ORIGINAL ARTICLE

Clostridium difficile infection in Alberta's long-term care facilities

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ABSTRACT

Background: *Clostridium difficile* infection (CDI) is prevalent in long-term care (LTC) facilities in the United States, Canada, Europe and Australia. However, to our knowledge, CDI surveillance in LTC facilities has not been documented provincially in Alberta or any other Canadian province. This study aims to identify the incidence of CDI in LTC facilities and describe the demographic characteristics of the affected population.

Methods: Administrative data from 172 LTC facilities in Alberta, Canada, was obtained from April 1, 2012, and September 30, 2013.

Results: The majority of LTC CDI cases were either residents who resided in a LTC facility for more than 72 hours and had no hospitalizations in the previous four weeks (65.7%), or residents who had a hospital visit between 72 hours and four weeks prior to their CDI case (30.3%). Fluid and electrolyte disorders, congestive heart failure, and cardiac arrhythmias were the most common co-morbidities. Approximately 30% of residents died within 60 days of their CDI episode.

Conclusions: There is a need to implement routine surveillance to continue monitoring CDI in LTC facilities to assess these findings further and to evaluate changes over time in response to improvement initiatives related to CDI prevention and clinical management.

KEY WORDS

long-term care, *Clostridium difficile*, surveillance

INTRODUCTION

Clostridium difficile is a Gram-positive, anaerobic, spore-forming bacterium with a range of clinical presentations from mild diarrhoea to toxic megacolon, which can lead to sepsis and even death (1). *Clostridium difficile* infection (CDI) is the most common cause of hospital acquired (HA) diarrhoea in the developed world and occurs primarily in older adults; infection rates in adults over the age of 65 are ten times higher than those under the age of 65 (2-4).

Although the increased risk of infection has been reported with increasing age, it is unclear if this association is due to age itself (and associated physiologic changes), or an increasing frequency of comorbidities and antibiotic use in an older population. It has been recommended that a comprehensive analysis of CDI should take into consideration the frequency, severity and type of comorbidities to determine potential predetermining factors that lead to CDI (5).

Survival following CDI is much worse for older adults; they are 3.5 times more likely to die as a result of CDI exposure (6). In Canada, the rate of CDI-attributable mortality has been increasing. Between 1997 and 2005, HA CDI-attributable mortality increased from 1.5% to 5.7% (6). More generally, a 2013 study by Inns et al. found that in 1,426 acute care patients with CDI, there was a 25.7% 30-day and 38.1% 90-day all-cause mortality (7).

Since it is difficult to determine CDI-attributable mortality due to the labour intensive process required to affirm the direct cause leading to mortality, all-cause mortality may be more feasible to identify CDI in long-term care (LTC) facilities (8). A review of C. *difficile* by Mitchell & Gardner (2012) found an all-cause mortality at 30 days ranging between 9%-38% and 90-day all-cause mortality with a range of 27%-30% (9).

Although CDI is prevalent in LTC facilities in Canada, United States and Europe, little is known about the population who experience CDI in LTC facilities (5). A recent study by Rodriguez et al. describes the colonization

