MAJOR ARTICLE

Incidence and Costs of *Clostridium difficile* Infections in Canada

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Background. Limited data are available on direct medical costs and lost productivity due to *Clostridium difficile* infection (CDI) in Canada.

Methods. We developed an economic model to estimate the costs of managing hospitalized and community-dwelling patients with CDI in Canada. The number of episodes was projected based on publicly available national rates of hospital-associated CDI and the estimate that 64% of all CDI is hospital-associated. *Clostridium difficile* infection recurrences were classified as relapses or reinfections. Resource utilization data came from published literature, clinician interviews, and Canadian CDI surveillance programs, and this included the following: hospital length of stay, contact with healthcare providers, pharmacotherapy, laboratory testing, and in-hospital procedures. Lost productivity was considered for those under 65 years of age, and the economic impact was quantified using publicly available labor statistics. Unit costs were obtained from published sources and presented in 2012 Canadian dollars.

Results. There were an estimated 37 900 CDI episodes in Canada in 2012; 7980 (21%) of these were relapses, out of a total of 10 900 (27%) episodes of recurrence. The total cost to society of CDI was estimated at $281 million; 92% ($260 million) was in-hospital costs, 4% ($12 million) was direct medical costs in the community, and 4% ($10 million) was due to lost productivity. Management of CDI relapses alone accounted for $65.1 million (23%).

Conclusions. The largest proportion of costs due to CDI in Canada arise from extra days of hospitalization. Interventions reducing the severity of infection and/or relapses leading to rehospitalizations are likely to have the largest absolute effect on direct medical costs.

Keywords. *Clostridium difficile*; economic burden; epidemiology; hospital-acquired infections; model.

Evidence is accumulating that the epidemiology of *Clostridium difficile* infection is worsening, with marked increases in both incidence and case-fatality in Canada [1], the United States [2, 3], Europe [4], and other countries [5]. Although the reasons are multifactorial, 1 cause is the emergence of a new, "hypervirulent" strain designated restriction endonuclease analysis type BI, North American pulsed-field gel electrophoresis type 1 (NAP1), or polymerase chain reaction (PCR) ribotype 027 (ie, BI/NAP1/027) [6]. Although it was first identified in Quebec [7], transmission of this strain is now of global concern [8]. In addition, although it is not known whether recurrence rates have changed, reduced susceptibility and increased rates of *C difficile* infection are being observed in the community [9].

The existing literature on the burden of illness of *C difficile* infection is sparse, with incidence estimates derived primarily from teaching hospitals [1]. As such, there are no published Canada-wide estimates of the prevalence or the economic burden attributable to *C difficile* infection. The objective of this study was to estimate the annual number of persons infected with *C difficile* in Canada in 2012 and the direct medical and lost productivity costs.

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METHODS

Using prevalence-based burden of illness model, we estimated the annual mean number of persons infected with *C difficile* in Canada and the direct medical costs and lost productivity costs [10]. Numbers of infected persons were tabulated by treatment location (acute care hospital, community-dwelling, and long-term care) and, for those in acute care, stratified by first versus recurrent infection, disease severity, and age group [11].

Given its episodic nature, the mean number of infections per province between 2010 and 2012 was estimated. These data are from a laboratory that uses PCR methods for diagnosis of *C difficile*. Resource use and costs of typical management patterns were estimated for each treatment location and other stratification variables. A societal perspective was adopted by including lost productivity costs. The model was developed in Microsoft Excel 2010, and the statistical analyses were conducted in Stata 12.

Data Sources

Sources of data used included the following: (1) the number of bed-days attributed to persons infected with *C difficile* in Canadian acute care hospitals, from the Canadian Institute for Health Information (CIHI); (2) the estimated proportion of recurrent acute care infections, from the Providence Health Care ([PHC] Vancouver, British Columbia) Infection Prevention and Control *C difficile* infection surveillance program dataset; and (3) the estimated proportions of infections occurring among hospital- and community-based individuals and distributions of severity, obtained from the literature [12, 13].

