Water, Sanitation, and Hygiene Interventions to Improve Health among People Living with HIV/AIDS: A Systematic Review

Running Head: WASH and HIV Systematic Review

Rachel L. PELETZ [a], Thomas MAHIN [b], Mark ELLIOT [c], Mamie SACKEY HARRIS [d], Ka Seen CHAN [a], Myron S. COHEN [d], Jamie K. BARTRAM [c], Thomas F. CLASEN [a]

[a] Department of Disease Control, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine

[b] Massachusetts Department of Environmental Protection

[c] UNC Water Institute, University of North Carolina – Chapel Hill

[d] Institute for Global Health & Infectious Diseases, University of North Carolina – Chapel Hill

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Correspondence and reprint requests to:

Dr Thomas Clasen, Department of Disease Control, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel St, London WC1E 7HT, UK

Email: thomas.clasen@lshtm.ac.uk

CONFLICTS OF INTEREREST AND SOURCE OF FUNDING

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ABSTRACT

Design: People living with HIV/AIDS (PLHIV) are at increased risk of diarrhoeal disease and enteric infection. This review assesses the effectiveness of water, sanitation, and hygiene (WASH) interventions to prevent disease among PLHIV.

Methods: We searched MEDLINE, EMBASE, Global Health, The Cochrane Library, Web of Science, LILACS, Africa-wide, IMEMR, IMSEAR, WPRIM, CNKI, and WanFang. We also hand searched conference proceedings, contacted researchers and organizations, and checked references from identified studies. Eligible studies were those involving WASH interventions among PLHIV that reported on health outcomes and employed a controlled study design. We extracted data, explored heterogeneity, sub-grouped based on outcomes, calculated pooled effects on diarrhoeal disease using meta-analysis, and assessed studies for methodological quality.

Results: Ten studies met the eligibility criteria and are included in the review, of which nine involved water quality interventions and one involved promotion of handwashing. Among eight studies that reported on diarrhoea, water quality interventions (seven studies, pooled RR=0·57, 95%CI: 0·38-0·86) and the handwashing intervention (one study, RR=0·42, 95%CI: 0·33-0·54) were protective against diarrhoea. One study reported that household water treatment combined with insecticide treated bednets slowed the progression of HIV/AIDS. The validity of most studies is potentially compromised by methodological shortcomings.

Conclusions: No studies assessed the impact of improved water supply or sanitation, the most fundamental of WASH interventions. Despite some evidence that water quality interventions and handwashing are protective against diarrhoea, substantial heterogeneity and the potential for bias raises questions about the actual level of protection.

Key Words: HIV, AIDS, water, sanitation, hygiene, systematic review

INTRODUCTION

An estimated 34 million people have HIV/AIDS (PLHIV), 69% of whom are in sub-Saharan Africa [1]. PLHIV are more susceptible to diarrhoeal disease, a serious cause of morbidity and mortality responsible for over 800,000 deaths per year [2]. Depending on disease stage and infective agent, PLHIV may become ill at lower levels of pathogen exposure, and may have substandard immune responses, affecting the severity and duration of health effects [3, 4]. There is also compelling evidence that PLHIV are at increased risk of enteric infections including *Cryptosporidium* spp. and other pathogens transmitted through the faecal-oral route, particularly in low-income settings [5-10]. Gastrointestinal infections may increase the progression of HIV [11] and lead to environmental (tropical) enteropathy, particularly in poor environmental conditions [12, 13]. Environmental enteropathy and diarrhoeal disease can inhibit normal consumption of foods and absorption of nutrients [14], increasing the risk of death and disease [15]. Furthermore, household members of PLHIV including young children born to HIV-positive mothers may experience increased health risks [16, 17].

Diarrhoeal disease and enteric infections are largely caused by unsafe water, sanitation, and hygiene (WASH), and basic WASH improvements have the potential to drastically reduce morbidity and mortality [18]. WASH improvements are a particular priority in sub-Saharan Africa, where the majority of PLHIV live and where access to safe water and adequate sanitation is most limited [1, 19]. The need for safe water and adequate sanitation for PLHIV has been recognized by the WHO [20] and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) [21, 22] with ensuing policy reforms ~~and international organizations~~ calling for an integration of WASH activities in HIV/AIDS programs [23-26].

