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Clostridioides difficile infection Data snapshot report: 2020 and 2021

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Summary

Clostridioides difficile, also known as *Clostridium difficile,* is a gram-positive, spore-forming bacterium that most often causes infection associated with excessive antimicrobial exposure, for example, antimicrobial-associated diarrhoea.[1,2]

Antimicrobial exposure is the most important risk factor for CDI.[3] Other common risk factors for CDI include gastric acid suppression medication, age over 65 years, recent hospitalisation and underlying chronic medical conditions, such as renal disease and immunosuppression.[2,4] Understanding the relationship between risk factors and the onset of CDI can improve awareness for prevention, early detection and treatment.[4]

CDI is a preventable and significant healthcare-associated infection (HAI), and surveillance of CDI in Australia focuses mainly on hospital-identified CDI rates. However, the rate of community-onset CDI is increasing, which suggests that CDI is a larger health problem in the community than previously understood.[1,5,6]

Key findings

What do the analyses show about CDI in Australia?

In Australian public hospitals:

- separations with a CDI diagnosis increased by 29% from 2020 and 2021
- community-onset CDI (pre-existing CDI symptoms on admission) accounted for over 80% of separations
- healthcare-associated hospital-onset CDI accounted for less than 20% of all CDI diagnoses.

What do these findings mean and why are they important?

Monitoring the national burden of CDI helps to identify changes in the epidemiology of CDI in Australia. The findings from this report suggest that:

- community-onset CDI is a significant health problem in Australia
- hospital-based strategies to prevent healthcare-associated hospital-onset CDI are effective
- changes in CDI rates coinciding with the response to COVID-19 may be linked to improved infection prevention and control strategies and changes in access to healthcare during the pandemic.

These findings can be used to raise awareness of the prevalence of CDI in public hospitals and the community, as well as supporting the development of targeted resources for the prevention of CDI, and the promotion of hospital- and community-based interventions such as antimicrobial stewardship (AMS) programs.

What can be done to improve CDI rates in Australia?

These findings will inform development of targeted resources for CDI diagnosis, management, prevention, and control for community settings.

Introduction

About *Clostridioides difficile*

C. difficile is commonly found in the environment, however, the other important reservoirs include animals (canine, feline, porcine, bovine, equine and avian) as well as asymptomatic and symptomatic patients.[1,2] Symptomatic *C. difficile* infection (CDI) results in fever, abdominal pain, nausea, vomiting, and diarrhoea. Infections range from mild to severe and can cause colitis, toxic megacolon, and pseudomembranous colitis.[2,7]

About this report

Data for the analyses for this report were extracted from the Admitted Patient Care National Minimum Data Set (APC NMDS), which provides information on patient diagnoses and the care provided during a patient's admission to an Australian public hospital.[8] 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 and referred to in this report as a CDI diagnosis.[8] Patient administrative data from the 2019–2020, 2020−2021 and 2021−2022 APC NMDS have been analysed to estimate the rate of CDI in Australian public hospitals.[8]

Use of the APC NMDS for monitoring CDI rates nationally by the Commission commenced in 2016 and was supported by the Commission's Inter-Jurisdictional Committee. Patient administrative data are comparable to hospital-identified CDI (HI-CDI) for surveillance.[6,9,10] 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.[6]

Method

Exclusion and filtering criteria have not been applied to the APC NMDS. 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.[11] This includes a total hospital stay (from admission to separation), or a portion of a hospital stay that begins or ends with a change in the type of care provided to a patient. The term separation describes completion of a patient's care from hospital by discharge, death or transfer.[11]

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)[11,12]. 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[8,13]

- 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[8,13]

- A **non-principal diagnosis COF1** refers to a condition that has arisen during the episode of admitted care that would not have been present or suspected on admission.[13] Separations coded as a non-principal CDI diagnosis with a COF1 may be described as healthcare-associated inpatient-onset CDI

- A **non-principal diagnosis COF2** refers to a condition previously existing or suspected on admission such as the presenting problem, a comorbidity or chronic disease.[11] Separations coded as 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 subsequent validation of the dataset. Currently there is a 14-month delay between documentation of diagnosis at the hospital and submission, validation, and availability of the APC NMDS to the Commission.