Resources expended for diagnosing persons in Canada infected with *C difficile* came from published literature, clinician interviews, and data from PHC Infection Prevention and Control and other Canadian surveillance programs (Table 1). Costs were obtained from PHC Infection Prevention and Control and PHC Finance. Clinical experts included hospital (n = 3) and community (n = 1) physicians and infection control experts (n = 2), medical directors of long-term care facilities (n = 3), and acute care nurses who care for patients infected with *C difficile* (n = 2). Lost productivity was quantified using labor statistics [14]. Use of the PHC Infection Prevention and Control data was approved by the ethical review boards of PHC and the University of British Columbia.

Number of Infected Persons With *Clostridium difficile* in Canada

The annual aggregated number of initial and recurrent infections in Manitoba was obtained from published sources [12, 15]. Other than Manitoba, there is no published information on the numbers of *C difficile* in Canadian provinces or territories so these estimates were derived indirectly (Figure 1). In step 1, the province-specific mean annual estimated rates of persons newly infected in hospital were multiplied by the total number of patient days per province from CIHI [12, 16–20]. In step 2, the numbers of person newly infected while living in the community or in long-term care were estimated by using the ratio of hospital- to community-based source of infections observed in Manitoba: 64.2 to 35.8 [12]. In step 3, the province-specific numbers of infections were determined by adding in the estimated proportion of *C difficile* infections that were recurrent (0.271). Because of different definitions of time periods reported by different agencies, recurrent infections included both relapses (variously defined as within 4, 6, or 8 weeks of initial infection) and reinfections.

Table 1. Estimated Mean Number of Initial and Recurrent Infections of *Clostridium difficile* Occurring in Canadian Hospitals, 2012

Province	Rate of New *C difficile* Infections per 10 000 Bed-Days[a]	Total Number of Bed-Days[b]	Number of Infections in Hospital
Newfoundland and Labrador	2.8	422 501	118
Prince Edward Island	2.8	126 014	35
Nova Scotia	2.8	806 400	226
New Brunswick	2.8	735 996	206
Quebec	17.0	5 560 668	9453
Ontario	6.0	6 924 115	4154
Manitoba			
Saskatchewan	3.4	829 701	282
Alberta	6.6	2 430 875	1636
British Columbia	8.3	2 834 776	2353
Yukon	6.3	15 138	10
Northwest Territories	6.3	24 208	15
Nunavut	6.3	4946	3
Canada			18.492

[a] Mean rate from Canadian Nosocomial Infection Surveillance Program for fiscal years 2011 and 2012 for all jurisdictions except British Columbia (Provincial Infection Control Network), Manitoba (back calculated from Manitoba Health), and the Territories (national average).

[b] From the Canadian Institute for Health Information.

Stratification

The costs of treating *C difficile* depend on the severity of illness, location of treatment, and patient age. Severity was classified according to the Society for Healthcare Epidemiology of America-Infectious Diseases Society of America (SHEA-IDSA) guidelines definitions of mild-to-moderate, severe, and fulminant infection [11]. Estimates of the distribution of infections by severity were taken from the literature [21] and from the PHC Infection Prevention and Control program, which showed that 2.1% of hospital infections result in fulminant disease.

As a result of a lack of population-based Canadian data, the proportion of infections managed in hospital (53%) was based on data from the Rochester Epidemiology Project [22]. In the base case, the number of infections (n = 1605) managed in

