Estimated numbers of community cases of illness due to *Salmonella*, *Campylobacter* and verotoxigenic *Escherichia coli*: Pathogen-specific community rates

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OBJECTIVE: To estimate the annual number of cases of illness due to verotoxigenic *Escherichia coli* (VTEC), *Salmonella* and *Campylobacter* in the Canadian population, using data from the National Notifiable Disease registry (NND), estimates of under-reporting derived from several National Studies on Acute Gastrointestinal Illness, and the literature.

METHODS: For each of the three pathogens (VTEC, *Salmonella* and *Campylobacter*), data were used to estimate the percentage of cases reported at each step in the surveillance system. The number of reported cases in the NND for each pathogen was then divided by these percentages. In cases where the pathogen-specific estimates were unavailable, data on acute gastrointestinal illness were used, accounting for differences between those with bloody and nonbloody diarrhea.

RESULTS: For every case of VTEC, *Salmonella* and *Campylobacter* infection reported in the NND, there were an estimated 10 to 47, 13 to 37, and 23 to 49 cases annually in the Canadian population, respectively.

CONCLUSIONS: The authors estimate that a significant number of infections due to VTEC, *Salmonella* and *Campylobacter* occur each year in Canada, highlighting the fact that these enteric pathogens still pose a significant health burden. Recognizing the significant amount of under-reporting is essential to designing appropriate interventions and assessing the impact of these pathogens in the population.

Key Words: *Burden;* Campylobacter*; Canada; Incidence;* Salmonella*; VTEC*

Évaluation du nombre de cas de maladie attribuables à *Salmonella*, à *Campylobacter* et à *Escherichia coli* producteur de vérotoxine : taux d'infection à certains micro-organismes pathogènes dans la collectivité

BUT : L'étude avait pour but d'évaluer le nombre annuel de cas de maladie attribuables à *Escherichia coli* producteur de vérotoxine (ECPV), à *Salmonella* et à *Campylobacter* dans les collectivités au Canada, et ce, à partir du relevé national des maladies à déclaration obligatoire, d'évaluations de sous-notification des maladies provenant de plusieurs études nationales des maladies gastro-intestinales aiguës et de la documentation scientifique.

MÉTHODE : Nous avons utilisé, pour chacun des micro-organismes pathogènes (ECPV, *Salmonella* et *Campylobacter*), des données pour évaluer le pourcentage de cas déclarés à chaque étape du système de surveillance. Nous avons ensuite divisé, pour chacune des bactéries, le nombre de cas déclarés dans le relevé par les pourcentages ainsi obtenus. Dans les cas où il n'y avait pas d'évaluation sur des germes pathogènes particuliers, nous avons eu recours à des données sur des maladies gastro-intestinales aiguës en distinguant les diarrhées sanglantes des diarrhées non sanglantes.

RÉSULTATS : Pour chaque cas d'infection à ECPV, à *Salmonella* et à *Campylobacter*, déclaré dans le relevé, il y avait respectivement de 10 à 47, de 13 à 37 et de 23 à 49 cas annuels de maladie dans la collectivité, au Canada.

CONCLUSIONS : Les auteurs sont d'avis qu'un nombre important d'infections à ECPV, à *Salmonella* et à *Campylobacter* se produit chaque année, au Canada; c'est donc dire que ces entérobactéries pathogènes posent encore un important problème de santé. Il est essentiel de reconnaître l'ampleur de la sous-notification de ces infections afin d'élaborer des interventions appropriées et de bien évaluer l'effet de ces germes dans la population.

Gastrointestinal illness (GI) is a public health concern for all countries (1-8). Traditionally, reportable disease data have been the main source of information used to describe the burden of specific pathogenic causes of GI in the population (9-14). However, such data capture only a fraction of the true number of cases (3,15,16). In Canada, the National Notifiable Disease registry (NND) is a legislated mechanism that captures information on culture-confirmed cases of nationally reportable enteric pathogens. Case capture in this registry depends on many steps: patients must be sick enough to visit a physician; the physician must request a sample; the sample must be submitted to a laboratory; the sample must test positive; and the positive result must be reported to the local health authority, to the provincial health authority, and finally to the NND. Although this registry has the advantage of being highly specific, it is subject to significant under-reporting. However, if the extent of under-reporting was known, registry data could be adjusted to provide an estimate of the true number of cases in the population.

