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John M. Colford

Timothy J. Wade

Sukhminder K. Sandhu

Catherine C. Wright

Sherline Lee

See next page for additional authors

Authors

John M. Colford, Timothy J. Wade, Sukhminder K. Sandhu, Catherine C. Wright, Sherline Lee, Susan Shaw, Kim Fox, Susan Burns, Anne Benker, M. Alan Brookhart, Mark van der Laan, and Deborah A. Levy

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A Randomized, Controlled Trial of In-Home Drinking Water Intervention to Reduce Gastrointestinal Illness

John M. Colford, Jr.[1], Timothy J. Wade[1,2], Sukhminder K. Sandhu[1,3], Catherine C. Wright[1], Sherline Lee[3], Susan Shaw[4], Kim Fox[5], Susan Burns[6], Anne Benker[6], M. Alan Brookhart[1,7], Mark van der Laan[7], and Deborah A. Levy[3]

[1] Centers for Occupational and Environmental Health and Family and Community Health, University of California, Berkeley, School of Public Health, Berkeley, CA.
[2] National Health and Environmental Effects Research Laboratory, US Environmental Protection Agency, Chapel Hill, NC.
[3] Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, GA.
[4] Office of Groundwater and Drinking Water, US Environmental Protection Agency, Washington, DC.
[5] US Environmental Protection Agency National Homeland Security Research Center, Cincinnati, OH.
[6] University of California, Berkeley Survey Research Center, Berkeley, CA.
[7] Division of Biostatistics, University of California, Berkeley, School of Public Health, Berkeley, CA.

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Trials have provided conflicting estimates of the risk of gastrointestinal illness attributable to tap water. To estimate this risk in an Iowa community with a well-run water utility with microbiologically challenged source water, the authors of this 2000–2002 study randomly assigned blinded volunteers to use externally identical devices (active device: 227 households with 646 persons; sham device: 229 households with 650 persons) for 6 months (cycle A). Each group then switched to the opposite device for 6 months (cycle B). The active device contained a 1-μm absolute ceramic filter and used ultraviolet light. Episodes of "highly credible gastrointestinal illness," a published measure of diarrhea, nausea, vomiting, and abdominal cramps, were recorded. Water usage was recorded with personal diaries and an electronic totalizer. The numbers of episodes in cycle A among the active and sham device groups were 707 and 672, respectively; in cycle B, the numbers of episodes were 516 and 476, respectively. In a log-linear generalized estimating equations model using intention-to-treat analysis, the relative rate of highly credible gastrointestinal illness (sham vs. active) for the entire trial was 0.98 (95% confidence interval: 0.86, 1.10). No reduction in gastrointestinal illness was detected after in-home use of a device designed to be highly effective in removing microorganisms from water.

drinking; epidemiologic studies; gastrointestinal diseases; intervention studies; randomized controlled trials; water; water supply

Abbreviations: CDC, Centers for Disease Control and Prevention; CI, confidence interval; EPA, US Environmental Protection Agency; HCGI, highly credible gastrointestinal illness.

Although infectious disease outbreaks can result from mistakes in the management of drinking water systems, there are questions regarding the extent to which such illness can be attributed to drinking water in systems that operate properly (1, 2). Previous drinking water trials produced conflicting results (3–6). In 1996, the US Congress amended the Safe Drinking Water Act (7). One of the Act's provisions that focuses on the above uncertainties (Section 1458 (d) (1)) required the Centers for Disease Control and Prevention (CDC) and the US Environmental Protection Agency (EPA) to conduct studies on waterborne disease occurrence and to provide a national estimate of waterborne disease. After a lengthy public discussion and planning process (8, 9), the CDC and the EPA funded a pilot and a large-scale drinking water trial as well as several smaller studies to estimate the risk of illness from using municipal tap water.

Correspondence to Dr. John M. Colford, Jr., University of California, Berkeley, School of Public Health, Division of Epidemiology and Public Health Biology, 140 Warren Hall #7360, Berkeley, CA 94720 (e-mail: jcolford@socrates.berkeley.edu).

We report here the results of the Water Evaluation Trial, a full-scale trial designed after a pilot trial was completed (6). This full-scale trial was a randomized, controlled, triple-blinded, crossover intervention study performed in Davenport, Iowa, and its surrounding communities along the Mississippi River. The principal objective was to measure the change in the incidence of gastrointestinal illness from use of supplemental in-home drinking water treatment by a healthy population consuming tap water. This tap water was supplied by a municipal system using conventional treatment methods to purify microbiologically contaminated river water while maintaining the system to meet all current US regulatory standards.

MATERIALS AND METHODS

The study and the informed consent process were reviewed, approved, and monitored by institutional review boards at the University of California, Berkeley; the CDC; the EPA; the state of California; and Public Health Foundation Enterprises of Los Angeles, California.

Active and sham water treatment devices and installation

Point-of-use devices for the trial were solicited in a national bid with more than 20 respondents and were selected to maximize microbial disinfection while minimizing effects on taste and chemical properties. On the basis of our experience in the pilot study (6), countertop units were chosen to minimize difficulties with installation and use.

