

Enteric illness risks before and after water treatment improvements

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ABSTRACT

This study evaluated whether occurrence of acute gastrointestinal illnesses declined after filtration and ozonation were added to a previously unfiltered, chlorinated high-quality surface water source in a northwest United States city. Enteric and other illnesses were recorded for two 6-month periods for control and intervention sites in the same city. During phase 1, chlorinated, unfiltered drinking water for both sites was obtained from protected watersheds. During phase 2, the intervention site received chlorinated, filtered and ozonated drinking water. The water was not altered in the control site. No overall differences were found in the risk of any of the illnesses after the new water treatment plant was completed. There was a significantly increased risk of diarrhoea and highly credible gastrointestinal illness in participants with three or more episodes of the same type of illness during phase 1.

Key words | cryptosporidiosis, gastrointestinal diseases epidemiology, natural immunity, water supply standards

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INTRODUCTION

Waterborne disease remains a major cause of morbidity and premature mortality for much of the world, resulting from either a lack of water for washing or a lack of safe water for drinking (World Health Organization 1997). However, few of the waterborne diseases common in developing countries are common in developed countries. Enteric viruses and bacteria are commonly implicated or suspected in groundwater-related outbreaks; however, filtration and disinfection of

surface water removes or inactivates most of these organisms. In the United States (US), the two agents most often implicated in waterborne disease outbreaks are *Giardia* and *Cryptosporidium* (Craun *et al.* 2002, 2003, 2006). *Giardia* and *Cryptosporidium* oocysts are commonly identified in both unfiltered and filtered surface water sources in the US and elsewhere (LeChevallier & Norton 1995; Aboytes *et al.* 2004). Sources of contamination include human sewage discharges

and wild and domestic animals. Protozoa such as *Giardia* and *Cryptosporidium* are more difficult to disinfect than bacteria and viruses found in water sources.

It has long been suspected that endemic waterborne illness not associated with outbreaks is also an important but unrecognized risk (Frost *et al.* 1996). However, there is conflicting evidence about whether drinking water that meets conventional standards contributes to endemic gastroenteritis in the community (Payment *et al.* 1991, 1997; Hellard *et al.* 2001, 2002; McConnell *et al.* 2001; Khalakdina *et al.* 2003). Studies have also identified sub-populations such as the elderly and young children who may be at higher risk of enteric illness under current treatment practices (Schwartz *et al.* 1997, 2000). Thus, drinking water regulators in the US and elsewhere are concerned about both endemic and outbreak waterborne disease risks in these groups. They are requiring either improved or additional treatment for many water systems (Environmental Protection Agency 2003). Unfiltered surface water supplies, even those supplied by protected watersheds, have new requirements that will require many water utilities to filter the water unless they can consistently maintain a very high water quality.

The health benefits from new technologies such as filtration and ozonation at the water treatment plant have not been thoroughly studied, even though they can effectively remove and inactivate *Giardia* and *Cryptosporidium* oocysts. Goh *et al.* (2005) found that microfiltration was associated with a reduction in sporadic cases of cryptosporidiosis at a United Kingdom site. Several randomized household intervention studies have been conducted in Australia, Canada and the US (Payment *et al.* 1991; Hellard *et al.* 2001; Colford *et al.* 2005). The Canadian study found a significantly increased annual incidence of gastrointestinal illness in tap water drinkers compared with filtered water drinkers (Payment *et al.* 1991). In contrast, studies in Australia and the US did not detect evidence of reduced enteric illnesses from adding highly efficient home drinking water filtration systems (Hellard *et al.* 2001; Colford *et al.* 2005).

The purpose of this study was to evaluate whether the occurrence of acute gastrointestinal illnesses declined after filtration and ozonation were added to a previously unfiltered but chlorinated high-quality surface water source. This surface water differs from most other surface water in

the world in that there are no sources or evidence of human sewage contamination. The only human pathogens known to be present in the source water are *Cryptosporidium* and *Giardia*, probably from wild animals. Even for *Cryptosporidium*, the absence of grazing domestic animals in the watershed probably minimizes the concentration of *Cryptosporidium* oocysts in the environment. This study compared illness rates before and after addition of filtration and ozonation for one of two protected unfiltered surface sources for the city.

