

Water Filter Provision and Home-Based Filter Reinforcement Reduce Diarrhea in Kenyan HIV-Infected Adults and Their Household Members

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Abstract. Among human immunodeficiency virus (HIV)-infected adults and children in Africa, diarrheal disease remains a major cause of morbidity and mortality. We evaluated the effectiveness of provision and home-based reinforcement of a point-of-use water filtration device to reduce diarrhea among 361 HIV-infected adults in western Kenya by comparing prevalence of self-reported diarrhea before and after these interventions. After provision of the filter, 8.7% of participants reported diarrhea compared with 17.2% in the 3 months before filter provision (odds ratio [OR] = 0.39, 95% confidence interval [95% CI] = 0.23–0.66, $P < 0.001$). The association was similar among 231 participants who were already taking daily cotrimoxazole prophylaxis before being given a filter (OR = 0.47, 95% CI = 0.25–0.88, $P = 0.019$). Educational reinforcement was also associated with a modest reduction in self-reported diarrhea (OR = 0.50, 95% CI = 0.20–0.99, $P = 0.047$). Provision and reinforcement of water filters may confer significant benefit in reducing diarrhea among HIV-infected persons, even when cotrimoxazole prophylaxis is already being used.

INTRODUCTION

Among human immunodeficiency virus (HIV)-infected adults and children in sub-Saharan Africa (SSA), diarrheal disease remains a major cause of morbidity and mortality.^{1,2} Diarrheal episodes in HIV-infected persons are more frequent and lead to more days of work and school lost than among individuals who are not infected with HIV.³ Diarrhea among HIV-infected individuals has been associated with increased HIV viral load, decreased CD4 counts, and increases in opportunistic infections, malnutrition, and death.^{4,5} Rates of diarrhea and diarrhea-related consequences in children are higher in households in which one or more adults are living with HIV (HIV-affected household), irrespective of the child's HIV status.^{6–8}

In resource-limited settings, where access to safe water and sanitation can be limited, it is estimated that 40–80% of moderate to severe diarrheal episodes in children are attributed to infectious causes.⁹ Repeated exposure to these contaminated environments contributes to increased intestinal permeability, impaired gut immune function, and malabsorption.^{10–12} This syndrome of environmental enteric dysfunction (previously termed tropical enteropathy) increases the risk of malnutrition and malnutrition-associated morbidity and mortality. Because HIV-infected individuals are at increased risk of both diarrheal disease and enteric dysfunction, interventions that reduce pathogen exposure and infection are particularly relevant.

Cotrimoxazole (CTX) prophylaxis is associated with dramatic reductions in diarrhea and opportunistic infections and the World Health Organization (WHO) recommends universal treatment in HIV-infected individuals.^{13–16} However, increased levels of circulating CTX drug resistance in low- and middle-income country (LMIC) settings may eventually lead to suboptimal effectiveness in eliminating gastrointestinal pathogens.^{15,17} Combination antiretroviral therapy (ART) in HIV-infected adults and children also reduces risk of diar-

rhea and enteric infection.^{13,14,18} However, it is estimated that only 34% of 28.3 million HIV-infected individuals globally currently receive ART.¹⁹

Water filtration devices reduce waterborne pathogens and subsequent diarrheal illness without contributing to antibiotic selective pressure or requiring clinic visits, and they can be used at any CD4 count.^{20–25} Thus, the WHO recommends that HIV-infected persons treat their drinking water at the point of use.²⁶ Although the efficacy of water filtration devices has been shown, there is limited evidence about what level of use is required for clinical benefit, how adherence might be improved, and in HIV-infected individuals, whether filters provide incremental benefit above CTX prophylaxis. The goal of the present study was to evaluate effectiveness of provision and reinforcement of a point-of-use water filtration device to reduce self-reported diarrhea in a population of HIV-infected adults and their household members.

MATERIALS AND METHODS

Study setting and participants. The study was nested in a prospective cohort study in which ART-naïve, HIV-1-infected adults were enrolled to determine the impact of a point-of-care water filtration device (Lifestraw Family Filtration Device; Vestergaard Frandsen, Lausanne, Switzerland) and long-lasting insecticide treated bed nets (LLINs) on HIV disease progression.²⁷ The filter removes particles larger than 20 nm and in controlled settings, reduces waterborne bacteria, viruses, and protozoan cysts by at least 99.9%.²⁸ Three hundred sixty-one individuals who received a water filtration device and LLIN between September of 2009 and July of 2010 were included in this analysis and followed for up to 2 years. Eligible individuals were 18 years of age or older, HIV-1-infected, ART-naïve (with enrollment CD4 count > 350 cells/mm³), WHO clinical stage I or II, and not pregnant. The study was conducted according to the procedures approved by the University of Washington Institutional Review Board (IRB) and the Kenya Medical Research Institute (KEMRI) Ethical Review Committee.

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Study visits and data collection. At the enrollment visit, all participants received a water filter and LLIN and completed a standardized questionnaire assessing medical history, socioeconomic status, living conditions, level of education, and occupation. As part of the medical history, participants were asked whether anyone in the household, including themselves, had experienced one or more acute diarrhea episodes, defined according to the WHO definition (three or more loose/watery stools in a 24-hour period lasting less than 14 days), within the last 3 months.²⁹ This information was used to estimate the prevalence of household diarrhea at each time point. The ages of all household members with acute diarrhea reported were also ascertained. Detailed information was collected about the participants' primary and other residences to facilitate patient tracing and home visits. Participants were allowed to opt out of home visits. Also, at enrollment, participants provided a blood sample for full blood count, measurement of CD4 count, and determination of plasma HIV RNA. Study staff sensitized participants on proper use, storage, and cleaning of the water filtration device and LLIN. Participants were asked to return to the health facility every 3 months for clinic visits to assess changes in health, including acute diarrhea episodes ascertained like they were at enrollment, and medication use (including ART and CTX) using a standardized questionnaire.