A recent study by Voetsch et al (17) from the United States estimated the number of cases of salmonellosis in the population using nationally reported disease data, combined with

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TABLE 1
Data sources used to estimate the percentage of cases that are reported at each step in the surveillance system in Canada

Parameter step	Data source (reference)	Surveillance step	Verotoxigenic *Escherichia coli* (%)	*Campylobacter* (%)	*Salmonella* (%)
h	Assumption	Province reports to the NND	100	100	100
g	NSAGI Public Health Reporting Survey (38)	Local health authority reports to province	94	97	97
f	NSAGI Laboratory Survey (48)	Laboratory reports to local health authority	93	89	94
e	International literature (39-44)	Test is positive:			
		High sensitivity	100	89	100
		Low sensitivity	52.5	72.5	85
d	NSAGI Laboratory Survey (38,48)	Laboratory tests for pathogen	99	99	100
c	NSAGI Population Survey (2)	Sample is submitted for those with:			
		Bloody diarrhea	75	75	75
		Nonbloody diarrhea	100	100	100
b	NSAGI Population Survey (2)	Sample is requested for those with:			
		Bloody diarrhea	50	50	50
		Nonbloody diarrhea	18.03	18.03	18.03
a	NSAGI Population Survey (2)	Case* visits physician for those with:			
		Bloody diarrhea	33.33	33.33	33.33
		Nonbloody diarrhea	16.18	16.18	16.18

**A case was defined as someone who had diarrhea (ie, three or more loose stools or stools with abnormal liquidity in 24 h) lasting more than 24 h. NND National Notifiable Disease registry; NSAGI National Studies on Acute Gastrointestinal Illness*

estimates of under-reporting derived from population-based surveys, laboratory level surveys and the literature. In Canada, the Public Health Agency of Canada's National Studies on Acute Gastrointestinal Illness (NSAGI) initiative has performed similar population- and laboratory-level surveys. Thus, using methods similar to those outlined by Voetsch et al (17), the objective of the present study was to estimate the number of cases of illness due to verotoxigenic *Escherichia coli* (VTEC), *Salmonella* and *Campylobacter* in the Canadian population, using data from the NND, estimates of under-reporting derived from several NSAGI studies, and the literature.

METHODS

Analytical approach

For each of the three pathogens (VTEC, *Salmonella* and *Campylobacter*), data from various sources were used to estimate the percentage of cases reported at each step in the surveillance system. In cases where pathogen-specific data were unavailable, data on GI were used, accounting for differences between those with bloody and nonbloody diarrhea. The number of reported cases in the NND for each pathogen was then divided by these percentages using the equation in the Appendix. Because there were two or more available estimates for the percentage of cases reported (eg, test sensitivity) at some steps in the reporting chain, the estimated number of community cases was calculated for both the most conservative and liberal of scenarios. By calculating a range of values, the authors attempted to reflect the variability and uncertainty of the estimates. An example calculation is provided in the Appendix to illustrate the methods used. Final estimates are reported as the number of community cases, ranges of annual rates per 1000 population, and ratios per reported case. Data were analyzed in SAS 9.1 (SAS Institute Inc, USA) and Microsoft Excel 2000 (Microsoft Corporation, USA).

Data

Percentage of cases reported at each step in the surveillance system: Table 1 outlines the data sources used to estimate the percentage of cases reported at each step in the surveillance system, by pathogen. These data sources are described here in detail, starting at the first step in the reporting chain.

The percentage of patients that visit the physician, the percentage of patients visiting a physician who are requested to submit a sample, and the percentage of patients who actually submit the sample (Table 1, steps a to c) were all estimated using data from the NSAGI Population Surveys, which were conducted in Hamilton, Ontario in 2001/2002 (2) and in British Columbia in 2002/2003 (18). Briefly, these two studies collected information over a 12-month period on the incidence and health care burden of GI using retrospective telephone surveys of randomly selected community members. The combined sample size was 8108. For this analysis, a case was defined as someone experiencing diarrheal illness before being interviewed, the same definition used in the study by Voetsch et al (17). Diarrheal illness was defined as diarrhea that lasted longer than 24 h, and diarrhea was defined as three or more loose stools or stools with abnormal liquidity in 24 h. Individuals were excluded from the case group if they reported that their symptoms resulted from a chronic or other medical condition previously diagnosed by a physician (eg, pregnancy, Crohn's disease, irritable bowel syndrome).

