Long-term Health Sequelae Following *E.coli* and *Campylobacter* Contamination of Municipal Water

Population Sampling and Assessing Non-participation Biases

Amit X. Garg, MD^{1,2}

Jennifer Macnab, PhD^{1,2}

William Clark, MD¹

Joel G. Ray, MD, MSc³

John K. Marshall, MD, MSc⁴

Rita S. Suri, MD¹

P.J. Devereaux, MD^{4,5}

Brian Haynes, MD, PhD^{4,5}

on behalf of the Walkerton Health Study Investigators

ABSTRACT

Background: Following bacterial contamination of a municipal water system in the rural town of Walkerton, Ontario, over 2,300 cases of acute gastroenteritis were documented. The Walkerton Health Study is currently underway to assess for long-term health sequelae among consenting inhabitants of Walkerton, related to the original outbreak. We explored whether the association between the acute exposure and preliminary long-term health outcomes may have been biased through differences between early- and late-recruited study participants.

Methods: Using multiple data sources, including the 1996 and 2001 Canadian Census, and records from the Regional Health Unit, hospital and Walkerton Health Study, we determined both sample representativeness and the anticipated effects of intensifying study participant recruitment. Selection bias was assessed by examining for differences between initial and late participants, and their subsequent risk of having hypertension, proteinuria and reduced renal clearance.

Results: Of the 4,315 participants, 2,756 were permanent residents of Walkerton, representing 55% of the town's total population. The sample was demographically similar to the population of interest, although statistically women were more likely to participate than men (55% of sample were women compared to 52% of population, $p < 0.01$), and the proportion of both young and very elderly adults was smaller than expected (13% of sample were ≥ 65 years of age compared to 18% of population, $p < 0.01$). Comparing the initial 3,959 participants to the 356 persons additionally recruited with substantial effort, the latter were more likely to be free of symptoms during the outbreak (21% vs. 7%, $p < 0.001$), but were otherwise similar in terms of age, sex, the use of medical care resources and underlying health state predating the outbreak. The risk of long-term hypertension or renal sequelae did not significantly differ between initial and late study recruits.

Conclusions: Participants in the Walkerton Health Study represent the population of interest, and comprise those who were acutely ill during the infected water outbreak. The available study sample should provide reasonably unbiased estimates of the associated risk between acute bacterial gastroenteritis and long-term health sequelae.

MeSH terms: Cohort studies; epidemiologic studies; water supply; sampling studies; selection bias; *Escherichia coli* O157

La traduction du résumé se trouve à la fin de l'article.

1. Division of Nephrology, University of Western Ontario, London, Ontario

2. Department of Epidemiology and Biostatistics, University of Western Ontario

3. Department of Medicine, University of Toronto, Toronto, Ontario

4. Department of Medicine, McMaster University, Hamilton, Ontario

5. Department of Clinical Epidemiology and Biostatistics, McMaster University

Correspondence: Dr. Amit Garg, Kidney Clinical Research Unit, Room A01, Westminster Tower, London Health Sciences Centre, 800 Commissioners Road East, London, ON N6A 4G5, Tel: 519-685-8502, E-mail: Amit.Garg@lhsc.on.ca

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Walkerton is a small rural town located in one of Ontario's prime agricultural areas, 180 kilometres northwest of Toronto. In May 2000, municipal water in Walkerton became contaminated with *Escherichia coli* O157:H7 and *Campylobacter* species. At the time of the outbreak, heavy rainfall contributed to the surface transport of live-stock fecal contaminants into inadequately chlorinated drinking water, supplied from three drilled wells. Many individuals were either primarily or secondarily exposed to the bacteria, including permanent residents of Walkerton, individuals employed in the town, and visitors from neighbouring communities. This outbreak produced an estimated 2,300 cases of acute gastro-intestinal illness, over 750 emergency room visits, 65 hospital admissions, 27 cases of identified hemolytic uremic syndrome (HUS), and 6 fatalities.¹

While initial medical care focussed on the acute management of infected persons, attention has now shifted towards long-term health matters. 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 HUS. Initiated in 2002, the Walkerton Health Study provides a unique and rare opportunity to characterize new and existing epidemiological associations between acute gastroenteritis and chronic diseases, including post-infectious irritable bowel syndrome, arthritis, hypertension, renal disease, and diabetes mellitus.²⁻⁷ Additionally, any psychosocial sequelae of this stressful environmental disaster may be better characterized.^{8,9} As part of the Walkerton Health Study, we invited citizens from the region to attend a special clinic in the local hospital, to undergo a standardized interview, physical examination, and blood and urine testing.

