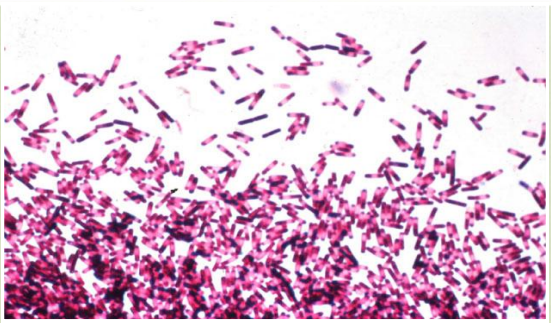
# HEALTHCARE- ASSOCIATED *CLOSTRIDIUM DIFFICILE* INFECTIONS IN CANADIAN ACUTE-CARE HOSPITALS

## SURVEILLANCE REPORT JANUARY 1st, 2007 TO DECEMBER 31st, 2012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## Information to the reader of healthcare-associated *Clostridium difficile* infection in Canada

The Public Health Agency of Canada (Agency) collects national data on various healthcare-associated infections, including healthcare-associated *Clostridium difficile* infection (HA-CDI) through the Canadian Nosocomial Infection Surveillance Program (CNISP), a collaborative effort of the Centre for Communicable Diseases and Infection Control, the National Microbiology Laboratory and sentinel hospitals across Canada who participate as members of the Canadian Hospital Epidemiology Committee (a subcommittee of the Association of Medical Microbiology and Infectious Disease Canada). As of December 2012, 54 largely, university-affiliated tertiary care hospitals (i.e., major hospitals that offer a range of specialist services such as burn units, transplant units, trauma centres, specialized cardiac surgery etc. to which patients are referred from smaller hospitals) from ten provinces participate in CNISP (Appendix 1). Of these, nine hospitals are stand-alone pediatric hospitals, 14 hospitals provide adult and pediatric patients, and the remaining 31 hospitals provide services to adult patients only. CNISP surveillance provides key information that informs the development of federal, provincial and territorial infection prevention and control programs and policies and provides rates and trends on healthcare-associated infections and antimicrobial resistant organism. The Agency surveillance reports are intended to provide up to date, timely CNISP rates to healthcare professionals and the provincial and territorial health authorities. The results are subject to change as new data is made available by the participating hospitals.

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## AT A GLANCE

The Public Health Agency of Canada (Agency) has collected data on hospitalized patients with healthcare-associated *Clostridium difficile* infections (HA-CDI) in Canadian acute-care hospitals through the Canadian Nosocomial Infection Surveillance Program (CNISP) since 2007. This report describes the epidemiology of HA-CDI and *Clostridium difficile* strain types in Canada from 2007 to 2012. The following are highlights of this surveillance report.

- The overall HA-CDI rates in Canada peaked in 2008 but remained stable between 2009 and 2012.

- HA-CDI rates per 1,000 patient admissions in adults showed no significant trend over time while HA-CDI rates per 10,000 patient-days in adults decreased slightly over the surveillance period.

- HA-CDI rates per 1,000 patient admissions in adults varied by region.

    - The Central had the highest rates with a slight decreasing trend over time.
    - The Eastern region had the lowest rates with a decreasing trend over time.
    - The Western region had the similar rates to the Central region; however, it showed no significant trend over time.

- HA-CDI rates per 1,000 patient admissions in children were stable during the surveillance period while HA-CDI rates per 10,000 patient days showed significant increasing trends over time in children.

- The all-cause mortality and the attributable mortality rates were stable in both adults and children populations.

- NAP1 strain type remains the most dominant *Clostridium difficile* strain type followed by NAP4.

## BACKGROUND

*Clostridium difficile*, commonly called *C. difficile*, is a bacterium that causes diarrhea and other serious intestinal conditions. It is the most common cause of infectious diarrhea in hospitals and long-term care facilities in Canada. [1] *C. difficile* causes disease by releasing toxins that destroy the lining of the bowel which, in turn, causes bloating and frequent, watery diarrhea. Other symptoms such as severe abdominal pain and tenderness, and/or fever may occur. *C. difficile* infections (CDI) are also the most common cause of pseudomembranous colitis (or inflammation of the colon).In rare instances, *C.difficile* can progress to more severe, life-threatening disease such as perforation of the bowel or toxic megacolon (or enlargement of the colon). [2] People can also acquire *C.difficile* without developing CDI and remain without symptoms.

*C.difficile* is an anaerobic, spore-forming bacterium which means it can resist cleaning and disinfection, and can persist in the environment. The acquisition of *C. difficile* occurs through ingestion of the spores, which are found in feces. Spores resist the acidity of the stomach then germinate into the vegetative form in the small intestine. Disruption to the normal gut flora can lead to the proliferation of *C.difficile* and the development of CDI.

Hospitalised patients can acquire *C.difficile* if they touch surfaces contaminated with feces (e.g. toilet seats, bedrails, door handles, soiled linens, etc.), and then touch their mouths. *C.difficile* may also spread from patient to patient via the contaminated hands of health care workers. The population at risk of acquiring CDI includes the elderly, or people with certain antibiotics exposure, immunocompromising conditions or serious underlying disease. A number of other risk factors have been suggested that may contribute to the onset of CDI, including the use of proton pump inhibitors (a type of stomach ulcer drug) and other medications that suppress the stomach acid. The association between acid-suppressing medications and CDI is difficult to establish as most patients with CDI have other significant risk factors, such as underlying severity of illness and duration of hospital stay. [3] It is very uncommon for patients to develop CDI without prior antibiotic use. Patients who have frequent hospital admissions and prolonged and excessive length of hospital stays are also at risk. [4]

Beginning in the last half of 2002, several hospitals in Quebec experienced a dramatic increase in the incidence, severity and number of relapses (or recurrences) associated with CDI. [5] Similar reports were seen in other provinces, notably Ontario and British Columbia; as well as in other industrialized countries. An analysis of US hospital discharge data revealed that CDI rates increased abruptly beginning in 2001, with a doubling of national rates from 2000 to 2003. [6] Reports also suggested that the fatality rate has increased in recent years. In Canada, the attributable mortality increased from 1.5% in 1997 to 5.7% in 2005. [7] Severe outcomes, other than death, have also increased; including admission to ICU for complications associated with CDI, toxic shock; and colectomy. This increase was most prominent for patients 65 years of age and older.

There are several hypotheses that have been examined to explain the dramatic increase in incidence, severity and recurrence associated with CDI. Shortly after the appearance of reports of more relapses and severe disease in patients with CDI, a previously unknown strain of *C.difficile* was identified. The strain is characterized as North American pulsed-field Type 1 with a restriction enzyme analysis type BI and PCR ribotype 027, hence the name NAP1/B1/027 (more commonly referred to as simply NAP1). This strain has been shown to produce greater quantities of toxins which may explain the association between NAP1 and more severe disease and relapse. Other studies have suggested that antibiotic usage, the physical layout of the

facility including the presence or absence of sinks for hand washing, and lapses in infection prevention and control measures has played a role in the overall incidence of CDI in Canada.

To diagnose CDI, a stool sample is taken from the patient and forwarded to a microbiology laboratory. Until recently, the most common test used to identify the bacteria in the stool has been an enzyme-linked immunosorbent assay (EIA) test which isolates the toxins in the stool sample. Many laboratories now test for *C.difficile* toxin with real-time polymerase chain reaction (PCR) which can improve the laboratory diagnoses of CDI as it more sensitive and faster as compared with EIA.

This report provides a review of available healthcare-associated *Clostridium difficile* infection (HA-CDI) surveillance data in Canada from January 1, 2007 to December 31, 2012.

## METHODS

### Surveillance network

The Public Health Agency of Canada (Agency) collects data on hospitalized patients with healthcare-associated *Clostridium difficile* infections (HA-CDI) in Canadian acute-care hospitals through the Canadian Nosocomial Infection Surveillance Program (CNISP). HA-CDI surveillance is compulsory for all participating CNISP hospitals; however hospitals have the option to opt out of the surveillance in any given calendar year. Surveillance of HA-CDI at participating hospitals is considered to be within the mandate of hospital infection prevention and control programs and does not constitute human research. While this surveillance project is observational and does not involve any alteration in patient care, Institutional Review Board (IRB) review may be sought at some hospital sites.

The HA-CDI Working Group is comprised of members of the Canadian Hospital Epidemiology Committee (CHEC), an Agency epidemiologist and an Agency laboratory representative. The working group is responsible for developing and regularly updating the surveillance protocol, which includes standardized data collection forms and a data dictionary. Surveillance protocols are revised at the beginning of each surveillance year which runs from January to December. In-service sessions are organised at the beginning of the surveillance year by the Agency for all participating hospitals. The purpose of the in-service sessions are to provide training to Infection Control Practitioners (ICPs) on how to follow the surveillance protocol and complete the data collection forms, and to ensure consistency across the participating hospitals in the understanding of each question on the data collection forms. This ensures that the data are comparable between the participating hospitals and between the provinces and regions.

### Case definitions

A patient is identified as having CDI if:

- they have diarrhea or fever, abdominal pain and/or ileus, and a laboratory confirmation of a positive toxin assay or positive polymerase chain reaction (PCR) test for *C.difficile*; or
- they have a diagnosis of pseudomembranes on sigmoidoscopy or colonoscopy or histological/pathological diagnosis of CDI; or
- the patient is diagnosed with toxic megacolon (in adult patients only).

In addition, a patient is considered to have HA-CDI if:

- the patient's CDI symptoms occur in the admitting hospital less than 72 hours after admission; or
- CDI is seen in a patient who had been hospitalized in the admitting hospital and discharged within the previous four weeks.

It is important to note that individuals who are in outpatient settings such as emergency departments and clinics are not considered admitted to the hospital and are therefore not included in the surveillance. Patients in psychiatry wards/units are also excluded from the surveillance. All hospitalized patients 1 year of age and older meeting the case definition for CDI were eligible for enrolment. The collected specimens are sent to the hospital's laboratory to determine if the patient's stool is positive for *C.difficile*.

Only healthcare-associated cases from the admitting facility are included in this surveillance. A case is considered to be healthcare-associated if the patient's CDI symptoms occur in the hospital

72 hours or more after admission or if CDI is seen in a patient who had been hospitalized and discharged within the previous four weeks. Only primary episodes are included in this surveillance. Primary episodes are defined as either the first episode of CDI or a new episode of CDI which occurs more than eight weeks after the first positive toxin assay[a]. This assessment is determined based on information available in the patient chart at the time of data collection. Episodes which did not meet the criteria for disease (i.e., positive test, but criteria for diarrhea or other symptoms not met), and recurrence, were not included in the surveillance.

**Data collection and submission**

When a possible CDI case is identified by the hospital's laboratory, a standardized patient questionnaire is completed through concurrent or retrospective chart review by an ICP. The questionnaire includes patient demographics and clinical information, the ward/unit the patient was on when the symptoms for CDI started, and outcome information. The detailed patient questionnaire was collected only between March 1st and April 30th of each year during the 2007 and 2008 surveillance year. Aggregate patient information was provided from January 1st to February 28th and from May 1st to December 31st of each year. In 2009, HA-CDI was expanded to cover the full calendar year. Detailed patient questionnaires were provided for the entire surveillance year; i.e. between January 1st and December 31st of each year.

