A review of household drinking water intervention trials and an approach to the estimation of endemic waterborne gastroenteritis in the United States

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ABSTRACT

The incidence of acute gastrointestinal illness (AGI) attributable to public drinking water systems in the United States cannot be directly measured but must be estimated based on epidemiologic studies and other information. The randomized trial is one study design used to evaluate risks attributable to drinking water. In this paper, we review all published randomized trials of drinking water interventions in industrialized countries conducted among general immunocompetent populations. We then present an approach to estimating the incidence (number of cases) of AGI attributable annually to drinking water. To develop a national estimate, we integrate trial results with the estimated incidence of AGI using necessary assumptions about the estimated number of residents consuming different sources of drinking water and the relative quality of the water sources under different scenarios. Using this approach we estimate there to be 4.26–11.69 million cases of AGI annually attributable to public drinking water systems in the United States. We believe this preliminary estimate should be updated as new data become available.

Key words | drinking, epidemiologic studies, gastrointestinal diseases, intervention studies, randomized controlled trials, water

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INTRODUCTION

Household drinking water intervention trials are used to investigate risks attributable to drinking water. In these trials one group of households typically is assigned randomly to use an in-home intervention device while another group uses a sham (or no other) device. These trials are similar to clinical trials to evaluate medical treatments comparing a drug to a placebo; in such water trials the sham water treatment device may be considered the placebo treatment. The incidence of gastrointestinal illness is recorded in each group. Under the assumption that the active group participants have no gastrointestinal illnesses attributable to water, the excess incidence of illnesses observed in the sham-device group theoretically represents the burden of waterborne disease and is called the attributable risk. Several such drinking water

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studies have been published using this design (Payment *et al.* 1991, 1997; Hellard *et al.* 2001; Colford *et al.* 2002, 2005).

In this paper, we first review the design and results of published drinking water trials conducted in industrialized countries in immunocompetent populations. This review intentionally focuses on household drinking water intervention trials conducted in countries with relatively high quality water supply and municipal water treatment similar to those seen in the United States. Studies in developing countries designed to address the efficacy of a specific treatment are not directly relevant to a US national estimate of waterborne disease and are not included in this review. We then present an approach to estimate the incidence of endemic acute gastrointestinal illness (AGI) specifically attributable to drinking water. This approach combines the published estimates of risk attributable to drinking water based on information available from household drinking water trials, the estimates of total AGI and several estimates and assumptions about water consumption and source water quality for community water systems in the United States based on the best data currently available to us. Estimates of the incidence of AGI in various populations can be obtained from many published studies. Roy *et al.* have provided estimates of acute gastrointestinal illness (due to infectious and noninfectious causes, excluding episodes of diarrhea or vomiting due to any long-lasting or chronic illness or condition) in the United States based on a comprehensive review of these published data, and we use these estimates (Roy *et al.* 2006) The proposed approach incorporates a range of estimates for the relative contributions of the source of water (such as groundwater or surface water), the water treatment system, and the distribution system. The framework uses available data whenever possible and assumptions when necessary. We then apply this approach to all currently available published data to arrive at an estimate of the number of cases of AGI attributable to drinking water annually in the United States.

We sought to develop an approach that could provide updated estimates of annual US episodes of AGI when additional data become available from new studies estimating waterborne attributable risk, new studies estimating AGI incidence, new surveys estimating the proportions of the population receiving drinking water from various sources across the country, and new estimates of the impact of the distribution system. This approach can subsequently be extended to estimate waterborne AGI incidence for specific sub-populations such as the elderly, children, the immunocompromised (e.g. cancer or HIV infection), when the necessary data are available for these specific subgroups.

PUBLISHED HOUSEHOLD DRINKING WATER INTERVENTION TRIALS

Through a literature search of MEDLINE and EMBASE (and searches of the bibliographies of relevant articles) we identified five published household interventions trials conducted in municipal water supplies whose results are relevant to the development of a national estimate of waterborne disease for the United States (Payment *et al.* 1991, 1997; Hellard *et al.* 2001; Colford *et al.* 2002, 2005). The key features of each of these studies are described in Table 1 and are reviewed briefly below. Trials that are underway currently were not eligible for inclusion.

Trials in Canada

Payment *et al.* (1991)

The first household intervention trial was conducted in the late 1980s in a suburban area of Montreal. The area received tap water from a surface water source mainly contaminated by human sewage, but the treated water quality met or surpassed all Canadian and US regulatory standards.

In this trial, 299 eligible households were supplied with domestic water filters (reverse-osmosis) to eliminate microbial and chemical contaminants from their water, and 307 households were left with their usual tap water without a filter. Gastrointestinal symptoms were evaluated by means of a family health diary maintained prospectively by all study families over a 15-month period. The principal outcome measured was episodes of "highly credible gastrointestinal illness (HCGI)", defined as shown in Table 1. The study results were reported for two separate periods: Period 1 (March 1988–June 1988) and Period 2 (September 1988–June 1989). The study was suspended during the summer months of 1988 because of summer vacations and travel of the participants. The estimated

Table 1 | Study characteristics of randomized controlled trials of drinking water in Australia, Canada, and the United States (1991–2005)