Since more severe acute illness is often associated with worse long-term outcomes,⁶ self-selection bias may lead to the erroneous finding of either no association, or an overestimate of the association, between previous gastroenteritis and subsequent chronic disease. For example, those who decide to attend a study health clinic or who choose to volunteer for a study may differ from non-participants (non-respondents). Non-participation may be due to denial, selec-

tive migration or differences in health-seeking behaviours. As a group, if volunteers differ from non-participants in their association between acute illness and long-term sequelae, then the measure of association may be distorted, and the generalizability of the results threatened.¹⁰

Here, we assessed for study sample representativeness, and explored whether the association between the acute exposure and preliminary long-term health outcomes may have been biased by differences between early study participants and those who agreed to participate after more intense recruiting efforts.¹¹

METHODS

We posed the following three questions: 1) Were study volunteers similar in age and sex to the general population of Walkerton and the wider municipality of Brockton? 2) What proportion of those who were acutely ill during the contaminated water outbreak agreed to participate in the long-term study? 3) What was the effect of intensifying efforts at participant recruitment? For the latter, we examined for differences between initial and late recruits, in terms of demographics, medical conditions predating the outbreak, and acute illness characteristics. Additionally, we explored whether the associated risk between having acute gastroenteritis and certain subsequent health measures differed between early and late study respondents.

Data sources

Both the 1996 and 2001 Canadian Census counted individuals in relation to their usual place of residence. According to the Census, non-commuter rural communities experienced a population decline due to both an emigration of young adults and the death of aged residents.¹² Similarly, the municipality of Brockton, Ontario, which includes the town of Walkerton, experienced a 5% population decline over this five-year period. At the time of the outbreak in May 2000, Census, local postal and voting records suggested that there were 5,000 persons living in the town of Walkerton, and 10,000 persons in the municipality of Brockton, a land area of 565 square kilometres (Figure 1). A formal investigation at the time of the outbreak by the Regional Health Unit identified all

Figure 1. Map of Walkerton, Ontario and municipality of Brockton (shaded stripes)

individuals who were acutely ill by considering the following: i) persons who contacted the Regional Health Unit directly, ii) those who underwent laboratory stool cultures, and iii) all emergency room visits and admissions to any of the three local hospitals in Owen Sound, Walkerton and Hanover, Ontario.¹ A total of 1,346 cases were identified from a history of diarrhea, positive stool cultures or recognized hemolytic uremic syndrome. The Regional Health Unit also conducted a random sample telephone survey at the time of the outbreak, to calculate age- and sex-specific attack rates for the town of Walkerton in the month of May 2000. By applying these estimates to age- and sex-specific population estimates provided by the 1996 Canadian Census, it was concluded that only 58% of cases had likely been identified. Accordingly, it was estimated that about 2,300 area residents had, in fact, been acutely ill at the time of the outbreak.

Beginning in February 2002, individuals who either lived in the Walkerton area or who had consumed municipal water in

May 2000, irrespective of whether they developed an acute illness, were invited to participate in the Walkerton Health Study through word of mouth, the local media (radio and television), mailed leaflets, and a town hall meeting. Subsequently, in 2003, a detailed recruitment and telephone campaign was conducted, inviting non-participants from Walkerton to attend the health clinic in the local hospital. Posters with recruitment targets were placed in the post office and pharmacies, and 1,147 non-participating households were called using the local phone book. Both initial and additional participants were given a small honorarium of \$10 to \$20 Canadian for travel costs. In addition, satellite clinics were set up in the local high school and nursing home. Data obtained at the time of the standardized interview, physical assessment and laboratory testing were entered into a computer database by trained staff unaware of the acute exposure status of the participant.