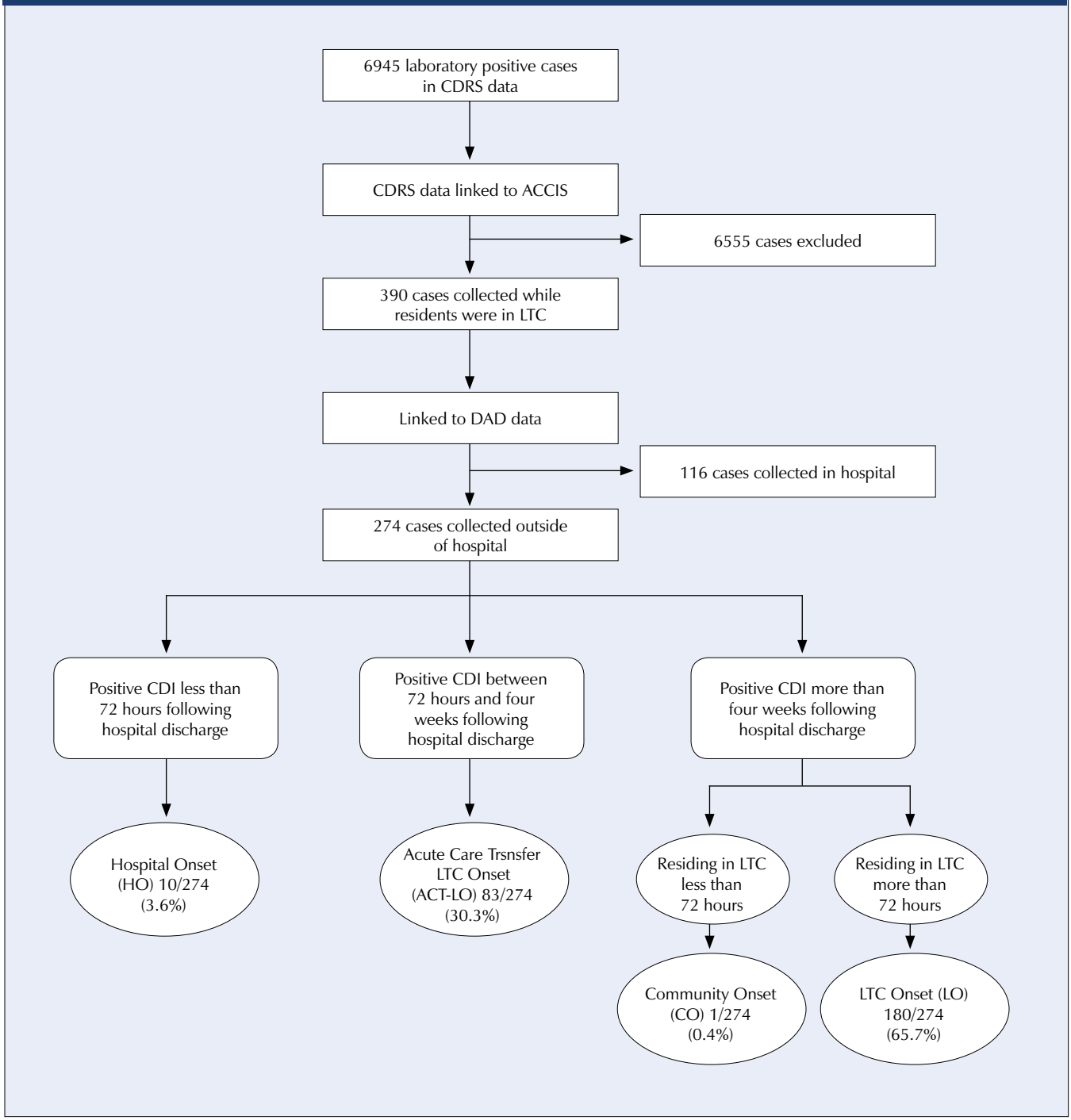
of *C. difficile* as 10 times higher among those residing in LTC facilities than those who were not (10). Therefore, there is a need to assess the incidence of CDI in LTC facilities as older adults tend to be the majority of residents and few studies have estimated the incidence of *C. difficile* in LTC facilities (10). This study investigates the incidence of CDI in Alberta's LTC facilities and presents data that describe the distribution of gender, age, the frequency of and type of co-morbidities, and proportion of all-cause mortality.

METHODS

Study population

The province of Alberta, Canada, has a population of approximately 3.7 million, of whom 405,000 (11%) are over the age of 65 (11). Alberta's LTC delivery is provided by Alberta Health Services (AHS) and its contracted partners. In the 2011/12 fiscal year, AHS provided 5,051,241 LTC resident days across 172 LTC facilities (n=78; 45.3% urban facilities) in five geographic zones.

FIGURE 1: Data Linkages and Case Classification Flow Chart



All residents with an incident case of CDI in LTC in Alberta between April 1, 2011, and September 30, 2013 (18 months), were included in this study.

There were no age restrictions on the study population, and inclusion into the study depended on the cases' identification.

