



## Research Article

*Clostridium difficile* Infection: Incidence in an Australian SettingBrett G. Mitchell, PhD<sup>\*</sup>

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## SUMMARY

**Purpose:** The aim of this study is to determine the incidence of *Clostridium difficile* infection (CDI) in an Australian hospital and highlight considerations for other Asian countries that are considering establishing or modifying existing CDI surveillance programs.

**Methods:** An observational study design with dynamic population was used. Data from all persons hospitalized for more than 48 hours over 4 years in a tertiary hospital in Australia were analyzed. Persons with healthcare associated, healthcare facility onset CDIs were identified. The calculation of the relative risk was performed to compare the occurrence of CDI in different groups.

**Results:** Of the total 58,942 admissions examined, 158 admissions had CDI. The incidence of CDI per 1,000 admissions for the entire study period was 2.68 (95% confidence interval [2.28, 3.13]). There was a statistically significant increase in the incidence of CDI in 2010 compared to that of 2007 ( $p < .001$ ). The incidence of CDI increased from the 30–39-year age group onwards.

**Conclusion:** Comparisons between this study and others are challenging due to the lack of standardized definitions for CDI internationally. Noting the increases of CDI internationally and the associated mortality, there is increasing importance to monitor and report the incidence of this infection worldwide.

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## Introduction

*Clostridium difficile*, a bacterium that is a common cause of diarrhea in hospitalized patients, can cause a variety of infections, ranging from mild diarrhea to pseudomembranous colitis. The incidence and severity of *C. difficile* infection (CDI) is increasing around the world, particularly in the northern hemisphere (Collins, Hawkey, & Riley, 2013). The primary mode of transmission of *C. difficile* is person to person via the fecal-oral route (National Health and Medical Research Council, 2010). *C. difficile* can exist in vegetative or spore form, with spores acting as a reservoir for transmission, particularly in the healthcare environment via the healthcare workers' hands (Dumford, Nerandzic, Eckstein, & Donskey, 2009; Stuart & Marshall, 2011). The ingestion of the organism does not necessarily result in infection due to the protective effects of the colonic flora (Cartman, Heap, Kuehne, Cockayne, & Minton, 2010). Disruption of the normal flora can occur following exposure to antibiotics, chemotherapy, antiperistaltic drugs, and gastroenterological surgery (Cartman et al., 2010; Kassavin, Pham, Pascarella, Yen-Hong, & Goldfarb, 2013; Kuijper, Coignard, & Tull,

2006). Antibiotics are thought to be an important risk factor for CDI, with a large number of studies supporting the association between antibiotics and CDI (Pepin, Valiquette, & Cossette, 2005; Polgreen et al., 2007; Thomas, Stevenson, & Riley, 2003).

Diagnosis of CDI occurs through the testing of fecal samples at a microbiology laboratory. The laboratory diagnosis of CDI is made through the detection of *C. difficile* by culture and/or by detection of its toxins. Treatment for symptomatic CDI usually involves stopping the use of antibiotics where possible and/or prescribing either vancomycin or metronidazole. Prevention of CDI primarily consists of three elements. First, appropriate antibiotic usage, including correct administration, is important. Second, early instigation and continued use of CDI prevention and control strategies, such as isolation of symptomatic persons, can assist in preventing the spread within a healthcare environment. Third, ensuring high standards of environmental cleanliness in healthcare settings can assist in the prevention and control of CDI (Van Gessel, Riley, & McGregor, 2009). Nurses play a key role in each of these three strategies. The importance of these measures and the ways to understand the risks that CDI pose to patients are best demonstrated through studies examining mortality.

Recent literature examining mortality and CDI indicates that CDI has a significant adverse effect on hospitalized patients (Karas, Enoch, & Aliyu, 2010; Mitchell & Gardner, 2012; Mitchell, Gardner, & Hiller, 2013). In two reviews examining this topic,

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only one study examining CDI and mortality in an Asian setting was found. Furthermore, there have been limited studies published in English that described the incidence of CDI in Asia (Collins et al., 2013). Studies investigating the incidence and mortality of CDI in settings outside of Europe and North America are needed so that the epidemiology of CDI in these regions can be understood with appropriate interventions planned. This paper describes a study exploring the incidence of CDI in a large Australian hospital. It also highlights important considerations for other Asian countries that are considering establishing or modifying existing CDI surveillance programs. In addition, it is hoped that by highlighting this infection in an Asian journal, it will encourage others to publish in this area and address the current gap in epidemiological knowledge in the region.

