An approach for developing a national estimate of waterborne disease due to drinking water and a national estimate model application

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ABSTRACT

In this paper, the US Environmental Protection Agency (EPA) presents an approach and a national estimate of drinking water related endemic acute gastrointestinal illness (AGI) that uses information from epidemiologic studies. There have been a limited number of epidemiologic studies that have measured waterborne disease occurrence in the United States. For this analysis, we assume that certain unknown incidence of AGI in each public drinking water system is due to drinking water and that a statistical distribution of the different incidence rates for the population served by each system can be estimated to inform a mean national estimate of AGI illness due to drinking water. Data from public water systems suggest that the incidence rate of AGI due to drinking water may vary by several orders of magnitude. In addition, data from epidemiologic studies show AGI incidence due to drinking water ranging from essentially none (or less than the study detection level) to a rate of 0.26 cases per person-year. Considering these two perspectives collectively, and associated uncertainties, EPA has developed an analytical approach and model for generating a national estimate of annual AGI illness due to drinking water. EPA developed a national estimate of waterborne disease to address, in part, the 1996 Safe Drinking Water Act Amendments. The national estimate uses best available science, but also recognizes gaps in the data to support some of the model assumptions and uncertainties in the estimate. Based on the model presented, EPA estimates a mean incidence of AGI attributable to drinking water of 0.06 cases per year (with a 95% credible interval of 0.02–0.12). The mean estimate represents approximately 8.5% of cases of AGI illness due to all causes among the population served by community water systems. The estimated incidence translates to 16.4 million cases/year among the same population. The estimate illustrates the potential usefulness and challenges of the approach, and provides a focus for discussions of data needs and future study designs. Areas of major uncertainty that currently limit the usefulness of the approach are discussed in the context of the estimate analysis.

Key words | attributable risk, Bayesian statistics, community water systems, drinking water, gastrointestinal illness, household-intervention, microbial risk, Monte Carlo analysis, national estimate, waterborne disease, water distribution systems

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OVERVIEW AND PURPOSE OF THE PAPER

In this paper, the US Environmental Protection Agency (EPA) presents a conceptual approach for developing a national estimate of endemic acute gastrointestinal illness

(AGI) due to drinking water and a national estimate analysis developed through a model application. We first present the approach from a theoretical perspective and then with our national estimate analysis that considers currently available data. The national estimate analysis illustrates the application of the theoretical approach to stimulate discussion on this approach as EPA considers how to best measure illness due to drinking water. It also serves as an example for discussions on the information required to adequately develop a metric of disease due to drinking water for the purpose of evaluating public health issues and improvements related to drinking water regulations.

In developing our conceptual approach, we assume a capacity to quantify differences on a national basis in the incidence of drinking water related illness in the population drinking water from public water systems. Differences in risk factors among systems that affect the likelihood of drinking water related illness include the type of source water and level of microbial contamination, different types of water treatment and levels of treatment performance, and distribution system characteristics that contribute to different levels of microbial risk from the growth or intrusion of pathogens. Recognizing a lack of data on some of the basic elements of information needed to apply the proposed approach, we present a national estimate based on best available information on these risk factors. The estimate includes elements that are based on assumptions for which there is currently sparse or no data. Areas of current uncertainty that limit the usefulness of the approach are discussed in the context of the estimate. The authors hope by presenting their approach and the estimate, to focus discussion not only on the approach, the analysis and the data gaps, but also on the goals and reasons for developing a national estimate of illness due to drinking water in the US.

Reasons for developing the paper

This paper addresses the following objectives:

(1) Response to the Safe Drinking Water Act (SDWA) requirement that EPA and the Centers for Disease Control and Prevention (CDC) conduct studies on waterborne disease occurrence and develop a national estimate of occurrence of waterborne disease.
(2) Present an approach on how to measure the incidence of drinking water related AGI illness in a community, and how to measure changes in incidence due to changes in source water, treatment, or distribution system microbial risk characteristics, or due to changes in population characteristics.
(3) Identify the type of data and studies needed to measure waterborne disease or appropriate indicators at the community level and better inform a national estimate.
(4) Inform a national microbial waterborne disease estimate considering exposure to pathogens as a mixture of pathogens rather than from exposure to a single specific pathogen.
(5) Stimulate discussion on how a national estimate and the understanding of the basis behind the estimate might be used to evaluate the impact of drinking water regulations.

We are particularly interested in developing an approach for estimating national microbial risk from a mixtures perspective. Historically, EPA, in developing its drinking water regulations has estimated baseline levels of national microbial risk for specific pathogens, e.g. for *Giardia* in the Surface Water Treatment Rule (US EPA, 1989*a*) and for *Cryptosporidium* in the Interim Enhanced Surface Water Treatment Rule (US EPA, 1998). However, the risks from exposure to all types of pathogens in drinking water is probably much greater than that indicated for specific pathogens such as *Giardia* or *Cryptosporidium*. If such estimates could be made, they could inform the actual benefits of achieving higher national compliance rates with existing drinking water regulations and/or provide a focus for additional regulation or guidance.

Recently, under the Stage 2 Disinfection Byproducts Rule (US EPA, 2006*a*), EPA used epidemiology studies, and national water quality and treatment information to estimate national bladder cancer risk from exposure to the mixture of known and unknown chlorinated disinfection by-products (DBP) in drinking water. This analysis indicated potential order of magnitude higher cancer risks from all chlorinated DBPs based on epidemiology studies versus those based only on the limited sub-set of known DBPs with

available toxicology data (US EPA, 2005). While the nature of risk from DBPs is substantially different than the nature of risk from pathogens, there may be order of magnitude differences in risk between pathogens that are regulated (e.g. *Cryptosporidium*) and the risk from the total mixture of pathogens that people may be exposed to from drinking water. EPA's strategy to control for pathogens as a mixture has focused on controlling for those pathogens known to be most resistant to treatment and thereby prevent significant risk from most other less resistant pathogens. While this strategy may work for many pathogens originating in the source water, it is not clear how many other types of treatment resistant pathogens exist in source water or to what extent treatment upsets occur which would compromise EPA's regulatory strategy. Also, it is not clear to what extent mixtures of pathogens may enter the distribution system and survive, and how significant such risks are relative to source/treatment uncertainty.

Why focus on AGI?

The focus of the national estimate is on AGI in the population served by community water systems (CWS). AGI, with a range of symptoms including diarrhea, vomiting, nausea and cramps, is the illness typically associated with microbial contamination of drinking water, i.e. it is the illness most often recognized and reported in drinking water related disease outbreaks. Although our focus here is exclusively on AGI and associated symptoms, we recognize that other types of diseases occur, including some with more serious health outcomes. These other diseases also may be important measures of illness associated with drinking water.

It reasonable to use AGI as a metric because it is the broadest indicator of the health effects associated with most waterborne pathogens. In addition, it can be measured by observation, i.e. it does not require complicated and expensive sample collection and analytical procedures necessary to identify the specific pathogen that caused the illness. It is also a measure of the health effects of those waterborne pathogens that cause AGI and for which there are no analytical methods. We recognize the limitation with using AGI as the sole indicator since it is not a specific measure of waterborne disease. A national estimate based on AGI requires carefully designed epidemiology studies to statistically differentiate the incidence of AGI due to drinking water from the incidence of AGI due to other sources, e.g. food, recreational water.

Household-intervention studies (sometimes referred to as "drinking water trials" because of the similarity of design with drug trials) and community-intervention studies have the most useful study designs and can provide the most useful information for estimating AGI incidence rates due to drinking water in a given community (Calderon & Craun, 2006; Colford *et al.* 2006).

In a household-intervention study, participants are randomly assigned to drinking water that is either regular tap water, or tap water that has received additional treatment to reduce the level of any pathogens that might have been contaminating regular tap water. Four such studies (not counting pilot studies, and studies conducted in subpopulations of a community, e.g. in the HIV-positive subpopulation of the San Francisco area) have been conducted in communities in economically developed countries: two in Canada (in Laval, a suburb of Montreal), one in Australia (Melbourne), and one in the United States (Davenport and surrounding communities, IA) (Colford *et al.* 2006).

Community-intervention studies measure the incidence of AGI from drinking water by comparing the incidence in a community before and after a major change in the source or the treatment of drinking water. The assumption is that these changes improve the quality of drinking water and reduce the associated incidence of AGI. Three such studies have been, or are being, conducted in the US; the results are awaiting publication (Calderon & Craun 2006).

Both the household-intervention and the community-intervention studies used the incidence of AGI (with varying definitions of symptom combinations) as their primary measure. Some of the studies collected data on illness due to specific pathogens as a secondary measure (i.e. serum samples for antibody analysis, stool samples for analysis of selected pathogens). The national estimate presented in this report uses the results of household-intervention studies when feasible.

Focusing on AGI due to drinking water also allows for comparison to national estimates of incidence of AGI illness due to all causes. The most recent published CDC

estimate of AGI due to all causes in the US, or more specifically, acute diarrheal illness (only diarrhea, not vomiting, was included in the case definition), is 0.72 illnesses per person-year (Imhoff *et al.* 2004). The case definition and other information on the survey is presented in section 3.1 in table 2 along with AGI cases definitions of some of the drinking water household-intervention studies. The AGI rate can be more clearly understood when translated to a number of cases expected in a year for a given population. For example, when applying the 0.72 case rate to a population of 100 people, 72 cases of AGI illness would be expected over the course of one year from all types of exposures (e.g. food, person-to-person transmission, water, air, etc). The study also reported a rate of AGI diarrhea that, either because of the shorter duration of the symptoms, or because the person did not suffer any impairment to their daily activities, was considered a diarrheal episode, rather than a diarrheal illness. The rate of episodes reported was nearly twice that of the rate of illness, i.e. 1.3 per person-year. This estimate is based on data collected in a retrospective cross-sectional population survey conducted under the FoodNet program during a 12-month period in 1998–1999. The telephone survey, using random-digit dialing, asked questions about AGI symptoms and questions relating to severity of illness during the previous 4 weeks. The survey covered a sample population of 29 million persons (~11% of the total US population) in 8 states. The population included those living in both rural and urban areas.

A more recent FoodNet AGI estimate using data from 2000–2003 is also presented in this special issue of the *Journal of Water and Health* (Roy *et al.* 2006). However, we decided to use the Imhoff estimate for a number of reasons. Although the more recent estimate included vomiting without diarrhea in its case definition (the same as in the household-intervention studies) it was also more restrictive than the household-intervention studies because it only counted cases with symptoms lasting longer than 24 hours or impairment of normal daily activities. In addition, the more recent estimate excludes cases with AGI symptoms if respondents also report concurrent respiratory symptoms– the household-intervention studies did not exclude these cases. Based on our comparison of the case definitions we felt that the Imhoff *et al.* case definition was probably closer to the one used in the household-intervention studies. When comparing the incidence of AGI symptoms due to drinking water in our conclusions we compare the rate due to drinking water to the rate of diarrheal episodes from the Imhoff *et al.* publication.

Why focus on risk in Community Water Systems?

We focused on the population served by Community Water Systems (CWS) because the majority of the US population (approximately 273 million persons or 94% of the US population) lives in a community that is served by a CWS. We recognize that risks from pathogens in non-community water systems (NCWS) may be significant and substantially contribute to the national incidence of disease due to drinking water; however, very little data are available to estimate risks associated with these systems. Much more data is available on CWSs, in particular on those systems that use surface water sources. Information available on CWSs allows some consideration of the effect of governmental policies and regulations on the quality of drinking water.

CONCEPTUAL APPROACH

Our approach is based on the premises that:

(1) each CWS has a certain, but unknown, mean AGI incidence rate due to drinking water,
(2) the type and spread of the distribution of mean AGI incidence rates among populations served by CWS can be estimated,
(3) a percentile AGI incidence rate for the distribution in (2) can be estimated, and
(4) the statistical distribution derived from (2) and (3) can be integrated to inform a mean national estimate of AGI due to drinking water.

In developing our approach, we identify three steps (as outlined below) to address these premises.

Regarding step 1, we believe that the mean endemic AGI incidence due to drinking water among CWS can vary substantially and the range of this variability can be estimated. CWS at the low end of a range of microbial

risk would have a well established quality management system, no pathogens in their source water and a tight and well-maintained distribution system not subject to mains breaks and accidental pathogen intrusion. CWS at the high end of a range of microbial risk would lack an established quality management system, have a highly contaminated source water, treatment deficiencies and leaky, poorly designed and maintained distribution systems.

Step 2 in our approach is to develop a national microbial risk matrix that classifies systems according to their relative levels of microbial risk. The microbial risk matrix scheme can then be used to estimate the relative range of risk among CWSs (e.g. 4 orders of magnitude difference in risk between lowest vs. highest risk systems). It is important to determine what type of statistical distribution to assign to this relative range of risk, e.g. lognormal or other.

In implementing this concept we need to recognize the influence of risk associated with source water/treatment deficiencies, as well as distribution system deficiencies. The variability and the range of microbial risk related to the source/treatment depends on:

- the frequency and concentration of pathogens from different types of sources as water enters the treatment plant,
- different levels of treatment (including reliability) at the plant,
- frequency and concentration of pathogens entering the distribution system and their survival at the consumer's tap.

The variability and the range of microbial risk in the distribution system depends on the frequency, concentration and the likelihood of pathogens originating in the distribution system and the health effects associated with the pathogens that originate in the distribution system and survive to the consumer's tap.

Step 3 is to use the mean AGI incidence rates determined to be due to drinking water in epidemiology studies and link the AGI rate due to drinking water to one or more of the risk factors common to the epidemiology study site and CWSs in general. Epidemiology studies that include data on the system's source water quality, treatment characteristics, and distribution system characteristics provide information that can be used in comparing the system's relative level of risk with that of other systems. The comparison of risk provides a basis for extrapolating health effects from the study community to other communities at the same or different level of risk. There is a lot of uncertainty in the extrapolation, more in some areas than others. Much more work has been done to characterize relative degrees of potential risk associated with source/treatment risk factors than for distribution system risk factors. Uncertainty related to the epidemiology study results and the lack of any epidemiology studies in groundwater systems also contribute to uncertainty in extrapolation between communities served by very different types of systems. Most of the epidemiology studies to date have been conducted at sites presumed to have certain high source water risk factors to increase the likelihood of detecting waterborne disease associated with drinking water. In spite of the selection of systems with presumably high source water risks as the location for drinking water epidemiology studies, only a few studies were able to enumerate mean AGI incidence due to drinking water. These are the studies that we will consider in our current application of this conceptual approach.

This is probably the most challenging step in our approach because of the limits in the sensitivity of epidemiology studies conducted to date (i.e. to differentiate risk due to drinking water from the background levels of risk due to all other relevant exposures). However, as shown later in our analysis, data from only a few studies can still be informative for a national estimate of disease, given our analytical approach.

While data to inform our proposed conceptual approach are limited, studies currently in progress or planned for the near future will contribute to a better vision of variability of microbial risk and the factors that could be used as indicators of microbial risk. We expect that improvements in the national distribution of microbial risk factors will be a focus of planning to address data gaps for any national estimate of drinking water related illness. Some areas where our current knowledge is limited and can be improved to inform this approach include: the variability of system risk characteristics, the uncertainty in the national distribution of source/treatment risk, the

uncertainty in understanding what factors are most important indicators of distribution system risk, and the limited number of epidemiology studies that have measured illness associated with drinking water in communities that could be considered representative of one of the microbial risk elements.

