EFFECT OF HOME-BASED WATER CHLORINATION AND SAFE STORAGE ON DIARRHEA AMONG PERSONS WITH HUMAN IMMUNODEFICIENCY VIRUS IN UGANDA

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Abstract. Diarrhea is frequent among persons infected with human immunodeficiency virus (HIV) but few interventions are available for people in Africa. We conducted a randomized controlled trial of a home-based, safe water intervention on the incidence and severity of diarrhea among persons with HIV living in rural Uganda. Between April 2001 and November 2002, households of 509 persons with HIV and 1,521 HIV-negative household members received a closed-mouth plastic container, a dilute chlorine solution, and hygiene education (safe water system [SWS]) or simply hygiene education alone. After five months, HIV-positive participants received daily cotrimoxazole prophylaxis (160 mg of trimethoprim and 800 mg of sulfamethoxazole) and were followed for an additional 1.5 years. Persons with HIV using SWS had 25% fewer diarrhea episodes (adjusted incidence rate ratio [IRR] = 0.75, 95% confidence interval [CI] = 0.59–0.94, \( P = 0.015 \)), 33% fewer days with diarrhea (IRR = 0.67, 95% CI = 0.48–0.94, \( P = 0.021 \)), and less visible blood or mucus in stools (28% versus 39%; \( P < 0.0001 \)). The SWS was equally effective with or without cotrimoxazole prophylaxis (\( P = 0.73 \) for interaction), and together they reduced diarrhea episodes by 67% (IRR = 0.33, 95% CI = 0.24–0.46, \( P < 0.0001 \)), days with diarrhea by 54% (IRR = 0.46, 95% CI = 0.32–0.66, \( P < 0.0001 \)), and days of work or school lost due to diarrhea by 47% (IRR = 0.53, 95% CI = 0.34–0.83, \( P < 0.0056 \)). A home-based safe water system reduced diarrhea frequency and severity among persons with HIV living in Africa and large scale implementation should be considered.

INTRODUCTION

The human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic presents profound challenges to health care providers and policy makers. In sub-Saharan Africa 5–30% of the adult population is infected with HIV. Because of scarce resources and limited infrastructure, treatment of HIV/AIDS has lagged far behind that available in industrialized world. In addition, environmental issues such as tropical infections, poor living conditions and limited access to safe drinking water and sanitation facilities expose persons with HIV to increased risks of opportunistic infections, including diarrhea. In sub-Saharan Africa, diarrhea is an important cause of morbidity and mortality in people living with HIV.1–4 Inexpensive interventions that prevent diarrhea could be important components of a care package for persons with HIV whether or not antiretroviral treatment is available.

The Safe Water System (SWS), a household-based water quality intervention developed by the Centers for Disease Control and Prevention (CDC) and the Pan American Health Organization, consists of water treatment using locally produced sodium hypochlorite solution and safe water storage in a narrow-mouth container (Figure 1).5 6 The SWS reduces the risk of water-borne diarrheal diseases in developing country settings.7–9 However, because the causes of diarrhea and the proportion of diarrhea associated with water-borne pathogens may be different among persons with and without HIV, we evaluated the effectiveness of SWS among persons with HIV and their family members living in rural Uganda.

Cotrimoxazole (trimethoprim-sulfamethoxazole) prophylaxis has been shown to decrease the incidence of diarrhea and mortality among persons with HIV in Africa, but has not been well evaluated in areas of high bacterial resistance to cotrimoxazole.10–12 The SWS and cotrimoxazole might additively reduce the incidence of diarrhea because the SWS potentially decreases the incidence of diarrhea associated with water-borne pathogens, but would not affect non–water-borne pathogens, and cotrimoxazole potentially decreases the incidence of diarrhea caused by cotrimoxazole-sensitive bacteria and parasites regardless of source, but would be less effective against resistant organisms. We designed a randomized controlled trial to evaluate both interventions and the potential for an additive effect on reducing the incidence of diarrhea in an area previously reported with bacterial resistance to cotrimoxazole greater than 70%.13,14 Here we present data on the effect of the SWS and cotrimoxazole on diarrhea. The effect of cotrimoxazole prophylaxis alone on morbidity and mortality has been reported elsewhere.14

METHODS

The study was reviewed and approved by the Science and Ethics Committee of the Uganda Virus Research Institute, the Uganda National Council of Science and Technology, and the Institutional Review Board of CDC.

