Observational epidemiologic studies of endemic waterborne risks: cohort, case-control, time-series, and ecologic studies

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ABSTRACT

Observational studies have assessed endemic waterborne risks in a number of countries. Time-series analyses associated increased water turbidity with increased gastroenteritis risks in several public water systems. Several cohort studies reported an increased risk of gastroenteritis in populations using certain public or individual water systems. Although several case-control studies found increased waterborne risks, they also found increased risks associated with other exposures. An increased risk of campylobacteriosis was associated with drinking untreated water from non-urban areas and some tap waters; other significant risks included contaminated poultry and foreign travel. Increased risks of cryptosporidiosis and giardiasis were associated with drinking water in some populations; other risk factors included foreign travel, day care exposures, and swimming. These observational studies provide evidence that some populations may be at an increased risk of endemic or sporadic illness from waterborne exposures, but not all studies found an increased risk. Differences in waterborne risks may be due to differences in water quality. System vulnerabilities and contamination likely differed in the areas that were studied. The information from these studies may help inform estimates of waterborne illness for the US population but is inadequate to estimate a population attributable risk.

Key words | Campylobacteriosis, case-control studies, cohort studies, cryptosporidiosis, ecologic studies, endemic waterborne illness, gastroenteritis, giardiasis, time-series analysis

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INTRODUCTION

We evaluated the available information about endemic waterborne risks from cohort, case-control, time-series, and ecologic studies conducted in the United States and other developed countries. Risks of waterborne campylobacteriosis, cryptosporidiosis, giardiasis, and gastrointestinal illness of unspecified etiology (AGI) are summarized in Tables 1–4. The studies are reviewed based on study type and illness. Although most of these observational studies are relatively recent, some were published as earlier as 1977. Several cross-sectional studies and surveys are included among the studies reviewed in the cohort and case-control sections.

For a discussion of the various study designs, readers are referred to a previous article (Craun *et al.* 2006*a*) in this special issue of the *Journal of Water and Health*. Community-intervention studies (Calderon & Craun 2006), experimental, household-intervention studies (Colford *et al.* 2006) are reviewed elsewhere in this special issue.

COHORT STUDIES

Studies in Canada, France, and Norway assessed waterborne AGI risks. Studies in the United States and New Zealand assessed waterborne giardiasis risks. Participants were selected on the presence or absence of certain characteristics, a specific event, or their exposure status (e.g. chlorinated or

Table 1 | Cohort studies, endemic waterborne risks in community water systems

Disease	Study location	Population	Univariate RR (95% CI) [90% CI]	Water exposure
Giardiasis	Vermont, USA (Birkhead & Vogt 1989)	Residents	1.9 (1.1, 3.3)	Unfiltered surface water
Giardiasis	Dunedin, NZ (Fraser & Cooke 1991)	Residents	3.32 [1.1, 10.1]	Unfiltered surface water
Gastroenteritis	Norway (Kuusi et al. 2003)	Child < 15 yrs.	0.5 (0.2–1.2)	Community water systems
			0.4 (0.2–0.9)	Chlorinated water
Gastroenteritis	France, 52 Alpine villages (Zmirou et al. 1987)	Residents	0.27 (0.14–0.51) 1.14 (0.67–1.92)	Untreated wells; + fecal coliform & no fecal streptococci: < 400 population > 400 population
Gastroenteritis	France, Alpine villages (Gofti-Laroche et al. 2003a)	Residents	1.19 (0.96–1.48) 1.24 (1.06–1.45)	10–20 Giardia cysts/100 l > 20 cysts/100 l in tap water
Gastroenteritis	France, Alpine villages (Gofti-Laroche et al. 2003b)	Residents	1.51 (1.17–1.94)	Astrovirus in water

unchlorinated drinking water, water source, or coliform bacteria levels in water). Disease incidence was determined during the follow-up period, and disease rates (i.e. rate difference (RD) and rate ratio or relative risk (RR)) were compared for the exposed and unexposed groups. The risk attributable to water may be computed if the study is not confounded or affected by one or more sources of bias (Rothman & Greenland 1986; Monson 1990).

Canada

Raina et al. (1999) studied AGI incidence among 442 Southern Ontario families. For 195 of the families, at least

one well-water sample was found to exceed the Ministry of Environmental standards for coliform bacteria. One contact person in each household completed a daily family diary describing illness events; AGI was defined as an episode in which diarrhea with or without vomiting was reported. Interviewers also collected information about well-water consumption, water treatment, and other risk factors. During a site visit, the well depth and distance from a septic tank was obtained. During the one-year follow-up period, 213 gastrointestinal (0.40 per person-year) and 945 non-gastrointestinal (1.78 per person-year) episodes were reported. At least one episode of AGI was reported for 31.6% of persons with *Escherichia coli* positive wells

Table 2 | Cohort studies, endemic waterborne risks in individual water systems

Disease	Study location	Population	Univariate RR (95% CI)	Water exposure
Gastroenteritis	Ontario, Canada (Raina et al. 1999)	Residents	2.16 (1.04–4.42) 0.46 (0.07–2.95)	Septic tank distance from +E. coli well: > 20 meters < 20 meters
Gastroenteritis	Ontario, Canada (Strauss et al. 2001)	Residents	1.52 (0.33–6.92) 0.39 (0.10–1.50)	Wells exceeding limit for: E. coli total coliforms
Gastroenteritis	Norway (Kuusi et al. 2003)	Child < 15 yrs.	3.1 (1.4–7.1)	Well or surface water

compared to 25.8% of persons with *E. coli* negative wells. After adjusting for other risk factors and confounders, a significant association was observed between *E. coli* positive wells and illness. The association was modified by the distance from the household septic tank to the well. When the septic tank was greater than 20 meters from an *E. coli* positive well, an increased AGI risk was found (OR = 2.16; 95% CI = 1.04–4.42). When the well was within 20 meters, the risk was not increased. The investigators suggested that study participants whose septic tank was close to their well may have had higher levels of immunity to AGI because of consistent exposure to waterborne pathogens.

During April to July 1995, Strauss *et al*. (2001) conducted a prospective study of 235 households (647 individuals) randomly selected from four rural hamlets in eastern Ontario. A self-administered questionnaire, a diary of self-reported symptoms, and two drinking water samples provided information about the cohort. Although a high prevalence of the private, individual wells (20% of households) were contaminated with coliforms or *E. coli* above the standards, the study found no statistically significant associations between these indicator bacteria and AGI. The case definition for AGI was similar to that used by Payment *et al*. (1991): either (1) vomiting or liquid diarrhea, or (2) nausea or soft, loose diarrhea combined with abdominal cramps.

In a year-long study, Isaac-Renton *et al*. (1996) found *Giardia* cysts in 77–98% of treated drinking water samples from two British Columbia communities; a health survey suggested low-level endemic waterborne transmission in these communities. An increased prevalence of laboratory-confirmed cases was also found in both communities compared to a nearby community with a less vulnerable water system.

France

Zmirou *et al*. (1987) conducted a prospective study for 64 weeks in 52 French Alpine villages with public water systems that used untreated groundwater. Weekly water samples were collected for indicator bacteria; 42% of the samples exceeded bacteriological standards. Cases of AGI were reported through physicians, pharmacists, and primary school teachers. Although most cases were sporadic, one outbreak of 50 cases was observed during the study period. The investigators concluded that the best predictor of AGI risk was fecal streptococcus in water; fecal coliforms enhanced this effect. When only fecal coliforms were present, a decreased AGI risk was observed in the smaller villages (<400 population: RR = 0.27; 95% CI = 0.14–0.51), and no increased risk was found in the larger villages (Table 1). Increased AGI risks were observed in both small and large villages where both fecal coliforms and streptococci were present. For example, when fecal coliforms were present and fecal streptococci counts were 1–5 per 100 ml, the RR = 4.3 (95% CI = 2.1–8.6) in the smaller villages and the RR = 2.7 (95% CI = 1.6–4.1) in the larger villages. Total bacterial count or the presence of total coliforms in the water made no independent contribution to risk, and about one-fourth of all cases were reported when all water quality indicators were absent.

In a nine-month period during 1998 and 1999, Gofti-Laroche *et al*. (2001, 2003*a, b*) followed a panel of 544 volunteers exposed to either of the following community water systems: a surface water source surrounded by farm and human activity; an unprotected groundwater with potential sources of contamination; an untreated groundwater system under the direct influence of surface water (GWUDI), or a GWUDI that received chlorination. The bacterial, virological, and parasitic quality of tap water was assessed at least monthly, and information about AGI (defined as an episode of abdominal pain, nausea, vomiting, and/or diarrhea) was obtained by weekly phone calls. The highest incidence of AGI was in the participants using an unprotected groundwater source (4.7 cases per person-day; 95% CI = 4.0–5.3). During the study, fecal indicators were found in all of the raw water samples and 20% of the tap water samples. Of 36 tap water samples analyzed for protozoa, eight were positive for *Giardia* and three for *Cryptosporidium*.

The final risk model of Gofti-Laroche *et al*. included the presence of *Giardia* in tap water and several confounding factors (e.g. age, month, water intake, and compliance with water quality criteria). The presence of more than 20 *Giardia* cysts per 100 l was associated with an increased AGI risk (RR = 1.24; 95% CI = 1.06–1.45). For tap water

with 10–20 *Giardia* cysts per 100 l, the risk was slightly increased but not statistically significant (RR = 1.19; 95% CI = 0.96–1.48).