Patient administrative data are not sufficiently sensitive to link comorbidities to the COF codes or identify severity of disease, and the effects of these elements are not adjusted for in the methodology. These data cannot 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. It is assumed that the 48-hour threshold for the onset of symptoms after admission used in hospital-based CDI surveillance programs can be applied to COF coding. However, this may limit the accuracy of applying CDI case exposure classifications to data from the APC NMDS.

Any association between length of stay and CDI should be interpreted with care. Length of stay may be impacted by many factors such as underlying comorbidities, severity of disease and treatment modalities; as such, a prolonged separation cannot solely be attributed to the acquisition of CDI.[14]

Findings

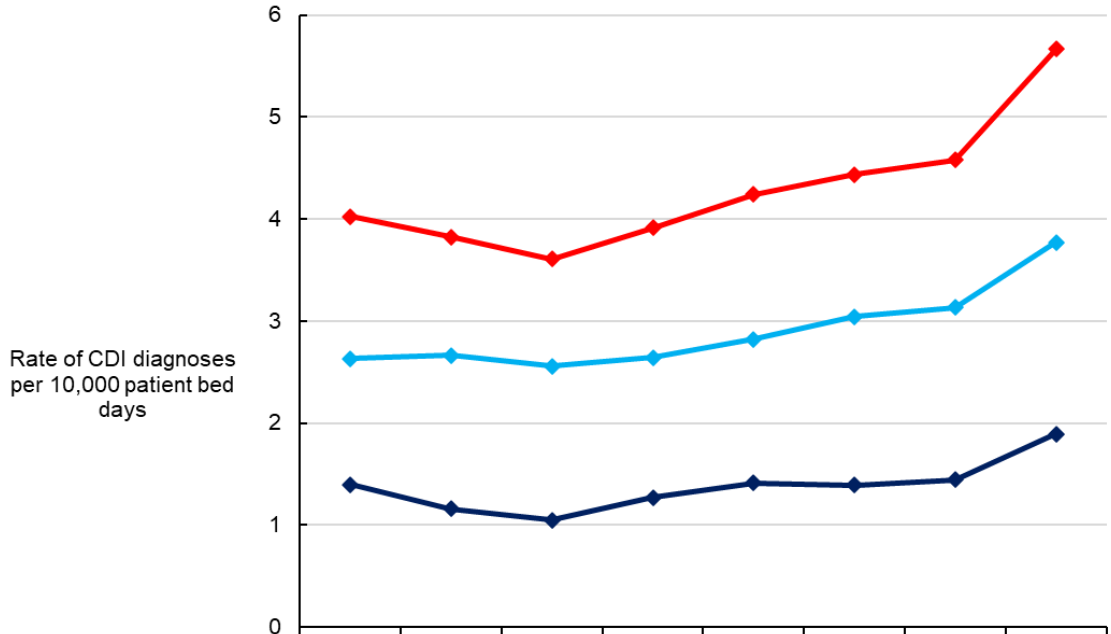
Rate of CDI diagnoses for 2022 and 2021

Rates of CDI diagnoses during 2020 remained stable, however the rate of all CDI diagnoses increased sharply throughout the last quarter of 2021 (Figure 1).

In 2020, there were 8,127 separations with a CDI diagnosis, and in 2021 there were 10,512 separations with a CDI diagnosis. Principal CDI diagnoses accounted for 33% of all CDI diagnoses in 2020 and 34% of all CDI diagnoses in 2021. Non-principal CDI diagnoses accounted for 67% of all CDI diagnoses in 2020 and 66% of all CDI diagnoses in 2021.

The average rate of all CDI diagnoses in 2020 was 3.95 diagnoses per 10,000 patient bed days. In 2021, the average rate of all CDI diagnoses increased to 4.82 diagnoses per 10,000 patient bed days.

