MAJOR ARTICLE

Health Care–Associated *Clostridium difficile* Infection in Adults Admitted to Acute Care Hospitals in Canada: A Canadian Nosocomial Infection Surveillance Program Study

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(See the editorial commentary by Bouza on pages 577–9)

Background. *Clostridium difficile* infection (CDI) is the most frequent cause of health care–associated infectious diarrhea in industrialized countries. The only previous report describing the incidence of health care–associated CDI (HA CDI) in Canada was conducted in 1997 by the Canadian Nosocomial Infection Surveillance Program. We re-examined the incidence of HA CDI with an emphasis on patient outcomes.

Methods. A prospective surveillance was conducted from 1 November 2004 through 30 April 2005. Basic demographic data were collected, including age, sex, type of patient ward where the patient was hospitalized on the day HA CDI was identified, and patient comorbidities. Data regarding severe outcome were collected 30 days after the diagnosis of HA CDI; severe outcome was defined as an admission to the intensive care unit because of complications of CDI, colectomy due to CDI, and/or death attributable to CDI.

Results. A total of 1430 adults with HA CDI were identified in 29 hospitals during the 6-month surveillance period. The overall incidence rate of HA CDI for adult patients admitted to these hospitals was 4.6 cases per 1000 patient admissions and 65 per 100,000 patient-days. At 30 days after onset of HA CDI, 233 patients (16.3%) had died from all causes; 31 deaths (2.2%) were a direct result of CDI, and 51 deaths (3.6%) were indirectly related to CDI, for a total attributable mortality rate of 5.7%.

Conclusions. The rates are remarkably similar to those found in our previous study; although we found wide variations in HA CDI among the participating hospitals. However, the attributable mortality increased almost 4-fold (5.7% vs. 1.5%; $P < .001$).

Clostridium difficile infection (CDI) is the most frequent cause of health care–associated infectious diarrhea in industrialized countries [1–3] and affects >300,000 hospitalized patients yearly in the United States [4–5]. Clinical manifestations range from asymptomatic colonization to severe diarrhea, pseudomembranous colitis, toxic megacolon, and death [6].

To our knowledge, the only previous comprehensive report that described the incidence of CDI in Canada was conducted in 1997 by the Canadian Nosocomial Infection Surveillance Program (CNISP). The CNISP examined the incidence of health care–associated CDI (HA CDI) within 19 hospitals in 8 Canadian provinces over a six-week surveillance period and found that HA CDI was most frequent in older patients and those hospitalized >2 weeks in medical or surgical wards [7]. The incidence of HA CDI cases was 66 infections per

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Table 1. Reported rates of health care–associated *Clostridium difficile* infection (CDI), by province or region, among adults hospitalized in Canadian Nosocomial Infection Surveillance Program hospitals ($n = 1430$).

Hospital location	No. of cases of CDI	No. of hospital admissions	No. of cases per 1000 hospital admissions	No. of patient-days	No. of cases per 100,000 patient-days
British Columbia	128	42,197	3.0	279,911	46
Alberta	153	75,728	2.0	372,966	41
Saskatchewan and Manitoba	67	25,214	2.7	184,153	36
Ontario	666	112,658	5.9	824,658	81
Quebec	282	21,964	12.8	217,507	130
Atlantic Canada	134	30,270	4.4	333,137	40
Total	1430	308,031	4.6	2,212,332	65

100,000 patient-days (95% CI, 3.75–95.1) and 5.9 infections per 1000 patient hospital admissions (95% CI, 3.4–8.4). A subsection of the initial study reported that of the 41 patients (15.2%) who died during the 30 days after onset of disease, 4 (1.5%) of these deaths were attributable to HA CDI [8]. These reports were pivotal in providing baseline rates with which other Canadian hospitals could compare, and they are currently the only available description of the burden of HA CDI in Canadian hospitals.

More-recent reports have suggested an increase in incidence, severity, and/or risk of relapse of CDI in Canada [9]. Since the last half of 2002, several hospitals in Quebec, Canada (located mostly in Montreal and Sherbrooke), have experienced a dramatic increase in the incidence, severity, and number of relapses associated with HA CDI [9, 10–13], with mean rates of 25 cases per 1000 hospital admissions [14].