Although astrovirus RNA was detected in only one of 44 tap water samples, it was detected in seven of 24 raw water samples, and Gofti-Laroche *et al.* found an increased risk of AGI (RR = 1.51; 95% CI = 1.17–1.94) associated with the presence of astrovirus RNA in raw or tap water. The investigators felt that chlorination, as practiced during the study, was insufficient to disinfect astrovirus and, thus, considered the raw water quality as representative of the finished water quality. The presence of rotavirus RNA (10 of 88 samples) or *Cryptosporidium* was not associated with increased AGI.

Norway

As part of a population-based prospective survey to determine the incidence of AGI during 1999 and 2000, Kuusi *et al.* (2003) collected information about selected exposures, including drinking water. A questionnaire mailed to 3000 randomly selected persons was completed by 61% of the persons contacted. AGI was defined as having the following symptoms in the four weeks before completing the questionnaire: (1) diarrhea (three or more loose stools in 24 hours) or (2) at least three of these four symptoms–vomiting, nausea, abdominal cramps or fever (38°C or higher). Among adults 20 to 40 years old, traveling abroad was associated with illness (RR = 1.8; 95% CI = 1.0–3.0). Among children less than 15 years of age, drinking water from a private, individual water system (well or surface source) was associated with an increased illness risk (RR = 3.1; 95% CI = 1.4–7.1) while using chlorinated water was protective (RR = 0.4; 95% CI = 0.2–0.9).

United States

An association between giardiasis and drinking water exposure was suggested in a survey of intestinal parasites in two Washington counties. Harter *et al.* (1982) reported a 7.1% *Giardia* prevalence among 518 children, one to three years of age; a higher prevalence was associated with unfiltered surface water. Only one of 37 (2.7%) children

residing in a home using filtered surface water was found to be infected with *Giardia* compared with 10 of 175 (6.9%) children residing in homes using unfiltered surface water. An increased prevalence of infection was also associated with drinking untreated surface water from streams or lakes during recreational activities. A survey of 383 Utah National Guard members found that 15% had symptoms suggestive of giardiasis (Laxer 1985). The guardsmen were at risk of contracting giardiasis by drinking contaminated water during field exercises in Utah; 62% of the men who had symptoms drank untreated water from lakes, streams, and a cattle watering trough.

In Vermont, Birkhead & Vogt (1989) studied 1211 cases of laboratory-confirmed giardiasis that were reported through a laboratory-based active surveillance system during 1983 to 1986. Excluding outbreak cases, the lowest incidence of giardiasis was found among populations using municipal surface water systems with filtration (1.5 cases per 100 000 person-years). An incidence of 28.6 per 100 000 person-years was found among populations using unfiltered municipal surface water systems (RR = 1.9; 95% CI = 1.1–3.3), and 32.8 per 100 000 person-years was found among populations using private, individual water systems (RR = 2.2; 95% CI = 1.3–3.6).

Sorvillo *et al.* (1998) examined seasonality and other factors associated with *Cryptosporidium* infection in a cohort of 4247 HIV-infected patients in Los Angeles County during 1990 to 1996. Cryptosporidiosis was diagnosed in 120 patients (2.8%). Although cryptosporidiosis among HIV-infected persons exhibited a modest spring and fall seasonality, the pattern was temporally unrelated to local rainfall patterns and the possible contamination of open drinking water reservoirs.

New Zealand

Fraser & Cooke (1991) found that the incidence of laboratory-confirmed giardiasis was higher (RR = 3.3; 90% CI = 1.1–10.1) in an area of Dunedin where surface water was mechanically microstrained through a 23 μm screen and chlorinated compared to other areas where drinking water was more thoroughly treated (i.e. coagulation, flocculation, dual media filtration, and chlorination).

Summary of cohort studies

Studies in Canada and France found no consistent association between AGI risk and coliform bacteria in drinking water from small community and individual systems. However, risks in France were associated with other indicators of fecal contamination, and about one-fourth of all AGI episodes occurred when bacteriological indicators were not detected. More recent studies in France found that the presence of astrovirus RNA or high levels of *Giardia* in village water systems was associated with an increased AGI risk, but the presence of *Cryptosporidium* or rotavirus RNA was not associated with an increased risk.

Strauss *et al*. (2001) did not find a significant association between AGI and coliforms or *E. coli* above the standard; other studies had similar findings (Zmirou *et al*. 1987; Fattal *et al*. 1988; Meara 1989; Raina *et al*. 1999). Strauss *et al*. offered two possible explanations. The relatively low levels of indicator bacteria in the systems studied may have indicated an insufficient amount of contamination to cause illness or some amount of exposure to contaminated drinking water may be protective of AGI. In support of a protective effect, Strauss *et al*. noted that, in their study, older persons and a longer duration of residence were independently associated with contaminated well water and that the incidence of AGI was significantly lower in older persons. Long-term older residents had more frequent exposure to contaminated water and, thus, a greater opportunity to develop protective immunity. In Norway, Kuusi *et al*. (2003) found increased AGI risks among children, but not adults, who drank water from individual water systems; using chlorinated water was protective for children. Kuusi *et al*. also noted that children may be more susceptible to illness while adults may have developed some protective immunity from previous infections.

Early studies in the United States suggested that endemic giardiasis was associated with the consumption of untreated surface water and water from private, individual systems. Studies in Vermont and New Zealand found that an increased risk of giardiasis was associated with community systems that do not filter surface water sources.

CASE-CONTROL STUDIES

Individuals enter a casecontrol study solely on the basis of disease status without knowledge of their exposure status. A single disease or health outcome (e.g. giardiasis or cryptosporidiosis) is usually selected for study. Diseased persons and a comparison group (controls) in which the condition or disease is absent are selected from a defined geographical area or population. The frequency of existing or past attributes and exposures thought to be relevant in the development of the disease are determined for all participants and compared among cases and controls. Because study participants are selected according to their disease status, the exposure odds ratio (OR) is determined. The OR can be interpreted similar to the RR (Miettinen 1976).

The studies reviewed here considered various risk factors and exposures, including tap water, untreated water, and bottled water. Studies of endemic campylobacteriosis, cryptosporidiosis, and giardiasis were conducted in the United States, United Kingdom, Australia, Canada, Denmark, Finland, Norway, and New Zealand. Our literature search uncovered no published case-control studies of AGI and waterborne risks.

Campylobacteriosis

Canada

In Quebec, Michaud *et al*. (2004) studied 158 culture-confirmed cases of campylobacteriosis reported from July 2000 to September 2001 and 314 controls matched for age and gender. Excluded were persons who had traveled outside of Quebec during the ten days prior to the onset of illness. Study participants were interviewed by telephone. A univariate analysis found that drinking tap water at home or work was associated with an increased risk for infection (OR = 1.90, $p = 0.03$), and in the county with the highest incidence, tap water from a deep well was the only risk factor identified (OR = 3.96, $p = 0.06$). Conditional multivariate analysis identified three independent risk factors: consuming raw or undercooked poultry, raw milk or milk products, or poultry in a restaurant. These three factors accounted for only 46% of the cases, and Michaud *et al*.

noted that the importance of drinking water as a source of endemic infection may be underestimated.

Denmark

During 1996 to 1997, Neimann *et al.* (2003) studied 282 culture-confirmed cases of campylobacteriosis and 319 controls matched for age, gender, and county in 9 of the 16 Danish counties. A univariate analysis identified, among other risk factors, an increased risk of campylobacteriosis associated with drinking water. Risk of infection was increased in households where drinking water had a bad taste or smell in the 14 days prior to illness onset (OR = 4.23; 95% CI = 1.18–15.04). Neimann *et al.* noted that the only waterborne outbreak of campylobacteriosis in Denmark had occurred in a community where the water had a bad taste or smell due to sewage contamination.

Increased risks were also associated with having an individual well as the household supply (OR = 2.09; 95% CI = 0.90–6.16). Other risk factors included consumption of under-cooked poultry (OR = 8.24; 95% CI = 1.07–63.12) and drinking unpasteurized milk (OR = 11.78; 95% CI = 1.97–70.32). Protective factors included proper kitchen hygiene practices. Neimann *et al.* concluded that water is a source of sporadic infections in Denmark. More than 99% of the registered public water supply in Denmark comes from groundwater sources, and most systems are not chlorinated.

Finland

Schonberg-Norio *et al.* (2004) studied 100 patients and 137 controls from three geographic areas during a seasonal peak of infections in 2002. A case-patient was a person who had a stool culture that was positive for either *Campylobacter jejuni* or *C. coli* and who had not traveled abroad within two weeks before illness. Controls were selected from a register of Finnish residents and matched for age, gender and municipality; persons who were ill or had traveled abroad were excluded. Information about risk factors was obtained by mailed questionnaire. A univariate analysis identified drinking water from a dug well (adjusted OR = 3.19; 95% CI = 1.58–6.15) as a significant risk factor; other risk factors included eating or tasting raw meat

and swimming in natural sources of water. No increased risk was associated with drinking bottled water, water from a bedrock-aquifer well, or water from a small water system. Possible protective factors included eating carrots (adjusted OR = 0.44; 95% CI = 0.24–0.82) and drinking water from a large water public system (adjusted OR = 0.52; 95% CI = 0.26–1.02). Large systems in Finland use surface water with multistage purification and disinfection, whereas dug wells are susceptible to surface water contamination and are usually not disinfected.