Between May and September of 2010, study staff trained in home tracing and patient confidentiality visited the homes of willing participants to assess the frequency, location, functionality, appearance, proper use, and cleaning of the water filtration device using a standardized questionnaire (filter reinforcement home visit). Average use of the filter by the HIV-infected participant was determined by the question: "In the last five times you prepared water for drinking, how many of those times did you use the water filtration device?". Participants demonstrated use and cleaning of the device and after assessment was performed, were engaged in a discussion of the risk of drinking unfiltered water. In addition, study staff demonstrated proper cleaning and use of the device. Although this visit was scheduled, participants were not informed of the reason for this home visit. Interviewers assessed whether the filtration device was being used based on the location of the device at the time of the home visit (hung up on the wall and ready to use versus in a closet, on the floor, or any other place where the device could not be readily used). If, on a given visit, the participant was not home, the household was visited up to three times. If, by the third visit, the participant was not available, they were considered lost to follow-up in the home visit assessment. A random subset of individuals were visited a second time, because of resource constraints, to evaluate changes in frequency of self-reported filter use as well as to obtain detailed information of water consumption and filtering behaviors.

Statistical analysis. Baseline demographics, laboratory measures, medication use, and self-reported filter use information were described with frequencies and percentages or medians and interquartile ranges (IQRs). *t* tests and χ^2 tests were used to determine differences between participants who did and did not elect to receive home visits. Any acute diarrheal episode within the last 3 months in the household and specifically, among HIV-infected partici-

pants and children under 5 years of age, were the outcomes of interest.

To evaluate the impact of water filter provision on acute diarrhea, we compared the odds of diarrhea (over the last 3 months) as recorded at baseline with the odds reported at the subsequent 3-month visit using McNemar's test of equality and reported odds ratios (ORs) and 95% confidence intervals (95% CIs) from conditional logistic regression models. Because daily CTX prophylaxis was provided to all HIV-infected participants as part of this study and is associated with reductions in diarrhea and other opportunistic infections in HIV-infected persons, we evaluated the filter provision analysis separately by baseline daily CTX status. In addition to assessing the relationship between filter provision and reductions in diarrheal disease, we also determined whether self-reported use by the HIV-infected participant was associated with their likelihood of reporting a diarrhea episode within the subsequent 3 months using logistic regression. We evaluated whether the location of the device at the time of the interview (a surrogate for use) was associated with household diarrhea using logistic regression. Additionally, the association between diarrhea among the HIV-infected participant and their household members was determined using logistic regression with clustered standard errors to account for within-household correlation of reporting. To understand the agreement between diarrhea reported from the HIV-infected participant and other household members (as reported by the HIV-infected participant), we evaluated the association of self-reported diarrhea between the two groups using McNemar's test of equality.

Among those participants in whom the home reinforcement visit occurred at least 3 months after provision of the water filter, we evaluated the impact of the filter reinforcement home visit on diarrheal episodes by comparing the odds of household diarrhea at the clinic visit before and the clinic visit after the home visit using McNemar's test of equality and conditional logistic regression. In the random subset of individuals visited a second time, McNemar's test was used to compare the odds of exclusive use (defined as using the water filter all of the last five times that drinking water was prepared) at the first home visit with the odds reported at the second visit.

HIV-infected participants who initiated ART in between any two time points at which self-reported diarrhea was ascertained were excluded, because ART has been shown to reduce diarrhea and thus, would confound any observed effect of the water filter. Fisher exact *P* values were calculated if any expected cell counts were less than five participants. All analyses were conducted using STATA 10.1, with statistical significance criteria set at $P \leq 0.05$.

RESULTS

Baseline characteristics. Three hundred sixty-one participants from the parent study received the water filtration device and LLIN between September of 2009 and July of 2010. Participants were relatively young (median age = 31 years; IQR = 25–39 years), 81.4% were female, 65.4% were married, and 19.9% were widowed (Table 1). Most participants (70.1%) had at least a primary school education, with 13.9% reporting post-secondary training. Close to one-half (43.9%) of participants had a communal water source, such as a shared

TABLE 1

Baseline characteristics of HIV-infected participants and their households ($N = 361$)

	Number median	Percent* (IQR)
HIV-infected participant factors		
Female sex	294	81.4
Age, years	31	25–39
Clinic location		
Kisii	193	53.5
Kisumu	168	46.5
Marital status		
Married	236	65.4
Education (highest completed)		
Less than primary	108	29.9
Income-generating occupation		
Farmer	99	27.4
Other	209	57.9
None	53	14.7
CD4 count (cells/ μ L)	531.4	446–667
Cotrimoxazole use [†]		
Daily	231	65.1
Less than daily	30	8.5
Never	94	26.5
Household-level factors		
Monthly income (Kenyan shillings)		
< 5,000	285	79.0
5,000+	72	19.9
Missing	4	1.1
At least one other person living in house	350	97.0
At least one child (≤ 5 years old) living in house	206	57.1
No. of persons living in house		
< 5 years	1	0–1
5–15 years	1	0–2
> 15 years (including HIV-infected participant)	2	2–3
Water source		
Piped water into house	21	5.8
Communal source	158	43.8
Environmental water source	85	23.6
Well/water source outside house	96	26.6
Missing	1	0.3
Type of toilet		
Pit latrine	344	95.3
Flush toilet	10	2.8
Bush	7	1.9

*Percentage of those individuals with complete data.