Figure 1: Rate of *Clostridioides difficile* diagnoses* in Australian public hospitals per 10,000 patient bed days, 2020–2021



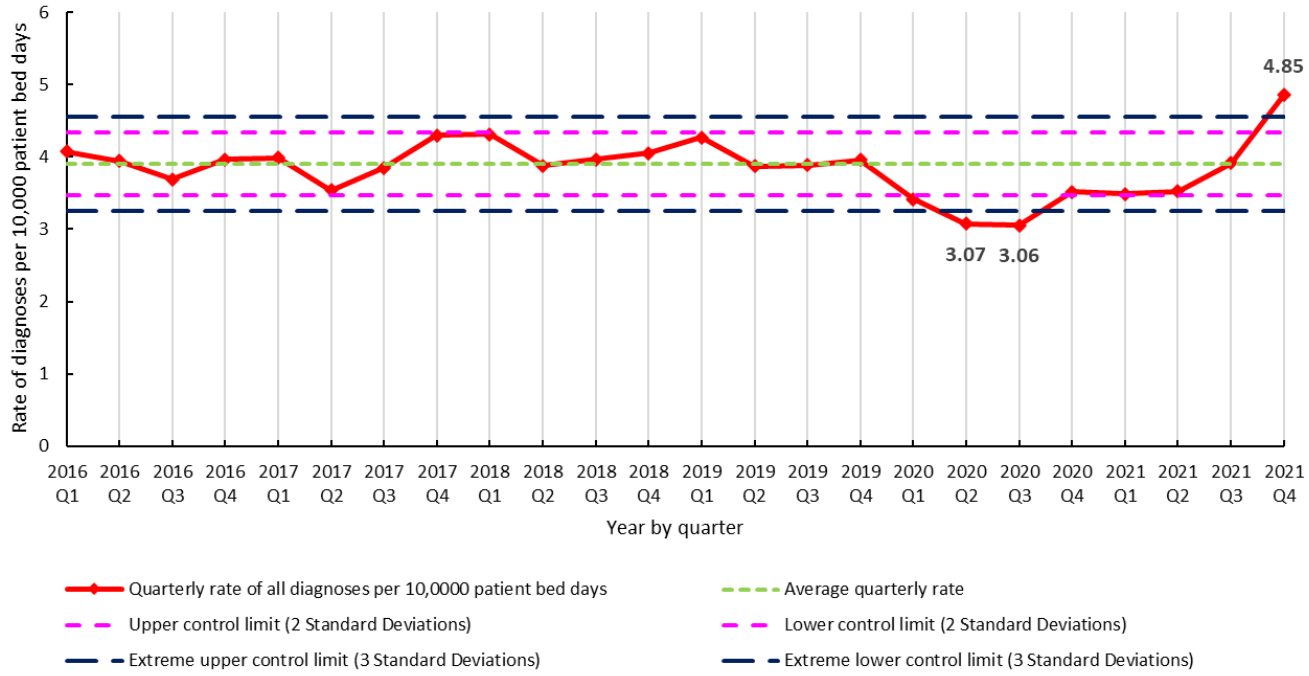
	2020 Q1	2020 Q2	2020 Q3	2020 Q4	2021 Q1	2021 Q2	2021 Q3	2021 Q4
Rate of all diagnoses	4.03	3.83	3.61	3.91	4.24	4.44	4.58	5.66
Rate of non-principal diagnoses	2.63	2.66	2.56	2.64	2.82	3.04	3.13	3.77
Rate of principal diagnoses	1.40	1.16	1.05	1.27	1.42	1.39	1.45	1.89

*Diagnostic code A04.7 (*Gastroenterocolitis caused by Clostridium difficile*)
Notes: Number of Australian public hospitals was 683 in both 2020 and 2021.
Total hospital separations 2020, *n* = 7,242,690
Total hospital separations 2021, *n* = 7,580,271

The quarterly rate of CDI diagnoses from 2016 to 2021 is presented in Figure 2. The use of a quarterly data interval is sensitive enough to identify sustained changes in the epidemiology of CDI over several years and is robust enough to filter out single-point events.[15]

There is no national benchmark for rates of CDI, therefore the average quarterly rate of CDI diagnosis does not represent a benchmark. The upper and lower control limits displayed on the chart are set at two and three standard deviations, based on the average quarterly rate of CDI for the 5-year period. The average and the control limits were calculated from the first quarter of 2016 through to the last quarter of 2021. The control limits have been applied to assist with identification of changes in rates and seasonal patterns of CDI diagnosis.