Because data on microbial risk factors and AGI incidence rates are not consistently measured and available for every CWS, national estimates will always rely on assumptions in quantifying the variability of different risk factors and categorizing systems' microbial risk and associated population. However, as more studies and relevant information become available, assumptions become better informed, thus narrowing confidence bounds around a given estimate.

With this paper we begin to explore questions on statistical approaches to quantify variability of microbial risk among systems and uncertainty in risk characterization. We note data gaps throughout the paper to stimulate discussion of their relative importance in the construction of a robust estimate.

ANALYTICAL FRAMEWORK

In this section we provide an analytical framework for implementing the conceptual approach.

- First, we provide information on household-intervention studies and how AGI is measured and defined in these studies. This helps provide a perspective on what we mean when later using the same definition as the proxy measure for generating a national estimate of AGI illness due to drinking water.
- Second, we provide information pertaining to risk characterization of public water supplies on a national level. We discuss waterborne disease outbreak data, criteria and timing of national drinking water regulations, source water and treatment characterizations for surface water systems–all of which are used to inform our model development.
- Third, we discuss specific modeling considerations and introduce the modeling approach used in the national estimate presented in section 4.

Household-intervention studies and measures of AGI

Household-intervention studies, or drinking water trials, can, under the right conditions, measure the rate of AGI due to drinking water in a community. The design of a household-intervention study relies on the random assignment of participants to different types of drinking water (e.g. regular tap water vs. tap water with subsequent treatment to remove any pathogens), the conscientious reporting by participants of AGI symptoms in a health diary, and the conscientious use of their assigned drinking water. The random assignment is necessary because it is the basis for the assumption that different groups are likely to have similar characteristics with the exception of their drinking water, and that therefore any difference in a health endpoint known to be associated with contaminated drinking water, among other things, is due to the difference in the type of drinking water (illness due to the "other things" being equal among the groups). Blinding of participants to their treatment assignment, similar to the protocol in drug trials, is a desirable additional study design feature to reduce potential bias in reporting. Unblinded trials have been criticized because of a concern that participants could differentially influence how they report AGI symptoms because of knowing whether or not their drinking water has been subject to additional treatment.

One of the factors that affects the likelihood of detecting AGI due to drinking water in a study is the rate of non-compliance by individuals from the treatment group with their assigned treatment. In the case of the household-intervention studies, treatment is drinking water that has undergone additional treatment to remove pathogens that might be present in regular tap water. Non-compliance reduces the likelihood of detecting a difference in rates of AGI and results in an underestimate of drinking water related illness.

It is also very important that the study includes enough participants to be able to detect a statistically significant difference in the measured health end-point between the different treatment intervention groups. As the quality of drinking water improves and the associated rate of illness declines, the number of participants needed to be able to detect a difference in illness increases exponentially. Another factor that is often unknown before the study begins is the background rate of AGI in the study community. The size of

the study needed to detect a difference between treatment groups increases exponentially with an increase in the background rate of AGI. Of the four full-scale household-intervention studies, only were two were adequately sized to detect the rate of drinking water attributable illness, the two Canadian studies in Laval (Payment *et al.* 1991, 1997). The Davenport and Melbourne (Hellard *et al.* 2001; Colford *et al.* 2005) studies had a higher minimum detection level (11% and 15%, respectively), as well as lower levels of microbial risk. Both Davenport and Melbourne were blinded studies. Table 1 summarizes some of the design features and the results of the 4 studies.

Household-intervention studies are typically designed with the following elements. One group drinks regular tap water (from the tap or from a sham household point-of-use treatment device), and other groups receive drinking water that is of higher quality (either the water that has received another level of treatment to remove pathogens that may not be completely removed by the community system treatment and/or to remove any pathogens that might originate in the distribution system). Participants are asked to drink their assigned drinking water when at home and are usually encouraged to bottle their assigned water to drink away from home. For the duration of the study, participants are required to report on a regular basis any AGI symptoms and other specified health information recorded in a health diary they agree to maintain.

Four full-scale household-intervention studies used the incidence of AGI symptoms, including diarrhea, vomiting, nausea, and abdominal cramps, as the primary measure of illness. The two Laval studies and Davenport study used the same measure of the incidence of AGI symptoms defined as Highly Credible Gastrointestinal Illness (HCGI); the Melbourne study used a similar measure that it called Highly Credible Gastroenteritis (HCG). The case definition of HCG of the Melbourne study was slightly more restrictive than HCGI used in the other studies in that HCG excludes some cases of HCGI that probably occurred and would have been counted using the HCGI definition, i.e. the incidence of HCGI in a community would be higher than the incidence of HCG. Table 2 provides details on how the different endpoints for AGI were measured in each of the household-intervention studies and in the FoodNet AGI cross-sectional population survey. For our concept discussion we refer generally to AGI. However, the reader should note that in discussions of our national estimate analysis we refer to HCGI, the measure used in the two Laval studies.

The incidence of AGI due to drinking water from household-intervention studies can be used as an indicator of drinking-water-related AGI in other communities when one can estimate the relative level of risk (microbial risk/waterborne disease risk) in comparing communities. Therefore, we assume that in communities with a level of microbial/waterborne disease risk an order of magnitude, or 10 times, lower than in a study community, the incidence rate of AGI due to drinking water is also expected to be 10 times lower. For example, if the AGI incidence rate in the study community due to drinking water is 100 cases per 1000 people per year (or 0.10), then, in communities with approximately one order of magnitude lower level of risk, the AGI rate due to drinking water would be expected to be approximately 10 cases per 1000 people per year (or 0.010). This assumption is key to the approach we use in developing our model of the national distribution of drinking water microbial risk and associated AGI.

HCGI due to drinking water in first Laval household-intervention study

In the first study (Payment *et al.* 1991), conducted between January 1988 and June 1989, two groups of approximately 300 families (a total of 2407 individuals) were randomly assigned to either the "placebo" (regular tap water) group or the "treatment" group (tap water with additional point-of-use carbon and reverse osmosis filtration to remove pathogens). Participants maintained diaries over a 15-month observation period recording any HCGI symptoms and measures of severity, such as duration and visits to health care providers. Non-compliance with assigned drinking water consumption among those assigned to the "treatment" group as measured by the percentage of regular tap water consumption was 20–30%. The incidence of HCGI among all the participants in the "treatment" group was 0.50 cases per person-year and 0.76 in the "placebo" group. The difference in incidence between the groups of 0.26 cases of HCGI per person-year represents the estimated attributable risk to drinking tap water.

Table 1 | Summary of household-intervention studies and results

Primary author, publication year	Payment *et al.* (1991)	Payment *et al.* (1997)	Hellard *et al.* (2001)	Colford *et al.* (2005)
Study area	Suburban area of Montreal, Canada	Suburban area of Montreal, Canada	Melbourne Australia	Davenport, Iowa
Yearly rate of illness (treatment arm) Units: Person-years	0.50	Purified: 0.58 Plant: 0.60 Tap-valve: 0.70	0.79	Period 1: 2.42 Period 2: 1.96
Yearly rate of illness (placebo or tap water arm) Units: Person-years	0.76	0.66	0.82	Period 1: 2.40 Period 2: 1.82
Primary result:	Attributable Risk (Incidence): 0.26 cases/pers-year	Attributable Risk (Incidence): 0.08 cases/pers-year attributable to tap water	No difference in treated and sham groups: IRR = 0.99 (95% CI 0.85–1.15)	No difference in treated and sham groups: IRR = 0.98 (95% CI 0.87–1.10)
Attributable Risk due to drinking water/minimum detectable AR	Attributable Risk (% of all GI cases): 35%	Attributable Risk %: 14% excess cases in tap water group No excess cases in bottled plant water group	Min. detectable Attributable Risk > 15%	Min. detectable Attributable Risk: > 11%
Study design	Randomized trial	Randomized trial	Randomized trial	Randomized trial (cross-over design)
Blinding	No	No	Yes	Yes
Placebo or sham treatment device	No	No	Yes	Yes
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
Dates of study	January 1988–June 1989	September 1993–Dec. 1994	March 1997–December 1998	October 2000–May 2002

Table 1 | (continued)

Primary author, publication year	Payment et al. (1991)	Payment et al. (1997)	Hellard et al. (2001)	Colford et al. (2005)
Length of follow-up	12 months	16 months	17 months	12 months
Sample size (HH/Individuals)	607/2407	1062/5253	600/2400	456/1296
Treatment arms	Reverse osmosis and filter	Tap water w/purge valve	Ultraviolet and 1 micron filter (active arm)	Ultraviolet and 1 micron filter (active arm)
		Bottled plant water		
	Regular tap water	Bottled purified water	Inactive device (placebo arm, blinded)	Inactive device (placebo arm, blinded)
		Tap water		

Modified from Colford et al. (2006).

HCGI due to drinking water in second Laval household-intervention study

In the second study (Payment *et al.* 1997), conducted between September 1993 and December 1994, a total of 1062 families (5253 individuals) were enrolled into four separate treatment arms (regular tap water, continuously running tap water, bottled treatment plant water, bottled purified water). Bottled purified water was either treated plant water subsequently treated by reverse osmosis, or ozonated spring water, delivered to the home approximately every two weeks. Bottled treatment plant water was fully treated plant water collected for bottling every 2 weeks and delivered to the home. The type of bottled water provided to the two bottled water groups was not identified. The "running tap" group had a diversion valve installed in the cold water pipe under the kitchen sink that maintained constant flow so as to equilibrate water quality in household plumbing and water quality in the distribution system main. One of the reasons for this intervention was to determine if the elevated levels of HPC bacteria, typical of water quality in room-temperature stagnant water in household plumbing, were associated with a higher incidence of HCGI (Payment *et al.* 1993).

Significant differences in the incidence of HCGI between groups were only observed between bottled water groups and tap water groups. The groups' HCGI incidence and the relative rate of HCGI compared to the purified bottled water group (shown in parentheses) are as follows: 0.58 (1.00) in bottled purified water group; 0.60 (1.07) in bottled plant water group, 0.66 (1.14) in the regular tap water group and 0.70 (1.25) in the running tap group. Compliance with treatment assignment was lower in this study than in the first study; the average "regular tap water" consumption in those persons assigned to drinking bottled water groups was 40%. This undoubtedly would lead to an underestimation of the difference in HCGI between the tap water and bottled water groups.

In developing our analysis of the Laval studies, we only used HCGI incidence data from the persons assigned to the bottled purified water (0.58 cases per person-year) and the regular tap water group (0.66 cases per person-year). We considered using the "running water" group's higher HCGI incidence of 0.70 cases per person-year in the model

Table 2 | Definitions of health endpoint measures (household-intervention studies and FoodNet cross-sectional survey)

Authors of study, publication year, study identifier and type	Endpoint/reported summary measure	Endpoint/case definition health-based exclusion criteria	Data collected
Payment *et al.* (1991)	HCGI episode /	HCGI (Highly Credible Gastrointestinal Illness)	Daily symptoms, duration of symptoms, physician visit, absence from school or work and hospitalization.
Laval, Canada, household-intervention #1	Incidence of HCGI in different treatment groups and attributable risk due to drinking water.	1) Liquid diarrhea OR 2) vomiting OR 3) nausea with abdominal cramps OR 4) soft (diarrhea) stools with abdominal cramps AND 5) 6 symptom-free days between episodes	Telephone follow-up for persons with AGI
	HCGI "illness"	Not reported Health-based Exclusion Criteria: HCGI reports with plausible etiologies apart from illness due to drinking water (e.g. food overindulgence, pregnancy, and visits to countries with high endemic levels of GI illness) were excluded from consideration in the statistical analysis of the results.	Question regarding possible etiology, e.g. excessive eating, pregnancy
Payment *et al.* (1997)	HCGI episode/	Same as above.	Same as above
Laval, Canada, household-intervention #2	Incidence of HCGI in different treatment groups and attributable risk due to drinking water.	Health-based Exclusion criteria: No known medical conditions that could affect the outcome. Only healthy individuals included in the study.	
Hellard *et al.* (2001)	Two definitions of HCG /	HCG (Highly Credible Gastroenteritis)	Daily AGI symptoms, medical treatment, potential risk factors, including pet ownership, swimming
Melbourne, AU, household-intervention	Incidence of HCG 1 and HCG 2 in different treatment groups and attributable risk due to drinking water.	Primary endpoint: "HCG def. 1" Any of following symptoms in 24-hr period: 1) 2 or more loose stools; OR 2) 2 or more episodes of vomiting; OR 3) 1 loose stool with abdominal pain, nausea, or vomiting; OR 4) 1 episode of vomiting with abdominal pain or nausea. AND 5) 6 symptom-free days between episodes	

Table 2 | (*continued*)

Authors of study, publication year, study identifier and type	Endpoint/reported summary measure	Endpoint/case definition health-based exclusion criteria	Data collected
		Secondary, less stringent gastroenteritis endpoint similar to Payment studies: "HCG def. 2" Any of following symptoms in 24-hr period: 1) 2 or more loose stools; OR 2) 1 loose stool with abdominal pain or nausea, 3) 1 or more episodes of vomiting 4) 1 episode of abdominal pain with nausea AND 5) 6 symptom-free days between episodes Health-based Exclusion Criteria: Persons with immunocompromising conditions	
Colford *et al.* (2005)	HCGI episode	Any of the 4 conditions: 1) Vomiting 2) watery diarrhea 3) soft diarrhea and abdominal cramps 4) nausea and abdominal cramps AND 5) 6 disease-free days between episodes	Daily symptoms, days of work/school missed, visited physician for GI illness
Davenport household-intervention	Incidence of HCGI Days of HCGI	Health-based Exclusion Criteria: Persons with immunocompromising conditions	
Imhoff *et al.* (2004	Incidence of diarrheal illness	AGI: diarrhea (3 or more loose stools in 24-hr period) with or without vomiting that lasted more than one day or was associated with impaired daily activities during past 4 weeks. Vomiting only not included.	Symptoms associated with AGI during past 4 weeks and duration /one day of not being able to conduct normal daily activities.
FoodNet, cross-sectional population-based survey of AGI; (1998-1999)		AGI illness definition: AGI symptoms last >24 hrs, or impairment to normal daily activities Exclusion criteria: No chronic diarrhea (colitis, irritable bowel syndrome, part of stomach surgically removed).	

(or 0.68 case per person-year: the mean of the incidence associated with regular and running water HCGI); however, we felt that drinking water from a running tap did not reflect normal tap water consumption or normal water quality exposure in the general population.

Information pertaining to risk characterization of public water supplies on a national level

Waterborne disease outbreak data

Over the years, waterborne disease outbreak trends have provided evidence of the causes of drinking water related illness that are informative at the national level. Since 1970, information on waterborne disease outbreaks has been compiled in the Waterborne Disease Outbreak Surveillance System database. In the decades since 1971, and in the 2-year period since 2001, the number of outbreaks has declined overall from over 200 in both the 1970 s and 1980 s to 140 in the 1990 s and 21 in the first two years of the current decade (Craun *et al.* 2006).