[†]Frequency and percentage of CTX use differ slightly from the primary publication, in which any CTX use was reported.

pipe, and the remaining one-half had either an environmental source (23.6%) or a personal well or pipe outside of the house (26.7%). The most common occupation was self-employed/business (36.5%) followed by farming (27.4%), casual laborer (13.3%), and other (8.1%), whereas 14.7% reported being unemployed. Almost all participants (97.0%) had one or more persons living in their household, and a little more than one-half (57.1%) had at least one child under 5 years old in the household. Median CD4 count at enrollment into the study was 531 cells/ μ L (IQR = 446–667 cells/ μ L); 261 (73.5%) of 355 participants who answered the question reported currently taking CTX prophylaxis at study enrollment. Of those participants, 231 participants reported using it daily, and 30 participants reported using it less than daily. All participants received CTX at enrollment and the 3-month follow-up visit, 351 (97.2%) participants reported using it daily, 3 (0.8%) participants reported using it less than daily, and 7 (1.9%) participants did not answer the question.

Follow-up. The first follow-up clinic visit occurred a median of 92 days after enrollment (IQR = 90–95 days), and retention at that visit was high (98.0%). At the time of the first clinic visit after enrollment, none of the participants had initiated ART. The majority (82.8%) consented to at least one home visit to reinforce the importance of filter use, document frequency of use, and assess the condition and location of the filter. Among these 299 participants, the first home visit occurred at a median of 7.0 months (IQR = 2–9 months) after enrollment. In addition, 211 (70.6%) participants were visited a second time at a median of 12.1 months (IQR = 8.1–16.3) after enrollment. Participants who elected not to be visited at their home did not differ from those participants who did with regard to any baseline characteristics other than employment; participants who agreed to be visited at home were more likely to be farmers (34.8%) compared with participants who did not agree to home visits (15.9%, $P = 0.013$). Many of the participants who chose not to be visited had not disclosed their HIV status to family members and refused home visitation for fear of unintended disclosure.

Water filter assessment. At the initial home visit, the majority (57.1%) of 299 participants reported exclusively using the water filter for drinking water, only 1.4% reported never using the device, and 5.7% did not respond to the question. The 188 households with the device hanging and ready for use at the time of the home visit were more likely to report exclusive use of the device than the 94 households with the device not ready to use (62.8% versus 45.7%, $P = 0.006$). When asked to demonstrate cleaning of the filter cartridge, 90.1% of participants demonstrated correct cleaning; however, there was some heterogeneity in the reported frequency of cleaning: 72.9% reported cleaning it daily, 22.8% reported cleaning it occasionally, and 4.3% reported never cleaning the cartridge. Participants were less likely to report exclusive use of the filter by the second home visit (30.8%) compared with the first home visit; however, participants who reported using the device exclusively at the first home visit were more likely to report exclusive use at the subsequent visit ($P < 0.001$). Less than one-half (39.4%) of participants reported consuming water outside of their homes, and of these participants, less than one-third (29.7%) reported filtering the outside water.

Self-reported diarrhea. Only one participant had initiated ART at the time of the clinic visit preceding the reinforcement visit, and this individual was excluded from the analysis. Eighty visited participants were excluded, because their home reinforcement visit occurred within the first 3 months of the study enrollment, thereby precluding the possibility of distinguishing filter provision from home reinforcement. An additional 22 participants were excluded, because they were missing a diarrhea assessment at the most recent 3-month clinic visit, leaving 196 participants for whom we evaluated whether the reinforcement impacted self-reported diarrhea.

Participant diarrhea was significantly lower at the first follow-up visit than at enrollment in the study (8.7% versus 17.2%; OR = 0.39, 95% CI = 0.23–0.66, $P < 0.001$) (Figure 1). Among 124 participants who were not on daily CTX prophylaxis at enrollment, the odds of diarrhea were reduced by more than 70% (7.1% versus 18.5%; OR = 0.26, 95% CI = 0.10–0.70, $P = 0.008$), and this effect was similar after excluding 30 participants who reported non-daily use of CTX at enrollment (5.5% versus 17.9%; OR = 0.27, 95% CI = 0.09–0.80, $P = 0.019$).

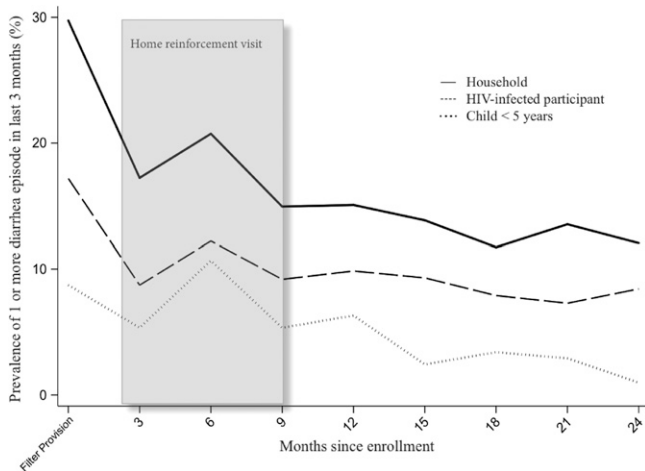


FIGURE 1. Percentage of households reporting any acute diarrhea episode experienced by the HIV-infected participant or other household member in the previous 3-month period.

