AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

Trim: D21-21335

December 2021

Clostridioides difficile infection

2019 Data Snapshot Report

Published by the Australian Commission on Safety and Quality in Health Care
Level 5, 255 Elizabeth Street, Sydney NSW 2000

Phone: (02) 9126 3600

Email: mail@safetyandquality.gov.au
Website: www.safetyandquality.gov.au

ISBN: 978-1-922563-27-9

The Commission's preference is that you attribute this publication (and any material sourced from it) using the following citation:

> Australian Commission on Safety and Quality in Health Care. *Clostridioides difficile* infection 2019 Data Snapshot Report. Sydney: ACSQHC; 2021

Disclaimer

The content of this document is published in good faith by the Commission for information purposes. The document is not intended to provide guidance on particular healthcare choices. You should contact your health care provider for information or advice on particular healthcare choices.

The Commission does not accept any legal liability for any injury, loss or damage incurred by the use of, or reliance on, this document.

Introduction

Clostridioides difficile[*] (*C. difficile*) is a spore-forming bacterium most commonly associated with excessive antimicrobial use and antimicrobial-associated diarrhoea.[1,2] The use of other medications such as proton pump inhibitors (PPIs) and chemotherapy agents may also contribute to *Clostridioides difficile* infection (CDI) for some patients.[2] This bacterium is typically found in the natural environment, agriculture, food production and many animal species, as well as in built environments.[1] Transmission of *C. difficile* occurs by ingestion of spores either through person-to-person contact, animal-to-person contact or environment-to-person contact.[3]

Symptomatic CDI is mediated through toxin production by the bacterium. Production of toxin A and toxin B results in hyper-inflammation and necrosis of the gut lining.[4] The spectrum of disease associated with *C. difficile* ranges from asymptomatic colonisation through to fulminant colitis and peritonitis.[2,5] Approximately 20% of patients with an initial infection will have at least one recurrent episode of symptomatic infection, usually within 21 days of the initial episode.[6]

CDI is a significant hospital-acquired healthcare-associated infection (HAI), and surveillance of CDI in Australia has mainly focused on hospital-identified CDI (HI-CDI) rates. However, rates of hospital-onset CDI are declining, and there is growing evidence indicating that CDI is a greater community health problem than initially understood.[1,7-10] The increasing burden of community-onset CDI raises new challenges for healthcare workers and health service organisations nationally. Compared to the hospital setting, the implementation of antimicrobial stewardship (AMS) programs in primary care is still in its early stages, and the implementation of infection prevention and control interventions in the community may be more challenging. In the community, there are a greater number of factors influencing the risk of infection, such as the influence of animal health, food production, asymptomatic carriage and transmission of CDI and under reporting and low rates of testing of acute diarrhoea in the community.[1,8,9]

A recent report by the Australian Commission on Safety and Quality in Health Care (the Commission) identified that the epidemiology of CDI in Australia is changing from a hospital-onset infection to a community-onset infection.[10] *The Technical report: Monitoring the national burden of Clostridioides difficile infection in Australian public hospitals: 2016 to 2018* found that between 2016 and 2018:

- The number of separations identified with a CDI diagnosis increased by 8.4%
- 24,247 separations had a CDI diagnosis, with CDI symptoms present prior to hospital admission in 76.5% of these separations
- Patients who developed CDI symptoms during their hospital admission accounted for around a third (32.5%) of all separations with a CDI diagnosis.[10]

There have been continuing, and increasing, efforts into the prevention and control of HAIs and antimicrobial resistance for some time in the Australian hospital setting. These efforts include the implementation of antimicrobial stewardship programs (AMS) and the National Safety and Quality Health Services (NSQHS) Standards actions relating to infection prevention and control.

[*] *Clostridioides difficile*, also known as *Clostridium difficile*.

The direct outcomes of these actions remain difficult to quantify, and the impact on hospital-onset CDI rates are yet to be observed.[7]

Surveillance of hospital-identified CDI using patient administrative data is an important and valuable strategy to monitor and identify the local burden of CDI, detect outbreaks and factors or interventions that influence rates of CDI such as changes in local testing, antimicrobial prescribing practices or environmental cleaning practices. The information provided in this data snapshot report can be used by health and medical professionals for the development of targeted treatment and management protocols for CDI and used to inform and support locally developed CDI interventions that may further reduce the rates of CDI.

Monitoring the burden of CDI at a national level helps to identify changes in the overall epidemiology of CDI in Australia. The use of patient administrative data allows for a standardised approach to CDI surveillance in the absence of national laboratory-based CDI surveillance. At a national level, this information can be used to raise awareness of the prevalence of CDI in both the community and in the hospital system, and for the development of targeted resources for the prevention of CDI, such as the promotion of community-based AMS programs.

Methods

The Commission has monitored the rate of CDI in Australian public hospitals since 2016. The 2019 Data Snapshot is the fourth report in a series published by the Commission.