Outcome information was defined as a severe outcomes if the patient was admitted to the intensive care unit (ICU) for complications related to HA-CDI, underwent a colectomy (surgical removal of a portion of the large bowel) or died. All cases of death within 30 days after the date of the onset of symptoms were assessed by the CHEC member or a designated physician to determine if the death was attributable to CDI. Cause of death was determined by the following criteria: 1) CDI was directly related to the death of the patient; that is, the patient had no other underlying condition that would have caused death during this hospitalization; or 2) CDI was indirectly related to death; that is, the CDI contributed to the patient's death but was not the primary cause; or 3) the patient died with CDI but CDI was not related to death. Outcome information including attributable mortality was provided from March 1st to April 30th each year.

Data were submitted via paper forms or submitted electronically through a web based information management system to the Surveillance and Epidemiology Division of the Agency for further analysis and storage.

**Laboratory data collection and analysis**

Whenever possible, frozen stool specimens from patients with laboratory confirmed HA-CDI were forwarded to the National Microbiology Laboratory (NML) in Winnipeg for *C. difficile* isolation and molecular characterization. Stool specimens in adult patients 18 years of age and older with HA-CDI were submitted between March 1st and April 30th of each year. Therefore, the number of *C.difficile* isolate tested is a subset of number of cases submitted. Stool specimens of children aged one year to less than 18 years with HA-CDI were submitted year round to NML. *C.difficile* was isolated from the stools using an alcohol shock procedure. Toxigenic strains were confirmed using polymerase chain reaction (PCR) to detect *tcdA* and *tcdB* genes. PCR was also used to confirm the species, detect variations in the *tcdC* gene and to detect the presence of the binary toxin (*cdtB*). Pulsed-field gel electrophoresis (PFGE) was used to type the strains to define the North American Pulsed Field pattern (NAP type).

[a] This was an arbitrary cut-off value to distinguish a relapse case from a new episode of CDI, because patients with CDI do not undergo repeat testing till negative test as a "test of cure" following treatment.

**Denominator data**

Participating hospitals provide the Agency with the number of patient-admissions and the number of patients-days for the corresponding surveillance year. These denominator data are used to calculate the annual incidence rates presented in this report.

**Data analysis**

Data submitted to the Agency by participating hospitals (patients' clinical and demographic data) and the NML (results of laboratory analysis) were extracted, validated and statistically analysed as appropriate.

Annual incidence rates were calculated using patient admissions and patient-days. Rates are calculated only using hospitals that provided both the number of CDI cases and denominator data. For reporting purposes and to ensure confidentiality, the provinces were grouped into three regions: Western (British Columbia, Alberta, Saskatchewan and Manitoba), Central (Ontario and Quebec), and Eastern (Nova Scotia, New Brunswick, Prince Edward Island and Newfoundland and Labrador). For pediatric hospitals, the rates were not stratified by the region to ensure confidentiality. The territories do not currently submit data to the Agency and Prince Edward Island only began submitting data in 2011. HA-CDI incidence rates are presented from 2007 to 2011. HA-CDI incidence rates trends over the surveillance period were examined using the Cochrane-Armitage test with a significance level of 0.05. [6] Logistic regression analyses were performed to determine the rate trend (increasing or decreasing) with a significance level of 0.05.

**Rate calculations**

Infection rate per 1,000 patient admissions = $\frac{Number\ of\ CDI\ cases}{Total\ number\ of\ admisisons}$ per year × 1,000

Infection rate per 10,000 patient days = $\frac{Number\ of\ CDI\ cases}{Total\ number\ of\ patient\ days}$ per year × 10,000

All-cause mortality rate = $\frac{Number\ of\ all\ cause\ deaths}{Total\ number\ of\ CDI\ cases}$ per year × 100

Attributable mortality rate = $\frac{Number\ of\ deaths\ directly\ and\ indirectly\ related\ to\ CDI}{Total\ number\ of\ CDI\ cases}$ per year × 100

Patient admissions are defined as the total number of individuals admitted as an in-patient in the hospitals participating in HA-CDI surveillance during a surveillance year.

Patient-days are defined as the sum total of the number of days all patients stayed in the hospital in a given surveillance year.

All-cause mortality rate is defined as death in a patient with HA-CDI from all causes within 30 days after the date of the first positive *C.difficile* test.

Attributable mortality rate is defined as all deaths directly or indirectly related to HA-CDI 30 days after the date of the first positive *C.difficile* test.

# RESULTS

## Section 1. Healthcare-associated *Clostridium difficile* Infection Incidence Rates from January 1, 2007 to December 31, 2012

### 1.1 Overall HA-CDI in Canada: National and Regional HA-CDI Incidence Rates

Table 1 provides the number of adult and pediatric HA-CDI cases and rates per 1,000 patient admissions and 10,000 patient-days by year and region. The national rate of HA-CDI in 2012 was 4.80 cases per 1,000 patient admissions and 6.04 cases per 10,000 patient days. There was no statistically significant increase or decrease in HA-CDI rates by patient admission over the surveillance period (p-value: 0.74). There was a significant decrease in HA-CDI rates by patient-days, although the rates annually fluctuated, resulting in an overall minimal decrease over time throughout the surveillance period. For instance, HA-CDI rates per 10,000 patient-days increased from 2007 to 2008 and decreased from 2008 to 2009.

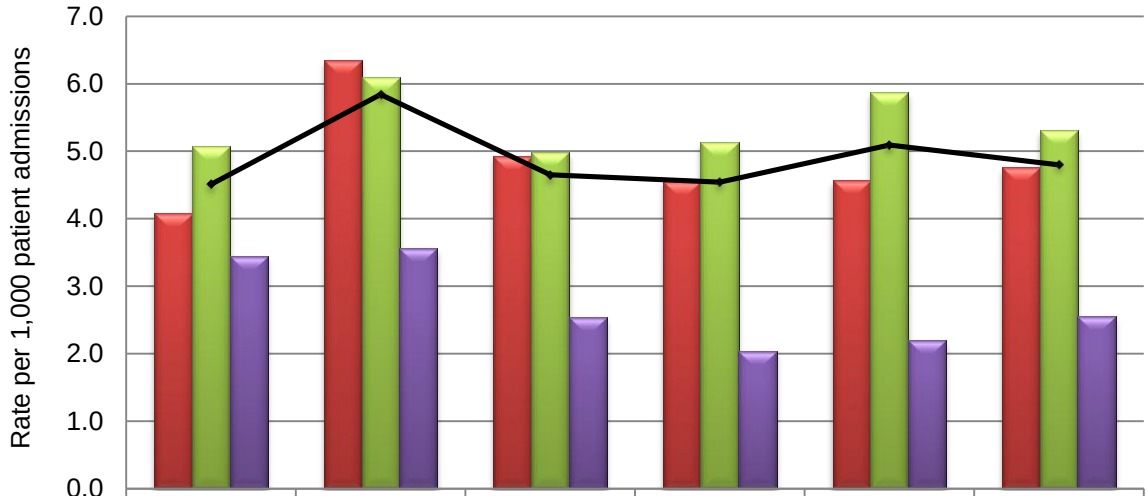
**Table 1. National and regional HA-CDI rates per 1,000 patient admissions and 10,000 patient days, January 1, 2007 to December 31, 2012, N = 18,871**

| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | *p* |
|---|---|---|---|---|---|---|---|
| **National** | | | | | | | |
| No. of HA-CDI cases | 3,271 | 3,192 | 2,483 | 3,026 | 3,417 | 3,482 | |
| No. of total patient admissions | 726,004 | 546,753 | 533,967 | 666,459 | 670,857 | 724,964 | |
| No. of total patient days | 4,832,597 | 4,274,020 | 4,270,868 | 4,945,856 | 5,141,450 | 5,766,774 | |
| Rate per 1,000 patient admissions | 4.51 | 5.84 | 4.65 | 4.54 | 5.09 | 4.80 | 0.74 |
| Rate per 10,000 patient days | 6.77 | 7.47 | 5.81 | 6.12 | 6.65 | 6.04 | <0.0001 |
| No. of reporting hospitals[b] | 49 | 44 | 49 | 52 | 54 | 54 | |
| **West** | | | | | | | |
| No. of HA-CDI cases | 1,180 | 1,060 | 907 | 1,282 | 1,241 | 1,282 | |
| No. of total patient admissions | 289,084 | 167,050 | 183,827 | 280,881 | 271,328 | 269,411 | |
| No. of total patient days | 1,947,982 | 1,314,608 | 1,357,052 | 1,879,003 | 2,150,998 | 2,245,105 | |
| Rate per 1,000 patient admissions | 4.08 | 6.35 | 4.93 | 4.56 | 4.57 | 4.76 | 0.86 |
| Rate per 10,000 patient days | 6.06 | 8.06 | 6.68 | 6.82 | 5.77 | 5.71 | <0.0001 |
| **Central** | | | | | | | |
| No. of HA-CDI cases | 1,831 | 1,876 | 1,401 | 1,589 | 2,075 | 1,997 | |
| No. of total patient admissions | 361,442 | 307,800 | 281,251 | 309,625 | 353,604 | 375,884 | |
| No. of total patient days | 2,226,341 | 2,295,426 | 2,371,581 | 2,382,999 | 2,639,924 | 2,795,627 | |
| Rate per 1,000 patient admissions | 5.07 | 6.09 | 4.98 | 5.13 | 5.87 | 5.31 | 0.37 |
| Rate per 10,000 patient days | 8.22 | 8.17 | 5.91 | 6.67 | 7.86 | 7.14 | <0.0001 |
| **East** | | | | | | | |
| No. of HA-CDI cases | 260 | 256 | 175 | 155 | 101 | 203 | |
| No. of total patient admissions | 75,478 | 71,903 | 68,889 | 75,953 | 45,925 | 79,709 | |
| No. of total patient days | 658,274 | 663,986 | 542,235 | 683,854 | 350,528 | 726,042 | |
| Rate per 1,000 patient admissions | 3.44 | 3.56 | 2.54 | 2.04 | 2.20 | 2.55 | <0.0001 |
| Rate per 10,000 patient days | 3.95 | 3.86 | 3.23 | 2.27 | 2.88 | 2.80 | <0.0001 |

[b] The variation in the number of reporting hospitals each year reflects the changes in the number of participating hospitals, which has increased over time. In 2008, five hospitals opted out of CNISP surveillance during that calendar year.

