The Sonoma Water Evaluation Trial: A Randomized Drinking Water Intervention Trial to Reduce Gastrointestinal Illness in Older Adults

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Objectives. We estimated the relative rate of highly credible gastrointestinal illness (HCGI) per year associated with active versus sham household water filtration devices among older adults in a community receiving tap water meeting current US standards.

Methods. We conducted a randomized, triple-blinded, crossover trial in 714 households (988 individuals), which used active and sham water filtration devices for 6 months each. We estimated the annual incidence rate ratio of HCGI episodes and the longitudinal prevalence ratio of HCGI days at population and individual levels with a generalized estimating equation (GEE) and generalized linear mixed models (GLMMs), respectively, adjusted for covariates associated with outcome.

Results. The incidence rate ratios (active versus sham) were 0.88 (95% confidence interval [CI]=0.77, 1.00) and 0.85 (95% CI=0.76, 0.94) HCGI episodes per year estimated by GEE and GLMM models, respectively. The corresponding longitudinal prevalence ratios were 0.88 (95% CI=0.74, 1.05) and 0.84 (95% CI=0.78, 0.90) HCGI days per person per year.

Conclusions. We observed reductions in population- and individual-level measures of HCGI associated with use of the active filtration device. These findings suggest the need for further research on the impact of drinking water on the health of sensitive subpopulations. (*Am J Public Health.* 2009;99:1988–1995. doi:10.2105/AJPH.2008.153619)

Widespread outbreaks of gastrointestinal infectious illness have occurred in the United States at times when public water treatment systems have failed.[1,2] This has led to intense public interest in whether the microbial content of drinking water might present a health risk even when public water treatment systems are believed to be functioning properly.[3–5]

Several randomized intervention trials with supplemental in-home drinking water treatment have been reported in general populations[6–10]; none focused on older individuals. Estimates of the annual number of cases of acute gastrointestinal illness related to drinking water in the United States, drawn from a variety of data sources and study designs, vary from 1.8 million to 16.4 million cases per year in the general population.[11–13] The US Environmental Protection Agency has called attention to the differential burden of drinking water–related disease among those who may be at increased risk of infection and serious illness from exposure to microbial pathogens, such as the elderly, children, and persons who are immunocompromised by infection, malignancy, or chemotherapy.[14–16] Older adults may be particularly susceptible to gastrointestinal infections and to severe illness once infected.[17–19]

We conducted the first drinking water trial exclusively studying older adults (aged ≥55 years). The study, performed in Sonoma County, California, was a randomized, controlled, triple-blinded (participants, investigators, analysts), crossover intervention trial. Our goal was to estimate the efficacy of an in-home water filter to reduce the risk of highly credible gastrointestinal illness (HCGI) among older adults living in a community whose tap water met or exceeded current US drinking water standards.

METHODS

We used a type of water treatment device (a modified version of model E-8301J; Amway Access Business Group, Ada, Michigan) that was used and described in an earlier general population trial in Iowa.[10] The point-of-use countertop device was selected to provide maximum microbial disinfection while minimizing effects on taste and chemical properties. The active devices included 1-μm filtration and ultraviolet treatment. Water consumption from the device was measured by an internal, electronic flow meter (totalizer).

Study Area and Water Supply

We selected Sonoma County as the study site for several reasons. A cohort of older adults in the county was already participating in a longitudinal study of aging and physical performance supported by the National Institutes of Health. Sonoma County also met several important criteria: a large enough community to meet our overall recruitment goals, drinking water meeting all US microbial regulatory standards[20–22] through conventional treatment methods, and a community receiving drinking water from 1 source.

The residents in the study area receive their drinking water through several suppliers (local water districts), which receive water from the Sonoma County Water Agency (SCWA). Drinking water is obtained from the Russian River, which is fed by 3 primary reservoirs (Lake Sonoma, Lake Pillsbury, and Lake Mendocino). Collector wells built adjacent to the river extract water from its deep gravel underflow. A typical collector has a 13-foot-diameter concrete pipe extending 50 to 60 feet below the streambed surface. Perforated pipes

(horizontal wells) extend radially from the bottom of each concrete pipe into the aquifer. Each collector well houses 2 large electric pumps. Sand beds beneath the Russian River provide natural filtration. During late summer and fall, SCWA augments infiltration by diverting water directly from the river to infiltration ponds. SCWA treats collected water with chlorine disinfection and pH adjustment. An aqueduct system consisting of storage tanks, pipelines, booster (pump) stations, and emergency wells carries water to the local water districts for distribution (http://www.scwa.ca.gov).