The Admitted Patient Care National Minimum Data Set (APC NMDS) provides information on patient diagnoses and the care provided during a patient's admission to an Australian public hospital.[11] Patient diagnoses are assigned a diagnostic ICD-10 code. The diagnostic code A04.7 *Gastroenterocolitis caused by Clostridium difficile* is used to identify separations affected by CDI. Patient administrative data from the 2018–2019 and 2019–2020 APC NMDS have been used in this report to estimate the rate of CDI in Australian public hospitals. For the purposes of this analysis, the diagnosis code A04.7 *Gastroenterocolitis caused by Clostridium difficile* will be referred to as a CDI diagnosis in this report

Use of the APC NMDS for monitoring national CDI rates was established by the Commission in 2016 and supported by the Commission's Inter-Jurisdictional Committee. Patient administrative data is comparable to hospital-identified CDI (HI-CDI) for surveillance.[10,12,13] As such, traditional CDI case exposure classifications including healthcare-associated healthcare facility (HCA-HCF) onset CDI, healthcare-associated community-onset CDI and community-associated CDI can potentially be applied to CDI diagnostic code categories.[10]

Exclusion and filtering criteria have not been applied to the APC NMDS. Data are based on the state or territory of the hospital that collected the data. Patient bed days were extracted from the APC NMDS and are defined as the total number of days for all patients who were admitted for an episode of care and who separated during a specific reference period.[14] This includes a total hospital stay (from admission to discharge, transfer or death), or a portion of a hospital stay that begins or ends with a change in the type of care provided to a patient.[15] The term separation describes discharges, deaths and transfers from the hospital.[14]

CDI diagnoses are categorised as either a principal diagnosis or a non-principal diagnosis. A non-principal diagnosis is further classified by Conditional Onset Flags (COFs). These terms are described as:

- A **principal diagnosis** describes the primary condition resulting in admission of an individual to hospital. This may include cases of CDI that develop in the community or may be attributed to a previous hospital admission.[11,16]
- A **non-principal diagnosis** describes a condition that may have contributed to the admission but is not the main reason for admission to hospital. This category of patients includes cases of CDI that develop during an inpatient admission.[11,16]
- A **non-principal diagnosis COF 1** refers to a condition that has arisen during the episode of admitted care that would not have been present or suspected on admission.[16] Separations coded as a non-principal CDI diagnosis with a COF1 may be described as healthcare-associated inpatient-onset CDI.
- A **non-principal diagnosis COF 2** refers to a condition previously existing or suspected on admission such as the presenting problem, a comorbidity or chronic disease.[11]

Separations coded as a non-principal CDI diagnoses with a COF2 may describe either a healthcare-associated community-onset CDI or a community-associated CDI.

Limitations and considerations for the interpretation of data

Access to information in the APC NMDS is dependent on the submission of hospital-level data by the states and territories and the subsequent validation of the dataset. Currently there is an 18 month lag between documentation of diagnosis at the hospital and submission, validation and availability of the APC NMDS to the Commission.

Patient administrative data is not sensitive enough to link co-morbidities to the COF codes or identify severity of disease, and the effects of these elements are not adjusted for in the methodology. Nor can the data be adjusted to account for or measure the impact of changes in CDI testing.

Unlike established HAI surveillance case exposure classification definitions, the definition for a COF does not include a time frame for when the onset of a condition is considered to have arisen during an episode of care. This may limit the accuracy of applying CDI case exposure classifications to data from the APC NMDS.

Findings

Rate of CDI diagnoses

In 2019, principal CDI diagnoses accounted for 31% of all CDI diagnoses (Figure 1). The average rate of all CDI diagnoses in 2019 was 4.00 diagnoses per 10,000 patient bed days. The monthly rate varied throughout 2019:

- The rates of all CDI diagnoses ranged from 3.65 to 4.44 diagnoses per 10,000 patient bed days
- The rate for non-principal CDI diagnoses ranged from 2.54 to 3.09 diagnoses per 10,000 patient bed days
- The rate of principal CDI diagnoses ranged from 1.01 to 1.52 CDI diagnoses per 10,000 bed days