Figure 1 illustrates the trend in annual HA-CDI rates per 1,000 patient admissions from 2007 to 2012. HA-CDI rates per 1,000 patient admissions varied by region. In the Western region, there was no statistically significant increase or decrease over time (p-value: 0.86). The incidence rate of HA-CDI per 1,000 patient admissions peaked in 2008 at 6.35 cases per 1,000 patient admissions, decreased from 2009 to 2010 and remained stable from 2010 to 2012 (4.76 cases per 1,000 patient admissions in 2012, representing a decrease of 25% when compared to 2008). HA-CDI in the Central region also increased from 2007 to 2008, before decreasing in 2009. Since 2010, the incidence rate per 1,000 patient admissions has remained relatively constant at 5.31 cases per 1,000 patient admissions in 2012. HA-CDI rates in the Eastern region have remained lower than the other regions in Canada over the entire surveillance period (Table 1, Figure 1). In 2012, the Eastern region had an incidence rate of 2.55 per 1,000 patient admissions, representing almost half the rates observed in the Western and Central regions of Canada.

**Figure 1. National and regional HA-CDI incidence rates per 1,000 patient admissions, January 1, 2007 to December 31, 2012, N = 18,871**



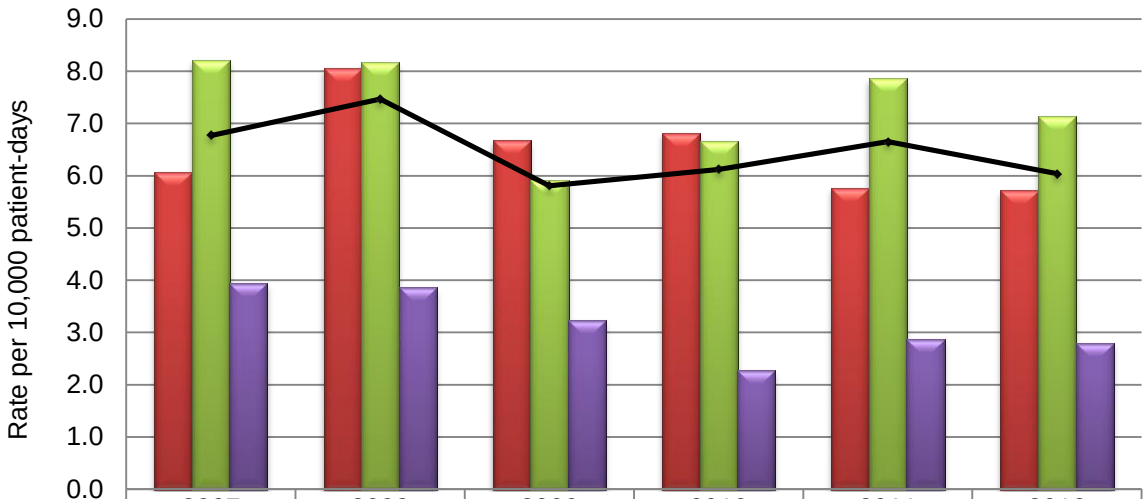

| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| West | 4.08 | 6.35 | 4.93 | 4.56 | 4.57 | 4.76 |
| Central | 5.07 | 6.09 | 4.98 | 5.13 | 5.87 | 5.31 |
| East | 3.44 | 3.56 | 2.54 | 2.04 | 2.20 | 2.55 |
| Overall | 4.51 | 5.84 | 4.65 | 4.54 | 5.09 | 4.80 |

Figure 2 illustrates the trend in annual HA-CDI rates per 10,000 patient-days from 2007 to 2012. Although the rates fluctuated annually, there was an overall downward trend over time throughout the surveillance period ($p < 0.0001$).

Regionally, all three regions showed a similar decrease in HA-CDI rates per 10,000 patient-days over time. HA-CDI rates per 10,000 patient-days in the Western region increased from 2007 to 2008; however, it has since been decreasing. In 2012, the rate of HA-CDI in the Western region was 5.71 cases per 10,000 patient-days. In the Central region, HA-CDI rates per 10,000 patient-days decreased between 2007 and 2009; after which the rate of HA-CDI has steadily increased. The rate of HA-CDI in the Central region in 2012 was 7.14 cases per 10,000 patient-days. In the Eastern region, HA-CDI rates per 10,000 patient-days decreased between 2007 and 2010 but the trend reversed with a slight increase in 2011 (Table 1, Figure 2). Overall, the

rate of HA-CDI in the Eastern region remain significantly lower compared to the Western and Central regions (2.80 vs. 5.71 and 7.14 cases per 10,000 patients-days, respectively in 2012).

**Figure 2. National and regional HA-CDI incidence rates per 10,000 patient-days, January 1, 2007 to December 31, 2012, N = 18,871**




| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| West | 6.06 | 8.06 | 6.68 | 6.82 | 5.77 | 5.71 |
| Central | 8.22 | 8.17 | 5.91 | 6.67 | 7.86 | 7.14 |
| East | 3.95 | 3.86 | 3.23 | 2.27 | 2.88 | 2.80 |
| Overall | 6.77 | 7.47 | 5.81 | 6.12 | 6.65 | 6.04 |

**1.2 HA-CDI in Adults: National HA-CDI surveillance from January 1, 2007 to December 31, 2012**

Table 2 provides the number of HA-CDI cases and rates in adults 18 years of age and older per 1,000 patient admission and 10,000 patient-days by year and region. Rates are calculated only using hospitals that provided both the number of HA-CDI cases and denominator data. Both adult only and mixed (adult and pediatric) hospitals are included in the calculation of the adult rates. However, the percentage of pediatric cases in mixed hospitals is less than one percent of the overall (n= 97).

The rates of HA-CDI in adults ranged from a low of 4.61 per 1,000 patient admissions in 2007 to a high of 7.62 cases per 1,000 patient admissions in 2008. The rate of HA-CDI in adults in 2012 was 5.07 cases per 1,000 patient admissions and 6.12 cases per 10,000 patient-days.

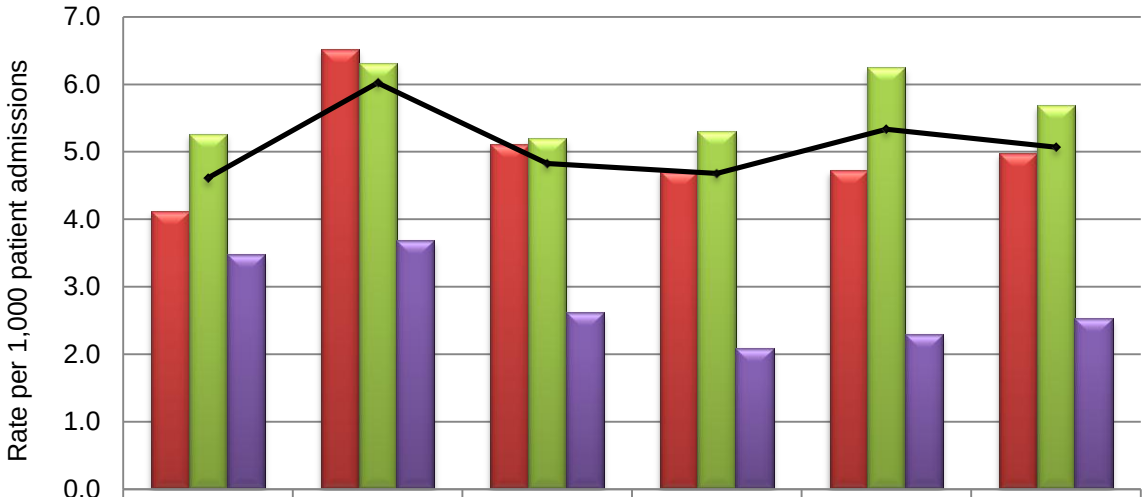
**Table 2. National and regional HA-CDI rates in adults per 1,000 patient admissions and 10,000 patient days in adults, January 1, 2007 to December 31, 2012, N= 18,291***

| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | *p* |
|---|---|---|---|---|---|---|---|
| **National** | | | | | | | |
| No. of HA-CDI cases | 3,207 | 3,095 | 2,402 | 2,924 | 3,289 | 3,374 | |
| No. of total patient admissions | 695,520 | 513,990 | 497,754 | 625,086 | 616,620 | 664,966 | |
| No. of total patient days | 4,629,377 | 4,063,201 | 4,054,478 | 4,711,277 | 4,896,429 | 5,511,426 | |
| Rate per 1,000 patient admissions | 4.61 | 6.02 | 4.83 | 4.68 | 5.33 | 5.07 | 0.07 |
| Rate per 10,000 patient days | 6.93 | 7.62 | 5.92 | 6.21 | 6.72 | 6.12 | 0.002 |
| No. of reporting hospitals | 42 | 37 | 42 | 44 | 46 | 45 | |
| **West** | | | | | | | |
| No. of HA-CDI cases | 1,162 | 1,043 | 890 | 1,248 | 1,198 | 1,253 | |
| No. of total patient admissions | 282,302 | 160,111 | 173,913 | 264,653 | 253,987 | 251,543 | |
| No. of total patient days | 1,885,499 | 1,240,773 | 1,283,433 | 1,772,646 | 2,040,029 | 2,135,069 | |
| Rate per 1,000 patient admissions* | 4.12 | 6.51 | 5.12 | 4.72 | 4.72 | 4.98 | 0.48 |
| Rate per 10,000 patient days* | 6.16 | 8.41 | 6.93 | 7.04 | 5.87 | 5.87 | <0.0001 |
| No. of reporting hospitals | 16 | 13 | 16 | 17 | 17 | 17 | |
| **Central** | | | | | | | |
| No. of HA-CDI cases | 1,791 | 1,796 | 1,338 | 1,522 | 1,990 | 1,935 | |
| No. of total patient admissions | 340,207 | 284,276 | 257,276 | 286,786 | 318,733 | 339,929 | |
| No. of total patient days | 2,096,075 | 2,169,116 | 2,237,899 | 2,264,145 | 2,515,734 | 2,680,937 | |
| Rate per 1,000 patient admissions* | 5.26 | 6.32 | 5.20 | 5.31 | 6.24 | 5.69 | <0.0001 |
| Rate per 10,000 patient days* | 8.54 | 8.28 | 5.98 | 6.72 | 7.91 | 7.22 | <0.0001 |
| No. of reporting hospitals | 21 | 19 | 21 | 23 | 23 | 23 | |
| **East** | | | | | | | |
| No. of HA-CDI cases | 254 | 256 | 174 | 154 | 101 | 186 | |
| No. of total patient admissions | 73,011 | 69,603 | 66,565 | 73,647 | 43,900 | 73,494 | |
| No. of total patient days | 647,803 | 653,312 | 533,146 | 674,486 | 340,666 | 695,420 | |
| Rate per 1,000 patient admissions* | 3.48 | 3.68 | 2.61 | 2.09 | 2.30 | 2.53 | <0.0001 |
| Rate per 10,000 patient days* | 3.92 | 3.92 | 3.26 | 2.28 | 2.96 | 2.67 | <0.0001 |
| No. of reporting hospitals | 5 | 5 | 5 | 5 | 6 | 5 | |

*Includes 97 pediatric cases

Figure 3 illustrates the trend in annual HA-CDI rates in adults per 1,000 patient admissions from 2007 to 2012. There was no statistically significant trend over time although a rate variation was observed during the surveillance period. For instance, HA-CDI rates per 1,000 patient admissions increased from 4.61 to 6.02 cases from 2007 to 2008 decreased from 6.02 cases per 1,000 patient admissions in 2008 to 4.68 cases per 1,000 patient admissions through 2010 and then reversed in 2011 when incidence rates once again began to rise. The rate in 2012 was 5.07 cases per 1,000 patient days.