Participants and enrollment. Persons with HIV-1 infection who were clients of The AIDS Support Organization (TASO) in the rural Tororo district in Uganda and without access to chlorinated municipality water were consecutively enrolled in

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Antimicrobial resistance was measured for Escherichia coli cysts. Frozen stool, stool samples were cultured on Mac- 
Shigella Aeromonas 927 using standard proce-

Evergreen Concentrate Kits (formalin-ethyl acetate, 

At enrollment, households of persons with 
/H11350 

Campylobacter was taken from each plate, stored in glycerol broth,

1. The safe water system. It is composed of a 20-liter 
polyethylene vessel with a spigot that prevents recontamination, a 
bottle of 0.5% sodium hypochlorite solution, and a locally produced cloth. Twenty liters of water are poured through the cloth into the 
vessel and one or two capfuls (equivalent to 10–20 mL) of sodium hypochlorite solution are added for disinfection.

SAFЕ WATER SYSTEM FOR DIARRHEA PREVENTION IN PERSONS WITH HIV

During weekly visits, study staff administered a question-
naire to all household members regarding diarrhea episodes, 

days with diarrhea, days of school or work lost, and hospital-
ization or death of a household member in the previous seven 
days. Seriously ill participants were encouraged to come to the 
study clinic and/or hospital and be treated free-of-charge. 
For cases of diarrhea, defined as ≥ 3 loose or watery stools in 
24 hours, a stool specimen was collected and aliquoted. Field 
workers inserted two swabs into stool samples, transferred 
them to a tube of Cary Blair transport media, then placed one 
portion of stool in a tube of formol saline, and another into a 
stainless container for storage. All samples were placed on ice 
packs in a cooler, transported to the project laboratory, and 
refrigerated. All Cary Blair specimens were cultured within 
48 hours of collection or frozen for future testing. Persons 
unable to provide a sample immediately were asked to insert 
two rectal swabs that were immediately transferred into Cary 
Blair transport media, and were also given a specimen cup for 
a stool specimen that was retrieved later the same day. Diar-
rhea was treated with oral rehydration solution and, if indi-
cated, antimicrobial and antimitoty agents. Only one stool 

Figure 1. The safe water system. It is composed of a 20-liter polyethylene vessel with a spigot that prevents recontamination, a bottle of 0.5% sodium hypochlorite solution, and a locally produced cloth. Twenty liters of water are poured through the cloth into the vessel and one or two capfuls (equivalent to 10–20 mL) of sodium hypochlorite solution are added for disinfection.

the study between January and March 2001 (Figure 2). After 
written, informed consent was provided, study staff visited 
participants’ homes to conduct a census and obtain consent 
from household members. Consent forms and questionnaires 
were translated into six local languages and back-translated 
into English. A household was defined as persons who shared 
a hearth and slept in the same house or cluster of houses for 
at least five days of the week for the preceding three months. 
A finger stick sample of blood was collected from household 
members on filter paper for HIV testing. All persons were 
encouraged to receive HIV test results and counseling at 
home or at the project clinic at Tororo Hospital. The HIV test 
result counseling was provided to study participants alone, or 
with partners. For participants 10–17 years of age, counseling 
included both the child and parent or legal guardian, and 
for those 0–9 years of age, only the parent or legal guardian 
was counseled. Consent for HIV testing or receiving test re-
results were not requirements for enrollment, but only persons 
for whom HIV test results were available were included in 
analyses.