Figure 1: CDI (A04.7) diagnoses in Australian public hospitals (n=744), 2019

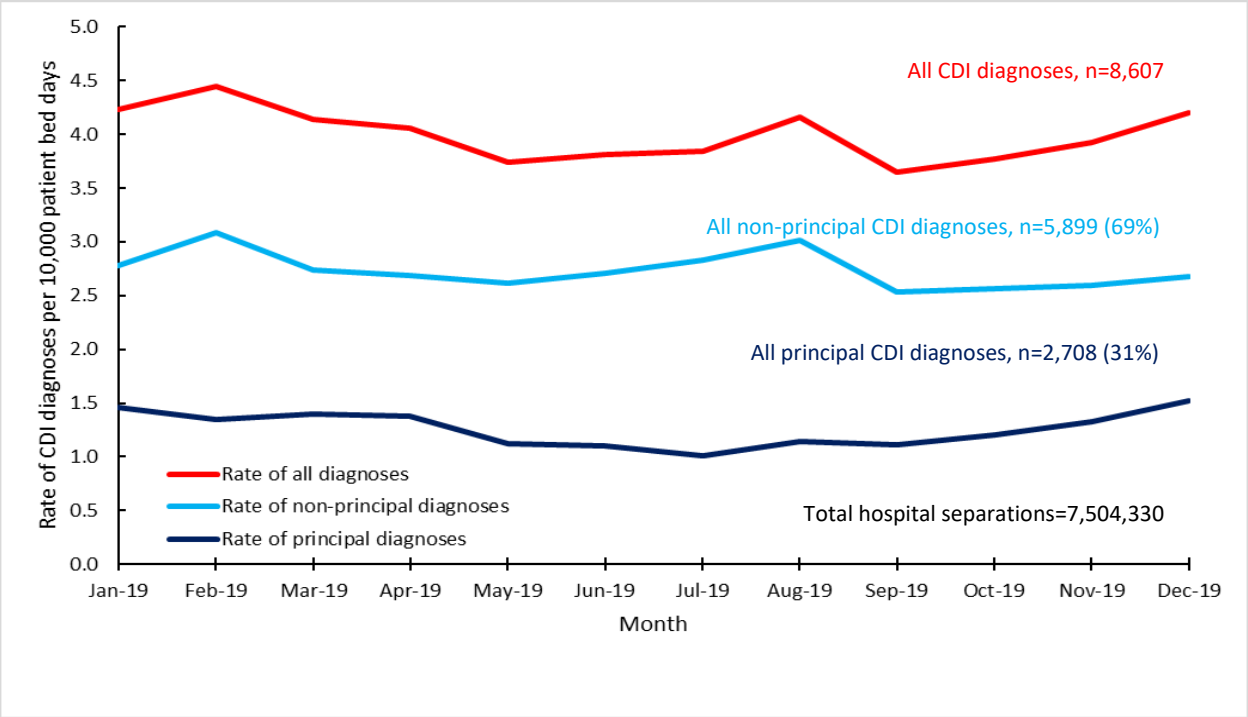
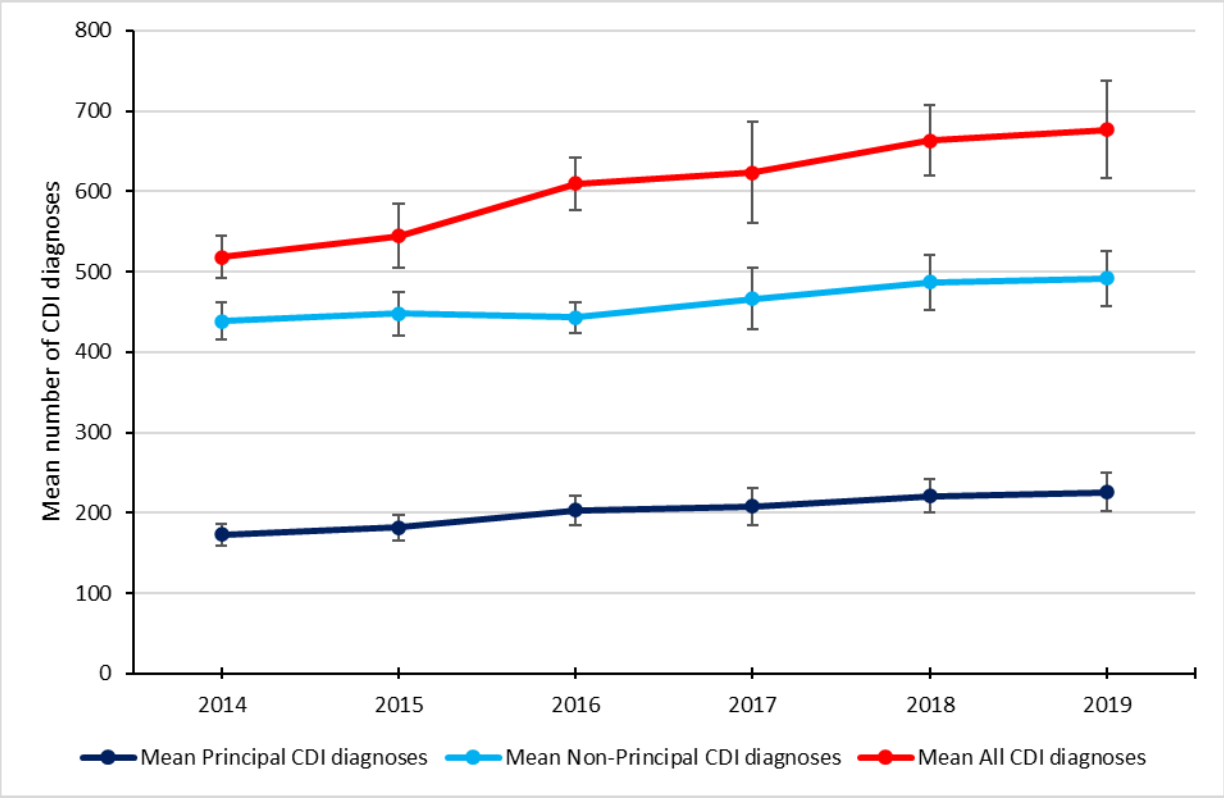
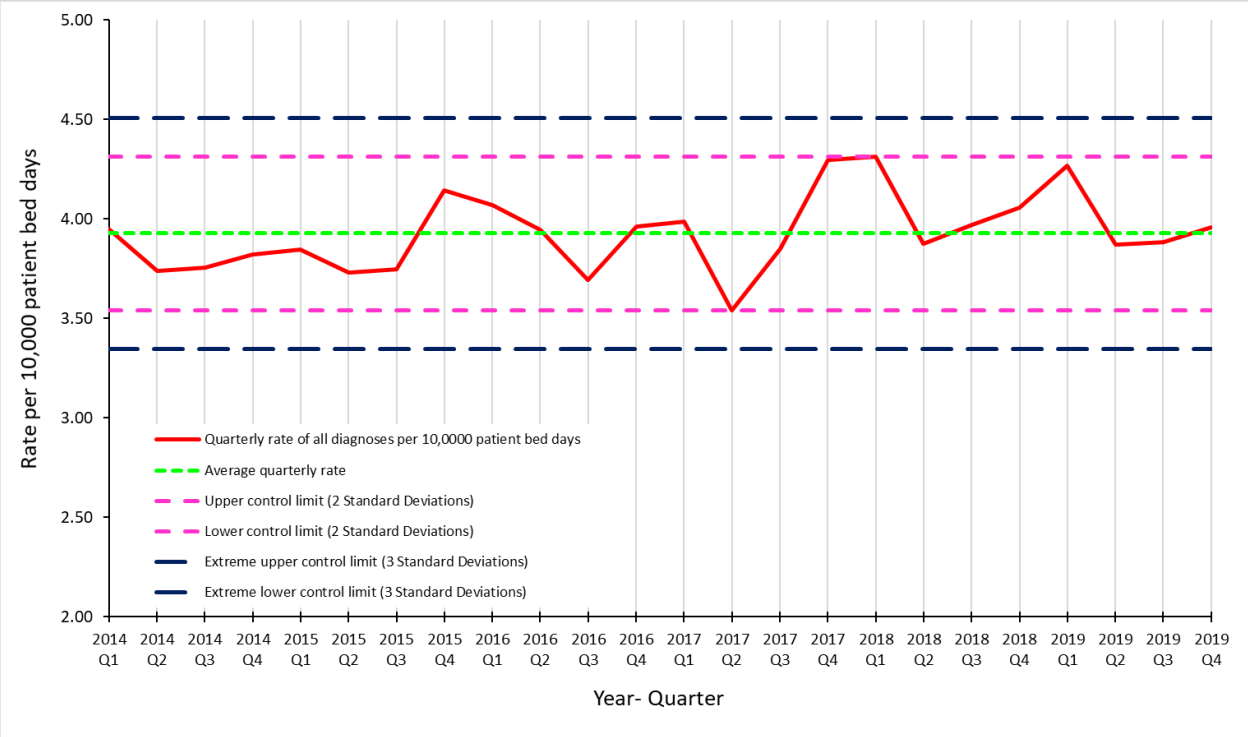