	Payment *et al.* (1991)	Payment *et al.* (1997)	Hellard *et al.* (2001)	Colford *et al.* (2002)	Colford *et al.* (2005)
Study design	Randomized trial (parallel arms)	Randomized trial (parallel arms)	Randomized trial (parallel arms)	Randomized trial (parallel arms)	Randomized trial (cross-over design)
Blinding	No	No	Yes	Yes	Yes
Placebo or Sham Device	No	No	Yes	Yes	Yes
Study area	Suburban area of Montreal, Canada	Suburban area of Montreal, Canada	Melbourne Australia	Contra Costa County, California, United States	Davenport, Iowa, United States
Study population	General population: homeowners with one child age 2–12	General population: homeowners with one child age 2–12	General population: homeowners with one child age 2–12, excluding those with immunocompromising conditions	General population: excluding those with immunocompromising conditions	General population: excluding those with immunocompromising conditions
Dates of study	January 1988–June 1989	September 1993–December 1994	September 1997–February 1999 (not including two 4-week periods over Christmas)	March 1999–October 1999	October 2000–May 2002
Length of follow-up	12 months	16 months	17 months	4 months	12 months
Sample size (households/individuals)	606/2408	1062/5253	600/2811	77/236	456/1296
Source water quality	River (surface) water contaminatedw/enteric viruses, coliforms, fecal coliform	River(surface) water contaminated by enteric viruses, oocysts and coliphages	Single surface water source; originates from protected catchments. Average compliance with water quality guidelines.	Surface water source. Contaminated by industrial and agricultural run off. Evidence of *Cryptosporidium* spp. in source water	Surface water source: Mississippi River. Contaminated with fecal indicator bacteria, *Cryposporidium, Giardia*, other pathogens
Water treatment	Alum flocculation, rapid sand filtration, ozonation, chorination and chlorine dioxide	Alum flocculation, settling, rapid sand filtration, ozonation, or chlorination	Chlorinated, not filtered	Standard conventional treatment with chlorimation; ozononation added to PWS during study	Standard conventional treatment: coagulation, flocculation, sedimentation, granular activated carbon/sand filters, and chlorination.
Treated water quality	Free of any detectable fecal bacteria or viruses, met all regulatory standards	Finished water turbidity <0.1 NTU, free of fecal bacteria and viruses. Met all regulatory standards	Total coliform bacteria not detected	Generally meets all federal guidelines. No additional testing conducted	High quality; met or surpassed all regulatory standards

Table 1 | (*continued*)

	Payment *et al.* (1991)	Payment *et al.* (1997)	Hellard *et al.* (2001)	Colford *et al.* (2002)	Colford *et al.* (2005)
Distribution system water quality	Not described	No evidence of fecal bacteria	Total coliforms detected in 18% of samples; 13% of HPC measures greater than 500; poorer than US/WHO standards	Data not collected	Less than 5% of samples positive for total coliform, within regulatory standards
Treatment arms	Reverse osmosis, tap water (unblended)	Tap water w/purge valve, bottled plant water, bottled purified water, tap water	Ultraviolet and 1-micron polypropylene filter, inactive device (sham, blinded)	Ultraviolet and 1-micron filter, inactive device (sham, blinded)	Ultraviolet and 1-micron filter, inactive device (sham, blinded)
Outcome definition	Highly credible GI(HCGI): vomiting or liquid diarrhea or nausea or soft diarrhea combined with abdominal cramps with or without confinement to bed, consultation with doctor or hospitalization required 6 consecutive symptom-free days between episodes	Same as Payment *et al.* (1991)	*Primary*: Any of the following symptoms in a 24-h period: two or more loose stools, two or more episodes of vomiting, one loose stool together with abdominal pain or nausea or vomiting, or one episode of vomiting with abdominal pain or nausea. *Secondary*: two or more loose stools, one loose stool together with abdominal pain or nausea, one or more episodes of vomiting, or an episode of abdominal pain with nausea.	Blinding of participants GI illness: HCGI similar to Payment *et al.* (1991).	GI illness: HCGI similar to Payment, 1991. Blinding of participants
Yearly rate of illness in treatment arm cases/ person-year	0.50	0.58 – purified bottled water group (average incidence for Periods 1 and 2)	0.79	2.63	(crossover trial) Period 1: 2.42 Period 2: 1.96
Yearly rate of illness in sham-device or tap water arm(s) cases/ person-year	0.76	0.66 – tap water group (average incidence for Periods 1 and 2) 0.70 – tap valve group (average incidence for Periods 1 and 2) 0.60 – bottled plant water group (average incidence for Periods 1 and 2)	0.82	3.48	Period 1: 2.40 Period 2: 1.82
Attributable risk	0.26	0.08 (tap water) 0.12 (tap valve) 0.02 (plant)	0.03	0.85	Period 1: −0.02 Period 2: −0.14

Table 1 | (*continued*)

	Payment *et al.* (1991)	Payment *et al.* (1997)	Hellard *et al.* (2001)	Colford *et al.* (2002)	Colford *et al.* (2005)
Primary result	AR% = 34% of all GI cases attributable to tap water	AR% = 12% excess cases in tap water group	No difference in treated and sham groups: IRR = 0.99 (95% CI 0.85–1.15)	Blinding was successful: BI = 0.64 (95% CI 0.51–0.78);	No difference in treated and sham groups: IRR = 0.98 (95% CI 0.87–1.10)
		AR% = 17% excess cases in tap-valve group	AR% = 4% of all GI cases attributable to tap water	Rate of illness in sham vs. active group:	Period 1 AR% = −0.008% of all GI cases attributable to tap water
		AR% = 3% excess cases in plant group		IRR = 1.32 (95% CI = 0.75–2.33)	Period 2 AR% = −0.08% of all GI cases attributable to tap water
				AR% = 24% of all GI cases attributable to tap water	
Limitations	Unblinded	Unblinded; high drop out rates (50% in bottled plant water group)		Designed to assess blinding, sample size too small to evaluate illness. Short follow up time.	

annual incidence of HCGI was 0.76 (episodes of HCGI/person/year) among tap water drinkers compared with 0.50 among filtered water drinkers ($p < 0.01$). The excess was consistent across age, sex and period. The investigators observed a significant trend between the amount of water consumed and illness among those in the tap water group. These findings were consistently observed in all population subgroups. The investigators estimated that, overall, 35% of the reported gastrointestinal illnesses among the tap water drinkers were drinking water-related and preventable.