Case identification

Cases of CDI were defined as a positive *C. difficile* toxin assay or positive polymerase chain reaction (PCR) test. Confirmatory testing by PCR was introduced in Alberta in April 2013 for indeterminate results of the toxin assay. All laboratories in Alberta report all *C. difficile*-positive laboratory results to the Ministry of Health's Communicable Disease Reporting System (CDRS). Incident cases were defined as either the first case in the dataset in the study time period, or those greater than eight weeks from the previous incident case. Repeated cases less than eight weeks from the previous incident case were excluded from the analysis as cases less than eight weeks from the previous case would be considered a relapse and related to the previous case and not a new episode as per the National Healthcare Safety Network (NHSN) guidelines definition for CDI (12). No symptomatic or clinical criteria were used for inclusion into the analysis.

Province-wide CDI toxin assay/PCR data from the CDRS were matched to the long-term care registry Alberta Continuing Care Information System (ACCIS) and to the Discharge Abstract Database (DAD) using residents' Alberta Provincial Health Number (PHN) to identify LTC residents. The ACCIS database is a long-term care registry that captures all admissions and discharges from an Alberta LTC facility. The DAD captures administrative, clinical, and demographic information related to an acute care hospitalization.

To identify which *C. difficile* toxin assay/PCR-positive results occurred while the person was residing in LTC, the specimen collection date for *C. difficile* was compared to the admission and discharge dates from both acute care hospitals and LTC facilities (Figure 1). If the specimen collection date for *C. difficile* occurred on or in between the admission and discharge date from a LTC facility and not while a patient was admitted to an acute care facility, that *C. difficile* toxin assay/PCR-positive result was assumed to have occurred in LTC.

All CDI cases were linked to Vital Statistics Canada data using PHN to identify all-cause mortality up to December 31, 2013.

Case definitions

Incident cases occurring in LTC facilities were classified according to their likely location of acquisition. Case classification definitions were based on the NHSN definitions for laboratory identified CDI (12). Those residents with CDI between 72 hours and four weeks after a hospital discharge were referred to as *acute care transfer long-term care facility onset* (ACT-LO). Those who had CDI greater than four weeks after an acute care hospital discharge and who had been a LTC resident for more than 72 hours were referred to as a *long-term care facility onset* (LO) classification. Those who had CDI less than or equal to 72 hours following a hospital discharge were referred to as *hospital-onset* (HO). Finally, those who had CDI more than four weeks following a hospital discharge and resided in LTC for less than 72 hours were referred to as *community-onset* (CO) (Figure 1).

Admission(s) to acute care hospital that occurred in the six months prior to the LTC-incident CDI case were identified using DAD data and International Classifications of Disease, 10 revision, Canada (ICD-10-CA) (i.e., diagnosis codes) were used to identify Elixhauser comorbidities. A single comorbidity documented more than once during the six-month period was only counted once for the LTC resident.

Data analysis

A descriptive analysis was performed for age, gender, location of CDI, and co-morbidity information. Frequencies and proportions were reported. Incidence rates were calculated by dividing the number of incident CDI in LTC facilities over the number of resident-days per 100,000. A test of proportions was used to compare categorical variables between the LO and ACT-LO case classifications. For all statistical comparisons a p-value <0.05 was deemed statistically significant. All data linkages and some of the analyses were conducted using IBM SPSS, Version 19. Comorbidity significance testing was performed using Stata/IC,Version 10 (StataCorp).

RESULTS

Between April 1, 2011, and September 30, 2013, 6,945 CDI cases were identified in the CDRS database. Six thousand five hundred fifty five cases did not overlap when patients were registered in a LTC facility. Three hundred ninety (5.6%) of the CDI cases occurred while the residents were registered in a LTC facility. Of the 390 CDI cases, 274 (70.3%) incident CDI cases occurred in a LTC facility and not during a hospitalization. Of the 274 episodes, 180 (65.7%) were LO, 83 (30.3%) were ACT-LO, 10 (3.6%) were HO and one (0.4%) was CO (Figure 1). Because 263 (96.0%) fell into either the ACT-LO or LO categories, only these two groups were analyzed further.

The provincial incidence rate for the entire study period was 0.7 per 100,000 resident days for ACT-LO and 1.4 per 100,000 resident days for LO.

Table 1 shows that there were more female cases in both the ACT-LO (61.4%) and LO groups (63.4%). The median age is 85 years (Interquartile Range (IQR) 12) for ACT-LO and 86 years (IQR 15) for LO.