Norway

Kapperud *et al.* (2003) studied campylobacteriosis risks among 212 cases and 422 population controls in three counties which contained 24% of Norway's population. A case was a resident who had not traveled abroad within two weeks before illness and had culture-confirmed campylobacteriosis caused by *C. jejuni* or *C. coli* during July 1999 to June 2000. Controls were matched by age, gender, and area. Information about risk factors were obtained by mailed questionnaire with a follow-up telephone interview. In a univariate analysis, drinking undisinfected water in the two weeks prior to the onset of illness was associated with an increased risk of infection (OR = 1.8; 95% CI = 1.2–2.6). Further analyses found that persons who drank water directly from a surface source during outdoor activities were not at increased risk (OR = 1.5; 95% CI = 0.9–2.5), but persons who drank water from private wells were at increased risk (OR = 2.0; 95% CI = 1.2–3.2). In a conditional logistic regression analysis that included factors associated with increased and decreased risks, undisinfected water was independently associated with an increased risk (OR = 2.5; 95% CI = 1.2–5.4). Other factors associated with an increased risk included eating at barbeques and eating poultry bought raw. Barbequing provides opportunities for under-cooking meats, and raw poultry provides opportunities for cross-contamination during meal preparation.

United Kingdom

Adak *et al.* (1995) obtained information from eleven public health laboratories to conduct a study of 598 cases and 598

Table 3 | Case-control studies, endemic waterborne risks in community water systems

Disease	Study location	Population	OR[1] (95% CI) [90% CI]	Water exposure
Giardiasis	Dunedin, NZ (Fraser & Cooke 1991)	Residents	1.8 [0.5–6.5]	Unfiltered SW
Giardiasis	Auckland, NZ (Hoque et al. 2003)	Children <5 yrs.	8.6 (3.5–21.2)	CWS other than Auckland
Giardiasis	Southwest England (Stuart et al. 2003)	Residents, lab +	1.3 (1.1–1.5)[1]	Each additional glass of treated tap water daily
Campylobacteriosis	Quebec, Canada (Michaud et al. 2004)	Residents, lab +	1.9, $p = 0.03$	Tap water[2]
Campylobacteriosis	Denmark (Neimann et al. 2003)	Residents, lab +	4.23 (1.18–15.04)	Water with bad taste or smell[2]
Campylobacteriosis	Finland (Schonberg-Norio et al. 2004)	Residents, lab +	0.52 (0.26–1.02)	Large CWS
			0.80 (0.37–1.72)	Small CWS
Campylobacteriosis	Christchurch, NZ (Ikram et al. 1994)	Residents, lab +	0.6 (0.1–1.9)	Towns other than Christchurch
Campylobacteriosis	Cardiff, Wales (Evans et al. 2003)	Residents, lab +	1.51 (1.06–2.18)	Tap water[2]
Cryptosporidiosis	Adelaide (Robertson et al. 2002)	Residents, lab +	1.0 (0.7–1.6)	Filtered SW
Cryptosporidiosis	Melbourne (Robertson et al. 2002)	Residents, lab +	1.3 (0.9–2.1)	Unfiltered SW
Cryptosporidiosis	San Francisco Bay (Aragon et al. 2003)	AIDS patients, lab +	6.76 (1.37–33.5)[1]	Tap water, home[2]
			3.16 (1.23–8.13)[1]	Tap water outside home
			1.19 (0.34–4.20)[1]	Unfiltered SW
			0.77 (0.35–1.74)[1]	Mixed
Cryptosporidiosis	San Francisco Bay (Khalakdina et al. 2003)	Immunocompetent, lab +	0.92 (0.16–5.30)	Tap water[2]
Cryptosporidiosis	North West England (Goh et al. 2004)	Residents, lab +	1.40 (1.14–1.71)[1]	Tap water[3]; Per pint daily
Cryptosporidiosis	North West England & Wales (Hunter et al. 2004)	Residents, lab +	1.135 (1.010–1.265)[1]	Tap water[2]; Per glass daily
Cryptosporidiosis	United States, 7 states (Roy et al. 2004)	Residents, lab +	0.7 (0.4–1.1)	Tap water

[1]Multivariate; all others univariate; [2]Presumed study population used a CWS; [3]98% of study population used CWS (at least 65% of used unfiltered SW, 35% used either filtered or unfiltered SW); CWS = community water system; SW = surface water.

Table 4 | Case-control studies, endemic waterborne risks in individual water systems

Disease	Study location	Population	OR[1] (95% CI)	Water exposure
Giardiasis	Auckland, NZ (Hoque et al. 2003)	Children <5 yrs.	8.3 (2.6–26.7)	Rain water from roof
			10.4 (1.0–55.8)	River
			9.9 (0.6–158.3)	Bored well
			2.4 (0.7–8.1)	Bottled water
Giardiasis	New Hampshire, USA (Chute et al. 1987)	Dartmouth-Hitchcock Clinic; lab +	2.1 (1.3–3.2)[1]	Shallow well
Giardiasis	Southwest England (Stuart et al. 2003)	Residents, lab +	1.6 (0.9–2.9)	Bottled water
			0.9 (0.5–1.7)	Water filter at home
Giardiasis	Avon, Somerset UK (Gray et al. 1994)	Residents, lab +	4.4 (0.3–60.3)[1]	Contaminated water
Campylobacteriosis	Denmark (Neimann et al. 2003)	Residents, lab +	2.09 (0.90–6.16)	Well
Campylobacteriosis	Finland (Schonberg-Norio et al. 2004)	Residents, lab +	3.36 (1.37–8.24)[1]	Dug well
			1.96 (0.89–4.34)	Bedrock well
			0.75 (0.37–1.51)	Bottled water
Campylobacteriosis	Norway (Kapperud et al. 2003)	Residents, lab +	2.5 (1.2–5.4)[1]	Undisinfected water (model 2)
			1.5 (0.9–2.5)	Untreated surface water
			2.0 (1.2–3.2)	Private wells
Campylobacteriosis	Christchurch, NZ (Ikram et al. 1994)	Residents, lab +	2.7 (0.9–8.3)	Rural sources
Campylobacteriosis	NZ (Eberhart-Phillips et al. 1997)	Residents, MD notified; most lab +	2.20 (1.04–4.65)	Rain water from roof
Campylobacteriosis	Cardiff, Wales (Evans et al. 2003)	Residents, lab +	1.41 (1.02–1.95)[1]	Bottled water
Cryptosporidiosis	Adelaide (Robertson et al. 2002)	Residents, lab +	3.1 (1.5–6.5)	River or lake
Cryptosporidiosis	Melbourne (Robertson et al. 2002)	Residents, lab +	1.5 (0.8–2.7)	River or lake
Cryptosporidiosis	San Francisco Bay (Aragon et al. 2003)	AIDS patients, lab +	0.09 (0.03–0.37)	Bottled water always, home
			0.75 (0.28–2.06)	Bottled water always, outside home
Cryptosporidiosis	San Francisco Bay (Khalakdina et al. 2003)	Immunocompetent, lab +	0.74 (0.11–5.02)	Filtered tap water or bottled water
Cryptosporidiosis	United States, 7 states (Roy et al. 2004)	Residents, lab +	1.5 (1.0–2.4)	Well
			1.0 (0.7–1.4)	Bottled water
			0.6 (0.4–0.9)	Filtering drinking water

[1]Multivariate; all others univariate.

controls matched on age, gender, and geography of residence. Conditional logistic regression analysis identified the following significant risk factors: occupational exposure to raw meat (OR = 9.37; 95% CI = 2.03–43.3), having a pet with diarrhea (OR = 2.39; 95% CI = 1.09–5.25), and drinking untreated water from lakes, rivers, and streams (OR = 4.16; 95% CI = 1.45–11.9) within the 10 days before becoming ill with campylobacteriosis.

Evans et al. (2003) conducted a case-control study in the Cardiff area among persons who had consulted a physician for gastrointestinal symptoms and subsequently submitted a fecal sample for analysis. The study included 213 symptomatic persons who were positive for *Campylobacter spp.* and 1144 case-patients who tested negative; 91 patients who tested positive for other pathogens were excluded. Increased risks were found for several exposures including drinking water, contact with cows or calves, and eating chicken, salad vegetables, or berries. Unadjusted risks were reported for drinking cold tap water (OR = 1.51; 95% CI = 1.06–2.18) and drinking bottled water (OR = 1.98; 95% CI = 1.48–2.67). The final model included a risk for bottled water (adjusted OR = 1.41; 95% CI = 1.02–1.95). The highest attributable fractions were found for eating chicken (31%), eating salad (21%), or drinking bottled water (12%).