**Figure 3. National and regional HA-CDI incidence rates in adults per 1,000 patient admissions, January 1, 2007 to December 31, 2012, N= 18,291**

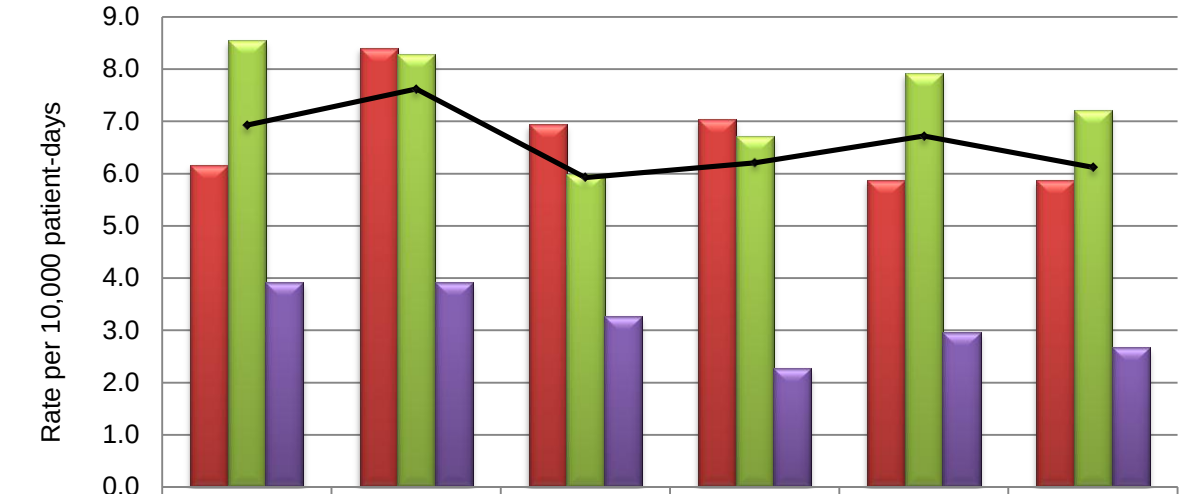



| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| West | 4.12 | 6.51 | 5.12 | 4.72 | 4.72 | 4.98 |
| Central | 5.26 | 6.32 | 5.20 | 5.31 | 6.24 | 5.69 |
| East | 3.48 | 3.68 | 2.61 | 2.09 | 2.30 | 2.53 |
| Overall | 4.61 | 6.02 | 4.83 | 4.68 | 5.33 | 5.07 |

Figure 4 illustrates the trend in annual HA-CDI rates per 10,000 patient-days from 2007 to 2012. Nationally, there was a decrease in HA-CDI rates per 10,000 patient-days, although the decrease was minimal due to the rate fluctuation throughout the surveillance period. HA-CDI rates per 10,000 patient-days increased from 6.93 per 10,000 patient-days in 2007 to 7.62 per 10,000 patient-days in 2008 and decreased from 7.62 per 10,000 patient-days in 2008 to 5.92 per 10,000 patient-days in 2009; since 2010, HA-CDI rates have been increasing.

Regionally, HA-CDI rates per 10,000 patient-days in the Western region increased from 2007 to 2008; however, it has since been decreasing. In the Central region, HA-CDI rates per 10,000 patient-days decreased between 2007 and 2009; after which the rate of HA-CDI has steadily increased. HA-CDI rates per 10,000 patient-days in the Eastern region decreased between 2007 and 2010 but showed a slight increase 2011. Overall, although all three regions had a statistically significant decrease in their rates, annual fluctuation in the rates showed that this decrease is small (Table 2, Figure 4).

**Figure 4. National and regional HA-CDI incidence rates in adults per 10,000 patient-days, January 1, 2007 to December 31, 2012, N= 18,291**




| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| West | 6.16 | 8.41 | 6.93 | 7.04 | 5.87 | 5.87 |
| Central | 8.54 | 8.28 | 5.98 | 6.72 | 7.91 | 7.22 |
| East | 3.92 | 3.92 | 3.26 | 2.28 | 2.96 | 2.67 |
| Overall | 6.93 | 7.62 | 5.92 | 6.21 | 6.72 | 6.12 |

### 1.3 HA-CDI in Children in Canada: National HA-CDI surveillance from January 1, 2007 to December 31, 2012

Table 3 provides the number of HA-CDI cases and rates in children between one years of age and less than 18 years of age per 1,000 patient admission and 10,000 patient-days by year and region. This section reports on the nine pediatric stand-alone hospitals only. Pediatric patients admitted to a hospital providing services to both adult and pediatric patients are not included in the calculation of pediatric HA-CDI rates. The rates are also not provided by geographic region as there are too few hospitals to make a comparison by region.

A total of 677 children with HA-CDI were reported to CNISP. Of these 580 were reported by the pediatric stand-alone hospitals. The remaining 97 children were reported from a hospital providing services to both adult and pediatric patients.

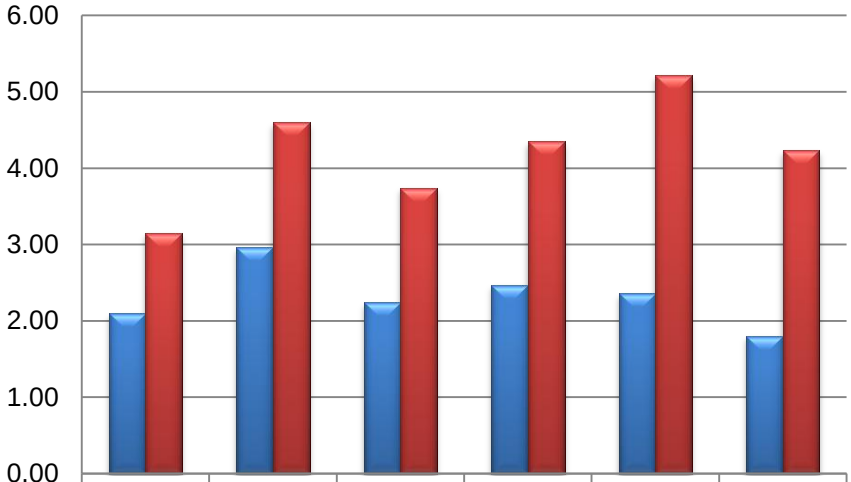
The overall rate of HA-CDI in children aged one year to less than 18 years of age was 1.80 cases per 1,000 patient admissions and 4.23 cases per 10,000 patient-days in 2012. The incidence rate decreased by almost quarter between 2011 and 2012; with the addition of one new pediatric hospital.

**Table 3. National HA-CDI rates in children admitted to stand-alone pediatric hospitals, January 1, 2007 to December 31, 2012, N = 580**

| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | *p* |
|---|---|---|---|---|---|---|---|
| **National** | | | | | | | |
| No. of HA-CDI cases | 64 | 97 | 81 | 102 | 128 | 108 | |
| No. of patient admissions | 30,484 | 32,763 | 36,213 | 41,373 | 54,237 | 59,998 | |
| No. of total patient days | 203,220 | 210,819 | 216,390 | 234,579 | 245,021 | 255,348 | |
| Rate per 1,000 admissions | 2.10 | 2.96 | 2.24 | 2.47 | 2.36 | 1.80 | 0.05 |
| Rate per 10,000 patient-days | 3.15 | 4.60 | 3.74 | 4.35 | 5.22 | 4.23 | 0.0005 |
| No. of hospitals | 7 | 7 | 7 | 8 | 8 | 9 | |

Figure 5 illustrates the national trend in annual HA-CDI rates in children from 2007 to 2012. Overall, there was no statistically significant change in HA-CDI rates per 1,000 patient admissions over (Table 3). The rate of HA-CDI in children per 1,000 patient admissions has significantly decreased over the surveillance years to a low of 1.80 cases per 1,000 patients admissions in 2012 ($p = 0.05$). However, the rate of HA-CDI per 10,000 patient-days has increased from 3.15 cases in 2007 to 5.22 cases in 2011, representing an increase of 65% ($p = 0.0005$). This increase may be related to the more severely ill children staying longer in hospitals whereas the less ill children have shorter hospital stays. The trend reversed in 2012.

**Figure 5. National HA-CDI rates in children per 1,000 patient admissions and 10,000 patient-days, January 1, 2007 to December 31, 2012, N = 580**




| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| per 1,000 admissions | 2.10 | 2.96 | 2.24 | 2.47 | 2.36 | 1.80 |
| per 10,000 patient-days | 3.15 | 4.60 | 3.74 | 4.35 | 5.22 | 4.23 |

## SECTION 2. Epidemiology of HA-CDI patients in Canada

### 2.1 Epidemiology of HA-CDI in Adult patients

A total of 18,194 adult cases of HA-CDI were reported to CNISP during the 6-year surveillance period. Detailed patient information was available on 10,517 (57.8% of all cases) adult patients as some hospitals report only aggregate (combined) data.

Table 4 provides the mean age and range of this group by year. The mean and median age remained relatively unchanged over the surveillance period.

**Table 4. Age and gender distribution of adult patients with HA-CDI, N = 10,517**

| | 2007 (n=656) | 2008 (n=477) | 2009 (n=1,627) | 2010 (n=2,310) | 2011 (n=2,797) | 2012 (n=2,650) |
|---|---|---|---|---|---|---|
| **Age (years)** | | | | | | |
| Mean | 70.5 | 70.7 | 69.6 | 70.4 | 69.4 | 69.6 |
| Median | 74 | 75 | 73 | 74 | 73 | 73 |
| Range | 18-101 | 20-100 | 18-101 | 18-109 | 18-104 | 18-103 |
| **Gender** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** |
| Male | 336 (51.2) | 245 (51.4) | 862 (53.0) | 1,130 (48.9) | 1,340 (47.9) | 1,374 (51.8) |

Table 5 shows location of the patient location at the time of CDI symptoms onset. The location at the time of onset was known for 10,328 cases. For the remaining 189 adults with HA-CDI, the location of the patient at the time of CDI symptoms onset could not be determined. Of the total cases, approximately half (51.1%) of the HA-CDI patients were in the medical ward at the time of CDI symptoms onset. The proportion of patient location remained relatively unchanged during the surveillance years.