We selected 1-μm filtration and ultraviolet treatment to reduce potential microbial contamination with minimal effect on taste and other qualities of the water. Unlike reverse osmosis devices and devices that use carbon filtration, the device that was used does not change the chemical composition of the water. This characteristic was desirable to maintain participant blinding.

The device selected was designed and manufactured by a firm selling similar devices in domestic and international markets. The active device consisted of a 1-μm ceramic prefilter and ultraviolet treatment with an output of 35,000–38,000 μW-second/cm^2. Except for replacement of the pressed activated carbon block filter with a ceramic 1-μm filter (to avoid noticeable changes in the water's taste and odor usually associated with the use of carbon filters), the device is identical to a commercially available model (class A) certified by the National Sanitary Foundation (model E-8301J; Amway Access Business Group, Ada, Michigan), used extensively in Asia. The installed devices were rectangular, with approximate dimensions of 5 1/2 (13.34 cm) inches wide by 8 inches (20.32 cm) long by 11 1/2 inches (29.21 cm) high. A diverter was attached to the faucet and was connected to the device. The diverter could be set to receive water through the treatment device (treated water) or directly through the kitchen faucet (untreated water).

Sham devices were identical to active devices in every respect but had an empty filter chamber, and the ultraviolet bulb was surrounded by an ultraviolet absorbing glass sleeve instead of the quartz sleeve present in the active devices. This sleeve effectively blocks transmission of radiation while providing the same light and heat associated with ultraviolet lamps surrounded by the quartz sleeve.

Study area

Several criteria were used to select the site: the community had to receive drinking water from one microbiologically challenged (i.e., with known upstream-contaminated discharges containing human waste) surface water (river) source; the source water had to be treated at one water treatment plant; the water had to be treated by conventional drinking water treatment methods to meet all US microbial regulatory standards (10–12); and the community had to be large enough so that we could recruit 400 households for a study (estimated to be about 100,000 households based on participation rates in prior trials) (3–6). An additional consideration was the willingness of the utility to provide data on treatment performance. The source water for the study site was one of the most contaminated of among 300 systems on which pathogen data were available (13).

Finding a study site that could provide useful data as one piece of information in the development of a national estimate of disease occurrence was a key concern in developing and weighing the importance of the different selection criteria. The goal was to select a system "typical" of the type that serves a large percentage of the US population (e.g., a large system that complies with drinking water regulations), and, recognizing that an affordable-size study would be able to detect only a large fraction of illness, such as measured in prior Canadian studies (3, 4), it was important that the system be subject to a high level of microbial risk (i.e., a system with extremely challenged source water). Other studies conducted at other sites in the United States with different water treatment characteristics would be needed to fully estimate a national attributable risk.

Numerous municipalities were considered by the CDC, the EPA, and our team. Ultimately, the Davenport/Bettendorf area of Scott County, Iowa, best fulfilled these criteria. The trial was performed in the cities of Davenport and Bettendorf and the associated neighboring communities of Panorama Park and Riverdale, all located in Scott County, Iowa, and served by the Iowa American Water Company.

Municipal water supply and treatment

The residents in the study area received their municipal water from a single source, the Mississippi River, which is treated at a single plant. Extensive monitoring for pathogens and indicators of fecal contamination conducted by the local water utility from 1990 to 1998 indicated that the Mississippi River at Davenport was a challenged source with evidence of human fecal contamination (14). Sampling during the time of the trial showed similar levels (data available on request from the authors). Finished water consistently met all state and federal standards for the year prior to the trial and during the trial. The utility is also one of a select group of utilities that have received the Directors' Award from the Partnership for SafeWater (an organization founded by EPA, state regulators, and the drinking water industry) for their efforts to