This review evaluates the effectiveness of WASH interventions to improve health for PLHIV in (i) reducing diarrhoeal disease (ii) reducing enteric infection, (iii) slowing the rate of HIV/AIDS progression, (iv) reducing environmental enteropathy, and (v) improving nutritional status.

METHODS

Eligible study designs included randomized controlled trials (RCTs), quasi-randomized controlled trials, controlled before and after studies, interrupted time series studies, and historically controlled studies [27]. We excluded non-controlled studies. Participants included PLHIV, their household members and children born to HIV-positive mothers.

Interventions included any measure aimed at improving drinking water quality, quantity, and/or accessibility; improving coverage or use of sanitation facilities; and/or improving hygiene through the promotion of handwashing with soap. Control participants consisted of study participants advised to continue with their usual WASH practices rather than the prescribed intervention. Primary outcomes included diarrhoea-related morbidity, enteric infections, HIV/AIDS disease progression measured by changes in CD4 counts, nutritional status, and environmental enteropathy [28].

We searched the following databases: MEDLINE, EMBASE, Global Health, The Cochrane Library, Web of Science, LILACS (Latin America & Caribbean), Africa-wide (Africa), IMEMR (East Mediterranean), IMSEAR (South East Asia), WPRIM (Western Pacific), and CNKI and WanFang (Chinese databases). We searched the conference proceedings of: International Water Association and the Water, Engineering and Development Centre (WEDC) (1973-2011); University of North Carolina Water and Health Conference (2010-2012); and International AIDS conference (2006-2012). We contacted experts working in the sector and checked reference lists of key articles.

After an initial screening of titles retrieved through the search strategy, abstracts and full texts were reviewed by two authors for eligibility. We assessed methodological quality using the Cochrane EPOC risk of bias tool [29] using pre-defined classifications. Assessments included the allocation sequence, allocation concealment (RCTs only), balance of baseline characteristics, loss to follow-up, blinding of intervention, protection against contamination, and reporting results on all outcomes. As no studies employed clustered designs we did not assess for clustering adjustments in statistical analyses. Interventions were primarily allocated at the household level with one primary participant per household. For reporting bias, we did not have an adequate number of studies to conduct funnel plots [27, 30].

Data synthesis

We tabulated all outcomes by study. If risk measures were not reported directly, we extracted the original data from the publication and, if necessary, contacted the author directly for the data. We calculated the appropriate measure of relative risk (risk ratio or rate ratio) and 95% confidence interval (CI) using standard techniques [31]. For studies that included non-HIV populations, we included only data from HIV-positive individuals and members of their households. Diarrhoeal data were compiled using STATA 12 and displayed graphically in forest plots. An overall pooled point estimate and 95% CI was calculated for diarrhoeal disease morbidity using a random effects model meta-analysis. Heterogeneity was examined both visually with forest plots and statistically using χ^2 test and the I^2 test for consistency. For other outcomes, a narrative synthesis was used to describe the results due to insufficient data for a meta-analysis. We did not perform subgroup analyses to explore heterogeneity due to the small number of studies identified [27].

RESULTS

Study characteristics

The combined search strategies identified 4,128 potentially relevant studies of WASH interventions for people living with HIV/AIDS (Figure 1). After the title screening, 166 abstracts were reviewed and full text of 28 articles was obtained to assess eligibility. Ten studies met the eligibility criteria and are included in the review (Table 1). Two papers were found of complementary studies; in these cases, we refer to the main intervention study paper.