METHODS

Study sites and population

This prospective cohort study was conducted in two distinct geographic areas (control and intervention) in a north-western US city during two time periods: phase 1 from June to November 2000 and phase 2 from June to November 2001. Both the intervention and the control sites were in the same city and were served by one water utility. However, they were supplied by different unfiltered, chlorinated surface water sources. Both surface water sources came from well-protected watersheds with no source or evidence of human sewage contamination. Treated water from both sources was stored in uncovered distribution system reservoirs. The water utility had a reservoir protection programme that included security, monitoring and maintaining chlorine residuals in water leaving the reservoirs. Water from both sources was chlorinated during the entire study period. Drinking water for both sites, before and after the treatment changes, met the current US Environmental Protection Agency (EPA) Safe Drinking Water Standards for coliform bacteria.

Prior to the beginning of phase 2, a new water treatment facility was completed for the intervention site. Treatment included ozone for primary disinfection, coagulation/flocculation, high-rate granular filtration (anthracite) and chlorine as a secondary disinfectant. Fluoride and chemicals for corrosion control were also added. Turbidity for the intervention site declined following filtration. In the control site, there was no change in the treatment facility and treatment processes which included only chlorination.

Eligibility

Two separate institutional review boards (Lovelace Clinic Foundation and Children's Hospital of Seattle) approved this study prior to recruitment of subjects. Free and informed consent of the participants or their legal representatives was obtained and the study protocol was approved by the Lovelace Institutional Review Board, Albuquerque, New Mexico, in February 2000. Families recruited from both sites were eligible to participate if: 1) a household member included either a child aged 2 to 10 years or an adult at least 65 years of age; 2) the household drank municipal water and did not have a home filtration system; and 3) family members had lived in the residence for at least six months and planned to stay in the community for the next two years. In addition, the family must have lived in an area where the water came from only one source. In some parts of the city, there was a blending of water from both sources. Only family members in self-reported overall good mental and physical health were enrolled.

Recruitment

Families were recruited from both sites for phase 1 of the study through advertisements and household mailings.

Table 1 | Characteristics of study participants living in the control and intervention sites who were enrolled in phase 1 and phase 2 of the study

	Control site	Intervention site
No. of individuals enrolled both phases	361	711
% of phase 1 enrolment	77	78
No. of individual families enrolled both phases	164	277
Age group (years):		
2–19	130	314
20–64	140	268
65 and older	91	129
Total diary days in town:		
Phase 1	33,435	72,242
Phase 2	48,742	102,876
Mean diary days in town per individual:		
Phase 1	92.1	101.6
Phase 2	134.3	144.7

Families from both sites who were recruited for phase 2 had to be previously enrolled in phase 1. Study enrolment and diary-days by age and area (intervention versus comparison site) are given in [Table 1](#).

Families with children were paid US\$20 per month of completed diaries. Families with senior citizens were paid US\$15 per month of completed diaries. We attempted to collect both sera and stools from participants. Results of the analysis of the sera have been previously reported [Frost *et al.* \(2005a\)](#). We were unable to collect a sufficient number of stools for a meaningful analysis.

Outcomes

Illnesses were tracked for participants of the two sites for both phase 1 and phase 2 of the study. A daily illness diary recorded illnesses for each family member for each 6-month period in phase 1 and phase 2. A designated person from each family was responsible for completing the enrolment and illness diary forms for the entire family. The daily diary recorded whether each person was out-of-town, well or had diarrhoea (loose/watery stools), vomiting, nausea or other symptoms of colds and so on. At the end of each week, the diaries were mailed to the study office. The majority of information was submitted through the mail, with some collected by telephone.