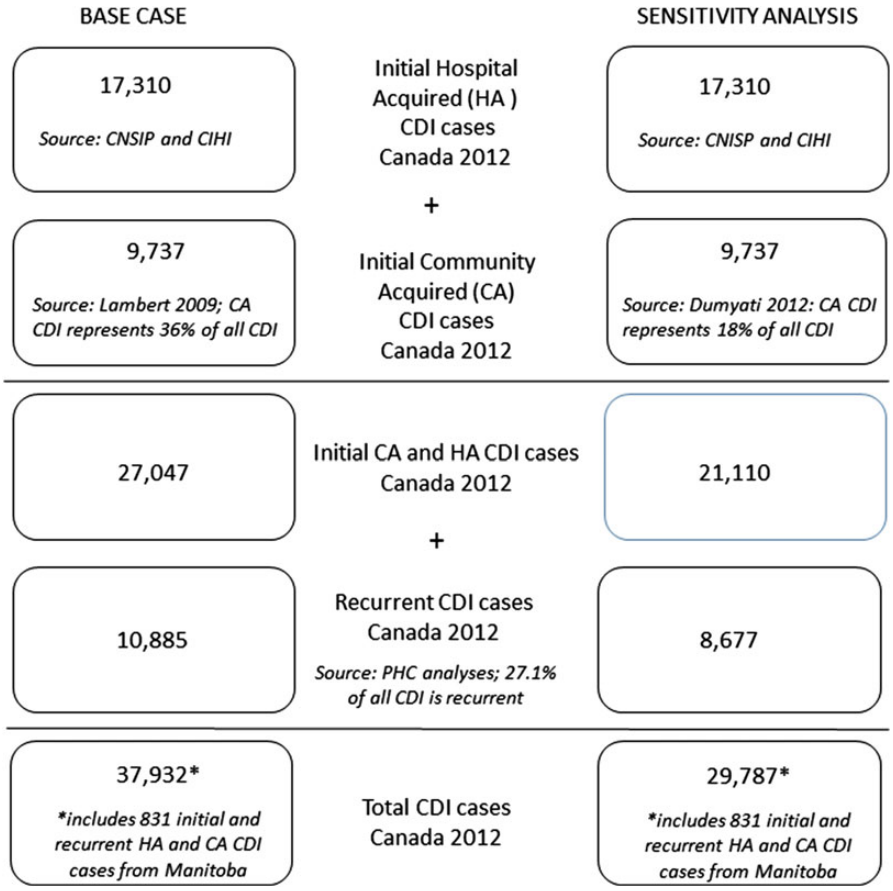

Figure 1. Estimated number of infections and of *Clostridium difficile* in Canada in 2012, base infection assumptions and sensitivity analysis.

long-term care was imputed based on a recent US population-based study [22].

Management and Resource Use

The frequency of tests among community-managed *C difficile* infections was estimated from the literature [23, 24], and the severity-specific mean number of physician visits was elicited from clinical experts. Pharmacologic treatment was assumed to follow the SHEA-IDSA guidelines for hospitalized patients [11]. The costs of managing severe or recurrent *C difficile* infections in the community were based on 2011 data [25, Personal Communication with community pharmacist in Ontario, February 13, 2012].

Costs

Direct costs attributable included the following: laboratory tests, hospitalizations for other causes that were extended due to infection, rehospitalization due to infection, medication, surgical procedures, and physician visits (Appendix Table 1) [26, 27]. Incremental costs of in-hospital resource use were estimated from the PHC Infection Prevention and Control dataset using a generalized linear regression model.

Estimates for lost productivity while in hospital were derived by multiplying the number of days in hospital attributable to *C difficile* infection by age-specific probabilities of being employed, of working full time, and by the 2012 mean daily wage rate [14].

Unit costs were inflated to 2012 Canadian dollars ($CAD) where necessary using the healthcare component of the Canadian consumer price index. Costs of infection control practices and of direct nonmedical resources were excluded.

Sensitivity Analyses

Key parameters were varied in sensitivity analyses. The proportion of infections managed in hospital was varied in sensitivity analyses, assuming the frequency of hospital treatment for *C difficile* infections was as high as 70% of all infections (based on clinical experts). In another sensitivity analysis, it was assumed that 7108 infections would be managed in long-term care based on recent population-based data from Canada and the United States (suggesting that 25% of cases originate from the long-term care, and that 10% of these require hospitalization) [12, 22].

In the absence of robust data, a plausible range of number of infections was determined as ±10% of the base case. This

Table 2. Estimates of the Incidence of *Clostridium difficile* Infection in Canada in 2012 According to Treatment Location, Type of Infection, Disease Severity, and Age Group

Patient Location	Characteristic of the Infection	Proportion	Number of Infections
Hospital			
	Type of Infection		
	New infection	0.73	14 593
	First relapse	0.16	3134
	Subsequent relapse	0.05	1020
	Reinfection	0.06	1254
	Disease Severity		
	Mild to moderate	0.61	12 155
	Severe	0.37	7435
	Fulminant infection	0.02	412
	Age Group (years)		
	<65	0.30	5944
	65–74	0.16	3161
	≥75	0.54	10 897
Community			
	Incidence		16 326
	Disease Severity		
	Mild to moderate	0.80	13 061
	Severe	0.20	3265
	Fulminant infection	0	0
Long-term care			
	Incidence		1604