The ten studies included six randomized controlled trials [4, 32-36], two controlled before/after studies [37, 38], one interrupted-time series [39], and one historically controlled trial [40]. Primary participants were PLHIV for eight studies; two studies examined young children born to HIV-positive mothers whose HIV status was not fully ascertained [36, 40]. Two studies reported outcomes for all members of the household in addition to the primary participants (PLHIV or children born to HIV-positive mothers) [4, 36]. With the exception of Sorvillo et al. that examined filtration at the water treatment plant level, the intervention allocation occurred at the household level. Three studies were carried out in the United States and seven in sub-Saharan Africa. While the US-based studies had predominantly male participants (75%-98%), females constituted 74%-100% of participants in the sub-Saharan Africa studies. The follow-up period ranged from 16 weeks [32] to eight years [37]. The studies covered 12,690 participants with HIV/AIDS (primarily from 10,988 in the Sorvillo study) and 591 children born to HIV-positive mothers, totalling 13,281 individuals. The studies were published from 1994 to 2012, with one study under review for publication at the time of this review.

Interventions

Except for one study that examined a handwashing intervention [33], all study interventions consisted of measures to improve drinking water quality. One study was of a filtration addition to a water treatment plant [37], and eight studies were of household water treatment interventions, including five filtration studies [two ceramic pot filters [34, 35], two LifeStraw® Family filters [36, 38], one filter combined with ultraviolet disinfection [32]] and three household chlorination studies [4, 39, 40]. Four studies included safe water storage containers as part of the intervention [4, 36, 39, 40]; additionally, the two ceramic pot filter studies integrated water storage as part of the device [34, 35]. In one study, the intervention was a combination of a long-lasting insecticide-treated bednet and LifeStraw® Family filter [38]; therefore the outcomes cannot be separated for the two interventions. One study examined the combined effect of cotrimoxazole prophylaxis and household chlorination after examining chlorination alone for five months [4]; only the results for chlorination alone are included in this review.

Adherence/Compliance

Intervention adherence is characterized as *correct, consistent and sustained use*, also referred to as compliance [41]. Studies varied in whether and how they assessed participant adherence to the WASH intervention. Three studies assessed adherence based on participant self-reports [33, 36, 38], two studies of household chlorination reported on chlorine residual levels [39, 40], and three studies compared microbial water quality in control and intervention arms [4, 35, 36]. For reported adherence, household filtration was reported in the intervention group in 93% of households in the Walson study and 96% in the Peletz study. In the Huang study, handwashing was more frequently reported in the intensive handwashing intervention group compared to the control (seven vs. four times a day, $p<0·05$). Chlorine residual was present in 50-80% of intervention households [39] or 80-92% of intervention households [40]. Microbial water quality was significantly improved in intervention households compared to control households ($p<0·001$) in Lule and Peletz studies; this comparison is not evaluated statistically in Potgieter. Neither Colford nor Sorvillo studies reported on adherence; although assumed high since Colford et al. attached the water treatment intervention to the main faucet of the household and Sorvillo et al. examined filtration at the water treatment plant.

<u>Outcomes measures and effect estimates</u>

<u>Diarrhoea</u>

Nine studies examined diarrhoea-related morbidity and results were reported by eight (results not reported in Potgieter 2010) (Figure 2). With the exception of the Harris study that used clinic visits for diarrhoea, studies with diarrhoea as an outcome relied on self-reports by participants. For the case definition of diarrhoea, six studies used the WHO definition (≥three loose stools per day), one study used 'highly credible gastrointestinal illness' which counts vomiting or abdominal cramps as well as diarrhoea [32] and one study did not provide a definition [39].

Households were visited or called periodically to assess self-reported diarrhoea-related outcomes. Pictorial diarrhoea diaries or health logs were used in four studies where participants were instructed to record health outcomes daily [32-35]. Household interviews were used in four studies, ranging from weekly [4, 36,39] to quarterly visits [38], where participants were asked about diarrhoea in the preceding time period

Diarrhoea outcomes were reported as rate ratios [4, 34], risk ratios [32, 38, 39], longitudinal prevalence ratio [36], difference in absolute diarrhoea episodes per year [33], or difference in absolute clinic visits per month [40]. While some papers presented adjusted ratios [4, 32], we used crude ratios in our analysis to avoid pooling ratios that were adjusted for different factors; for the Lule study we chose to use diarrhoea episodes as the main outcome though days with diarrhoea were also reported.