Using pre-specified algorithms, persons with abnormal results were flagged for

TABLE I

Age- and Sex-distribution Data of Residents of Walkerton and Surrounding Areas Compared to the 1996 and 2001 Canadian Census Data

	Canadian Census Data				Walkerton Health Study Participants (n = 4,315)	
	Municipality of Brockton 1996	Municipality of Brockton 2001	Town of Walkerton 1996	Town of Walkerton 2001	Residents Municipality of Brockton 2000	Residents Town of Walkerton 2000
Number	10,163	9,655	5,036	4,845	3,124	2,756
Female (%)	52.0	50.1	52.0	52.2	55.4	55.1
Age years (%)						
≤4	6.6	5.0	6.6	5.1	6.6	6.4
5-14	15.3	14.0	15.3	13.3	18.4	18.0
15-19	6.6	9.0	6.6	8.8	7.4	7.5
20-24	5.9	5.2	5.9	5.5	3.5	3.6
25-54	39.0	40.8	39.0	39.6	40.2	40.1
55-64	8.8	10.6	8.8	8.9	11.4	11.0
65-74	8.5	8.2	8.5	8.6	8.4	8.9
≥75	9.2	7.3	9.2	10.3	4.2	4.6

These data refer to permanent residents. The age of the Walkerton Health Study participants was according to May 1, 2000.

The sample was demographically similar to the population of interest, although statistically women were more likely to participate than men (55% of sample were women compared to 52% of population, $p < 0.01$), and the proportion of both young and very elderly adults was smaller than expected (13% of sample were 65 years of age or older compared to 18% of population, $p < 0.01$).

TABLE II

Illness Characteristics of Walkerton Health Study Participants and Non-participants in Relation to the Initial Outbreak of Water-contaminated *Escherichia coli* O157:H7 and *Campylobacter* Species

	Participants	Non-participants	All Persons
Total no.	4315	Unknown	—
No. individuals with recognized hemolytic uremic syndrome*	20	10	30
No. individuals with acute gastroenteritis confirmed by the Regional Health Unit	848	587	1346
No. individuals with self-reported acute gastroenteritis	1893	407	2300 †,‡
No. individuals with stool cultures performed during outbreak	571	104	675
No. individuals with positive <i>E. coli</i> O157:H7 stools during outbreak	134	42	176

* Subsequent to the initial investigation, at least 3 more cases of hemolytic uremic syndrome have been identified. Of the 10 non-participants, 6 died within weeks of the outbreak.

† Estimated by the Regional Health Unit.

‡ The true number of individuals who drank contaminated municipal water or who were secondarily exposed to infection is unknown.

Based on self-reported and laboratory-confirmed definitions of acute illness, between 63% and 85% of all those identified as having been acutely ill are current participants in the study.

referral to a medical specialist for consultation, while other laboratory test results were forwarded to the participant's family physician for attention. Specifically, based on predetermined cut-point measures of blood pressure, urine dipstick and/or 24-hour total protein and estimated glomerular filtration rate, persons with any abnormality received a nephrology consultation. The algorithm used therein depended on the individual's age, sex and diabetes status. To illustrate, non-diabetic adults aged 20 to 50 years were flagged for consultation in the presence of either elevated blood pressure (i.e., a systolic blood pressure ≥ 180 mm Hg or a diastolic blood pressure ≥ 100 mm Hg averaged over three readings); proteinuria (i.e., a 24-hour urine protein ≥ 0.5 g, a random urine dipstick protein ≥ 1.0 g/L or a urine albumin: creatinine ratio ≥ 50 mg/mmol), or renal impairment (i.e.,

serum creatinine ≥ 104 μ mol/L in women or ≥ 137 μ mol/L in men).