The main potential limitation of this study with respect to its design was the lack of blinding: the tap water group participants were aware they had no reverse-osmosis device installed. This could have conceivably led to an over-reporting of illness among those in the tap water group, together with the possibility of under-reporting of illness in the reverse-osmosis group. The authors, however, acknowledging the potential for this bias, point out that symptoms such as vomiting and liquid diarrhea are not subjective, and that the excess was constant over time. Moreover, the presence of a dose–response relationship between the amount of water consumed and HCGI is unlikely to be explained by such biases.

Payment *et al.* (1997)

A second household intervention trial was conducted in another study group in the same Montreal region. This study was designed to investigate the nature of the excess risk observed in the first study, and established four treatment arms: tap water; purified bottled water; tap water with a continuously purged tap valve; and plant bottled water. The tap water group served as the exposed or baseline group, and the purified bottled water group served as the control, or unexposed, group. The tap water group with a purge valve was included to assess any relationship between illness and microbial regrowth in or contamination of the household water lines. The authors state: "It was postulated that, by maintaining a constant flow of water in the household pipes, water consumed by the subjects would be close in quality to water in the distribution system mains". The plant bottled water group was included to establish the contribution of the distribution system to the illness rate. The main outcome was HCGI (Table 1).

Over 350 households were initially enrolled in each treatment group. Overall, approximately 20% of participants dropped out of the study, but the bottled plant water group had a much higher dropout rate of 50%, with many citing taste and odor problems with the water as their primary reason for discontinuing the study. While low bacterial counts were found in the purified bottled water group, the plant bottled water group had extremely high heterotrophic plate counts with a geometric mean of over 1 million colony forming units per 100 ml.

The highest rates of illness were observed in the tap-valve group, followed by the tap group. The rate of illness in the plant bottled water group was no different than the rate of illness in the purified bottled water group despite the excessive regrowth of bacteria observed in the plant bottled water group. The attributable risk (AR) for the tap group was 0.08 (attributable risk percent [AR%] = 12% and the AR for the tap valve group was 0.12 (AR% = 17%).

The authors concluded that, because installation of a tap valve did not result in a lower rate of illness (in fact it resulted in a higher rate of illness compared to the tap water group), bacterial regrowth and contamination of the household pipes was not a likely cause of the excess illness. The authors speculated that since the rate of HCGI in the plant group was equivalent to or less than that in the purified bottled group the distribution system may have been the source of the differences observed, and that excess HCGI may be primarily due to distribution-related contamination rather than source water contamination.

This study had several limitations. There was a high dropout rate, particularly in the plant bottled water group, as discussed above, raising concerns regarding conclusions about this group. As in the first study, subjects were unblinded. The authors report that there was also a lower than expected compliance in the bottled water groups and that these groups frequently used other sources for their water.

Trials in Australia

Hellard *et al.* (2001)

The first blinded household intervention trial was conducted in Australia. This study had different goals than the Payment studies and was conducted in an area of Melbourne that receives its water from protected catchments of high water quality. The community was considering adding filtration to the treatment process and the study was therefore designed to examine whether additional treatment would be effective in reducing the incidence of gastrointestinal illness.

This study addressed the issue of blinding by including a sham device. The treatment device was selected to have minimal effect on the taste of the water (ultraviolet treatment combined with 1-micron filtration) but which should have removed or inactivated waterborne pathogens.

The primary outcome differed slightly from Payment in that at least two loose stools and two episodes of vomiting were required for an AGI episode. Participants completed a weekly health diary for each of the 68 weeks of the study. Six hundred families with 2811 individuals were randomized. There was a low dropout rate in this study, less than 7%.

After more than one year of follow up, the rates of illness in the treatment and sham groups were nearly identical. There was no difference in the type of fecal pathogens isolated from stool specimens in the two treatment arms. The authors also reported high compliance in that participants used the majority of their unboiled water from the treatment or sham device. The authors noted that water in the distribution system would not meet regulations for the United States and guidelines of the World Health Organization in that detection of coliform bacteria was relatively common.

This study had several strengths, including its randomized design, blinding of participants, low dropout rate, and long follow-up period–addressing many of the limitations of the earlier Payment studies.

Trials in the United States

Colford *et al.* (2000)

The first household intervention trial in the United States was conducted in Contra Costa County, California. This was a pilot study designed to assess the feasibility and methodology for a larger study, and to determine whether participants could be successfully blinded to the type of water treatment device they received. Household

recruitment began in January 1999 and follow-up was completed in December 1999.

The study area included single-family dwellings served by the Contra Costa Water District, around the community of Walnut Creek, California. The treatment plant serving the study area used standard conventional treatment with chloramination. A new ozonation plant was completed during the study period, so that after May 1999 the water supply was also ozonated. Source water from the San Joaquin River delta contained agricultural and industrial runoff and pathogens, including *Cryptosporidium*. The finished water met all Federal and state drinking water treatment standards and requirements.

Participants 12 years of age and older were asked to record each day in diaries whether they had symptoms such as nausea, vomiting, diarrhea, abdominal cramps, cough, and fever; index respondents were asked to record these data for children younger than 12 years of age and other household members who might need assistance.

The active water treatment device contained a 1-micron absolute prefilter cartridge and a UV lamp secured in a quartz sleeve that permitted transmission of UV light. Dual treatment was selected to provide optimal removal of waterborne parasites, bacteria, and viruses.

One study investigator, who remained unblinded throughout the trial and had no role in data analyses, prepared randomly coded labels and sent them to the manufacturer; the manufacturer then permanently affixed labels to the devices that could be decoded later to distinguish active from sham devices. All other study investigators, the plumbing contractor who installed the devices, and the study subjects were blinded to the household device assignment throughout the trial, including the analysis phase, resulting in a triple-blinded trial.

The principal health outcome measured in the trial was similar to the highly credible gastrointestinal illness reported by Payment *et al*. (Payment *et al.* 1991). A new episode, defined before the analysis was performed, was any of the following four conditions, preceded by at least 6 HCGI-free days: (1) vomiting; (2) watery diarrhea; (3) soft diarrhea and abdominal cramps occurring together on any day; or (4) nausea and abdominal cramps occurring together on any day.