Figure 2: Mean yearly rate of CDI (A04.7) diagnoses, per 10,000 patient bed days, Australian public hospitals, 2014–2019



Since 2014, the number of CDI diagnoses in Australian public hospitals has increased year on year. In 2014, the average number of all CDI diagnoses were 518 case per month. In 2019, the average number of CDI diagnoses were 677 cases per month. The standard deviation for all CDI diagnoses also increased each year. While Figure 2 shows a steep increase in the number of CDI diagnoses between 2017 and 2018, there is reduced steepness in the average numbers CDI diagnoses between 2018 and 2019. This is most noticeable for principal CDI diagnoses from 2018 to 2019.

Figure 3: Statistical process control chart for CDI (A04.7) diagnoses in Australian public hospitals, 2014–2019



The quarterly rate of CDI diagnosis from 2014 to 2019 is presented in Figure 3. The use of a quarterly data interval is sensitive enough to identify sustained changes in the epidemiology of CDI over several years but is also robust enough to filter out single-point events.[17]

There is no national benchmark for rates of CDI, therefore the average quarterly rate of CDI diagnosis (represented by the green line) does not represent a benchmark or a desirable rate of CDI. The upper and lower control limits displayed on the chart are set at two (±2SD) and three (±3SD) standard deviations based on the average quarterly rate of CDI for the entire period. The average and the control limits were calculated from the first quarter of 2014 through to the last quarter of 2019. The control limits have been applied to assist in the identification of changes in rates and seasonal patterns of CDI diagnosis.

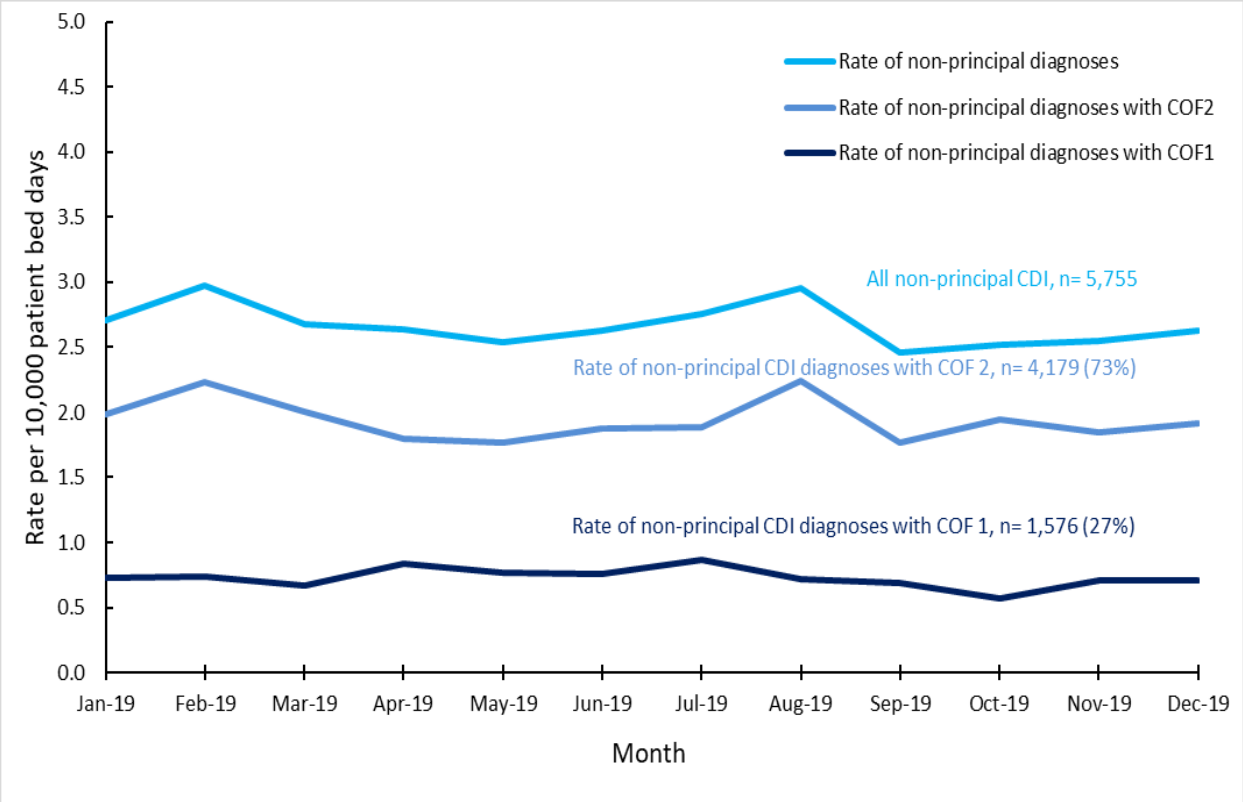
While quarterly rates of CDI were equal to the upper and lower control limits in previous years, the rates of CDI diagnoses in 2019 remained within the upper and lower control limits on the graph. This suggests that rate of CDI diagnosis did not vary greatly over the 12 months.