number was derived as follows: Manitoba Health reported 831 hospital or community, initial or recurrent, *C difficile* infections over 2010–2012. Using the algorithm used here based on Canadian Nocosomial Infection Surveillance Program data, we calculated that 752 infections occurred in Manitoba over the same period, indicating that the algorithm underestimated the actual number of infections by 9%. To estimate a plausible range of direct costs, the PHC Infection Prevention and Control dataset was bootstrapped 1000 times; the generalized linear model was fit at each iteration, and the estimated cost was recorded. Costs were log transformed, and a log likelihood with Gamma link model was fit to the data. A confidence interval was then calculated from the 2.5th and 97.5th percentiles of the bootstrapped estimates [28]. A detailed description of the cost analyses is available upon request.

RESULTS

There were an estimated 37 932 (plausible range, 34 139–41 725) *C difficile* infections in Canada in 2012, including 20 002 (plausible range, 18 018–22 022) in hospital, 16 326 (plausible range, 14 693–17 959) in the community, and 1604 (plausible range, 1444–1764) in long-term care institutions (Figure 1). The total number of bed-days attributable to (Table 2) infections with *C difficile* was highest in Quebec, followed by Ontario, British Columbia, and Alberta. Of those in hospital, approximately 73% were new infections and 27% were recurrent, 61% were mild to moderate, and 54% occurred in those aged 75 years and older. Quebec had the highest total number of infections, followed by Ontario, British Columbia, and Alberta (Figure 2).

Resource use and unit cost estimates are provided in Appendix Table 2. The largest component was the incremental hospitalization costs of *C difficile* infection, with an estimated mean of $11 930 for the initial episode and $15 330 for a recurrent episode. The largest portion of this difference was due to the longer mean number of hospital days attributable to *C difficile* for recurrent infections.

The economic burden was estimated to surpass CAD $280 million dollars (plausible range, $254 to $309 million dollars), almost 90% of which was incurred in hospital (Table 3). Treating 5400 recurrent infections in the hospital was estimated to account for over $80 million. Four percent ($12 million) of the burden was incurred as direct medical costs in the community, and 4% ($10 million) was due to lost productivity.

The key inputs to which the model results were the most sensitive included the following (Table 4): (1) the length of stay in hospital attributable to *C difficile*, which resulted in a decrease in total costs of 40% when the mean number of days was reduced from 13.6 to 6.0; and (2) the ratio of hospital-based to community-based management, which resulted in an increase in total costs of 65% when the ratio changed from 53:47 to 70:30.

DISCUSSION

Management of hospital-acquired infections in Canada has been broadly characterized as "crisis-motivated" or "reactive", with an influx of resources when an outbreak becomes severe, such as the hypervirulent strain of *C difficile* in Quebec [31]. As such, most Canadian infection control programs do not meet expert recommendations with regards to investments in infection controls programs [32].

Applying reasonable assumptions to the limited existing Canadian data, there were an estimated 38 000 infections of *C difficile* infection in 2012 that, under conservative assumptions, cost CAD $280 million dollars to Canadian society. Extended hospital stays and rehospitalizations accounted for the lion's share—92%—of the total. The 37 932 number of cases we estimated in Canada in 2012 was approximately 8% of the 453 000 estimated in the United States in 2011 [33], and the Canadian cost estimate of $280 million was approximately 9% of the $3.2 billion dollars per year in the United States [34], with both estimates nearly proportionate to the population sizes. For context, the estimated $272 million in direct medical costs represents 0.1% of the CAD $207 billion spent on healthcare in Canada in 2012.

The annual burden of illness is likely increasing due to the aging demographics of the population, leading to increased