Similar reports have been published in other industrialized countries [15, 16]. One of the earliest North American reports of highly lethal CDI was from Pittsburgh, Pennsylvania, in 2000 [17]. An analysis of US hospital discharge data revealed that CDI rates increased abruptly beginning in 2001, with a doubling of national rates between 2000 and 2003 [18]. This increase was most prominent for patients ⩾65 years of age. Reports also suggested that the attributable mortality rate (or fatality rate) had increased as well. On the basis of the data from Quebec, the attributable mortality rate for CDI was estimated to be 6.9% [11].

The CNISP elected to re-examine the incidence of HA CDI in Canada, with an emphasis on patient outcomes. The objectives of the surveillance were to determine the incidence and burden of illness associated with HA CDI in CNISP hospitals and to determine whether there was an increase in severe outcomes (mortality and morbidity associated with CDI) in 2005, compared with 1997. The present report describes the epidemiology of HA CDI involving adults aged ⩾18 years who were hospitalized in Canadian acute care facilities that participate in CNISP.

METHODS

The CNISP is a collaborative effort of the Canadian Hospital Epidemiology Committee, a subcommittee of the Association of Medical Microbiology and Infectious Disease Canada, the National Microbiology Laboratory, and the Centre for Communicable Diseases and Infection Control of the Public Health Agency of Canada (PHAC). Twenty-nine hospitals in 9 Canadian provinces participated in a prospective surveillance for HA CDI from 1 November 2004 through 30 April 2005. All hospitalized patients aged ⩾18 years were eligible for enrollment.

The case definition for CDI was (1) documented diarrhea (6 watery stools during the previous 36 h, 3 unformed stools in a 24-h period over 2 days, or 8 unformed stools during a 48-h period), (2) fever, abdominal pain, and/or ileus plus laboratory confirmation of a stool sample positive for *C. difficile* toxin A or B or a positive tissue culture assay, (3) diagnosis of pseudomembranous colitis on colonoscopy, or (4) histological or pathological diagnosis of CDI. The infection was considered to be health care associated if the patient's symptoms occurred at least 72 h after hospital admission or if symptoms resulted in readmission of a patient who had been hospitalized within the 2 months before the symptom onset date and who was not a resident in a long-term care facility or nursing home.

Eligible patients were identified by daily review of results of toxin assay of *C. difficile* in stool samples tested in the clinical microbiology laboratory or a review of relevant pathology reports or operating room records. The charts of patients with stool samples positive for *C. difficile* toxin were examined by experienced and trained infection-control professionals or trained research personnel associated with each hospital. Basic demographic data were collected on all patients, as well as the

Table 2. Reported mortality rates for adults with health care–associated *Clostridium difficile* (HA CDI) infection who were hospitalized in Canadian Nosocomial Infection Surveillance Program hospitals at 30 days after onset of disease ($n = 1430$).

Hospital location	No of cases of HA CDI	No. of patients who died	Mortality rate per 100 cases	No. of deaths related to HA CDI		No. of deaths attributable to HA CDI per 100 cases
				Directly	Indirectly	
British Columbia	128	22	17.2	1	7	6.3
Alberta	153	14	9.2	1	1	1.3
Saskatchewan and Manitoba	67	10	14.9	1	0	1.5
Ontario	666	108	16.2	7	20	4.1
Quebec	282	64	22.7	20	22	14.9
Atlantic Canada	134	15	11.2	1	1	1.5
Total	1430	233	16.2	31	53	5.7

NOTE. Attributable deaths, deaths directly or indirectly related to HA CDI 30 days after onset; mortality rate, death from all causes within 30 days after onset of HA CDI.

date of onset of diarrhea, initial treatment of CDI, and medical and treatment inventions.

Data regarding adverse events were collected 30 days after the date of diarrhea onset and included information about death, intensive care unit admission, surgery, bowel perforation, gastrointestinal bleeding, toxic megacolon, dehydration, hypokalemia, and relapse. All deaths were assessed by the hospital epidemiologist or a designated physician to determine whether the death was attributable to CDI—either CDI that was directly related to the death or CDI that indirectly contributed to the patient's death but was not the primary cause. Severe outcome was defined as an admission to the intensive care unit for complications of CDI, colectomy due to CDI, and/or death attributable to CDI.