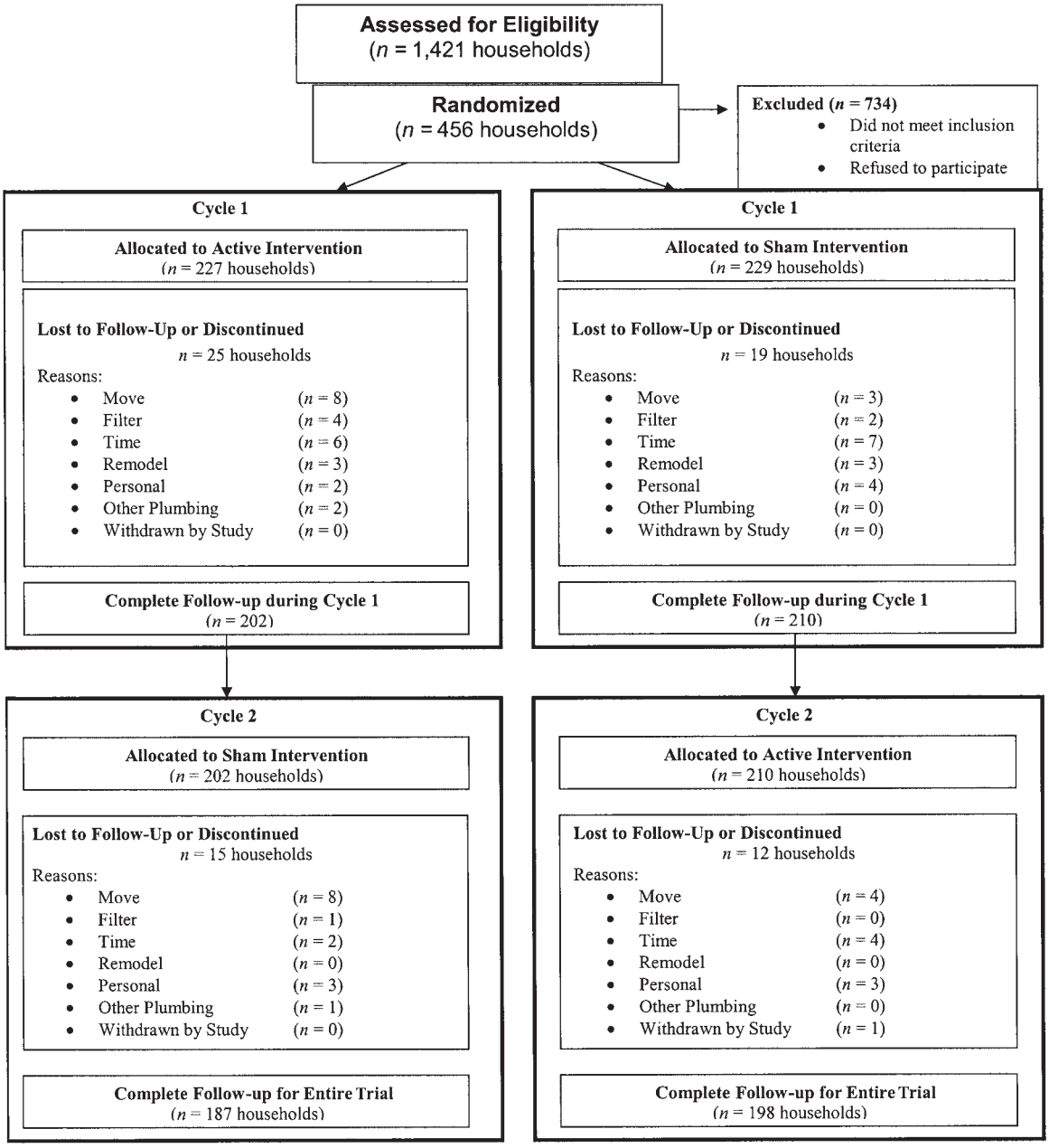

FIGURE 1. Flow chart of the random assignment, crossover, and completion of 456 households enrolled in a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002.

produce water that exceeds current regulatory filtration performance standards (15, 16).

The water utility uses "conventional" treatment consisting of coagulation, flocculation, sedimentation, filtration through granular activated carbon/sand filters, and chlorination. Granular activated carbon is used as a combination filtration/adsorption medium to remove organics and to treat objectionable tastes and odors (refer to the following website: www.iawater.com). Treatment performance and management of the distribution system during the intervention trial period are discussed in detail in a separate report (17).

Recruitment and enrollment

Recruitment began on October 16, 2000. The eligible population consisted of households served by the Iowa

TABLE 1. Baseline characteristics of 1,296 participants enrolled in the Water Evaluation Trial, a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002

Characteristic	Active-device group (n = 646)		Sham-device group (n = 650)	
	No. of persons	%	No. of persons	%
Gender (% male)	320	50	324	50
Currently in school	215	33	242	37
Currently working	342	53	345	53
No. of persons in the household				
1	26	11	30	13
2	88	39	87	38
3	42	19	46	20
4	46	20	38	17
5	17	7	17	7
6	7	3	9	4
7–9	1	0.4	2	0.9
Self-reported health				
Excellent	224	35	230	35
Very good	255	39	253	39
Good	135	21	137	21
Fair	28	4	22	3
Poor	3	0.5	5	1
Missing	1	0.2	3	0.5
History of heartburn	72	11	85	13
History of diverticulitis	14	2	15	2
Irritable bowel syndrome	30	5	34	5
History of cramps				
Frequently	23	4	27	4
Occasionally	326	50	351	54
Never	294	46	267	41
Missing	3	0.5	5	1
History of diarrhea				
Frequently	17	3	22	3
Occasionally	335	52	369	57
Never	293	45	255	39
Missing	1	0.2	4	1
History of nausea				
Frequently	10	2	7	1
Occasionally	294	46	321	49
Never	336	52	317	49
Missing	6	1	5	1
History of vomiting				
Frequently	4	1	3	0.5
Occasionally	241	37	246	38
Never	400	62	398	61
Missing	1	0.2	3	0.5
Fever				
Frequently	4	1	2	0.3
Occasionally	332	51	349	54
Never	305	47	294	45
Missing	5	1	5	1
Any current medication use	266	41	279	43
Pregnant at enrollment	5	2	5	2
Self-estimated total daily water consumption*				
0	14	2	9	1
<1	5	1	5	1
1–5	335	52	315	48
6–10	232	36	245	38
11–15	35	5	26	4
16–20	5	1	2	0.3
>20	2	0.3	3	0.5
Missing	18	3	45	7
Self-estimated daily water consumption* (home only)				
0	20	3	22	3
<1	15	2	11	2
1–5	409	63	397	61
6–10	151	23	152	23
11–15	18	3	10	2
16–20	1	0.2	1	0.25
>20	1	0.2	1	0.2
Missing	31	5	56	9
Self-estimated daily bottled water consumption*				
0	505	78	513	79
<1	31	5	23	4
1–5	63	10	54	8
6–10	6	1	5	1
11–15	0	0	0	0
16–20	0	0	0	0
>20	1	0.2	1	0.2
Missing	40	6	54	8

Table continues

* Number of 8-ounce (240-ml) glasses.