Health conditions that predated the outbreak were first identified through self-report, and confirmed by data abstraction from hospital and family physician records. Those with renal disease or hypertension pre-dating the outbreak were excluded from the analysis comparing early- and late-recruited participants and their development of new renal sequelae. If participants were seen more than once, we used the data obtained at their first visit following the outbreak. While the Walkerton Health Study is ongoing until 2009, the study results reported herein are current up to February 2004.

Statistical analysis

Chi-squared goodness-of-fit tests were used to assess for age and sex differences

between population Census data and those of the Walkerton Health Study participants. Chi-squared or Fisher's Exact tests were used to assess for differences between initial and subsequent volunteers. Relative risks for long-term renal sequelae after acute gastroenteritis and their 95% confidence intervals were calculated¹³ and graphed on a logarithmic scale. Statistical significance was set at a p-value < 0.05 . All analyses were conducted using SPSS 10.0 (SPSS, Inc., Chicago, IL, USA) and Excel 2000 (Microsoft Corporation, Redmond, WA, USA). All participants provided written informed consent, and the study was approved by the University of Western Ontario Research Ethics Board.

RESULTS

By February 2004, 4,315 study participants were recruited, of whom 2,756 (64%) were residents of Walkerton and 3,124 (72%) were residents of the wider municipality of Brockton. This represents about 55% of all Walkerton inhabitants and 31% of Brockton inhabitants at the time of the initial outbreak.

Study participants from Walkerton and Brockton were similar in age and sex to the Canadian Census figures for 1996 and 2001 (Table I), with the exception of a smaller proportion of young and very elderly adults (13% of sample were ≥ 65 years of age compared to 18% of population, $p < 0.01$), and a higher representation of women (55% of sample were women compared to 52% of population, $p < 0.01$). Demographic differences between the Census and study sample were consistent

in those with and without gastrointestinal symptoms at the time of the outbreak (data not shown).

Specific characteristics of Walkerton Health Study participants and non-participants at the time of the contaminated water outbreak are presented in Table II. Based on self-reported and laboratory-confirmed definitions of acute illness, between 63% and 85% of all those identified as having been acutely ill are current participants in the study.

Following the 2003 campaign, an additional 356 initial non-participants were successfully recruited from Walkerton (Table III). Compared to initial participants, additional recruits were more likely to have been symptom-free at the time of the outbreak (21% vs. 7%, $p<0.001$), middle-aged ($p<0.01$) and have a family history of hypertension (35% vs. 42%, $p<0.01$). Otherwise, they were comparable to those recruited soon after the contaminated water outbreak (Table III).

Of the 4,315 study participants, 907 had evidence of hypertension or renal disease pre-dating the outbreak. Of the remaining participants, 1,135 described no symptoms at the time of the outbreak, 773 had confirmed acute gastroenteritis, and 1,500 were suspect cases. While recognizing the relatively small number of additionally-recruited participants, their risk of hypertension and renal sequelae necessitating nephrological consultation was similar to that of the early recruits (Table IV and Figure 2). The inclusion of the additional study participants to the whole study sample did not change the overall risk of long-term sequelae following acute gastroenteritis (Figure 2).

DISCUSSION

The Walkerton Health Study was designed to identify whether persons infected with *E.coli* O157:H7 or *Campylobacter* species are at extended risk of adverse health outcomes. For the purpose of screening and prognosis, this requires that the association between acute infection and long-term sequelae be characterized accurately. While a "target population" usually refers to those individuals to whom a study is applicable, it is difficult and/or impractical to study an entire population, even after a fixed and relatively contained outbreak, like that which

TABLE III

Baseline Characteristics of Initially- and Additionally-recruited Study Participants