Study design. At enrollment, households of persons with 
HIV were randomly assigned to receive either a 20-liter poly-
ethylene vessel with a narrow mouth and a spigot (Nampak 
Co., Johannesburg, South Africa), one 500-mL bottle of 0.5% 
sodium hypochlorite solution, a cloth, and basic hygiene edu-
cation alone. Field workers educated participants in the intervention group how to use the SWS, and 
replenished the solution as needed during weekly visits. To 
minimize confounding by exposure to health education mes-
ges, field workers instructed both intervention and comp-
parison households on hygiene and sanitation. After five 
months, all participants with HIV were provided cotrimox-
azole prophylaxis, and data on the incidence of diarrhea con-
tinued to be collected until the end of November 2002.

Data collection and main outcome measures. At baseline, 
participants were interviewed about household demographic 
and socioeconomic characteristics, and water, hygiene, and 
sanitary practices. All HIV-positive participants received an 
assessment by a physician and provided blood samples for 
viral load and CD4 cell count.

During weekly visits, study staff administered a question-
naire to all household members regarding diarrhea episodes, 
days with diarrhea, days of school or work lost, and hospital-
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a stool specimen that was retrieved later the same day. Diar-
rhea was treated with oral rehydration solution and, if indi-
cated, antimicrobial and antimitoty agents. Only one stool 

Laboratory testing. Stool samples in Cary Blair media were 
cultured for Salmonella, Shigella, Campylobacter, Vibrio cholerae, Plesiomonas, and Aeromonas using standard proce-
dures. To test for enterotoxigenic Escherichia coli and entero-
pathogenic E. coli, stool samples were cultured on Mac-
key agar. A sweep of colonies with appearance typical of 
E. coli was taken from each plate, stored in glycerol broth, 
and subsequently tested by polymerase chain reaction using 
DNA probes.15 Antimicrobial resistance was measured for 
bacterial stool pathogens using standard, disk-diffusion tech-
niques.16 Evergreen Concentrate Kits (formalin-ethyl acetate, 
feecal parasite concentrator; Evergreen Scientific, Los Ange-
les, CA) were used to identify ova, cysts, and parasites from 
formalinized whole stool samples. Modified Ziehl Neelsen 
stain was used to identify Cryptosporidium cysts. Frozen stool 
samples were thawed and tested for Rotavirus using the 
Murex Rotavirus enzyme-linked immunosorben assay kit 
(Med-Ox Diagnostics, Inc., Ottawa, Ontario, Canada).

Plasma samples were screened for HIV infection using two 
enzyme-linked immunoassays (EIAs) in parallel (Recom-
bigen HIV-1/HIV-2; Trinity Biotech, Dublin, Ireland and 
Murex HIV 120; Abbot Diagnostics, Chicago, IL). Specimens
negative on both EIA screening tests were considered negative and specimens positive on both assays were considered positive. Specimens with discordant results were re-tested by Western Blot (LAV Blot, Bio-Rad Laboratories, Hercules, CA). HIV testing of dried blood spots consisted of a screening EIA (Vironostika HIV; BioMerieux, Durham, NC) and confirmation of reactive specimens by Western blot. The polymerase chain reaction was conducted on all HIV-reactive specimens from children less than 24 months of age. The CD4 cell counts and HIV viral loads were measured using standard procedures (FACScount; Becton-Dickinson, La Jolla, CA and Cobas Amplicor Monitor version 1.5; Roche, Nutley, NJ).

At baseline, a random sample of 20% of study households was selected for microbiologic testing of source and stored water. In October 2001 and October 2002, follow up microbiologic water quality testing was conducted on additional random samples of 20% of the households. Field workers collected water samples in sterile 500-mL plastic containers and transported them to the project laboratory in a cooler with ice packs. Samples were processed on the day of collection using the membrane filtration technique with *E. coli* as the indicator organism (Hach Co., Loveland, CO).17

**Data analysis.** Data were analyzed using SAS version 9 software (SAS Institute, Cary, NC). Multivariable Poisson regression models using a log link function were developed for assessing associations between SWS and diarrhea episodes, days with diarrhea, and days of work or school lost due to diarrhea, adjusting for age, sex, time of year in three-month intervals, cotrimoxazole use, water quality, presence of latrine in compound, soap at home, and household wealth, including World Health Organization clinical stage and CD4 cell count for persons with HIV. The CD4 count measured at the beginning of the study was used as a baseline for the time period before cotrimoxazole prophylaxis, and the CD4 count measured just before starting treatment with cotrimoxazole was used as a baseline for the cotrimoxazole period. The combined effect of SWS and cotrimoxazole prophylaxis was assessed by comparing the rates of diarrhea in the intervention arm during cotrimoxazole prophylaxis with the rates in the control arm before cotrimoxazole prophylaxis.