**Table 5. Location of the adults with HA-CDI at the time of onset, N = 10,517**

| Location* | 2007 (n=656) No. (%) | 2008 (n=477) No. (%) | 2009 (n=1,627) No. (%) | 2010 (n=2,310) No. (%) | 2011 (n=2,797) No. (%) | 2012 (n=2,650) No. (%) |
|---|---|---|---|---|---|---|
| Medical ward | 384 (58.5) | 262 (54.9) | 782 (48.1) | 1,196 (51.8) | 1,412 (50.5) | 1,339 (50.5) |
| Surgical ward | 127 (19.4) | 117 (24.5) | 400 (24.6) | 589 (25.5) | 740 (26.5) | 719 (27.1) |
| Intensive Care unit | 43 (6.6) | 31 (6.5) | 161 (9.9) | 223 (9.7) | 272 (9.7) | 268 (10.1) |
| Combined ward | 22 (3.4) | 13 (2.7) | 53 (3.3) | 72 (3.1) | 94 (3.4) | 158 (6.0) |
| Emergency | 8 (1.2) | 5 (1.1) | 11 (0.7) | 12 (0.5) | 25 (0.9) | 20 (0.8) |
| Long-term care facility | 10 (1.5) | 8 (1.7) | 21 (1.3) | 16 (0.7) | 15 (0.5) | 10 (0.4) |
| Home | 47 (7.2) | 33 (6.9) | 110 (6.8) | 159 (6.9) | 181 (6.5) | 84 (3.2) |
| Other | 2 (0.3) | 1 (0.2) | 8 (0.5) | 17 (0.7) | 16 (0.6) | 35 (1.3) |
| Unknown location | 13 (2.0) | 7 (1.5) | 81 (5.0) | 27 (1.2) | 44 (1.6) | 17 (0.6) |

* Combined ward includes medical and surgical patients. Other includes another acute care facility other than the reporting facility, case room, retirement homes or group homes etc.

### Severe outcomes in adults

Severe outcomes in adults aged 18 years and older with HA-CDI were collected between March 1st and April 31st of each year. Of the 18,194 total adult cases of HA-CDI reported to CNISP over the course of the 6-year surveillance period, 3,226 (17.7%) cases were reported during March and April of each year. The proportion of patients admitted to ICU for HA-CDI complications ranged from a low of 0.6% in 2012 to a high of 2.9% in 2010 (Table 6).

**Table 6. Admissions to ICU among adult patients with HA-CDI, N= 3,226***

| Admissions to ICU | 2007 (N=626) No. (%) | 2008 (N=465) No. (%) | 2009 (N=560) No. (%) | 2010 (N=479) No. (%) | 2011 (N=564) No. (%) | 2012 (N=532) No. (%) |
|---|---|---|---|---|---|---|
| Yes, for the complication of CDI | 13 (2.1) | 6 (1.3) | 12 (2.1) | 14 (2.9) | 10 (1.8) | 3 (0.6) |
| Yes, for reasons other than CDI | 50 (8.0) | 32 (6.9) | 30 (5.4) | 13 (2.8) | 25 (4.4) | 27 (5.1) |

*Admissions to ICU data were collected during the two-month (March and April of each year) for adults aged 18 years and older.

Table 7 shows the number of adults with HA-CDI who required a colectomy due to complications associated with CDI. The proportion of patients requiring a colectomy remained relatively constant over the 6-year surveillance period ranging from 1.1% in 2011 to 1.9% in 2010.

**Table 7. Colectomy among adult patients with HA-CDI, N= 3,226***

| Colectomy | 2007 (N=626) No. (%) | 2008 (N=465) No. (%) | 2009 (N=560) No. (%) | 2010 (N=479) No. (%) | 2011 (N=564) No. (%) | 2012 (N=532) No. (%) |
|---|---|---|---|---|---|---|
| Yes | 9 (1.4) | 8 (1.7) | 9 (1.6) | 9 (1.9) | 6 (1.1) | 9 (1.7) |

*Colectomy data were collected during the two-month (March and April of each year) for adults for adults aged 18 years and older.

Table 8 provides the number of patients who died from all causes 30 days after the onset of HA-CDI. A total of 454 (14.1%) adult patients with HA-CDI died within 30 days of onset of HA-CDI. The all-cause mortality ranged from 12.5% in 2010 to 15.8% in 2007. The all-cause mortality rate fluctuated and showed no clear trend over time during the 6-year surveillance period (p-value: 0.22).

**Table 8. All-cause mortality in adult patients with HA-CDI 30 days after the onset, N= 3,226***

| Outcome | 2007 (N=626) | 2008 (N=465) | 2009 (N=560) | 2010 (N=479) | 2011 (N=564) | 2012 (N=532) | *p* |
|---|---|---|---|---|---|---|---|
| No. of deaths | 99 | 62 | 81 | 60 | 84 | 68 | |
| All-cause mortality (%) | 15.8 | 13.3 | 14.5 | 12.5 | 14.9 | 12.8 | 0.22 |

* Mortality data were collected during the two-month (March and April of each year) for adults 18 years of age and older

Table 9 provides information on the number of deaths in adults with HA-CDI that were related to CDI. The medical records of all 454 adult patients with HA-CDI who died within 30 days of onset were assessed by the CHEC member or his/her delegate to determine if HA-CDI was directly related to the death of the patient or if HA-CDI had contributed to the death of the patient but was not the primary cause.

Of the 454 cases who died, 152 were directly or indirectly related to HA-CDI. The overall attributable mortality rate was 4.7%. The attributable mortality rate increased by 33.3% from 2007 to 2011, though there was a marked decrease in 2009 (Table 9).

**Table 9. Number of adult patients with HA-CDI that died and the attributable mortality rate 30 days after onset, N = 3,226***

| Outcome | 2007 (N=626) | 2008 (N=465) | 2009 (N=560) | 2010 (N=479) | 2011 (N=564) | 2012 (N=532) | *p* |
|---|---|---|---|---|---|---|---|
| No. of deaths directly or indirectly related to HA-CDI | 30 | 23 | 13 | 26 | 36 | 24 | |
| No. of deaths not related to HA-CDI | 62 | 34 | 47 | 25 | 44 | 37 | |
| No. of deaths but unable to judge | 7 | 5 | 21 | 9 | 4 | 7 | |
| Attributable mortality rate (%)* | 4.8 | 4.9 | 2.3 | 5.4 | 6.4 | 4.5 | 0.43 |

* Deaths directly or indirectly related to HA-CDI 30 days after the onset of symptoms. Data on the cause or contributing factor to death are collected during the two-month (March and April of each year) for adults 18 years of age and older.

### 2.2 Epidemiology of HA-CDI in Children

A total of 677 children with HA-CDI were reported to CNISP. Of these, 580 were reported by the pediatric stand-alone hospitals. The remaining 97 children were reported from a hospital providing services to both adult and pediatric patients.

Detailed information on children with HA-CDI was collected only between March 1st and April 30th in 2007 and 2008. Starting in 2009, detailed information was collected over the course of the entire surveillance year, i.e. January 1st to December 31st of each year.

Table 10 provides the age distribution of the children by year. The mean and median age remained relatively unchanged over the surveillance period. The majority were children aged between 2 and less than 12 year of age (n = 391, 57.8%) followed by children aged 12 to less than 18 years of age (n = 242, 35.7%). Only 6.5% (n=44) of the pediatric cases were children between aged one year to less than two years of age.

### Table 10. Age and gender distribution of children with HA-CDI, N = 677

| | 2007 (n=33) | 2008 (n= 22) | 2009 (n=148) | 2010 (n=148) | 2011 (n=174) | 2012 (n=152) |
|---|---|---|---|---|---|---|
| **Age (years)** | | | | | | |
| 1 to < 2 | 3 (9.1) | 3 (13.6) | 8 (5.4) | 10 (6.8) | 6 (3.5) | 14 (9.2) |
| 2 to <12 | 18 (54.5) | 13 (59.1) | 90 (60.8) | 86 (58.1) | 102 (58.6) | 82 (54.0) |
| 12 to <18 | 12 (36.4) | 6 (27.3) | 50 (33.8) | 52 (35.1) | 66 (37.9) | 56 (36.8) |
| **Gender** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** | **No. (%)** |
| Male | 12 (36.4) | 13 (59.1) | 72 (48.6) | 82 (55.4) | 99 (56.9) | 92 (60.5) |

Table 11 provides the locations of the children with HA-CDI at the time of symptom onset. More than a quarter (27.2%, n = 184) of the children with HA-CDI were on a hematology/oncology ward at the time of symptom onset. Of the remaining children with HA-CDI, 126 (18.6%) were on a medical ward and 105 (15.5%) were a surgical ward. In addition 76 children were on high risk units; i.e. 48 (7.1%) in an intensive care unit and 28 (4.1%) on a dedicated bone marrow transplant unit.

### Table 11. Location of the children with HA-CDI at the time of onset, N= 677*

| Location* | 2007† (n= 33) No. (%) | 2008 (n= 22) No. (%) | 2009 (n=148) No. (%) | 2010 (n= 148) No. (%) | 2011 (n= 174) No. (%) | 2012 (n= 152) No. (%) |
|---|---|---|---|---|---|---|
| Hematology/Oncology | 4 (12.1) | 2 (9.1) | 49 (33.1) | 32 (21.6) | 49 (28.2) | 48 (31.6) |
| Medical ward | 0 | 9 (40.9) | 24 (16.2) | 37 (25.0) | 31 (17.8) | 25 (16.5) |
| Surgical ward | 4 (12.1) | 3 (13.6) | 27 (18.4) | 19 (12.8) | 28 (16.1) | 24 (15.8) |
| Combined ward | 5 (15.2) | 2 (9.1) | 13 (8.8) | 16 (10.8) | 2 (1.2) | 18 (11.8) |
| Home | 9 (27.3) | 4 (18.2) | 7 (5.0) | 17 (12.0) | 14 (9.7) | 4 (2.6) |
| Intensive care units | 2 (6.1) | 0 | 8 (5.4) | 12 (8.1) | 8 (4.6) | 18 (11.8) |
| Bone marrow transplant | 1 (3.0) | 1 (4.6) | 10 (6.8) | 5 (3.4) | 7 (4.0) | 4 (2.6) |
| Other | 0 | 0 | 1(0.7) | 3 (2.0) | 2 (1.2) | 2 (1.3) |
| Unknown location | 8 (24.2) | 1 (4.6) | 9 (6.1) | 7 (4.7) | 33 (19.0) | 9 (5.9) |

* Combined ward includes medical and surgical patients; Other includes technology dependant unit or other (unspecified).
† Detailed information on children with HA-CDI was collected only in March and April in 2007 and 2008

### Severe outcomes in children

Severe outcomes in children aged one to less than 18 years with HA-CDI were collected between March 1st and April 31st in 2007 and 2009. Starting in 2009, information on severe outcomes was collected throughout the surveillance year, i.e. January 1st to December 31st in 2009 to 2012.

Table 12 provides information on the number of children with HA-CDI who were admitted to an intensive care unit (ICU) for complications related to HA-CDI. Approximately 1% of HA-CDI patients admitted to ICU were due to complications from CDI. Five (0.7%) HA-CDI patients required a colectomy due to CDI.