All studies reporting on diarrhoea found some reduction in morbidity, ranging from 17% [4] to 77% [34], though the 25% reduction reported by Colford was not statistically significant (Figure 2). The single handwashing study [33] reported a reduction of 58% (RR=0·42, 95% CI: 0·33-0·55). The pooled reduction from the water quality interventions was 43% (RR=0·57, 95% CI 0·38-0·86) (Figure 2). However, there was substantial heterogeneity of the water quality studies (probability of heterogeneity, χ^2 = p<0·001) and 95·0% consistency (I^2, p<0·001).

Only the Barzilay study stratified diarrhoea by intervention adherence; diarrhoea was significantly reduced among high frequency chlorination users (46% reduction, p=0·04) but not among low-frequency users (15% reduction, p=0·47) [39]. Only two studies reported results for all members of households with an HIV-positive individual. For household members in the Lule study, there were borderline significant reductions in diarrhoea episodes (adjusted RR=0·80, 95% CI 0·64-1·0, p=0·047) and days with diarrhoea (adjusted RR=0·74, 95% CI: 0·54-1·01, p=0·055) [4]. For household members in the Peletz study, there was a significant reduction in diarrhoea (LPR=0·46, 95% CI: 0·30-0·70, p<0·001) but not persistent diarrhoea (≥14 days) (LPR=0·75, 95% CI: 0·37-1·53, p=0·43) [36].

Enteric Infection

Cryptosporidiosis

Two studies examined cryptosporidiosis as a primary outcome; one household ceramic filter study in South Africa [34] and one study including filtration at a water treatment plant in the United States [37]. Cryptosporidiosis was verified by stool samples [34] or records from the national AIDS surveillance for all PLHIV [37].

Abebe et al. found no significant difference in cryptosporidiosis prevalence at the end of the study (7% household filtration group vs. 22% control , *p*=0·11), though they did find a significant reduction between baseline and final visits in the intervention group (25% reduction, *p*=0·02) and not in the control (4% reduction, *p*=0·74) [34]. Sorvillo et al. found no effect from water treatment plant filtration. Though prevalence declined by 20% (from 4·2% to 3·4%) after the filtration addition, prevalence also declined by 47% (from 6.2% to 3.3%) in a neighbouring area that had not changed their water treatment plant technology during the same time period [37]. In the Lule and Huang studies, participants with diarrhoea were tested for *Cryptosporidium* spp. in addition to other pathogens as secondary outcomes, no significant difference was found between intervention and control groups [4, 33].

Other enteric infections

Three studies examined other enteric infections of PLHIV as secondary outcomes, by collecting stool samples of participants with diarrhoea [4, 33], or using a new bio-wipes technique [35]. Lule et al. tested for hookworms*, Strongyloides stercoralis*, enterotoxigenic *Escherichia coli,* enteropathogenic *E. coli, Aeromonas* spp., *Shigella* spp., *Salmonella* spp., *Campylobacter* spp., *Vibrio cholerae*, and *Pleisiomonas* spp. Huang et al. tested participants with diarrhoea for *Shigella* spp., *Campylobacter* spp., enteroaggregative *E. coli*, *Clostridium difficile*, *Yersinia enterocolitica, Salmonella* spp., human cytomegalovirus, adenovirus, norovirus, rotavirus, *Giardia lamblia*, *Entamoeba histolytica, a*nd *Microsporidium*. In the study by Potgieter, samples were tested for pathogenic *E. coli* (five types), *Shigella flexneri,* and *Salmonella typhimurium*. None of the studies assessed exposure for enteric infections specifically.

The Lule and Huang studies reported no significant differences between intervention and control groups in rates of the infection among PLHIV except in the case of *G. lamblia* in the Huang study (2% vs. 6%, $p < 0{\cdot}05$) [33]. For HIV-negative members of the household in the Lule study, the intervention group had lower rates of hookworm than the control (27% vs. 40%, p=0·0138) and *Shigella* species (1% vs. 5%, p=0·0292) [4]. In the Potgieter study, results were not stratified by intervention group for PLHIV.

