

Consultation on surveillance and
monitoring of *Clostridium difficile*
infection in Australia

Discussion paper

April 2015

This discussion paper is available on the website of the Australian Commission on Safety and Quality in Health Care (the Commission) www.safetyandquality.gov.au

The Commission will be accepting online and written submissions up to (5 June 2015). The discussion paper contains ten consultation questions that should provide the basis for your comments. The consultation questions are summarised in section 9 of the paper.

Online submissions should be made using the online submission page at:
<https://www.surveymonkey.com/r/cdidiscussionpaper>

Written submissions marked '*Clostridium difficile* infection discussion paper' may be forwarded to: Director, National Healthcare Associated Infection Prevention Program, Australian Commission on Safety and Quality in Health Care, GPO Box 5480, Sydney NSW 2001 or emailed to: HAI@safetyandquality.gov.au

Please be aware that in order to ensure transparency and promote a robust discussion, all submissions will be published on the Commission website, including the names of individuals or organisations making the submission. The Commission will consider requests to withhold the contents of any submissions made in whole or part.

Acknowledgments

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FOREWORD

The Australian Commission on Safety and Quality in Health Care (the Commission) is undertaking consultation with key stakeholders with the aim of providing recommendations to inform national strategies to reduce *Clostridium difficile* infection (CDI) in Australia. Since 2007, clinical experts have identified CDI as a significant priority for patient harm reduction.¹ In 2008, Australian Health Ministers endorsed a Commission recommendation that jurisdictions collect information to identify epidemic strains should they emerge in Australian patients.

Between 2007 and 2012, the Commission took the lead with jurisdictions to develop standardised definitions, a data-set specification and a surveillance implementation guide for CDI. It was recognised during this work that it was very complex and resource intensive to accurately attribute a case of CDI as either healthcare acquired or community acquired. The advice from clinical experts was to concentrate on the number of cases identified in hospital patients. This was in keeping with the aim of the recommendations to Health Ministers to garner information on the presence of epidemic strains and outbreaks. The surveillance definition of CDI was modified to include a category of hospital identified cases. This allowed for determination of healthcare acquired versus community acquired cases to continue, where it was possible to distinguish between the two.

As the result of epidemic strains of CDI identified in patients in two states during 2010, the Commission sponsored a symposium with representatives from the state and territory health departments, public and private hospital sectors, laboratories and professional associations. The main objectives of the symposium were to provide an understanding of the potential impact of epidemic strains of *C. difficile* and an overview of the prevalence of CDI, and to formulate strategic options to prevent epidemic CDI from gaining a foothold in Australia.

As a result of the symposium, the Commission funded PathWest to undertake a snapshot survey of *C. difficile* in Australia, to determine the molecular epidemiology of *C. difficile* and identify epidemic *C. difficile* strains within Australian patients. The Australasian Society of Infectious Diseases published guidelines for the management and diagnosis of CDI at this time.

During 2011, an upward trend in CDI cases across all states was reported by members of the Commission's Healthcare Associated Infection (HAI) Technical Working Group. A subsequent publication of CDI rates from all states and the ACT showed an increase in the annual incidence between 2011 and 2012.² A peak in the number of cases was evident in 2011, and a smaller peak occurred in 2012. These two peaks in the number of CDI cases in 2011 and 2012 were not maintained into 2013, however the upward trend in the rate of CDI has remained above the 2010 baseline.

The reason for the upward trend in CDI rates since 2011 is not clear, with several causes postulated, including improved measurement and reporting, better laboratory practice or an unidentified food source. Two further projects were undertaken during 2012 in an attempt to provide answers to the increase:

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- The Commission funded PathWest to undertake a second survey that included not only ribotyping, but also the collection of patient information and Potential risk factors for CDI.
- The Communicable Diseases Network of Australia undertook a risk assessment to test the hypothesis that the increased rates of *C. difficile* were linked to transmission by food.

Despite these actions, a clear epidemiological picture of CDI in Australia has still not emerged.

Further work undertaken by the Commission in 2013 included a survey of jurisdictional surveillance units to identify and compare the CDI surveillance methodology used in each jurisdiction. The results of the survey indicated that the nationally agreed definition for CDI surveillance and reporting CDI were being used to identify cases in hospital patients. However, not all cases could be reported as either acquired during health care or in the community.³

By providing an overview of the current issues and potential solutions, this paper aims to stimulate discussion and build on issues identified by jurisdictions, professional organisations and clinicians. The responses from this discussion paper will inform the development of national recommendations regarding CDI in Australia.