	Initial Participants 3959	Additional Participants 356
No.		
Caucasian (%)	99.0	98.9
Female (%)	56.1	55.9
Age (%)		
≤4	8.0	4.5
5-14	17.7	15.4
15-19	8.0	4.8
20-24	4.1	3.7
25-54	41.1	46.3
55-64	10.6	14.0
65-74	7.3	7.6
≥75	3.3	3.7
Medical conditions predating outbreak (%)*		
Renal impairment	4.7	4.5
Hypertension	18.2	19.9
Diabetes mellitus	4.2	4.8
Myocardial infarction	2.1	3.1
Stroke	1.4	1.4
Gallstones	6.3	7.3
Irritable bowel syndrome	5.2	3.1
Smoking	18.5	21.9
Elevated cholesterol	11.1	11.8
Family history (%)*		
Diabetes mellitus	20.6	18.9
Hypertension	35.4	41.8
General medical check-up in the year prior to the outbreak (%)*	64.3	65.4
Number with hemolytic uremic syndrome	19	1
Acute gastroenteritis confirmed by the Regional Health Unit (%)	20.8	7.0
Stool culture performed at outbreak (%)	14.0	4.8
Stool culture performed and positive for <i>E.coli</i> O157:H7 (%)	3.2	2.0

* Most responses were either self-reported and/or from a review of a family physician's medical chart, or as reported by the local laboratory or Regional Health Unit.

Compared to initial participants, additional recruits were more likely to have been symptom-free at the time of the outbreak ($p<0.001$), middle-aged ($p<0.01$), and have a family history of hypertension ($p<0.01$). Otherwise, they were comparable to those recruited soon after the contaminated water outbreak.

occurred in Walkerton. After such an unpredictable event, establishing methods of collecting clinical and laboratory data on more than 4,300 participants living in a remote community requires funding, planning and time. In the case of Walkerton Health Study, two years had elapsed before the first participant was enrolled. As such, inferences must be drawn from a convenience sample of voluntary and consenting participants, who may differ from non-participants according to important baseline and prognosticating variables.¹⁴ The data presented herein suggest that, in a small and willing community, and using a variety of baseline sampling and ongoing recruitment strategies, study participants do appear to be representative of the population of interest. While those recruited through additional efforts were less likely to have been acutely ill during the outbreak, they were otherwise comparable to those recruited soon after the outbreak. Thus, non-participation has not significantly biased estimates of certain health conditions that predated the exposure of interest.

A true measure of non-participation bias is usually not possible, since non-participants cannot be assessed on how they differ from study volunteers in the relationship between an acute exposure and a long-term outcome. A large uncontrolled municipal water outbreak is particularly challenging in this regard, as the true number of exposed individuals remains unknown, and the methods of establishing a comprehensive sampling frame of eligible participants and non-participants remains elusive, often referred to as 'non coverage'. Nevertheless, our results establish a framework by which selection biases can be partially assessed in this health study, by comparing associations in those who initially volunteered to those who were recruited only after substantial effort. This commonly used technique¹¹ is imperfect, since for late recruits a longer period of time has elapsed between the initial exposure and the first study contact and collection of baseline and current data. There will also always be a fixed number of late recruits, and in some cases a limited sample size may provide inade-

TABLE IV

Incidence of Newly Diagnosed Hypertension, Proteinuria or Reduced Glomerular Filtration Rate Prompting Nephrology Referral Among Initial Participants and Those Additionally Recruited Through a Telephone Campaign

	Initial Participants (n = 1773)*		Additional Participants (n = 135)*		Total Participants (n=1908)*	
	No Symptoms at the Time of the Outbreak	Confirmed Gastroenteritis at the Time of the Outbreak	No Symptoms at the Time of the Outbreak	Confirmed Gastroenteritis at the Time of the Outbreak	Confirmed Gastroenteritis at the Time of the Outbreak	No Symptoms at the Time of the Outbreak
No.	1026	747	109	26	1135	773
No. (%) referred for nephrology consultation	42 (4.1%)	28 (3.7%)	3 (2.8%)	2 (7.7%)	45 (4.0%)	30 (3.9%)

* Those with pre-existing hypertension or renal disease, and those with suspected but unconfirmed gastroenteritis, were excluded from this analysis. Appreciating the relatively small number of additionally-recruited participants, the risk of hypertension and renal sequelae necessitating nephrological consultation in additionally-recruited participants did not statistically differ from that of early recruits.