Outbreaks in public water systems are classified by one of the following causes: deficiency in water treatment, distribution system deficiency, untreated ground water, miscellaneous/unknown deficiency, and untreated surface water. Trends in causes of outbreaks, as measured by the percentage of outbreaks in each category, are noteworthy. Categorized by deficiency, the relative percentage of outbreaks in the same time period in untreated groundwater systems remained fairly stable in the 20–30% range; however, the percentage of outbreaks due to deficiencies in water treatment has declined from over 40% in the first two decades to just over 30% in the 1990 s, and to 14% since 2001. By contrast, during the same period, the percentage of outbreaks due to distribution system deficiencies has been on the rise from less than 20% to a high of more than 50% in the most recent 2-year period. The decline in reported surface water outbreaks since the 1980 s is undoubtedly due to the implementation of well-defined regulations with measures of treatment performance (Craun *et al.* 2006).

From drinking water microbial risk evident in the outbreak data, we proceed to considering how drinking water regulations relate to levels of microbial risk.

Criteria and timing of national drinking water regulations

Table 3 provides a summary of all drinking water regulations that we considered in developing our model. We believe that each of these regulations has a constraining influence on AGI incidence due to drinking water. The drop in waterborne disease outbreaks in the 1990s versus the previous two decades, as described above, may largely be due to the effects of implementing the Surface Water Treatment Rule (SWTR) (US EPA 1989*a*) and Total Coliform Rule (TCR) (US EPA 1989*b*).

The Surface Water Treatment Rule (SWTR) established filtration and disinfection requirements that were designed to reduce the concentration of *Giardia* by 99.9%, and that of enteric viruses by 99.99%. The effectiveness of filtration and disinfection is frequently described in terms of log-units. "Log removal" refers to the logarithm of the fraction of organisms physically removed by treatment that includes filtration and "log inactivation" refers to the logarithm of the fraction inactivated by chlorine or other disinfectants. For example, the SWTR requirements are to provide a 3 log, or a 99.9% reduction of *Giardia*; for filtered systems the 3 log reduction can be achieved by removal through conventional treatment (2 log) plus 1 log *Giardia* inactivation by meeting *CT* (the concentration of disinfectant residual multiplied by residual contact time) requirements of disinfection (1 log).

Treatment performance in filtered systems is measured by filter effluent turbidity plus disinfection performance at the treatment plant, measured by *CT*. Unfiltered surface water systems with adequately protected watersheds are required to meet source water quality criteria and the same overall treatment performance by disinfection performance as measured by *CT*.

One limitation of the SWTR was the range of tolerance for treatment upsets to occur while a system is still in compliance. For example, combined filter effluent spikes could occur at levels up to 5 NTU and combined filter turbidity performance could exceed 0.5 NTU up to 5% of the time and the system could still be in compliance. Also, even though continuous disinfection for surface water is stated as a rule objective, disinfectant residuals leaving the plant could theoretically be absent for up to four hours without the system incurring a treatment technique

violation. While the duration of intervals of treatment upset may be small and infrequent, if pathogens occur in source waters at such times, there could be significant increases in microbial risk.

Enhancements of the SWTR, i.e. Interim Enhanced Surface Water Treatment Rule (IESWTR) (US EPA 1998) and Long Term 1 Enhanced Surface Water Treatment Rule (LT1) (US EPA 2002), to remove *Cryptosporidium* required improvements in filtration performance (i.e. a decrease in the acceptable level of the combined filter effluent turbidity) and on-line turbidity monitoring of individual filters (see Table 3). While these requirements significantly constrain possible plant upsets, treatment upsets can still occur while systems are in compliance. Since systems were not required to come into compliance with the IESWTR until the end of 2001 and the LT1 until the beginning of 2005, the effects of these regulations are only recently being realized.

Source water pathogen occurrence and treatment from studies performed and data collected in the development and implementation of the various rules (SWTR, IESWTR, LT1, Long Term 2 ESWTR or LT2) provide a wealth of information for characterizing the range of microbial risk nationally. Furthermore the national range of microbial risk due to drinking water is constrained by this regulatory framework.

Areas with the most uncertainty in their risk characterization are the areas of pathogen occurrence in groundwater and the occurrence and survival of pathogens that enter the distributions system post-entry-point to the distribution system, e.g. as the result of cross-connections or due to improperly maintained storage tanks. There are as yet no Federal treatment requirements for groundwater sources that are vulnerable to microbial contamination.

The quantity and quality of data on the occurrence of pathogens in source water and on the type and the levels of treatment for surface water systems is on a completely different scale than the data available on groundwater systems. This is due in part to research being driven by the need to balance the health risks associated with disinfection by-products (mostly a problem in surface water systems) and to improve the level of microbial protection for a broader suite of pathogens (e.g. *Giardia* and *Cryptosporidium*) than are generally found in groundwaters.

Characterization of source water quality and treatment in surface water supplies

Under the Information Collection Rule (ICR) (US EPA 1996), CWS with treatment plants serving more than 100,000 persons were required to collect data on pathogens, microbial indicators and treatment data over an 18-month period between 1997 and 1998. In addition, during the 1980s and 1990s many laboratory and pilot plant research studies were conducted to determine treatment efficiencies for a variety of pathogens. We used data collected from research studies and the ICR to inform our assumptions on relative microbial risk among CWS.

Research conducted on filtration performance since the SWTR has increased our understanding of the conditions under which increased performance can be achieved. Pilot plant filtration studies on *Cryptosporidium* have shown a range of filtration performance between 2 and 5 log. As part of the risk assessment to support the LT2, EPA assumed that *Cryptosporidium* removal rates ranged between 2 and 5 log. The effectiveness of filtration is not the same for all pathogens. Based on viral challenge studies it appears that filtration plants can generally remove 1–2 log of viruses.

Pathogens have a wide range of resistance to disinfection. *Cryptosporidium* is the most resistant among known pathogens to all commonly used forms of chemical disinfection (while ultraviolet light is effective at inactivating *Cryptosporidium*, it has not yet been used by many plants in the US). Free chlorine, the most commonly used disinfectant, achieves virtually no inactivation of *Cryptosporidium* but appears very effective for inactivating most viruses.

Information from the ICR indicated that average *E.coli* or fecal coliform concentrations in source water among plants ranged over approximately 5 orders of magnitude. Measured mean source water concentrations for viruses, *Cryptosporidium*, and *Giardia*, ranged more than 3 log (or 3 orders of magnitude) for each of these organisms among ICR plants. Statistical estimates for mean *Cryptosporidium* and *Giardia* source water concentrations (which included plants having all measurements below detection limits) ranged over more than 5 log. Based on this source water data we believe that mean pathogen concentrations among systems probably range about 5 log and use this range to inform our modeling effort.

Table 3 | National regulations expected to limit the level of endemic AGI and reduce the occurrence of waterborne disease outbreaks in 2004

Rule and promulgation date	Community water systems, population served	Treatment requirements	Effective date of treatment requirements and measures of treatment performance	Expected effect
Surface Water Treatment Rule 6/1989	All surface water systems	All systems to provide treatment (filtration and disinfection) that achieves a 3-log reduction of *Giardia lamblia* cysts and 4-log reduction of viruses.	Maximum combined filter effluent of 5 NTU, 95% combined filter effluent of 0.5 NTU	Reduce outbreaks and endemic level of AGI in communities served by surface water systems
	Total pop: 182 million	Systems with protected watersheds and meeting defined water quality criteria can meet the treatment requirements by disinfection alone.	Inactivation requirements: Disinfectant residual CT: (concentration of disinfectant residual x and contact time)	
	* Pop. Viol: 8.1 million	Disinfectant residual at entry point to the distribution system of 0.2 mg/L and detectable in 90% of distribution system samples.	Effective date for unfiltered systems: 12/91	
			Effective date for filtered systems: 6/93	
Total Coliform Rule 6/1989	All systems (ground water and surface water)	Monitor microbial water quality in distribution system for total coliform and fecal coliform bacteria. Number of samples /month ranging from 1–480 based on community system size. Repeat samples required if sample total coliform positive	Effective beginning 12/1990	Surveillance of distribution system microbial water quality and actions by systems to maintain compliance (e.g. increase the rate of disinfection in groundwater systems not previously disinfecting) expected to reduce the risk of outbreaks due to distribution system contamination, and reduce endemic level of AGI.
	Total pop: 272.5 million		Not more that 5% of samples total coliform positive No fecal coliform or *E. coli* bacteria and total coliform bacteria in subsequent samples.	

Table 3 | (*continued*)

Rule and promulgation date	Community water systems, population served	Treatment requirements	Effective date of treatment requirements and measures of treatment performance	Expected effect
	* Pop. viol: 10.6 million		Violations to be addressed by protection of well from microbial contamination, disinfection in distribution system and proper maintenance of distribution system.	
Interim Enhanced Surface Water Treatment Rule 12/1998	All surface water systems serving population of 10 000 or more	Enhanced filtration performance to increase removal of *Cryptosporidium*	Effective beginning 12/2001	Reduce outbreaks due to filtration deficiencies, reduce risk of endemic illness due to disinfectant resistant pathogens.
	Total pop: 163.4million		Maximum combined filter effluent of 1 NTU, 95% combined filter effluent of 0.3 NTU Monitor individual filter effluent	
Long Term 1 Enhanced Surface Water Treatment Rule 1/2002	All surface water systems serving population of less than 10 000	Enhanced filtration performance to increase removal of *Cryptosporidium*	Effective beginning 1/2005	Reduce outbreaks due to filtration deficiencies, reduce risk of endemic illness due to disinfectant resistant pathogens.
	Total pop: 18.6 million		Maximum combined filter effluent of 1 NTU, 95% combined filter effluent of 0.3 NTU Monitor individual filter effluent	

*Population served by systems in violation in 2004 (data from 2004 freeze of SDWIS database).

Laboratory studies have shown that relatively low *CT* values with free chlorine are needed to achieve > 4 log virus inactivation. On the other hand extremely high *CT* values for chloramines are needed to inactivate only a few logs of viruses. To achieve compliance with the SWTR, most plants that use chloramine as a residual disinfectant first provide enough *CT* with free chlorine to achieve at least 2 or 3 log inactivaton. The ICR data indicate that, based on *CT* values, viral inactivation among water treatment plants ranged from <2 log to > 10 log. However, an important caveat to these theoretical inactivation calculations based on *CT*s derived from laboratory studies is that viruses were found in finished water among 7 ICR plants that used ozone or chorine inactivation within the plant (Shaw *et al.* 2002). Three of the seven had theoretical log inactivation rates of 8 log or more which, if actual, would lead to no viruses being detected in their finished waters. The ICR data on viral inactivation indicates that inactivation efficiencies derived from laboratory studies either overstate viral inactivation in the environment or that viruses are breaking through plants during treatment compromises or upsets.

Due to the log scale of treatment removal or inactivation efficiencies, treatment plant compromises or upsets of even short duration can have a significant impact on overall removal or inactivation efficiencies. For example, if a treatment plant had achieved only 2 log removal for 1% of the year (for about 90 hours) because of treatment inefficiencies its mean removal for the year could be no more than 4 log for the entire year, regardless of how much removal and/or inactivation was achieved during the other 99% of operational time[1].

Multiple very short duration treatment failures (e.g. during extreme storm events) can also significantly influence mean pathogen removal or inactivation efficiency. For example, if a treatment process had complete failure cumulatively over a year for only 0.01% of the time (for about 0.9 hours), its mean removal for the year could be no more than 4 log for the entire year, regardless of how much removal or inactivation efficiency was achieved during the remaining time. Similarly, if a treatment process had complete failure cumulatively over a year for 0.1% of the time (for about 9 hours) its mean removal for the year could be no more than 3 log for the entire year.

[1] One example of this level of treatment compromise could pertain to removal of pathogens by filtration because of less filtration removal efficiency during the beginning and end of each of the 200 or so filtration cycles that may occur during the year. The more stringent turbidity monitoring and performance criteria under the IESWTR and LT1 were intended to largely address this particular treatment issue. However, the extent that overall removal efficiency is compromised during the beginning and ending of each filtration cycle on a national level remains unknown.

Characterization of the population served by CWSs

Data on the US population served by CWSs is compiled in the Safe Drinking Water Information System (SDWIS) (US EPA 2006b). Approximately 182 million persons of the US population are served by community water systems that use surface water (or groundwater under the direct influence of surface water). Of the 182 million served by surface water systems, approximately 90% (163 million) are served by systems supplying water to more than 10,000 persons and approximately 6% are served by the largest unfiltered systems (i.e. Portland ME, Portland OR, Tacoma WA, San Francisco CA, New York NY).

Approximately 90.5 million people are served by community water systems using groundwater (not under the direct influence of surface water). Of this 90.5 million, approximately 37% are served by small systems that serve fewer than 10,000 persons. Approximately 10 million people served by CWSs receive untreated groundwater and most of the remaining 80.5 million people receive water that has undergone some level of disinfection.

Selecting a reference year for generating the national estimate

Having a baseline mean estimate of AGI due to drinking water for a given year provides a reference point from which to evaluate changes in risk over time. In developing a national estimate, we used 2004 as the base year since it is the most recent year for which we have regulatory compliance data for the SWTR, TCR and IESWTR. The more stringent turbidity filtration performance requirements of LT1, the small system equivalent of the IESWTR, only became effective at the beginning of 2005.

As discussed earlier, microbial risk is expected to decline over time as new regulations impose tighter monitoring and treatment performance controls, and as states implement the minimum operator certification requirements. We expect the

rate of AGI illness due to drinking water to decline in surface water systems over the next 10 years under the influence of LT1 and the Long Term 2 Enhanced Surface Water Treatment Rule (LT2). The LT2 will require an increased level of treatment for filtered surface water systems of all sizes with high levels of *Cryptosporidium* in their source water. In addition, the LT2 will also require unfiltered systems to disinfect (UV treatment) for *Cryptosporidium*. Forthcoming regulatory requirements for groundwater systems are also expected to reduce the incidence of AGI nationally. However, it is possible that infrastructure degradation over time could have an opposite effect, especially on the distribution system component of microbial risk.

A link between microbial risk factors and rates of AGI illness

We elaborate discussion of the risk–illness link in the model development. We provide the following descriptions of the Laval system during each of the household-intervention studies to begin to provide the link between microbial risk factors and rates of illness. We focus specifically on the Laval studies, because they form the basis of our national estimate distribution of AGI. Our intention is to provide enough information to understand and evaluate our analysis. Payment *et al.* (1991, 1993, 1997) provide a detailed summary of the studies they conducted in Laval. We remind the reader that in our concept discussion we generally referred to AGI in discussing waterborne gastrointestinal illness. However, the reader should note that in discussion of our model application and analysis we refer to HCGI, the measure used in the two Laval studies.

Drinking water microbial risk factors in first Laval study

In this section we provide a summary of source water characteristics, treatment and distribution system conditions from the Laval systems during the period of the first study. In our national estimate analysis, we use this data on the Laval system in the 1980s, with its attributable risk of 0.26 cases of HCGI per person-year, to consider how Laval might fit into the range of microbial risk associated with drinking water from US surface water supplies in 2004. We also consider the likelihood of the system complying with regulations that were in effect in 2004, but not at the time the first Laval study was conducted. The comparison between Laval and US systems will be further analyzed in the discussion of our model assumptions. The data on the first Laval study (Payment *et al.* 1991, 1995) are presented below. Some additional data on characteristics that affect microbial risk of the Laval system during both studies are summarized in Table 4.