(Figure 2). Among participants who were already taking daily CTX by the time that they were given the filter, the odds reduction was approximately 50% (9.6% versus 16.5%; OR = 0.47, 95% CI = 0.25–0.88, $P = 0.019$) (Figure 2). There were significantly fewer households with any diarrhea at the first follow-up visit (17.2% versus 29.7%; OR = 0.37, 95% CI = 0.24–0.59, $P < 0.001$) compared with the enrollment visit. In the subgroup of 206 children < 5 years old living in the household, 5.3% had experienced diarrhea in the 3 months after receipt of the water filter compared with 8.8% in the 3 months before (OR = 0.53, 95% CI = 0.23–1.26, $P = 0.15$). There was substantial concordance between diarrhea among the HIV-infected participants and their household members; at enrollment, of 56 participants self-reporting diarrhea, 34 (60.7%) participants also reported that a household member had diarrhea, whereas 15.4% of participants who did not experience diarrhea had a household member who did ($P < 0.001$)

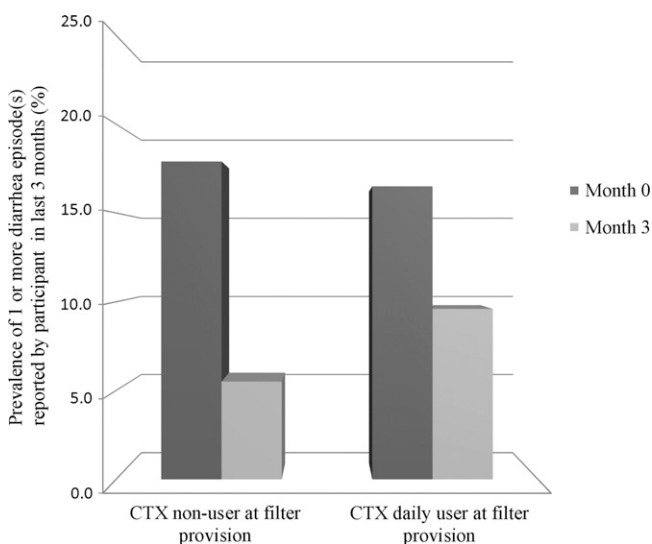


FIGURE 2. Prevalence of self-reported diarrhea at filter provision and the 3-month clinic visit among participants taking daily CTX prophylaxis at filter provision ($N = 231$) and participants not taking CTX at the time of filter provision ($N = 94$).

(Table 2). Similarly, at the 3-month visit, 10 (34.5%) of 29 participants who reported diarrhea also had a household member with diarrhea, whereas only 9.6% of 314 participants who did not report diarrhea had a household member with diarrhea ($P < 0.001$) (Table 2). Although self-reported diarrhea was predictive of one or more diarrhea episodes by other members of the household, 15.4% and 9.6% of participants who did not report diarrhea themselves reported diarrhea of another household member at enrollment and month 3, respectively. Conversely, 39.3% and 65.5% of participants reporting diarrhea at enrollment and month 3 visits, respectively, reported no diarrhea episodes among household members.

Data on the use and location of the device and diarrhea at the subsequent clinic visit within 3 months were available for 282 of 299 participants who agreed to be visited. Participants who reported exclusive filter use did not differ from participants reporting less than exclusive filter use in terms of self-reported diarrhea (7.3% versus 7.3%; OR = 0.99, 95% CI = 0.4–2.6, $P = 0.99$). Among three participants who reported never using their device in whom we had diarrhea data available, one (33.3%) participant reported diarrhea; 12 (6.5%) of 184 participants who had the device hung up and ready to use at the time of the interview reported diarrhea at the subsequent visit, whereas 9 (9.2%) of those participants without the device hanging reported diarrhea (OR = 0.69, 95% CI = 0.3–1.7, $P = 0.42$).

Self-reported diarrhea was lower in 3 months after the home reinforcement visit compared with 3 months before the home visit (7.7% versus 13.3%; OR = 0.50, 95% CI = 0.20–0.99, $P = 0.047$). Any household diarrhea was not significantly lower in 3 months after the filter reinforcement compared with before the filter reinforcement (15.8% versus 19.4%; OR = 0.70, 95% CI = 0.4–1.3, $P = 0.277$) (Figure 3). In the subgroup of 120 children under 5 years of age, there was no association between filter reinforcement and diarrhea (5.0% versus 6.7%; OR = 0.90, 95% CI = 0.40–2.1, $P = 0.835$).

DISCUSSION

In this nested pre-/post-effectiveness study, the provision of a point-of-use water filtration device to ART-naïve, HIV-infected adults resulted in significant reductions in self-reported diarrheal disease episodes among those individuals as well as their household members. The reduction in self-reported diarrhea among HIV-infected participants was independent of CTX use, suggesting that both these interventions are important in improving the health of HIV-infected individuals who are not yet on ART. Reductions in reported diarrheal disease occurred despite only 57.1% of participants reporting exclusive use of the filter. Reinforcement of the need to use the device at the household further decreased diarrheal episodes among the participants. The results of this study suggest that provision of water filters to HIV-affected households may confer significant benefit in reducing diarrhea among the HIV-infected individual and their household members, even when reported use of the filter is suboptimal.