American Water Company in the communities of Davenport, Bettendorf, Riverdale, and Panorama Park. Apartments were excluded because of concern that their water may not be representative of the water in the community because of the potentially increased risk of plumbing cross-connections within apartment buildings. The water utility provided a list of all 40,403 residential service addresses. Of these, 2,050 addresses with post office boxes (likely to be businesses or apartments), out-of-service addresses, addresses outside the study area, and apartment numbers were excluded. Solicitations for enrollment were sent to the remaining 38,353 addresses in randomly selected blocks, taking a proportionate number of addresses from each ZIP Code between October 16, 2000, and January 25, 2001.

TABLE 2. Daily average water consumption* by participants enrolled in the Water Evaluation Trial, a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002

	Active device					Sham device					*p* value†
	Minimum	25% IQR‡	Median	75% IQR	Maximum	Minimum	25% IQR	Median	75% IQR	Maximum	
Cycle 1	0	5.1	9.4	17.9	75.7	0	5.5	8.5	16.2	57.8	0.34
Cycle 2	0	3.0	6.4	11.5	47.2	0	2.1	6.0	11.5	46.8	0.69

* Number of 8-ounce (240-ml) glasses per day as measured by an electronic totalizer.
† *p* value for a two-sided *t* test comparing sham- with active-device water usage during each cycle of the study.
‡ IQR, interquartile range.

The mailing provided information about the study, with a toll-free telephone number and a postcard. Households were excluded if they contained an employee of the Iowa American Water Company, had an address outside the local utility water service area, consumed less than 75 percent of their in-home drinking water from the tap, contained an immunocompromised person (including one with human immunodeficiency virus or active cancer under treatment), or included any member who had been advised by a physician to drink only bottled or specially treated water.

For each participant, the entire trial was 54 weeks long (26 weeks during cycle A, a 2-week washout period, and 26 weeks during cycle B). During the washout period, participants used no device but continued to complete health diaries. The length of the washout period was chosen to be longer than the symptomatic period of most likely infectious causes of gastrointestinal illness (18). Enrollment was completed on May 30, 2001, with a final enrollment of 456 households and 1,296 individual persons.

Randomization and (triple) blinding

Households were randomly assigned by block in blocks of 14 with equal probability to receive either an active or a sham device. A randomized list of device assignment codes was prepared by an unblinded staff member not involved with installation or analysis and was sent to the manufacturer. Device assignments were hidden from the investigators and installers, the study subjects, and the data analysts. All analyses were conducted by using a noninformative code for device type. Investigators remained blinded to household assignment until after all analyses were completed and finalized and the first draft of this manuscript had been written and circulated. Households contacted the research center or returned postcards to participate. After consent forms were returned, randomly assigned devices were allocated from an offsite list.

Health outcomes

Adult household members recorded daily occurrences of illness in their health diaries. An adult member recorded responses for children under age 12 years. The principal health outcome measured was episodes of "highly credible gastrointestinal illness" (HCGI), a previously published measure (3–6). A new episode was defined as any of the following four conditions, preceded by at least six HCGI-free days: 1) vomiting, 2) watery diarrhea, 3) soft diarrhea and abdominal cramps, or 4) nausea and abdominal cramps. The requirement for six disease-free days between episodes was used to increase the likelihood that separate episodes truly represented distinct infections (rather than a prolonged course of one infection) (3–6).

Statistical methods

Blinding Index. Blinding was measured by using the "Blinding Index" of James et al. (19). Full details on its use in a drinking water intervention trial were reported in the pilot study (6).

Analysis of HGCI. The primary statistical analysis presented in this paper evaluated the effect of in-home water treatment on two individual-level outcomes: counts of the numbers of episodes of HCGI (the primary outcome of the study) and counts of the days (a prespecified secondary outcome) during each treatment cycle. We denote the outcome as $Y_{i,j}$, the number of person-years of observation time as $T_{i,j}$, and $a_{i,j}$ as the treatment assignment for the ith individual during the jth cycle. The treatment variable $a_{i,j} = 0$ if the individual was in a household receiving the active device during the jth cycle; otherwise, $a_{i,j} = 1$. For the initial 6-month observation period (cycle A), we let $j = 0$, while, after the crossover, $j = 1$.

To estimate a treatment effect that can take into account both a cycle effect (before vs. after crossover) and a treatment-by-cycle interaction, we fit a log-linear generalized estimating equation model (20). This statistical model is appropriate for correlated count outcomes that may exhibit extra-Poisson variability. Using this approach, we modeled the log of the mean incidence rate for each individual measurement as follows: $\log E(Y_{i,j}) = \beta_0 + \log T_{i,j} + \beta_1 j + \beta_2 a_{i,j} + \beta_3 j a_{i,j}$.