The community's source water has very high levels of fecal contamination, as indicated by the high mean levels of viruses (78 infectious units/100 L) and fecal coliforms (3674 cfu/L). The source water is subject to multiple discharges of untreated sewage from combined stormwater and sewage overflows (http://www.menv.gouv.qc.ca/eau/regions/region13/13-laval.htm, http://www.menv.gouv.qc.ca/eau/regions/region06/06-mtl.htm). No coliform bacteria or enteric viruses were detected in weekly samples of treated water (no analysis of samples for *Giardia* or *Cryptosporidium*). Payment *et al.* (1991) report that the system met US microbial drinking water regulations in effect during the study period, i.e. the National Interim Primary Drinking Water Regulations (NIPDWR) (US EPA 1975). We believe that the system probably also would have met the more stringent treatment performance requirements of the SWTR that went into effect in mid-1993 because of the reported multiple disinfection steps (pre-disinfection with chlorine, chlorine dioxide or ozone, and post disinfected with chlorine or chlorine dioxide) and the performance of the physical removal process (sedimentation process and plant effluent turbidity rarely over 0.5 NTU) (Payment *et al.* 1993).

The distribution system coliform monitoring results complied with the NIPDWR (US EPA 1975) coliform requirements; however the data presented by Payment *et al.* (1991, 1993) do not provide the type of information necessary to determine whether the system would have met the current requirements of the TCR (US EPA 1989*a*) that went into effect in 1991, i.e. total coliform MCL based on presence/absence of total coliforms and the new fecal coliform/*E. coli* MCL.

When we consider the sources of contamination in the watershed upstream from the system's intake (the high average concentrations of fecal indicator bacteria and enteric viruses measured at the intake), and compare the levels of viruses and fecal coliforms to those measured at the

intake of US systems in samples collected under the ICR requirements, it is apparent that Laval's source water ranks high among the most contaminated. Its average virus concentration was exceeded by only one system in the ICR data set (Shaw *et al.* 2002). Its treatment by 2004 standards would be considered below average for a surface water system of its size because it does not meet the IESWTR treatment requirements.

Drinking water microbial risk factors present in the second Laval study

The second Laval study was conducted during a 16-month period in 1993–1994. The microbial risk factors described in the study report (Payment *et al.* 1997) are presented here and in Table 4 in some detail to provide a perspective of rate of illness associated with a system that has highly contaminated source water, but provides treatment that would probably meet the microbial regulations in effect in 2004. The improvements in treatment are of particular interest because they offer an explanation of the decline from the first study in drinking water attributable HCGI (from 0.26 to 0.08 cases per person-year). The microbial risk factors will be further discussed in the Laval model analysis.

There were no changes in the sources of microbial contamination in the watershed and source water microbial quality did not change between the first and second epidemiology study. Drinking water quality, or at least water quality leaving the treatment plant, was better in the second study because of improvements at the treatment plant, including enhancements to the chlorination and ozonation processes and lower combined filter effluent turbidity levels. Average plant effluent turbidity decreased from 0.26 NTU in the first study to 0.1 NTU in the second, and the maximum level decreased from "only rarely" to "never" exceeding 0.5NTU. Definitely, the treatment must have met the SWTR treatment requirements because plant effluent turbidity never exceeded 0.5 NTUs, the maximum monthly 95th % turbidity level under the SWTR. Individual filter effluent turbidity was monitored during the study. Filter effluent turbidity spikes (Payment *et al*. refer to them as microfailures) were identified during a one-month period and for short periods on other occasions. Whether the plant's effluent met the IESWTR requirements 95th % level of 0.3 NTU is difficult to say because only an average (not a 95%) combined filter effluent value is reported. *Giardia* was detected in filtered water in one of 32 samples, and *Cryptosporidium* in 7 of 32 (22%) samples; however, no pathogens were detected in finished water (clear well). Filtration reduced the geometric mean of 14 oocysts/100 L measured in raw water to a geometric mean of 0.3 oocysts/100 L in the filtered water, a 1.7 log reduction.

The detection of *Cryptosporidium* in filtered water is more common than might be expected based on the levels of *Cryptosporidium* measured in source water and the performance level assumed of the filtration process (2–3 logs on average for conventional filtration). In a recent study that summarized *Cryptosporidium* results in filtered water from 9 studies based on microscopic detection of oocysts (immunoflorescent antibody detection) the median percentage of positive samples was 17% (ranging from $<1\%$ to 46.2%) with maximum concentrations ranging from 0.8–48 oocysts/100 L (Aboytes *et al.* 2004). The main focus of the Aboytes study, however, was on infectious *Cryptosporidium* measured in the filtered water of 82 treatment plants using a different analytical method, cell culture–polymerase chain reaction, than detect live infectious oocysts and identify the species and strains (genotyping and subgenotyping). The study found that infectious oocysts were detected in 26.8% of the treatment plants and more than 70% of the positive samples were measured in filtered water samples of <0.1NTU and 20% were in water with a turbidity of <0.05. Clearly, even achieving very low effluent turbidity does not guarantee the absence of infectious oocysts in plants treating contaminated source water.

Disinfectant residual was not always present in distribution system samples collected in the service areas most distant from the Laval treatment plant; however, 99.4% of samples collected during the Laval study were free of total coliform, and no fecal coliforms were detected. Although the TCR requirement of no total coliforms in 95% of samples is based on monthly analysis, not analysis over a longer time period as reported by Payment *et al*. the 99.4% of samples testing negative makes compliance with the TCR more likely than not.

Further consideration of the link between microbial risk factors reported in the Laval studies (referred to as Laval 1 and 2) and the AGI results lead us to consider how they

Table 4 | Description of system water quality and treatment during epidemiology study

System, period of study	Source type and water quality	Post treatment microbial water quality	Treatment type and performance	Distribution system
Laval, Quebec 1988–1990	Sewage contaminated river water, including combined sewer overflows within 25 km upstream during heavy precipitation, weekly samples – mean concentrations reported: enteric viruses 78i.u. /100L),	Weekly samples Post filtration measured at plant:	Conventional filtration and pre- and post-disinfection (ozonation followed by chlorine or chlorine dioxide), treated water leaving plant: residual always presnt, averaging 0.6 mg/L total chlorine, and approximately 0.4 mg/L free chlorine.	Weekly samples were collected in distribution system for bacteriologic parameters: No bacterial or disinfectant residual results reported. Author reports that system is in compliance with 1979 US drinking water regulations (monthly average plant effluent of 1 NTU, the absence of fecal coliforms, and in majority of distribution system samples, the absence of total coliforms)
	Aerononas hydrophila 6,590 cfu/L	No coliforms, no enteric viruses detected	Filter performance: average leaving plant 0.26 NTUs and "only rarely >0.5NTUs.	
Data from references 1 and 2 below	*Clostridium perfringens* 623 cfu/L total coliforms, 57,530 cfu/L, fecal coliforms 3,674 cfu/L			
Laval, Quebec 1993–1994	Source description – same as above. Data from 33 bi-weekly samples	Data from 33 bi-weekly samples:	Same type of treatment as above, but plant was subject to "major overhaul, and quality of treatment was significantly enhanced, especially at the disinfection stage for both ozonation and final chlorination". Estimated *Giardia* removal/inactivation far exceeded SWTR 3-log requirements (min reported estimate of 7.4 logs). Estimated inactivation of viruses by chlorine alone always exceeded 10 logs. Turbidity leaving treatment plant averaged 0.1 NTU and never exceeded 0.5 NTU, but periods of "microfailures" in individual filter banks reported.	Distribution system: 99.4% of samples free of total coliforms, no fecal coliforms detected, but disinfectant residual not always present in some parts of distribution system.

Table 4 | (*continued*)

System, period of study	Source type and water quality	Post treatment microbial water quality	Treatment type and performance	Distribution system
Data from references 3 and 4 below.	Pathogen concentrations:	Post filtration, pre-disinfection - Geometric mean:		From Awwarf report on system B (ref 4): system subject to low-pressure transients when opening fire hydrant, significant pressure drops indicated potential for development of low and negative pressure transients.
	Geometric mean: enteric viruses 410 mpniu/100 L *Giardia* 200 cysts/100 L, *Cryptosporidium* 14 oocysts/100 L	No enteric viruses detected		
	Somatic coliphages 27 000 pfu/100 L, *C. perfringens* 2330 cfu/L No coliform data reported	*Giardia* - 0.2 cysts/100 L *Cryptosporidium* 0.3 oocysts/100 L Somatic coliphages 15 pfu /100 L, *C. perfringens* 0.3cfu/L Post disinfection: none of above pathogens/indicator organisms detected.		
Davenport, IA 2000 –2002	River water subject to upstream sources of fecal contamination, ave/median/max values: enteric viruses (MPN/100 L) 6.72/1.02/37.99)	Post-Treatment	Conventional filtration with chlorine pre-disinfection and addition of ammonia post filtration. Daily mean (range) turbidity leaving treatment plant averaged 0.05 (0.03 – 0.09) NTU. Some evidence of individual filter "microfailure" defined as daily average turbidity > 0.15 NTU.	Total chlorine residual detected in all distribution system samples
Data from references 5 and 6 below.	*Giardia* (cysts/100 L) 9/ 0 /110	Enteric viruses – none detected in 19 samples		TC + sample rare (2/2471) No FC/EC +
	Cryptosporidium (oocysts/100L) 2/0/30	*Cryptosporidium* – none detected in 71 samples using cell culture – PCR		System subject to negative pressure transients when pump shut down
	Somatic coliphages (pfu/100 L) *192 000/102,000/1645 000*	Somatic coliphages – none detected in 69 samples		

Table 4 | (*continued*)

System, period of study	Source type and water quality	Post treatment microbial water quality	Treatment type and performance	Distribution system
	C. perfringens (cfu/L) 416/250/4100	No coliforms detected in 408 samples		
	Total coliform (cfu/L) 46 200/20 880/350 000			
	Fecal coliform (cfu/L) 3420/1130/44 800			
Melbourne, AU, 1997 – 1999 Ref. 7	Protected watershed (no agriculture, human habitation or recreation), minimum of 12 months storage before use. No data on pathogenons in source water but water not considered "pathoge free" because fecal coliforms detected in reservoirs, typically 23% and 45% of 100 ml samples test positive.	68 weekly pooled water main samples: no No samples positive for *Clostridium perfringens* spores *No Cryptosporidium* detected (0/68 samples), viable *Giardia* detected (2/68).	No filtration, only chlorination.	Free chlorine residual in distribution system ranged from 0 to 0.94.mg/L, median 0.05 mg/L, 90^{th} pct <0.2. Total chlorine ranged from 0.01 – 1.1 mg/L, median 0.08 mg/L, 90^{th} pct <0.2 mg/L
		No analysis for viruses		No fecal coliforms detected in 1167 routine distribution system samples, 18% positive total coliform., 5.4% with >10cfu/ 100 ml

References: 1. Payment *et al*. (1990); 2. Payment *et al.* (1993); 3. Payment *et al.* (1997); 4. Kirmeyer *et al.* (2001); 5. Colford *et al.* (2005); 6. LeChevallier *et al.* (2004); 7. Hellard *et al.* (2001)

influence our perception of national level drinking water related microbial risk and illness in 2004 and what the range of AGI incidence might be for our analysis.

Characterizing how AGI relates to microbial risk factors is extremely complex and there are many unknowns in trying to quantify the risk: (1) we do not know the distribution of the different pathogens in source water, (2) different pathogen species and even strains of the same pathogen species vary in their ability to infect and cause illness, (3) different categories of waterborne pathogens (viruses, protozoa) respond differently to filtration and disinfection, and (4) the significance of differences between theoretical treatment performance and actual treatment performance is not well understood (e.g. the influence of treatment upsets on overall performance or differences between inactivation of viruses under laboratory conditions and in the treatment plant). While the risk implications of filtration treatment failure rate have probably been reduced due to the IESWTR and LT1, the risk implications of disinfection efficacy are less clear, especially for viruses.

In order to estimate the variability of microbial risk and AGI one needs to better understand the risk implications of these source and treatment variables. However, given our current knowledge, it is not possible to directly estimate the range of variability of risk. For our analysis, we use an indirect approach considering the Laval study results and the source/treatment risk factors in the context of what we know about other surface water systems in the US. For example, HCGI incidence due to drinking water in US. systems range could range from the 0.3 to 0.000 003 cases per person-year (i.e. from 3 in 10 cases to 3 in 100,000 cases attributable to drinking water).

- Laval 1 is an example of a system close to the upper end of this range (with 0.26 cases per person-year). Nationally, it falls at the high end of a range of mean source water risk with less than average treatment, i.e. probably meets SWTR but not the IESWTR.
- The other end of the range is based on source water pathogen levels measured in surface water systems in the US that vary in concentration up to 5 logs (discussed earlier).

In the following section on model development we propose a distribution to represent the variability of microbial risk and AGI on a national level that is based on the range of microbial risk described above.

Modeling considerations

Given the baseline incidence of AGI from all causes we need to estimate the fraction of the baseline AGI estimate that may be attributed to drinking water to derive a national estimate. We use a model that includes the steps described in this section.

Step 1: We assume a certain but unknown rate of AGI illness in each CWS is due to drinking water and further assume that the AGI incidence due to drinking water has a source/treatment component and a distribution component. In step 1, we estimate the relative proportions of source/-treatment risk and distribution system risk.. The AGI illness due to drinking water in each community is the sum of incidence due to pathogens present in water as it leaves a drinking water treatment facility (source/treatment risk) and the incidence due to entry of pathogens into the distribution system via deficiencies such as cross-connections, intrusion events, biofilm related organism growth and sloughing (distribution system risk).

What evidence or indicators do we have on the magnitude and variability of AGI and the relative importance of risk factors that vary among communities? Outbreak data provide an indication of AGI due to different microbial risk factors, including deficiencies ranging from lack of treatment in groundwater systems to treatment deficiencies and distribution system deficiencies in both surface water and groundwater systems. Analysis of outbreak reports since 1971 shows a decline in the percentage of outbreaks due to treatment deficiencies, in particular in surface water systems, and an increase in the percentage of outbreaks due to distribution system deficiencies (Craun *et al.* 2006). The decline in outbreaks due to treatment deficiencies probably reflects a national trend in the incidence of endemic AGI due to changes brought about by increasingly stringent treatment requirements and a better understanding of the factors that affect drinking water associated microbial risk from research in this area.

Although outbreaks provide useful information on national trends, it is difficult to use this trend information to derive a national distribution of endemic waterborne disease incidence. For our national estimate approach, we believe that

national endemic AGI illness rates can be more appropriately estimated by examining the prevalence of microbial risk factors and the effect of drinking water regulations.

In developing microbial regulations, we model the risk of illness based on a few specific target pathogens, e.g. *Cryptosporidium* for the IESWTR and LT1. The models use information on the occurrence of pathogens in source water, information on treatment effectiveness and a dose–response model to estimate the number of cases of illness due to drinking water, e.g. Cryptosporidiosis (AGI due to *Cryptosporidium*). Based on these models, we have estimated national baseline pathogen-specific illnesses and reductions in illnesses from baseline levels resulting from the SWTR, and the IESWTR/LT1. Even though the regulations undoubtedly reduce other pathogens in addition to the target pathogen, these models are not designed to estimate the rate of AGI due to all drinking water pathogens that cause AGI. Despite the deficiency in the regulatory model for quantifying the reduction in a mixture of pathogens and associated illness due to drinking water at the national level, the regulations, and the studies conducted to support them, provide a solid knowledge base on source water associated microbial risk and treatment performance.