**Table 12. Admissions to ICU and colectomies among children with HA-CDI, N= 677***

| Outcome | 2007* (n=33) No. (%) | 2008 (n-22) No. (%) | 2009 (n=148) No. (%) | 2010 (n=148) No. (%) | 2001 (n=174) No. (%) | 2012 (n=152) No. (%) |
|---|---|---|---|---|---|---|
| Admitted to ICU | 0 | 0 | 1 (0.7) | 2 (1.4) | 2 (1.1) | 2 (1.3) |
| Colectomy | 0 | 0 | 0 | 2 (1.4) | 0 | 3 (2.0) |

* Detailed information on children with HA-CDI was collected only in March and April in 2007 and 2008

Table 13 provides information on the children with HA-CDI who died within 30 days of onset of CDI. A total of eight (1.2%) children died from all causes within 30 days of onset of HA-CDI. The medical records of all eight children with HA-CDI who died within 30 days of onset were assessed by the CHEC member or his/her delegate to determine if HA-CDI was directly related to the death of the patient or if HA-CDI had contributed to the death of the patient but was not the primary cause. Only one (0.6%) death in 2009 was attributable to HA-CDI.

**Table 13. All-cause mortality in children with HA-CDI 30 days after the onset, N= 677***

| Outcome | 2007* (n=33) | 2008 (n=22) | 2009 (n=148) | 2010 (n=148) | 2011 (n=174) | 2012 (n=152) |
|---|---|---|---|---|---|---|
| Number of deaths | 0 | 0 | 2 | 2 | 4 | 0 |
| All-cause mortality (%) | 0 | 0 | 1.4 | 1.4 | 2.3 | 0 |
| Number of deaths directly or indirectly related to HA-CDI | 0 | 0 | 1 | 0 | 0 | 0 |

* Detailed information on children with HA-CDI was collected only in March and April in 2007 and 2008

### Section 3 *Clostridium difficile* Strain Types in Canada

Stool specimens in adult patients 18 years of age and older with HA-CDI were collected and submitted to NML between March 1st and April 30th of each year. Therefore, the number of *C.difficile* retrieved from the stool specimens and analysed is a subset of the number of cases HA-CDI reported in adult patients. Stool specimens of children aged one year to less than 18 years with HA-CDI were submitted year round to NML, starting in 2009. In 2007 and 2008, stool specimens from children with HA-CDI were only submitted between March 1st and April 30th in each year.

From 2007 to 2012, laboratory results were available for 2,497 HA-CDI cases in both adults and children from a total of 3,422 eligible cases. Toxigenic *C.difficile* were not isolated from the remaining 925 stool specimens although the patients all had a positive toxin assay or PCR test as determined by the hospital laboratory. The overall recovery rate for *C.difficile* was 73.0%.

### 3.1 National distribution of *Clostridium difficile* strain types

Table 14 provides information on the pulsed field gel electrophoresis (PFGE) strain type of the *C.difficile* isolates retrieved from the stool specimens submitted from patients with HA-CDI over the 6-year surveillance period. Overall, the North American pulsed field type 1 (NAP1) strain was the most dominant strain type; followed by the NAP4 strain and NAP2 strain. Of the 2,497 submitted stool specimens, the NAP1 strain was found in 1,059 (42.4%) specimens; 11.0% were NAP4 strain type and 10.3% were NAP2.

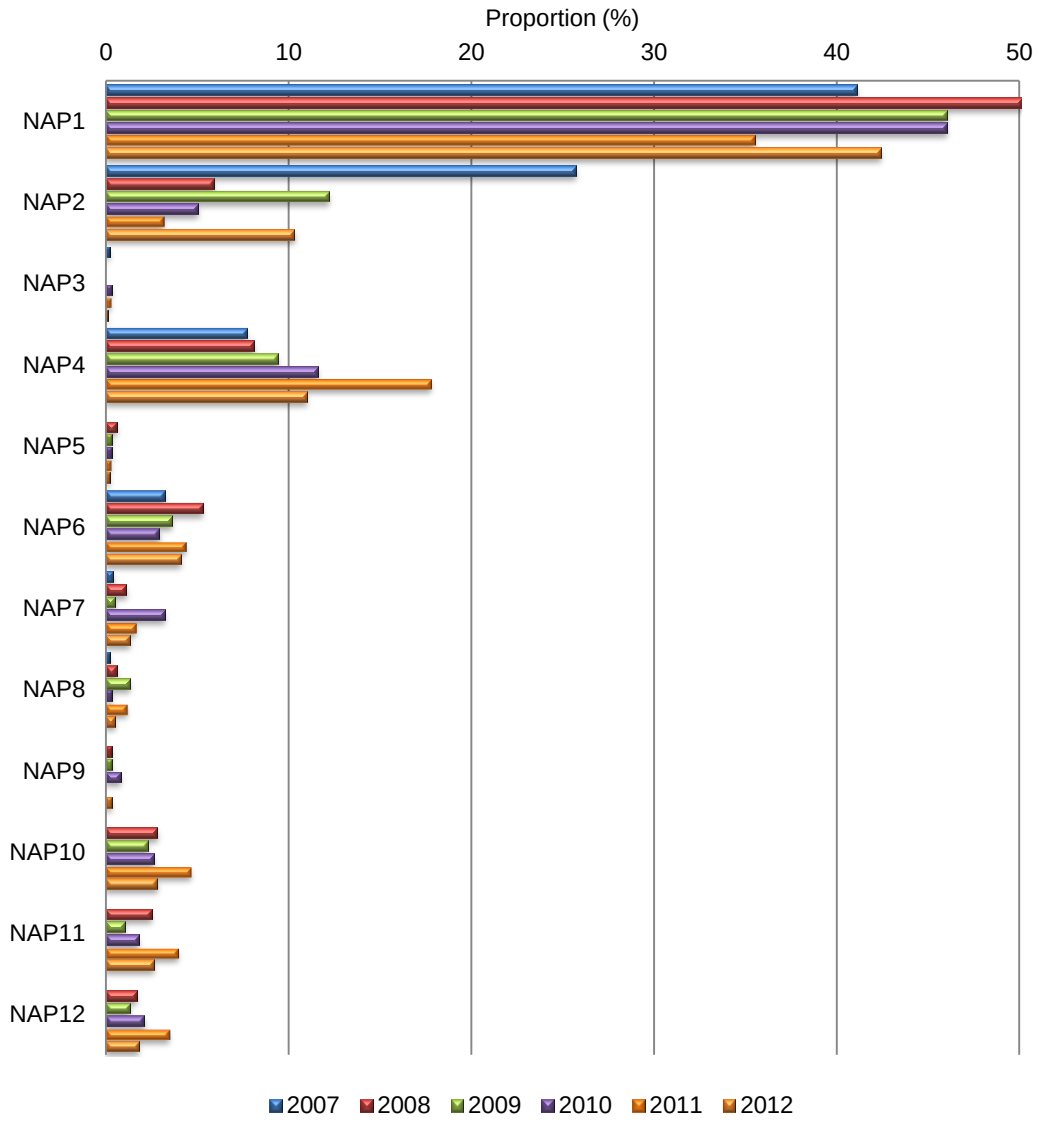
**Table 14. Number and proportion of *C.difficile* NAP strain types, 2007 to 2012, N=2,497**

| Strain type | 2007 (n=557) | 2008 (n=357) | 2009 (n=393) | 2010 (n=380) | 2011 (n=405) | 2012 (n=405) | Overall (n=2,497) |
|---|---|---|---|---|---|---|---|
| | No. (%) | No. (%) | No. (%) | No. (%) | No. (%) | No. (%) | No. (%) |
| NAP1 | 229 (41.1) | 179 (50.1) | 181 (46.0) | 175 (46.0) | 144 (35.5) | 151 (37.3) | 1,059 (42.4) |
| NAP2 | 143 (25.7) | 21 (5.9) | 48 (12.2) | 19 (5.0) | 13 (3.2) | 14 (3.5) | 258 (10.3) |
| NAP3 | 1 (0.2) | 0 (0.0) | 0 (0.0) | 1 (0.3) | 1 (0.3) | 0 (0.0) | 3 (0.1) |
| NAP4 | 43 (7.7) | 29 (8.1) | 37 (9.4) | 44 (11.6) | 72 (17.8) | 50 (12.4) | 275 (11.0) |
| NAP5 | 0 (0.0) | 2 (0.6) | 1 (0.3) | 1 (0.3) | 1 (0.3) | 0 (0.0) | 5 (0.2) |
| NAP6 | 18 (3.2) | 19 (5.3) | 14 (3.6) | 11 (2.9) | 18 (4.4) | 22 (5.4) | 102 (4.1) |
| NAP7 | 2 (0.4) | 4 (1.1) | 2 (0.5) | 12 (3.2) | 7 (1.7) | 6 (1.5) | 33 (1.3) |
| NAP8 | 1 (0.2) | 2 (0.6) | 5 (1.3) | 1 (0.3) | 5 (1.2) | 0 (0.0) | 14 (0.6) |
| NAP9 | 0 (0.0) | 1 (0.3) | 1 (0.3) | 3 (0.8) | 0 (0.0) | 2 (0.5) | 7 (0.3) |
| NAP10 | 0 (0.0) | 10 (2.8) | 9 (2.3) | 10 (2.6) | 19 (4.7) | 23 (5.7) | 71 (2.8) |
| NAP11 | 0 (0.0) | 9 (2.5) | 4 (1.0) | 7 (1.8) | 16 (4.0) | 30 (7.4) | 66 (2.6) |
| NAP12 | 0 (0.0) | 6 (1.7) | 5 (1.3) | 8 (2.1) | 14 (3.5) | 13 (3.2) | 46 (1.8) |
| Other-not assigned | 120 (21.5) | 75 (21.0) | 86 (21.8) | 88 (23.1) | 95 (23.4) | 94 (23.1) | 558 (22.3) |

There is a marked variability in the distribution of the strain types over the 6-year surveillance period (Table 14, Figure 6). The proportion of NAP1 strains ranged from 35.5% to 50.1%, peaking in 2008. In 2012, the proportion of NAP1 strains among all specimens was 37.3%. This represents a decrease of almost 30% when compared to 2008 where the NAP1 strain was found in 50.1% of all submitted stool specimens. Conversely, the NAP4 strain type more than doubled in the first five years of surveillance; from a low of 7.7% in 2007 to almost a fifth (17.8%) of all strains in 2011. The proportion of NAP4 strain type increased by 69.2% from 2008 to 2009 and by an additional 63.6% from 2010 to 2011. In addition, the NAP11 strain has also increased significantly in the 6-year surveillance period, from no strains in 2007 to 4.0% of all strains in 2011 (p-value: <0.0001). The proportion of all specimens with the NAP11 strain almost doubled between 2011 and 2012; from 4.0% in 2011 to 7.4% in 2012 (p-value: <0.0001). The proportion of NAP2 was the highest in 2007(25.7%) but has since declined more than 6-fold (3.5% in 2012). The NAP strain types 3, 5 and 9 were rare with respective proportions less than

1% for all surveillance years; whereas the proportion of other-not assigned NAP type stayed relatively consistent over the surveillance years.

**Figure 6. National distribution of *C.difficile* NAP strain types, 2007 to 2012, N=2,497***




*Other-non assigned strain types not shown

### 3.2 National and regional distribution of select *Clostridium difficile* strain types

Table 15 provides information on the number and proportion of the most common *C.difficile* NAP strain types by geographic region.