Figure 2. According to those recruited initially and subsequently, the risk of hypertension, proteinuria or reduced glomerular filtration rate 2 years after acute symptomatic gastroenteritis.

Appreciating the relatively small number of additionally-recruited participants, the risk of hypertension and renal sequelae necessitating nephrological consultation in additionally-recruited participants did not statistically differ from that of early recruits.

quate statistical power to detect selection biases, if in truth they do exist. These concerns notwithstanding, the long-term study outcomes defined herein were based on “objective” physical examination and laboratory measurements, to minimize self-reporting bias, as could be the case when participants are engaged in lawsuits for damages incurred.¹⁵

Recognizing the limitations related to small sample sizes and a follow-up period of three years or less, there was no overt difference in the risk of long-term hypertension and renal disease after acute gastroenteritis between early and late participants. The inclusion of another 356 late recruits did not change the overall associated risk of detectable long-term sequelae in the entire study sample. Thus, we believe that the Walkerton Health Study sample will provide reasonably unbiased estimates of the risk of long-term disease after acute bacterial gastroenteritis. In the future, these selection analyses will be repeated, and will include appropriate imputation methods and sensitivity scenarios on the

number of individuals who would need to be recruited to meaningfully change the observed association.^{16,17} Ongoing public health efforts will continue to ensure that medical sequelae can be identified, treated and prevented in those who remain non-participants.

In health surveys, eligible non-participants may be heterogeneous in nature. A change in the strength or direction of various associations due to non-participation may depend on the nature of the health survey, the sampling method used, and the uniformity of non-participant variables relative to those of enrollees. As observed by others, we found that non-participants were more likely to be male¹⁸⁻²² and elderly,^{18,22} and had less symptoms of acute illness.^{20,21,23,24} Others have suggested that non-participants are also less likely to be formally educated^{21,25} or employed,¹¹ are more likely to engage in smoking,^{18,21,25-28} poorer lifestyle behaviours^{19,29} and medication use,¹⁸ while receiving fewer routine health care visits²⁸ and having less health care expenditures.³⁰ In the special situation of a contained envi-

ronmental disaster, one study following an oil tanker spill highlighted the main reasons for non-participation to be attitudinal: non-participants had fewer concerns about their own health, or were either not interested in the study or did not think it was useful.³¹ While some have provided evidence to the contrary,²² it is encouraging that some large studies support our finding that a measure of association between an adverse exposure and an adverse health outcome is not appreciably influenced by the inclusion of late participants, as in our study, or the omission of a relatively small proportion of non-participants.^{19,21,28,32}

In conclusion, current participants of the Walkerton Health Study appear representative of the general population of interest, and include most individuals who were acutely ill during the outbreak. Our study sample should provide unbiased estimates of the risk of long-term disease after acute bacterial gastroenteritis. Ongoing and future epidemiological analyses will provide a unique opportunity to better charac-

terize these associations following this unfortunate catastrophe.