The main reason we separate risk due to source water and treatment deficiencies from risk due to distribution system deficiencies is to recognize that there are different factors that relate to the potential risk from each of these components of the risk paradigm. We considered these risk components to develop our model and recognized availability of a robust data set at the national level on source water and on the type and effectiveness of treatment in systems that must meet the SWTR, IESWTR and LT1 treatment technique requirements. We have no similar national base of knowledge that would allow us to quantify groundwater or distribution system risk factors. Moreover, we know much less about the relative importance of different types of distribution system deficiencies.

Step 2: We estimate the shape of the distribution (type and spread) of relative microbial risk based on an assessment of data pertaining to source water quality, treatment performance, and distribution system characteristics. We have discussed some of the issues on relative differences in community microbial risk based on data from the ICR, inferences based on compliance with regulations, and inferences on the magnitude of distribution system risk, all of which are elements that contribute to developing a national distribution of CWS drinking water microbial risk. We will now discuss an approach to quantifying the range of national microbial risk and the shape of the cumulative national microbial risk distribution curve.

For this step of the model development, we use a lognormal distribution of source/treatment and distribution system deficiency attributable mean AGI incidence rates. Lognormality is a reasonable assumption considering factors including source water variability, variability of treatment efficacy, and the differences between treatment facilities with respect to their likelihood of upsets and/or treatment failures. We discuss these factors below.

Environmental measurement data usually exhibit considerable asymmetry and are generally restricted to be non-negative. The normal distribution is not appropriate for these cases because it is symmetric and allows concentrations to fall below zero. The lognormal, Weibull, gamma, and beta distributions can be]tter describe environmental data and are often employed for this purpose (Gilbert, 1997). Of these, the lognormal appears to be the most popular. An online search for "log-normal distribution" or "lognormal distribution" in conjunction with the words "environmental," "concentration," and "risk" returned more hits on Google (www.google.com) than do the Weibull, gamma, or beta distributions:

Google search results, February 13 2006

Distribution	+ concentration and environmental and risk
Lognormal	28 300 citations
Log-normal	22 300 citations
Weibull	11 800 citations
Gamma	11 300 citations
Beta	841 citations

(NOTE: The word "distribution" was used in each case. Searches for "Gamma" without "distribution" returned many citations that addressed the risks of gamma radiation and other cases not related to distributional modeling.)

The log normal model appears to be the commonly selected model to represent environmental data based on this search; we will present more data below on why it is an

appropriate model for estimating microbial risk due to drinking water in our discussion of our analysis

Analysis of ICR *Cryptosporidium* source water densities indicates that the mean concentrations are reasonably represented by a lognormal distribution with a geometric standard deviation equal to $e^{2.35}$, which is approximately 10 (Messner & Wolpert 2002). ICR source water data for *Giardia*, enteric viruses, and *E. coli* concentrations also varied approximately according to a lognormal distribution.

Cryptosporidium densities in source waters for large and medium size systems in the ICR Supplemental Surveys (ICRSSs) also demonstrated lognormality with inter-location variability equivalent to geometric standard deviation ranges of approximately $e^{1.2} = 3.3$ and $e^{1.6} = 5.0$, respectively (US EPA 2003). The ICRSS collected source water data from a randomly selected sub-set of ICR systems (40 of 360 ICR systems or 11%) and medium size systems (40 of 2043 or 2%) using a methodology that reduced variability between samples by analyzing equal size sample volumes.

Thus, based on the ICR data, 95% of surface water systems have mean influent *Cryptosporidium* concentrations that fall within a factor of 10,000 (four log range). At the other extreme, the ICRSS estimates suggest that 95% of surface water systems have mean influent concentrations that fall within a factor of 100 (two log range). These observations are illustrated in Figure 1.

Cryptosporidium and other source water pathogens must overcome a number of barriers if they are to infect humans through the drinking water route. They must survive such physical treatment processes as coagulation, settling, and filtration. They are challenged by chemical disinfection in the distribution system, and can encounter additional barriers after they leave the tap (freezing, heating, in-home filtration). Finally, the pathogen must survive the human host's defenses (saliva, stomach acid, intestinal flora, antibodies) before it can initiate infection. Let $p[i]$ = the probability that a pathogen can survive barrier i in a community. If C is the pathogen concentration in the drinking water source, then $C[\text{tap}] = C \times p[1] \times p[2] \times \ldots \times [\text{tap}] = C \times p[1] \times p[2] \times \ldots \times p[n]$ will be the concentration following the n barriers it must pass before arriving at the tap. If all terms of that expression (C and all of the p's) are lognormally distributed across some set of drinking water systems, then their product, the tap water concentration, will also be lognormally distributed.

The mean HCGI incidence rate associated with distributed water from each treatment plant is proportional to the influent pathogen concentration and attenuation during water treatment. Thus, we assume that the mean rate of AGI attributable to drinking water from the source/treatment portion of CWSs is also approximately lognormal.

In this paper we characterize treatment variability (including brief periods of treatment upsets) in surface water systems, as having a mean pathogen reduction (combined physical and chemical) that ranges from 2–6 logs. When variable treatment performance and reliability are included, predicted variability of pathogen densities in finished water could be greater than their variability in the influent. Thus, for this analysis, we assume that the variability of the source/treatment attributable illness distributions are such that 95% of systems range from a low of 2 logs ($AR_{97.5\%}/AR_{2.5\%} = 100$) to a maximum of 5 logs ($AR_{97.5\%}/AR_{2.5\%} = 100{,}000$).

As previously discussed in the section on the analytical framework, we assume the same variability (2–5 log) for AGI due to drinking water is reasonable, given data on microbial risk factors and recognizing limited data are available on the range of AGI and microbial risk nationally.

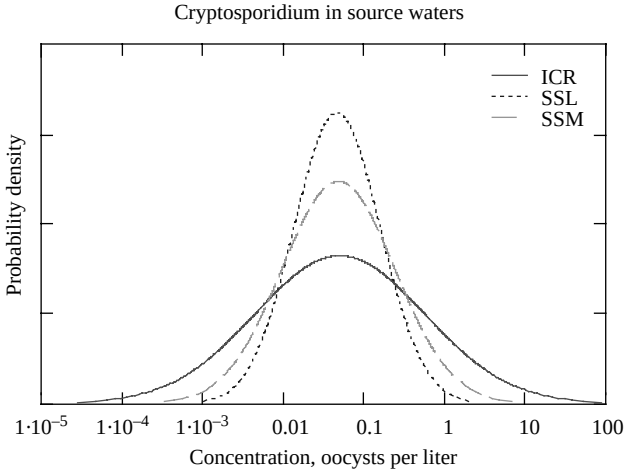

Figure 1 | Distributions of *Cryptosporidium* concentrations in source waters from Information Collection Rule (ICR) and ICR Supplemental Surveys (ICRSS).

For our present analysis, we assume that the range of source/treatment microbial risk and its variability apply equally to the populations served by CWSs that provide filtered surface water, unfiltered surface water and groundwater.

We also assume that the separate national distribution of distribution system related microbial risk has the same range and variability as the source/treatment microbial risk distribution (recognizing that limited data are currently available on distribution system related risk).

Step 3: We estimate a statistical distribution of AGI due to drinking water among all CWS in the US based on the distribution of relative microbial risk and considering data from epidemiology studies for individual CWSs. With the shape (type and spread) of the cumulative distribution of drinking water associated microbial risk established, the next step is to establish a link between the population's microbial risk exposure and the incidence of AGI associated with that exposure. In establishing this link, we rely on data from epidemiology studies on the incidence of AGI attributable to drinking water and the information on the level of microbial risk in the study community. We use this data to inform the placement of the study community in a cumulative national distribution of microbial risk. A key assumption in this step is that the range and the shape of the microbial risk distribution and that of the associated AGI distribution are the same.

We assume that characteristics of the source/treatment microbial risk distribution (developed based on data and analyses of microbial risk factors from communities served by surface water systems) also represents the distribution of the population served by CWSs (both groundwater and all surface water systems). This assumption allows us to translate 1:1 a percentage of CWSs to a percentage of the population. For filtered surface water systems this approximation may not be unreasonable because the data that informed the distribution was based on treatment plants that served similar sized populations (at 100,000 persons). The other assumption that we make is that the relative level of microbial risk translates directly to the relative level of HCGI risk. Quantifying the level of HCGI risk is where the positive results of epidemiology studies are required.

Theoretically only one data point (i.e. from one community) is needed to convert the level of population microbial risk exposure to a level of AGI attributable to drinking water. However, given the uncertainties in establishing levels of microbial risk at a national level and the uncertainties associated with establishing the incidence of AGI attributable to drinking water in a single community, one could produce a more robust estimate and increase the level of confidence in developing a national estimate using results from multiple studies in a range of different types of systems.

To date, only two household-intervention studies produced estimates of HCGI incidence attributable to drinking water that can be used in our analysis–the two studies conducted in Laval. Although we provide a summary of the data from all four studies in Tables 1 and 4, the main focus of this paper is on the two Laval studies. These are the studies that we use in our modeling approach.

The results of the Davenport study (no incidence of AGI attributable to drinking water) could not be incorporated into a model similar to the national estimate analysis based on the Laval studies. For studies in which no drinking water attributable illness was detected, we considered modifying the approach used in the Laval model to make use of professional judgment on the uncertainty of the estimate of disease incidence below the level of detection of a study. Information that might influence opinions on the likelihood of illness might include information on the participants (e.g. their compliance with the assigned intervention, the change in illness reporting over the duration of the study, the participant exclusion criteria) and drinking water microbial risk factors. Both the Davenport study and the Melbourne study did not detect any disease attributable to drinking water; they could not detect AGI attributable to drinking water unless its incidence was greater than 11% of all AGI cases (due to all causes) in the Davenport study, or 15% in the Melbourne study. We developed an estimate with a modification to the Laval model, using a Bayesian analysis, that relies to a great extent on the professional judgment of the authors and other EPA staff to develop a prior estimate of AGI due to drinking water and a likelihood function. An example of this approach applied to the Davenport study is provided in Appendix B as an example for discussion of the approach.

MODEL APPLICATION OF THE CONCEPTUAL APPROACH: AN ESTIMATE OF THE NATIONAL HCGI INCIDENCE DUE TO DRINKING WATER

Inputs to the model application (Steps 1 and 2)

Step 1: We assume a certain unknown mean rate of AGI illness in each CWS is due to drinking water and further assume that the mean AGI incidence due to drinking water has a mean source/treatment component and a mean distribution component as detailed below. In step 1, we estimate the relative proportions of mean source/treatment risk and mean distribution system risk. Unless specified otherwise in our discussion of a national distribution of drinking water attributable AGI and drinking water related microbial risk, all rates of illness and microbial risk are means.

In step 1, we decompose the mean microbial risk and mean HCGI incidence into a source/treatment associated component and a distribution system associated component. The mean AGI illness due to drinking water in each community is the sum of the mean incidence due to pathogens present in water as it leaves a drinking water treatment facility (source/treatment risk) and the mean incidence due to entry of pathogens into the distribution system via deficiencies such as cross-connections, intrusion event, biofilm related organism growth and sloughing (distribution system risk). Having decomposed the incidence of mean HCGI into source/treatment and distribution system components, we develop two lognormal national distributions of mean microbial risk: one due to mean source/treatment microbial risk and one due to mean distribution system risk. The following section describes Step 1 in our analysis based on the Laval studies.

Inference to source/treatment and distribution system risk from the Laval household-intervention studies

In our analysis, we use information from both of the Laval household-intervention studies. In evaluating the Laval studies to perform step 1, we first approach defining the distribution system associated component and then move to the source/treatment component, as described in this section of our paper. We use the reported HCGI incidence attributable to drinking water from the first Laval study (Payment *et al.* 1991) as an input parameter in our modeling effort. We only use the second Laval study (Payment *et al.* 1997) to inform our consideration of the incidence of HCGI reported in the first study so that we can decompose the first study's reported incidence into source/treatment associated HCGI and distribution associated HCGI for our model. It may seem counter-intuitive to only directly use data from one of the studies for model input–our discussion below clarifies how data from the studies converge in our analysis.

The two Laval studies provide a unique dataset–two household-intervention studies conducted at the same location at two different points in time with observed incidence of HCGI due to drinking water above the detection level in both studies. We take advantage of this combined dataset in our analysis to quantify one of the variables in the model–the level of HCGI associated with distribution system microbial risk. We do this by interpreting the difference in incidence due to drinking water between the two studies as reflective of changes in water treatment that reduce the level of microbial risk.

Payment *et al.* (1991, 1997) observed important differences between the first and the second study that relate to the source/treatment vulnerabilities of the Laval system–these differences inform our assumptions on the microbial risk components of our model. The authors reported improved disinfection and filtration performance during the second study (described above and summarized in Table 4). By contrast, no changes were reported in the distribution system's vulnerability. We do not know whether the microbial risk conditions presented by the distribution system were the same during both study periods, but for the purpose of this model application, we assume that any changes in distribution system microbial risk (or changes in other factors that could influence the estimate of HCGI) were of minimal significance, compared to the changes in source/treatment vulnerability, and would have a negligible effect on the reported incidence of HCGI due to drinking water.

Source/treatment versus distribution system attributable HCGI

The results from the two studies conducted in Laval (Table 1) indicate that there was a reduction in the waterborne HCGI rate between the two study periods

(from 0.26 compared to 0.08 cases per person-year). As described above, we presume that the reduction in waterborne HCGI incidence between the first and the second Laval studies was due primarily to major improvements in water treatment performance, and that the incidence of HCGI due to distribution system deficiencies did not change between the two studies.

Based on our assumption that the difference in drinking-water-related HCGI between the first and the second studies was due to improved water treatment and that there were no changes in distribution system attributable HCGI, we conclude that the HCGI rate from the distribution system was not greater than 0.08 (the HCGI rate due to drinking water observed in the second study). Given that the author discusses periods of filtration "microfailure," it is unreasonable to assume that no illness whatsoever was attributable to treatment deficiencies. We therefore assumed that on average half of the measured HCGI incidence could be attributable to treatment deficiencies (0.04 cases per person-year) with the other half due to the distribution system deficiencies. We set bounds around each estimate of 0.02–0.06 cases per person-year.

Now, having developed our estimate of HCGI due to deficiencies in the Laval distribution system, we can proceed with the development of the input parameters for a model based on the first Laval study. We assume that the waterborne HCGI rate observed during the first study (0.26 cases per person-year) was the sum of HCGI arising from the distribution system (on average 0.04, and ranging from 0.02–0.06 cases per person-year) and the HCGI arising from the combined effects of poor source water quality and inadequate source water treatment (source/treatment component) (complementarily ranging from an average of 0.22, and ranging from 0.20–0.24 cases per person-year).