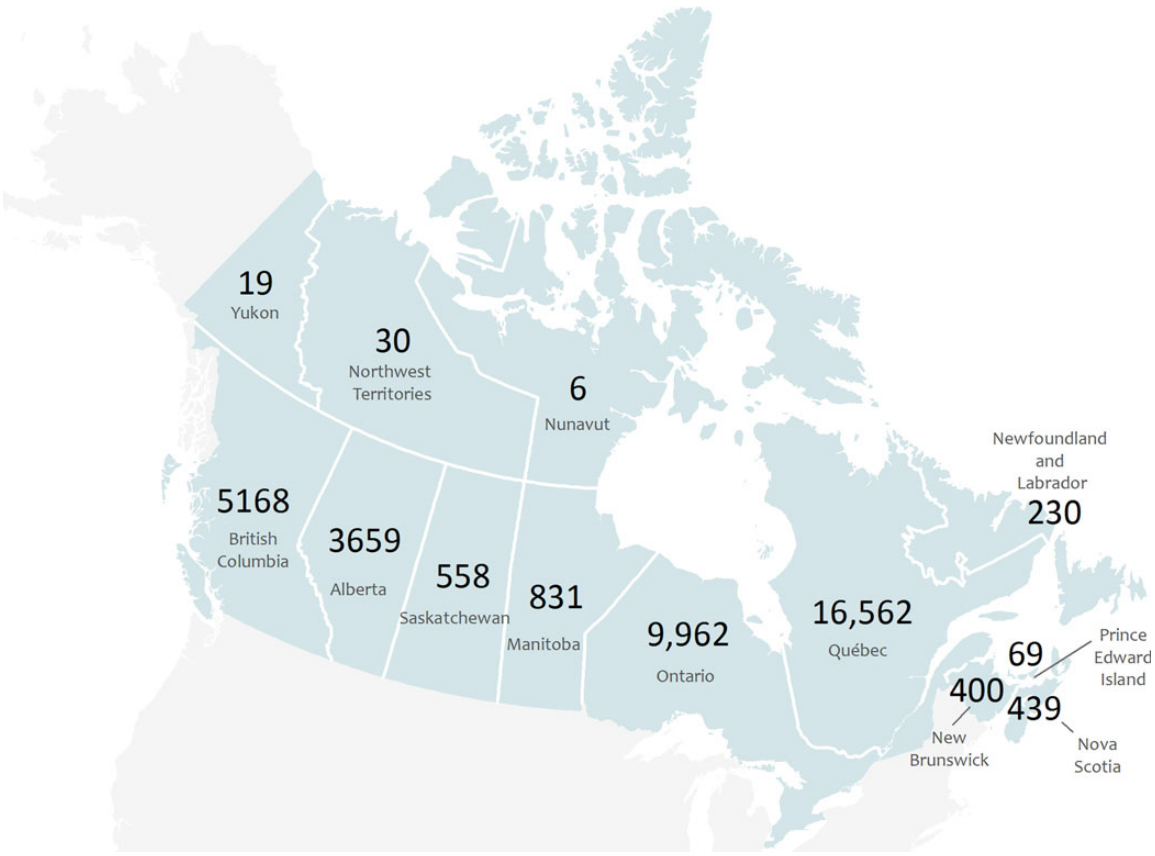

Figure 2. Estimated number of infections and of *Clostridium difficile* in Canadian provinces and Territories in 2012.

numbers of patients at risk, and the indiscriminate use of both antibiotics and proton pump inhibitors. From an economic perspective, hospital managers are often allocated inadequate funding for infection control because of a failure in budgetary mechanisms [35], the decentralization of budgets and responsibility, or uncertainty over the benefits of infection control [36]. Inadequate staffing, lower standards of hygiene in healthcare facilities, privatization of cleaning services, and overcrowding in hospitals have also been suggested as reasons why the number of *C difficile* infections in Canada have increased [32]. This burden will also potentially be affected by changing diagnostic practices with the expansion of new and more sensitive assays [37].

Table 3. Estimated Costs of Treating Initial and Recurrent Infection of *Clostridium difficile* in Canada, 2012, According to Patient Location and Category of Cost

Patient Location	Category of Cost	Total Estimated Cost (2012 $CAD, Thousands)
Direct medical costs		
Hospital	Pharmacotherapy	237
	Physician costs	6649
	Other hospitalization visits	252 709
	Total in-hospital	259 595
Community and long-term care	Tests and procedures	602
	Pharmacotherapy	6356
	Physician and nursing visits	5198
	Total community cost	12 157
Lost productivity		9613
Total costs	281 365	

Abbreviations: $CAD, Canadian dollars.