Here, β_1 is the period effect, β_2 is the effect of drinking untreated tap water, and β_3 is a treatment-cycle interaction. The parameter estimates are interpreted as being the change in a marginal log rate. For example, the parameter $\exp(\beta_2)$ can be interpreted as the ratio of the average rate of illness for an individual from an untreated household to the average rate of illness for an individual from a treated household during the first cycle. The effect of drinking untreated water during the second cycle is given by $\exp(\beta_2 + \beta_3)$. For maximal statistical efficiency, we used a

TABLE 3. Blinding, by device type, of participants enrolled in the Water Evaluation Trial, a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002

Cycle, month, and guess	Active device		Sham device		Overall		Blinding Index (entire cycle)	95% confidence interval
	No.	%	No.	%	No.	%		
Cycle 1								
First month								
Active device	140	31	122	28	262	29		
Sham device	43	9	64	14	107	12		
Don't know	271	60	258	58	529	59	0.77	0.74, 0.80
Last month								
Active device	117	27	95	23	212	25		
Sham device	44	10	41	10	85	10		
Don't know	278	63	275	67	553	65	0.82	0.79, 0.85
Cycle 2								
First month								
Active device	49	13	39	10	88	12		
Sham device	56	15	70	19	126	17		
Don't know	272	72	265	71	537	71	0.84	0.82, 0.87
Last month								
Active device	50	14	32	9	82	11		
Sham device	39	11	64	17	103	14		
Don't know	271	75	278	74	549	75	0.85	0.82, 0.87

working correlation matrix with a structure that accounted for both within-subject and within-household correlation. The standard errors of the parameter estimates are computed robustly and are asymptotically valid when the empirical variance-covariance matrix is used (20). Diggle et al. (21) illustrated the use of the generalized estimating equation approach to analyze data from a crossover trial with a dichotomous outcome.

Data (prior to dropout) from households that dropped out of the trial at any point after randomization were retained (intention-to-treat analysis).

Water consumption (exposure measurement)

Water consumption (i.e., the degree of exposure to the intervention) was measured in two ways. First, self-reported data were collected from participants by using questions inserted into the health diary at 2-week intervals. Participants estimated (in numbers of 8-ounce (240-ml) glasses) their daily consumption of drinking water at home (separately through the study device and through all other sources at home) and outside the home. Additionally, an electronic flow meter (a totalizer) had been installed in each device to measure the amount consumed and the time at which water was used.

Participants were provided with water bottles and were encouraged to carry water from the home device when outside the home. Mean water consumption was compared by study group using the two-sample *t* test.

RESULTS

Recruitment, enrollment, withdrawals, and completion

As detailed in the flow chart shown in figure 1, we screened 1,421 households that responded to our request for participation. Of these, 687 (48 percent) were eligible. We enrolled 456 households (1,296 individual persons) to meet our goal of 400 households (estimated to enable us to detect a relative rate of 1.15 with 80 percent power). The overall completion rates for the entire study were 82 percent for those originally assigned randomly to the active device group and 86 percent for those originally assigned randomly to the sham device group, resulting in complete 1-year follow-up for 84 percent of those initially enrolled. The most frequent reasons given for dropping out are detailed in figure 1.

Baseline characteristics of participants and completeness of data collection

Random assignment appeared to be successful, and participants in the groups were well balanced at baseline with respect to numerous factors (table 1). The median age of participants in the active group was 33 years (interquartile range, 13–47 years); those in the sham group were a median age of 32 years (interquartile range, 13–49 years).

Water consumption (exposure) patterns during the trial

Participants estimated how many 8-ounce glasses of unheated bottled water (all types) they drank each day (data

TABLE 4. Episodes and days of illness, by device and cycle, for participants enrolled in the Water Evaluation Trial, a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002

Event	Cycle A		Cycle B	
	Active device	Sham device	Active device	Sham device
Episodes of illness				
Highly credible gastrointestinal illness	707	672	516	476
Diarrhea*	208	208	186	142
Watery diarrhea†	138	147	131	103
Vomiting	214	196	170	175
Any watery diarrhea	407	391	300	269
Soft diarrhea and cramps	154	136	94	88
Nausea and cramps	217	220	186	171
Days of illness				
Highly credible gastrointestinal illness	1,423	1,585	977	929
Diarrhea	381	508	283	215
Watery diarrhea	227	394	182	152
Vomiting	288	299	261	241
Any watery diarrhea	774	921	494	538
Soft diarrhea and cramps	281	227	128	121
Nausea and cramps	380	458	386	313
Measures of disease impact				
Days of work or school missed	221	209	269	239
Visited physician for gastrointestinal illness	20	12	9	14
Years at risk				
Person-years at risk for highly credible gastrointestinal illness	292.58	280.57	263.26	260.83
Person-years at risk for missing work or school	229.43	224.24	221.30	212.86

* Reported three or more instances of diarrhea during the day.
† Reported three or more instances of diarrhea and indicated that diarrhea was watery.

not shown). Water consumption between the two groups appeared similar with respect to the amount of bottled water or untreated tap water consumed at or away from home. An electronic totalizer in each of the devices recorded no significant difference between the two groups (table 2).