Step 2: We estimate the shape of the distribution (type and spread) of relative microbial risk based on an assessment of data pertaining to source water quality, treatment performance, and distribution system characteristics. As described under step 2 of the modeling considerations, we propose to use separate lognormal distributions to represent the variability (or spread of the distributions) of community source/treatment and distribution system microbial risk. It is also important to remember at this point that in carrying out Step 3 of our analysis as described below we assume the mean HCGI incidence rates attributable to source/treatment and distribution system microbial risk vary from system to system, are directly proportional to the level of microbial risk, and can also be modeled as lognormal random variables.

The shape of the model is also defined by its spread or range. In our model application, we assume that 95% of microbial risk and AGI due to source/treatment deficiencies, and similarly 95% of microbial risk and AGI due to distribution system deficiencies, range on the order of 2–5 logs.

Model application (Step 3)

Step 3: We estimate a statistical distribution of AGI due to drinking water among all CWS in the US based on the distribution of relative microbial risk and considering data from epidemiology studies for individual CWSs. As we describe in our discussion of model considerations, the focus of step 3 is to establish a link between the population's microbial risk exposure and the incidence of AGI associated with that exposure. In this step, we use a Monte Carlo simulation methodology to estimate the national distribution of HCGI incidence (cases per person-year) associated with drinking water from CWSs based on the results of the intervention trials carried out in Laval. Before we describe the Monte Carlo modeling effort, we present information on our understanding of relative microbial risks for community water systems in the US and how we use this information to compare the Laval system to US CWSs. We also describe how we used professional judgment and our related assumptions to transition from comparing microbial risk in US systems and Laval (or "placing" Laval) to characterizing a national distribution of HCGI attributable to drinking water.

In transitioning to step 3 (our modeling approach) it is important for the reader to recognize a set of key assumption in our analysis. In step 2 we recognized that both HCGI and microbial risk vary from system to system and can be modeled as lognormal distributions. In developing the model, we make the following assumptions:

- We accept the distribution of CWS source/treatment and distribution system microbial risk (type and spread) and

consider the risk factors that were used in developing the spread in our "placement" of the Laval system within those distributions, considering its microbial risk characterization.

- We assume that the distribution of CWS microbial risk is the same distribution as the distribution of population exposure to microbial risk, i.e. that the distribution represents the risk that would be experienced if all of the information from CWSs that informed the distribution served the same-sized population.
- We assume that the range and the shape of the microbial risk distribution and that of the associated HCGI distribution are the same.
- In placing Laval, we can use the HCGI incidence due to drinking water from the study (and our assumptions regarding the proportion related to source/treatment risk and distribution system risk) to perform the model simulations and generate a distribution of expected mean HCGI incidence associated with drinking water from CWSs.

Microbial risk distribution and HCGI in filtered and unfiltered surface water systems

Approximately 94% of the US population served by surface water systems is served by systems that filter and disinfect their source water. Most filtered surface water systems in the US have a number of characteristics in common with those in Laval. That is, the majority of the public is served by CWSs that have a surface water supply and a centralized treatment system consisting of complete conventional treatment (flocculation, settling, filtration) and disinfection (271 of the 346 ICR plants, or 78%, used conventional treatment, Frey *et al.* 2002). The remaining filtered systems have some other type of treatment process, e.g. in-line or direct filtration, softening, slow sand filtration, membrane filtration. All surface water systems are required to disinfect the water to meet treatment requirements at the entry point to the distribution system.

Parallel regulations for unfiltered systems (serving the remaining 6% of the surface water population) require a similar level of microbial protection. Unfiltered systems are required to have very high quality source water (e.g. low maximum levels of both source water turbidity and indicators of fecal contamination) and protected watersheds. Currently, the water reaching the consumer in some of the unfiltered surface water systems may present a higher risk of HCGI than high quality filtered water due to parasites such as *Cryptosporidium* (because of their resistance to chemical disinfection) (US EPA 2003).

Although protection provided by the SWTR and the IESWTR regulations may not be equivalent, for the purpose of this analysis, no difference in the distribution of HCGI attributable to drinking water is assumed between filtered and unfiltered surface water systems in the US. In 2004, 4.45% of the population served by surface water systems did not fully comply with the SWTR treatment requirements, and a total of 4.5% did not comply with both the SWTR and the IESWTR, i.e. at least 4.45% of the population during at least one month were provided drinking water from systems with treatment that did not meet the minimum treatment requirements for *Giardia* and virus reduction (3 log and 4 log, respectively). At the other end of the treatment performance scale are some of the systems that have successfully adopted treatment management practices to optimize the performance of their filtration process with a goal to maintaining their plant effluent turbidity below 0.1 NTU and maintain a free chlorine *CT* to inactivate viruses. We do not know the percentage of the population served by such systems.

When the treatment and source water protection requirements in the recently promulgated LT2 rule are implemented both unfiltered and filtered systems with high levels of *Cryptosporidium* in their source water will be required to provide additional treatment to reduce the associated risk, thereby equalizing, or at least reducing, risk among surface water systems.

Microbial risk and HCGI distribution in groundwater systems

Groundwater systems are subject mostly to contamination by viruses and bacteria, both of which can be reduced by disinfection; however, there are no Federal regulations that require disinfection of groundwater that is vulnerable to contamination. Some groundwater systems (groundwater under the direct influence of surface water or GWUDI) are also subject to contamination by larger pathogens, e.g. *Giardia* and *Cryptosporidium*, and are required to comply

with the SWTR treatment requirements. However, not all systems that are vulnerable to contamination from surface water or from storm run-off are identified as GWUDI, and may therefore present a higher risk of AGI than surface water systems with contaminated source water.

There have been no household-intervention studies in communities served by groundwater systems. Hence, HCGI incidence data for CWSs using groundwater and GWUDI are virtually non-existent, with the exception of the evidence of a high level of microbial risk evident in systems that experienced outbreaks due to lack of treatment or deficient treatment. The relatively much higher rate of outbreaks occurring in untreated ground water systems in 2001–2002, as compared to surface water systems is an indication that untreated groundwater systems may present an even higher risk of HCGI than some of the high risk surface water systems. These untreated GW systems serve serving approximately 10% of the groundwater population. While acknowledging evidence from outbreak data on potential risk from untreated groundwater, we recognize the sparseness of data on a national level to characterize source water pathogens and treatment levels in groundwater systems. For the purpose of this example estimate, we assume that the distribution of microbial risk and the associated distribution of HCGI incidence due to groundwater is described by the same distribution as that of surface water microbial risk and associated HCGI.

Characterizing the national estimate based on professional judgment and the Laval intervention studies

As described above, for the purpose of this analysis, we assume that the variability of community source/treatment and distribution system microbial risk is represented by two lognormal distributions. Here in step 3 of our analysis, we also assume that the related mean HCGI incidence rates attributable to source/treatment and distribution system microbial risk vary from system to system and can be modeled as lognormal random variables.

HCGI incidence associated with source/treatment and HCGI associated with distribution system components are represented by independent lognormal distributions. The "placement" of a system within the national distribution is based on our professional judgment, considering the drinking water risk factors of the Laval system in the 1980 s (as described in Payment *et al.* 1991, 1993), and how those factors compare to those of other systems in the US.

Given the source water and water treatment conditions in Laval during the first household-intervention study, we assume that, under conditions in 2004, the Laval system's level of source/treatment microbial risk belongs somewhere in the upper 10% of US systems' source/treatment microbial risk distribution. Specifically, we assume that the mean waterborne HCGI incidence rate for the first Laval study is ranked between the 90th and the 99.5th percentile of all US systems. Our decision on the placement of the 1980 s Laval system is based on the extreme level of source water contamination, combined with a level of treatment that in 2004 would be considered below average and out-of-compliance with the IESWTR. Illustrative of the extreme level of source water contamination is the mean virus concentration of 78 infectious units/100 L, a level exceeded by only one of the 207 ICR plants that monitored viruses in their source water.

Among the other systems in the upper 10% of source/treatment microbial risk are those surface water systems in violation of the SWTR and IESWTR as well as other surface water systems not reported in violation of surface water regulations. We assume that a smaller percentage of the population served by groundwater systems and unfiltered systems would also be placed within the top 10% of microbial risk. Whether our placement of Laval assumption is reasonable in the context of considering groundwater microbial risk, is difficult to judge without more data, but as previously explained, for the purpose of this example estimate, we assume that groundwater and surface water microbial risk/HCGI incidence distributions are identical.

Information on microbial risk related to the distribution system is of a more qualitative nature relative to source/-treatment risks. Payment *et al.* (1991, 1993, 1997) report several potential microbial risk factors present in the Laval distribution system during the studies, e.g. mains breaks, exceptionally cold temperatures, and no residual disinfectant in areas most distant from the treatment plant. Based on the general lack of similar risk factor information on distribution systems on a national level (as well as the uncertainty in the relative importance of the risk factors),

we assume a greater degree of uncertainty in the placement of the Laval distribution system relative to current US systems. For the purpose of this analysis, we assume that the mean waterborne HCGI incidence from the Laval study distribution systems is ranked between the 50th and the 99th percentile of all US systems. It is more difficult to judge the placement of Laval in the national distribution of distribution system risk given the lack of information on the relative importance and relative prevalence of distribution system risk factors on a national level. Hence, we assume a broader range in placement of Laval in the national distribution system risk distribution than in the national source /treatment distribution.

Monte Carlo analyses

We employed a Monte Carlo simulation methodology to estimate the national distribution of HCGI incidence (cases per person-year) associated with drinking water from CWSs based on the results of the intervention trials carried out in Laval. In each simulation, one distribution of HCGI incidence was generated based on the risk associated with source/treatment characteristics and a second distribution of HCGI incidence was generated based on the risk associated with water distribution system characteristics.

The expected mean HCGI incidence from each simulation was computed as the sum of the mean values from those two distributions. This approach was repeated 10,000 times to generate a distribution of the expected mean HCGI incidence associated with drinking water from CWSs. Random variables used in the Monte Carlo simulation are summarized in Table 5.

Uniform distributions are used because, when considering any two ranges of equal size (within the stated boundaries) for a parameter, we agreed that they were equally likely (or equally unlikely) to contain the true parameter value. Note that the HCGI incidence attributable to the distribution system is not shown in Table 5. It is not included in the table because it is computed as the observed drinking water attributable HCGI incidence due to source/treatment and distribution system combined (0.26 cases per person-year) minus the HCGI rate selected within the range of Laval source/treatment associated HCGI (0.20 – 0.24). Therefore, the HCGI incidence attributable to the distribution system microbial risk varies from simulation to simulation. The process used to generate the national estimate based on Laval data is described in detail in Appendix A.

The cumulative distributions of national average attributable incidence rates (one for source/treatment, one for distribution system, and one for the total attributable incidence) for the Laval-based simulations are presented in Figure 2. These cumulative distributions present the uncertainty about the national average HCGI incidence attributable to CWSs as well as the source/treatment and distribution system components that comprise that risk.

Inspection of Figure 2 reveals that the slope of the source/treatment curve is steeper than the distribution system curve because there is greater uncertainty about the rate of HCGI attributable to distribution systems compared to that attributable to the source/treatment component.

The results of the national estimate analysis described below are summarized in Table 6. Based on our analysis, the estimated mean national incidence of HCGI attributable to drinking water is 0.11 cases per person-year with a 95% credible interval of 0.03 – 0.22. The mean national incidence attributable to the distribution system was 0.062 cases per person-year with a 95% credible interval of 0.005 – 0.16 cases per person-year, and mean national incidence attributable to source/treatment was 0.048 cases per person-year with a 95% credible interval incidence of 0.011 – 0.086 cases per person-year.

How does an incidence of 0.11 cases of HCGI per person-year relate to the overall incidence of 0.72 cases of AGI illness per person-year measured in the cross-sectional survey conducted by the FoodNet program in 1998 – 1999? If we assume, as discussed in section 1.2, that the incidence of HCGI due to all causes is similar to the 1.3 cases per person-year incidence of AGI episodes (or diarrheal episodes, to be more precise since the vomiting alone was not included in the case definition), then the percentage of episodes due to drinking water would be 8.5% (with a 95% credible interval of 2.3% and 17%). If we further assume that causal relationship remains the same for both the more inclusive AGI episodes and the more serious AGI illness (symptoms lasting more than 24 hours or resulting in impairment to normal daily activities) then we can also

Table 5 | Random variables used in Laval based Monte Carlo simulations

Variable	Distribution and parameters	Units
HCGI illness rate attributable to source treatment in first Laval study ('88-'89)	Uniform [0.20, 0.24]	Illnesses/personyear
Ranking of Laval source / treatment in '88-'89 relative to current US systems	Uniform [0.90, 0.995]	Unitless
Ranking of Laval distribution system ('88-'89)relative to current US systems	Uniform [0.5, 0.99]	Unitless
Variability of source treatment HCGI illness distribution	Uniform [2.0, 5.0]	log units. Corresponds to log10(97.5th %ile / 2.5th %ile)
Variability of distribution system HCGI illness distribution	Uniform [2.0, 5.0]	log units. Corresponds to log10(97.5th %ile / 2.5th %ile)

assume that 8.5% of AGI illness is attributable to drinking water. Based on these assumptions we estimate that the incidence of AGI illness due to drinking water is 0.06 cases per person-year (with a 95% credible interval of 0.02 – 0.12). The incidence of AGI illness due to source/treatment deficiencies and distribution system deficiencies with their respective 95% confidence intervals are 0.03 (0.006, 0.05) and 0.03 (0.003, 0.09), respectively.

The results presented above indicate that in a community of 100,000 people, it would be expected that over a 1-year period the community would experience approximately 72,000 cases of AGI illness (0.72 cases per person-year), of which 6,000 (95% credible interval of 2000 – 11 000) would be attributable to drinking water treated and distributed by the community system. In terms of AGI illnesses due to source water and treatment deficiencies, each would be associated with approximately 3000 cases of AGI. Nationally, the incidence due to drinking water contributes a total of 16.4 million cases of AGI illness to the total estimate of 196 million cases of AGI illness due to all causes among the 272.5 million persons served by CWS.

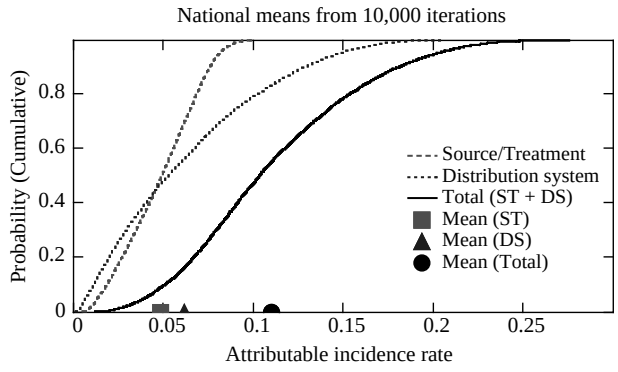

Figure 2 | Average HCGI incidence rates attributable to drinking water from CWSs based on Laval results.

One question of particular interest in the interpretation of this analysis is the percentage of cases of AGI illness due to the highest risk systems, e.g. the "systems" that are ranked within the top 20% because of their source/treatment characteristics or their distribution system characteristics. An additional analysis of the model output (included in Appendix A) shows that 81.6% of the attributable distribution system incidence is borne by the population served by the systems in the upper 20% of the distribution system attributable incidence distribution; similarly 82.9% of the attributable source/treatment incidence is borne by the those in the upper 20% of the source/treatment attributable incidence distribution.