New Zealand

Campylobacteriosis accounts for about two-thirds of all notifiable diseases in New Zealand. Eberhart-Phillips et al. (1997) studied 621 cases reported during June 1994 to February 1995. Controls were randomly selected from telephone directories, matched with cases for gender, age group, and home phone prefix in four urban centers. A univariate analysis identified a strong association of campylobacteriosis with the recent consumption of raw or undercooked chicken (OR = 4.52; 95% CI = 2.88–7.10) and overseas travel (OR = 4.43; 95% CI = 1.95–10.06). Drinking water was also identified as a risk factor. Risks were associated with using roof-collected rainwater as a home water source (OR = 2.20; 95% CI = 1.04–4.62) and non-city water outside the home in the 10 days before illness (OR = 1.63; 95% CI = 1.17–2.27). Rainwater systems are typically untreated, and birds, which are a major reservoir for *Campylobacter* species, can contaminate rainwater systems by roosting on house roofs.

Ikram et al. (1994) studied 100 cases identified by medical practitioners from stool isolates of *Campylobacter* spp. in the Christchurch area during the summer of 1992–1993. A control was selected by the same medical practitioner, matched by age and gender. Eating poorly cooked or handled chicken was a significant source of illness. An increased risk (OR = 4.94; 95% CI = 1.03–23.62) was associated with eating under-cooked chicken. Drinking water from a non-urban supply (OR = 2.70; 95% CI = 0.89–8.33) was among the risk factors; however, the risk was not statistically significant. Drinking water from another town was not a risk factor (OR = 0.56; 95% CI = 0.12–1.85).

Giardiasis

Canada

Mathias et al. (1992) found no increased risks of giardiasis associated with drinking water in Vancouver, a city served by an unfiltered, chlorinated water supply. Important risk factors were travel abroad and elsewhere within British Columbia. Isaac-Renton & Philon (1992) found that drinking local tap water was a risk factor for persons who traveled to rural areas of British Columbia. Persons who drank unfiltered, unchlorinated surface water were at a higher risk for laboratory-confirmed giardiasis than persons who drank well water. There was little difference in risk for persons who drank unfiltered, chlorinated surface water compared to persons who drank unfiltered, unchlorinated surface water.

New Zealand

In addition to a cohort study, Fraser & Cooke (1991) conducted a small case-control study in Dunedin to investigate the risk of endemic giardiasis. Higher, but statistically nonsignificant risks (OR = 1.8; 90% CI = 0.5–6.5) were associated with living in a part of the city where the municipal water was unfiltered.

Among children under five years of age (69 cases and 98 controls), Hoque et al. (2003) found an increased risk of giardiasis associated with using public water systems other

than the Auckland Metropolitan Mains (AMM) supply (adjusted OR = 8.6; 95% CI = 3.5–21.2) and consuming water away from home (adjusted OR = 4.7; 95% CI = 2.2–10.1). Risks were also associated with swimming at least once a week, exposure to children wearing diapers, and traveling domestically. Consuming water from other than AMM (PAR = 57.8%) and traveling (PAR = 33.2%) have a significant impact among this population.

United Kingdom

Using a postal questionnaire, Gray et al. (1994) obtained travel history, water consumption, and recreational water use for 74 patients having *Giardia*-positive stools and 108 matched controls in Avon and Somerset. Conditional logistic regression analysis identified swimming and travel as important risk factors. Drinking potentially contaminated water was not associated with increased risk (adjusted OR = 4.4; 95% CI = 0.3–60.3).

United States

In a survey of 256 Colorado residents with *Giardia*-positive stools and 256 controls matched by age, gender, race, and place of residence,Wright et al. (1977) found a higher proportion of cases among persons who visited Colorado mountains (69% vs. 47%), camped overnight (38% vs. 18%), and drank untreated mountain water (50% vs. 17%). In a survey of 78 Minnesota residents with *Giardia*-positive stools and no history of recent foreign travel, Weiss et al. (1977) found that 63% had consumed untreated water; unfortunately, an appropriate comparison group was not included in the study. In a study of 349 Washington State residents having *Giardia*-positive stools and 349 controls matched by age and gender, Harter et al. (1982) and Frost et al. (1983) found that consumption of untreated water, nursery school exposure for children, and foreign travel to developing countries was associated with a higher risk of acquiring *Giardia* infection.

Chute et al. (1985, 1987) collected information by mail survey about potential risk factors from 171 Hitchcock Clinic patients with giardiasis and an age- and sex-matched control group of 684 other clinic patients. Patients were identified during 1977 to 1984; Dartmouth students were

excluded. An increased risk (adjusted OR = 2.1; 95% CI = 1.3–3.2) of giardiasis was associated with the use of a shallow well or surface water for household drinking water compared to the use of drilled wells or municipal water. The etiologic fraction attributable to shallow wells or surface water was 18%. Other observed risks were travel outside the United States, family member diagnosed with giardiasis, family member in a day-care program, and camping. In a study of 273 cases and 375 matched controls during 1984 and 1985 in New Hampshire, Dennis et al. (1993) found that drinking water from shallow wells was a significant risk factor; other risk factors were contact with a person in day care and swimming in a lake, pond, stream or river.

Cryptosporidiosis

Australia

In an exploratory study in South Australia, Weinstein et al. (1993) found that only water-related exposures (i.e. consumption of rain and spring water) were significantly associated with cryptosporidiosis.

Robertson et al. (2002) assessed risk factors for sporadic cryptosporidiosis in Melbourne and Adelaide, both of which use surface water sources. Melbourne has high quality source water from highly protected catchments; the water undergoes minimal treatment with chlorination. Adelaide obtains water from unprotected catchments; the water undergoes full conventional water treatment including coagulation, sedimentation, filtration and chlorination. The study included 201 cases and 795 controls in Melbourne and 134 cases and 536 controls in Adelaide. Participants were recruited from the general communities, and four controls were matched for each case according to age and sex. A case was defined as having *Cryptosporidium* oocysts detected in a fecal specimen by an accredited pathology laboratory and an onset of diarrhea or vomiting within eight weeks before the administration of the questionnaire. A control was defined as not having diarrhea or vomiting in the 2 weeks before the onset of the matching case's illness. The most important risks were associated with swimming in public pools and having contact with a person with diarrhea. Other risk factors were similar for the two

cities. In Adelaide, an increased risk was associated with drinking unboiled water from a river or lake in rural Australia (adjusted OR = 3.1; 95% CI = 1.5–6.5). In Melborne, a small, non-statistically significant risk was associated with drinking unboiled water from a river or lake in rural Australia (adjusted OR = 1.5; 95% CI = 0.8–2.7).

The consumption of tap water was not associated with cryptosporidiosis in Adelaide (adjusted OR = 1.0; 95% CI = 0.7–1.6) or Melbourne (adjusted OR = 1.3; 95% CI = 0.9–2.1). Risks were not significantly different for the amount of tap water consumed, and there was no evidence of a trend of increased risk with increased consumption. In Adelaide, the following risks were reported: consumption of >4 glasses per day (adjusted OR = 0.8; 95% CI = 0.4–1.3), 2–4 glasses per day (adjusted OR = 1.2; 95% CI = 0.7–2.0), and less than 2 glasses per day (adjusted OR = 1.1; 95% CI = 0.7–2.0). In Melbourne, the following risks were reported: consumption of >4 glasses per day (adjusted OR = 1.5; 95% CI = 0.9–2.6), 2–4 glasses per day (adjusted OR = 1.0; 95% CI = 0.6–1.7), and less than 2 glasses per day (adjusted OR = 1.4; 95% CI = 0.9–2.4).

United States

In a small case-control study in New Mexico, Gallaher et al. (1989) found that sporadic cryptosporidiosis was statistically associated with use of untreated surface water. More recently, Roy et al. (2004) assessed risk factors for sporadic cryptosporidiosis among immunocompetent persons in seven sites of the Foodborne Diseases Active Surveillance Network (FoodNet). The study included 282 persons with laboratory-identified cryptosporidiosis and 490 age-matched and geographically matched controls. Risk factors included international travel, contact with cattle, contact with persons aged 2–11 years of age with diarrhea, and freshwater swimming. Eating raw vegetables was protective. None of the drinking water source variables studied (public water system, well water, bottled water, or filtered tap water) were found to be significantly associated with the development of cryptosporidiosis. Although filtering tap water was a protective factor in a univariate analysis, the association between filtered water and cryptosporidiosis was not statistically significant in a multivariate analysis that either included or excluded international travelers. The *Cryptosporidium*

sp. identified in each case-patient was not genotyped, and Roy et al. did not comment on differences in epidemiology between sporadic cases associated with bovine and human species. Roy et al. cautioned that the results should not be generalized to the US population because the seven FoodNet sites do not comprise a nationally representative sample, the study participants were mostly white and non-Hispanic, and half of the participants came from Minnesota.

Several studies were conducted in the San Francisco Bay area. Khalakdina et al. (2003) recruited cases from a population-based, active surveillance system. Age-matched controls were recruited using sequential random-digit dialing. Cases (n = 26) and controls (n = 62) were interviewed by telephone using a standardized questionnaire. Information was obtained about the following exposures: drinking water, recreational water, food items, travel, animal contact, person-to-person fecal contact, and sexual practices (for adults). The most important risk factor was travel to another country. No significant association with drinking water was detected in multivariate conditional logistic regression analyses. The consumption of tap water with no further treatment or processing was not associated with cryptosporidiosis when compared to consumption of boiled water. Although the results of this study did not find an increased risk associated with drinking tap water among an immunocompetent population, Khalakdina et al. noted that the study did not assess individual exposures to potential oocyst-contaminated water.