Randomized controlled trials (RCTs) of the effectiveness of water filters in preventing diarrhea report reductions ranging from 15% to 80%.^{20–24} An RCT conducted among HIV-infected women and evaluating the same filtration device used in this study found a similar magnitude of effect in the intervention group (a 54% lower longitudinal household

TABLE 2

Frequency of one or more acute diarrhea episodes in the last 3 months among HIV-infected participants and their household members at enrollment

HIV-infected participant	Enrollment visit			Month 3 visit		
	Other household members		Total	Other household members		Total
	Diarrhea, <i>N</i> (%)	No diarrhea, <i>N</i> (%)		Diarrhea, <i>N</i> (%)	No diarrhea, <i>N</i> (%)	
Diarrhea	34 (60.7)*	22 (39.3)	56	10 (34.5)	19 (65.5)	29
No diarrhea	44 (15.4)	242 (84.6)	286	30 (9.6)	284 (90.5)	314
Total	78	264	342†	40	303	343†

*Row percentages.

†Six HIV-infected participants were missing diarrhea information at baseline; 11 participants lived alone at both enrollment and month 3. At baseline, two participants did not know whether anyone in the household had experienced diarrhea, and one participant did not know at the month 3 visit.

diarrhea prevalence) compared with controls.²⁰ In addition, the trial reported a statistically significant 49% reduction in longitudinal diarrhea among children less than 5 years old living in the household, consistent with the 47% reduction (albeit in odds rather than risk) that we observed (although this reduction was not statistically significant in our study). The relatively small subset (206 of 365) of households with a child under 5 years of age and the restricted 3-month period of reporting may have limited our power to detect significant difference in these children. A recently published systematic review and meta-analysis of the effect of water quality interventions in preventing diarrhea in HIV-infected populations showed a pooled relative risk of 0.57 (95% CI = 0.38–0.86) among the eight included studies.³⁰ Although the magnitude of effect observed in our study of 0.39 fell within the confidence interval of the pooled effect size, we reported OR instead of relative risk; the ratio of diarrhea prevalence after filter provision (8.7%) compared with before filter provision (17.2%) is 0.51, a prevalence ratio that closely matches the pooled relative risk reported by Peletz and others.³⁰

HIV-infected participants benefited immediately from water filter provision, and importantly, this benefit occurred even among those participants already on daily CTX prophylaxis at the time of study enrollment. Similar findings were reported from a trial in Uganda, which compared a home-

based water chlorination and safe storage system with education alone; the study found that the water system not only decreased diarrhea incidence among the HIV-infected participants by 25% but that CTX did not alter the benefit of the intervention on diarrhea risk.³ The combination of the two interventions reduced diarrhea more than two times as much as the water intervention alone (67% versus 25%) in the Ugandan study. Although we could not explicitly address this question, we did find that individuals receiving CTX and the water filter had a 70% reduction in diarrhea prevalence compared with participants on CTX already, who had a 50% reduction with the addition of the water filter. Combined with evidence that water filters and CTX can delay progression of HIV disease, both water filters and CTX should be part of the health promotion package offered to HIV-infected persons who have not yet started ART.

Almost all participants reported some use of the filter, with slightly more than one-half reporting exclusive use and only 1.4% reporting not using the device at all. Because so few participants reported never using the device, we were not able to analyze differences in diarrhea between those participants who did and did not use the device. The lack of a difference in diarrhea comparing exclusive use with non-exclusive use could be because of a small sample size, or if real, could be because the relative gain in diarrhea reduction associated with

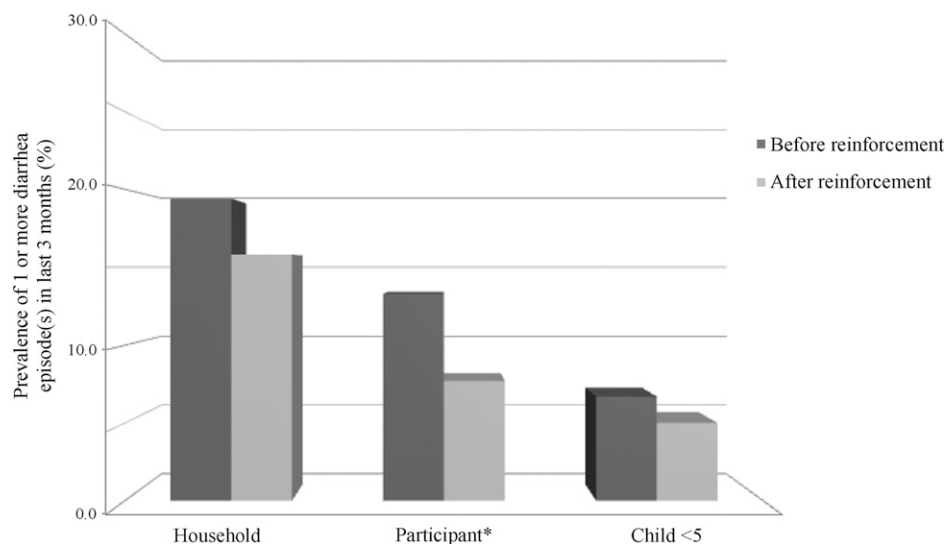


FIGURE 3. Any self-reported diarrhea in the last 3 months among households, HIV-infected participants, and children under 5 years old before and after the filter reinforcement home visit. Participants who did not consent to home visits ($N = 62$), whose home visit occurred within the first 3 months of enrollment ($N = 80$), who had initiated ART between visits ($N = 1$), and who did not have a clinic visit for diarrhea assessment within 3 months before and after home visit ($N = 22$) were excluded from the analysis. *Indicates McNemar's test (P value < 0.05).