Generalized estimating equation methods with an exchangeable correlation structure and an offset for the number of days at risk were used to control for intra-household and intra-individual disease clustering. A Wald test was used to
compare differences between groups. Multivariable results are presented unless otherwise specified. An intention-to-treat approach was used for analyses. Analysis of the effect of SWS on changes in CD4 cell count and viral load were calculated comparing the rate of change of CD4 cell count or viral load using analysis of covariance, adjusting for initial CD4 cell count or viral load for each period.

RESULTS

Baseline demographic and socioeconomic characteristics. A total of 509 persons with HIV and 1,521 HIV-negative household members were enrolled from 392 households (Figure 2). Seventy-four percent of the persons with HIV were female and median age was 34 years (interquartile range [IQR] = 28–40 years); 27 (5%) were less than five years old. At baseline, 27% of the persons with HIV had CD4 cell counts < 200 cells/mm$^3$, 37% had CD4 cell counts of 200–500 cells/mm$^3$, and 36% had CD4 cell counts > 500 cells/mm$^3$. Of the 1,521 HIV-negative family members, 730 (49.6%) were female and median age was 10 years, (IQR = 6–15 years); 255 (17%) were less than five years old.

The median follow-up time for persons with HIV was 547 days (IQR = 313–563 days) in the intervention group and 556 days (IQR = 469–567 days) in the comparison group (P = 0.059). There were no significant differences between intervention and comparison groups in baseline demographic characteristics, HIV status, CD4 cell count, or socioeconomic status.

Water, hygiene, and sanitation. Most households used springs or boreholes as water sources (Table 1). More than 90% of households’ stored water at home using wide-mouth containers. Of all water samples collected at baseline, more stored household samples had detectable E. coli than source samples (64 [90%] versus 40 [56%]; P < 0.0001), and stored household-water samples had higher levels of E. coli than source water samples (median = 158 [range = 0–40,000] versus 14 [range = 0–19,800] colony-forming units per 100 mL; P < 0.0001). Most households did not treat water. The only effective water treatment practices reported were boiling for 21% of intervention and 24% of comparison households, and bleach for one household (0.5%) in each group. Sanitary conditions, water sources, water handling practices, hygienic practices, and baseline E. coli colony counts were similar in both groups, except the intervention group had slightly worse E. coli contamination of source and stored water at baseline (P = 0.08 and 0.09, respectively), more often had water available for hand washing (P = 0.06), and more frequently reported hand washing after defecation (P = 0.07), although none of these findings were statistically significant (Table 1).

Diarrhea. During follow-up, 1,140 episodes of diarrhea and 6,861 days with diarrhea were reported. Persons with HIV, when compared with HIV-negative family members, had more diarrhea (1.2 versus 0.3 episodes per person-year; adjusted incidence rate ratio [IRR] = 6.03, 95% confidence interval [CI] = 4.94–7.36, P < 0.0001) and more days of work or school lost due to diarrhea (4.1 versus 0.3 days per person-year, IRR = 15.35, 95% CI = 11.44–20.58, P < 0.0001) (adjusted for age, presence of SWS, person in household taking cotrimoxazole, presence of soap and toilet, and quarter of year). Persons with HIV with CD4 counts < 200 cells/mm$^3$ had more episodes of diarrhea than persons with CD4 counts ≥