It was noted that 85.3% of ACT-LO resided in an urban zone of Alberta; 93.9% of LO resided in an urban zone.

One hundred three LO and 44 ACT-LO residents died following the incident CDI case. Of those, all-cause mortality at 30, 60 and 90 days was listed including the percent of the population who died within 30, 60 and 90 days (Table 1). It was found that 32.7% of LO and 30.1% of ACT-LO died within 60 days of the CDI diagnosis.

All ACT-LO cases had a previous acute care admission and therefore Elixhauser comorbidity data could be evaluated from the discharge diagnoses; however, only 43% (78/180) of the

TABLE 1. Resident Characteristics and Antibiotic Class Exposure

	LO N=180 n (%)	ACT-LO N=83 n (%)	p-value
Males (%)	66 (36.7)	32 (38.6)	0.77
Median Age, years (Interquartile Range, IQR)	86 (15)	85 (12)	
Urban Facilities (%)	169 (93.9)	71 (85.5)	0.03*
Deceased LTC Discharge Care Level			
30-day All-cause Mortality	40 (22.2)	16 (19.3)	0.59
60-day All-cause Mortality	59 (32.7)	25 (30.1)	0.67
90-day All-cause Mortality	64 (35.6)	29 (34.9)	0.92
Cases with Co-morbidity Data	n=78	n=83	
Fluid and Electrolyte Disorders	27 (34.6)	21 (25.3)	0.20
Congestive Heart Failure	15 (19.2)	19 (22.9)	0.40
Cardiac Arrhythmias	18 (23.1)	24 (28.9)	0.25
Chronic Pulmonary Disease	15 (19.2)	20 (24.1)	0.45
Renal Failure	10 (12.8)	14 (16.9)	0.47
Uncomplicated Hypertension	48 (61.5)	49 (59.0)	0.75
Valvular Disease	2 (2.6)	8 (9.6)	0.06
Drug Abuse	0 (0.0)	1 (1.2)	0.33
Coagulopathy	2 (2.6)	7 (8.4)	0.11
Blood Loss Anemia	2 (2.6)	3 (3.6)	0.70
Pulmonary Circulation Disorder	2 (2.6)	5 (6.0)	0.28
Other Neurological Disorder	10 (12.8)	12 (14.5)	0.76
Weight Loss	7 (9.0)	3 (3.6)	0.16
Depression	8 (10.3)	11 (13.3)	0.56
Peripheral Vascular Disease	3 (3.8)	4 (4.8)	0.76
Rheumatoid Arthritis	1 (1.3)	3 (3.6)	0.34
Liver Disease	0 (0.0)	2 (2.4)	0.17
Peptic Ulcer Disease (excluding Bleeding)	1 (1.3)	1 (1.2)	0.96
Paralysis	7 (9.0)	7 (8.4)	0.90
Diabetes uncomplicated	8 (10.3)	7 (8.4)	0.69
Diabetes complicated	27 (34.6)	23 (27.7)	0.34
Hypothyroidism	10 (12.8)	11 (13.3)	0.94
Solid tumor (w/out metastasis)	2 (2.6)	0 (0.0)	0.14
Obesity	4 (5.1)	3 (3.6)	0.64
Deficiency Anemia	5 (6.4)	8 (9.6)	0.45
Alcohol abuse	1 (1.3)	1 (1.2)	0.96
Psychoses	1 (1.3)	1 (1.2)	0.96
Hypertension complicated	2 (2.6)	1 (1.2)	0.52

*Difference between LO and ACT-LO is statistically significant at the .05 level

LO population had an acute care admission in the 6 months prior to the CDI event. Of those residents, 74 (89.2%) of the ACT-LO and 75 (96.2%) of the LO had at least one comorbidity identified (Table 1). Nine (10.8%) ACT-LO cases had no comorbidities listed, 22 (26.5%) had one or two comorbidities, and 52 (62.7%) had three or more comorbidities. For LO cases, 3 (3.8%) had no comorbidities, 31 (39.7%) had one or two comorbidities, 44 (56.4%) had three or more comorbidities. The most commonly found co-morbidity for both the LO (61.5%) and ACT-LO (59.0%) groups was uncomplicated hypertension, the second most common comorbidity was complicated diabetes for the LO group (34.6%) and cardiac arrhythmias for the ACT-LO group (28.9%), and the third most common comorbidity was fluid and electrolyte disorders for LO (34.6%) and complicated diabetes for ACT-LO (27.7%).