Disease Progression

Progression of HIV/AIDS was examined in three studies. In the Walson study where disease progression was the primary outcome, individuals receiving bednets and water filters were 27% less likely to reach the endpoint of CD4 count of <350 cells/mm^3 after controlling for baseline CD4 counts (HR=0·73, 95% CI: 0·57-0·95, p=0·02) [38]. CD4 decline was significantly lower in the intervention group (-54 vs. -70 cells/mm^3/year, p=0·03) [38].

The Lule and Potgieter studies reported on the impact of household water treatment on progression of HIV/AIDS, though this was not the primary outcome in either study. Lule et al. found household chlorination did not impact viral load, though diarrhoea episodes were significantly associated with viral load and HIV viral load increased by 0·40 log_{10} per person-year for PLHIV using household chlorination compared with 0·71 log_{10} per person-year in control [4]. Potgieter et al. found that household filtration did not significantly impact changes in CD4 counts (p=0·344) [35].

Nutrition

Only one study examined nutrition, measured as weight-for-age z-scores (WAZ) for children <2 years born to HIV-positive mothers [36]. This study found no impact of household filtration on mean WAZ scores (-1·21 vs. -1·24, respectively, p=0·92) as a secondary outcome [36].

Environmental enteropathy

None of the reviewed studies reported on the impact of WASH interventions on environmental enteropathy.

Mortality

Two studies reported mortality, though in neither case was it the primary outcome. Walson and colleagues reported that participants that received household filters and bednets were significantly less likely to die as a result of non-traumatic death or reach CD4 <350 cells/mm^3 during the surveillance period (HR 0·74, 95% CI: 0·58-0·95, *p*=0·02) [38]. Peletz and colleagues reported fewer deaths of children <2 years in the filtration intervention group, but these results were not significant (RR=0·56; 95% CI: 0·13 - 2·37, *p*=0·43) [36].

Methodological quality of included studies

Methodological quality of studies and assessment criteria details are summarized in Table 2. The intervention was allocated randomly in six studies; the others compared the intervention group to a separate control group [37, 38, 40] and/or the same group before they received the intervention [37, 39]. We classified two studies as blinded: Colford by design and the Sorvillo study by virtue of the fact that participants were not likely to be aware of the filtration addition to the water treatment plant. Neither blinded study found significant health effects, though both were conducted in the United States where water supplies are generally of good quality. The methodological quality criteria was completely met for only one RCT (Colford study) and one non-randomized controlled trial (Harris study). Four studies did not report on all criteria evaluated. Reported (subjective) outcomes were primary outcomes in five studies with non-blinded interventions, suggesting the potential of reporting bias. All studies reported on all outcomes with the exception of the Potgieter study; results on diarrhoeal disease were not available at the time of this review.

DISCUSSION

We reviewed water, sanitation and hygiene interventions to prevent disease among PLHIV. Ten studies covering 13,281 individuals in six countries met the review's eligibility criteria. Nine assessed water quality interventions and one study assessed a handwashing intervention. Significantly, we identified no studies that assessed the impact of water supply or sanitation, two of the most fundamental WASH interventions.

Evidence from the eight studies that reported on diarrhoea suggests that water quality interventions and handwashing interventions may be protective among PLHIV. Notably, however, all but one of such studies relied on self-reported diarrhoea and the only blinded study found no statistically significant result. Thus, we cannot rule out the possibility that the effect is exaggerated [42].

All seven water quality studies that reported on diarrhoeal disease were of household water treatment, a water quality intervention reported to be effective in preventing diarrhoea [43, 44]. Our pooled estimate of effect of 43% is within the range of estimates observed for household water treatment interventions, suggesting that the level of effectiveness among PLHIV is comparable to general populations. While most interventions consisted of household water treatment, they included a variety of filtration and chlorination approaches that have different levels of efficacy against important opportunistic agents for PLHIV [43]; for example, chlorination does not inactivate *Cryptosporidium* spp. [45], a pathogen of particular concern for PLHIV [46].