UNRESOLVED ISSUES WITH APPROACH

Our national estimate based on the Laval studies and the approach presented in this paper has the advantage that it can effectively make use of the wealth of data on microbial

Table 6 | Summary of national estimate model results of drinking water attributable illness

Source and endpoint	Mean incidence (cases per person-year)	Lower 95% credible bounds (cases per person-year)	Upper 95% credible bounds (cases per person-year)
Total HCGI (ST + DS)	0.11	0.03	0.22
Source/treatment HCGI	0.048	0.011	0.086
Distribution system HCGI	0.062	0.005	0.16
Total AGI (ST + DS)	0.06	0.02	0.12
Source/treatment AGI	0.03	0.006	0.05
Distribution system AGI	0.03	0.003	0.09

risk to make up for the sparseness of data from epidemiology studies. It is an approach that can be modified and refined as new data and analyses become available, but, even in its current form, it illustrates a method that can be used to estimate AGI associated with drinking water. Although the approach can make optimal use of water quality and CWS information, there are clearly some major water quality related data gaps, in particular regarding the extent and influence of treatment upsets, regarding disinfection practice, and microbial risk factors associated with groundwater systems and distribution systems. The data gaps range from not having a clear understanding of which risk factors provide the most representative measure of microbial risk (related to how to characterize different levels of microbial risk) to lack of information on the prevalence of risk factors in systems and the size of the associated population.

For groundwater systems the major unknowns are at the national level, i.e. the range and the variability of source water pathogen occurrence as well as the variability of treatment applied in groundwater systems. We know that in 2004, 5.3% of groundwater community systems (serving 5.4% of the population served by groundwater) were in violation of the total coliform rule. The extent to which these violations present source water deficiencies versus distributions system deficiencies is not clear.

Distribution system microbial risk is the area we think represents the most significant factor of uncertainty in the analysis because there is no established measure of distribution system microbial risk other than the presence or absence of total coliforms, and fecal coliforms and *E. coli*. TCR violations in surface water systems are probably not due to source or treatment problems because of the treatment plant disinfection requirements, so the violations of the TCR MCL that affect approximately 3% of the population served by surface water systems are due to distribution system problems. We know from research that leaky systems that are subject to occasional low or negative pressure events are subject to intrusion of pathogens, but we do not know the probability of such events, or range of variability among systems. A recent case-control study (Hunter *et al.* 2005) in the UK of sporadic *Cryptosporidiosis* showed a very strong association with low water pressure at the tap due to supply disruption likely related to mains breaks. Another question that deserves attention is the extent to which biofilms are associated with waterborne illness and the extent to which pathogens may grow (bacteria) or be released to reach the consumer. Biofilms have been shown to contribute to the survival of pathogens in the distribution system (Armon *et al.* 1997; Mackay *et al.* 1998).

Microbial risk associated with treatment upsets is also an area that requires more attention, in particular with regard to the uncertainty related to the risk in surface water systems with highly contaminated source water. A significant unknown is the frequency of treatment upsets that result in pathogens surviving through the treatment process and entering the distribution system. Ruptures or

lapses in treatment could occur for short periods even if systems are in full compliance and could cause a spike in waterborne disease. While treatment upsets in filtration processes should be reduced substantially due to improved compliance with the IESWTR and with LT1 (beginning in 2005), treatment upsets in the distribution process are less specifically controlled. The frequency and duration of upsets are currently not known but could be significant.

There is also uncertainty regarding health effects related to the sparseness of epidemiological data on AGI illness associated with drinking water from different types of systems (source, treatment and distribution system). This is an area where we need additional significant positive data on AGI incidence from a range of systems to supplement the incidence and microbial risk data provided by the Laval studies.

SUMMARY AND CONCLUSIONS

Our conceptual approach and national estimate represent the use of available information to measure illness due to drinking water. We plan to refine the approach and incorporate new information and analyses to improve our ability to measure AGI, or some other appropriate indicator or health end-point due to drinking water. Our goal is to use the approach of a national distribution of microbial risk and associated illness to measure the effect of new regulations on the incidence of AGI illness in the years following their implementation. If, as illustrated by the analysis, the contribution of the upper 20% in both the source/treatment and the distribution system distribution of AGI illness incidence explains approximately 80% of the cases, we may be able to measure the effect of new regulations or non-compliance with existing microbial regulations (SWTR, TCR, IESWTR, LT1 ESWTR) if we concentrate on the high risk systems. The new regulations that are expected to reduce AGI illness include the LT2, the future groundwater rule, and, currently in the planning stages, modifications to the TCR and a possible distribution system rule. The LT2 is expected to reduce the incidence of AGI due to *Cryptosporidium* and other pathogens in high risk surface water systems through its graded treatment and source water protection requirements that are based on the level of source water *Cryptosporidium*. Identification and remediation of high-risk groundwater systems is also anticipated under the forthcoming groundwater rule. Developing criteria by which to identify and remediate high risk distribution systems will be challenging but a possible outcome of future regulatory efforts.

In terms of filling data gaps, our primary focus is on collecting information to improve our assessment of microbial risk factors and associated illness in groundwater systems and due to distribution system deficiencies in all types of systems, not only on the individual system basis, but also at the national level. In addition to analyzing the results of ongoing epidemiology studies and new research on drinking water microbial risk models, we will also focus on how to conduct new epidemiology studies to improve our estimate of AGI or of exposure to waterborne pathogens.

While our primary purpose in developing this estimate, using the best available data, is to address, in part, the 1996 Safe Drinking Water Act Amendments, we remind readers that an equally important objective is consideration of the conceptual approach and the model as an application of this approach. We used many simplifying assumptions to bridge gaps in data that may have introduced significant over- or underestimates and recognize that consideration of this approach for future estimates or measures should consider new information in addressing these data gaps.

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DISCLAIMER

The views expressed in this article are those of the individual authors and do not necessarily reflect the views and policies of the US Environmental Protection Agency.

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APPENDIX A: MATHEMATICAL DETAILS FOR LAVAL EXAMPLE APPLICATION OF THE DRINKING WATER ATTRIBUTABLE HCGI RISK MODEL

The mathematical modeling presented herein was carried out using Mathcad 12 software (Mathsoft Engineering and Education, Inc., www.mathsoft.com). The definitions and descriptions below include several Mathcad functions. A brief summary of those functions is included for clarity.

- qnorm(p,m,s) = x returns the inverse of the cumulative normal distribution with mean m and standard deviation s.
- dnorm(x,m,s) returns the probability density and pnorm(x,m,s) = p returns the cumulative probability associated with x.
- ln(x) is the natural log (base e).
- K is a large multiplier to ensure that integration covers virtually 100% of the probability mass. (This is needed because the numerical integration routine cannot deal with infinite limits.)
- X is the expected, or average national attributable incidence rate, the result of the numerical integration.

Step 1. Select from their respective uniform distributions, the following random variables:

a. HCGI rate that is attributable to source/treatment component in the 1991 Laval study. This rate is converted to a fraction by dividing it by the total observed drinking water attributable rate, 0.26 (ST_Fraction). This fraction is a uniform variable on the range [0.2/0.26, 0.24/0.26]. *For example, the first simulation produced ST_Fraction = 0.769.*
b. Ranking (percentile) of the 1991 Laval study's source treatment attributable incidence in the US distribution (ST_Pctile). *For example, the first simulation produced ST_Pctile = 0.954 = 95.4%ile.*
c. Ranking (percentile) of the 1991 Laval study's distribution system attributable incidence in the US distribution (DS_Pctile). *For example, the first simulation produced DS_Pctile = 0.562 = 56.2%ile.*
d. Variability of source treatment GI illness distribution (ST_Logs). *For example, the first simulation produced ST_Logs = 2.193. Thus, the width of the central 95% interval is then 10^(ST_Logs) or in this example, approximately a factor of 156.*
e. Variability of distribution system HCGI distribution (DS_Logs). *For example, the first simulation produced DS_Logs = 2.881. Thus, the width of the central 95% interval is then 10^(DS_Logs) or in this example, approximately a factor of 760.*

Step 2. Compute fraction of HCGI that is attributable to the distribution system in the 1991 Laval study: DS_Fraction = 1–ST_Fraction. *For example, the first simulation produced ST_Fraction = 0.769. Thus, DS_Fraction = 1 – 0.769 = 0.231.*

Step 3. Compute mean and standard deviation values for the distributions of source/treatment and distribution system risk based on variables values computed in Steps 1 and 2.

f. The US distribution of source/treatment attributable risk is lognormal. Natural log of source treatment risk is therefore normally distributed with mean STμ and standard deviation STσ. They are derived as follows:

i. STσ = ln(10^ST_Logs)/3.92. *In the first simulation, STσ = ln(156)/3.92 = 1.29*

ii. STμ = ln(ST_Fraction * 0.26)-STσ * qnorm (ST_Pctile,0,1). *In the first simulation, STμ ln (0.769 * 0.26) – 1.29 * qnorm(0.954,0,1) = -1.61 – 1.29 * 1.69 = -3.78.*

g. Similarly, the US distribution of distribution system attributable risk is lognormal with mean DSμ and standard deviation DSσ:

i. DSσ = ln(10^DS_Logs)/3.92. *In the first simulation, DSσ = ln(760)/3.92 = 1.69.*

ii. DSμ = ln(DS_Fraction * 0.26)-DSσ * qnorm(DS_ Pctile,0,1). *In the first simulation, DSμ = ln*

*(0.231 * 0.26) – 1.69 * qnorm(0.562,0,1) = -2.81 – 1.69 * 1.57 = -3.08.*

Step 4. Perform numerical integration to derive the national average incidence rates attributable to source/-treatment and distribution system components. Upper limits for integration are set at 2 cases per person-year (Limit):

$$ST_{sim} := \frac{\int_{ST\mu - K \cdot ST\sigma_{sim}}^{\min\left(\begin{pmatrix} ST\mu_{sim} + K \cdot ST\sigma_{sim} \\ \ln(Limit) \end{pmatrix}\right)} e^{x} \cdot dnorm(x, ST\mu_{sim}, ST\sigma_{sim})dx}{plnorm(Limit, ST\mu_{sim}, ST\sigma_{sim})}$$

In the first simulation, the ST integral's value is 0.052 cases per person-year.

$$DS_{sim} := \frac{\int_{DS\mu_{sim} - K \cdot DS\sigma_{sim}}^{\min\left(\begin{pmatrix} DS\mu_{sim} + K \cdot DS\sigma_{sim} \\ \ln(Limit) \end{pmatrix}\right)} e^{x} \cdot dnorm(x, DS\mu_{sim}, DS\sigma_{sim})dx}{plnorm(Limit, DS\mu_{sim}, DS\sigma_{sim})}$$

In the first simulation, the DS integral's value is 0.137.

Step 5. Store the mean values from the source/treatment and distribution system distributions.

The final step in the process was to generate cumulative distributions from the results of all 10,000 simulations.

The national distributions (one for source/treatment and the other for distribution system) associated with the first simulation are presented in Figure A1. In Figure A1, the circles mark the placement of the 1991 Laval study's source/treatment and distribution system incidence rates (as noted above, in the first simulation, the percentile associated with source treatment (ST_Pctile) was 0.952, and that associated with distribution system (DS_Pctile) was 0.562).

The cumulative distributions of national average attributable risk or attributable incidence rates (one for source/treatment and one for distribution system) based on 10 000 simulations are presented in Figure A2. These cumulative distributions present the uncertainty about the national average HCGI rates attributable to the source/treatment and distribution system components.

Inspection of Figure A2 indicates that the slope of the source/treatment curve is steeper than the distribution system curve. This observation indicates that there is greater uncertainty about the rate of HCGI attributable to distribution systems compared to that attributable to the source/treatment component.

Based on the results of this analysis, the mean incidence attributable to drinking water is 0.111 cases per person-year with a 95% confidence interval of 0.032 – 0.22. This result indicates, for example, that in a community of 100,000 people, it would be expected that over a 1-year period the community would experience approximately 72 000 cases of GI illness (0.72 cases per person per year), of which 8000 (95% confidence interval of 2300 – 16 000) would be attributable to drinking water treated and distributed by the community system.

The mean incidence attributable to distribution systems risk was 0.062 cases per person-year with a 95% confidence interval of 0.005 – 0.16 cases per person-year, and mean incidence attributable to source/treatment was 0.048 cases per person-year with a 95% confidence interval incidence is 0.011 – 0.86 cases per person-year.

80/20 percent analysis

The first expressions (p80ds and p80st) in the equations below identify the 80th percentiles of the truncated DS and

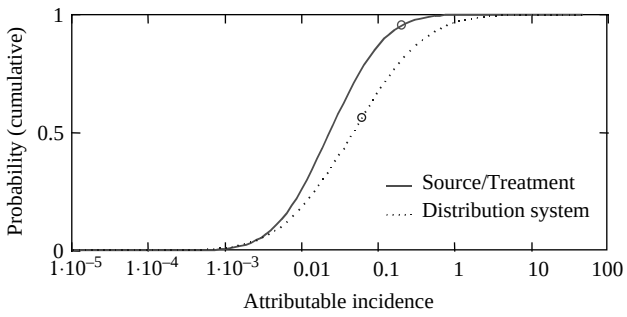

Figure A1 | first iteration: national distributions of source/treatment and distribution system risk.

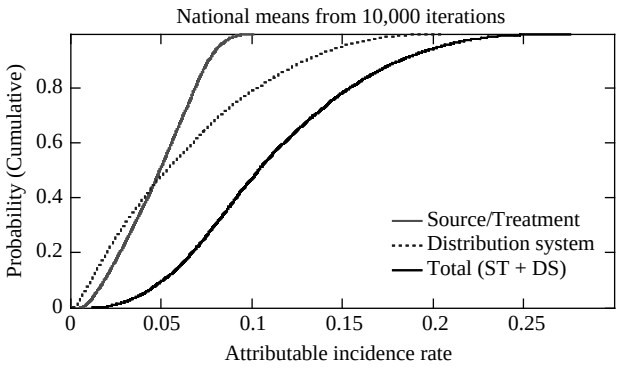

Figure A2 | Cumulative distribution of national average incidence rates attributable to drinking water from cwss based on Laval results.

