA, Cairncross S. Effect of city-wide sanitation programme on reduction in rate of childhood diarrhoea in northeast Brazil: assessment by two cohort studies. *The Lancet* 2007;**370**:1622–28.
- <sup>34</sup> Haggerty PA, Muladi K, Kirkwood BR, Ashworth A, Manunebo M. Community-based hygiene education to reduce diarrhoeal disease in rural Zaire: impact of the intervention on diarrhoeal morbidity. *Int J Epidemiol* 1994;**23**:1050–59.
- <sup>35</sup> Stanton BF, Clemens JD. An educational intervention for altering water-sanitation behaviors to reduce childhood diarrhea in urban Bangladesh. *Am J Epidemiol* 1987;125: 292–301.
- <sup>36</sup> Schmidt WP, Cairncross S. Household water treatment in poor populations: is there enough evidence for scaling up now? *Environ Sci Technol* 2009;**43**:986–92.
- <sup>37</sup> Clasen T, Bartram J, Colford J et al. Comment on Schmidt & Cairncross. Environ Sci Technol 2009;43:5542–44.

- <sup>38</sup> Moe CL, Sobsey MD, Samsa GP, Mesolo V. Bacterial indicators of risk of diarrhoeal disease from drinking-water in the Philippines. *Bull World Health Organ* 1991;69:305–17.
- <sup>39</sup> Payment P, Richardson L, Siemiatycki J, Dewar R, Edwardes M, Franco E. A randomized trial to evaluate the risk of gastrointestinal disease due to consumption of drinking water meeting current microbiological standards. *Am J Public Health* 1991;**81**:703–8.
- <sup>40</sup> Luby SP, Agboatwalla M, Painter J *et al.* Combining drinking water treatment and hand washing for diarrhoea prevention, a cluster randomised controlled trial. *Trop Med Int Health* 2006;**11:**479–89.
- <sup>41</sup> Hoque BA, Mahalanabis D, Alam MJ, Islam MS. Postdefecation handwashing in Bangladesh: practice and efficiency perspectives. *Public Health* 1995;109:15–24.
- <sup>42</sup> Strina A, Cairncross S, Barreto ML, Larrea C, Prado MS. Childhood diarrhea and observed hygiene behavior in Salvador, Brazil. *Am J Epidemiol* 2003;**157**:1032–38.
- <sup>43</sup> Bartram J, Cairncross S. Hygiene, sanitation and water; forgotten foundations of health. *Lancet*, in press.
- <sup>44</sup> Victora CG, Smith PG, Vaughan JP *et al*. Water supply, sanitation and housing in relation to the risk of infant mortality from diarrhoea. *Int J Epidemiol* 1988;17: 651–54.
- <sup>45</sup> Fung IC, Cairncross S. Ascariasis and handwashing. *Trans R Soc Trop Med Hyg* 2009;**103**:215–22.

Downloaded from http://ije.oxfordjournals.org/ by guest on December 9, 2015