Pooled estimates of the impact of the intervention on diarrhoea should be interpreted with caution due to important differences in the studies. Populations varied in terms of demographics, access to sanitation, water supplies, hygiene practices, viral load, access to ARVs, and other factors. Adherence with household water treatment, a major factor affecting exposure and potential health impact [41], also varied among studies or was not measured at all. Differences in study design, case definitions, and the method of diarrhoea assessment limited the potential utility of pooled estimates of effect.

The one study evaluating a handwashing intervention among PLHIV reported the intervention to be effective against diarrhoea [33]. The 58% reduction in risk exceeds the pooled estimate of a previous systematic review not focused on PLHIV (four trials, IRR 0·68, 95% CI: 0·52 to 0·90) [47]; however, it is not possible to conclude from this single study whether handwashing is more effective among PLHIV compared to the general population.

Despite this evidence of effectiveness on reported diarrhoea, results on other objective outcomes provide only limited evidence of a protective effect. The studies reporting on cryptosporidiosis and other enteric infections generally lacked significant findings, though studies could have been underpowered. Reductions in disease progression and non-traumatic death were reported in only one study [38], though since the intervention included provision of insecticide treated nets, it is not possible to ascribe these results solely to the WASH (water filter) component.

Most studies included in this review presented issues of methodological quality. Four of the ten studies employed a non-randomized study design; populations assessed in different geographical locations and/or at different time periods may limit study population comparability. In addition to the issues noted above concerning self-reported outcomes (e.g., diarrhoeal disease) in non-blinded trials, some studies reporting on diarrhoea used longer diarrhoea recall periods that may be unreliable [48]. The one blinded study that met all criteria of methodological quality did not report the water quality intervention to be protective against diarrhoea [32]. However, this study was conducted in the United States where the potential impact may have been reduced due to generally higher levels of water quality. Most of the studies included in the review were small in scale with three studies had fewer than 100 HIV-positive participants. Results from pooling multiple small-scale studies should be interpreted with caution. Furthermore, the included studies had relatively short follow up periods, a factor that has been shown to exaggerate the effect of WASH interventions [49].

In conclusion, the evidence of the health impact of WASH interventions among PLHIV is limited and mixed. Future studies should examine the impact of improved water supply and sanitation, two of the most fundamental of WASH interventions. Though blinding of most WASH interventions may be impossible, assessments should employ study designs and objective outcomes that minimize the risk of bias. They should also carefully measure compliance as a possible effect modifier and track the impact of the intervention on reducing pathogen exposure, a necessary condition for achieving health benefits from WASH interventions.

RESPONSIBILITY AND ACKNOWLEDGEMENTS

RP and TC designed the study. RP conducted all searches (except the Chinese databases), reviewed results for eligibility, extracted data from included studies, conducted the analysis, and assessed quality of the included studies. KC conducted database searches of the Chinese databases and reviewed subsequent results for eligibility. TM reviewed database results for study eligibility. MH and ME reviewed gray literature for eligibility. TC contacted agencies for grey literature, resolved any disagreements on eligibility, and helped with quality assessment. RP and TC wrote the paper. All authors contributed to drafts of this report and interpreted findings.

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Figure 1: Search flow diagram

Figure 2: Forest plot and meta-analysis of the impact of drinking water and hygiene interventions on diarrhoeal disease.

Effects size was calculated from crude data for Colford, Barzilay, Huang, and Harris. All data were unadjusted. Results are for PLHIV with the exception of Peletz and Harris, where they are for children born to HIV-positive mothers.