using the filter exclusively, compared with using it sometimes, is minimal. In real world situations, interventions that offer substantial benefit, despite imperfect adherence, are often the most sustainable interventions to implement. No trials that we found performed an as-treated analysis that considered whether there is a dose–response relationship between filter use and its effectiveness in preventing diarrhea among study participants. A meta-analysis performed using 11 trials of water quality interventions with various reported compliance levels ($\geq 50\%$ versus $< 50\%$) found that studies with higher compliance levels reported larger benefits associated with the intervention than studies with lower compliance levels.²¹ However, this classification of compliance does not offer insight into differences between benefit levels among those participants who do use the intervention, because the studies with compliance $< 50\%$ also include participants who did not use the interventions at all.³¹

It is possible that our question of self-reported filter use in the last five times that drinking water was prepared was not an accurate reflection of the longer-term filter use during the salient period for enteric infection risk. Despite this potential response bias in self-reported use questions, there was substantial agreement between those participants reporting exclusive use and the device being easily accessible and ready for use at the time of the interview. Methods for measuring adherence to water filters are limited; unlike chlorine, which can be detected in water, or a biomarker, which could potentially be measured in blood, filters do not have a reliable measure of adherence other than self-report and location of the device at the time of the interview. In the absence of a gold standard adherence measure for filter use, reliability studies are needed to identify the ideal period of time to maximize recall of water filter use, and this measure should be standardized across future studies for between-study comparisons.

Home visits by study staff, in which the water filter device use was reinforced and assessed, were associated with a reduction in odds of diarrhea among the HIV-infected participants. Although the mechanism by which this type of reinforcement influenced diarrheal episodes was not explicitly explored, we hypothesize that repeated advocacy about the importance of clean water and a personal demonstration on how to use the device motivated participants to use the device correctly more frequently, resulting in less diarrhea. We did not observe a notable reduction in diarrhea among the household members after the reinforcement home visit. The lack of an effect, particularly among children under 5 years of age, could be because the magnitude of benefit is small, and we lacked power to detect such an effect with data for only 120 children. We cannot exclude the possibility that diarrhea prevalence would have gone down, even in the absence of the home reinforcement visit. Independent of the reinforcement visit, participant awareness of the benefits of the filter and/or sanitation could be increasing over time, or participants may have reported less diarrhea over time from participant fatigue. A future RCT would be useful to quantify the additional benefit of such reinforcement on household diarrhea episodes. Additionally, the benefit of reinforcement, relative to provision alone, should be assessed taking into account the cost of such personalized counseling.

The present study was limited by its pre-/post-observational design; it could be that participants reported less diarrhea

after enrollment in the study because of response bias rather than the true causal effect of the water filter. However, because the primary aim of this study, which was communicated to participants, was to slow down HIV disease progression, we do not believe participants were compelled to underestimate their diarrheal episodes after enrollment in the study. We considered earlier time points within the same individuals to be the control group; however, an independent group of participants enrolled in the study without the filter provision and educational reinforcement would have better estimated non-intervention changes in self-reported diarrhea prevalence. The infrequent assessment of diarrhea was another limitation; participants were asked about diarrhea at every 3-month visit, whereas research has shown that the most accurate recall of morbidity events is in the last 3 days.³² Diarrhea among household members was also ascertained from the HIV-positive participants who may or may not have been aware of diarrheal episodes among all household members, possibly resulting in underreporting of household diarrhea. Although the infrequent ascertainment of self-reported and household diarrhea by only a single household member may have been imprecise, the imprecision within a given household is unlikely to differ between time points; because the analytic comparisons were made within households, we do not believe that differential bias occurred.

Another limitation of the present study is that we assume that the filter was effectively improving water quality. Although efficacy studies of the Lifestraw Family Filtration device clearly show reductions in fecal contamination as measured by thermotolerant coliforms [TTCs], these studies assume proper use and cleaning of the device as well as safe storage of water.^{20,24,28} We were not able to ascertain TTCs in the present study; however, we did perform a single assessment of proper use and cleaning of the device at the reinforcement visit and found that almost all participants (96%) demonstrated proper use and cleaning of the device. However, not all participants (27.1%) reported cleaning the filter cartridge daily, and although we do not know the impact of improper cartridge cleaning on the efficacy of the filtration system, it is plausible that water was contaminated for this reason. Although participants were instructed to store water in clean containers with a cover, we did not provide these containers, which was done in other studies that found benefit associated with this filtration system.²⁰ Because filtered water can be recontaminated if placed in unsterile or uncovered storage containers, wide-scale implementation of water filtration systems will need to incorporate mechanisms for safe water storage.

Despite these limitations, this study suggests substantial benefit of providing water filter devices to HIV-infected individuals to prevent diarrheal disease in both these individuals and their household members. Cost-effectiveness analyses showed that 191 disability-adjusted life years (DALYs) and US\$48,123 per 1,000 participants could be averted through the provision of the US\$20 water filters to HIV-infected individuals.^{33,34} These data also suggest that there may be added benefit of simple home visitations to reinforce the use of the device; however, we do not have estimates on the cost effectiveness of such services. This type of reinforcement is likely cost effective only in settings where participants live within a reasonable distance from health facilities. Incorporating provision of water filtration devices into HIV care and treatment

programs may offer prophylactic benefit to HIV-infected adults when used correctly and also may confer benefit to their household members.