Given the high costs of hospitalization, preventing recurrence of *C difficile* is likely to lead to the largest reduction in direct medical costs by avoiding readmissions to hospital. Interventions that have been shown to reduce recurrence include the following: infection control measures; [36] reduced use of proton pump inhibitors which has been inferred based on 1.4- to 2.7-fold increase in risks of *C difficile* infections after observed use of these medications; [38] antimicrobial stewardship including removing concomitant systemic antibiotics and escalating antibiotic therapy when appropriate; [39] or the use of newly marketed antibiotics [13, 40]. While the technical and allocative efficiency of such programs and therapies is not yet adequately characterized in Canada, those that have the highest reduction in recurrence are likely to offer the highest value for money.

Table 4. The Impact of Varying Key Assumptions in Sensitivity Analyses on the Total Cost of Treating *Clostridium difficile* Infections in Canada, 2012

Model Input	Base Case Value (Source)	Sensitivity Analysis (Source)	Total Cost (2012 $CAD, Thousands)	% Change vs Baseline Estimated Cost
Low estimate of CDI-associated hospitalization cost ($CAD)	11 930 (IPAC[a])	3550 (IPAC[b])	148 598	–47
LOS in hospital (days)	13.6 (IPAC)	6 [27]	160 119	–43
Ratio of HB to CB infection	64:36 ([12])	82:18 ([29])	222 257	–21
Cost per recurrent infection ($CAD)	15 330 (IPAC[c])	11 930 (IPAC[a])	267 233	–5
% of infections that were recurrent	20.8 (IPAC[d])	13.7 (IPAC[e])	279 171	–1
Incidence in LTC	1604 ([22])	7108 ([12], [30])	280 773	–0
Baseline estimate			281 365	0
Ratio of HB to CB management	53:47 ([22])	70:30 (EO)	366 869	30
High estimate of CDI-associated hospitalization cost ($CAD)	11 930 (IPAC[a])	19 930 (IPAC[f])	408 224	45

Abbreviations: $CAD, Canadian dollar; CB, community-based; CDI, *Clostridium difficile* infection; EO, expert opinion; HB, hospital based; IPAC, Providence Healthcare Infection Prevention and Control dataset; LOS, length of stay; LTC, long-term care.

[a] Adjusted cost per infection.

[b] 2.5th percentile of bootstrapped adjusted cost per infection.

[c] Adjusted cost per recurrent infection.

[d] Infections ≤8 weeks of initial infection.

[e] Infections ≤4 weeks of initial infection.

[f] 97.5th percentile of bootstrapped adjusted cost per infection.

This study has important limitations. First, by comparing against data reported from Manitoba with the algorithm developed here, we noted a 9% underestimate in the number of *C difficile* infections. If this was the case in all provinces, the results reported here would underestimate the actual burden. Second, the estimated incremental hospital costs may have been confounded by the fact that hospitalized patients with *C difficile* infection had more comorbid medical conditions and longer lengths of stay than uninfected hospitalized patients. This was addressed by developing additional statistical models to adjust for health status unrelated to *C difficile* infection using the PHC Infection Prevention and Control dataset (available upon request). Third, we assumed that treatment followed the SHEA-IDSA guidelines [11], recognizing that this likely underrepresented the variability in treatment patterns between facilities in Canada. Fourth, the impact of excluding emerging therapies such as fecal transplant was low because use of new therapies is still rare in Canada. Fifth, costs that were excluded because of lack of data included: (1) Infection prevention and control procedures and services in hospitals (specifically, staffing levels of nurses, doctors, and epidemiologists in the infection prevention and control team, the proportion of those persons' time spent on infection surveillance and control, and the actual implementation and monitoring of prevention and control strategies) were excluded. Although potentially substantial, it would be challenging to validly allocate a proportion of these costs to *C difficile* because these procedures and services focus on all hospital-acquired infections; (2) No adequate data exist on lost productivity or on other direct medical and non-medical costs (such as caregiver burden). Lost productivity costs are challenging to quantify in a population such as this, which tends to have high levels of comorbidity and advanced age, and few people are able to return to paid work once they leave hospital, which would mean that using mean age-specific employment rates would inflate estimates of economic impact. On the other hand, there are serious equity implications of valuing lost time only among employed persons. Additional data collected via a patient or caregiver survey would be of value to quantify the magnitude of this burden. Finally, there were other potential, less influential sources of misclassification such as the use of clinical experts other than Public Health Agency of Canada Working Groups, interprovincial differences in costs, and others. We are confident that the results using different values of resource utilization or costs from these sources would be contained within the results sensitivity analyses presented.