Rate of non-principal CDI diagnoses

The data presented in Figures 4 and 5 are drawn from hospitals that reliably assigned COF coding criteria for cases of CDI in their facility. This dataset excludes:

- Hospitals with an overall low volume of activity (less than 100 episodes of care per month)
- Hospitals where COF coding was very low (less than 1%) for any condition arising during an episode of care
- Hospitals where the COF was coded as unknown on set for any diagnoses in more than 10% of patient records.[18]

Figure 4: Rate of CDI (A04.7) non-principal diagnoses by Condition of Onset Flag (COF) in Australian public hospitals, 2019*

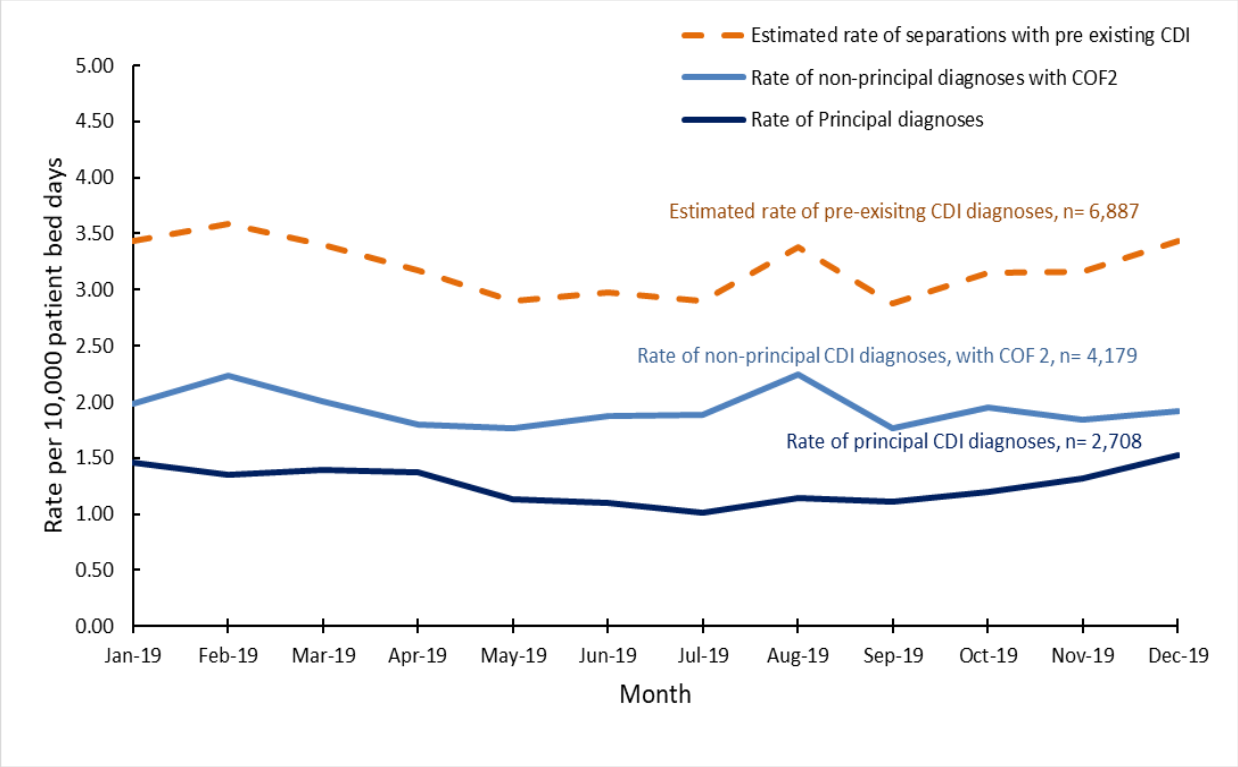


*Based on hospitals with highly reliable COF coding only (2019 n=547)

For 2019, a total of 744 hospitals were included in the APC NMDS. Of these, 547 hospitals were considered to have highly reliable COF coding, which assists to improve the accuracy of the findings in this report. The findings from Figure 4 are as follows:

- The average rate for all CDI non-principal diagnoses was 2.74 diagnoses per 10,000 patient bed days (range: 2.54 to 3.09 diagnoses per 10,000 patient bed days).
- Separations coded as a non-principal CDI diagnoses with a COF2 may include both healthcare-associated community-onset CDI and community-associated CDI. The average rate of non-principal CDI diagnoses flagged with a COF2 was 1.98 diagnoses per 10,000 patient bed days (range: 1.83 to 2.29 diagnoses per 10,000 patient bed days).
- Separations coded as a non-principal CDI diagnosis with a COF1 may be described as healthcare-associated hospital-onset CDI. The average rate of non-principal CDI diagnoses flagged with a COF1 was 0.73 diagnoses per 10,000 patient bed days (range: 0.57 to 0.84 diagnoses per 10,000 patient bed days).