Data were collected and entered manually onto patient data-extraction forms and were forwarded to PHAC for data entry and analysis. A unique identifier linked to the patient name was used only to identify patients at the participating hospital and was not transmitted to PHAC. Because this surveillance project was observational and did not involve any alteration in patient care, Review Ethics Board approval was not required by PHAC. However, individual institutional Review Ethics Board approval was obtained at some of the participating hospitals.

Statistical analysis. The CNISP hospitals were grouped by Canadian province or region, and rates of HA CDI were calculated using both the number of patient admissions and the number of patient-days for denominators. Crude mortality and attributable mortality rates were determined using the criteria described above. Descriptive and univariate analyses were performed. To assess differences between patient populations, continuous variables were expressed by means and were compared using Student's t test. Categorical variables were expressed as proportions and were compared using the χ^2 test and Fisher's exact test when necessary. All tests were 2 tailed, and a P value $<.05$ was considered to be statistically significant. Relative risks with corresponding 95% CIs were calculated according to standard methods. A multivariate logistic regression model was used to assess patient factors associated with a severe outcome. Variables were selected for entry into the regression model if $\geqslant 10$ of the patients had the characteristic and the variables were significantly associated with a severe outcome ($P \leqslant .25$) in the univariate analysis. The goodness of fit of the final model was tested using the deviance test. Statistical analysis was conducted using SAS, version 9.1 (SAS Institute).

RESULTS

A total of 1430 adults with HA CDI were identified during the 6-month surveillance period. There were 13 hospitals in Ontario; 4 in Alberta; 2 each in British Columbia, Saskatchewan, Manitoba, Quebec, and Newfoundland; and 1 each in New Brunswick and Nova Scotia. The overall rate of HA CDI for adult patients admitted to these hospitals for this 6-month period was 4.6 cases per 1000 patient admissions and 65 cases per 100,000 patient-days (table 1). The rate was higher in the hospitals in Quebec than it was in hospitals in the rest of Canada (12.8 vs. 4.0 cases per 1000 admissions and 130 vs. 58 cases per 100,000 patient-days; $P < .001$). At 30 days after onset of HA CDI, 233 patients had died from all causes, for a mortality rate of 16.3 deaths per 100 cases. Of these, 31 deaths (2.2% of all patients) were a direct result of CDI, and 51 deaths (3.6% of all patients) were indirectly related to CDI, for a total attributable mortality of 5.7% (table 2). The attributable mortality in Quebec was >4 times higher than that for the rest of Canada combined (14.9% vs. 3.5%, $P < .001$).

The mean age ± SD of the adults with HA CDI was 70 ± 16 years (range, 18–101 years); 996 patients (70%) were ⩾65 years of age; 735 (51%) were male patients (table 3). Patients aged ⩾65 years were more likely to acquire CDI under care

Table 3. Description of the adult patients with health care–associated *Clostridium difficile* infection.