Table 1: Baseline characteristics of water sources, handling, hygienic, and sanitation practices, and water contamination of intervention and comparison households.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention (n = 196)</th>
<th>Comparison (n = 196)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water source*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surface/shallow well</td>
<td>31 (16)</td>
<td>30 (15)</td>
<td>0.89</td>
</tr>
<tr>
<td>Spring</td>
<td>131 (50)</td>
<td>133 (50)</td>
<td>0.83</td>
</tr>
<tr>
<td>Borehole/tap</td>
<td>105 (53)</td>
<td>113 (46)</td>
<td>0.42</td>
</tr>
<tr>
<td>Water storage*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wide-mouth clay pot</td>
<td>172 (88)</td>
<td>176 (90)</td>
<td>0.52</td>
</tr>
<tr>
<td>Jerry can</td>
<td>21 (11)</td>
<td>18 (9)</td>
<td>0.61</td>
</tr>
<tr>
<td>Other</td>
<td>28 (15)</td>
<td>19 (10)</td>
<td>0.17</td>
</tr>
<tr>
<td>Water treatment*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>127 (65)</td>
<td>108 (55)</td>
<td>0.05</td>
</tr>
<tr>
<td>Boil</td>
<td>41 (21)</td>
<td>46 (24)</td>
<td>0.54</td>
</tr>
<tr>
<td>Sieve</td>
<td>28 (14)</td>
<td>48 (25)</td>
<td>0.01</td>
</tr>
<tr>
<td>Bleach</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hygiene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wash hands after defecation</td>
<td>146 (75)</td>
<td>128 (65)</td>
<td>0.07</td>
</tr>
<tr>
<td>Observed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soap in house</td>
<td>169 (86)</td>
<td>165 (84)</td>
<td>0.42</td>
</tr>
<tr>
<td>Water available for hand washing</td>
<td>17 (9)</td>
<td>8 (4)</td>
<td>0.06</td>
</tr>
<tr>
<td>Latrine</td>
<td>154 (79)</td>
<td>149 (76)</td>
<td>0.55</td>
</tr>
<tr>
<td>Feces in yard</td>
<td>102 (52)</td>
<td>116 (59)</td>
<td>0.16</td>
</tr>
<tr>
<td>Baseline water Escherichia coli count† (n = 71)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source water</td>
<td>22 [0–18,800]</td>
<td>0 [0–19,800]</td>
<td>0.08</td>
</tr>
<tr>
<td>Stored water</td>
<td>233 [0–40,000]</td>
<td>93 [0–40,000]</td>
<td>0.09</td>
</tr>
<tr>
<td>Water samples with contamination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline source water (n = 71)</td>
<td>27 (64)</td>
<td>13 (45)</td>
<td>0.10</td>
</tr>
<tr>
<td>Stored water (n = 71)</td>
<td>40 (95)</td>
<td>24 (83)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

* More than one response permitted, total may equal more than 100%.
† Median E. coli count in colony-forming units per 100 mL and range in brackets.
During the study, 936 (80%) episodes of diarrhea were observed, with Shigella species (4%) and E. coli (6%) being the most common. Among persons with HIV, SWS was associated with a 20% reduction in diarrhea episodes (IRR = 0.81, 95% CI = 0.75–0.87) and those 3–12 years old (IRR = 0.82, 95% CI = 0.71–0.94) experienced 26% fewer days with diarrhea (IRR = 0.74, 95% CI = 0.67–0.81). The SWS had no effect on hospitalizations and clinic visits among persons with HIV or HIV-negative family members.

**Stool pathogens**. During the study, 936 (80%) episodes of diarrhea were associated with stool specimens collected. Participants in the intervention group reported fewer stools with visible blood or mucus than the comparison group (28% versus 39%; P < 0.0001). The results were similar for persons with HIV (32% versus 42%; P = 0.0065) and HIV-negative family members (22% versus 36%; P = 0.0022). The proportion of different pathogens recovered from stool specimens collected from persons with HIV varied: hookworms (33%), Strongyloides stercoralis (15%), enterotoxigenic E. coli (14%), Aeromonas species (8%), enteropathogenic E. coli (7%), Shigella species (6%), Cryptosporidia parvum (6%), Salmonella species (3%), and Campylobacter species (4%). For persons with HIV, there was no difference in pathogens between the intervention group and comparison groups. Among HIV-negative family members, stool samples from participants in the intervention group had lower rates than the comparison group of hookworms (27% versus 40%; P = 0.0138) and Shigella species (1% versus 5%; P = 0.0292).