Effectiveness of blinding of participants

The data gathered during the first and last months of each of the two 6-month cycles are presented in table 3 and suggest that blinding was maintained throughout the trial. The Blinding Index (values greater than 0.50 are consistent with successful blinding (6, 19)) increased slightly from 0.77 in the first month to 0.85 by the 12th month.

Analysis of gastrointestinal illnesses

The principal outcome of the trial was episodes of HCGI. During cycle A, 707 episodes were reported by active-device participants, and 672 episodes were reported by sham-device participants (table 4). During cycle B, 516 and 476 episodes were reported in the active and sham device groups, respectively.

We also compared the groups with respect to differences in days of HCGI (table 4). Again, no significant differences between the groups were found.

We evaluated the risk of HCGI episodes for the active-device group versus the sham-device group (the a priori study goal) during the entire study by using the generalized estimating equation model described above. In addition to the full model, we examined models without the interaction term and with only the device term (table 5). The full model suggested no device effect nor any cycle-by-device interaction, indicating that the device yielded no reduction in the relative rate of HCGI for either cycle A or cycle B. The final model provided a relative rate estimate (sham-device vs. active-device group) of 0.98 (95 percent confidence interval (CI): 0.86, 1.10). Similar analyses were conducted with the outcome defined as days of HCGI and suggested no significant effect of the device (table 5).

Although our trial was randomized (which ideally will balance the distribution of known and unknown confounding factors across the two arms of the study), we also conducted

TABLE 5. Multivariate models for episodes and days of highly credible gastrointestinal illness using generalized estimating equations analysis for a sham vs. an active device among participants enrolled in the Water Evaluation Trial, a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002

Analysis	Model	Parameter	Relative rate	95% confidence interval	*p* value
Episodes of highly credible gastrointestinal illness	Interaction	Device (sham vs. active)	0.98	0.78, 1.22	0.83
		Cycle (B vs. A)	0.75	0.59, 0.97	0.03
		Cycle × device	1.00	0.64, 1.55	0.98
	No interaction	Device (sham vs. active)	0.98	0.87, 1.10	0.66
		Cycle (B vs. A)	0.75	0.67, 0.85	<0.001
	Device only	Device	0.98	0.86, 1.10	0.70
Days of highly credible gastrointestinal illness	Interaction	Device (sham vs. active)	1.11	0.78, 1.57	0.58
		Cycle (B vs. A)	0.66	0.48, 0.92	0.01
		Cycle × device	0.98	0.56, 1.71	0.94
	No interaction	Device (sham vs. active)	1.10	0.87, 1.38	0.44
		Cycle (B vs. A)			<0.001
	Device only	Device (sham vs. active)	1.10	0.86, 1.41	0.44
Episodes of highly credible gastrointestinal illness adjusted for additional covariates	Multivariate	Device	0.96	0.85, 1.08	0.47
		Cycle (B vs. A)	1.19	1.05, 1.35	<0.01
		Age (per year)	1.00	0.99, 1.00	0.14
		Total water consumption (per 8-ounce* glass)	1.01	1.00, 1.44	0.11
		Female vs. male gender	1.25	1.09, 1.44	<0.01
		Season (vs. spring)			
		Summer	1.93	1.63, 2.30	<0.01
		Fall	0.64	0.49, 0.84	<0.01
		Winter	2.48	2.12, 2.90	<0.01

* 8 ounces = 240 ml.

multivariate analyses to adjust for potential confounding by season, gender, water consumption, and age on the effect of the device on episodes of HCGI. The effect of the device remained unchanged (relative rate = 0.96, 95 percent CI: 0.85, 1.08) in these analyses. An additional model (not shown) adjusting for these same variables and for the proportion of water consumed outside the home (rather than for total water consumption) yielded no change in the conclusion about the effect of the device (relative rate = 0.96, 95 percent CI: 0.85, 1.08).

We also analyzed the correlation of outcomes within person and within household during the study. Within person, the correlation of HCGI was 0.68. Within household (within the same cycle), the correlation was 0.241. Within household (in a different cycle), the correlation was 0.239 for HCGI.

We investigated the possibility that the device effect might vary within different subgroups of age, gender, employment status, water consumption, and completeness of participation (table 6). In none of these analyses did we detect any significant differences.

Adverse events

Six deaths occurred (two while in the active-device group and four while in the sham-device group). Causes of death included one case each of suicide, cardiopulmonary arrest, cancer, myocardial infarction, pneumonia, and bacterial sepsis. Thirty hospitalizations were reported by participants during the trial (18 while in the active-device group and 12 while in the sham-device group). None of the deaths and none of the hospitalizations were believed to be trial related.

DISCUSSION

To our knowledge, this randomized trial of in-home drinking water intervention is the largest conducted in the United States and the first to measure exposure (i.e., device usage) electronically (prior studies relied exclusively on self-reported usage). Our results suggest no significant decrease in the incidence of gastrointestinal illness among immunocompetent persons from using an in-home drinking water treatment device with combined 1-μm filtration and ultraviolet light. A water treatment device with a 1-μm absolute filter is highly effective in removing *Giardia*, *Cryptosporidium*, and other similarly sized microorganisms that can cause gastrointestinal illness. Prior testing of the device's ultraviolet treatment unit demonstrated a 99.99 percent inactivation of viruses (22).