Aragon et al. (2003) studied cryptosporidiosis risks among persons with acquired immunodeficiency syndrome (AIDS). Cases (n = 49) were selected from patients who were reported to the San Francisco AIDS Registry; controls (n = 99) were individually matched on age, gender, race/ethnicity, CD4 + T lymphocyte count, date of CD4 + count, and date of diagnosis. In the multivariable analysis with adjustments for confounders, tap water consumption inside and outside the home at the highest exposure categories was associated with cryptosporidiosis. Risks were associated with water consumed inside the home (OR = 6.76; 95% C1 1.37–33.5) and outside the home (OR = 3.16; 95% C1 1.23–8.13). Aragon et al. estimated that as many as 85% of the cases of cryptosporidiosis in San Francisco AIDS patients may be attributable to tap water consumption (PAR = 85%).

Eisenberg *et al.* (2002) conducted a cross-sectional survey to measure risk factors, especially drinking water exposure, and their association with diarrhea among 226 HIV-infected men who were patients at the San Francisco Veterans Administration Medical Center. Diarrhea, defined as two or more loose or unformed stools in a day, was reported by 47% of the respondents. An increased risk of diarrhea was found for persons who always drank bottled water (OR = 3.0; 95% CI = 1.1–7.8). Always drinking boiled water (OR = 0.5; 95% CI = 0.2–1.6) or home filtered water (OR = 1.2; 95% CI = 0.6–2.5) was not associated with diarrhea. Taking medications with diarrhea side effects, however, was reported by a significant proportion of persons with diarrhea (OR = 2.1; 95% CI = 1.2–3.6). In discussing the results of this cross-sectional study, Eisenberg *et al.* (2002) presented a causal model that highlighted the complexities, potential biases, and possible confounding that should be kept in mind when studying AGI risks in populations where persons may be concerned about water quality and may be taking medications with diarrhea side effects.

United Kingdom

Goh *et al.* (2004) determined risk factors for sporadic cryptosporidiosis in 152 patients and 466 unmatched controls who resided in two local government districts in North Cumbria, North West England. Case-patients were defined as residents with (1) diarrhea (three or more loose stools in a 24-hour period), (2) onset from March 1 1996 to February 29 2000, and (3) a fecal smear positive for *Cryptosporidium* oocysts but negative for other enteric pathogens. Excluded were participants who had traveled outside the United Kingdom. Interviews were conducted face-to-face at the home. Most of the case-patients were children, suggesting that older persons in this study population were immune, possibly due to low-level intermittent contamination of water supplies and contact with livestock. Genotyping of 57 cases found that most were *C. parvum* (genotype 2 of animal and human origin). In the final multivariable model, the usual volume of cold, unboiled tap water consumed was independently associated with cryptosporidiosis (OR = 1.40, 95% C1 = 1.14–1.71 per pint consumed per day). No difference in risk was found

between the various water supply zones, some of which were supplied by private water supplies or unfiltered lake water. Infection was also associated with short visits to farms, and Goh *et al.* noted that livestock may have contributed substantially to sporadic cryptosporidiosis through low-level intermittent contamination of public water sources. Infection was not associated with the consumption of bottled water, ice, soft drinks or unpasteurized milk. A decreased risk was associated with the consumption of lettuce, tomatoes, mixed salad, and cream.

Hunter *et al.* (2004) studied sporadic cryptosporidiosis in North West England and Wales. Eligible for study were laboratory-confirmed cases during February 2001 to May 2002 with diarrhea within the two weeks before the stool specimen was collected. *Cryptosporidium* isolates from case-patients were genotyped, and risk factors were considered for specific genotypes. Controls were persons without diarrhea in the two weeks before completing the questionnaire and within the same age range and location. A postal questionnaire was completed by 427 patients and 427 controls. When all cryptosporidiosis cases were considered in the analysis, three variables were strongly associated with illness: travel outside the United Kingdom, contact with another person with diarrhea, and touching cattle. Helping a child to use the toilet and the number of glasses of tap water consumed at home each day were also independently positively associated with risk. For *C. hominis* infections (previously genotype 1 and primarily of human origin), significant risk factors were travel abroad and changing the diapers of children less than 5 years of age. For *C. parvum* (previously genotype 2), eating raw vegetables and eating tomatoes were protective whereas touching farm animals was associated with increased risk.

In the final multivariate model which included all case-patients, a small but statistically significant risk was the number of glasses of unboiled water consumed at home (adjusted OR = 1.135 per glass; 95% CI = 1.010–1.265). However, in the univariate analysis, tap water was not associated with an increased risk and use of a water filter or bottled water was not associated with a decreased risk. Hunter *et al.* noted the possibility of recall bias and suggested that tap water does not appear to be of major importance as a cause of sporadic cryptosporidiosis in this population.

Summary of case-control studies

An increased risk of campylobacteriosis was associated with drinking water from individual wells, untreated water from lakes, rivers, and streams, water from non-urban areas, or rainwater collected from roofs,. An increased risk was associated with tap water in Quebec Province but not in New Zealand. In Denmark, an increased risk was associated with household drinking water that had a bad taste or smell. In England, an increased risk of campylobacteriosis was associated with bottled water.

An increased risk of giardiasis was found among populations consuming untreated water, either surface or ground, or unfiltered municipal surface water. Other risk factors, especially person-to-person transmission and foreign travel may also be important, and drinking water may not be a significant risk factor in all areas. For example, Esrey *et al*. (1989) found that personal hygiene and person-to-person transmission in Lesotho, South Africa, were more important than water source in the transmission of giardiasis.

A study in seven states of the United States found that municipal water systems or well water was not associated with cryptosporidiosis risk among immmnuocompetent persons; international travel, contact with cattle, contact with persons 2–11 years of age with diarrhea, and freshwater swimming were important risk factors. In the San Francisco Bay Area, no significant association with drinking water was found for immmnuocompetent persons; however, tap water consumption at the highest exposure categories was an important risk for persons with AIDS.

In one study in England, consumption of tap water was not a major source of endemic cryptosporidiosis; significant risk factors included travel abroad, changing diapers of children, and touching farm animals. However, in another study which excluded persons who had traveled abroad, the consumption of tap water was a significant risk factor. This is the first study to show that drinking tap water is a significant risk factor for sporadic cryptosporidiosis among the general population, regardless of the water source and its treatment. In Australia, tap water from two large public systems with different quality water sources was not a significant risk factor for cryptosporidiosis; however, public swimming pools and person-to person transmission were important sources of infection. In several studies, the consumption of untreated

water from a lake, river, or spring and rainwater was significantly associated with cryptosporidiosis.

In summary, tap water may be a significant risk factor for cryptosporidiosis among some immmnocompetent as well as immunocompromised populations, and increased risks of campylobacteriosis and giardiasis may be associated with certain types of water systems. Some studies found no increased risks, and in one study, bottled water was implicated as a risk factor for campylobacteriosis. The findings of case-control studies emphasize that the importance of endemic waterborne risks depend on the water system type and vulnerability to contamination and, for some illnesses, the immune status or age of the population. Other risk factors and exposures may also be important and thus, should be considered when evaluating waterborne risks.

ECOLOGIC STUDIES

Because populations rather than individuals are studied, ecologic studies have limitations. These studies can assist in the development of hypotheses for further investigation. Results may also be informative about risks in situations where the group measures reflect individual exposures and health effects. We reviewed several studies that were conducted in Germany, Sweden, the United States and United Kingdom.

Campylobacteriosis

Sweden

Campylobacteriosis is a notifiable disease in Sweden, and both physicians and laboratories report cases. Because 60–70% of all cases are associated with foreign travel, Nygard *et al*. (2004) investigated the environmental factors and the incidence of 7280 domestically acquired infections reported during 1998 to 2000. Information on agricultural characteristics, including livestock density and water supply, was obtained for each of the 289 municipalities, and the population was categorized by degree of urbanization to control for potential confounding. A negative association was found between infection and the percentage of the population receiving water from a public water system

(incidence RR = 0.93; 95% CI = 0.91–0.95). These findings suggest that a public water system may protect against infection. However, positive associations were found with the average length of water pipe per person (incidence RR = 1.11; 95% CI = 1.08–1.15) and ruminant density (incidence RR = 1.12; 95% CI = 1.09–1.14). These findings suggest that livestock contamination may occur in the water distribution system. Several factors might contribute to contamination including leakage of pipes and low water pressure. In Sweden, about 20% of all water produced is lost through leakage, and in sparely populated areas long pipelines can lead to unstable water pressure resulting in contamination from backsiphonage or cross-connections.

Cryptosporidiosis

United States

An ecologic study in Los Angeles County (Sorvillo et al. 1994) found no difference in the prevalence of cryptosporidiosis among AIDS patients in areas with filtered and unfiltered surface water. However, these results should be interpreted with caution in light of a recently conduced case-control study in San Francisco (Aragon et al. 2003).