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REFERENCES

- van Eijk AM, Brooks JT, Adcock PM, Garrett V, Eberhard M, Rosen DH, Ayisi JG, Ochieng JB, Kumar L, Gentsch JR, Nahlen BL, Mintz ED, Slutsker L, 2010. Diarrhea in children less than two years of age with known HIV status in Kisumu, Kenya. *Int J Infect Dis* 14: e220–e225.
- Thea DM, St Louis ME, Atido U, Kanjinga K, Kembo B, Matondo M, Tshiamala T, Kamenga C, Davachi F, Brown C, Rand WM, Keusch GT, 1993. A prospective study of diarrhea and HIV-1 infection among 429 Zairian infants. *N Engl J Med* 329: 1696–1702.
- Lule JR, Mermin J, Ekwaru JP, Malamba S, Downing R, Ransom R, Nakanjako D, Wafula W, Hughes P, Bunnell R, Kaharuza F, Coutinho A, Kigozi A, Quick R, 2005. Effect of home-based water chlorination and safe storage on diarrhea among persons with human immunodeficiency virus in Uganda. *Am J Trop Med Hyg* 73: 926–933.
- Sadraei J, Rizvi MA, Baveja UK, 2005. Diarrhea, CD4+ cell counts and opportunistic protozoa in Indian HIV-infected patients. *Parasitol Res* 97: 270–273.
- Brink AK, Mahe C, Watara C, Lugada E, Gilks C, Whitworth J, French N, 2002. Diarrhea, CD4 counts and enteric infections in a community-based cohort of HIV-infected adults in Uganda. *J Infect* 45: 99–106.
- Ciara E, O'Reilly RO, Moke F, Ondeng A, Hukumu E, Ibworo V, Rajasingham A, Ochieng B, Farag TH, Nasrin D, Panchalingam S, Nataro JP, Kotloff KL, Levine MM, Oundo J, Parsons MB, Bopp C, Vulule J, Laserson K, Mintz ED, Breiman RF, 2011. *Moderate-to-Severe Diarrhea Among Children Less Than Five Years Old with HIV Infected Mothers in Rural Western Kenya*. Philadelphia, PA: The American Society of Tropical Medicine and Hygiene.
- Mermin J, Lule J, Ekwaru JP, Malamba S, Downing R, Ransom R, Kaharuza F, Culver D, Kizito F, Bunnell R, Kigozi A, Nakanjako D, Wafula W, Quick R, 2004. Effect of co-trimoxazole prophylaxis on morbidity, mortality, CD4-cell count, and viral load in HIV infection in rural Uganda. *Lancet* 364: 1428–1434.
- Peletz R, Simuyandi M, Sarenje K, Baisley K, Kelly P, Filteau S, Clasen T, 2011. Drinking water quality, feeding practices, and diarrhea among children under 2 years of HIV-positive mothers in peri-urban Zambia. *Am J Trop Med Hyg* 85: 318–326.
- Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, Wu Y, Sow SO, Sur D, Breiman RF, Faruque AS, Zaidi AK, Saha D, Alonso PL, Tamboura B, Sanogo D, Onwuchekwa U, Manna B, Ramamurthy T, Kanungo S, Ochieng JB, Omere R, Oundo JO, Hossain A, Das SK, Ahmed S, Qureshi S, Quadri F, Adegbola RA, Antonio M, Hossain MJ, Akinsola A, Mandomando I, Nhamposha T, Acacio S, Biswas K, O'Reilly CE, Mintz ED, Berkeley LY, Muhsen K, Sommerfelt H, Robins-Browne RM, Levine MM, 2013. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. *Lancet* 382: 209–222.
- Korpe PS, Petri WA Jr, 2012. Environmental enteropathy: critical implications of a poorly understood condition. *Trends Mol Med* 18: 328–336.
- Prendergast A, Kelly P, 2012. Enteropathies in the developing world: neglected effects on global health. *Am J Trop Med Hyg* 86: 756–763.
- Petri WA Jr, Miller M, Binder HJ, Levine MM, Dillingham R, Guerrant RL, 2008. Enteric infections, diarrhea, and their impact on function and development. *J Clin Invest* 118: 1277–1290.
- Chintu C, Bhat GJ, Walker AS, Mulenga V, Sinyinza F, Lishimpi K, Farrelly L, Kaganson N, Zumla A, Gillespie SH, Nunn AJ, Gibb DM, 2004. Co-trimoxazole as prophylaxis against opportunistic infections in HIV-infected Zambian children (CHAP): a double-blind randomised placebo-controlled trial. *Lancet* 364: 1865–1871.
- Nunn AJ, Mwaba P, Chintu C, Mwinga A, Darbyshire JH, Zumla A, 2008. Role of co-trimoxazole prophylaxis in reducing mortality in HIV infected adults being treated for tuberculosis: randomised clinical trial. *BMJ* 337: a257.
- Anglaret X, Chene G, Attia A, Toure S, Lafont S, Combe P, Manlan K, N'Dri-Yoman T, Salamon R, 1999. Early chemoprophylaxis with trimethoprim-sulphamethoxazole for HIV-1-infected adults in Abidjan, Cote d'Ivoire: a randomised trial. Cotrimo-CI Study Group. *Lancet* 353: 1463–1468.
- World Health Organization (WHO), 2006. *Guidelines on Co-Trimoxazole Prophylaxis for HIV-Related Infections Among Children, Adolescents and Adults: Recommendations for a Public Health Approach*. Available at: <http://www.who.int/entity/hiv/pub/guidelines/ctxguidelines.pdf>. Accessed July 26, 2013.
- Swierczewski BE, Odundo EA, Koech MC, Ndonge JN, Kirera RK, Odhiambo CP, Cheruiyot EK, Wu MT, Lee JE, Zhang C, Oaks EV, 2013. Surveillance for enteric pathogens in a case-control study of acute diarrhea in western Kenya. *Trans R Soc Trop Med Hyg* 107: 83–90.
- Monkemuller KE, Call SA, Lazenby AJ, Wilcox CM, 2000. Declining prevalence of opportunistic gastrointestinal disease in the era of combination antiretroviral therapy. *Am J Gastroenterol* 95: 457–462.