**Environmental and hygienic factors associated with diarrhea**. The first two quarters of the year, when compared with the last two quarters, were associated with more diarrhea episodes (January through March; relative risk [RR] = 1.41, 95% CI = 1.34–1.48, P < 0.0001). Days with diarrhea only among persons > 59 years old (IRR = 1.56, 95% CI = 1.32–1.84, P < 0.0001) and those 3–12 years old (IRR = 1.51, 95% CI = 1.31–1.75, P < 0.0001) had associated stool specimens collected. Participation in the intervention group was associated with fewer stools with visible blood or mucus compared with the comparison group (IRR = 0.59, 95% CI = 0.52–0.69, P < 0.0001). The SWS had no effect on hospitalizations and clinic visits among persons with HIV or HIV-negative family members.

**Table 2**

| Diarrhea episodes and days with diarrhea among persons with HIV and HIV-negative family members* |
|---------------------------------|--------|----------------|----------------|-----------------|
| **Intervention group** | **Comparison group** | **Intervention group** | **Comparison group** | **Intervention group** | **Comparison group** | **Intervention group** | **Comparison group** | **Intervention group** | **Comparison group** | **Intervention group** | **Comparison group** |
| | No. | PYO | Crude rate | | No. | PYO | Crude rate | | No. | PYO | Crude rate | | No. | PYO | Crude rate | | No. | PYO | Crude rate | |
| **Diarrhea episodes** | | | | | | | | | | | | | | | | | | | | |
| All participants | 488 | 1,077.4 | 0.45 | 652 | 1,176.5 | 0.55 | 0.82 (0.73–0.92) | 0.80 (0.64–1.00) | 0.047 |
| HIV-positive | | | | | | | | | | | | | | | | | | | | |
| Overall | 306 | 271 | 1.12 | 412 | 305 | 1.35 | 0.83 (0.72–0.96) | 0.75 (0.59–0.94) | 0.015 |
| ≥ 5 years old | 268 | 255 | 1.05 | 387 | 292 | 1.33 | 0.79 (0.68–0.93) | 0.79 (0.62–0.98) | 0.046 |
| < 5 years old | 36 | 16 | 2.32 | 25 | 13 | 1.93 | 1.20 (0.72–2.00) | 0.70 (0.23–1.10) | 0.525 |
| HIV-negative | | | | | | | | | | | | | | | | | | | | |
| Overall | 184 | 806 | 0.23 | 240 | 872 | 0.28 | 0.83 (0.68–1.00) | 0.84 (0.58–1.22) | 0.355 |
| < 3 years old | 80 | 69 | 1.16 | 80 | 76 | 1.05 | 1.11 (0.81–1.51) | 0.90 (0.51–1.59) | 0.722 |
| 3–12 years old | 60 | 448 | 0.13 | 105 | 468 | 0.22 | 0.60 (0.44–0.82) | 0.60 (0.38–0.94) | 0.025 |
| ≥ 59 years old | 36 | 252 | 0.14 | 36 | 292 | 0.12 | 1.16 (0.73–1.84) | 1.15 (0.57–2.33) | 0.692 |
| Days with diarrhea | | | | | | | | | | | | | | | | | | | | |
| All participants | 2,859 | 1,077.3 | 2.7 | 4,002 | 1,176.3 | 3.4 | 0.78 (0.74–0.82) | 0.74 (0.54–1.01) | 0.055 |
| HIV-positive | | | | | | | | | | | | | | | | | | | | |
| Overall | 1,863 | 270.6 | 6.9 | 2,785 | 304.8 | 9.1 | 0.75 (0.71–0.80) | 0.67 (0.48–0.84) | 0.001 |
| ≥ 5 years old | 1,637 | 255.1 | 6.4 | 2,652 | 292.0 | 9.1 | 0.71 (0.66–0.75) | 0.71 (0.51–0.99) | 0.044 |
| < 5 years old | 226 | 15.6 | 14.5 | 133 | 12.9 | 10.0 | 1.41 (1.14–1.75) | 0.83 (0.21–3.37) | 0.797 |
| HIV-negative | | | | | | | | | | | | | | | | | | | | |
| Overall | 996 | 806.7 | 1.2 | 1,217 | 871.5 | 1.4 | 0.88 (0.81–0.96) | 0.88 (0.54–1.43) | 0.602 |
| < 3 years old | 483 | 68.8 | 7.0 | 498 | 76.2 | 6.5 | 1.07 (0.95–1.21) | 0.82 (0.38–1.80) | 0.626 |
| 3–12 years old | 234 | 417.6 | 0.6 | 434 | 438.6 | 1.0 | 0.66 (0.57–0.76) | 0.67 (0.40–1.15) | 0.146 |
| ≥ 59 years old | 179 | 251.9 | 0.7 | 128 | 292.1 | 0.4 | 1.62 (1.29–2.04) | 1.58 (0.74–3.38) | 0.242 |