In 1991, Payment et al. (3) published the results of the first randomized, controlled drinking water intervention trial using reverse osmosis filtration in a system with a chal-

TABLE 6. Subgroup analyses of relative rate (sham vs. active device), using generalized estimating equations episodes, of highly credible gastrointestinal illness among participants enrolled in the Water Evaluation Trial, a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002

Subgroup	Adjusted relative rate	95% confidence interval
Time in study		
Weeks 1–18	1.01	0.87, 1.18
Weeks 19–36	0.94	0.79, 1.12
Weeks >36	0.98	0.82, 1.17
Water consumption (8-ounce* glasses per day)		
Low (0–2.08)	0.88	0.72, 1.08
Medium (2.09–3.54)	0.97	0.82, 1.16
High (>3.54)	1.00	0.85, 1.17
Gender		
Male	0.95	0.83, 1.08
Female	0.98	0.87, 1.09
Age (years)		
0–5	1.13	0.89, 1.43
6–20	0.87	0.72, 1.04
21–49	0.95	0.83, 1.08
>49	0.97	0.81, 1.17
Employment status		
Full-time job	1.00	0.82, 1.23
Part-time job	0.86	0.57, 1.28
None	0.91	0.69, 1.19

* 8 ounces = 240 ml.

lenged source water. Filters were installed in 299 households (including 1,206 individual persons), and another 307 households (1,202 individuals) were followed as controls (no device installed). During a 15-month period, these investigators concluded that 35 percent of the self-reported gastrointestinal illness was attributable to tap water.

Subsequently, Payment et al. (4) conducted a second drinking water trial that included treatment groups receiving regular tap water, tap water from a continuously purged tap, bottled treatment plant water, or purified bottled plant water in a system that met all Canadian and equivalent US water microbial treatment standards. This study, conducted in the same community as the first trial, concluded that 14–40 percent of gastrointestinal illness could be attributed to tap water, depending on the comparison group. Participants in the first study and in the two groups in the second study who did not receive bottled water were not blinded to their treatment assignments. Although bottled water recipients were not informed of their group assignment, 50 percent of those receiving bottled water from the treatment plant withdrew from the trial, citing taste and odor problems. No significant difference in gastrointestinal illness rates was observed between the two groups drinking bottled water. The only significant differences were observed between the bottled water and the tap water groups. The authors noted that it was possible that reporting of gastrointestinal illness could have been affected by this lack of blinding. In our study, there was strong evidence, measured by the Blinding Index, that participants were successfully blinded. In both Payment studies (3, 4), the source water was contaminated by sewage and other materials, similar to the setting in which our trial was conducted.

In a randomized, controlled, drinking water trial in Australia, Hellard et al. (5) reported no difference in the rates of illness between sham and active treatment groups. A sham device was used in the Australian trial to blind participants, as in our trial. In the Australian trial, the source water was reported to be of high quality, from protected catchments unaffected by human activity, which differs markedly from the challenged source (Mississippi River) water used in our study.

Recently, our group published results from a randomized, controlled trial in Walnut Creek, California, among households consuming water from a contaminated source that was conventionally treated to meet all US federal standards (6). This trial confirmed that blinding of participants could be maintained successfully during such a drinking water study. Although the point estimate of the effect in the pilot trial (relative rate = 1.32, 95 percent CI: 0.75, 2.33) was consistent with the point estimate reported in the prior Payment studies (3, 4), this study was not large enough to be likely to detect a statistically significant effect.

The primary health outcome was episodes of HCGI, chosen both because of its high sensitivity (any of several different symptoms constitute an episode) and because of its use in prior trials (3, 5, 6). In an effort to be specific about significant illness, we also measured days lost from work or school. We found no significant differences between the devices within either cycle or over the entire trial.

We measured as a secondary (but specified a priori) outcome total days of HCGI. This measure was intended to provide a sense of the burden of illness in the two groups. Again, no differences between the groups were found.

Using data on water usage from the device reported by participants, we found no difference between groups with respect to use of the device during either cycle of the trial. Analysis of the data from the electronic totalizer in each device supported this finding, which suggests that our findings are not attributable to differential exposure to the untreated municipal water.

We noted a decline in the frequency of HCGI episodes over time in both groups (figure 2) very similar to that reported by others (3, 5). Although HCGI does have a strong seasonal component (table 5), we hypothesize that the decline seen during cycle 2 (equal in both groups) is more likely due to a loss of enthusiasm for reporting illness. Half of the subjects were randomly assigned to the active device in cycle 1 and the other half to the inactive device, and the decline in reporting was equivalent in the two arms. We also noted a strong effect of cycle (table 5). Because of the two-period crossover study design, cycle effects were not likely to bias the principal relation between device and HCGI, and there is no evidence that they did bias this relation (table 5).