DISCUSSION

To our knowledge, this was the first province-wide study in Canada that assessed the incidence and characteristics of CDI that occurred in LTC facilities. The purposes of the study were to provide baseline CDI rates in these facilities, to inform future research, and to add to the demographic literature related to CDI in LTC facilities.

A relatively low number of studies have estimated the incidence of *C. difficile* in nursing homes and other LTC facilities (10). A comprehensive study from the Ohio Department of Public Health on the burden of CDI in LTC facilities found that the overall rate for initial cases of CDI was lower in nursing homes compared to hospitals (1.7-2.9 vs. 6.4-7.9 cases/10,000 patient days, respectively); however, the absolute number of CDI in the nursing homes exceeded those in acute care by more than 50% (13). The Alberta provincial incidence rate for LO was much lower than that found by the Ohio Department of Public Health (0.14 per 10,000 resident days).

Based on our analysis, it is difficult to pinpoint why there were more LO cases than ACT-LO cases. One potential explanation is the potential exposure to systemic antibiotics in long-term care patients. Daneman et al found a 5.9% antibiotic use based on a point-prevalence in 363 Ontario Long Term Care facilities (14). The three most prevalent antibiotics Daneman et al found were most prescribed in the context of urinary tract infections including: nitrofurantoin (15.4%), trimethoprim/sulfamethoxazole (14.3%) and ciprofloxacin (12.8%) (14). Another possibility is that in our jurisdiction patients are not often discharged from acute care to long-term care if they continue to be symptomatic with diarrhea or have an indication of CDI. This is supported by the fact that only 3.6% of cases among long-term care residents occurred in the first 72 hours following an acute care discharge (i.e., hospital-onset CDI).

The median age for CDI cases in LTC facilities in this study was 86 years for LO and 85 years for ACT-LO (Table 1). This is a similar finding to age-related demographic information found in CDI-related literature about the age of CDI patients. In acute care, the rate of CDI based on discharge diagnoses was several-fold higher in patients over the age of 65 than patients 45-64 years ($p<0.05$) (16). The probability of CDI increases with age: patients with CDI were nearly 20 years older (67.9 vs. 48.1 years), and patients $\geq$85 years had the highest rate of CDI (1,089 per 100,000 population) compared with patients less than 18 years (11 per 100,000 population) (16). Previous studies have highlighted factors that make people over 65 years of age more susceptible to *C. difficile* including antibiotic treatment, age-related changes in intestinal flora and host defences, and possibly underlying illnesses (10, 17).

Most cases of CDI in both the LO and ACT-LO groups occurred in LTC facilities located in urban settings. This may be due to increased laboratory testing for CDI in urban LTC facilities compared to rural facilities. Further work is required to identify other possible explanations for this finding.

Using all-cause mortality, less than 23% of both the ACT-LO and LO cases died within 30 days of CDI diagnosis. A British study by Karas et al. assessed the rate of all-cause mortality in acute care and indicated that 37.9% of patients died 30 days after a CDI episode (18). We cannot state why there is a disparity between studies. Although CDI-attributable mortality data was unavailable, all-cause mortality data for the ACT-LO and LO group suggests that the prognosis of those with CDI is poor.

Only 43.3% of residents with LO CDI had acute care data with comorbidity information that could be matched to laboratory-identified CDI case data, since comorbidity information was only available when a resident was previously admitted to an acute care facility within six months prior to the CDI case. The most common co-morbidities were uncomplicated hypertension, complicated diabetes, fluid and electrolyte disorders and cardiac arrhythmias. Studies have shown that hypertension, diabetes, and electrolyte imbalance are common comorbidities among individuals with CDI (19-21). The connection between these comorbidities and CDI is unclear; they may be related to independent medical condition(s) and not due to CDI. Further research to examine quality of life and severity of illness indicators in LTC residents before a CDI episode is needed to determine if any of these factors predispose residents to CDI. Additional research should compare CDI cases to a control group who did not get a CDI.