Because the percentage of cases who (a) visited a physician, (b) were asked to submit a sample and (c) submitted a sample was different for those with bloody diarrhea versus nonbloody diarrhea, and because the proportion of cases expected to have bloody diarrhea was thought to vary for the three pathogens, separate percentages for those with bloody and nonbloody diarrhea were used for these three steps accordingly. The results of recent Canadian and international outbreak investigations (19-37) were used to obtain

TABLE 2
Estimates of the percentage of cases with bloody diarrhea

	Verotoxigenic *Escherichia coli*		*Campylobacter*		*Salmonella*	
	High estimate	Low estimate	High estimate	Low estimate	High estimate	Low estimate
Estimated percentage of cases with bloody diarrhea	91	18	29	4	59	6.5

Data from references 19 to 37

TABLE 3
The annual reported and estimated number of cases and rates of illness due to verotoxigenic *Escherichia coli*, *Salmonella* and *Campylobacter* in Canada*, as reported in the Canadian National Notifiable Disease registry in 2000 and 2001

		Annual reported		Estimated (conservative)		Estimated (liberal)	
Pathogen	Year	Number of cases	Rate per 1000 population	Number of cases	Rate per 1000 population	Number of cases	Rate per 1000 population
Verotoxigenic *E coli*	2000	3011	0.10	29,898	1.0	142,760	4.6
	2001	1334	0.04	13,246	0.4	63,249	2.0
	Average	2173	0.07	21,572	0.7	103,005	3.3
Salmonella	2000	5692	0.18	72,840	2.4	207,461	6.7
	2001	6072	0.20	77,702	2.5	221,311	7.1
	Average	5882	0.19	75,271	2.5	214,386	6.9
Campylobacter	2000	12,641	0.41	291,765	9.4	618,109	19.9
	2001	11,886	0.38	274,339	8.9	581,191	18.8
	Average	12,264	0.40	283,052	9.1	599,650	19.3

**Canadian population approximately 31 million*

both a conservative and liberal estimate of the percentage of cases with bloody diarrhea, by pathogen (Table 2).

The NSAGI Laboratory Survey (38), a Canada-wide survey of all community and hospital laboratories conducted in the year 2000, collected information on routine laboratory methods, numbers of samples tested, and the reporting of test results to public health authorities. The percentage of samples that were tested in a routine stool test for each pathogen, as identified in the NSAGI Laboratory Survey, was used for the percentage of cases for which a laboratory tests for the pathogen (Table 1, step d).

An extensive review of the international microbiology literature, circa 2000, on pathogen-specific test sensitivity (39-44) was conducted for the percentage of cases for which the test was found to be positive. For each pathogen, the highest and lowest test sensitivities reported in the literature were used (Table 1, step e).

The percentage of Canadian laboratories that reported confirmed cases of illness due to VTEC, *Salmonella* and *Campylobacter* to the local public health authority at least 80% of the time, as reported in the NSAGI Laboratory Survey (described above), was used as the estimate of the percentage of cases reported from the laboratories to the local health authorities (Table 1, step f).

The percentage of cases reported from the local health authorities to the provinces was estimated using data from the NSAGI Public Health Reporting Survey (38). Briefly, this study was a mail survey conducted with all local health authorities in Ontario and British Columbia between 2000 and 2001. For each of the three pathogens, the percentage of cases reported from the health units to the provincial health authority was used (Table 1, step g).

A reporting rate of 100% was assumed for the percentage of cases reported from the provinces to the NND because cases of infection of VTEC, *Salmonella* and *Campylobacter* are all required by legislation to be reported nationally (Table 1, step h).