Figure 2: Statistical process control chart for CDI (A04.7) diagnoses in Australian public hospitals, 2016–2021



During 2020 and 2021 there was a large variation in the rates of CDI diagnoses. The quarterly rates of CDI diagnoses declined from the last quarter to 2019 to the third quarter of 2020 and were below the lower control limits for the first time since 2016. During the second quarter of 2021, the rates of CDI diagnoses increased steadily, and exceeded the upper control limits in the last half of 2021. There were 4.85 CDI diagnoses per 10,000 patient bed days in the last quarter of 2021, which was the highest rate reported since monitoring commenced in 2016. At this time, it is not clear if or how the COVID-19 pandemic has impacted on the rates of CDI during 2020 and 2021.

Rates of non-principal CDI diagnoses

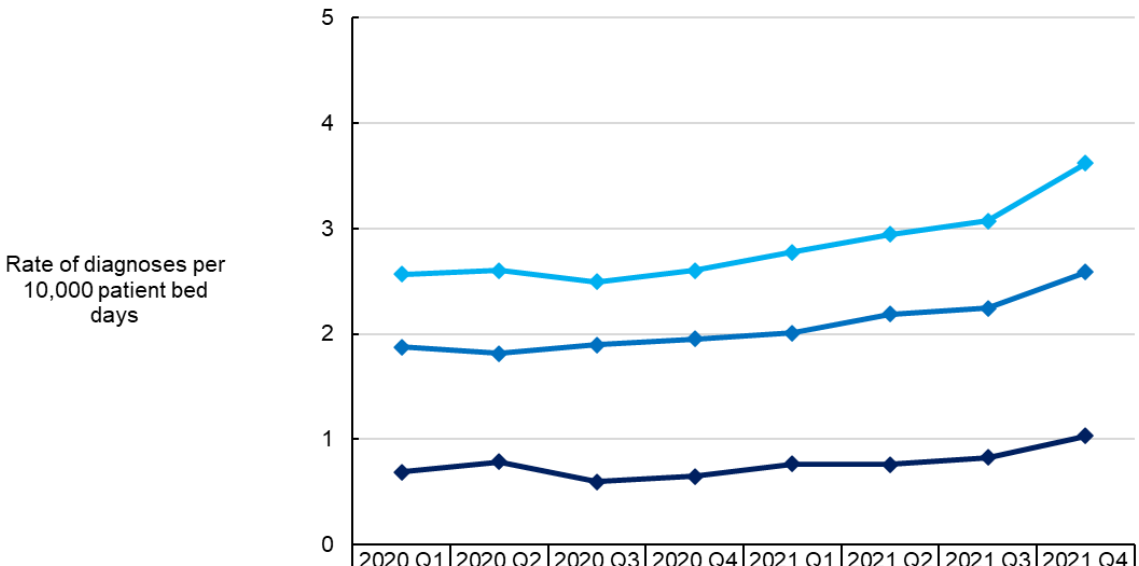
The data presented in Figure 3 and Figure 4 are drawn from hospitals that reliably assigned COF coding criteria for cases of CDI. This dataset excludes:

- 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 onset for any diagnoses in more than 10% of patient records.[16]

Of the 683 hospitals nationally, 502 hospitals in 2020 and 519 hospitals in 2021 were considered to have highly reliable COF coding.

In 2020 and 2021, there were 5,357 separations and 6,783 separations respectively with a non-principal CDI diagnosis. Separations coded as non-principal CDI diagnoses with a COF2 may include both healthcare-associated community-onset CDI and community-associated CDI. In 2020 and 2021, non-principal CDI diagnoses with a COF2 accounted for 74% (*n*= 3,986) and 73% (*n*= 4,948) of all non-principal CDI diagnoses respectively. Separations coded as a non-principal CDI diagnosis with a COF1 may be described as healthcare-associated hospital-onset CDI. In 2020 and 2021, non-principal CDI diagnoses with COF1 accounted for less than 20% of all CDI diagnoses respectively (*n* = 1,371 in 2020 and *n* = 1,835 in 2021). The average rate of non-principal CDI diagnoses was 2.62 diagnoses per 10,000 patient bed days and increased to 3.19 diagnoses per 10,000 patient bed days in 2021.