Four categories of illness were defined based on the reported symptoms. Diarrhoea was defined as at least two episodes of soft or loose stools. Gastrointestinal illness was defined as having nausea, any vomiting or abdominal cramps. Highly credible gastrointestinal illness (HCGI), described by [Payment *et al.* \(1991\)](#), was defined as at least one of the following: 1) vomiting or liquid diarrhoea; or 2) nausea or diarrhoea combined with abdominal cramps. Other illness was defined as reported fever, chills, headache or cold without enteric symptoms. Illnesses could be classified in more than one illness category if symptoms in more than one category were reported. For example, an illness was classified as both HCGI and diarrhoea if the person reported nausea and soft stools.

Symptoms occurring within five days of each other were considered to be related and were counted as one episode. A new diarrhoea or gastrointestinal episode could begin

after 6 or more days without diarrhoea or gastrointestinal symptoms. For example, the following would be classified as a single diarrhoea episode of six days duration: a person with no diarrhoea for six days experiences diarrhoea on day 7 and 8, no diarrhoea on days 9 and 10, diarrhoea on days 11 and 12, and no diarrhoea during the next six days.

Poisson regression

Analyses were performed using SAS version 8.2 statistical software. Illness episodes were discrete counts and rare episodes, characteristic of a Poisson distribution of counts. Individual diaries encompassed varying lengths of time each year. Adjustments for these varying lengths were made in the analysis models. Illness episodes per 1,000 diary days were modelled using a Poisson regression that included variables for site location (i.e. intervention and control), rates of illness reports per diary days in phase 1, gender (reference, female), age (less than 20 years, 20 to 64 years and 65 years and older, reference age 20 to 64 years). Separate analyses were also conducted for each age group. Exponentiation of the main effect coefficient in the Poisson model estimates the regression-adjusted incidence density ratio (IDR) for the effect. The incidence density is the number of new illness episodes divided by the fraction of the year the person contributed daily diary records. The IDR is the incidence density of illnesses in the exposed population divided by the incidence density of illnesses in

the unexposed or reference population. A statistically significant ratio that is less than 1.0 is consistent with a protective effect from the exposure; a ratio of more than 1.0 indicates an increased risk.

RESULTS

There were 906 individuals enrolled from the intervention site and 471 from the control site. Of these, 711 from the intervention site and 361 from the control site successfully completed both study phases and were included in this analysis. We did not attempt to match individuals between the intervention and comparison populations. The number of different families and diary days are shown in [Table 1](#). We did not collect or analyse socio-economic data, but the population appeared to be well educated. In fact, one mother enrolled so that her children might better understand the occupation of their late father, an epidemiologist.

For both the control and intervention sites, the mean number of reported illnesses in each category per diary-year declined for all age groups during phase 2, except for a slight increase in HCGI in participants 20–64 years of age in the intervention group ([Table 2](#)). The decline in illness rates was greater in participants less than 20 years of age and those 65 years and older. Only a relatively small decline in gastrointestinal and diarrhoea illness rates occurred for the 20–64-year-old age intervention group.

Table 2 | Mean number of gastrointestinal (GI), diarrhoea, HCGI and other illness episodes per diary-year by site and age group

Site	Age group (years)	No. of people	GI episodes per diary-year		Diarrhoea episodes per diary-year		HCGI episodes per diary-year		Other illnesses* per diary-year	
			Phase 1	Phase 2	Phase 1	Phase 2	Phase 1	Phase 2	Phase 1	Phase 2
Control	2–19	130	1.98	1.38	2.01	0.95	2.33	1.54	7.98	6.12
	20–64	140	3.04	1.54	3.28	1.62	3.24	1.86	8.85	5.93
	65 +	91	2.05	1.26	2.73	1.30	2.09	1.07	5.69	3.00
	All ages	361	2.37	1.38	2.92	1.30	2.61	1.50	7.70	5.21
Intervention	2–19	314	1.98	1.38	1.22	0.83	1.90	1.46	7.15	5.25
	20–64	268	1.90	1.78	1.86	1.78	1.94	1.98	6.91	5.85
	65 +	129	2.37	1.15	2.25	1.22	2.09	1.30	5.77	2.73
	All ages	711	2.01	1.50	1.66	1.26	1.94	1.62	6.83	5.02

*Fever, chills, headache or cold without enteric symptoms.