Study Cohort

Recruitment began in August 2001. Households were eligible if they included 1 or more persons aged 55 years or older. Initially we recruited among an existing study cohort of persons aged 55 years and older within the city of Sonoma who were followed by researchers at the University of California, Berkeley, as part of a study of physical performance and age-related changes in Sonoma residents. We also recruited other residents in our target age range in areas served by the SCWA, including the City of Sonoma, Valley of the Moon, Oakmont, Glen Ellen, Cotati, Kenwood, Temelec, and Santa Rosa. Addresses and phone numbers of households with residents meeting our age criteria were purchased from a marketing firm. Both samples were recruited by random selection from countywide population sampling frames. Potential participants were sent mailers with information and a callback number or were called by study staff.

Interested households were excluded if they included an employee of the SCWA or any water district, included a household member who was unwilling to sign an informed consent form agreeing to have the water treatment device installed, consumed less than an estimated 75% of their in-home drinking water from the household tap, or included an immunocompromised individual (including persons with HIV or active cancer and transplant recipients).

Enrollment was completed in May 2005, with a total of 714 households and 988 individuals. Each participant was enrolled for 54 weeks (26 weeks during cycle 1, 26 weeks in cycle 2, and a 2-week washout period between cycles).

Households were block-randomized in blocks of 10, with an equal probability of receiving either a sham or an active device. The identical appearance of the active and sham devices and (assumed) identical taste of the water they produced were designed to ensure that participants remained unaware of the sequence of their device assignments. An unblinded author (C.W., who was not involved with the participants or data analysis after unblinding) generated a randomized list of device assignment codes, preassigned the devices to randomized households, sent device labels to the manufacturer, and provided interviewers and installers with the appropriate device number to install.

After consent forms were signed, the device was installed in the participant's home. All study staff involved in installation and contact with participants were blinded to device assignments throughout the trial. Finally, all analyses were conducted with a noninformative code for device type and household assignment, and the investigators and analysts remained blinded until after all coauthors had reviewed the first draft of this article.

Health Outcomes

Participants recorded daily occurrences of illness in health diaries, which they mailed to the field office once a month. Our primary efficacy outcome, also measured in previous similar studies, was episodes of HCGI.[6,8–10] A single episode of HGCI was defined as any of the following 4 conditions, preceded by at least 6 HCGI-free days: (1) vomiting, (2) watery diarrhea, (3) soft diarrhea and abdominal cramps, and (4) nausea and abdominal cramps. Requiring 6 disease-free days between episodes increased the likelihood that separate episodes represented distinct infections.

The daily longitudinal prevalence of HCGI, defined as the total days of illness divided by the total days in the study, was measured as our secondary efficacy outcome. We reported estimates and analyses from both episodes of HCGI and longitudinal prevalence in a manner analogous to other drinking water intervention trials.[10,23]

Statistical Methods

As suggested by Rees et al.,[24] participants were asked to guess their treatment assignment (active, sham, or don't know) at the start and end of both cycles. We assessed the possibility of unblinding by comparing sequence groups' beliefs (i.e., active–sham or sham–active) at the end of cycle 2 with the Fisher exact test.

We analyzed the intervention's effect on HCGI by modeling the incidence of new episodes of HCGI (primary outcome) and the longitudinal prevalence of HCGI (secondary outcome). The outcome was denoted as $Y_{i,j}$, the number of person-days of observation as $T_{i,j}$, and the treatment assignment as $a_{i,j}$ for the ith individual during the jth cycle. In the incidence models, $T_{i,j}$ only included days at risk; it did not include days during which an individual had illness or the 6 days following the conclusion of an episode. In the longitudinal prevalence models, $T_{i,j}$ included all person-days in cycle j. The treatment variable $a_{i,j}=1$ if individual i was in a household receiving the active device during the jth cycle, otherwise $a_{i,j}=0$. We let $j=1$ for the initial 6-month observation period (cycle 1), and $j=0$ after crossover (cycle 2).