Variable	All patients (n = 1430)	Aged 18–64 years (n = 434)	Aged ⩾65 years (n = 996)	P
Age at onset, mean years ± SD (range or median)	70 ± 16.73 (18–101)	50 ± 12 (54)	79 ± 8 (78)	
Male sex	735 (51)	238 (55)	497 (50)	NS
Length of stay before onset, mean days ± SD (median)	25 ± 50 (11)	25 ± 57 (8)	25 ± 46 (12)	NS
Type of care				<.001
Acute	1242 (87)	415 (96)	827 (83)	
Long term	188 (13)	19 (4)	169 (17)	
Admitted from				
Home	1073 (75)	346 (80)	727 (73)	.007
Another hospital	175 (12)	65 (15)	110 (11)	.037
Long-term care facility	127 (9)	11 (3)	116 (12)	<.001
Other	55 (4)	12 (3)	43 (4)	NS
Location at infection onset				
Medicine unit	609 (43)	130 (30)	479 (48)	<.001
Surgery unit	327 (23)	123 (28)	204 (21)	.001
Intensive care unit	142 (10)	53 (12)	89 (9)	NS
Home	92 (6)	33 (8)	59 (6)	NS
Long-term-care facility	58 (4)	5 (1)	53 (5)	<.001
Oncology/hematology unit	53 (4)	31 (7)	22 (2)	<.001
Combined medicine/surgical	45 (3)	16 (4)	29 (3)	NS
BMT/transplant unit	22 (2)	18 (4)	4 (0.4)	<.001
Other	82 (5)	25 (6)	57 (6)	NS
Chronic disease[a]				
Diabetes	331 (23)	82 (19)	249 (25)	.012
Heart	514 (36)	76 (18)	438 (44)	<.001
Lung	327 (23)	57 (13)	270 (27)	<.001
Cancer	290 (20)	125 (29)	165 (17)	<.001
Liver	62 (4)	38 (9)	24 (2)	<.001
Kidney	229 (16)	63 (15)	166 (17)	NS
Dementia	101 (7)	5 (1)	96 (10)	<.001
Immunocompromised status	120 (8)	72 (17)	48 (5)	<.001
Other	338 (24)	103 (24)	235 (24)	NS

NOTE. Data are no. (%) of patients, unless otherwise indicated. BMT, bone marrow transplant; NS, not significant.

[a] May have >1 chronic disease.

on a medical ward (48% vs. 30%, $P < .001$), whereas the adults aged 18–64 years were more likely to have acquired CDI under care on a surgical or oncology/hematology unit (28% vs. 21% [$P = .001$] and 7% vs. 2% [$P < .001$], respectively).

Only 81 patients (6%) did not receive treatment for the episode of CDI. Among the 1430 patients with CDI, 1215 (85%) were prescribed metronidazole, 230 (16%) received vancomycin, and 51 (4%) also received probiotics. A total of 168 patients (12%) were receiving both metronidazole and vancomycin. Probiotics were given in addition to either metronidazole or vancomycin. Patients ⩾65 years of age were 1.5 times more likely to receive vancomycin than were patients aged 18–64 years (18% vs. 12%, $P = .005$). Patients with CDI in the province of Quebec were 9 times more likely to receive vancomycin than were patients in the rest of Canada (56% vs. 6%, $P < .001$) (table 4).

A total of 319 adult patients with HA CDI (22%) developed complications during the first 30 days after onset of CDI; 104 patients (7.3%) had a severe outcome (table 5). Relapse was the most common complication, which involved 125 patients (9%). Dehydration was more likely to be seen in the patients ⩾65 years of age (7% vs. 3%; $P = .005$), whereas gastrointestinal bleeding that required blood transfusions was more likely to be seen in adults aged 18–64 years (2% vs. 0.7%; $P = .029$).

The attributable mortality was 3.5 times higher in patients aged >65 years, compared with the patients aged 18–64 years (7.3% vs. 2.2%; $P < .001$). The attributable mortality was highest in patients aged >90 years: 14.7%. For patients aged 81–90 years, the attributable mortality was 10.4%; at 71–80 years of age, the attributable mortality was 5.9%; at 61–70 years of age, the attributable mortality was 5.4%; at 51–60 years of age, the

Table 4. Description of the treatments and medical interventions for adult patients with health care–associated *Clostridium difficile* infection (CDI).

Variable	All patients (n = 1430)	Aged 18–64 years (n = 434)	Aged ⩾65 years (n = 996)	P
Initial CDI treatment[a]				
No treatment	81 (6)	28 (7)	53 (5)	NS
Metronidazole[b]	1215 (85)	381 (88)	834 (84)	.049
Vancomycin	230 (16)	52 (12)	178 (18)	.005
Cholestyramine	18 (1)	3 (1)	15 (2)	NS
Intravenous immunoglobulin	3 (0.2)	0 (0)	3 (<1)	NS
Probiotics	51 (4)	13 (3)	38 (4)	NS
Other intervention				
Discontinued antibiotics	181 (13)	68 (16)	113 (11)	.024
Endoscopy	51 (4)	21 (5)	30 (3)	NS
Surgical consult	44 (3)	18 (4)	26 (3)	NS
Infectious disease or gastroenterologist consult	12 (1)	2 (1)	10 (1)	NS
Initial treatment changed	246 (17)	63 (15)	183 (18)	NS
Reason for treatment change				
Failure to respond	145 (10)	28 (7)	117 (12)	.002
Intolerance to antibiotic	21 (2)	10 (2)	11 (1)	NS
Complications	12 (1)	2 (1)	10 (1)	NS
Inappropriate treatment	58 (4)	17 (4)	41 (4)	NS

NOTE. Data are no. (%) of patients, unless otherwise indicated. NS, not significant.