Table 3 | Unadjusted incidence density ratios (IDRs) for all participants for the four types of illness by site, age group and number of illness episodes in phase 1

	GI IDR (95% CI)	Diarrhoea IDR (95% CI)	HCGI IDR (95% CI)	Other illnesses* IDR (95% CI)
Site:				
Control	1.00	1.00	1.00	1.00
Intervention	1.12 (0.87–1.43)	1.01 (0.76–1.33)	1.09 (0.91–1.30)	0.99 (0.85–1.15)
Age group (years):				
2–19	1.00	1.00	1.00	1.00
20–64	1.21 (0.94–1.55)	1.99 (1.49–2.67)	1.03 (1.09–1.55)	1.07 (0.92–1.23)
65 +	0.86 (0.62–1.19)	1.45 (1.02–2.08)	0.82 (0.65–1.03)	0.52 (0.42–0.65)
No. illness episodes in phase 1:				
<3	1.00	1.00	1.00	1.00
3 +	4.90 (3.76–6.39)	5.04 (3.75–6.78)	4.32 (3.25–5.74)	2.73 (2.41–3.09)

*Fever, chills, headache or cold without enteric symptoms.

Unadjusted incidence density ratios (IDRs) for phase 2 comparing the control and intervention sites were calculated for the four categories of illnesses (Table 3). None of the IDRs was significantly elevated for any of the four illness categories. Unadjusted IDRs were also calculated for the age groups to determine whether certain age groups were at higher risk of illness in phase 2 (Table 3). Compared with participants aged 2–19 years, both older age groups (20–64 years of age and 65 + years of age) were at higher risk of diarrhoea in phase 2 (IDRs of 1.99 and 1.45). Participants 20–64 years old were also at a slightly higher risk of HCGI compared with the younger age group (IDR 1.03). The number of illness episodes in phase 1 was significantly associated with an increased IDR for the same category of illness in phase 2 (Table 3). Participants having three or more diarrhoea episodes in phase 1 had a fivefold higher risk of diarrhoea episodes compared with those participants who had less than three episodes in phase 1. A similar

magnitude of increased risk was also seen for gastrointestinal illness (IDR 4.90; 95% CI 3.76–6.39) and HCGI (IDR 4.32; 95% CI 3.25–5.74). The IDR for other illnesses was also increased (IDR 2.73; 95% CI 2.41–3.09).

Since both age and number of illness episodes were related to an elevated IDR, adjusted IDRs were calculated to examine the effect of the intervention (Table 4). Although we initially included age, food, travel and contact with animals, these were not significant variables in the final models and were not included in further analyses. We were able to examine the effect of the intervention on the two previous illness groups: 1) participants with less than three episodes of illness in phase 1; and 2) participants with three or more episodes of illness in phase 1. The IDRs comparing the intervention site with the control site for any of the four types of illness were not significantly elevated or reduced for participants with less than three illness episodes in phase 1. In contrast, for participants with three or more

Table 4 | Incidence density ratios (IDRs) for episodes of the four types of illness in the two sites by number of illness episodes in phase 1

	GI IDR (95% CI)	Diarrhoea IDR (95% CI)	HCGI IDR (95% CI)	Other illnesses* IDR (95% CI)
Participants with < 3 illness episodes in phase 1: <i>N</i> = 1026				
Control	1.00	1.00	1.00	1.00
Intervention	1.02 (0.80–1.30)	1.00 (0.75–1.33)	1.05 (0.87–1.26)	0.91 (0.75–1.10)
Participants with 3 + illness episodes in phase 1: <i>N</i> = 42				
Control	1.00	1.00	1.00	1.00
Intervention	1.86 (0.98–3.52)	2.23 (1.18–4.20)	2.67 (1.45–4.93)	1.16 (0.96–1.39)