United Kingdom

In Blackpool, Wyre, and Fylde, England, prospective and retrospective ecologic studies were conducted of incidence cases of cryptosporidiosis reported between 1987–92 and 1992–93 (Fewtrell & Delahunty 1995). In the retrospective study, most cases were reported in children under the age of four, and no significant differences in incidence were found when cases were evaluated according to water supply zones. The prospective study also found no differences in the incidence of cryptosporidiosis among water zones, and interviews identified recreational water and contact with farm animals as important risk factors.

Gastroenteritis

Germany

Dangendorf et al. (2002) conducted a retrospective study of AGI risks in the North Rhine-Westphalia area which is

characterized by different drinking water systems (surface or groundwater sources). The study excluded AGI due to *Salmonella* and *Shigella* because cases are primarily associated with travel and contaminated foods. Geo-statistical analyses revealed spatial variations in the incidence of AGI, and the amount of drinking water from surface or groundwater was correlated with age-standardized incidence rates. Districts supplied by surface water had a significantly lower illness incidence. Dangendorf *et al.* felt that the results reflected the high quality of drinking water provided by the surface water systems. Water treatment included carbon filtration and disinfection, whereas three of the four groundwater systems in the study were untreated.

United States

Aeromonas is ubiquitous in water and some strains have been shown to possess virulence traits. Borchardt et al. (2003) examined stool specimens from 2310 patients with acute diarrhea in Wisconsin and compared the molecular fingerprints of *Aeromonas* isolates from these patients with isolates from the patients' drinking water. Although 17 ($<$ 1%) stool specimens tested positive for *Aeromonas*, the stool and drinking water isolates were genetically unrelated, suggesting little waterborne risk.

Time-series studies

The time-series study, a variation of the cohort approach using ecologic methods, considers a series of observations at successive points in time. In the 1980s, the time-series approach was widely used to study the epidemiology of air pollution (Beaudeau, 2003). More recently, it has been used to study the epidemiology of drinking water contamination. The analysis is relatively inexpensive when routinely collected disease and water surveillance data are available. Usually, the study is conducted for at least one year so that seasonal changes can be assessed. For infectious waterborne illness, the method considers various time lags between the water exposure and illness because etiologic agents have different incubation periods ranging from 24 hours to several days or more. A major advantage is that the method tends to eliminate many possible confounding factors. Since the community serves as its own control, confounders are

restricted to risk factors or exposures that may vary over time. For a factor to confound the association in a time-series study, it must vary in a similar way as water quality data. Most important confounders are not expected to vary in the same way. However, if higher levels of water contamination occur in the fall and winter, then seasonal risk factors for AGI could confound waterborne associations.

The time-series analysis has been used to relate water turbidity and AGI, but other routinely measured water quality parameters can also be considered. Investigators have focused on more severe AGI since routinely collected surveillance data are available for emergency room visits, physician visits, and hospitalization admissions. Because of the large number of AGI events, these studies can, theoretically, detect very small relationships between changes in water quality and AGI. However, the interpretation of the findings may be limited because of the ecological measure of exposure, and it is not yet certain which water quality measures are most appropriate. For example, when assessing turbidity as a water quality indicator, the following questions come to mind: is a change in turbidity an adequate indicator for exposure to pathogens; if so, how large a change in turbidity should be considered; and are water quality tests at the water treatment plant adequate to assess individual exposures? In addition, the risks may vary based on water system vulnerabilities and type of water source and water treatment.

Gastroenteritis

Canada

Aramini et al. (2000) investigated the possible association between AGI (i.e. hospitalizations, physician visits, and visits to the British Columbia Children's Hospital emergency room) and water quality in Vancouver during 1992 to 1998. A Generalized Additive Modeling approach was used to quantify associations between AGI events and several water quality parameters, including turbidity, 1–39 days earlier. Investigators assumed that no AGI event resulted from water with a turbidity of less than or equal to 1 nephelometric turbidity units (NTU). For the Poisson model, the relationship between the daily number of health outcomes was assessed. For the binomial model, the relationship between

case status (gastrointestinal vs. respiratory conditions) and water quality was investigated. A winter rise in gastroenteritis was evident among all three health outcomes. Turbidity and fecal coliforms counts in all three watersheds also exhibited seasonal variation. Seasonal, long-term effects, and day-of-the-week effects were controlled.

No association was found between AGI risk and fecal coliform levels or rainfall. However, statistically significant turbidity–AGI relationships were found among multiple age groups for all three health outcomes. In general, the probability of AGI increased as turbidity increased. The turbidity–AGI relationships were strongest among 2–18 year olds and 18–65 year olds, and the following lag times: 3–6, 6–9, 12–16, and 21–29 days. These lag times are consistent with the incubation periods of waterborne bacterial and protozoan pathogens. Depending on the area of Vancouver, turbidity variations explained 0.8–2.1% of emergency AGI-related physician visits and 0.2–1.3% of AGI-related hospitalizations.

United States

Associations between drinking water turbidity and AGI were also reported in Milwaukee (Morris et al. 1996, Naumova et al. 2003) and Philadelphia (Schwartz et al. 1997, 2000, Schwartz & Levin 1999).

Schwartz et al. (1997) evaluated daily measures of drinking water turbidity and emergency visits and admissions to the Children's Hospital of Philadelphia for AGI, controlling for time trends, seasonal patterns, and temperature. The Philadelphia water system is filtered and in compliance with water quality standards. An interquartile range increase in turbidity levels (0.04 NTU) was associated with a 7.2% increase (95% CI = 2.8–11.7) in emergency visits four days later and a 6.7% increase (95% CI = 2.2–11.4) 10 days later. An age-stratified analysis showed the strongest association was in older children, especially for hospital admissions. For children over 2 years of age, an increase in admissions of 31.1% (95% CI = 10.8–55) was seen after 5–6 day lag period. For younger children, an increase in admissions of 13.1% (95% CI = 3.0–24.3) was seen after a 13 day lag period. This study caused considerable controversy. Major concerns included the use of turbidity as a proxy or surrogate measure for risk of

microbial contamination, likely exposure misclassification due to the very low levels of turbidity in the drinking water, and the large number of lag periods examined. These concerns were discussed by Schwartz & Levine (1999).

A similar study examined AGI-related hospital admissions for elderly persons in Philadelphia (Schwartz et al. 2000). All residents aged 65 and older in 1992–93 were studied through their Medicare records. An interquartile range increase in turbidity levels in drinking water was associated with a 9.0% increase (95% CI = 5.3–12.7) in gastroenteritis admissions 9–11 days later.

Morris et al. evaluated records for hospital admissions, emergency room visits, and outpatient visits for AGI for the period January 1 1992, to April 14 1993 in Milwaukee and turbidity at each of the two water filtration plants. During the 434 day period prior to the 1993 waterborne outbreak of cryptosporidiosis, an increase of 0.5 NTU at one of the treatment plants was associated with AGI events among persons aged less than 19 years (RR = 2.35; 95% CI = 1.34–4.12). Risks were primarily seen in emergency and inpatient gastroenteritis (RR = 2.80; 95% CI 1.28–6.12). These findings suggest that endemic waterborne AGI occurred prior to the outbreak. During the outbreak, the daily turbidity increased dramatically, and average daily rates for AGI events increased by 20–150%. Naumova et al. found a positive association between age and emergency room visits and hospitalizations due to AGI in persons 65 years of age and older in Milwaukee before the outbreak.

Summary of time-series studies

Increased risks of severe AGI events were associated with turbidity in both filtered and unfiltered surface water sources that meet current water quality standards. Because the nature of the turbidity and its relationship with pathogens may depend both on source water quality and its treatment, extrapolation of these findings to other water systems should be made with caution.

OTHER STUDIES OF INTEREST

Of interest, but not reviewed in this article, are several other studies that should be mentioned. Moe et al. (1991) conducted a study of diarrheal disease risks associated with bacterial

indicators in drinking water in the Philippines. Results of this study and a case-control study in urban Zambia (Nchito et al. 1998) are a reminder that waterborne contamination continues to be a substantial problem posing quite large risks in the developing world, especially for children.

Studies by Egorov et al. (2002) and Semenza et al. (1998) are a reminder that endemic illness may be associated not only with source water contamination and inadequate water treatment but also with water distribution system contamination. Egorov et al. associated an increased AGI risk with the deterioration of drinking water quality in the distribution system. Although water leaving the treatment plant at Cherepovets, Russia, was adequately disinfected, chlorine residuals declined rapidly within the system. An interquartile range decrease (0.22 mg/l) in free chlorine in the system was associated with an increased risk (RR = 1.42; 95% CI = 1.05–1.91) of self-reported AGI after controlling for socioeconomic, hygienic, and demographic factors. Semenza et al. found that 30% of households in Nukus, Uzbekistan, lacked a detectable chlorine residual despite two-stage water treatment of the public supply. Persons living in houses without residuals experienced 60% more cases of diarrhea than those with a residual. Payment et al. (1997) and Hunter et al. (2005) also associated endemic waterborne risks with distribution system contamination, and in the United States, this source of contamination is increasingly associated with reported waterborne outbreaks (Craun et al. 2006b).