[a] Patients may be undergoing >1 treatment.

[b] Administered orally or intravenously.

attributable mortality was 2.8%; and at age of <50, the attributable mortality was 3.0%.

For univariate analysis, the factors that were associated with a severe outcome are presented in table 6. In the multivariate logistic regression model for severe outcome, the following characteristics were all independently associated: advanced age, hospital admission from another hospital or a long-term care facility, liver disease, receipt of vancomycin as initial treatment, and having a change in the initial treatment for HA CDI (table 7). Location of the patient in the hospital at infection onset was not independently associated with severe outcome.

DISCUSSION

The results from this surveillance project represent the most comprehensive surveillance of HA CDI in adults hospitalized in Canada that have been reported to date. The rates are remarkably similar to those found in our previous study [7]; however, we found wide variations in HA CDI among the participating hospitals (range, 20–167 cases per 100,000 patients-days). The underlying reasons for this variation remain unclear. There may be a surveillance artifact: in different hospitals, the threshold for testing stool samples for *C. difficile* toxin may vary (especially in Quebec, where heightened public attention may have led to increased testing). Variation in toxin testing methods may also contribute, because these tests are not uniformly sensitive [19] Although it has been suggested that these discrepant findings may be the result of differing methodologies [20], this is not the case for our surveillance. Our study was conducted using a previously piloted methodology with a standardized case definition and patient questionnaire. However, previous studies have suggested that antibiotic usage; the physical layout of the institution, including the presence or absence of sinks for hand washing; and both the infection-prevention and infection-control practices and isolation practices, particularly in adherence to and agents used for hand hygiene, have played a role in the overall incidence of HA CDI [3, 21, 22].

Wide variations are also seen among provinces and regions in Canada. The rate of HA CDI in CNISP hospitals in central Canada (e.g., Ontario and Quebec) was more than twice the incidence of HA CDI in other areas of the country (7.0 vs. 2.8 cases per 1000 hospital admissions and 91 vs. 41 per 100,000 patient-days; $P < .001$). Although there is notable stability in the rate of HA CDI in Canada since 1997 (65 vs. 66 cases per 100,000 patient-days in 1997); our surveillance found a significant increase in the number of deaths attributable to HA CDI. Compared with the CNISP surveillance conducted in 1997, the percentage of deaths directly or indirectly related to HA CDI has increased almost 4-fold (from 1.5% to 5.7%; $P < .001$) [8]. These results are comparable, because we used the same methodology with the current surveillance that was used in 1997, and this would indicate that HA CDI is an emerg-

Table 5. Frequency of adverse outcomes among adult patients with health care–associated *Clostridium difficile* infection (CDI) in the first 30 days after onset of disease.

Variable	All patients (n = 1430)	Aged 18–64 years (n = 434)	Aged ⩾65 years (n = 996)	P
Complications of CDI	319 (22)	88 (20)	231 (23)	NS
Type of complication				
Relapse	125 (9)	39 (9)	86 (9)	NS
Bowel perforation	1 (<1)	1 (<1)	0 (0)	NS
Gastrointestinal bleed, transfusion	16 (1)	9 (2)	7 (1)	.029
Toxic megacolon	17 (1)	3 (1)	14 (1)	NS
Bacteremia	22 (2)	7 (2)	15 (2)	NS
Dehydration	84 (6)	14 (3)	70 (7)	.005
Hyopkalemia	39 (3)	11 (3)	28 (3)	NS
Other[a]	47 (3)	15 (3)	32 (3)	NS
Admitted to the intensive care unit	31 (2)	7 (2)	24 (2)	NS
Colectomy	12 (1)	4 (1)	8 (1)	NS
Death				
All causes	233 (16)	35 (8)	198 (20)	<.001
Related to CDI	82 (6)	9 (2)	73 (7)	<.001
Directly related	31	1	30	
Indirectly related	51	8	43	
Severe outcome[b]	104 (7)	17 (4)	87 (9)	.001

NOTE. All data are no. (%) of patients, unless otherwise indicated. NS, not significant.