We analyzed each outcome with 2 estimation strategies: a generalized estimating equations (GEE) approach, which provided a marginal, population-averaged inference, and a generalized linear mixed-model approach (GLMM), which provided an individual-specific inference.[25] We estimated the treatment effect on HCGI with a log-linear base specification model:

$$(1)\quad \log \mathrm{E}\left(\mathrm{Y}_{i,j}\right) - \log\left(T_{i,j}\right) = \beta_0 + \beta_1 a_{i,j};$$

on the annual scale $\exp(\beta_0)$ was the mean rate of HCGI per year on the sham arm, and $\exp(\beta_1)$ was the mean rate ratio of HCGI for the active versus the sham device. We settled on this model for our primary analysis after finding that the unadjusted interaction term was not statistically significant according to either the GEE analysis ($P=.47$) or the GLMM analysis ($P=.09$). We also reported results from multivariable models that included the main effects for cycle 1 baseline covariates that had strong univariate associations ($P<.20$) with the outcome because recent theoretical and simulation results indicated the potential of this approach to increase the estimators' efficiency.[26]

In the GEE approach, the device effect was interpreted as the rate ratio of HCGI between

a population using a water treatment device and a population using a sham device. We used an exchangeable working correlation structure to account for within-individual and within-household correlation and computed robust standard errors on the coefficient estimates.[27]

In the GLMM approach, we added random intercepts for individual and household to our base specification and assumed that the random intercepts were normally distributed with mean zero and finite variance. This model posited that there was natural heterogeneity among households and individuals in their sham-associated level of HCGI. Because the device effect was conditional on the individual random intercept, we interpreted it as the rate ratio of HCGI for an individual in the population.[25] We used Stata version 10 (StataCorp, College Station, TX) for all data management and analyses.[28]

Mislabeled Devices and Consumption Measurement

During a scheduled quality assurance review at the midpoint of the study, in October 2003, an unblinded author (C.W., who was involved with neither the participants nor data analysis) discovered that a batch of 180 devices had been mislabeled during the manufacturing process. Most of these devices had already been used in the study. This error resulted in 157 households receiving the same type of device during their entire time in the study, rather than receiving the appropriate crossover device after 6 months. After discussion with our National Institutes of Health Data Safety and Monitoring Board, we agreed to drop these 157 households from our primary analysis because they could not provide crossover data, an important design element in our study. To compensate for this loss of participants, we extended recruitment and enrollment for the study by 9 months. Quality assurance procedures were subsequently changed so that each batch of devices was checked by an unblinded staff member on the day of delivery from the manufacturer rather than after removal from the household at the study midpoint.

In the primary analyses, all data collected after randomization and prior to dropout were retained and analyzed according to each individual's assigned treatment, among only participants with properly labeled devices. In

TABLE 1—Sample Baseline Characteristics, by Initial Assignment (Active or Sham Water Treatment Device): Sonoma Water Evaluation Trial, Sonoma County, CA, 2001–2006