CONCLUSIONS AND RECOMMENDATIONS

An increased risk of endemic waterborne disease (campylobacteriosis, giardiasis, cryptosporidiosis, and AGI) has been epidemiologically associated with some drinking water sources and their treatment. These studies provide evidence that some populations using public or non-public drinking water systems may be at increased risk of endemic or sporadic illness. However, not all of the studies found an increased risk of illness. The differences in illness risk may be associated with different exposures due to various watershed characteristics and water system vulnerabilities in the areas that were studied. Observational studies offer little information about AGI risks in public systems, and it is not possible to use the current information from these

studies to help estimate the population attributable risk for endemic waterborne AGI in the United States.

These studies suggest that more information is needed to characterize the risks associated with the various water systems serving the US population. Additional cohort and case-control studies in the United States can expand the database of information about risks associated with different water sources and treatment. In particular, we recommend that additional case-control studies be considered using the FoodNet population. Although the FoodNet population is not representative of the US population, it does represent a large population with exposure to potentially different public water systems. After assessing the range of water sources, treatment, and water quality in the seven states, the feasibility should be assessed of conducting a case-control study of AGI. Alternatively, investigators can consider a nationwide study that is representative of the raw water sources and water treatment for public water systems in the United States.

Additional case-control studies should also be considered for those diseases caused by pathogens that are important causes of waterborne outbreaks. Additional ecological studies may offer additional hypotheses for further study, and time-series analyses can help clarify turbidity–AGI relationships in various public water systems. Other water quality parameters should be considered for time-series analyses.

Endemic risks associated with distribution system deficiencies should be better characterized in the United States and differentiated from endemic risks associated with source water quality and its treatment.

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REFERENCES

Adak, G. K., Cowden, J. M., Nicholas, S. & Evans, H. S. 1995 The Public Health Laboratory Service national case-control study of primary indigenous sporadic cases of campylobacter infection. *Epidemiol. Infect.* **115**(1), 15–22.

Aragon, T. J., Novotny, S., Enanoria, W., Vugia, D. J., Khalakdina, A. & Katz, M. H. 2003 Endemic cryptosporidiosis and exposure to municipal tap water in persons with acquired immunodeficiency syndrome (AIDS): a case-control study. *BMC Public Health* **3**, 2.

Aramini, J., McLean, M., Wilson, J., Holt, J., Copes, R., Allen, B. & Sears, W. 2000 Drinking water quality and health-care utilization for gastrointestinal illness in greater Vancouver. *Can. Commun. Dis. Rep.* **26**(24), 211–214.

Beaudeau, P. 2003 Time series analysis. In *Drinking Water and Infectious Disease-Establishing the Links* (eds. Hunter, P. R., Waite, M. & Ronchi, E.), pp. 155–164. CRC Press, London.

Birkhead, G. & Vogt, R. L. 1989 Epidemiologic surveillance for endemic Giardia lamblia infection in Vermont. *Am. J. Epidemiol.* **129**(4), 762–768.

Borchardt, M. A., Stemper, M. E. & Standridge, J. H. 2003 Aeromonas isolates from human diarrheic stool and groundwater compared by pulsed-filed gel electrophoresis. *Emerging Infect. Dis.* **9**(2), 224–228.

Calderon, R. L. & Craun, G. F. 2006 Estimates of endemic waterborne risks from community-intervention studies. *J. Wat. Health* **4**(Suppl. 2), 89–100.

Craun, G. F., Calderon, R. L. & Wade, T. J. 2006a Assessing waterborne risks: an introduction. *J. Wat. Health* **4**(Suppl. 2), 3–18.

Craun, M. F., Craun, G. F., Calderon, R. L. & Beach, M. J. 2006b Waterborne outbreaks reported in the United States. *J. Wat. Health* **4**(Suppl. 2), 19–30.

Chute, C., Smith, R. & Baron, J. 1985 Risk factors for endemic giardiasis. *Am. J. Epidmiol.* **122**, 515.

Chute, C. G., Smith, R. P. & Baron, J. A. 1987 Risk factors for endemic goardiasis. *Am. J. Public Health* **77**, 585–587.

Colford, J. M., Roy, S., Beach, M., Hightower, A., Shaw, S. & Wade, T. 2006 A review of household drinking water intervention trials and a proposal for using their results in the estimation of endemic acute gastrointestinal illness attributable to drinking water in the United States. *J. Wat. Health* **4**(Suppl. 2), 71–88.

Dangendorf, F., Herbest, S., Reintjes, R. & Kistemann, T. 2002 Spatial patterns of diarrhoeal illnesses with regard to water supply structures–a GIS analysis. *Int. J. Hyg. Environ. Health* **205**, 183–191.

Dennis, D. T., Smith, R. P., Welch, J. J., Chute, C. G., Anderson, B., Herndon, J. L. & von Reyn, C. F. 1993 Endemic giardiasis in New Hampshire: a case-control study of environmental risks. *J. Infect. Dis.* **167**(6), 1391–1395.

Eberhart-Phillips, J., Walker, N., Garrett, N., Bell, D., Sinclair, D., Rainger, W. & Bates, M. 1997 Campylobacteriosis in New Zealand: results of a case-control study. *J. Epidemiol. Comm. Health* **51**, 686–691.

Egorov, A., Ford, T., Tereschenko, A., Drizhd, N., Segedevich, I. & Fourman, V. 2002 Deterioration of drinking water quality in the distribution system and gastrointestinal morbidity in a Russian city. *Int. J. Environ. Health Res.* **12**, 221–233.

Eisenberg, J. N. S., Wade, T. J., Charles, S., Vu, M., Hubbard, A., Wright, C. C., Levy, D., Jensen, P. & Colford, M., Jr. 2002 Risk factors in HIV-associated diarrheal disease: the role of drinking water, medication, and immune status. *Epidemiol. Infect.* **128**, 73–81.

Esrey, S. A., Collett, J., Miliotis, M. M., Koornhof, J. & Makhale, P. 1989 The risk of infection from Giardia lamblia due to drinking water supply, use of water, and latrines among preschool children in rural Lesotho. *Int. J. Epidemiol.* **18**(1), 248–253.

Evans, M. R., Ribeiro, C. D. & Salmon, R. L. 2003 Hazards of healthy living: bottled water and salad vegetables as risk factors for campylobacter infection. *Emerging Infect. Dis.* **9**(10), 1219–1225.

Fattal, B., Gutman-Bass, N., Agursky, T. & Shuval, H. I. 1988 Evaluation of health risk associated with drinking water quality in agricultural communities. *Wat. Sci. Technol.* **20**(11-12), 409–415.

Fewtrell, L. & Delahunty, A. 1995 The incidence of cryptosporidiosis in comparison with other gastro-intestinal illnesses in Blackpool. *Wyre, and Fylde. JCIWEM* **9**(12), 598–601.

Fraser, G. G. & Cooke, K. R. 1991 Endemic giardiasis and municipal water supply. *Am. J. Public Health* **81**, 760–762.

Frost, F., Harter, L., Plan, B., Fukutaki, K. & Holman, B. 1983 Giardiasis in Washington State. Project Summary. US Environmental Protection Agency (EPA-600/S1-82-016), Research Triangle Park, NC.

Gallaher, M. M., Herndon, J. L., Nims, L. J., Sterling, C. R., Grabowski, D. J. & Hull, H. F. 1989 Cryptosporidiosis and surface water. *Am. J. Public Health* **79**(1), 39–42.

Gofti-Laroche, L., Demanse, D., Joret, J-C. & Zimirou, D. 2003*b* Health risks and parasitical quality of water. *J. AWWA* **95**(5), 162–172.

Gofti-Laroche, L., Gratacap-Cavallier, B., Demanse, D., Genoulaz, O., Seigneurin, M. & Zimirou, D. 2003*a* Are waterborne astrovirus implicated in acute digestive morbidity (E.MI.R.A.)? *J. Clin. Virol.* **27**, 74–82.

Gofti-Laroche, L., Gratacap-Cavallier, B., Genoulaz, O., Joret, J-C., Hartemann, Ph., Seigneurin, J. M. & Zimirou, D. 2001 A new analytical tool to assess health risks associated with the quality of water (E.MI.R.A. study). *Wat. Sci. Technol.* **43**(12), 39–48.

Goh, S., Reacher, M., Casemore, D. P., Verlander, N. Q., Chalmers, R., Knowles, M., Williams, J., Osborn, K. & Richard, S. 2004 Sporadic cryptosporidiosis, North Cunbria, England, 1996-2000. *Emerging Infect. Dis.* **10**:6 1007–1015.

Gray, S. F., Gunnell, D. J. & Peters, T. J. 1994 Risk factors for giardiasis: a case-control study. *Epidemiol. Infect.* **113**, 95–102.

Harter, L., Frost, P. & Jakubowski, W. 1982 Giardia prevalence among 1-to-3-year-old children in two Washington State counties. *Am. J. Public Health* **72**(4), 386–388.

Hoque, M. E., Hope, V. T., Scragg, R. & Kjellstrom, T. K. 2003 Children at risk of giardiasis in Auckland: a case-control study. *Epidemiol. Infect.* **131**, 655–662.

Hunter, P. R., Hughes, S., Woodhouse, S., Syed, Q., Verlander, N. Q., Chalmers, R. M., Morgan, K., Nichols, G., Beeching, N. & Osborn, K. 2004 Sporadic cryptosporidiosis case-control study with genotyping. *Emerging Infect. Dis.* **10**:7 1241–1249.