* HIV = human immunodeficiency virus; PYO = person-years of observation; CI = confidence interval.
† Multivariate analysis adjusted for age group, sex, quarter of year, cotrimoxazole use, water quality, presence of latrine in the compound, presence of soap at home, and household wealth for all participants. For persons with HIV, adjustments were made for age group, sex, CD4 cell count, quarter of year, cotrimoxazole use, water quality, presence of latrine in the compound, presence of soap at home, and household wealth.
‡ P values of adjusted incidence rate ratio.
SAFE WATER SYSTEM FOR DIARRHEA PREVENTION IN PERSONS WITH HIV

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TABLE 3

<table>
<thead>
<tr>
<th>Stored water quality among households at baseline and during follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td>--------------------</td>
</tr>
<tr>
<td><strong>Households with <em>Escherichia coli</em> contamination in stored water</strong></td>
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<tr>
<td>Baseline</td>
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<tr>
<td>October 2001</td>
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<tr>
<td>October 2002</td>
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<td><strong>Stored water <em>E. coli</em> contamination</strong>†‡</td>
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<td>Baseline</td>
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<tr>
<td>October 2001†</td>
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<td>October 2002</td>
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* Median *E. coli* count in colony-forming units per 100 mL (mean [range]).
† Stored water samples from the intervention households collected in October 2002 did not have any *E. coli* contamination.
‡ Stored water samples from the intervention households collected in October 2001.

95% CI = 1.13–1.76, P = 0.002 and April through June; RR = 1.24, 95% CI = 1.02–1.51, P = 0.032. Among persons with HIV, the presence of a latrine in a compound, compared with those without a latrine, was associated with fewer episodes of diarrhea, (IRR = 0.69, 95% CI = 0.53–0.91, P = 0.009), fewer days with diarrhea, (IRR = 0.63, 95% CI = 0.40–1.00, P = 0.048), and fewer days of work or school lost due to diarrhea (IRR = 0.63, 95% CI = 0.41–0.97, P = 0.038). Among persons with HIV, the presence of soap in the house was also associated with fewer days with diarrhea, (IRR = 0.58, 95% CI = 0.35–0.97, P = 0.038), and fewer days of work or school lost due to diarrhea (IRR = 0.56, 95% CI = 0.34–0.93, P = 0.024), but not episodes of diarrhea (IRR = 0.79, 95% CI = 0.60–1.07, P = 0.134). The presence of a latrine or soap were not associated with significant reductions in diarrhea episodes, days of diarrhea, or days of work or school lost due diarrhea among HIV-negative family members.

**Association between diarrhea, HIV viral load, and SWS.** Each diarrhea episode was associated with a 0.12 logₐ₁₀ copies/mL per year increase in viral load (95% CI = 0.01–0.23, P = 0.037). The HIV viral load increased by 0.40 logₐ₁₀ per person-year for persons with HIV using SWS compared with 0.71 logₐ₁₀ per person-year for those not using SWS (adjusted mean pairwise difference = -0.14 logₐ₁₀ per person-year, 95% CI = -0.55 to 0.27, P = 0.510).