Over the 6-year surveillance period, NAP1 remained the most common strain type isolated In the Western and Central regions although the proportion in the Central region was almost double the proportion in the Western region (48.7% vs. 27.0% in the Central and Western regions, respectively, $p$ = <0.0001). The NAP 1 strain type was isolated in 16.7% of stool

specimens from the Eastern region. In 2007 and 2008, the proportion of NAP1 strain types isolated in the Eastern region was unusually high (56.3% and 30.0%, respectively). These results must be interpreted with caution due to the small number of *C.difficile* isolates that were typed from this region. Less than 10% of eligible stool specimens were submitted in 2007 and 2008 (n = 48 of a total of 510 eligible cases).

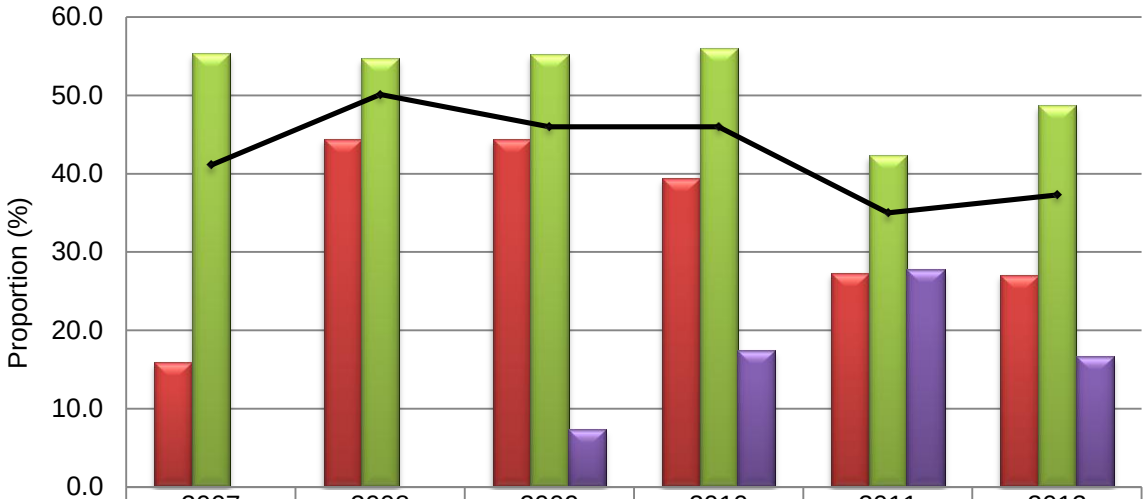
**Table 15. Number and proportion of select *C.difficile* NAP strain types by geographic region, 2007 to 2012, N=2,497**

| Strain Type | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| | No. (%) | No. (%) | No. (%) | No. (%) | No. (%) | No. (%) |
| **National, n = 2,497** | (n =557) | (n =357) | (n =393) | (n = 380) | (n = 405) | (n =405) |
| NAP1 | 229 (41.1) | 179 (50.1) | 181 (46.0) | 175 (46.0) | 144 (35.5) | 151 (37.3) |
| NAP2 | 143 (25.7) | 21 (5.9) | 48 (12.2) | 19 (5.0) | 13 (3.2) | 14 (3.5) |
| NAP4 | 43 (7.7) | 29 (8.1) | 37 (9.4) | 44 (11.6) | 72 (17.8) | 50 (12.4) |
| Other NAP types* | 22 (3.9) | 53 (14.8) | 41 (10.4) | 54 (14.2) | 81 (20.0) | 96 (23.7) |
| Other-not assigned | 120 (21.5) | 75 (21.0) | 86 (21.8) | 88 (23.1) | 95 (23.4) | 94 (23.1) |
| **West, n = 1,076** | (n =195) | (n = 133) | (n = 212) | (n =175) | (n = 165) | (n =196) |
| NAP1 | 29 (14.9) | 59 (44.4) | 94 (44.3) | 69 (39.4) | 45 (27.3) | 53 (27.0) |
| NAP2 | 101 (51.8) | 11 (8.2) | 28 (13.1) | 16 (8.4) | 12 (6.1) | 5 (2.6) |
| NAP4 | 17 (8.7) | 14 (10.5) | 16 (7.5) | 23 (13.1) | 30 (18.2) | 29 (14.8) |
| Other NAP types* | 4 (2.1) | 15 (11.3) | 21 (10.0) | 25 (14.2) | 26 (15.8) | 57 (29.1) |
| Other-not assigned | 44 (22.6) | 34 (25.6) | 53 (25.0) | 42 (24.0) | 52 (31.5) | 52 (26.5) |
| **Central, n = 1,293** | (n =324) | (n = 214) | (n = 154) | (n =182) | (n = 222) | (n =197) |
| NAP1 | 179 (55.3) | 117 (54.7) | 85 (55.2) | 102 (56.0) | 94 (42.3) | 96 (48.7) |
| NAP2 | 42 (12.8) | 10 (4.7) | 16 (9.0) | 3 (1.4) | 4 (1.5) | 9 (4,6) |
| NAP4 | 23 (7.1) | 14 (6.5) | 17 (11.0) | 18 (9.9) | 36 (16.2) | 18 (9.1) |
| Other NAP types* | 18 (5.6) | 36 (16.8) | 13 (8.4) | 22 (12.1) | 46 (20.7) | 38 (19.3) |
| Other-not assigned | 62 (19.1) | 37 (17.3) | 23 (14.9) | 37 (20.3) | 42 (18.9) | 36 (18.3) |
| **East, n = 128** | (n =38) | (n = 10) | (n = 27) | (n =23) | (n = 18) | (n =12) |
| NAP1 | 21 (56.3) | 3 (30.0) | 2 (7.4) | 4 (17.4) | 5 (27.8) | 2 (16.7) |
| NAP2 | 0 | 0 | 6 (20.0) | 1 (3.7) | 1 (4.6) | 0 |
| NAP4 | 3 (7.9) | 1 (10.0) | 4 (14.8) | 3 (13.0) | 6 (33.3) | 3 (25.0) |
| Other NAP types* | 0 | 0 | 5 (18.5) | 6 (26.1) | 5 (27.8) | 1 (8.3) |
| Other-not assigned | 14 (36.8) | 4 (40.0) | 10 (37.0) | 9 (39.1) | 1 (5.6) | 6 (50.0) |

*Other NAP strain types include NAP3, NAP5, NAP6, NAP7, NAP8, NAP9, NAP10, NAP11 and NAP12.

Figure 7 shows the distribution of *C.difficile* NAP1 strain type by region over the 6-year surveillance. The proportion of the NAP1 strain type in the Eastern region is not shown for 2007 and 2008 as less than 10% of the eligible stool specimens were submitted during those two surveillance years.

**Figure 7. Distribution of *C.difficile* NAP1 strain type by region, 2007 to 2012 (N=1,059)***




| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| West | 15.9 | 44.4 | 44.3 | 39.4 | 27.3 | 27.1 |
| Central | 55.3 | 54.7 | 55.2 | 56.0 | 42.3 | 48.7 |
| East | | | 7.4 | 17.4 | 27.8 | 16.7 |
| Overall | 41.1 | 50.1 | 46.0 | 46.0 | 35.0 | 37.3 |

*****The proportion of NAP1 reported in the Eastern region in 2007 and 2008 is not presented as the sample size is too small to make a comparison with the other geographic regions.

## LIMITATIONS

Several limitations should be considered when interpreting the data presented in this report.

First, surveillance data understates the magnitude of HA-CDI and subsequently does not represent the total number of inpatients with HA-CDI in Canada. Surveillance data can only tell us about inpatients who have been tested and diagnosed with HA-CDI and not those who remain untested and undiagnosed. In addition, 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.

Second, these data only include hospitalized patients, therefore cases identified in outpatient settings such as emergency departments and clinics are not captured by this surveillance system. Furthermore, only cases who were hospitalized at participating hospitals were included. Seasonal variations in CDI incidence may also influence the overall annual rates.

Third, participating hospitals may not be representative of all Canadian hospitals. Hospitals which submit HA-CDI data to the Agency are large, tertiary acute care centres located in major cities. HA-CDI data from small hospitals and those in rural and northern areas are underrepresented.

Fourth, antibiotic prescribing practices and implementation of infection prevention and control measures may vary between hospitals, but because the Agency does not collect data regarding these factors, it was not possible to correlate them with the occurrence of HA-CDI. As well, since the diagnosis of a 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.

Fifth, healthcare-associated infection surveillance methodologies are not standardized across countries. For this reason, caution must be used when comparing rates between countries without knowing the details of their surveillance strategies.

## DISCUSSION

When comparing the surveillance data in this report with the previously reported 2005 HA-CDI rates, HA-CDI has risen slightly in Canada. [7] Between 2007 and 2012, the average overall rate of HA-CDI was 4.89 (ranged from 4.51 to 5.84) cases per 1,000 patient admissions and 6.56 (ranged from 5.81 to 7.47) cases per 10,000 patient-days. In comparison, the prospective surveillance by CNISP in 2005 reported the rate of HA-CDI for all patients (adult and pediatric patients combined) was 4.5 cases per 1,000 patient admissions and 6.4 cases per 10,000 patient-days from 2004 to 2005. The slight increase in overall HA-CDI rates reported during this surveillance period is probably due to two HA-CDI peaks experienced one in 2008 (5.84 cases per 1,000 patient admissions) and another in 2011 (5.09 cases per 1,000 patient admissions). This trend could also be driven by the regional variations where the Western and Eastern HA-CDI rates peaked in 2008 and 2012, respectively. This regional variation contributed to the overall HA-CDI fluctuation where it decreased by 20% (per 1,000 patient admissions) in 2009, remained stable through 2010, before increasing again by 5% in 2012.

There are several reasons that could explain such fluctuations in the data experienced over a relatively short period of time. Firstly, the downward trend in 2009 coincided with the time when *C.difficile* became recognized as a Nationally Notifiable Disease in Canada and a reportable disease in several provincial jurisdictions. This trend is akin to other countries such as England, which experienced a significant decrease in CDI rates following the implementation of a mandatory reporting system. Such public reporting heightens awareness in healthcare settings that promotes better prevention strategies, antimicrobial stewardship as well as more rigorous use of the CDI criteria. All these factors may have contributed to reduction of HA-CDI that was potentially triggered by mandatory reporting. Another possible factor for such variation in the HA-CDI rate could have been the arrival of H1N1 in 2009, which may have contributed to under-reporting of CDI due to human resource challenges. As well, the increase in HA-CDI in 2011 may be due in part to several CDI outbreaks that occurred across the country in 2011.