Figure 3: Rate of CDI (A04.7) non-principal diagnoses by Condition of Onset Flag (COF) in Australian public hospitals, 2020–2021*

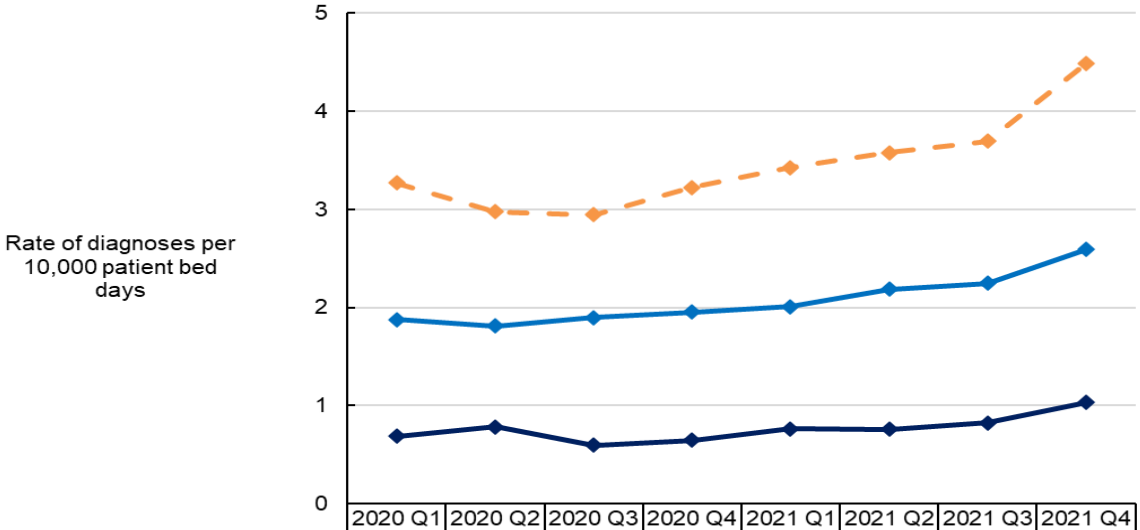


	2020 Q1	2020 Q2	2020 Q3	2020 Q4	2021 Q1	2021 Q2	2021 Q3	2021 Q4
Rate of non-principal diagnoses	2.56	2.60	2.49	2.60	2.77	2.95	3.07	3.62
Rate of non-principal diagnoses with COF2	1.87	1.81	1.89	1.95	2.01	2.19	2.25	2.59
Rate of non-principal diagnoses with COF1	0.69	0.79	0.60	0.65	0.76	0.76	0.83	1.03

*Based on hospitals with highly reliable COF coding only (2020 *n* = 502, 2021 *n* = 519)

Figure 4 describes the estimated rates of patients admitted to Australian public hospitals with pre-existing CDI symptoms in 2020 and 2021. This cohort includes patients with a principal CDI diagnosis and patients with a non-principal CDI diagnosis with a COF2 (*C. difficile* acquired either in the community or during a previous healthcare admission [healthcare-associated community-onset CDI, community-associated CDI, or indeterminate CDI onset]). Separations with pre-existing CDI accounted for over 80% of all patients with a CDI diagnosis, which is consistent with 2019 data.[17] In 2020, there 6,630 separations with pre-existing CDI; this increased to 8,499 separations with pre-existing CDI in 2021.

Figure 4: Estimated rates of pre-existing CDI (A04.7) presenting to Australian public hospitals, 2020–2021*



	2020 Q1	2020 Q2	2020 Q3	2020 Q4	2021 Q1	2021 Q2	2021 Q3	2021 Q4
Estimated rate of separations with pre-existing CDI	3.27	2.98	2.94	3.23	3.42	3.58	3.69	4.48
Rate of non-principal diagnoses with COF2	1.87	1.81	1.89	1.95	2.01	2.19	2.25	2.59
Rate of non-principal diagnoses with COF1	0.69	0.79	0.60	0.65	0.76	0.76	0.83	1.03

*Based on Australian public hospitals with highly reliable COF coding only (2020 *n* = 502, 2021 *n* = 519)

The rate of separations with pre-existing CDI symptoms has increased each year since 2016.[6,17] The highest rate of separations with pre-existing CDI symptoms (3.80 separations per 10,000 bed days) occurred in 2021. Table 1 provides a summary of separations with pre-existing CDI symptoms from 2016 to 2021.