[a] Pseudomembraneous colitis and/or gastrointestinal bleed not requiring transfusion.

[b] Admission to intensive care unit, colectomy and/or death, directly or indirectly related to CDI. A total of 21 patients had >1 severe outcome.

ing cause of mortality among hospitalized patients in Canada, especially among older patients. Our results are similar to those of other recent studies, which demonstrated that age-specific attributable mortality increased sharply after age 60 years [23]. This may explain, in part, why we found a similar rate of HA CDI during 2004–2005, compared to 1997, whereas the attributable mortality increased sharply—by 400%. In the present study, 50% of the patients were ⩾73 years of age; in 1997, the patients were somewhat younger, with 50% of patients ⩾68 years of age.

The increase in the attributable mortality between 1997 and the current study may also be related to the heightened awareness of the severe outcomes associated with CDI, especially in the provinces that have experienced numerous outbreaks in recent years. Although the hospital epidemiologist or another qualified physician determined the cause of death in patients with HA CDI, attribution of mortality is always subjective and can be interpreted differently by different clinicians. In Quebec, all death rates are reviewed by 2 physicians before a consensus is reached. In the participating hospitals from other provinces, only 1 assessment was performed. We found that the attributable mortality from HA CDI was much higher in the CNISP hospitals in Quebec, followed by British Columbia and Ontario. However, although only 2 hospitals in Quebec participated in the surveillance project, our findings support previously published reports describing increased fatality in Quebec [9–14, 23].

Although the analysis of the *C. difficile* strain characterization was not the object of this study, subsequent examination of the strains on a subset of the CNISP surveillance revealed that the NAP1/027 "hypervirulent" strain of *C. difficile,* first described in Quebec before the 2004–2005 surveillance period, was now isolated in 6 more Canadian provinces, but mostly in Quebec, British Columbia, and Ontario [24]. Previous studies have found a definite association between NAP1/027 and more-severe disease, especially in older patients with CDI [23–26].

The association between vancomycin use as therapy for HA CDI and a worse outcome is contradictory to recent data that suggest that it is superior to metronidazole [27, 28]. We believe that this association is attributable to 2 factors. First, more vancomycin was used in Quebec, where more severe CDI outcomes were observed. Second, we believe that vancomycin was used preferentially for patients with more severe disease at the time of CDI diagnosis, a practice ensuing from the influence of Montreal hospitals, which used vancomycin this way since the outbreaks in 2002 (M. Miller, personal communication). Therefore, the association between vancomycin use as CDI therapy and severe outcome should be viewed with caution. Approximately 70% of all vancomycin use was in Quebec, where the majority of infecting isolates are of the NAP1/027

Table 6. Univariate analysis of variables associated with severe outcome in patients with health care–associated *Clostridium difficile* infection.