1 EXECUTIVE SUMMARY

Clostridium difficile infection (CDI) is an infection that commonly affects hospitalised patients and people in the community. The transmission, prevention and control of CDI are complex. Internationally, the incidence of CDI has increased significantly over the past 10 years. In Australia, the epidemiology of CDI is unclear as there has been variability in the rates reported over time, with peaks and a general upward trend in the number of cases reported. Understanding the epidemiology of CDI is paramount in developing and evaluating strategies to reduce the incidence of CDI. Data from both research and surveillance systems with timely dissemination of information will enhance prevention and control strategies. In Australia to date, the current understanding of CDI has been hampered as there is no aligned, co-ordinated approach to the analysis of data collated through the jurisdictional surveillance units.³ Commonwealth, state and territory jurisdictions and professional organisations have developed a range of prevention and control strategies that would be enhanced by a national approach to surveillance and reporting.

The diagnosis of CDI is based on a combination of observed signs and symptoms and laboratory findings. Variation in laboratory practices across the country impacts the quality of available data and the ability to accurately understand the epidemiology of CDI. This is further compounded by gaps in CDI surveillance. Hospital-based CDI surveillance, using a standardised definition, commenced in recent years through the work of the Commission and jurisdictional health departments. This system provides a surrogate marker of CDI epidemiology in a targeted population. However, the data do not distinguish between healthcare associated (HCA) and community associated cases of CDI, nor robustly identify cases that occur in the community and can be potentially difficult to interpret given variations in laboratory practice.

CDI tends to have a higher prevalence and poorer health outcomes in people who are elderly, chronically unwell or who are immunocompromised. Many of these people have frequent admissions to hospitals. In many cases, identifying where CDI was acquired is difficult using the current surveillance definitions. In addition, the current data collection does not provide information on patient outcomes, such as disease severity or mortality.

The prevention and control of CDI is multifaceted and complex. Until the understanding of CDI in Australia is improved, developing and implementing further interventions will be challenging and an incomplete picture of the disease in Australia will remain.

Advice from clinical experts suggests the strategies required will be based primarily on the issues covered in this discussion paper: coordinated surveillance; standardisation of laboratory testing and practice; and the identification of research priorities. Communication and oversight will be imperative to ensure that Australia has a system in place that can identify and respond to changes in CDI epidemiology, and to avoid outbreaks associated with high patient morbidity and mortality.

2 INTRODUCTION

2.1 The Commission

The Australian Commission on Safety and Quality in Health Care (the Commission) was jointly established in 2006 by Australian, state and territory governments. The role of the Commission is to provide health ministers with strategic advice on best practices to improve safety and quality in the health system. The Commission is also responsible for developing and supporting national safety and clinical standards; formulates and implements national accreditation schemes; and develops national health related data sets. HAI has been a priority program since the inception of the Commission. The HAI Program coordinates national programs including clinical capacity building, infection control guidelines, hand hygiene and the National Safety and Quality Health Service Standards, Standard 3.

The *National Health Reform Act 2011* specifies the Commission's roles and responsibilities, these include:

- formulating standards, guidelines and indicators relating to healthcare safety and quality matters;
- advising health ministers on national clinical standards promoting, supporting and encouraging the implementation of these standards and related guidelines and indicators;
- monitoring the implementation and impact of these standards;
- promoting, supporting and encouraging the implementation of programs and initiatives relating to healthcare safety and quality matters;
- formulating model national schemes that provide for the accreditation of organisations that provide healthcare services and relate to healthcare safety and quality matters;
- collecting, analysing, interpreting and disseminating information relating to healthcare safety and quality matters;
- publishing reports and papers relating to healthcare safety and quality matters.

One component of the Commission 2013–16 work plan is the responsibility for nationally coordinated action to address healthcare associated infections. Key priorities include the development of a coordinated and efficient national approach to the reporting and surveillance of healthcare associated infections across Australia, and the sharing of experience and best practice.