CONCLUSIONS

This study highlights gaps in understanding the epidemiology and burden of *C difficile*, including the frequency and management in the community, robust estimates of incremental length of stay attributable to the infection, and costs of infection prevention and control programs and services in hospitals. Future studies can incorporate the information presented here to estimate the value of information of new research [41]. Understanding the relationship between recurrence and total costs,

as well as the interplay among in-hospital, nursing home, and community-based costs, is critical for evaluating efforts designed to minimize the burden of *C difficile* infection.

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Potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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APPENDIX

Appendix Table 1. Resource Use and Costs (2012 $CAD) Used to Estimate the Total Cost of Treating *Clostridium difficile* Infections in Canada, 2012

Description	Value	Source
Resource Use		
Incremental number of physicians visits for CDI in hospital		
Internists or hospitalists, mild-to-moderate CDI	2	Assumption
Internists or hospitalists, severe CDI	2	Assumption
Radiologists, severe CDI	1	Assumption
Internists or hospitalists, fulminant CDI	7	Assumption
Infectious disease practitioners, fulminant CDI	1	Assumption
Radiologists, fulminant CDI	1	Assumption
General surgeons, fulminant CDI (for those requiring colectomy)	2	Assumption
Pathologists, fulminant CDI (for those requiring colectomy)	1	Assumption
Incremental number of physicians visits for *CDI* in community-based patients		
General practitioners, mild- to-moderate CDI	3	Assumption
Infectious disease physicians, recurrent CDI	1	Assumption; 3 or 4 visits over 6 to 9 mo
Number of Interventions delivered to community-based *C difficile* patients		
Flexible sigmoidoscopy; for multiple recurrent infections	1	Assumption
Flexible colonoscopy; for multiple recurrent infections	1	Assumption
Incremental number of healthcare contacts for CDI in long-term care		
Nursing visits (per day)	4	Assumption
Personal support staff (per day)	4	Assumption
General practitioner/Hospitalist/Admitting physician (per week)	1	Assumption
Frequency of blood tests in long-term care		
Complete blood count, white blood cell count, hematocrit	1	Assumption
Electrolytes	1	Assumption
Serum creatinine	1	Assumption
Albumin	1	Assumption

Appendix Table 1 continued.