Characteristic	Active Device, No. (%)	Sham Device, No. (%)
Gender (% men)	171 (43.3)	160 (42.7)
Age at enrollment, y		
55–64	113 (28.6)	105 (28.0)
65–74	115 (29.1)	117 (31.2)
75–84	127 (32.2)	115 (30.7)
≥85	40 (10.1)	38 (10.1)
Employment status		
Full-time	55 (13.9)	51 (13.6)
Part-time	54 (13.7)	47 (12.5)
Unemployed	286 (72.4)	277 (73.9)
No. of persons in household		
1	173 (61.1)	174 (63.5)
2	108 (38.2)	99 (36.1)
3	2 (0.7)	1 (0.4)
Self-reported health		
Excellent	126 (31.9)	122 (32.5)
Good	211 (53.4)	203 (54.1)
Fair	51 (12.9)	42 (11.2)
Poor	7 (1.8)	8 (2.1)
Data missing	0 (0.0)	0 (0.0)
History of heartburn	108 (27.3)	88 (23.5)
History of diverticulitus	40 (10.1)	31 (8.3)
History of irritable bowel syndrome	36 (9.1)	49 (13.1)
Symptoms in past 2 wk		
Cramps	56 (14.2)	51 (13.6)
Diarrhea	54 (13.7)	43 (11.5)
Nausea	22 (5.6)	21 (5.6)
Vomiting	7 (1.8)	6 (1.6)
Fever	6 (1.5)	5 (1.3)
Any current medication use	365 (92.4)	346 (92.3)
Medications, no.		
0–2	105 (26.6)	103 (27.5)
3–5	153 (38.7)	152 (40.5)
6–8	93 (23.5)	83 (22.1)
9–11	26 (6.6)	25 (6.7)
≥12	18 (4.6)	12 (3.2)
Data missing	0 (0.0)	0 (0.0)
Total daily water consumption, 8 oz glasses[a]		
0	2 (0.5)	2 (0.5)
<1	0 (0.0)	0 (0.0)
1–5	174 (44.1)	186 (49.6)
6–10	191 (48.4)	170 (45.3)
11–15	25 (6.3)	14 (3.7)
16–20	1 (0.3)	3 (0.8)
>20	2 (0.5)	0 (0.0)
Missing	0 (0.0)	0 (0.0)

Continued

supplemental analyses we repeated the process with the inclusion of participants who received mislabeled devices. In the primary and supplemental analyses all participants were analyzed according to their original randomization assignment.

A totalizer was installed in each device to measure the amount of water used from the device in each household. Participants were provided with water bottles and encouraged to carry water from the home device when outside the home. Mean water consumption in each cycle was compared by initial device assignment with the 2-sample *t* test.

RESULTS

As detailed in the CONSORT (Consolidated Standards for Reporting Trials) flowchart (Figure A, available as a supplement to the online version of this article at http://www.ajph.org),[29] we screened 4391 households that responded to our requests for participation. Of these, 714 households (16.3%) were eligible, agreed to participate, and were enrolled. After 157 households that received devices from a mislabeled batch and thus did not undergo a crossover were dropped, our total sample was 557 households (770 individuals), which slightly exceeded our original goal of 540 households. Among households initially assigned to receive an active device, 89% completed cycle 1 and 83% also completed cycle 2; among households initially assigned to receive a sham device, 90% completed cycle 1 and 82% also completed cycle 2 (the most frequent reasons given for dropping out were fatigue [33%], no reason [22%], and moved [17%]; detailed in Figure A, available as an online supplement).

Thirteen participants died during the study (7 while using the active device and 6 while using the sham device). Causes of death included respiratory failure, cardiac arrest, septicemia, cancer, intracerebral hemorrhage, and other, ill-defined conditions. Participants reported 69 hospitalizations during the trial (35 while using the active device and 34 while using the sham device.). Hospitalizations were primarily attributable to disorders of the circulatory system, respiratory system, musculoskeletal system, and digestive system. Only 1 hospitalization was classified by the treating physician as infectious gastroenteritis.

TABLE 1—*Continued*

Daily water consumption at home, 8 oz glasses[a]		
0	14 (3.5)	12 (3.2)
<1	0 (0.0)	0 (0.0)
1–5	236 (59.7)	219 (58.4)
6–10	126 (31.9)	131 (34.9)
11–15	16 (4.1)	9 (2.4)
16–20	1 (0.3)	2 (0.5)
>20	1 (0.3)	0 (0.0)
Missing	1 (0.3)	2 (0.5)
Daily bottled water consumption, 8 oz bottles[a]		
0	329 (83.3)	318 (84.8)
<1	1 (0.3)	1 (0.3)
1–5	58 (14.7)	49 (13.1)
6–10	6 (1.5)	5 (1.3)
11–15	0 (0.0)	0 (0.0)
16–20	0 (0.0)	0 (0.0)
>20	0 (0.0)	0 (0.0)
Missing	1 (0.3)	2 (0.5)

Note. Sample size for the active device was n = 395; sample size for the sham device was n = 375.
[a]Self-estimated.