REFERENCES

- Anonymous. The investigative report of the Walkerton outbreak of waterborne gastroenteritis May-June 2000. Bruce-Grey-Owen Sound Health Unit. 2000;1-67.
- Neal KR, Hebden J, Spiller R. Prevalence of gastrointestinal symptoms six months after bacterial gastroenteritis and risk factors for development of the irritable bowel syndrome: Postal survey of patients. *BMJ* 1997;314(7083):779-82.
- Parry SD, Stansfield R, Jelley D, Gregory W, Phillips E, Barton JR, et al. Does bacterial gastroenteritis predispose people to functional gastrointestinal disorders? A prospective, community-based, case-control study. *Am J Gastroenterol* 2003;98(9):1970-75.
- Hannu T, Mattila L, Rautelin H, Pelkonen P, Lahdenne P, Siitonen A, et al. Campylobacter-triggered reactive arthritis: A population-based study. *Rheumatology (Oxford)* 2002;41(3):312-18.
- Bremell T, Bjelle A, Svedhem A. Rheumatic symptoms following an outbreak of campylobacter enteritis: A five year follow up. *Ann Rheum Dis* 1991;50(12):934-38.
- Garg AX, Suri RS, Barrowman N, Rehman F, Matsell D, Rosas-Arellano MP, et al. Long-term renal prognosis of diarrhea-associated hemolytic uremic syndrome: A systematic review, meta-analysis, and meta-regression. *JAMA* 2003;290(10):1360-70.
- Suri R, Clark W, Mahon J, Garg AX. Incidence of diabetes mellitus after diarrhea associated hemolytic-uremic syndrome: A systematic review. *Submitted for review*.
- Bertazzi PA. Industrial disasters and epidemiology. A review of recent experiences. *Scand J Work Environ Health* 1989;15(2):85-100.
- Lyons RA, Temple JM, Evans D, Fone DL, Palmer SR. Acute health effects of the Sea Empress oil spill. *J Epidemiol Community Health* 1999;53(5):306-10.
- Ives DG, Traven ND, Kuller LH, Schulz R. Selection bias and nonresponse to health promotion in older adults. *Epidemiology* 1994;5(4):456-61.
- Sheikh K. Predicting risk among non-respondents in prospective studies. *Eur J Epidemiol* 1986;2(1):39-43.
- Statistics Canada Census Operating Division. A profile of the Canadian population: Where we live. *Statistics Canada* 2004; Catalogue: 96F003XIE0 no1.
- Gardner MJ, Altman DG. Statistics with confidence. *BMJ* 1994;51-52.
- Ganguli M, Lytle ME, Reynolds MD, Dodge HH. Random versus volunteer selection for a community-based study. *J Gerontol A Biol Sci Med Sci* 1998;53(1):M39-M46.
- Roht LH, Vernon SW, Weir FW, Pier SM, Sullivan P, Reed LJ. Community exposure to hazardous waste disposal sites: Assessing reporting bias. *Am J Epidemiol* 1985;122(3):418-33.
- Rowland ML, Forthofer RN. Adjusting for non-response bias in a health examination survey. *Public Health Rep* 1993;108(3):380-86.
- Brick JM, Kalton G. Handling missing data in survey research. *Stat Methods Med Res* 1996;5(3):215-38.
- Korkeila K, Suominen S, Ahvenainen J, Ojanlatva A, Rautava P, Helenius H, et al. Non-response and related factors in a nation-wide health survey. *Eur J Epidemiol* 2001;17(11):991-99.
- Van Loon AJ, Tjihuis M, Picavet HS, Surtees PG, Ormel J. Survey non-response in the Netherlands: Effects on prevalence estimates and associations. *Ann Epidemiol* 2003;13(2):105-10.
- Kotaniemi JT, Hassi J, Kataja M, Jonsson E, Laitinen LA, Sovijarvi AR, et al. Does non-responder bias have a significant effect on the results in a postal questionnaire study? *Eur J Epidemiol* 2001;17(9):809-17.
- Brogger J, Bakke P, Eide GE, Gulsvik A. Contribution of follow-up of nonresponders to prevalence and risk estimates: A Norwegian respiratory health survey. *Am J Epidemiol* 2003;157(6):558-66.
- Chou P, Kuo HS, Chen CH, Lin HC. Characteristics of non-participants and reasons for non-participation in a population survey in Kin-Hu, Kinmen. *Eur J Epidemiol* 1997;13(2):195-200.
- de Marco R, Verlato G, Zanolin E, Bugiani M, Drane JW. Nonresponse bias in EC Respiratory Health Survey in Italy. *Eur Respir J* 1994;7(12):2139-45.
- Buchner DM, Pearson DC. Factors associated with participation in a community senior health promotion program: A pilot study. *Am J Public Health* 1989;79(6):775-77.
- Shahar E, Folsom AR, Jackson R. The effect of nonresponse on prevalence estimates for a reference population: Insights from a population-based cohort study. *Atherosclerosis Risk in Communities (ARIC) Study Investigators. Ann Epidemiol* 1996;6(6):498-506.
- Hill A, Roberts J, Ewings P, Gunnell D. Non-response bias in a lifestyle survey. *J Public Health Med* 1997;19(2):203-7.
- O'Neill TW, Marsden D, Silman AJ. Differences in the characteristics of responders and non-responders in a prevalence survey of vertebral osteoporosis. *European Vertebral Osteoporosis Study Group. Osteoporos Int* 1995;5(5):327-34.
- Nakai S, Hashimoto S, Murakami Y, Hayashi M, Manabe K, Noda H. [Response rates and non-response bias in a health-related mailed survey]. *Nippon Koshu Eisei Zasshi* 1997;44(3):184-91.
- Hoeymans N, Feskens EJ, Van Den Bos GA, Kromhout D. Non-response bias in a study of cardiovascular diseases, functional status and self-rated health among elderly men. *Age Ageing* 1998;27(1):35-40.
- Etter JF, Perneger TV. Analysis of non-response bias in a mailed health survey. *J Clin Epidemiol* 1997;50(10):1123-28.
- Foster K, Campbell D, Crum J, Stove M. Non-response in a population study after an environmental disaster. *Public Health* 1995;109(4):267-73.
- Siemiatycki J, Campbell S. Nonresponse bias and early versus all responders in mail and telephone surveys. *Am J Epidemiol* 1984;120(2):291-301.