According to a previously published Blinding Index, participants were not able to successfully distinguish what type of water device they were assigned (James *et al.* 1996). The Blinding Index was 0.64; an index of 0.50 or above indicates successful blinding. Overall, more subjects tended to guess that they had received the active device.

In the sham-device group there were 103 episodes of HCGI and 10,790 days on which these subjects were at risk for HCGI (3.48 episodes per person-year; adjusted 95% CI 2.26, 5.34). In the active group there were 82 episodes of HCGI during 11,380 days at risk (2.63 episodes per person-year; adjusted 95% CI 1.82, 3.79). The incidence rate ratio was 1.32 episodes per person-year (adjusted 95% CI 0.75, 2.33) when all household respondents were analyzed and 1.09 (95% CI 0.63, 1.90) when data were analyzed only from the index respondent in each household.

The study concluded that subjects could be successfully blinded to an in-home water treatment device.

Colford *et al.* (2005)

This full-scale household intervention trial was conducted as planned as a follow-up to the pilot study conducted in Contra Costa, California. The goal of this study was to determine whether or not additional treatment of tap water at home was effective in reducing the incidence of gastrointestinal illness. The study began in October 2000 and follow-up was completed in June 2002.

Some significant differences in this study include the use of a cross-over design, where each subject effectively served as self-controls; the use of a countertop treatment device; and the partnering with the water utility for a related study to conduct a detailed water quality characterization (LeChevallier *et al.* 2003).

Several criteria were used to select a study location: the entire community had to receive its drinking water from one microbiologically challenged surface water 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, and the community had to be large enough to recruit for a study of 400 households. An additional consideration was the willingness of the utility to provide data on microbial water quality and treatment performance.

This trial was performed in Davenport, Iowa and its surrounding communities along the Mississippi River.

Letters inviting households to participate in the study were sent to 38,353 customers of the Iowa American Water Company. Households were excluded if the household: contained an employee of the Iowa American Water Company; had an address outside the local utility water service area; drank less than an estimated 75% of in-home drinking water from the household tap; contained an individual with a known immunocompromising condition (including HIV and active cancer under treatment); or if any member of the household had been advised by a physician to drink only bottled or specially treated water.

Households were randomized to receive either an active water treatment device or an identical looking sham device. Active water treatment devices were designed to reduce or eliminate any pathogens that remained in the water. Sham devices were identical to active devices 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 glass sleeve blocked transmission of ultraviolet radiation. After 6 months, the devices were replaced with a device of the alternate type. Water treatment devices were connected to the kitchen faucet.

Each member of the household recorded their daily occurrence of gastrointestinal symptoms, such as diarrhea, nausea, and vomiting, for a period of approximately 1 year. Adult household members recorded daily occurrences of illness in their health diaries. An adult member recorded responses for children younger than 12 years of age. The principal health outcome measured was episodes of HCGI, a previously published measure.. 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.

A moderate dropout rate was observed with 84% of those households initially randomized completing the entire study. Participants were successfully blinded to their treatment device as measured by the Blinding Index. No difference was seen in the rates of HCGI in the two treatment arms (IRR = 0.98, 95% CI 0.86–1.10). Furthermore, no difference was observed in subgroup analysis by age, sex, water consumption, or season. Also, no difference was observed among those reporting that 90% or more of their water was from the treatment device. A significant flood occurred in the study area in the Spring of 2001 whereby raw water bypassed sewage treatment and contaminated the source water supply. A related paper reported an increase in the incidence of HCGI during this time, but this increase occurred among study participants using both treatment and sham devices (Wade *et al.* 2004).

The authors speculate that the reason for the lack of a difference in HCGI between the two study arms may be a result of the high quality of water treatment and the high quality of water throughout the distribution system. The authors also recognize that "conservative" biases such as consumption of water outside the home may have reduced the power of the study to detect an effect. The authors conclude that less than 10% of HCGI illness is attributable to water in a community with a well-operated municipal water utility using conventional treatment of surface water.

Although no differences were found among study groups, considerably higher rates of HCGI were observed in this study compared to the Payment and Hellard studies. The reason for this is unknown since the outcomes were similarly defined. It is possible that these differences might be attributable to differences in water quality, water system vulnerability, water source and treatment, or other factors including consumption of water outside the home.

SUGGESTED APPROACH FOR THE ESTIMATION OF ACUTE GASTROINTESTINAL ILLNESS IN THE UNITED STATES ATTRIBUTABLE TO DRINKING WATER

Unlike current efforts which attempt to relate gastrointestinal illnesses to food (i.e. the Foodborne Diseases Active Surveillance Network (FoodNet, http://www.cdc.gov/foodnet/), there is no surveillance system that captures and reports the incidence of acute gastrointestinal illness believed attributable to drinking water in the United States. Additionally, although there does exist a surveillance system for waterborne disease outbreaks, this system does not track endemic waterborne illness (Craun *et al.* 2006*a*). We suggest here a procedure to estimate the incidence of acute gastrointestinal illness (AGI) occurring in community

water systems in the United States that integrates the following estimates:

(1) the estimated national incidence of AGI;
(2) the estimated proportion of these AGI cases attributable to drinking water derived from the randomized drinking water trials done in community water systems reviewed above;
(3) the estimated number of persons receiving drinking water from surface water versus groundwater sources in community water systems;
(4) the estimated proportion of the total risk for waterborne AGI attributable to problems with either the source water and water treatment (SW/TR) or attributable to problems with water arising from the distribution system (DS);
(5) the estimated proportion of the population consuming water from community systems with a history of water quality or treatment problems.

We have used published data for each of the estimates when such data were available. When no such data were available, we have made assumptions, stated the rationale for our choices, and examined the impact of these assumptions across a wide range of possible values.