Randomization and Blinding

Randomization appeared to have been successful, and dropouts appeared to have caused little imbalance across sequences. Device groups were well-balanced at both the cycle 1 and the cycle 2 baseline with respect to numerous factors (cycle 1 shown in Table 1; cycle 2 is shown in Table A, available as a supplement to the online version of this article at http://www.ajph.org). Water consumption was higher during cycle 1 than cycle 2 but did not significantly differ between the 2 devices (Table B, available as a supplement to the online version of this article at http://www.ajph.org). However, because of the crossover study design, this resulted in more exposure to active filtration for participants randomized to device sequence active–sham than for those randomized to sham–active.

We observed a phenomenon also seen in 1 of our previous water intervention trials[24]: at randomization but not at other time points, the majority (71%) of participants willing to guess (40%) optimistically believed they were randomized to the active device, regardless of actual assignment. At the end of each cycle, more than half the participants in each sequence group did not hazard a guess, with a higher proportion in cycle 2 (Table C, available as a supplement to the online version of this article at http://www.ajph.org). Among participants willing to guess, 52% and 56% of those randomized to device sequence active–sham believed they were using the active device at the ends of cycles 1 and 2, respectively; among those randomized to device sequence sham–active, 55% believed they were using the sham device at the end of cycle 1 and 53% at the end of cycle 2 (Table C, available as an online supplement). At the end of cycle 2, we found no difference in the distribution of 3-level guesses between sequence groups (2-sided Fisher exact test, $P=.40$).

Analysis of Gastrointestinal Illnesses

The primary efficacy outcome of the trial was episodes of HCGI. During cycle 1, participants using the active device reported 2.83 episodes per year (ascertained by calculating an average rate for 6 months and scaling that rate to years), and participants using the sham device reported 2.76 episodes per year (Table 2). During cycle 2, there were 1.69 and 2.29 episodes per year in the active and sham groups, respectively. Participants reported more episodes during cycle 1 than cycle 2, regardless of their allocated device sequence, which is very

TABLE 2—Model-Free Estimates of Episodes and Days of Illness per Year, by Device and Cycle: Sonoma Water Evaluation Trial, Sonoma County, CA, 2001–2006

	Cycle 1		Cycle 2	
Estimates	Active Device	Sham Device	Active Device	Sham Device
Episodes of illness per y, mean				
HCGI	2.83	2.76	1.69	2.29
Diarrhea	3.64	3.23	2.26	2.78
Vomiting	0.44	0.46	0.27	0.45
Watery diarrhea	2.07	2.02	1.32	1.67
Diarrhea and cramps	0.97	0.92	0.64	0.71
Nausea and cramps	0.52	0.53	0.28	0.30
Days of illness per y, mean				
HCGI	7.06	5.88	3.68	6.21
Diarrhea	9.38	8.06	4.69	7.92
Vomiting	0.97	0.66	0.45	0.88
Watery diarrhea	4.85	4.21	2.59	4.62
Diarrhea and cramps	1.78	1.45	1.16	1.68
Nausea and cramps	1.19	0.98	0.74	0.95
Measures of disease impact, mean				
Days of work missed per y	1.29	1.05	0.71	1.55
Physician visits for gastrointestinal illness per y	0.21	0.17	0.14	0.34
Risk, mean				
Person-years at risk for HCGI	173.77	165.92	135.23	141.62
Person-years at risk for missing work	34.98	31.34	25.22	27.73
Total person-years under observation	185.17	176.29	140.37	149.40

Note. HCGI = highly credible gastrointestinal illness.

similar to findings reported by others (Figure B, available as a supplement to the online version of this article at http://www.ajph.org).[6,8]

The adjusted incidence of HCGI episodes per person-year for the sham device was 1.98 (95% confidence interval [CI]=0.78, 5.02); the active-versus-sham incidence ratio was 0.88 (95% CI=0.77, 1.00) according to the GEE model. The corresponding values from the GLMM model were 1.58 (95% CI=0.54, 4.63) and 0.85 (95% CI=0.76, 0.94), respectively (Table 3).

The secondary outcome of the trial was the longitudinal prevalence of HCGI (days of HCGI divided by days at risk). During cycle 1 there were 7.06 and 5.88 days of HCGI per year for active and sham participants, respectively. During cycle 2 there were 3.68 and 6.21 days of HCGI per year in active and sham groups, respectively (Table 2).