Hunter, P. R., Chalmers, R. M., Hughes, S. & Syed, Q. 2005 Self-reported diarrhea in a control group: a strong association with reporting of low pressure events in tap water. *Clin. Infect. Dis.* **40** e32–e34.

Ikram, R., Chambers, S., Mitchell, P., Brieseman, M. A. & Ikram, O. H. 1994 A case-control study to determine risk factors for Campylobacter infection in Christchurch in the summer of 1992–3. *NZ Med. J.* **107**, 430–432.

Isaac-Renton, J., Moorehead, W. & Ross, A. 1996 Longitudinal studies of Giardia contamination in two community drinking water supplies: cyst levels, parasite viability, and health impact. *Appl. Environ. Microbiol.* **62**(1), 47–54.

Isaac-Renton, J. L. & Philon, J. J. 1992 Factors associated with acquiring giardiasis in British Columbia residents. *Can. J. Public Health* **83**(2), 155–158.

Kapperud, G., Espeland, G., Wahl, E., Walde, A., Herikstad, H., Gustavsen, S., Tveit, I., Natas, O., Bevanger, L. & Digranes, A. 2003 Factors associated with increased and decreased risk of Campylobacter infection: a prospective case-control study in Norway. *Am. J. Epidemiol.* **158**(3), 234–242.

Khalakdina, A., Vugia, D. J., Nadle, J., Rothrock, G. A. & Colford, J. K, Jr 2003 Is drinking water a risk factor for endemic cryptosporidiosis? A case-control study in the immnuocompetent general population of the San Francisco Bay area. *BMC Public Health* **3**, 11.

Kuusi, M., Aavitsland, P., Gondrosen, B. & Kapperud, G. 2003 Incidence of gastrenteritis in Norway–a population-based survey. *Epidemiol. Infect.* **131**, 591–597.

Laxer, M. A. 1985 Potential exposure of Utah army national guard personnel to giardiasis during field training exercise: a preliminary survey. *Military Med.* **150**(1), 23–26.

Mathias, R. G., Riben, P. D. & Osei, W. D. 1992 Lack of an association between endemic giardiasis and a drinking water source. *Can. J. Public Health* **83**(5), 382–384.

Meara, J. L. 1989 An investigation of health and lifestyle in people who have private water supplies at home. *Comm. Med.* **11**, 131–139.

Michaud, S., Menard, S. & Arbeit, R. D. 2004 Campylobacteriosis, eastern townships, Quebec. *Emerging Infect. Dis.* **10**(10), 1844–1848.

Miettinen, O. S. 1976 Estimability and estimation in case-referent studies. *Am. J. Epidemiol.* **103**, 226.

Moe, C. L., Sobsey, M. D., Samsa, G. P. & Mesolo, V. 1991 Bacterial indicators of risk of diarrheal disease from drinking water in the Philippines. *Bull. World Health Org.* **69**, 305–317.

Monson, R. R. 1990 *Occupational Epidemiology*, 2nd edn. CRC Press, Boca Raton, FL.

Morris, R. D., Naumova, E. N., Levin, R. & Munasinghe, R. L. 1996 Temporal variation in drinking water and diagnosed gastroenteritis in Milwaukee. *Am. J. Public Health* **86**(2), 237–239.

Naumova, E. N., Egorov, A. I., Morris, R. D. & Griffiths, J. K. 2003 The elderly and waterborne Cryptosporidium infection: gastroenteritis hospitalizations before and during the 1993 Milwaukee outbreak. *Emerging Infect. Dis.* **9**(4), 418–425.

Nchito, M., Kelley, P., Sianongo, S., Luo, N. P., Feldman, R., Farthing, M. & Baboo, K. S. 1998 Cryptosporidiosis in urban Zambian children: an analysis of risk factors. *Am. J. Trop. Med. Hyg.* **59**(3), 435–437.

Neimann, J., Engberg, J., Molbak, K. & Wegner, H. C. 2003 A case-control study of risk factors for sporadic campylobacter infections in Denmark. *Epidemiol. Infect.* **130**, 353–366.

Nygard, K., Andersson, Y., Rottingen, J. A., Svensson, A., Lindback, J., Kistemann, T. & Giesecke, J. 2004 Association between environmental risk factors and campylobacter infections in Sweden. *Epidemiol. Infect.* **132**, 317–325.

Payment, P., Richardson, L., Siemiatycki, J., Dewar, R., Edwardes, M. & Franco, E. 1991 A randomized trial to evaluate the risk of gastrointestinal disease due to the consumption of drinking water meeting currently accepted microbiological standards. *Am. J. Public Health* **81**, 703–708.

Payment, P., Siemiatycki, J., Richardson, L., Renaud, G., Franco, E. & Prevost, M. 1997 A prospective epidemiological study of gastrointestinal health effects due to the consumption of drinking water. *Int. J. Environ. Health Res.* **7**, 5–31.

Raina, P. S., Pollari, F. L., Teare, G. F., Gross, M. J., Barry, A. J. & Wilson, J. B. 1999 The relationship between E. coli indicator bacteria in well-water and gastrointestinal illness in rural families. *Can. J. Public Health* **90**(3), 172–175.

Robertson, B. V., Sinclair, M. I., Forbes, A. B., Veitch, M., Kirk, M., Cunliffe, D., Willis, J. & Fairley, C. K. 2002 Case-control studies of sporadic cryptosporidiosis in Melbourne and Adelaide. *Australia. Epidemiol. Infect.* **128**(1), 419–431.

Rothman, K. J. & Greenland, S. 1986 *Modern Epidemiology*. Little, Brown, Boston, MA.

Roy, S. L., DeLong, S. M., Stenzel, S. A., Shiferaw, B., Roberts, J. M., Khalakdina, A., Marcus, R., Segler, S. D., Shah, D. D., Thomas, S., Vugia, D. J., Zansky, S. M., Dietz, V. & Beach, M. J. 2004 Risk factors for sporadic cryptosporidiosis among immunocompetent persons in the United states from 1999 to 2001. *J. Clin. Microbiol.* **42**:7 2944–2951.

Schonberg-Norio, D., Takkinen, J., Hannien, M-L., Katila, M-L., Kaukoranta, S-S., Mattila, L. & Rautelin, H. 2004 Swimming and Campylobacter infections. *Emerging Infect. Dis.* **10**(8), 1474–1477.

Schwartz, J. & Levin, R. 1999 Drinking water turbidity and pediatric hospital use for gastrointestinal illness in Philadelphia. *Epidemiol.* **10**(1), 86–90.

Schwartz, J., Levin, R. & Goldstein, R. 2000 Drinking water turbidity and gastrointestinal illness in the elderly of Philadelphia. *Epidemiol. Comm. Health* **54**, 45–51.

Schwartz, J., Levin, R. & Hodge, K. 1997 Drinking water turbidity and pediatric hospital use for gastrointestinal illness in Philadelphia. *Epidemiol.* **8**(6), 615–620.

Semenza, J. C., Roberts, L., Henderson, A., Bogan, J. & Rubin, C. H. 1998 Water distribution system and diarrheal disease transmission: a case study in Uzebekistan. *Am. J. Trop. Med. Hyg.* **59**(6), 941–946.

Sorvillo, F., Beall, G., Turner, P. A., Beer, V. L., Kovacs, A. A., Kraus, P., Masters, D. & Kerndt, P. R. 1998 Seasonality and factors associated with cryptosporidiosis among individuals with HIV infection. *Epidemiol. Infect.* **121**(1), 197–204.

Sorvillo, F., Leib, L. E., Nahlen, B., Miller, J., Mascola, L. & Ash, L. R. 1994 Municipal drinking water and cryptosporidiosis among persons with AIDS in Los Angeles county. *Epidemiol. Infect.* **113**, 313–321.

Strauss, B., King, W., Ley, A. & Hoey, J. R. 2001 A prospective study of rural drinking water quality and acute gastrointestinal illness. *BMC Public Health* **1**, 8.

Stuart, J. M., Orr, H. L., Warburton, F. G., Jeyakanth, S., Pugh, C., Morris, I., Sarangi, J. & Nichols, G. 2003 Risk factors for sporadic giardiasis: a case-control study in southwestern England. *Emerging Infect. Dis.* **9**(2), 229–233.

Weinstein, P., Macaitis, M., Walker, C. & Cameron, S. 1993 Cryptosporidial diarrhoea in South Australia. An exploratory cases-control study of risk factors for transmission. *Med. J. Australia* **158**(2), 117–119.

Weiss, H. B., Winegar, D. A., Levy, B. S. & Washburn, J. W. 1977 Giardiasis in Minnesota 1971–1975. *Minn. Med.* **60**, 815–820.

Wright, R. A., Spencer, H. C., Brodsky, R. E. & Vernon, T. M. 1977 Giardiasis in Colorado: an epidemiologic study. *Am. J. Epidemiol.* **105**, 330–336.

Zmirou, D., Ferley, J. P., Collin, J. F., Charrel, M. & Berlin, M. S. 1987 A followup study of gastrointestinal diseases related to bacteriologically substandrad drinking water. *Am. J. Public Health* **77**(5), 582–584.