Table 1: Rate of separations with pre-existing CDI symptoms, 2016–2021

Year	Rate of separations with pre-existing CDI symptoms (diagnoses per 10,000 bed days)
2016	2.92
2017	2.95
2018	3.18
2019	3.19
2020	3.22
2021	3.89

Separations for 2020 and 2021

The total number of separations from Australian public hospitals declined between 2019 (*n* = 7,504,330) and 2020 (*n* = 7,242,690) by 3.46%.[17] This was influenced by the introduction of COVID-19 pandemic restrictions, which reduced usual hospital activity, including restrictions on elective procedures.[12]

Separations increased by 4.66% from 2020 to 2021 as health services attempted to return to routine service provision in 2021. Separations with CDI diagnoses also increased for each category between 2020 and 2021 (Table 2). However, the increase in separations with a CDI diagnosis may be influenced by other factors, in addition to the resumption of inpatient services in 2021.

Table 2: Number of CDI-related separations (A04.7) in Australian public hospitals* in 2020–2021

Separations	2020	2021	Relative change between 2020 and 2021
Number of separations in Australian public hospitals	7,242,690	7,580,271	↑ 4.66%
Number of separations with a CDI diagnosis	8,127	10,512	↑ 29.35%
Number of separations with a principal CDI diagnosis	2,644	3,551	↑ 34.30%
Number of separations with a non-principal CDI diagnosis	5,483	6,961	↑ 26.96%
Number of separations with a non-principal CDI diagnosis, with COF1*	1,371	1,835	↑ 33.84%
Number of separations with a non-principal CDI diagnosis, with COF2*	3,986	4,948	↑ 24.13%
Estimated pre-existing burden Principal CDI + non-principal CDI, COF2*	6,630	8,499	↑ 28.19%

*Australian public hospitals with highly reliable COF coding only (2020 *n* = 502, 2021 *n* = 519)

Length of stay for patients with CDI diagnoses

Table 5 shows the progressive 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 all public hospital admissions was 3 days between 2019–2020 and 2.9 days between and 2020–2021.[12]

Overall, the average length of stay for patients with a CDI diagnosis has remained steady since 2015. Generally, patients with CDI diagnoses continue to remain in hospital up to nearly five times longer (16.58 days) than the average length of stay (2.9 days).

Table 3: Average length of stay (days) for patients with a *Clostridioides difficile* diagnosis in Australian public hospitals, 2012–2021

Year	Length of stay in days		
	Principal CDI diagnosis	Non-principal CDI diagnosis	Any 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
2020	7.30	19.39	15.46
2021	7.45	19.89	15.69

A lengthy hospital stay has major impacts on patient outcomes and healthcare resources.[14] Patients who have an extended length of stay generally require invasive treatments and interventions, are often elderly, have chronic underlying comorbidities and have a higher risk of acquiring infections.[14] These are generally the same factors that increase the risk for CDI.[2,4]

Discussion

The rates of CDI diagnosis fluctuated across 2020 and 2021. The lowest rates of CDI since 2016 were recorded in the first three quarters of 2020, and the highest rates of CDI since 2016 were recorded in the last two quarters of 2021. The rise in the rate of CDI was most noticeable for community-onset CDI (separations with pre-existing CDI symptoms). In 2020 and 2021, community-onset CDI accounted for over 80% of all separations with a CDI diagnosis. Healthcare-associated hospital-onset CDI accounted for less than 20% of all CDI diagnoses.

Community-onset CDI includes separations defined as healthcare-associated community-onset CDI, community-associated CDI, indeterminate CDI onset CDI[18], and patients with recurrent disease who are readmitted to hospital for further treatment.[5] The increasing burden of community-onset CDI is likely to increase pressure on healthcare services and present new challenges for healthcare workers and health service organisations nationally.