Figure 5: Estimated rates of pre-existing CDI (A04.7) presenting to hospitals, 2019*



*Based on hospitals with highly reliable Condition Onset Flag (COF) coding (n=547)

Note: COF 1: Conditional Onset Flag 1, 'refers to a condition that has arisen during the episode of admitted patient care that would not have been present or suspected on admission'.
COF 2: Condition Onset Flag 2, 'refers to a condition previously existing or suspected on admission such as the presenting problem, a comorbidity or chronic disease'. [11] For further information on Conditional Onset Flags, see: Australian Institute of Health and Welfare. Episode of admitted patient care- condition onset flag, code N [online]: Available from: https://meteor.aihw.gov.au/content/index.phtml/itemId/496512

Figure 5 describes the estimated rates of patients admitted to Australian public hospitals in 2019 with pre-existing CDI symptoms. This cohort represents patients that acquired *C. difficile* either in the community or during a previous healthcare admission (healthcare-associated community-onset CDI, community-associated CDI or indeterminate CDI onset). In 2019, this

cohort of patients accounted for 80% (n=6,887) of all patients with a CDI diagnosis (n= 8,607). The rate of separations with pre-existing CDI symptoms has been increasing since 2016 (2016: 2.92 CDI diagnoses per 10,000 bed days, 2017: 2.95 CDI diagnoses per 10,000 bed days, 2018: 3.18 CDI diagnoses per 10,000 bed days, and 2019: 3.19 diagnoses per 10,000 bed days).[10]

Table 1: Number of CDI-related separations (A04.7) in Australian public hospitals (n=744), 2018 and 2019

	2018	2019	Relative change
Number of separations in Australian public hospitals	7,238,129	7,504,330	↑ 3.68%
Number of separations with a CDI diagnosis	8,496	8,607	↑ 1.31%
Number of separations with a principal CDI diagnosis	2,654	2,708	↑ 2.03%
Number of separations with a non-principal CDI diagnosis	5,842	5,899	↑ 0.98%
Number of separations with a non-principal CDI diagnosis, with COF1*	1,699	1,576	↓ 7.24%
Number of separations with a non-principal CDI diagnosis, with COF2*	4,010	4,179	↑ 4.21%
Estimated pre-existing burden Principal CDI+ non-principal CDI, COF2*	6,664	6,887	↑ 3.35%

*Based on hospitals with highly reliable COF coding only (2019 n=547)

Since 2016, the number of all separations from Australian public hospitals has increased, as has the number of all separations with a CDI diagnosis (2016 n= 7,836, 2017 n= 8,095, 2018 n=8,496, 2019 n= 8,607).[10] Separations classified as a non-principal CDI diagnosis with a COF1 decreased by 7.24% between 2018 and 2019, indicating that there was a reduction in the number of separations where the onset of CDI occurred during an inpatient admission.

During the same time, the number of all CDI diagnoses only slightly increased (1.31%), but the estimated proportion of pre-existing CDI increased by 3.35%, and separations classified as non-principal CDI diagnosis with a COF2 code increased by 4.21%. This suggests CDI symptom onset originates while an individual is in the community rather than during an inpatient admission.

Hospital length of stay for patients with a CDI diagnoses

Table 2: Average length of stay (days) for patients with a CDI (A04.7) diagnosis in Australian public hospitals, 2012–2019

Year	Principal CDI diagnosis	Non-principal CDI diagnosis	All CDI diagnosis
2012	8.34	22.73	18.69
2013	7.91	20.91	17.17
2014	7.79	22.10	18.05
2015	7.60	20.68	16.91
2016	7.38	19.78	16.08
2017	7.76	19.99	16.16
2018	7.01	19.56	15.64
2019	6.94	20.11	15.97
Overall average	**7.59**	**20.73**	**16.83**
Overall rate of change (slope), 2012-2019	-0.174	-0.385	-0.395
p value	<0.01	0.01	<0.01

Table 2 shows the progressive and significant reduction in the length of stay each year since 2012 for patients admitted to Australian public hospitals with a diagnosis of CDI. Data from the Australian Institute of Health and Welfare (AIHW) indicate that the average length of stay for any admission in an Australian public hospital was three days for 2019–20.[19,20] This is slightly higher than previous years (2015–2016 the average length of stay was 2.8 days, and in 2017–2018 and 2018–2019 the average length of stay was 2.7 days).[11] Similarly, the average length of stay for patients with a CDI diagnosis has also been reducing, though a slight increase in the average length of stay in 2019 for patients admitted with a non-principal CDI diagnosis was observed. Generally, patients with a CDI diagnoses continue to remain in hospital up to nearly seven times longer than the average length of stay.

A lengthy hospital stay has major impacts on patient outcomes and healthcare resources.[15] Patients who have an extended length of stay, generally require invasive treatments and interventions, are often elderly, have chronic underlying co-morbidities and in turn have a higher risk of acquiring infections.[15] These factors are also the same factors that increase the risk for CDI in most patients.[2] Aside from the clinical impact, there is also a significant socio-economic impact to the patient and their families that is often overlooked, can have long lasting impacts and are difficult to quantify economically.[21] However, any association between length of stay and CDI should be interpreted with care. Length of stay can be impacted by many factors such as underlying co-morbidities, severity of disease and treatment modalities; as such, a prolonged separation cannot solely be attributed to the acquisition of CDI.[15]

Conclusion

CDI is largely a preventable HAI. Knowing the burden of CDI in Australia can assist in identifying at-risk groups for CDI and targeting interventions to minimise the risk of CDI to these groups within the clinical setting. Since 2016, the Commission has been monitoring the burden of CDI in Australian public hospitals. During this time, separations with a CDI diagnosis have increased by 9.84% (2016 n= 7,836, 2017 n= 8,095, 2018 n=8,496,[10] and 2019 n=8,607). However, these separations have not increased at the same rate of overall separations, which increased by 11.22% (2016 n = 6,747,532, 2017 n = 7,021,452, 2018 n = 7,238,129[10] and 2019 n= 7,504,330) over the same time period.