Number of cases reported in the NND: The number of cases of illness due to VTEC, *Salmonella* and *Campylobacter* reported in Canada for the years 2000 and 2001 were obtained from the NND (Table 3) (45), and the means of these years were used to determine the pathogen-specific community estimates, circa 2000, for *Salmonella* and *Campylobacter*. Of note, the number of cases of VTEC reported by the NND in 2000 appears anomalous, likely due to the large waterborne outbreak of *Escherichia coli* in Walkerton, Ontario (46); thus, the 2001 NND data likely provide a better estimate of VTEC-specific community cases circa 2000.

RESULTS

The estimated annual number of community cases and community rates per 1000 population due to infection by VTEC, *Salmonella* and *Campylobacter* are shown in Table 3. For every case of VTEC infection reported in the NND, there were an estimated 10 to 47 cases annually in the Canadian population. Similarly, for every case of *Salmonella* and *Campylobacter* infection reported in the NND, there were an estimated 13 to 37 cases and 23 to 49 cases annually in the Canadian population, respectively.

DISCUSSION

Due to factors such as underdiagnosing and under-reporting, the actual number of cases of illness due to VTEC, *Salmonella* and *Campylobacter* infection in the Canadian population is unknown. However, by combining data from the NND with estimates of the percentage of cases reported at each step in the reporting chain, the number of community cases can be estimated. Here, we estimated that approximately 2.5 to 6.9 cases of salmonellosis and 9.1 to 19.3 cases of campylobacteriosis occur each year per 1000 Canadians (circa 2000). We also estimated the community incidence rate for VTEC for both 2000 and 2001. Because the year 2000 appears to be an anomalous year in the NND, it is likely that the incidence reported herein for 2001 (0.4 to 2.0 cases annually per 1000 Canadians) represents our best estimate circa 2000. The results of the present

study highlight the fact that these three pathogens represent a potential significant health burden in the Canadian population

Our estimated range of the ratio of the number of salmonellosis cases in the community per reported case (13 to 37 cases) is very similar to previous estimates of 38.6 (17) and 39 (47) from studies conducted in the United States that used similar methodology. However, our estimate is higher than that reported in a previous study conducted in England (3), where an estimated 3.2 community cases occurred per reported case. Similarly, our estimated range of the ratio of the number of campylobacteriosis cases in the community per reported case (23 to 49 cases) is greater than that reported in the English study, where an estimated 7.6 community cases occurred per reported case (3). Such differences may be due to methodological differences (eg, calculations, surveillance systems, laboratory practices and case definitions used in population surveys), differences in the health care-seeking behaviour of patients, or possibly true differences in the epidemiology of these pathogens.

Interestingly, our estimated range of the ratio of the number of cases due to VTEC in the community per reported case (10 to 47 cases) is higher than the previously reported Ontario estimate of four to eight community cases per reported case (16). It is possible that this difference reflects a true difference in the reporting of VTEC infection in Ontario compared with the overall Canadian rates, but it is more likely that the difference in the estimates is due to methodological differences in the analyses, particularly in the data sources that have become available since the study, which was reported in 2000, was performed. Data used in steps b and c of Table 1 of our analysis were obtained from the NSAGI Population Surveys (2,18); in the Ontario study (16), however, these steps were combined and data from the literature were used to estimate the percentage of symptomatic patients from whom stool samples were obtained. Similarly, the percentage used in step d of Table 1 was obtained from the NSAGI Laboratory Survey, whereas the Ontario study relied on the assumption that 100% of submitted stool samples were tested. Here, the percentages used in steps f and g of Table 1 were obtained from the NSAGI Laboratory and Public Health Reporting Surveys, whereas the Ontario study combined these steps and used a value between 99% and 100% obtained through personal communication. It is likely that these differences in data used are the reasons for differences in the final estimates.