Estimated national incidence of AGI

From 1996 to 2003, the Foodborne Diseases Active Surveillance Network (FoodNet) conducted four 12-month cycles of a population-based telephone survey to determine the prevalence of self-reported diarrheal illness in the United States (Hawkins *et al.* 2002; Herikstad *et al.* 2002; Imhoff *et al.* 2004; Jones *et al.* in press).

Cycles one and two did not record information on vomiting without diarrhea and/or respiratory symptoms but the subsequent two cycles did (Herikstad *et al.* 2002; Imhoff *et al.* 2004). Using the data from FoodNet cycles three and four, the estimated incidence of AGI in the United States is 0.65 episodes per person-year (Hawkins *et al.* 2002; Jones *et al.* in press). This estimate falls within the range of estimates presented by other national and international studies of varying design that assessed the burden of AGI (Roy *et al.* 2006). For this FoodNet estimate, AGI was defined as diarrheal illness (three or more loose stools in a 24-hour period resulting in an impairment of daily activities or diarrhea duration greater than 1 day) and/or vomiting, excluding those with respiratory symptoms (cough and/or sore throat). In this context, AGI included diarrhea and/or vomiting of infectious or non-infectious origin but excluded episodes of diarrhea or vomiting due to any long-lasting or chronic illness or condition.

Estimated proportion of AGI attributable to drinking water

As reviewed above, drinking water intervention trials provide a direct estimate of the rate of illness in each of the treatment and comparison groups. For example, in the Payment *et al.* (1997) study described above the rate of HCGI in the treatment (purified bottled water) group (I_{Treat}) was estimated as 0.58 episodes/person-year and the rate in the comparison group was 0.66 episodes/person-year (I_{Tap}). Two concepts, attributable risk and attributable risk percent, are needed to make use of these results (see the companion article by Craun *et al.* (2006*b*)). Attributable risk (AR) is defined as the difference in the rate of illness in the two groups:

$$\text{AR} = I_{\text{Tap}} - I_{\text{Treat}}.$$

Using the Payment data, $\text{AR} = (0.66 - 0.58) = 0.08$ episodes/person-year. The AR may be thought of, and is sometimes referred to as, "excess risk" since the rate in the sham or tap water group is presumed to be greater than or equal to that in the treated group in a properly randomized trial in which the two groups differ only with respect to their drinking water (and in which there is no harmful effect from water treatment).

Attributable risk percent (AR%) is a related measure which provides an estimate of the proportion of the total burden of HCGI among tap water drinkers is represented by the AR:

$$\text{AR}\% = (\text{AR}/I_{\text{Sham}}) \times 100.$$

In the Payment example, $\text{AR}\% = (0.08/0.66) \times 100 = 12\%$. The assumption is that the remaining 88% of cases of HCGI are due to causes not related to the drinking water.

Using the five published trials of drinking water interventions conducted in general populations in Canada,

Australia, and the United States, we make an initial estimate of the attributable risk for the general population (Payment *et al.* 1991, 1997; Hellard *et al.* 2001; Colford *et al.* 2002, 2005). All of these trials involved consumption of tap water from surface water sources with varying levels of contamination and treatment. The AR in these studies ranged from a low of 0.14 (Colford *et al.* 2005) to a high of 0.85 (Colford *et al.* 2002). The median AR of these five estimates is 0.08 with a median AR% of 12%. We use this median estimate of AR% = 12% in our subsequent calculations. Because these studies were all conducted in sites using surface water as a source, a similar direct estimate of the proportion of cases due to contaminated groundwater is not possible. Instead, we assume that the AR% for groundwater systems is the same for surface water systems.

Estimated number of persons receiving water from drinking specific water sources (surface vs. groundwater)

For the purposes of this estimate, we consider two components of the drinking water system, each of which may be responsible for a portion of the total risk: (1) the source water and its subsequent treatment (SW/TR), and (2) the drinking water distribution system (DS). There are two types of source water to consider: surface water and groundwater. In 2004, an estimated 182.0 million persons in the United States relied on community water systems using surface water supplies or groundwater supplies under the influence of surface water. In the same year, an estimated 90.5 million persons relied on community water systems using groundwater. Therefore, the total estimated number of persons using community or public drinking water systems in 2004 was 272.5 million (SDWIS 2004), which represented 92.8% of the US population (2004 population estimate 293,655,404) (Census 2004). This estimate does not include the population using private water systems, typically household wells. The water quality of private systems is not subject to the Environmental Protection Agency's (EPA) national drinking water regulations. Without the required microbial monitoring and limits on the presence of fecal bacteria imposed by regulations, the variability of microbial water quality in private systems nationwide is expected to be more extreme than that in regulated community water systems. The calculations that follow represent only persons using community water systems under regulation by the US EPA.

The proportion of risk attributable to problems with source water or water treatment vs. problems with the distribution system

The proportion of risk for waterborne AGI that is attributable to contamination of water at the source or inadequate water treatment (SW/TR) is likely to be different than the proportion of risk attributable to contamination of water in the distribution system. However, the magnitudes of these proportions are unknown and assumptions must be made. We first assume that 90% of the risk for AGI is due to a contaminated water source or inadequate treatment (SW/TR) and that 10% is due to contamination of the drinking water in the distribution system (Table 2). To evaluate the effect of the assumption of the distribution of risk between source water/treatment vs. distribution, in Table 3 we have reversed these estimates, assuming only a 10% risk for AGI due to a contaminated water source and 90% risk due to contamination in the distribution system.