The rates of non-principal CDI diagnoses with a COF1, as reported by the AIHW, are declining (2016= 0.87, 2017= 0.92, 2018= 0.81[10] and 2019 =0.73 diagnoses per 10,000 patient bed days). Patients with a non-principal CDI diagnosis with a COF1, include episodes of CDI identified as healthcare-associated healthcare facility-onset CDI using hospital-identified CDI surveillance methods. In 2019, separations coded as non-principal CDI diagnoses with a COF1 accounted for 18.31% of all CDI separations. The reduction in the rate of non-principal CDI diagnoses with a COF1 may be attributable to the implementation of a bundle of infection prevention and control interventions including hospital AMS programs, environmental cleaning programs, improved detection of CDI, and better management and treatment modalities for CDI.[3,7,22] These interventions have an impact on reducing the acquisition and spread of HAIs, such as CDI, but measuring the effectiveness of these interventions remains difficult to quantify and require ongoing efforts to ensure sustainable outcomes.[3]

Conversely, the rates of separation for patients with pre-existing CDI symptoms have been increasing since 2016 (2016= 2.92, 2017=2.95, 2018= 3.18[10] and 2019= 3.19 diagnoses per 10,000 patient bed days). Based on the dataset used for this analysis, patients identified as having pre-existing CDI symptoms on admission to hospital, include patients who may have acquired CDI in the community and those who were recently discharged from a health service organisation. In 2019, this group of patients accounted for 80% of separations with a CDI diagnosis.

Community-onset CDI remains prevalent in both the hospital and community setting, and antimicrobial, PPI and immunosuppressive agents continue to be factors influencing CDI acquisition in both settings. [9] However, effective antimicrobial stewardship in the community is challenging, and many factors that influence antimicrobial use are outside the scope of hospital-based interventions.[8] [9] The role of general practitioners in improving medication use and prescribing PPIs and antimicrobial use in the community and aged care is crucial, and should not be underestimated.[23] Information from AURA 2021, indicates that inappropriate and over prescribing of antimicrobials in the community remains common.[23] Of particular concern is the amount of antimicrobials routinely prescribed for common conditions such as influenza and acute bronchitis, as well as the high rates of antimicrobial prescriptions for children under four years of age and adults over 65 years of age.[23] The Commission has developed a number of resources to support general practitioners and healthcare providers in the community to improve antimicrobial usage and support AMS in primary healthcare and residential aged care services.

Community-onset CDI also appears to affect younger individuals and those who have not had any recent antimicrobial or healthcare exposure, suggesting that factors other than antimicrobial exposure may have an impact on the burden of CDI in the community; for example, age and other underlying medical conditions.[7-9,22] Exposure to other medications such as proton pump inhibitors (PPIs) or immunosuppressive agents also may increase the risk of CDI in the community in the absence of antimicrobial use.[7] PPIs act to reduce the acidity of the gastrointestinal tract and this change in pH may increase a person's susceptibility to CDI, although this mechanism still remains poorly understood.[6,7] Immunosuppressive agents are known to reduce a person's antibody response and increase their susceptibility to opportunistic infections including CDI.[6] Exposure to PPIs and immunosuppressive agents may be common in among older people or in the outpatient setting, though further information on the relationship between these medications and CDI acquisition in the Australian community setting is needed. The role of food and water contamination, and person-to-person transmission from symptomatic and asymptomatic individuals, such as transmission from children under the age of two years, who are naturally colonised with *C. difficile,* may also have underestimated roles in the transmission of community-onset CDI.[8,9] As such, ongoing research into how these factors may influence the rates of community CDI is still required.

Surveillance of community-onset CDI is limited, and case numbers are likely to be under-reported in Australia.[8] Further work is required to better understand community-onset CDI; the impact of these infections on the health system, the types of interventions required to reduce the risk of CDI in the community and, in turn, limit the spread of community-onset CDI entering hospitals. General practitioners can play a role in reducing the burden of community-onset CDI. For example, general practitioners could increase testing of acute episodes of diarrhoea[9], which would improve the early detection and management of CDI, and may result in fewer CDI-related admissions to hospital.[22]

The Commission utilises information from the APC NMDS to generate these reports to better understand the burden of CDI in Australia. Information in this dataset is provided to the AIHW by all public hospitals in Australia. Data from the APC NMDS is uniform and validated and does not rely on different jurisdictional HAI reporting requirements. There are some of limitations with using this dataset for CDI surveillance, such as the lack of patient level details, the time lag between the submission of data to AIHW from health services and when it becomes available for use by the Commission, and the inability to measure the impact of changes in CDI testing. The findings of this report should be considered by health services in the context of available local surveillance and hospital-acquired complications (HAC) data and should be used to help inform local intervention to keep CDI rates and morbidity low.

In addition to the actions of the National Safety and Quality Health Services (NSQHS) Standards, health service organisations should develop local interventions to prevent and control HAIs including CDI. The Preventing and Controlling Infections Standard aims to improve patient safety and infection prevention and control, through actions that support AMS, and reduce the spread of antimicrobial resistant organisms and CDI. To assist health service organisations meet these actions and promote the use of standard and transmission-based precautions and prevent the spread of CDI, a range of resources have been developed by the Commission to support local infection prevention and control programs. These resources can provide health service organisations with guidance on environmental cleaning programs, the implementation of AMS programs and the surveillance of hospital-identified CDI. Used together,

these interventions can provide a bundled approach to preventing the spread of CDI in hospitals. These resources can be adapted for use in the community, primary care settings and residential aged care, to support interventions to reduce the risk of CDI acquisition and transmission in the community.