**Water testing.** During repeat water testing in October 2001, only stored household water samples from the comparison arm households had *E. coli* contamination. In October 2002, more samples from households of the comparison arm had *E. coli* contamination than the intervention arm. However, the median *E. coli* counts of the contaminated water samples evaluated in October 2002 did not differ by arm (P = 0.308) (Table 3).

**Water, hygiene, and sanitation.** The use of water sources with better water quality increased during the follow-up, e.g., in the intervention households the use of boreholes increased from 46% to 61% (P = 0.005) and in comparison households from 42% to 65% (P < 0.0001). Hand washing also increased in intervention (from 74.9% to 90.4%; P < 0.0001) and comparison households (from 65% to 80.1%; P = 0.002).

**DISCUSSION**

A simple, household-based, water purification and safe storage system used by persons with HIV was associated with 25% fewer episodes of diarrhea, 33% fewer days with diarrhea, and 24% fewer episodes of diarrhea with blood or mucus in stool. This is the first study to examine the impact of a safe drinking water intervention on diarrhea among persons with HIV in the less industrialized world. The results occurred even though participants had a high degree of access to uncontaminated water sources at baseline, and access to better quality water and hygienic practices increased during the study. The magnitude of diarrhea risk reduction was comparable to findings of studies of the health impact of SWS in other populations. Since there was no interaction between cotrimoxazole and the effect of SWS on diarrhea, the effects of SWS and cotrimoxazole on diarrhea were complementary.

Among HIV-negative family members, the SWS was effective only among certain age groups, i.e., children 3–12 years old and adults > 59 years old, but not in other age groups. These findings are consistent with previous studies that have shown similar reductions in these age groups. It may be that the effect of SWS was restricted to those persons most likely to be at home during the day and able to access the intervention (children and adults > 59 years old). The SWS may have been effective among adults with HIV between 13 and 59 years of age because they were more likely to be at home due to illness and a decreased ability to work. This added benefit for some family members improves the cost-effectiveness of the intervention. Among children with HIV less than five years of age, the SWS was associated with a non-significant 30% reduction in diarrhea episodes. This was likely due to limited power because only 27 children with HIV participated in the study.

In this cohort, source water quality was relatively good and improved over the course of the study. The beneficial effect of the SWS may be greater in populations with more fecal contamination of drinking water. In addition, although water stored in the home is at risk of contamination, this risk may have been reduced in the study by good hygienic practices and a high degree of access to soap and toilet facilities, all of which lower the burden of pathogens in the household environment. Hand washing and access to latrines have been associated with reduced risk of diarrhea. The association of soap and latrines with reduced risk and severity of diarrhea in persons with HIV support these findings. Weekly home visits may have influenced adherence to the SWS and improved hygiene practices. Although the effect of health education on sanitation and hygiene practices would likely be similar across both study arms, the effectiveness of the SWS during large-scale programmatic implementation might be less than what
was seen in this study because of lower adherence rates in a less intensive intervention.

Diarrhea is common in persons with HIV and in this study was associated with increased HIV viral load. Although this has not been previously examined, other studies have shown associations between opportunistic infections, viral load, and HIV disease progression.\textsuperscript{21–25} Interventions such as SWS that prevent diarrhea could potentially slow down the progression of HIV disease, although this study did not have sufficient power to address this question.

Point-of-use water quality interventions, such as the SWS, are the most cost-effective water interventions currently available.\textsuperscript{26} The cost per family for locally produced sodium hypochlorite solution is less than $0.01 per day, and the initial cost of buying the water vessel is approximately $3. This excludes costs to families of transport to obtain a vessel and chlorine or to the healthcare system for distribution, which were provided by the study infrastructure.

The results of this study support the statement by Lee Jongwook, the Director-General of the World Health Organization, that “successful treatment [of HIV] depends on safe water . . . .”\textsuperscript{27} Simple, inexpensive interventions such as the SWS and cotrimoxazole prophylaxis should be considered as components of a basic care package provided to all persons with HIV in resource-poor settings. The SWS might be especially useful in settings where diarrhea is common and drinking water quality is poor.

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