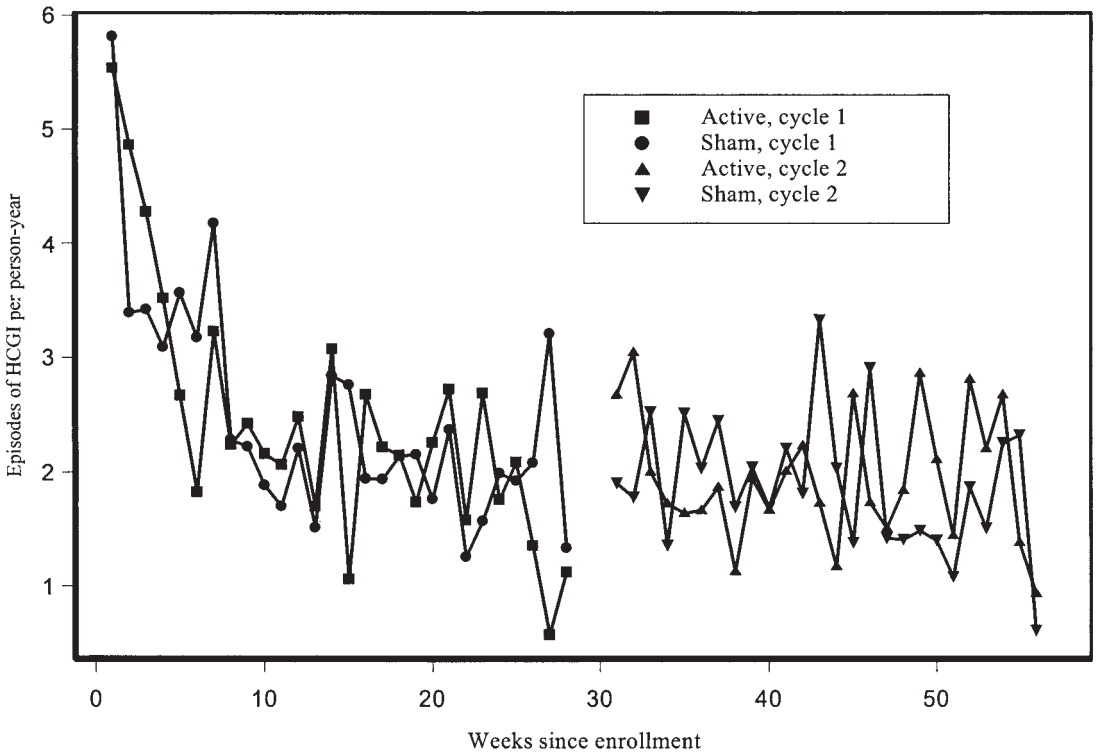

FIGURE 2. Weekly rates of "highly credible gastrointestinal illness (HCGI) after enrollment of 1,296 participants in a randomized controlled trial of an in-home drinking water intervention in Davenport, Iowa, and neighboring communities, October 2000–May 2002.

The correlation of HCGI within households was essentially identical both within the same cycle (0.241) and across the different cycles (0.239) of the study. This consistency across the different cycles (which could be detected with only a crossover design) suggests that secondary transmission is not as important within a household as are other factors related to gastrointestinal illness. If true, the presence of other factors associated with gastrointestinal illness within a family highlights the importance of random assignment of households in such studies.

We examined the possibility that the effect of the device might differ within important subgroups defined by age (prior studies had reported such differences (23)), length of participation, level of use of the device (i.e., a type of dose response), gender, or employment status. In none of these subgroup analyses was a significant effect detected (table 6).

We considered the possibility that the lack of an observed effect of the device may have been attributable to use of water outside the home. This possibility would have had the effect of attenuating any true effect the device may have had in reducing illness. We examined the device effect for only those subjects who reported that 90 percent or more of their water consumption was from the device (relative rate = 1.08, 95 percent CI: 0.85, 1.37), suggesting that the results were not likely explained by water consumption outside the home.

Our trial has limitations. It is possible that subjects in both groups, faced daily with the device, were reminded constantly about the study and altered their behavior or illness reporting in unknown ways so as to change their incidence of reporting of gastrointestinal illness (and thus drive the results toward a null effect). We have no data to evaluate this possibility. In future trials, a third, unblinded group of subjects with no device could be enrolled as an additional comparison group, but such data might be difficult to interpret because of a lack of blinding. It is possible that any true device effect was too small to be detected by the study. Since subjects drank water away from home and were exposed to pathogens in food, water, and other sources, it is possible that any reduction in the incidence of gastrointestinal illness attributable to the device could not be detected by the study because of its size. The confidence interval in the Australian trial indicated that less than 15 percent of gastrointestinal illness is likely caused by drinking water (5); this finding is very similar to our results suggesting that less than 11 percent of gastrointestinal illness is likely attributable to drinking water. Our study was not designed to address important questions about risk in immunocompromised persons. Studies suggest that human immunodeficiency virus-positive persons may be more susceptible to some waterborne infections during both outbreak situations and times without any known outbreak under way (24–27). Finally, because our study was conducted in a community with documented high standards of water quality treatment (refer to the Materials and Methods section), the generalizability of our results to other communities with different treatment efficiencies cannot be determined with our data.

Conclusion

We found no evidence that in-home drinking water treatment with combined filtration and ultraviolet light is effective in reducing the incidence of gastrointestinal illness in immunocompetent persons using water that exceeds regulatory standards. The results suggest that less than 11 percent of the gastrointestinal illnesses observed in a community with such standards can be attributed to the consumption of tap water among those who use tap water as their primary source of drinking water.

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