The proportion of the population consuming high-risk drinking water

Not all source water, water treatment processes, and distribution systems are alike. Therefore, the risk of AGI also varies within each component of the drinking water system. One approach to characterizing high-risk drinking water is to base the characterization on whether it meets the standards of the US EPA national microbial drinking water regulations, i.e. the treatment technique requirements of the Surface Water Treatment Rule (SWTR) for surface water systems, and the Maximum Contaminant Level of the Total Coliform Rule for both surface- and groundwater systems (SWTR & TCR 2006). The SWTR sets standards for removal by filtration and/or the inactivation by disinfection of pathogens in surface water. The TCR requires systems to monitor the microbial quality of the water in their distribution systems and to take remedial actions if they violate the MCL of more than 5% of samples in a month testing positive for total coliform bacteria. Additional

requirements apply if fecal coliform or *E. coli* bacteria, indicators of recent fecal contamination, are detected. Detection of fecal coliforms represents a higher level of risk to public health and a single positive sample can result in an acute violation of the TCR MCL. Data from the Safe Drinking Water Information System (SDWIS), the USEPA's database of systems, population served, and violations of drinking water regulations, was used to calculate the population percentages served by systems in violation of the SWTR or the TCR (SDWIS 2004).

In 2004, 7.6% of the population served by community water systems using surface water or groundwater under the influence of surface water was served by systems in violation of the treatment technique requirements of the SWTR (4.5%) or by systems in violation of the TCR MCL (3.1%), including acute public health violations. During the same year, 5.4% of the population served by community water systems using groundwater was served by systems with violations, including acute public health violations of the TCR. For the following calculations, we will consider persons served by community water systems with the above violations in 2004 to be at high risk for AGI. All others will be considered to be at low risk for AGI. We will also assume that the risk varies by an order of magnitude (10-fold) between the high-risk category and the low-risk category.

SAMPLE ESTIMATE OF ACUTE GASTROINTESTINAL ILLNESS ATTRIBUTABLE TO COMMUNITY DRINKING WATER SYSTEMS IN THE UNITED STATES

In Tables 2–6, using the methods and assumptions described above, we demonstrate an approach that can be used to estimate the annual incidence of endemic AGI cases attributable to community drinking water systems in the United States. These estimates exclude cases attributable to private water systems not regulated by the US EPA. These calculations rely on many assumptions and estimates, and the degree of uncertainty around these estimates is unknown. Furthermore, these calculations are made using only a limited number of relevant variables–other variables could be included in this approach if data were available. Therefore, the estimates presented here are not meant to represent a rigorous evaluation of the risk for AGI. Rather, they are meant to illustrate a methodology that can and should be further refined as more data become available and to highlight data gaps where further research and investigation may be warranted.

Estimates of AGI due to community drinking water supplies in the population receiving surface water (Tables 2 and 3)

In Table 2 we estimate the number of cases of AGI occurring among the 182.0 million people using community water systems (CWS) supplied by surface water, under the assumption that 90% of the risk was due to the source water or inadequate treatment (SW/TR) and that 10% of the risk was due to the distribution system. We first assumed that 7.6% (13.84 million) of the population was receiving high-risk surface water. We categorized the risks arising from the source water and treatment (SW/TR) and the risks from the distribution system as either "high" or "low" and assumed one order of magnitude of difference in these estimates. We then added the number of cases under all possible combinations of risks (high/low separately in the SW/TR and distribution systems) and estimated 2.93 million cases of AGI annually in those consuming surface water. In the second part of Table 2 we arbitrarily assumed that equal proportions of persons received water from high- and low-risk sources (i.e. 50% received high-risk surface water rather than the 7.6% based on the violation data). Under this assumption, 7.81 million cases of AGI were estimated to occur annually.

Table 3 provides similar calculations (again for surface water systems), except now under the assumption that 10% (rather than 90%) of the risk arose from SW/TR and 90% (rather than 10%) arose from the distribution system. Under these assumptions, we estimated 7.27 million cases annually if 7.6% of the population received high-risk source water and 7.81 million cases of AGI if 50% of the population received high-risk source water.

Estimates of AGI due to community drinking water supplies in the population receiving groundwater (Tables 4 and 5)

We used 90.5 million as the estimated number of persons using community drinking water systems supplied by

Table 2 | Provisional estimate of the number of cases of acute gastrointestinal illness in the United States attributable to drinking water in surface water systems where 90% of the risk is associated with contamination of the source water or inadequate treatment

7.6% of population with high-risk source water (violation data)

		SW/TR risk level			Distribution system risk level			SW/TR + Dist
Population[a] (millions)	Incidence rate[b] (cases / person-year)	SW/TR[c]	Attributable risk percent[d]	Cases attributable to SW/TR (millions)	Distribution system	Attributable risk percent[d]	Cases attributable to dist. system (millions)	Cases attributable to drinking surface water (millions)
6.92	0.65	High	0.108	0.49	High	0.012	0.05	0.54
6.92	0.65	High	0.108	0.49	Low	0.0012	0.01	0.49
84.08	0.65	Low	0.0108	0.59	High	0.012	0.66	1.25
84.08	0.65	Low	0.0108	0.59	Low	0.0012	0.07	0.66
182.0				2.15			0.78	2.93
50% of population with high-risk source water (upper end assumption)								
Population[e] (millions)								
45.50	0.65	High	0.108	3.19	High	0.012	0.35	3.55
45.50	0.65	High	0.108	3.19	Low	0.0012	0.04	3.23
45.50	0.65	Low	0.0108	0.32	High	0.012	0.35	0.67
45.50	0.65	Low	0.0108	0.32	Low	0.0012	0.04	0.35
182.0				7.03			0.78	7.81

[a]7.6% of population is assumed to be in the high-risk SW/TR category; 92.4% of population is assumed to be in the low-risk SW/TR category.
[b]estimate based on third and fourth cycles of the FoodNet Population Survey.
[c]SW/TR = source water / treatment (see text).
[d]The median value of the attributable risk percent from five intervention studies is 12%. In this calculation we assume 90% of this risk is associated with SW/TR and 10% with the distribution system. There are high and low risk SW/TR and Distribution Systems categories where risk due to each component varies by an order of magnitude.
[e]Population evenly distributed across risk categories.