This study shows that CDI is prevalent in LTC facilities. It is important to stress the need for evidence-based practices being employed in infection prevention and control including the use of private rooms, contact procedures, environmental cleaning, and hand hygiene to reduce CDI in LTC facilities. The Public Health Agency of Canada lists precautions and procedures that need to be upheld in order to decrease the number of people with CDI (22). Education and awareness of the severity of this infection in terms of morbidity and mortality must be stressed with LTC facilities' staff. This could potentially inform initiatives to improve clinical management of residents to decrease the reservoir and burden of CDI in these facilities.

There are several limitations with this study. The acute care database only included diagnostic code information six months prior to the CDI case. The acute care diagnostic codes were the only source of information for co-morbidity data. It is likely that these data do not give a complete depiction of all co-morbidities, particularly of residents with no hospital

admission in the six month period prior to the CDI case. Resident-level linkages to other electronic medical records such as primary care records would provide more information about the comorbidities for this population.

The NHSN guidelines for laboratory-identified CDI is recommended for CDI identification in LTC. The limitation with this guideline is that it differs from the CDI definition for acute care which requires a clinical evaluation of symptoms and it relies on CDI testing practices in LTC facilities. The rationale for using the NHSN guideline is that it could be assumed that symptoms were present in order for a stool specimen to be collected and tested. The feasibility of collecting CDI-related symptomatic information would be challenging in LTC facilities with the limited resources available in infection prevention and control.

Finally, the mortality information within the analysis only included all-cause mortality; CDI-attributable mortality was not determined in this analysis because the data source used did not include attributable-mortality information. To include CDI-attributable mortality, a health care professional would have to assess each case to determine if CDI contributed to or was the cause of death. Using all-cause mortality does not indicate death due to CDI; this distinction should be considered when reviewing mortality-related literature.

CONCLUSION

The study found demographic homogeneity in both ACT-LO and LO classifications; there were similar distributions of gender, age, all-cause mortality, and co-morbidities. Although there were more LO situations, there was little demographic variation between the two groups. The key difference between the two case classifications was the variation in acute care exposure. Future work is warranted to further assess CDI in LTC facilities to determine if there are similar findings.

Based on these findings, we recommend routine annual provincial surveillance of CDI in all Albertan LTC facilities to identify and explain changes in CDI incidence over time. Routine annual surveillance would replicate this laboratory event surveillance on an annual basis, using the same strategy and definitions to measure incidence without requiring extensive Infection Prevention and Control support for data collection.