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RÉSUMÉ

Contexte : Après la contamination bactérienne du réseau municipal d'alimentation en eau de la collectivité rurale de Walkerton, en Ontario, plus de 2 300 cas de gastro-entérite aiguë ont été documentés. L'étude sur la santé de Walkerton évalue actuellement les séquelles à long terme de cette flambée épidémique sur la santé des habitantes et des habitants de Walkerton ayant accepté de participer. Nous avons cherché à déterminer si l'association entre l'exposition aiguë et les premiers résultats sanitaires à long terme pouvait comporter des biais en raison des différences entre les recrues initiales et tardives.

Méthode : Nous avons utilisé des données de plusieurs sources, dont les recensements canadiens de 1996 et de 2001 et les dossiers de la circonscription sanitaire, de l'hôpital et de l'étude sur la santé de Walkerton, pour déterminer la représentativité de l'échantillon et les effets escomptés de l'intensification du recrutement. Pour évaluer le biais de sélection, nous avons cerné les différences entre les recrues initiales et tardives et leur risque ultérieur de souffrir d'hypertension artérielle, de protéinurie et de clairance rénale réduite.

Résultats : Des 4 315 personnes participantes, 2 756 étaient des résidents permanents de Walkerton, soit 55 % de la population de la ville. Sur le plan démographique, l'échantillon était semblable à la population de Walkerton, bien que statistiquement, les femmes aient eu plus tendance à participer que les hommes (l'échantillon comportait 55 % de femmes, alors qu'elles représentent 52 % de la population, $p < 0,01$), et que les proportions de jeunes et de personnes très âgées aient été plus faibles que prévu (l'échantillon comportait 13 % de personnes de plus de 65 ans, alors qu'elles représentent 18 % de la population, $p < 0,01$). Si l'on compare les 3 959 recrues initiales aux 356 personnes recrutées plus tard au prix d'un effort considérable, ces dernières étaient plus susceptibles d'avoir été asymptomatiques durant la flambée (21 % c. 7 %, $p < 0,001$), mais sur tous les autres plans (âge, sexe, recours aux soins médicaux et état de santé avant la flambée), les deux groupes étaient semblables. Le risque d'hypertension artérielle ou de séquelles rénales à long terme ne différait pas de façon significative chez les recrues initiales et tardives de l'étude.

Conclusions : Les participantes et les participants de l'étude sur la santé de Walkerton sont représentatifs de la population de Walkerton, et ils comprennent les personnes atteintes d'infections aiguës durant la flambée d'origine hydrique. L'échantillon disponible pour l'étude devrait donc fournir des estimations raisonnablement impartiales du risque associé entre la gastro-entérite bactérienne aiguë et les séquelles à long terme sur la santé.