The adjusted longitudinal prevalence of HCGI for the sham device was 3.19 (95% CI=1.06, 9.65) according to the GEE model; the active-versus-sham prevalence ratio was 0.88 (95% CI=0.74, 1.05). The corresponding values from the GLMM model were 2.80 (95% CI=1.73, 4.51) and 0.84 (95% CI=0.78, 0.90), respectively (Table 3). GEE models estimated the population-average device effect, by averaging over the variety of sham device HCGI rates in the study population. They assessed the overall effect of the device on HCGI in the target population. By contrast, GLMM models estimated the mean subject-specific device effect, conditional on participant-specific sham device HCGI rates. They assessed the effect on HCGI in an individual who used a water-filtration device.

GEE models fit a common intercept (HCGI rate on the sham device) for all participants, whereas GLMM models fit different intercepts for each participant; both fit a common slope (device effect). A consequence of this model difference was that any variation in sham device HCGI rates across participants had to be absorbed by the device effect estimate of the GEE model. Thus, in general as well as in our HCGI findings, GEE estimates are attenuated and have wider confidence intervals than do GLMM estimates (Table 3; for further discussion, see Fitzmaurice et al[25]).

We repeated the analyses by including the available data from the 218 participants who had received mislabeled devices and who therefore did not cross over to the other device type during the study. These results were consistent with those in the principal analyses (Table D, available as a supplement to the online version of this article at http://www.ajph.org).

We also examined the device effect in a model that accounted for device sequence (active–sham or sham–active). We found that the estimate of the mean of the sequence-specific device effects essentially matched the estimate of the overall device effect. For example, in the unadjusted GEE model of HCGI incidence, the mean of the sequence-specific device effects was 0.87 (95% CI=0.76, 0.99), whereas the overall device effect was 0.90 (95% CI=0.79, 1.03; Table 3).

Subgroup Analyses

The study was not designed to test hypotheses about differential device effects between subgroups; however, we felt that several subgroups were worthy of exploration. For example, because participants reported more episodes during cycle 1 than cycle 2, regardless of their assigned device sequence (Table 2; Figure B, available as an online supplement), we examined the device effect separately for the 2 cycles. In the adjusted GEE model, the device effect (rate ratio for episodes per person-year of HCGI) was 1.02 (95% CI=0.80, 1.31) and 0.75 (95% CI=0.54, 1.04) in cycles 1 and 2, respectively (Table 4). However, when we stratified the results by cycle, we lost the power of the crossover design, because individuals no longer served as their own control for estimating the device effect; this was scientifically unbiased because of randomization but was less statistically efficient and did not reflect the original study design.

In the adjusted GEE analyses, the device effect among men (relative risk [RR]=0.76; 95% CI=0.60, 0.95) appeared to be different

TABLE 3—Unadjusted and Adjusted Estimates of Episodes and Days of Highly Credible Gastrointestinal Illness (HCGI) With Use of an Active Versus a Sham Water Treatment Device: Sonoma Water Evaluation Trial, Sonoma County, CA, 2001–2006