Table 3 | Provisional estimate of the number of cases of acute gastrointestinal illness in the United States attributable to drinking water in surface water systems where 90% of the risk is associated with contamination in the distribution system

7.6% of population with high-risk source water (violation data)

		SW/TR risk level			Distribution system risk level			SW/TR + Dist
Population[a] (million)	Incidence rate[b] (cases / person-year)	SW/TR[c]	Attributable risk percent[d]	Cases attributable to SW/TR (million)	Distribution system	Attributable risk percent[d]	Cases attributable to dist. system (million)	Cases attributable to drinking water (million)
6.92	0.65	High	0.012	0.05	High	0.108	0.49	0.54
6.92	0.65	High	0.012	0.05	Low	0.0108	0.05	0.10
84.08	0.65	Low	0.0012	0.07	High	0.108	5.90	5.97
84.08	0.65	Low	0.0012	0.07	Low	0.0108	0.59	0.66
182.0				0.24			7.03	7.27
50% of population with high-risk source water (upper end assumption)								
Population[e] (million)								
45.50	0.65	High	0.012	0.35	High	0.108	3.19	3.55
45.50	0.65	High	0.012	0.35	Low	0.0108	0.32	0.67
45.50	0.65	Low	0.0012	0.04	High	0.108	3.19	3.23
45.50	0.65	Low	0.0012	0.04	Low	0.0108	0.32	0.35
182.0				0.78			7.03	7.81

[a]7.6% of population is assumed to be in the high-risk SW/TR category; 92.4% of population is assumed to be in the low-risk SW/TR category.
[b]estimate based on third and fourth cycles of the FoodNet Population Survey.
[c]SW/TR = source water / treatment (see text).
[d]The median value of the attributable risk percent from five intervention studies is 12%. In this calculation we assume 90% of this risk is associated with the distribution system and 10% with SW/TR. There are high and low risk SW/TR and Distribution Systems categories where risk due to each component varies by an order of magnitude.
[e]Population evenly distributed across risk categories.

Table 4 | Provisional estimate of the number of cases of acute gastrointestinal illness in the United States attributable to drinking water in ground water systems where 90% of the risk is associated with contamination of the source water or inadequate treatment

5.4% of population with high-risk source water (violation data)

		SW/TR risk level			Distribution system risk level			SW/TR + Dist
Population[a] (million)	Incidence rate[b] (cases / person-year)	SW/TR[c]	Attributable risk percent[d]	Cases attributable to SW/TR (million)	Distribution system	Attributable risk percent[d]	Cases attributable to dist. system (million)	Cases attributable to drinking water (million)
2.44	0.65	High	0.108	0.17	High	0.012	0.02	0.19
2.44	0.65	High	0.108	0.17	Low	0.0012	0.00[f]	0.17
42.81	0.65	Low	0.0108	0.30	High	0.012	0.33	0.63
42.81	0.65	Low	0.0108	0.30	Low	0.0012	0.03	0.33
90.5				0.94			0.39	1.33
50% of population with high-risk source water (upper end assumption)								
Population[e] (millions)								
22.625	0.65	High	0.108	1.59	High	0.012	0.18	1.76
22.625	0.65	High	0.108	1.59	Low	0.0012	0.02	1.61
22.625	0.65	Low	0.0108	0.16	High	0.012	0.18	0.34
22.625	0.65	Low	0.0108	0.16	Low	0.0012	0.02	0.18
90.5				3.49			0.39	3.88

[a]5.4% of population is assumed to be in the high-risk SW/TR category; 94.6% of population is assumed to be in the low-risk SW/TR category and 10% with the distribution system. There are high and low risk SW/TR and Distribution Systems categories where risk due to each component varies by an.
[b]estimate based on third and fourth cycles of the FoodNet Population Survey.
[c]SW/TR = source water / treatment (see text).
[d]The median value of the attributable risk percent from five intervention studies is 12%. In this calculation we assume 90% of this risk is associated with SW/TR.
[e]Population evenly distributed across risk categories.
[f]This number is actually 0.0019 million or approximately 1900 cases. We consider cases less than 5,000 to be negligible in this national estimate. order of magnitude.

Table 5 | Provisional estimate of the number of cases of acute gastrointestinal illness in the United States attributable to drinking water in ground water systems where 90% of the risk is associated with contamination in the distribution system

		SW/TR risk level			Distribution system risk level			SW/TR + Dist
Population[a] (million)	Incidence rate[b] (cases / person-year)	SW/TR[c]	Attributable risk percent[d]	Cases attributable to SW/TR (million)	Distribution system	Attributable risk percent[d]	Cases attributable to dist. system (million)	Cases attributable to drinking water (million)
2.44	0.65	High	0.012	0.02	High	0.108	0.17	0.19
2.44	0.65	High	0.012	0.02	Low	0.0108	0.02	0.04
42.81	0.65	Low	0.0012	0.03	High	0.108	3.01	3.04
42.81	0.65	Low	0.0012	0.03	Low	0.0108	0.30	0.33
90.5				0.10			3.49	3.60
50% of population with high-risk source water (upper end assumption)								
Population[e] (millions)								
22.625	0.65	High	0.012	0.18	High	0.108	1.59	1.76
22.625	0.65	High	0.012	0.18	Low	0.0108	0.16	0.34
22.625	0.65	Low	0.0012	0.02	High	0.108	1.59	1.61
22.625	0.65	Low	0.0012	0.02	Low	0.0108	0.16	0.18
90.5				0.39			3.49	3.88

[a]5.4% of population is assumed to be in the high-risk SW/TR category; 94.6% of population is assumed to be in the low-risk SW/TR category.
[b]estimate based on third and fourth cycles of the FoodNet Population Survey.
[c]SW/TR = source water / treatment (see text).
[d]The median value of the attributable risk percent from five intervention studies is 12%. In this calculation we assume 90% of this risk is associated with the distribution system and 10% with SW/TR. There are high and low risk SW/TR and Distribution Systems categories where risk due to each component varies by an order of magnitude.
[e]Population evenly distributed across risk categories.