The data snapshot reports produced by the Commission provide valuable information on the national burden of CDI. However, due to a number of factors including the COVID-19 pandemic, delays in access to data and a shift from healthcare-associated healthcare facility-onset CDI to community-onset CDI, the direction of future CDI surveillance remains under consideration. The Commission will consider including national monitoring of CDI as part of its program for the surveillance of resistance microorganisms, subject to laboratory surveillance data for CDI being available. Over time, this data from laboratory surveillance could be used to monitor the changing burden of community-onset CDI in Australia and laboratory-based definitions could be applied to this data, improving the interpretation and utility of the results. The Commission will also undertake work to continue to increase the awareness of community-onset CDI, including the promotion of community-based AMS for the prevention of community-onset CDI, and strategies to reduce the risk of readmission to hospital for CDI.

References

1. Knight DR, Riley TV. Genomic Delineation of Zoonotic Orgins of Clostridium difficile. Frontiers in Public Health. 2019;7.
2. Guh AY, Kutty PK. Clostridioides difficile Infection. Annals of internal medicine. 2018 Oct 2;169(7):Itc49-itc64.
3. Brain D, Yakob L, Barnett A, Riley TV, Clements A, Halton K, et al. Economic evaluation of intervention designed to reduce Clostridium difficile infection. PLOS ONE. 2018.
4. Awad MM, Johanesen PA, Carter GP, Rose E, Lyras D. Clostridium difficile virulence factors: Insights into an anaerobic spore-forming pathogen Gut Microbes. 2014;5:579-593.
5. Napolitano LM, Edmiston CE. Clostridium difficile disease: Diagnosis, pathogenesis, and treatment update Surgery 2017;162:325-348.
6. Kachrimanidou M, Malisiovas N. Clostridium difficile infection: A comprehensive review. Critical Reviews in Microbiology 2011;37:178-187.
7. Fu Y, Luo Y, Grinspan AM. Epidemiology of community-acquired and recurrent Clostridioides difficile infection. Therapeutic advances in gastroenterology. 2021;14:17562848211016248.
8. McLure A, Clements ACA, Kirk M, Glass K. Modelling diverse sources of Clostridium difficile in the community: importance of animals, infants and asymptomatic carriers. Epidemiol Infect. 2019;147:e152-e152.
9. Tracey L, Kirke A, Armstrong P, Riley TV. From the hospital to the home--the rise and rise of Clostridium difficile infection. Australian family physician. 2015 Oct;44(10):712-717.
10. Australian Commission on Safety and Quality in Health Care. Technical report: Monitoring the national burden of Clostridioides difficile infection in Australian public hospitals: 2016 to 2018. ACSQH: Sydney, 2021.
11. Australian Institute of Health and Welfare. Admitted patient care NMDS 2019-20. [Internet] 2020 [cited 16 June 2021] Available from: https://meteor.aihw.gov.au/content/index.phtml/itemId/699728.

12. Daveson K, Kennedy K. Hospital-acquired complications and Clostridium difficile surveillance in the Australian context. Poster session at the Antimicrobial Society Australia conference; February 2019; Sydney2019.
13. Public Health Services, Department of Health and Human Services. Clostridium difficile infection (CDI) surveillance. The sensitivity and PPV of administrative data sets. Presentation at Healthcare-Associated Infections Advisory Committee meeting, ACSQHC November 2019; Sydney.
14. Australian Institute of Health and Welfare. National Health Data Dictionary. Canberra: AIHW, 2012.
15. Jeon CY, Neidell M, Jia H, Sinisi M, Larson E. On the role of length of stay in Healthcare-Associated Bloodstream Infection. Infection Control and Hospital Epideminology. 2012;33(12):1213-1218.
16. Australian Institute of Health and Welfare. Principal diagnosis data cubes. 2017. Available from: http://www.aihw.gov.au/hospitals-data/principal-diagnosis-data-cubes/.
17. Australian Commission on Safety and Quality in Health Care. Clostridium difficile infection: Monitoring the national burden of Clostridium difficile. Sydney: ACSQHC, 2018.
18. Pricing and Funding for Safety and Quality. Risk Adjustment Model for Hospital Acquired Complications – March 2019. 2019.
19. Australian Institue of Health and Welfare. Overnight hospital stays becoming shorter and same-day hospitalisations increasing. [Internet] 2020 [updated 09 Jult 2020] Available from: https://www.aihw.gov.au/news-media/media-releases/2020/july/overnight-hospital-stays-becoming-shorter-and-same.
20. Australian institue of Health and Welfare. Admitted patient activity. [Internet] 2020 Available from: https://www.aihw.gov.au/reports-data/myhospitals/intersection/activity/apc.
21. Plowman R. The socioeconomic burden of hospital acquired infection. Euro Surveillance. 2000;5(4):pii=4.
22. Guh AY, Mu Y, Winston LG, Johnston H, Olson D, Farley MM, et al. Trends in U.S. Burden of Clostridioides difficile Infection and Outcomes. The New England journal of medicine. 2020 Apr 2;382(14):1320-1330.
23. Australian Commission on Safety and Quality in Health Care. AURA 2021: fourth Australian report on antimicrobial use and resistance in human health. Sydney: ACSQHC, 2021.