	Episodes of HCGI		Days of HCGI	
	GEE Model, RR (95% CI)	GLMM Model, RR (95% CI)	GEE Model, Prevalence Ratio (95% CI)	GLMM Model, Prevalence Ratio (95% CI)
Device (active vs sham), unadjusted estimate	0.90 (0.79, 1.03)	0.88 (0.79, 0.98)	0.90 (0.76, 1.08)	0.87 (0.81, 0.92)
Adjusted multivariable model				
Device (active vs sham)	0.88 (0.77, 1.00)	0.85 (0.76, 0.94)	0.88 (0.74, 1.05)	0.84 (0.78, 0.90)
Cycle (1 vs 2)	1.45 (1.26, 1.66)	1.47 (1.32, 1.64)	1.30 (1.09, 1.56)	1.30 (1.21, 1.39)
Men (vs women)	0.76 (0.60, 0.98)	0.64 (0.51, 0.79)	0.98 (0.60, 1.60)	0.54 (0.49, 0.60)
Age (per 10 y)	0.93 (0.83, 1.06)	0.88 (0.75, 1.03)	0.92 (0.79, 1.06)	0.84 (0.79, 0.89)
Self-reported health (vs excellent)				
Good	0.74 (0.53, 1.03)	0.68 (0.54, 0.86)	1.01 (0.70, 1.46)	0.69 (0.60, 0.79)
Fair	0.87 (0.54, 1.41)	0.81 (0.52, 1.27)	0.87 (0.38, 1.97)	0.67 (0.56, 0.81)
Poor	0.87 (0.52, 1.45)	1.49 (0.64, 3.48)	1.72 (0.56, 5.26)	2.55 (1.98, 3.30)
Medications, no.	1.09 (1.05, 1.13)	1.10 (1.06, 1.15)	1.12 (1.06, 1.19)	1.11 (1.09, 1.13)
Irritable bowel syndrome at baseline	1.49 (1.08, 2.06)	1.80 (1.24, 2.61)	1.43 (0.85, 2.39)	1.52 (1.32, 1.75)
Diarrhea at baseline	2.58 (1.93, 3.45)	4.62 (3.69, 5.80)	4.00 (2.18, 7.34)	4.76 (4.30, 5.28)
Total daily water consumption, 8 oz glasses	1.03 (0.98, 1.07)	1.02 (0.97, 1.06)	1.03 (0.98, 1.09)	1.03 (1.01, 1.05)

Note. CI = confidence interval; GEE = generalized estimating equations; GLMM = generalized linear mixed model; RR = rate ratio. All estimates are adjusted except where indicated. All adjusted estimates for the device and all of the covariates were run in the same multivariable model. All GEE models estimated with exchangeable correlation and robust SEs. All GLMM specifications included random intercepts for individual and household.

from that among women (RR=0.99; 95% CI=0.85, 1.17; Table 4).

We did not detect any differences in the effect of the device in subgroups defined by water consumption, employment status, or age (age was stratified into 4 quartiles defined by balanced person-cycles in the trial). Our results were similar for all of the subgroup analyses in the adjusted GLMM models (Table 4).

DISCUSSION

Ours was the first randomized drinking water trial conducted exclusively among older adults, defined as persons aged 55 years and older. We found evidence of 12% mean reductions in population incidence and prevalence of gastrointestinal illness episodes per year during use of a device with combined filtration and ultraviolet light treatment. Higher frequencies of "don't know" guesses and incorrect beliefs about treatment assignment in cycles 1 and 2 suggested that participants remained blinded throughout the trial. In earlier published tests of this device, the ultraviolet treatment achieved a 99.99% inactivation of viruses, and the 1-μm filter was shown to remove virtually all bacteria and parasites.[30]

We focused on older adults for several reasons. The Environmental Protection Agency and others have identified the elderly as a sensitive subpopulation for which more research is needed about risks from drinking water.[14,15] Persons aged 65 years and older represent approximately 13% of the US population, and this proportion is expected to increase to approximately 20% by 2030.[31] Hospitalizations for enteric infections increased in this age group by 43% between 1990 and 2002.[31] Between 1979 and 1995, diarrheal disease accounted for 14.4 deaths per 1000 hospital discharges in persons aged 65 to 75 years and 24.9 deaths per 1000 discharges in those older than 75 years.[32] Another study reported that 51% of deaths caused by diarrhea over a 9-year period occurred in individuals older than 74 years.[33]

Drinking water has been shown to contribute to an increased risk of severe gastrointestinal illness in the elderly (defined as aged 65 years and older) during waterborne outbreaks.[19] Our results are in agreement with evidence from a study in Philadelphia, Pennsylvania, that suggested that drinking water regulated by federal water quality standards contributed to the endemic incidence of gastrointestinal illness in the persons aged 65 years and older.[18]

Our results may provide useful input to inform risk assessment methods to develop a national estimate of waterborne diseases.[12,34] Such a risk assessment process can serve also to identify necessary studies to fill in other empiric gaps in support of drinking water regulations.

It is possible that participants in both groups, faced daily with the device in their homes, were reminded constantly about the study and altered 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).