The main limitation of this type of analysis is that it requires several assumptions. First, we assumed that the behaviour of patients with respect to seeking care and submitting samples for testing was the same regardless of pathogen because, unfortunately, such pathogen-specific information is expensive to obtain and is currently unavailable for Canada. In an attempt to address this issue, however, we did account for differences in these behaviours by severity of illness (ie, bloody diarrhea), as well as for differences in severity by pathogen. Second, we used international literature, circa 2000, to obtain the sensitivities of the pathogen tests because information specifically on test sensitivity for Canadian laboratories was unavailable. However, our range of sensitivity estimates of 52.5% to 100% for VTEC were within the range of that used in the Ontario study (mean ± SD 51.8±10.4%) (16). Our range of sensitivity for *Salmonella* (85% to 100%) was slightly higher than that used by Voetsch et al (70%) (17). Third, the percentages obtained from the NSAGI Population Surveys for those who submitted stool samples (Table 1, step c), sorted by bloody and nonbloody diarrhea, were based on small numbers, as was the case in the study by Voetsch et al (17). Given this potential limitation, we reran the analysis with a pooled number of 93% for both those with bloody and nonbloody diarrhea. Using the pooled numbers made little difference to the results, producing estimates of eight to 43, 11 to 37, and 20 to 50 per reported case of VTEC, *Salmonella* and *Campylobacter,* respectively. Finally, the NSAGI Population Surveys were conducted in the city of Hamilton, Ontario, and the province of British Columbia; as such, the surveys may not be representative of the entire Canadian population.

In summary, we estimated that a significant number of infections due to VTEC, *Salmonella* and *Campylobacter* occur each year in the Canadian population, highlighting the fact that these enteric pathogens pose a significant health burden in Canada. These methods can be replicated in other countries, although it would be necessary to evaluate, on a country-by-country basis, how appropriately the multipliers used here can serve as proxy for each country-specific system. Estimates for other pathogens may be conducted in a similar manner using these methods as well, taking into account inherent differences between pathogens.

To further our understanding of the disease burden, an understanding of the pathogen-specific costs of illness is necessary. As well, recognizing the significant amount of under-reporting of cases that result from these three pathogens is essential to designing appropriate interventions, assessing the impact of pathogens in the population and identifying risk exposures.

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APPENDIX
Calculation of the estimated number of community cases of *Salmonella*, *Campylobacter* or verotoxigenic *Escherichia coli* infection

$$y = \frac{x}{[(pBD \times a_1 \times b_1 \times c_1 \times d \times e \times f \times g \times h) + (pNBD \times a_2 \times b_2 \times c_2 \times d \times e \times f \times g \times h)]}$$

Where:

x = The number of reported cases in the National Notifiable Disease registry

y = The number of cases estimated in the community

pBD = Percentage of cases with bloody diarrhea

pNBD = Percentage of cases with nonbloody diarrhea

a = Percentage of cases that visit a physician*

b = Percentage of cases that have a stool sample requested of them*

c = Percentage of cases that submitted a sample*

d = Percentage of laboratories that test for the pathogen

e = Sensitivity of laboratory pathogen test†

f = Percentage of laboratories that report to local health authority

g = Percentage of local health authorities that report to provincial health authorities

h = Percentage of provincial health authorities that report to the National Notifiable Disease registry

Continued on next page

APPENDIX – continued
Calculation of the estimated number of community cases of *Salmonella*, *Campylobacter* or verotoxigenic *Escherichia coli* infection

Example calculation of the conservative estimate of the number of community cases of *Salmonella* infection in the year 2000:

$$y = \frac{5{,}692}{\left[(0.59 \times 0.3333 \times 0.50 \times 0.75 \times 1.00 \times 1.00 \times 0.94 \times 0.97 \times 0.98) + (0.41 \times 0.1618 \times 0.1803 \times 1.00 \times 1.00 \times 1.00 \times 0.94 \times 0.97 \times 0.98)\right]}$$

$$y = 72{,}840$$

Where:

$x = 5692$

y = The number of cases estimated in the community

$pBD = 0.59$

$pNBD = 0.41$

$a_1 = 0.3333$

$b_1 = 0.50$

$c_1 = 0.75$

$a_2 = 0.1618$

$b_2 = 0.1803$

$c_2 = 1.00$

$d = 1.00$

$e = 1.00$

$f = 0.94$

$g = 0.97$

$h = 0.98$

**Where 1 and 2 represent the percentages for those with bloody and nonbloody diarrhea, respectively; †This calculation was performed using both high and low test sensitivities*

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