*Fever, chills, headache or cold without enteric symptoms.

episodes of illness in phase 1, IDRs were elevated for all four types of illness (though not significantly for gastrointestinal and other illnesses) and ranged from 1.16 to 2.67. For diarrhoea, the IDR was significantly increased at 2.23 (95% CI 1.18–4.20), as was the IDR for HCGI (IDR 2.67; 95% CI 1.45–4.93).

DISCUSSION

This study found no overall differences in the risk of any of the four types of illness after the completion of a new water treatment plant. However, there was a significantly increased risk of diarrhoea and HCGI in participants with three or more previous episodes of the same type of illness. The risk for diarrhoea was 2.23-fold higher in the intervention group compared with participants in the control group; for HCGI, it was 2.67-fold higher. This study suggests that prior gastrointestinal illness history or the propensity to report the illness might be a significant risk factor for increased risk of current reported gastrointestinal events, in addition to other factors such as food, travel to another country and contact with animals. In fact, in our study, these other risk factors were not significantly associated with an increased risk of any of the four types of illness.

There was an overall decline in the number of reported illnesses per diary-year from phase 1 to phase 2 that affected all sites. This decline may have been due to reporting fatigue. Alternatively, the number of daily diary days was higher for phase 2 than for phase 1 for both sites. This occurred because there were no delays in phase 2 due to recruitment of participants; they had already been enrolled in the study in phase 1. The difference in number of daily diary days could have affected overall disease reporting since illness rates increased slightly during the winter months. However, the intervention and comparison sites were comparably affected.

It has long been assumed that improved water treatment will reduce the endemic as well as outbreak risks of enteric illness (Environmental Protection Agency 2003). While some studies have found a decreased risk of endemic enteric illness to be associated with improved water treatment, this and other studies have not (Hellard *et al.* 2001, 2002; McConnell *et al.* 2001; Goh *et al.* 2005). A study in northwest England estimated a 79% reduction in the

incidence of cryptosporidiosis after the introduction of membrane filtration (Goh *et al.* 2005). However, our overall observation of no differences in illness rates in phase 1 and phase 2 agrees with studies in Australia that found no differences in gastroenteritis fecal specimens and emergency and hospital admission rates before and after implementation of water treatment (Hellard *et al.* 2001, 2002; McConnell *et al.* 2001).

We examined the geographic distribution of participants and illness risks in both populations (intervention and comparison sites). In fact, we dropped from the analysis a previously planned groundwater comparison site because of evidence of groundwater contamination and elevated illness risks. For the intervention and this comparison population we also examined the geographic distribution of illnesses and did not observe any geographic or temporal clustering.

It is not likely that the observed increased risks of enteric illness were due to higher levels of waterborne enteric pathogens because the enhanced water treatment should have been at least as effective as the water treatment it replaced. However, other studies have hypothesized that improved water quality may, in fact, reduce the protective immunity to *Cryptosporium* and result in higher rates of illness with gastrointestinal symptoms and diarrhoea (Casemore *et al.* 1997; Goh *et al.* 2005; Frost *et al.* 2005a,b). Although our discussion has focused on protective immunity to *Cryptosporidium*, it is possible, if not likely, that other chlorine-resistant waterborne organisms can and have initiated a similar protective immune response. As we have postulated for *Cryptosporidium*, their inactivation or removal could also account for an increased disease risk. Our study, which used an experimental pre-post-intervention design, provides additional evidence to support a protective immunity hypothesis.

In our study, participants at very low risk of enteric illness were unaffected by enhanced treatment of high quality drinking water. However, those participants with higher incidence of diarrhoea or gastrointestinal illness in phase 1 prior to the intervention appeared to experience even higher illness rates after the improvements in water treatment. This suggests that the risk of the occurrence of future gastrointestinal, diarrhoea and other illness episodes may be strongly dependent on individual characteristics and/or susceptibility such as age or prior illness rates.