Description	Value	Source
Proportion of the population that is used		
15 to 24 y	0.55	Statistics Canada Labour force survey estimates
25 to 44 y	0.81	Statistics Canada Labour force survey estimates
45 to 64 y	0.71	Statistics Canada Labour force survey estimates
65 to 69 y	0.23	Statistics Canada Labour force survey estimates
≥70 y	0.06	Statistics Canada Labour force survey estimates
Proportion of the working population considered full time		
15 to 24 y	0.53	Statistics Canada Labour force survey estimates
25 to 44 y	0.88	Statistics Canada Labour force survey estimates
45 to 64 y	0.86	Statistics Canada Labour force survey estimates
65 to 69 y	0.61	Statistics Canada Labour force survey estimates
≥70 y	0.53	Statistics Canada Labour force survey estimates
Costs		
Cost of diagnostic testing for *C difficile* (2012 $CAD)		
Polymerase chain reaction	17.5	Assumption
Toxin A/B enzyme-linked immunosorbent assay	15.0	Badger et al [42]
Standard culture with cytotoxin neutralization assay (cell/stool culture)	5.0	Badger et al [42]
Other tests (assumed glutamate dehydrogenase and toxigenic assay)	12.0	Badger et al [42]
Cost of physicians visits for CDI in hospital (2012 $CAD)		
First visit, internist or hospitalist	77.2	Ontario MOHLTC schedule of benefits [43]
First visit, radiologist	50.0	Ontario MOHLTC schedule of benefits [43]
First visit, infectious disease practitioner	157.0	Ontario MOHLTC schedule of benefits [43]
First visit, general surgeon	90.0	Ontario MOHLTC schedule of benefits [43]
First visit, pathologist	102.0	Ontario MOHLTC schedule of benefits [43]
Subsequent visit, internist or hospitalist	58.8	Ontario MOHLTC schedule of benefits [43]
Subsequent visit, radiologist	50.0	Ontario MOHLTC schedule of benefits [43]
Subsequent visit, infectious disease practitioner	105.3	Ontario MOHLTC schedule of benefits [43]
Subsequent visit, general surgeon	60.0	Ontario MOHLTC schedule of benefits [43]
Subsequent visit, pathologist	102.0	Ontario MOHLTC schedule of benefits [43]
Costs of physicians visits for CDI in community-based patients (2012 $CAD)		
General physician	45.9	MOHLTC schedule of benefits [43]
Infectious disease physician	157	MOHLTC schedule of benefits [43]
Costs of Interventions delivered to community-based *C difficile* patients (2012 $CAD)		
Flexible sigmoidoscopy	116.29	BC guide to fees 2010 [44]
Flexible colonoscopy	251.23	BC guide to fees 2010 [44]
Costs of healthcare contacts for CDI in long-term care (2012 $CAD)		
Nursing visits	34.13	Median hourly wage, registered nurse in Canada; [45]
Support staff visits	18.13	Median hourly wage for a nurse aid in Canada; Canada [45]
Internist/General practitioner visits	32.3	MOHLTC schedule of benefits [43]
Costs of blood tests in long-term care (2012 $CAD)		
Complete blood count, white blood cell count, hematocrit	7.8	MOHLTC schedule of benefits [43]
Electrolytes	2.6	MOHLTC schedule of benefits [43]
Serum creatinine	2.6	MOHLTC schedule of benefits [43]
Albumin	2.6	MOHLTC schedule of benefits [43]
Mean hourly wage (2012 $CAD)		
15 to 24 y	13.6	Statistics Canada: CANSIM tables 282-0069 and 282-0073
25 to 44 y	25.5	Statistics Canada: CANSIM tables 282-0069 and 282-0073
45 to 64 y	25.2	Statistics Canada: CANSIM tables 282-0069 and 282-0073
65 to 69 y	24.9	Statistics Canada: CANSIM tables 282-0069 and 282-0073
≥70 y	24.9	Statistics Canada: CANSIM tables 282-0069 and 282-0073

Abbreviations: BC, British Columbia; $CAD, Canadian dollars; CDI, *Clostridium difficile* infections; MOHLTC, Ministry of Health and Long-Term Care.

Appendix Table 2. Parameter Estimates Used to Estimate the Total Cost of Treating *Clostridium difficile* Infections in Canada, 2012

Model Input	Estimate	Data Source
% New infection (of all infections)	72.9	PHC IPAC dataset
% Reinfection (of all infections)	6.3	PHC IPAC dataset
% First relapse (of all infections)	15.7	PHC IPAC dataset
% Subsequent relapses (of all infections)	5.1	PHC IPAC dataset
% infections <65 y	30.0	PHC IPAC dataset
% infections 65 to <75 y	16.0	PHC IPAC dataset
% infections ≥75 y	54.0	PHC IPAC dataset
% treated in hospital	52.7	Khanna et al [22]
Number of infections in the community from LTC	1604	Khanna et al [22]
% of hospitalized patients with mild infection	30.5	Louie et al [13]
% of hospitalized patients with moderate infection	30.2	Louie et al [13]
% of hospitalized patients with severe infection	39.2	Louie et al [13]
% of hospitalized patients with fulminant infection	2.1	PHC IPAC dataset
% of community classified as infections	20.0	Khanna et al [22]
Number of vancomycin 125 mg pills dispensed, Canada, 2011	421 213	BROGAN DATA; 2011 [25]
Number of vancomycin 250 mg pills dispensed, Canada, 2011	150 645	Brogan Data [25]
Vancomycin (500 qid oral tab; daily cost)	$124.88	Perras et al [46]
Metronidazole (500 mg IV; tid; daily cost)	$3.93	Perras et al [46]
Metronidazole (500 mg oral tab; tid; daily cost)	$0.36	Perras et al [46]
Incremental hospitalization cost, per initial infection, excluding pharmacotherapy cost	$11 928	Predicted from PHC IPAC dataset
Incremental hospitalization cost, per relapse, excluding pharmacotherapy cost	$15 330	Predicted from PHC IPAC dataset

Abbreviations: IV, intravenous; PHC IPAC, Providence Health Care Infection Prevention and Control.