Other countries have taken similar reporting initiatives to determine and report their national rates for HA-CDI while/after experiencing an increase in CDI rates. England for example is a country that has experienced a dramatic increase in HA-CDI rates since late 1990 to mid-2000. When the mandatory reporting was implemented in England in 2007, there was a reduction in HA-CDI rates. Following the mandatory reporting of CDI, the incidence rate per 10,000 patient-days was 3.4 in 2010 which is a 54% reduction from the rates in 2007 in England. [9] Finland has also reported a reduction in HA-CDI since the country launched its enhanced CDI surveillance in 2008. As a result, HA-CDI rates in Finland have decreased from 3.1 per 10,000 patient-days in 2008 to 2.3 per 10,000 patient-days in 2010. [10]

Data from the Center for Disease Prevention and Control (CDC) report documented that the HA-CDI rates in the US have declined 20% from 9.3 cases per 10,000 patient-days to 7.5 cases per 10,000 patient-days between May 2008 and October 2011. The study was based on 71 hospitals in three states (Illinois, Massachusetts and New York). [11] It is important to note that the HA-CDI rates from this report and the U.S are higher than the rates from countries mentioned previously. Although HA-CDI rates in Canada and in the US are both consistently higher than other countries, it is difficult to draw a direct comparison given that the healthcare systems of the respective countries differ greatly. The following summary table illustrates and compares the HA-CDI rates in Canada, US, England and Finland.

### Summary Table 1. Overall HA-CDI rates per 10,000 patient-days

| Country (Surveillance network) | 2007 | 2008 | 2009 | 2010 | 2011 |
|---|---|---|---|---|---|
| Canada (CNISP) | 6.77 | 7.02 | 5.80 | 6.09 | 6.82 |
| US-CDC | N/A | 9.3 | N/A | N/A | 7.5 |
| England* | 7.4 | 4.7 | 3.4 | N/A | N/A |
| Finland (SIRO) | N/A | 3.1 | 3.1 | 2.3 | N/A |

* Rates are calculated based on the financial years (i.e. 2007/2008, 2008/2009 etc.), N/A – not available
SIRO – Finnish Hospital Infection Program

In Canada, the overall pediatric HA-CDI rate per 1,000 patient admissions was 2.42, which remained relatively stable from 2007 to 2011, with a decrease in 2012. Since there is insufficient international data on the pediatric HA-CDI in the literature, a direct comparison of the pediatric HA-CDI trend over time between countries was not feasible. However, a US study reported that the incidence rate of pediatric hospitalizations with *C.difficile* infection increased from 7.24 to 12.80 per 10,000 hospitalizations between 1997 and 2006. [12] It is important to note that a direct comparison of the pediatric HA-CDI incidence rates from this study to the US study was not possible because their study period was different from the study period in this report. Further, the US study used the International Classification of Diseases, 9$^{th}$ revision, clinical modification (ICD-9-CM) to determine CDI cases in the administrative database whereas the cases in this study were determined by directly applying the CNISP surveillance definition to classify only HA-CDI cases. Therefore, the rate from the US study does not represent the HA-CDI rates; rather, it illustrates the overall CDI rates in a hospitalized pediatric population. Though we could not directly compare CDI rates between Canada and the US, it is important to acknowledge that the overall incidences of CDI in the pediatric population are on the rise.

In comparison to the stable pediatric HA-CDI rates per 1,000 admissions between 2007 and 2011 in this study, it shows that the pediatric HA-CDI rates per 10,000 patient-days have increased significantly from 3.15 in 2007 to 5.22 in 2011 before decreasing in 2012 to 4.23 per 10,000 patient-days. This increase may be related to the more severely ill children staying longer in hospitals whereas the less ill children have shorter hospital stays. A similar increase in the CDI rates per 10,000 patient-days among children was also reported in the US. A study by Kim et al. reported an increase in CDI rates among inpatients at children's hospitals in the US from 4.4 to 6.5 cases per 10,000 patient-days between 2001 and 2006. [13] Although the study period of this American study did not coincide with our study, the data still reflects the fact the pediatric incidence rate of CDI per 10,000 patient-days appears to be increasing over time in the US and Canada.

Although this study indicates that the pediatric HA-CDI rates per 10,000 patient-days have increased over time, the all-cause mortality rates have remained relatively unchanged. Although eight children with HA-CDI died over the 6-year surveillance period (all-cause mortality rate of 1.6%); CDI has been a contributing factor in only one child (CDI attributable mortality rate of 0.6%) individual since 2007. Similarly, a study from the US also reported that mortality rates among pediatric CDI patients did not change over time. [13]

The all-cause mortality at 30 days after the date of the first positive CDI culture in adults was 15.1% which remained relatively unchanged over time between 2007 and 2012. This finding is consistent with the previously published Canadian study in 2005 which reported a16.3% all-cause mortality in adults. [7] A similar all-cause mortality rate in adults was reported in other

countries. For example, a multicentre cohort study in 13 Dutch hospitals reported an all-cause 30-day mortality of 13%. [14]

The overall CDI attributable mortality rate in adults over the surveillance period was 5.0%. This represents a sizeable proportion of the patients with HA-CDI. The attributable mortality rate in this study was slightly lower than the previously reported rate of 5.7% in 2005 in Canada. [7] However, the overall attributable mortality data in this report should be interpreted with caution due to the wide variability across the respective surveillance years from 2.3% to 6.4% in adults. Further, the previously reported attributable mortality rate was based on a much shorter surveillance period of 6 months compared to this study.

Internationally, between 2005 and 2012, CDI attributable mortality rates varied from 5.7% to 6.9%. These rates were based on three separate studies (two from Canada, including the Agency's study from 2005, and one from the US). [15] The CDI attributable mortality rate of 5.0% for the 2007 to 2012 surveillance period presented here was slightly lower than other currently available rates.

Overall NAP1 was the most common strain type in CNISP hospitals, accounting for 43.4% of all HA-CDI episodes from 2007-2011. Comparative studies in the literature are limited, but the prevalence of NAP1 (ribotype 027) in 2010 from 6 US healthcare institutions was found to be 29% (95% CI 13-45%). [16] In this study, the prevalence of NAP1 has declined since 2008 from 50.1% to 35.5%. Similar trends have been reported in England, where the prevalence of NAP1 (ribotype 027) decreased markedly from 55% in 2007–2008 to 36% and 21% in 2008–2009 and 2009–2010, respectively [17]. NAP4 (ribotype 14/20) was the most prevalent strain type (16%) in a pan-European survey [18] and the second most prevalent strain type in this study and in 6 US healthcare institutions, accounting for 10.8% and 12% of typed isolates, respectively. [16] The proportion of NAP4 in CNISP hospitals has significantly increased from 7.7% in 2007 to 17.8% in 2011. Similar trends have been observed in England where NAP4 (ribotype 14/20) has increased from 3% in 2007-2008 to 8% in 2009-2010. [17]

In conclusion, the overall HA-CDI rates in Canada have fluctuated and varied by year and region. The rate peaked in 2008 but remained stable between 2009 and 2012. HA-CDI rates per 1,000 patient admissions in adults showed no significant trend over time while HA-CDI rates per 10,000 patient-days decreased between 2007 and 2012. The Central region had the highest rates with a slight decreasing trend over time; whereas the Eastern region had the lowest rates with a decreasing trend over time. The Western region had the similar rates to the Central region. HA-CDI rates per 1,000 patient admissions in children were stable during the surveillance period while HA-CDI rates per 10,000 patient days showed significant increasing trends over time in children.

The all-cause mortality and the attributable mortality rates were stable in both adults and children populations and the NAP1 strain type remains the most dominant *Clostridium difficile* strain type in Canada followed by the NAP4 strain type.

As a result, the Agency will continue to monitor HA-CDI on an ongoing basis in order to provide the benchmark rates and trend over time rates that hospitals and provincial and territorial authorities can use to develop and implement policies that can address HA-CDI.

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# APPENDIX

**Data sources**

The following individuals are members of the Canadian Nosocomial Infection Surveillance Program who submit CDI data to the Public Health Agency of Canada:

Natalie Bridger, Eastern Health-HSC, St. John's, NFLD;
Elizabeth Bryce, Vancouver Coastal Health Authority, Vancouver, BC;
John Conly, Foothills Medical Centre, Calgary, AB;
Janice de Heer, Interior Health Authority, Kelowna, BC;
John Embil, Health Sciences Centre, Winnipeg, MB;
Joanne Embree, Health Sciences Centre, Winnipeg, MB;
Gerald Evans, Kingston General Hospital, Kingston, ON;
Sarah Forgie, Stollery Children's Hospital, Edmonton, AB;
Charles Frenette, McGill University Health Centre, Montreal, QC;
Gregory German, Queen Elizabeth Hospital, Charlottetown, PEI;
David Haldane, Queen Elizabeth II Health Sciences Centre, Halifax, NS;
Deanna Hembroff, University Hospital of Northern BC, Prince George, BC;
Elizabeth Henderson, Alberta Health Services, Calgary, AB;
Michael John, London Health Sciences Centre, London, ON.;
Lynn Johnston, Queen Elizabeth II Health Sciences Centre, Halifax, NS;
Kevin Katz, North York General Hospital, Toronto, ON;
Pamela Kibsey, Royal Jubilee Hospital, Victoria, BC;
Magdalena Kuhn, South East Regional Health Authority, Moncton, NB;
Joanne Langley, IWK.Health Centre, Halifax, NS;
Bonita Lee, Stollery Children's Hospital, Edmonton, AB;
Camille Lemieux, University Health Network, Toronto, ON;
Victor Leung, Providence Health Care, Vancouver, BC;
Yves Longtin, SMBD-Jewish General Hospital, Montreal, QC;
Mark Loeb, Hamilton Health Sciences Corporation, Hamilton, ON;
Allison McGeer, Mount Sinai Hospital, Toronto, ON;
Dominik Mertz, Hamilton Health Sciences Corporation, Hamilton, ON;
Dorothy Moore, Montreal Children's Hospital, McGill University Health Centre, Montreal, QC;
Michael Mulvey, National Microbiology Laboratory, Public Health Agency of Canada;
Suzanne Pelletier, Health Sciences North, Sudbury, ON;
Caroline Quach, Montreal Children's Hospital, McGill University Health Centre, Montreal, QC;
Susan Richardson, Hospital for Sick Children, Toronto, ON;
Virginia Roth, The Ottawa Hospital, Ottawa, ON;
Andrew Simor, Sunnybrook Health Sciences Centre, Toronto, ON;
Stephanie Smith, University of Alberta Hospital, Edmonton, AB;
Paula Stagg, Western Memorial Hospital, Corner Brook, NL;
Kathryn Suh, The Ottawa Hospital, Ottawa, ON;
Geoffrey Taylor, University of Alberta Hospital, Edmonton, AB;
Nisha Thampi, Children's Hospital of Eastern Ontario, Ottawa, ON;
Eva Thomas, Children's and Women's Health Center, Vancouver, BC;
Nathalie Turgeon, CHUQ-Hôtel-Dieu, Québec, QC;
Mary Vearncombe, Sunnybrook Health Sciences Centre, Toronto, ON;
Joseph Vayalumkal, Alberta Children's Hospital, Calgary, AB;
Karl Weiss, Maisonneuve-Rosemont Hospital, Montreal, QC;
Alice Wong, Royal University Hospital, Saskatoon, SK.

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