REFERENCES

1. Leal, J. (2014). *Comparison of Two Clostridium difficile Surveillance Methods: Clinical Infection Surveillance vs. Laboratory Identified Event Surveillance*. (Unpublished manuscript). Calgary, AB: Alberta Health Services.
2. Karas, J., Enoch, D., & Aliyu, S. (2010). A review of mortality due to *Clostridium difficile* infection. *The British Infection Society,* 61(1), 1-8. doi: 10.1016/j.jinf.2010.03.025.
3. Kamboj, M., Son, C., Cantu, S., Chemaly R. F., Dickman, J., Dubberke, E., Sepkowitz, K. A. (2013). Hospital-onset *Clostridium difficile* infection rates in persons with cancer or hematopoietic stem cell transplant: A C3IC network report. *Infection Control and Hospital Epidemiology,* 33(11), 1162-1165. doi: 10.1086/668023
4. Pépin, J., Valiquette, L., Alary, M. E., Villemure, P., Pelletier, A., Forget, K., Pépin, K., & Choinard, D. (2004). *Clostridium difficile*-associated diarrhea in a region of Quebec from 1991 to 2003: A changing pattern of disease severity. *Canadian Association Medical Journal*, 171, 466–472.
5. Simor, A., Bradley, S., Strausaugh, L., Crossley, K., & Nicolle, L. (2002). *Clostridium difficile* in long-term-care facilities for the elderly. *Infection Control & Hospital Epidemiology*, 23(11), 696-703.
6. Gravel, D., Miller, M., Simor, A., Taylor, G., Gardam, M. McGreer, A., & Mulvey, M. (2009). Health care-associated *Clostridium difficile* infection in adults admitted to acute care hospitals in Canada: A Canadian nosocomial infection surveillance program study. *Clinical Infectious Diseases,* 48(5), 568-576. doi: 10.1086/596703
7. Inns, T., Gorton, R., Berrington, A., Sails, A., Lamagni, T., Collins, J. & Gould. K. (2013). Effect of ribotype on all-cause mortality following *Clostridium difficile* infection. *The Journal of Hospital Infection,* 84(3), 235-241. DOI: 10.1016/j.jhin.2013.04.008
8. Depestel, D. D., & Aronoff, D. M. (2013). Epidemiology of *Clostridium difficile* Infection. *Journal of Pharmacy Practice,* 26 (5), 464-465.
9. Mitchell, B. G., & Gardner, A. (2012). Mortality and *Clostridium difficile* infection: a review. *Antimicrobial Resistance & Infection Control,* 1:20, 1-6.
10. Rodriguez, C., Korsak, N., Taminiau, B., Avesani, V., Van Broeck, J., Delmee, M., & Daube, G. (2014). *Clostridium difficile* infection in elderly nursing home residents. *Anaerobe*, 30, 184-187. doi: 10.1016/j.anaerobe.2014.08.007
11. Statistics Canada. (2012). *Focus on Geography Series, 2011 Census*. Statistics Canada Catalogue no. 98-310-XWE2011004. Ottawa, Ontario. Analytical products, 2011 Census. Last updated October 24, 2012.Retrieved from, https://www12.statcan.gc.ca/census-recensement/2011/as-sa/fogs-spg/Facts-pr-eng.cfm?Lang=Eng&GK=PR&GC=48
12. Centre for Disease Control. (2012). Laboratory-identified Multidrug-Resistant Organism (MDRO) & *Clostridium difficile* Infection (CDI) Events for Long-term Care Facilities. https://www.cdc.gov/nhsn/pdfs/training/ltc/ltcf-labid-event-protocol_current.pdf
13. Campbell, R.J., Giljahn, L., Machesky, K., Cibulskas-White, K., Lane, L.M., Porter, K., . . . McDonald, L.C. (2009). Clostridium difficile infection in Ohio hospitals and nursing homes during 2006. Infection Control and Hospital Epidemiology, 6, 526–533.
14. Daneman, N., Gruneir, A., Newman, A., Fischer, H. D., Bronskill, S. E., Rochon, P. A. . . . & Bell, C. M. (2011). Antibiotic use in long-term care facilities. Journal of Antimicrobial Chemotherapy, 66, 2856-2863.
15. McDonald, C. L., Owings, M., & Jernigan, D. B. (2006). Clostridium difficile Infection in Patients Discharged form US Short-stay Hospitals, 2006-2003. Emerging Infectious Diseases, 12, 3, 409-415.
16. Lucado, J., Gould, C., & Elixhauser, A. (2012). Clostridium difficile Infections (CDI) in Hospital Stays, 2009. HCUP Statistical Brief #124. January 2012. Agency for Healthcare Research and Quality, Rockville, MD. http://www.hcup-us.ahrq.gov/reports/statbriefs/sb124.pdf.
17. Taslim, H. (2009). Clostridium difficile infection in the elderly. Acta Medica Indonesia, 41, 3, 148-151.
18. Karas, J., Bradshaw, S., Mahmud, W., & Enoch, D. A. (2010). Morality in hospitalized older adults associated with Clostridium difficile infection at a district hospital. Current Infectious Disease Reports, 2(1), 19-21.
19. Keddis, M., Khanna, S., Noheria, A., Baddour, L., Pardi, D., & Qian, Q. (2012). Clostridium difficile infection in patients with chronic kidney disease. Mayo Clinic Proceedings, 87(11), 1046-1053. doi: 10.1016/j.mayocp.2012.05.025
20. Sunenshine, R., & McDonald, C. (2006). Clostridium difficile-associated disease: New challenges from an established pathogen. Cleveland Clinic Journal of Medicine, 73(2), 187-197.
21. Qu, H., & Jiang, Z. (2014) Clostidium difficile infection in diabetes. Diabetes Research and Clinical Practice, 105(3), 285-294. doi: 10.1016/j.diabres.2014.06.002
22. Public Health Agency of Canada (2012). Clostridium difficile Infection: Infection prevention and control guidance for management in long-term care facilities. Ottawa, ON.