These measures must be taken into account in the analysis if an effect of an intervention is to be identified. For example, in our study, increased IDRs were not observed if these measures of susceptibility were not included in the analytic models. This suggests that the failure to make similar adjustments in other studies may account for the lack of detection of either increased or reduced enteric disease risks associated with an intervention.

Our other studies have suggested that increased diarrhoea illness risks may be due to declines in the population in protective immunity to cryptosporidiosis (Frost *et al.* 2005a,b). In this study, the enhanced water treatment should have reduced the low-dose exposures to waterborne pathogens such as *Cryptosporidium* oocyst compared with the water treatment it replaced. Improved water treatment in the intervention site would include more complete or total removal or inactivation of *Cryptosporidium* oocysts. Thus, we hypothesize that the level of protective immunity to *Cryptosporidium* oocysts would have been reduced in the intervention population. Reduced waterborne exposure to *Cryptosporidium* oocysts would have resulted in fewer mild or asymptomatic infections which likely enhance protective immunity and prevent the occurrence of more severe infections. In our study, the intervention population would experience more of the severe illness episodes because of reduced immunity. The control population would maintain its level of protective immunity over the two time periods.

Exposure to *Cryptosporidium* oocysts and other enteric pathogens can also occur from sources other than drinking water, and these exposures may help explain the increased risks. Water recreation can be an important source of exposure as are some foods, and exposures to these and other sources may have affected illness rates among the study population (Robertson *et al.* 2002; Roy *et al.* 2004; Craun *et al.* 2005; Dziuban *et al.* 2006). The importance of non-waterborne exposures was suggested by findings that people with high levels of raw vegetable consumption have half the risk of people who do not (odds ratio of 0.5; 95% CI 0.3–0.7) (Roy *et al.* 2004). Two other studies have found similar protective effects from consuming fresh fruit and vegetables (Casemore *et al.* 1997; Robertson *et al.* 2002). Furthermore, oocysts have been detected on fruits and vegetables (Robertson & Gjerde 2001).

The source water used by our study population came from well-protected watersheds with no source or evidence of human sewage contamination. Although there are wild animals residing in the two watersheds, there are no livestock located in the watersheds. The turbidity levels for both the intervention and comparison site were very low throughout the study. This may explain why no overall differences in risks were detected before and after the implementation of the new water treatment system. The water temperature increases somewhat during the summer months, but the area is not subject to extreme differences in temperature from winter to summer, suggesting the disinfection efficacy varies minimally from summer to winter. For these reasons, the results from this study also may not apply to populations where the source water is more heavily contaminated, especially with human or livestock sewage. This would include water from most lakes and rivers that receive sewage discharges. In these situations, the source waters may be contaminated by a wide variety of viral, bacterial and protozoan pathogens which will provide a greater challenge to water treatment facilities. Protective immunity is likely to be less important for waterborne exposures to viral and many bacterial enteric pathogens. If these pathogens survive water filtration and disinfection, increased endemic enteric illness would probably be detected in a study of similar design.

CONCLUSION

Even though the findings of this study are consistent with our earlier predictions of changes in protective immunity following enhanced water treatment, the evidence from this study is insufficient to conclude that the elevated risks in phase 2 were due to decreased levels of protective immunity. However, the findings do suggest that immunity may be important. If it is true that changes in the enteric illness risk following enhanced water treatment are due to reductions in protective immunity to cryptosporidiosis, then, additional studies should be completed of high-risk immunosuppressed populations. Such a population might include patients who are immunosuppressed as a result of medical interventions such as organ transplants. In this population, the risks of post-transplant diarrhoea or

gastrointestinal illness would be reduced if the patients have been previously exposed to low doses of pathogens such as *Cryptosporidium*.

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