

A gradient of acute gastroenteritis was characterized, to assess risk of long-term health sequelae after drinking bacterial-contaminated water

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Accepted 29 August 2005

Abstract

Objective: A municipal water system became contaminated with *Escherichia coli* O157:H7 and *Campylobacter* spp. Beginning 2 years after an outbreak, all residents from the region were invited to participate in a cohort study assessing the risk of long-term sequelae. We aimed to develop a method to grade the accuracy and severity of self-reported acute symptoms.

Study Design and Setting: We corroborated participant survey responses with health records at the time of the outbreak. Of the 4,135 participants, 1,388 were asymptomatic during the outbreak, 1,752 had symptoms of acute self-limited gastroenteritis that could neither be confirmed nor refuted by prior health records, and 995 had symptoms that necessitated medical attention (and thus were confirmed by prior health records).

Results: The gradient related to the severity of acute symptoms. Compared to those with unconfirmed gastroenteritis, participants with confirmed gastroenteritis were more likely to describe fever, bloody diarrhea, and prolonged diarrhea (all $P < .03$). The gradient also correlated with long-term plausible outcomes, including chronic gastrointestinal symptoms, chronic symptoms of arthritis or depression, and the avoidance of municipal water ingestion after the outbreak (P for trend consistently $< .03$). Conversely, for the outcome of chronic tinnitus, an association was neither expected nor observed (P for trend = $.26$).

Conclusion: We successfully characterized a gradient to be used in future primary analyses assessing the risk of long-term health sequelae after an outbreak. © 2006 Elsevier Inc. All rights reserved.

Keywords: Health survey; Cohort study; *Escherichia coli* O157; *Campylobacter*; Environmental exposure; Risk factors; Gastroenteritis; Bias

1. Introduction

Walkerton is a small rural town located in one of Ontario's prime agricultural areas. In May 2000, municipal water in Walkerton became contaminated with bacterial

pathogens *Escherichia coli* O157:H7 and *Campylobacter* spp. At the time of the outbreak, heavy rainfall contributed to the transport of livestock fecal contaminants into inadequately chlorinated drinking water, supplied from a shallow well [1,2]. Many individuals were either primarily or secondarily exposed to the bacteria, including permanent residents of Walkerton, commuters employed in the town, and visitors from neighboring communities. This outbreak produced an estimated 2,300 cases of acute gastrointestinal illness, > 750 emergency room visits, 65 hospital admissions, 27 recognized cases of hemolytic uremic syndrome, and 7 deaths [3]. The most serious case of water contamination in recent Canadian history, this event attracted worldwide media attention and sparked public concerns about the quality of drinking water [4].

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Initial medical care of course focused on the acute management of infected persons, but attention has now shifted toward long-term health sequelae. Previous biological and observational studies suggest that survivors of campylobacter gastroenteritis and severe *E. coli* O157:H7 infection may have poorer long-term health, regardless of whether they initially experienced overt hemolytic uremic syndrome. Beginning 2 years after the outbreak, all residents from the region were invited to participate in a large cohort study assessing the risk of long-term sequelae—the Walkerton Health Study. Individuals were eligible for study participation if they lived in the Walkerton area or had consumed municipal water in May 2000, whether or not they had developed an acute illness. The Walkerton Health Study provides a unique opportunity to characterize new and existing epidemiological associations between acute bacterial gastroenteritis and chronic diseases, including postinfectious irritable bowel syndrome, arthritis, hypertension, renal disease, and diabetes mellitus [5–11]. Additionally, any psychosocial sequelae of this stressful environmental disaster, as well as health care utilization after the outbreak, may be better characterized [12,13].

In observational studies, causality is inferred if an exposure is associated with specific outcomes supported by biological rationale [14]. The strength of association between exposure and outcome also requires consideration: stronger associations (i.e., larger relative risks) are more likely to indicate causality, although it is recognized that small relative risks do not imply lack of causality and may be important if the disease is common (i.e., the population attributable risk is high). Lastly, if the risk of the disease in question increases with the amount of exposure (termed biologic gradient, or dose response), this is considered superior evidence of causality [14].

To guide inferences of causality, we aimed to characterize a gradient of acute gastroenteritis at the time of the outbreak. It would have been ideal to enroll participants and elicit their symptoms immediately after the outbreak, but this proved unrealistic for a number of reasons. First, time was required to prepare the study protocol, obtain financial support, submit an application for ethical review, and develop local facilities and procedures. In addition, the community was not affiliated with an academic health center, and for months after the outbreak the public inquiry was the focus of attention. Accordingly, 2 years elapsed before the first participant was enrolled in the Walkerton Health Study and could be asked about symptoms of acute gastroenteritis experienced during the outbreak.

The accuracy of symptom recall is further limited by availability of government financial compensation for those who suffered acute enteric illness. Misclassification of truly asymptomatic individuals as ill could dilute any apparent relationship between acute gastrointestinal illness and chronic health outcomes. Alternatively, those with long-term health problems could exaggerate their recall of initial

symptoms, thus amplifying any association between that outcome and bacterial gastroenteritis.

Biased recall was empirically demonstrated in 405 health study participants who were questioned about acute symptoms by public health officials just after the outbreak [3], and again by Walkerton Health Study personnel 2 years later (Table 1). As many as 27% of participants recalled acute symptoms that they had denied just after the outbreak. We therefore elected not to categorize acute gastroenteritis solely by self-reported bloody diarrhea, frequency or duration of diarrhea, fever, vomiting, or abdominal pain.

Positive stool cultures for known enteric pathogens would provide the best confirmation of acute enteric illness. However, once the outbreak source and causative organisms were identified, local citizens were advised not to submit stool samples, in part because local health services were overwhelmed. Even so, stool cultures can lack sensitivity, and negative results do not exclude infection in the setting of acute symptoms during a large outbreak. We considered the use of serological testing for *E. coli* O157:H7 and campylobacter gastroenteritis during the outbreak, but such assays are not commercially available. (Some assays exist as research tools, they have not been approved for clinical use and antibodies might not persist 2 years after the outbreak.) Serology might also have proven unreliable in a rural population with considerable previous exposure to farm flora [15–17].

Given these concerns, we aimed to characterize a gradient of acute gastroenteritis using prior health records to confirm recalled gastrointestinal symptoms at the time of the outbreak. We divided participants into three groups: no history of gastroenteritis, a history of gastroenteritis that could be neither confirmed nor refuted by health records at the time of the outbreak because the individual did not seek medical attention (classed as unconfirmed gastroenteritis), and gastroenteritis that necessitated medical attention and thus was confirmed by a prior medical record (confirmed gastroenteritis).

We examined demographic and acute outbreak characteristics of children and adult study participants grouped

Table 1
Self-reported symptoms recalled 2 years after the outbreak, compared with original responses

Questions Posed*	Response unchanged, %	Response changed, %		κ
		Absence of symptom previously present	Presence of symptom previously absent	
Were you ill?	73	1	26	.49
Did you have a fever?	81	4	15	.40
Did you have abdominal pain?	71	2	27	.46
Did you have bloody diarrhea?	91	1	8	.59

* These questions were posed to 405 study participants by public health officials just after the outbreak, and again by Walkerton Health Study personnel 2 years later.

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