## Methods

The aim of this study is to determine the incidence of CDI between January 1st, 2007 and December 30th, 2010 in an Australian hospital.

### Study design

To address the research questions, a retrospective observational design with dynamic population is used.

### Setting and sample

All persons aged 2 years or older and who were hospitalized at a tertiary referral hospital in Australia for more than 48 hours between January 1st, 2007 and December 31st, 2010 formed the study population. Persons in the study population are referred to as “admissions” throughout this paper. The hospital is a 500-bed hospital that provides a full range of services including an emergency department, intensive care, surgery, renal, children, chemotherapy and maternity services.

From the available data, those persons who developed CDI during their hospital stay were subsequently identified. A person was defined as having CDI if he or she had a positive stool sample result for *C. difficile* using either a laboratory assay (enzyme immunoassay or polymerase chain reaction) detecting toxin A and/or toxin B or culture, resulting in the isolation of *C. difficile* that is subsequently shown to produce toxin A and/or toxin B. The positive stool sample had to be collected more than 48 hours after admission to capture cases of healthcare-associated healthcare facility onset episodes of CDI (McDonald et al., 2007). All infectious episodes included in this study were such episodes. Any positive stool sample for *C. difficile* occurring in patients less than 2 years old or occurring within 8 weeks of the last positive test was excluded.

During the full study period, the microbiology department tested all diarrheal samples from the hospitalized patients, regardless of reason for hospitalization for *C. difficile*. Diarrhea was defined as an unformed stool that took the shape of the container.

### Ethical considerations

Ethical approval for this research was granted by two human research ethics committees (Tasmanian Human Research Ethics Committee and Australian Catholic University).

### Data collection

Data were retrieved from four different sources. These sources comprised data from the clinical coding department at the hospital, a government surveillance unit (The Tasmanian Infection

Prevention and Control Unit [TIPCU]), the Infection Prevention and Control Unit at the hospital, and a review of the patient administration system and medical records of each person who has CDI during the period.

To identify the population, all admissions aged 2 years and older who were admitted to the hospital for more than 48 hours were identified by the clinical coding department at the request of the researcher. To allow for the identification of persons who developed CDI during their hospital stay, the TIPCU provided the researcher with details on all admissions who had an episode of CDI occurring at the hospital during the study period, consistent with the case definitions described earlier. Using the data provided by the TIPCU, further data were collected through a review of the records held on the hospital patient information system and on the individual medical records of those with CDI. The review of the medical records of each patient with CDI included reviewing medical and nursing documentation related to the frequency of diarrhea.

The Infection Prevention and Control Unit at the hospital collected data within the timeframe that a person with CDI was isolated under contact precautions. The researcher reviewed the data provided by this unit for when persons with CDI had contact precautions ceased. The rationale for using the cessation of contact precautions as a marker for infection cessation is described in more detail in the following section. Data using this process were only available from July 1st, 2009 until December 30th, 2010, as the infection control unit did not collect this data prior to July 1st, 2009. There were 11 instances within this timeframe where data were not available from the hospital infection control unit. Subsequently, a review of the medical notes of these admissions was conducted and pointed to the date a person was removed from isolation. Data on the isolation periods of a total of 72 persons (from July 1st, 2009 to December 30th, 2010) were obtained.

### Data items collected

The data items collected included date of birth, sex, age, admission and discharge date, date of infection, date of infection cessation and the diagnosis-related group. The issue of defining CDI cessation in an individual is challenging. As *C. difficile* may continue to be detected from asymptomatic colonization, laboratory testing for the clearance of CDI is not recommended (Stuart et al., 2011). The researcher undertook a review of 20 medical notes of admissions with CDI and found that medical records failed to document a formed stool or cessation of diarrhea reliably. Based on the findings from the review of the 20 medical records, it was considered that the cessation of contact precautions for persons with CDI was a simple, reliable, and practical method of determining the cessation of CDI and was consistent with literature (National Health and Medical Research Council, 2010). Additionally, the decision to cease contact precautions was made after a review done by an infection control professional at the time of making this clinical decision.

### Data analysis

Descriptive analysis on the characteristics of the admissions was performed using IBM SPSS Version 20.0 (International Business Machines Corporation, 2011). Distributions were analyzed using Q–Q plots and the Kolmogorov–Smirnov test. Univariate analysis was used to compare the clinical characteristics of persons with and without CDI using a chi-square test or Fisher’s exact test where numbers were small. Incidence for calendar years and age groups was calculated by using mid *p* exact test. The calculation of the relative risk was performed to compare the occurrence of CDI in

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