ST attributable incidence distributions. This is complex because both were truncated at Limit = 2 cases per person-year. In the fractions below, $risk20_{ds}$ and $risk20_{st}$ are risks above the 80th percentiles divided by the total risk (over all systems). The results of the analysis are: 81.6% of the attributable DS incidence is borne by those in the upper 20% of the DS attributable incidence distribution and 82.9% of the attributable ST incidence is borne by those in the upper 20% of the ST attributable incidence distribution:

$$risk20_{ds_{sim}} := \frac{\int_{\ln\left(p80_{ds_{sim}}\right)}^{\min\left(\begin{pmatrix} DS\mu_{sim} + K\,DS\sigma_{sim} \\ \ln(Limit) \end{pmatrix}\right)} e^{x}\,dnorm(x,\, DS\mu_{sim},\, DS\sigma_{sim})\,dx}{\int_{DS\mu_{sim} - K\,DS\sigma_{sim}}^{\min\left(\begin{pmatrix} DS\mu_{sim} + K\,DS\sigma_{sim} \\ \ln(Limit) \end{pmatrix}\right)} e^{x}\,dnorm(x,\, DS\mu_{sim},\, DS\sigma_{sim})\,dx}$$

$$Mean(risk20_{ds}) = 0\ 816$$

$$risk20_{st_{sim}} := \frac{\int_{\ln\left(p80_{st_{sim}}\right)}^{\min\left(\begin{pmatrix} ST\mu_{sim} + K\,ST\sigma_{sim} \\ \ln(Limit) \end{pmatrix}\right)} e^{x}\,dnorm(x,\, ST\mu_{sim},\, ST\sigma_{sim})\,dx}{\int_{ST\mu_{sim} - K\,ST\sigma_{sim}}^{\min\left(\begin{pmatrix} ST\mu_{sim} + K\,ST\sigma_{sim} \\ \ln(Limit) \end{pmatrix}\right)} e^{x}\,dnorm(x,\, ST\mu_{sim},\, ST\sigma_{sim})\,dx}$$

$$Mean(risk20_{st}) = 0\ 829$$

APPENDIX B: CHARACTERIZING THE NATIONAL ESTIMATE BASED ON PROFESSIONAL JUDGMENT AND THE DAVENPORT INTERVENTION STUDY

Davenport household-intervention study and comparisons with Laval

The Davenport study (Colford *et al.* 2005), conducted between October 2000 and May 2002, was the first full-scale household-intervention study conducted in the US The design of the study was similar to the Laval studies (Payment *et al.* 1991, 1997) in that households were randomly assigned a water treatment intervention and study participants maintained a health diary documenting AGI symptoms to be used as a measure of HCGI (using the same definition as that used by Payment in the Laval studies). Two aspects of the study design were different in that participants were blinded to their intervention assignments, and also, in addition to just comparing the incidence of AGI between individuals in households assigned to different treatment groups (sham treatment or real treatment), this study switched household treatment midway, after 6 months (cross-over study design), and also evaluated the treatment effect on individuals. The study enrolled 456 households (1296 individuals) and followed them for 12 months, 6 months with real and 6 months with sham treatment with a two-week wash-out period following the treatment switch. No difference in HCGI incidence was observed between real and sham treatment groups (Incidence Rate Ratio = 0.98 (95% CI 0.87 – 1.10). Another difference between the Laval studies and the Davenport studies is the difference in HCGI incidence. The incidence ranged from 1.76 to 2.42 cases per person year, compared to the 0.5 – 0.92 cases per person-year in Laval. The higher rate of HCGI was probably due to the relaxed inclusion criteria in study enrollment that included persons with chronic illnesses that have diarrhea as one of the associated symptoms, e.g. Irritable Bowel Syndrome.

A parallel study of water quality and treatment performance was conducted in Davenport and surrounding communities that were part of the study area served by Iowa American, the Davenport utility. Samples were collected to measure source water, filtered water and distribution system water quality (LeChevallier *et al.* 2004). The source water quality of the Mississippi River in Davenport is subject to high levels of fecal contamination. Upstream activities in the watershed that contribute to fecal contamination include agriculture, sewage treatment plant discharges, and combined sewer overflows. Comparing pathogen concentrations measured in Davenport to those measured in Laval's source water is not just a matter of comparing numbers because the analytical methods for the pathogens are different and probably have different recovery rates. However, fecal coliform analytical methods were the same with the exception of sample volume. In the first Laval study, the mean fecal coliform level was 3674 cfu/L; in Davenport the mean level was 3418 cfu/L, i.e., of the same order of magnitude; the mean concentration of enteric viruses was 78 infectious units/100 L in the first Laval study, and 6.72/100 L in Davenport. Based on the virus data and other pathogen measures (*Giardia lamblia* and *Cryptosporidium*) Davenport's source water appears to be slightly less contaminated than Laval's. Davenport's treat-

ment was similar to the treatment at Laval. It also consisted of conventional filtration and pre- and post-disinfection; however, filtration performance appears an order of magnitude better than that of Laval in the second study (average turbidity of water leaving the plant of 0.05 NTU versus 0.1 NTU, with a maximum of 0.09 NTU versus 0.5 NTU). No pathogens were detected in the finished water.

During the study period a total chlorine residual was maintained at all sampling locations and only 2/2469 coliform samples tested positive.

In the Davenport study, the level of HCGI attributable to drinking water was below the detectable level of the study (Colford *et al.* 2005). Thus, we were not able to use the data from the Davenport study in the same way that data from the Laval studies were used. This appendix describes an analysis that uses the Davenport data to estimate the national distribution of GI illness associated with drinking water from CWSs. In this analysis, Bayesian statistical methods are employed to update the team's prior judgments and estimate: (1) the amount of GI illness attributable to drinking water during the Davenport intervention trial, and (2) Davenport's relative placement in the national distribution conditioned on the magnitude of Davenport's attributable incidence.

Those two estimates result in a joint posterior distribution that was used to estimate the national distribution of GI illness associated with drinking water from CWSs. Following is an overview of the Davenport analysis and results. Mathematical details are available from the authors.

Davenport's attributable risk[2] due to drinking water (prior and posterior distributions)

The prior (cumulative probability) distribution for Davenport's attributable incidence of AGI due to drinking water illustrated in Figure B1was generated based on the following information from EPA staff scientists and engineers (referred to as the "team"). These scientists were asked to recall their beliefs at the time the Davenport study was being planned. At that time, these scientists were aware of the results from the two Laval intervention studies.

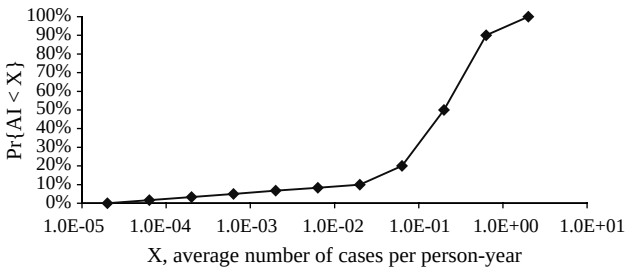

Figure B1 | Expected cumulative (prior) distribution for Attributable Risk or Attributable Incidence (AI) in Davenport.

- The maximum tenable attributable endemic risk was believed to be two HCGI cases per person-year (greater values would more likely be recognized by outbreak surveillance).
- The team thought it unlikely that the waterborne attributable illness rate in Davenport would be much greater than the rate found in the first Laval study (0.26 cases per person-year) or greater than the average total background rate of acute GI illness in the US (0.72 cases per person-year). Thus, 10% probability is allowed that the waterborne attributable rate in Davenport exceeds 0.63 (geometric mean of 0.2 and 2) cases per person-year.
- The team believed the Davenport study was likely to identify a statistically significant attributable risk (incidence) of HCGI. The study was designed to be able to detect an average attributable incidence rate of about 0.1 cases per person-year.
- In designing the study, it was thought that there was a 50/50 chance that the rate would be greater than 0.2 cases per person-year, and that it was unlikely (probability 0.1) that the rate would be less than 0.02 per person-year.
- In designing the study, the minimum reasonable risk was expected to be 2 cases per 100,000 person-years based on analysis of the ICR data (Messner & Wolpert 2002). If the source water were typical of US waters, and treatment removed 99.99% of *Cryptosporidium* oocysts, then the finished water would contain about 2 oocysts per 100,000 L. A consumer drinking 1 liter per day would expect to ingest 365 L $\times$ 2 oocysts/100,000 L $=$ 0.007 oocysts. If probability of illness, given one oocyst ingested, is on the order of 0.03, then the attributable risk due to *Cryptosporidium* in finished water would be about 0.0002. It was assumed that Davenport's risk due

[2] In Appendix B, some of the figures contain the notation "AI" or attributable incidence rather than AR or attributable risk. They both refer to exactly the same measure, i.e. the difference in the incidence of HCGI that is assumed to be attributable to drinking water.

to all pathogens in the source water plus the risk due to those entering the distribution system is not less than 1/10 of this amount, or 0.000 02.

The above figure displays the Prior probability distribution for Davenport's AI. The other piece needed to apply Bayes' theorem is the Likelihood Function. Ideally, the likelihood would be derived directly, using the study data. In this case, data were not available, but summary results were reported in terms of a central estimate and associated confidence limits (Colford *et al.* 2005)[3]. Based on these, the likelihood function for Davenport's attributable risk (incidence) was modeled as a Normal distribution with mean −0.042 and standard deviation 0.130 (Figure B2). This normal model is consistent with the nearly symmetric confidence intervals for illness rates in both exposed and unexposed groups.

Through Bayes' theorem, the prior and likelihood functions described above yielded a posterior distribution for Davenport's attributable risk (incidence) (Figure B2). As shown in Figure B2, Davenport's posterior attributable incidence distribution has a mean of 0.065 cases per person-year (median = 0.055) and a 95% confidence interval ranging from 0.0003 to 0.22 cases per person-year.

Davenport's relative placement in the national distribution

Similar to Davenport's prior distribution, the team provided information on their beliefs about the relative placement of Davenport in the national distribution conditional on (hypothetically) knowing Davenport's true attributable risk (AR). Those beliefs are summarized as follows:

- If Davenport's AR was 0.2 cases per person-year, then the team would be confident (95% level) that Davenport's placement would be in the upper portion of the US distribution, specifically in the interval (0.75, 0.95).
- If Davenport's AR was 0.04 cases per person-year, then the team expect its placement to fall in the interval (0.1, 0.95).
- If Davenport's AR was 0.003 cases per person-year, then the team expects its placement to fall in (0.01, 0.5).

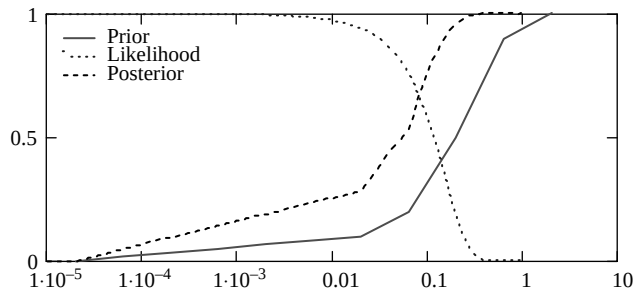

Figure B2 | Posterior and prior distribution functions for Attributable Risk (Incidence) due to drinking water in Davenport (also shown is the Likelihood Function).

- If Davenport's AR was 1 case per person-year, then the team expects its placement to fall above 0.95.

The data summarized above were logit transformed[4]. The logit transformation is a natural choice to achieve (or nearly achieve) homogeneity and normal uncertainty structure. Whereas probabilities are restricted to the range [0, 1], logits or log odds have no such limits. This transformation is often used to expressing estimates from case-control studies, as the error structure for simple studies (wherein a 2 × 2 contingency table conveys the information) is normal with regards to log odds.

Over the range of interest (Davenport's AR in the range of 0.000 02 to 2 cases per person-year), lines were fitted to the data via the method of least-squares to generate upper and lower credible bands. Those bands are linear in terms of logit, but appear as curves in Figure B3 (the blue circles are estimates for the selected values of AR and the red crosses are the expressed values for those same ARs).

Joint distribution of attributable risk and placement in the national distribution

The resulting joint distribution shows the relation between Davenport's attributable risk and placement in the national distribution (Figure B4). Inspection of Figure B4 indicates that the bulk of probability mass is in the corner of the figure which represents the upper ranges of both placement and attributable incidence. This is consistent with the prior belief that Davenport's AR was sufficiently great to produce a statistically significant finding by the household interven-

[3] The negative mean is due to finding a lower illness rate in the group receiving tap water.

[4] $\text{logit}(p) = \ln(\text{odds}) = \ln(p/(1\text{-}p))$.

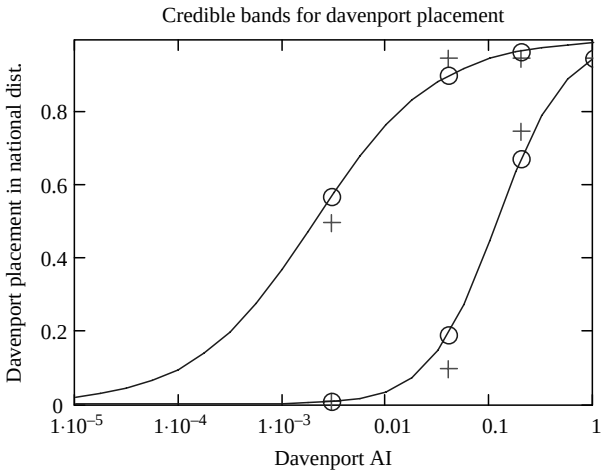

Figure B3 | Credible bounds for Davenport's placement in the national distribution of Attributable Risk (Attributable Incidence or AI).

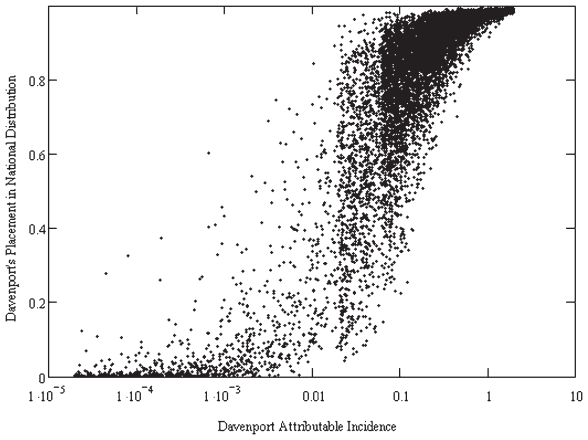

Figure B4 | Sample from joint distribution of AI and placement in the national distribution of AI.

tion study. The probability mass near zero reflects the possibility that Davenport's AR is very small.

Monte Carlo analysis to characterize the national estimate

Similar to the Laval PAR analysis, a Davenport-based Monte Carlo simulation was employed to estimate the national distribution of GI illness associated with drinking water from CWSs. In each simulation, the following uncertain variables were sampled:

- Davenport's attributable incidence (from the Bayesian posterior, Figure B2),
- Davenport's placement in the national distribution (from the conditional distribution, Figure B4),
- the variability of the national distribution (2–5 logs as described previously).

For each simulation, numerical integration was used to derive the expected national average attributable incidence. This process was repeated 10 000 times. The results from those simulations is a distribution that describes the uncertainty about the national average GI illness rates attributable to the drinking water, based on a combination of expert judgment and the results of the Davenport intervention trial (Figure B5).

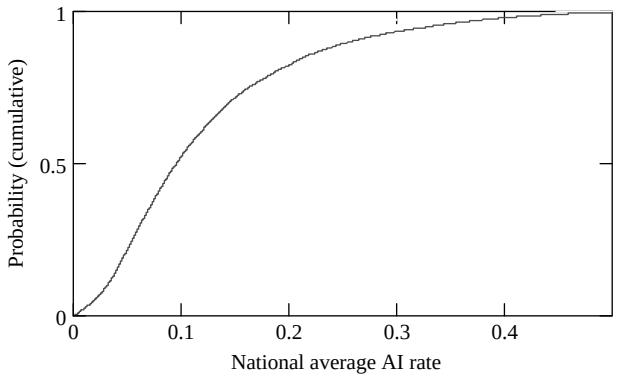

Figure B5 | Average incidence rates attributable to drinking water from CWSs based on Davenport results.

Based on the results of this analysis, the mean national average incidence attributable to drinking water is estimated to be 0.12 cases per person-year with a 95% credible interval of 0.01 to 0.39 cases per person-year.