Variable	No. of patients (n = 1430)	No. (%) of patients with severe outcome (n = 104)	RR (95% CI)	P[a]
Adults aged ⩾65 years	996	87 (8.7)	2.23 (1.34–3.70)	.001
Adults aged 18–64 years	434	17 (3.9)	Ref	
Long-term care	188	22 (11.7)	1.77 (1.14–2.78)	.012
Acute care	1242	82 (6.6)	Ref	
Age of the patient, years[b]				
⩾90	84	11 (13.1)	1.92 (1.05–3.51)	.034
80–89	311	35 (11.3)	1.61 (1.21–2.16)	.002
70–79	418	27 (6.5)	0.88 (0.63–1.23)	.447
60–69	275	17 (6.2)	0.84 (0.54–1.31)	.438
50–59	163	5 (3.1)	0.40 (0.17–0.96)	.028
40–49	86	3 (3.5)	0.46 (0.15–1.43)	.163
18–39	93	6 (6.5)	0.88 (0.39–1.96)	.753
Admitted from				
Home	1073	62 (5.7)	0.49 (0.34–0.71)	<.001
Another hospital	175	18 (10.3)	1.50 (0.92–2.43)	.101
Long-term-care facility	127	18 (14.2)	2.15 (1.34–3.45)	.002
Other	55	6 (10.9)	1.53 (0.70–1.05)	.285
Location at onset				
Medicine unit	609	47 (7.8)	1.11 (0.77–1.61)	.577
Surgery unit	327	12 (3.7)	0.44 (0.24–0.79)	.004
Intensive care unit	142	15 (10.6)	1.53 (0.91–2.57)	.112
Home	92	11 (12.0)	1.72 (0.96–3.10)	.074
Long-term-care facility	58	8 (13.8)	1.97 (1.01–3.86)	.051
Oncology/hematology unit	53	2 (3.8)	0.51 (0.13–2.01)	.426
Combined medicine/surgical unit	45	0 (0.0)	…	.072
BMT/transplant unit	22	1 (4.6)	0.62 (0.09–4.25)	>.999
Other	82	8 (9.8)	1.37 (0.69–2.72)	.378

NOTE. BMT, Bone marrow transplant; GI, gastroenterology; ID, infectious disease; IV, intravenous; PO, per os; RR, relative risk.

[a] By χ^2 or Fisher's exact test where appropriate.
[b] Comparing each category with all others.

type and where severe CDI is more common than it is in other provinces. In Quebec, vancomycin has been officially recommended as first-line therapy for severe CDI since 2004. Thus, the association of vancomycin and severe disease is most likely a correlation that is attributable to the provincial recommendations for treatment of this disease. Analysis of outcome and vancomycin use in patients outside Quebec failed to show a correlation, as expected.

There are limitations to our study, primarily inherent to large multicenter surveillance activities. First, although data collection was conducted by experienced and trained infection-control professionals using standardized definitions, the data collection remained unmonitored, and there may be inconsistencies between hospitals in identifying a case of HA CDI. Because the diagnosis of HA CDI is frequently based on laboratory findings, there may be some variability in the microbiological laboratory testing and identification of *C. difficile* at the different hospitals. Finally, the populations examined in this survey were in major teaching hospitals and so are likely not entirely representative of all hospitalized adult patients in Canada.

Despite these limitations, the data presented in this study are an important contribution to understanding the impact of HA CDI in adults admitted to Canadian hospitals participating in CNISP. The results are sufficiently robust to be used as baseline indicators for future comparisons within similar large teaching hospitals. Follow-up surveillance in the same hospitals will allow us to monitor the incidence of HA CDI, to follow the spread of *C. difficile* strains—more specifically, the spread of NAP1/027—in Canada, and to assess the impact on the morbidity and mortality associated with HA CDI. In addition, follow-up surveillance will allow for the assessment of seasonal

Table 7. Multivariate analysis of the characteristics of the adult patients with health care–associated *Clostridium difficile* infection (CDI) independently associated with severe outcome (stepwise logistic regression model) ($n = 1430$).

Variable	β Estimate	SE	OR (95% CI)	*P*
Increase per year of age, starting at age 18 years	0.0215	0.0079	1.02 (1.01–1.04)	.006
Admitted from another hospital or nursing home	0.7347	0.2202	2.09 (1.35–3.21)	.001
Liver disease	0.9637	0.4349	2.62 (1.12–6.15)	.027
Received vancomycin as initial treatment	0.9583	0.2407	2.61 (1.63–4.18)	<.001
Treatment for CDI was changed	0.7659	0.2428	2.15 (1.34–3.46)	.002

NOTE. Adjusted for location of the patient on onset of diarrhea: medicine department, surgery department, or intensive care unit.

variations in HA CDI. CDI is known to be more common in hospitalized patients during winter months—a factor in our decision to perform a survey during November–April [29]. Although our hospitals have reported similar rates throughout the year, year-round surveillance may show a lower national rate of HA CDI. National surveillance also provide opportunities for interhospital collaboration that may lead to more standardized use of surveillance methodology, including application of definitions and case finding methods, and effective infection-prevention and infection-control measures.

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