Table 1. Details of included studies on water, sanitation, and hygiene interventions for PLHIV

Reference	Design and setting (duration)	Number of participants	Intervention	Health Outcomes	Status
Abebe 2012	RCT (1 year) in Limpopo Province, South Africa.	74 HIV+	Household filter (ceramic)	Cryptosporidiosis, reported diarrhoeal disease	Submitted
Barzilay 2011	Interrupted-time series in Lagos, Nigeria (21 weeks)	242 HIV+ women	Household chlorination	Reported diarrhoeal disease	Published
Colford 2005	Blinded RCT in San Francisco, CA, USA (16 weeks)	50 HIV+ adults	Household filter + UV	Reported diarrhoeal disease (highly credible gastrointestinal illness)	Published
Harris 2009	Historically controlled in Kisumu, Kenya (1 year)	491 infants born to HIV+ women	Household chlorination	Clinic visits for diarrhoea	Published
Huang 2007	RCT in USA (1 year)	148 HIV+ adults	Handwashing	Reported diarrhoeal disease, enteric infections	Published
Lule 2005	RCT in Tororo district, Uganda (5 months/1 year)	509 HIV+, 1521 HIV- household members	Household chlorination	Reported diarrhoeal disease, enteric infections	Published
Peletz 2012	RCT in Chongwe district, Zambia (1 year)	120 children <2 years (100 of HIV+ mothers and 20 of HIV- mothers)	Household filter (LifeStraw Family)	Reported diarrhoeal disease, weight-for-age z-scores	Published

Potgieter 2010	RCT paired in Limpopo Province, South Africa (17 weeks)	90 HIV+, 1315 people total	Household filter (ceramic)	Diarrhoeal disease, enteric infection, disease progression	In preparation; report available
Sorvillo 1994	Controlled before/after in Los Angeles, CA, USA (8 years of records)	10,988 HIV+	Filtration at water treatment plant	Cryptosporidiosis	Published
Walson 2013	Prospective cohort in Kisii and Kisumu, Kenya (2 years) (controlled before/after study)	589 HIV+	Household filter + bednets	Disease progression, diarrhoeal disease	Published

Table 2. Methodological quality of included study

Reference	Allocation sequence	Allocation concealment (RCTs only)[1]	Balanced baseline[2]	Loss to follow-up[3]	Blinding	Protection against contamination[5]	Reporting all outcomes
Abebe 2012	Random	Adequate	Adequate	Inadequate	Open	Adequate	Adequate
Barzilay 2011	Non-random	N/A	N/A	Inadequate	Open	N/A	Adequate
Colford 2005	Random	Adequate	Adequate	Adequate	Triple Blind	Adequate	Adequate
Harris 2009	Non-random	N/A	Adequate	Adequate	Open	Adequate	Adequate
Huang 2007	Random	Unclear	Adequate	Unclear	Open	Adequate	Adequate
Lule 2005	Random	Unclear	Unclear	Unclear	Open	Unclear	Adequate
Peletz 2012	Random	Adequate	Adequate	Inadequate	Open	Adequate	Adequate
Potgieter 2010	Random	Unclear	Unclear	Unclear	Open	Adequate	Inadequate[6]
Sorvillo 1994	Non-random	N/A	Unclear	Adequate	Single Blind[4]	Adequate	Adequate
Walson 2013	Non-random	N/A	Adequate	Adequate	Open	Somewhat adequate	Adequate

RCT = Randomized Controlled Trial.

[1]Studies considered adequate if randomization was centralized so that participants and investigators enrolling participants were unable to foresee assignment, unclear if method not described or insufficiently described, and N/A if not a RCT.

[2]Baseline data were considered to be adequately balanced if data were provided for baseline characteristics and outcomes, and adjusted for appropriately if necessary; baseline was unclear if data were not provided for baseline characteristics and/or outcomes; and baseline was listed as N/A for the interrupted-time series study.

[3]Loss to follow-up was considered adequate if ≤15%, inadequate if >15%, and unclear if not reported.

[4]The Sorvillo study was officially not blinded, though it is probable that participants were not aware of the change in the water treatment plant.

[5]Protection against contamination was considered adequate if it was unlikely for the control group to receive the intervention; the Walson study is listed as somewhat adequate because in the control group, 76% reported drinking purified water and 83.1% reported having a bednet (vs. 99.5% and 97.7% in the intervention group, respectively), though the control group was primarily boiling (29.9%) or chlorinating (45.4%) their water rather than filtering (0.4%).

[6]Did not report on diarrhoea; however the final report/publication was not available.