Over recent years, simple, organisation-wide, interventions have been implemented to prevent and control CDI in hospitals.[2] Antimicrobial stewardship programs are one of the most important interventions for reducing the risk of CDI[3]; especially reducing inappropriate prescribing of antimicrobials such as, cephalosporins, which has had an impact on hospital-onset CDI.[19-21] Other interventions such as early detection and appropriate testing, environmental cleaning programs, the use of single rooms and ensuites and transmission-based precautions in addition to standard precautions for symptomatic patients, require an organisational approach to help to prevent disease transmission and target modifiable risk factors.[2,3,19]

For many patients, previous healthcare exposure is a risk factor for the onset of CDI in the community. Early discharge programs may be contributing to the increased rate of community-onset CDI. These programs involve continuing treatments such as antimicrobial therapy in the community, which can predispose patients to CDI.[5] [19]

Medications such as proton pump inhibitors (PPI) and antimicrobials are often associated with the onset of CDI.[3] Both these classes of mediation are widely used in the community and often inappropriately prescribed.[22] Like antimicrobial medication, PPI medication causes alterations in microflora of the gut, which can increase the risk of *C.difficile* spore germination.[23, 2] While community national dispensing data on these medications are available, there are limitations that make it difficult to compare dispensing data and rates of CDI.

Patients may also have been exposed to *C.difficile* during a hospital admission, and develop CDI symptoms or recurrent infection after discharge.[5] The role of recurrent CDI may be an underestimated factor that has contributed to the increased rate of community-onset CDI. Data on recurrent CDI are not collected by all Australian states and territories, however, between 25%[2] to 47%[4] of patients with an initial episode of CDI will experience recurrent disease. Recurrent CDI occurs most frequently within the first week after completion of CDI specific antimicrobial treatment, and up to 65% of patients will experience a second relapse of infection.[4,2] Conversely, there is an increasing number of patients who have had no recent healthcare exposure who develop CDI in the community.[5,19] The role of other factors, such as animal health and exposure, food production, and asymptomatic carriage and transmission of CDI, is not fully understood or easy to control.[1]

Impact of the COVID-19 pandemic on CDI rates in Australian public hospitals

It is not clear to what extent the COVID-19 pandemic and its impact on health service provision in Australia directly affected rates of CDI in 2020 and 2021, particularly the observed fluctuation in CDI rates. Restrictions on health service provision during 2020 and the reintroduction of health services such as elective surgery in 2021, impacted the number of all separations recorded during 2020 and 2021. In the community, there were less face-to-face general and specialist practitioner consultations, and an increase in the use telehealth. In acute health service organisations, elective surgery was suspended.[24]

During the pandemic response period in 2020 and 2021, antimicrobial use in the community decreased by 25.3%, and prescriptions for antimicrobials were issued at a lower rate compared to before the pandemic – from 16 per 100 general practitioner (GP) visits in 2019 to 7 per 100 GP visits in 2020 and 2021.[22] A greater awareness of and enhanced infection prevention and control practices in health service organisations may have helped to initially reduce the risk of hospital-onset CDI.[7,22,25] However, increased pressure on the health system throughout the pandemic, such as staff shortages and higher patient acuity and turnover, may have contributed to the increased CDI acquisition in many settings, including in the community in 2021.

There is early evidence that co-infection with COVID-19 and CDI leads to worse outcomes for patients. Patients co-infected with COVID-19 and CDI have longer and more severe infections, and are at an increased risk of death.[26] In addition, patients who have had past COVID-19 infection may represent a new risk group due to post-infection health complications.[7]

The reduction in hospital-onset CDI and the increase in community-onset CDI in Australia is consistent with international data.[19] Surveillance of community-onset CDI is limited in Australia, and case numbers are likely to be under-reported.[27]

What can be done to improve CDI rates in Australia?

These findings can be used to raise awareness of the prevalence of CDI in public hospitals and the community, as well as supporting the development of targeted resources for the prevention and control of CDI, and the promotion of hospital- and community-based interventions such as antimicrobial stewardship (AMS) programs.

Primary health care clinicians and residential aged care staff can play an important role in reducing the burden of community-onset CDI. Interventions such as:

- reducing inappropriate or prolonged prescribing of antimicrobials
- supporting the use of standard and transmission-based precautions for symptomatic patients and residents
- promoting high standards of environmental cleaning
- increased awareness of risk factors for CDI and high-risk patient groups
- increasing awareness for the risk of recurrent infection
- developing indicators for early detection and appropriate testing.[3,5,19]

The Commission will continue to monitor and report on the burden of CDI using patient administrative data and monitor for epidemiological changes.

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