Table 6 | Estimate of the number of cases of acute gastrointestinal illness in the United States attributable to drinking water

Scenario 1: 90% of the risk is associated with contamination of the source water or inadequate treatment

	Low estimate[a]	High estimate[b]	From
Surface water	2.93	7.81	Table 2
Ground water	1.33	3.88	Table 4
Total	4.26	11.69	

Scenario 2: 90% of the risk is associated with contamination in the distribution system

	Low estimate[c]	High estimate[d]	From
Surface water	7.27	7.81	Table 3
Ground water	3.60	3.88	Table 5
Total	10.87	11.69	

[a]Assumes 7.6% of the population uses high risk surface water sources, 5.4% of the population uses high risk ground water sources, and 90% of the risk is associated with the source water / treatment.
[b]Assumes 50% of the population uses high risk surface water sources, 50% of the population uses high risk ground water sources, and 90% of the risk is associated with the source water / treatment.
[c]Assumes 7.6% of the population uses high risk surface water sources, 5.4% of the population uses high risk ground water sources, and 90% of the risk is associated with the distribution system.
[d]Assumes 50% of the population uses high risk surface water sources, 50% of the population uses high risk ground water sources, and 90% of the risk is associated with the distribution system.

groundwater in the United States (SDWIS, 2004). In Table 4 we assumed that 90% of the risk of illness was due to SW/TR and 10% was due to the distribution system. Based on violation data, we also assumed that 5.4% (4.88 million) of the population received high-risk groundwater. As in the calculations for surface water (Tables 2 and 3), we again divided the population into four groups based on the joint distribution of the SW/TR and distribution system risk. Using these assumptions we estimate 1.33 million cases annually. In the second part of Table 4, we arbitrarily assumed that 50% of the population (rather than 5.4%) received high-risk groundwater. Using these assumptions, 3.88 million cases of AGI were estimated to occur annually.

In Table 5 we reversed these assumptions and assumed that only 10% of the risk in groundwater systems was due to SW/TR while 90% of the risk was due to the distribution system. Under these assumptions, we estimate 3.60 million cases of AGI annually if 5.4% of the population received high-risk groundwater and 3.88 million cases of AGI if 50% of the population received high-risk groundwater.

Summary of groundwater and surface water risks

In Table 6, we summarized the highest and lowest estimates made for annual cases of AGI in community drinking water systems supplied by both surface water and groundwater sources under all of the scenarios presented in Tables 2–4. Reviewing all the scenarios that we examined, we estimated the range in the number of cases of AGI from community drinking water systems in the United States to be 4.26–11.69 million cases annually.

Improving this estimate

This estimate can be updated easily as new data become available. For example, if additional drinking water trials are published they will provide additional estimates of the AR% for specific types of communities and subgroups of patients. We suggest that such new studies should include children, the elderly, and the immunocompromised (particularly HIV/AIDS patients and individuals undergoing immnunosupression during chemotherapy). Additionally, there is a pressing need for better estimates of attributable risk due to waterborne disease in the setting of groundwater systems–we were forced to rely in this estimate entirely on data from trials conducted in surface water systems. We recommend calibration of the results of expensive household-level drinking water trials with other study designs such as community-intervention studies or observational studies which are much more easily conducted. The ability to develop reliable estimates from cheaper designs would make it possible to provide more estimates in more communities and subgroups.

Our estimate makes several simplifying assumptions. One of these is that the generalization of the Attributable Risk percent (AR%) derived from intervention trials to the population level (Population Attributable Risk % or PAR%). The AR% estimated by intervention trials is most applicable to those communities in which most residents primarily

drink tap water for their drinking water. In communities where a large proportion of residents already use treated (e.g. bottled or filtered) water, the AR% estimates from intervention trials may not apply and the use of a Population Attributable Risk percent (PAR%) would be more appropriate. This is yet another example where community-specific information on drinking water usage could be used to refine the estimate further.

Since the current estimate is based on population survey data obtained at several FoodNet sites across the country, the estimate could also be refined by weighting based on the types of water sources used by persons in the different FoodNet catchment areas (these data are not presently available). Water sources would need to be categorized into surface water or groundwater for each responding FoodNet area code/phone exchange and classified according to the degree of risk for AGI, similar to the procedures described earlier. Another refinement to this calculation would be to separate risk from two categories (SW/TR and DS) into four categories (source, treatment, distribution system, and point of use). However, further information not currently available about these four risk categories would be required.

CONCLUSIONS

We have summarized the evidence available from randomized trials about the proportion of risk (i.e. the Attributable Risk percent) of acute gastrointestinal illness attributable to drinking water in immunocompetent populations (median estimate: AR% = 12%). We have presented a method by which the data from trials can be integrated with other data, including the estimated total AGI incidence due to acute infectious and non-infectious causes (0.65 cases/person/year based on the review by Roy *et al.* (2006)), and data concerning water sources and water quality in the United States, to arrive at an estimate of the total annual number of cases of AGI in the United States attributable to drinking water. Using this approach and necessary assumptions, we estimate there to be 4.26–11.69 million cases of acute gastrointestinal illness annually in the United States attributable to drinking water from community drinking water systems supplied by surface water and groundwater sources. The degree of uncertainty in this estimate is unknown but this approach makes explicit the assumptions that are applied and the additional data that could be gathered to improve the estimation. We caution that this approach can and should be refined for specific populations (e.g. the immunocompromised, the young, the elderly) or specific communities as additional data become available. Our approach and current estimates will be updated as appropriate new data become available.

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DISCLAIMER

The views expressed in this paper are those of the individual authors and do not necessarily reflect the views and policies of the US Environmental Protection Agency or the Centers for Disease Control and Prevention. The paper has been subject to the Environmental Protection Agency's peer review and approved for publication.

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