19. United Nations Programme on HIV/AIDS (UNAIDS), 2013. *Global Report: UNAIDS Report on the Global AIDS Epidemic 2013*. Geneva: UNAIDS.
20. Peletz R, Simunyama M, Sarenje K, Baisley K, Filteau S, Kelly P, Clasen T, 2012. Assessing water filtration and safe storage in households with young children of HIV-positive mothers: a randomized, controlled trial in Zambia. *PLoS ONE* 7: e46548.
21. Clasen T, Roberts I, Rabie T, Schmidt W, Cairncross S, 2006. Interventions to improve water quality for preventing diarrhoea. *Cochrane Database Syst Rev* 6: CD004794.
22. Clasen T, Schmidt WP, Rabie T, Roberts I, Cairncross S, 2007. Interventions to improve water quality for preventing diarrhoea: systematic review and meta-analysis. *BMJ* 334: 782.
23. Boisson S, Kiyombo M, Sthresley L, Tumba S, Makambo J, Clasen T, 2010. Field assessment of a novel household-based water filtration device: a randomised, placebo-controlled trial in the Democratic Republic of Congo. *PLoS ONE* 5: e12613.
24. Boisson S, Schmidt WP, Berhanu T, Gezahegn H, Clasen T, 2009. Randomized controlled trial in rural Ethiopia to assess a portable water treatment device. *Environ Sci Technol* 43: 5934–5939.
25. Fewtrell L, Kaufmann RB, Kay D, Enanoria W, Haller L, Colford JM Jr, 2005. Water, sanitation, and hygiene interventions to reduce diarrhoea in less developed countries: a systematic review and meta-analysis. *Lancet Infect Dis* 5: 42–52.
26. World Health Organization (WHO), 2008. *Essential Prevention and Care Interventions for Adults and Adolescents Living with HIV in Resource-Limited Settings*. Available at: <http://www.who.int/hiv/pub/plhiv/interventions/en/index.html>. Accessed August 21, 2013.
27. Walson JL, Sangare LR, Singa BO, Naulikha JM, Piper BK, Yuhua K, Onchiri FM, Otieno PA, Mermin J, Zeh C, Richardson BA, John-Stewart G, 2013. Evaluation of impact of long-lasting insecticide-treated bed nets and point-of-use water filters on HIV-1 disease progression in Kenya. *AIDS* 27: 1493–1501.
28. Clasen T, Naranjo J, Frauchiger D, Gerba C, 2009. Laboratory assessment of a gravity-fed ultrafiltration water treatment device designed for household use in low-income settings. *Am J Trop Med Hyg* 80: 819–823.
29. World Health Organization (WHO), 2007. *The Treatment of Diarrhoea. A Manual for Physicians and Other Senior Health Workers*. Geneva: WHO.
30. Peletz R, Mahin T, Elliott M, Harris MS, Chan KS, Cohen MS, Bartram JK, Clasen TF, 2013. Water, sanitation, and hygiene interventions to improve health among people living with HIV/AIDS: a systematic review. *AIDS* 27: 2593–2601.
31. Reller ME, Mendoza CE, Lopez MB, Alvarez M, Hoekstra RM, Olson CA, Baier KG, Keswick BH, Luby SP, 2003. A randomized controlled trial of household-based flocculant-disinfectant drinking water treatment for diarrhea prevention in rural Guatemala. *Am J Trop Med Hyg* 69: 411–419.
32. Feikin DR, Audi A, Olack B, Bigogo GM, Polyak C, Burke H, Williamson J, Breiman RF, 2010. Evaluation of the optimal recall period for disease symptoms in home-based morbidity surveillance in rural and urban Kenya. *Int J Epidemiol* 39: 450–458.
33. Kahn JG, Muraguri N, Harris B, Lugada E, Clasen T, Grabowsky M, Mermin J, Shariff S, 2012. Integrated HIV testing, malaria, and diarrhea prevention campaign in Kenya: modeled health impact and cost-effectiveness. *PLoS ONE* 7: e31316.
34. Kahn JG, Harris B, Mermin JH, Clasen T, Lugada E, Grabowsky M, Vestergaard Frandsen M, Garg N, 2011. Cost of community integrated prevention campaign for malaria, HIV, and diarrhea in rural Kenya. *BMC Health Serv Res* 11: 346.