Our finding of more episodes of HCGI earlier in the trial (cycle 1) than later (cycle 2) regardless of group (Figure B, available as an online supplement) is very similar to findings reported by others.[6,8] This might be attributable to a loss of enthusiasm for reporting illness as the trial progressed. It also could reflect inclusion of less serious episodes during cycle 1 reporting or restriction to more serious episodes in cycle 2. We have no data with which to evaluate this possibility. We detected no differential in the use of water from the devices, suggesting that our findings were unlikely to be attributable to differential exposure to the municipal water (Table B, available as supplement).

We found evidence in this randomized, triple-blinded, controlled intervention trial that supplemental in-home drinking water treatment with a device that combined filtration and

TABLE 4—Stratified Subgroup Results From 2 Models for Episodes of Highly Credible Gastrointestinal Illness With Use of an Active Versus a Sham Water Treatment Device: Sonoma Water Evaluation Trial, Sonoma County, CA, 2001–2006

Subgroup	No.	GEE Model, RR[a] (95% CI)	GLMM Model, RR[a] (95% CI)
Study cycle			
1	770	1.02 (0.80, 1.31)	0.96 (0.73, 1.26)
2	657	0.75 (0.54, 1.04)	0.71 (0.46, 1.11)
Participant time in study, wk			
1–13	56	0.35 (0.12, 1.06)	0.13 (0.05, 0.40)
14–26	53	1.26 (0.52, 3.07)	0.49 (0.21, 1.17)
27–39	40	0.58 (0.24, 1.44)	0.78 (0.27, 2.23)
>39	1278	0.92 (0.80, 1.05)	0.89 (0.80, 0.99)
Total daily water consumption, 8 oz glasses			
Low (<5)	431	0.88 (0.70, 1.12)	0.89 (0.73, 1.09)
Medium (5–7)	583	0.91 (0.74, 1.11)	0.87 (0.74, 1.02)
High (>7)	413	0.91 (0.71, 1.17)	0.90 (0.75, 1.08)
Gender			
Women	812	0.99 (0.85, 1.17)	0.97 (0.85, 1.10)
Men	615	0.76 (0.60, 0.95)	0.72 (0.60, 0.87)
Age, y, quartiles			
55–62	357	0.88 (0.70, 1.11)	0.85 (0.70, 1.03)
63–72	358	0.79 (0.58, 1.08)	0.81 (0.65, 1.00)
73–79	356	1.16 (0.90, 1.49)	1.09 (0.88, 1.36)
>79	356	0.84 (0.66, 1.07)	0.83 (0.67, 1.03)
Employment status			
Full-time	198	0.84 (0.61, 1.15)	0.77 (0.59, 1.02)
Part-time	184	0.77 (0.50, 1.16)	0.76 (0.58, 0.99)
Unemployed	1045	0.95 (0.81, 1.10)	0.93 (0.82, 1.05)

Note. CI = confidence interval; GEE = generalized estimating equations; GLMM = generalized linear mixed model; RR = rate ratio (episodes of illness). All GEE models estimated with exchangeable correlation and robust SEs. All GLMM specifications included random intercepts for individual and household.
[a]RR estimates are for active versus sham.

ultraviolet light reduced population- and individual-level incidence of HCGI among older residents of an area of northern California where municipal drinking water met US standards. ■

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Contributors

J.M. Colford Jr was the principal investigator, wrote and revised the article, was responsible for primary interpretation of the results, and helped conceptualize, design, and implement the study. J.F. Hilton helped design the study, revise the article, and interpret the results, particularly regarding the statistical models. C.C. Wright helped design and implement the study and draft the article. B.F. Arnold helped analyze data, interpret results, and draft the article. S. Saha helped design and implement the study. T.J. Wade helped conceptualize and design the study and develop the instruments. J. Scott helped analyze data and interpret results. J.N.S Eisenberg helped conceptualize, design, and implement the study. All authors helped to conceptualize ideas, interpret findings, and review drafts of the article.

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Human Participation Protection

All study activities were approved by the institutional review board at the University of California, Berkeley. The study was monitored by a Data Safety Monitoring Board appointed by the National Institutes of Health. Participants provided written informed consent and were remunerated according to the study protocol.

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