2.2 An introduction to *Clostridium difficile* infection

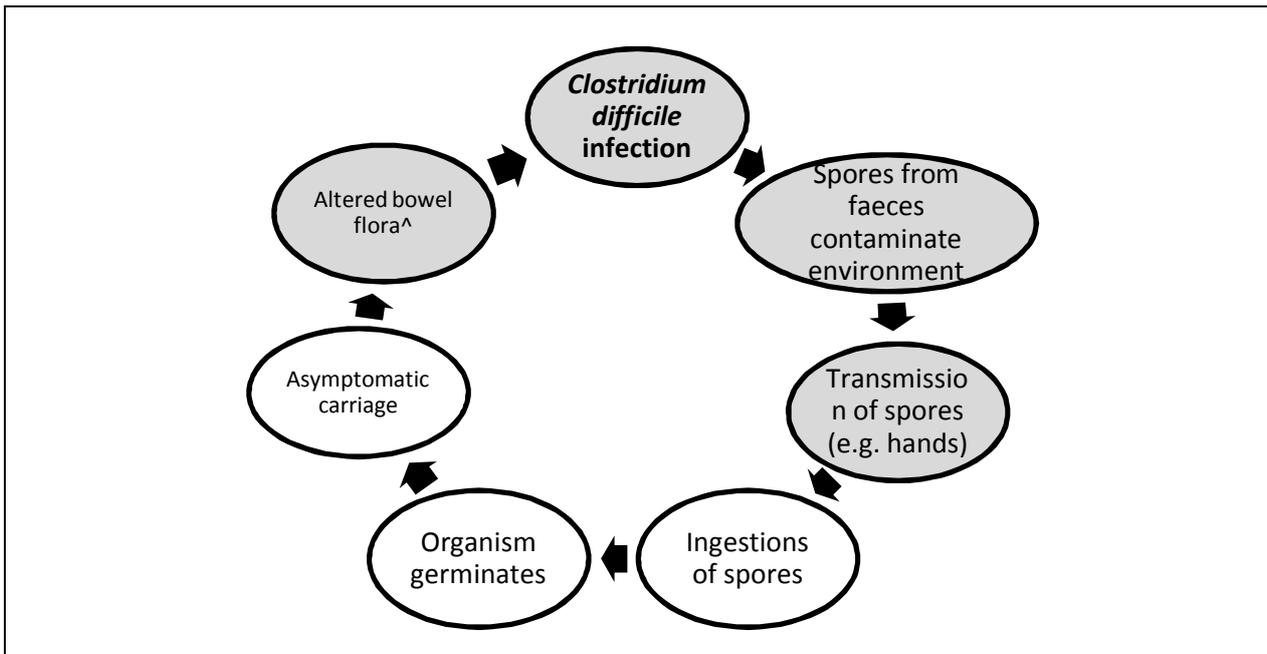
Clostridium difficile is a bacterium that commonly causes diarrhoea in hospitalised patients and individuals in the community. When *C. difficile* causes symptomatic illness in the past this has been called ‘*Clostridium difficile*-associated diarrhoea’, however, the term ‘*Clostridium difficile* infection’ (CDI) is now preferred.^{4,5} For the purposes of this discussion paper, CDI is used. Around the world, the incidence of CDI has been increasing since 2002. Explanations for this increase include a change in circulating strains of *C. difficile* – for example, the emergence of a strain known as ribotype (RT) 027 – and improved laboratory detection.⁶ Australia is not immune to the impacts of CDI: It is emerging as a public health risk, with an increase in cases between 2011 and 2012, which included an increase in community associated infections.² Reviews examining mortality and CDI indicate that CDI has a significant adverse effect on hospitalised patients, with suggested all-cause mortality at 30 days ranging from 9% to 38% and attributable mortality between 6% and 7%.^{7,8} CDI also has an impact on health services through prolonged length of stay in hospital.^{9–12}

Clostridium difficile can exist in vegetative or spore forms. Patients with CDI can contaminate the environment with spores, and this is exacerbated when patients have diarrhoea. The contaminated environment can subsequently act as a reservoir for transmission, for example, by the hands of healthcare workers.^{5,13} The primary mode of transmission of *C. difficile* is person-to-person by the faecal-oral route.¹⁴ As *C. difficile* spores can survive in the environment for prolonged periods of time, ongoing risk of transmission exists unless adequate decontamination occurs. Ingestion of the organism does not necessarily result in disease. Disruption of the bowel flora is an important factor, and occurs most commonly following exposure to antibiotics, chemotherapy, anti-peristaltic drugs and gastroenterological surgery.^{15,16} Antibiotics are thought to be a particularly important risk factor for CDI because they reduce the colonisation resistance of the bowel. Several studies have reported an association between antibiotic use and CDI.^{16–18}

Figure 1 summarises the CDI cycle based on current understanding. However, recently the use of whole genome sequencing suggests that there may be genetically diverse sources of *C. difficile*, in addition to symptomatic patients, that play a part in *C. difficile* transmission.¹⁹

It has been hypothesised that food could be as a possible source of *C. difficile* in community settings, but evidence to confirm or refute this hypothesis is incomplete.²⁰ Importantly, however, *C. difficile* is recognised as both a gut coloniser and cause of diarrhoea in food animals^{21–25} and hence CDI has the potential to be a ‘One Health’ issue in Australia.²⁶ In Australia there is no published evidence of transmission of *C. difficile* to humans from animals or agriculture and the Australian Scientific and Technical Antimicrobial Resistance Group does not currently recognise CDI as a One Health issue.

Figure 1. CDI cycle



Notes: ^ Altered bowel flora can occur in a number of ways, including exposure to antibiotics. Shaded areas indicate the stages at which strategies can be introduced to prevent ongoing transmission. Adapted from Mitchell, Gardner and Hiller (2014).²⁷

In a recent study, strong evidence suggested that strain type is an independent contributor to disease severity and outcome in HCA CDI.²⁸ However, what remains unclear is how this information should be translated into clinical care, with decisions based on host factors (age, healthcare association, co morbidities, concomitant medications, etc.) likely to remain the most important influences of care at present.²⁹

2.3 Purpose of this discussion paper

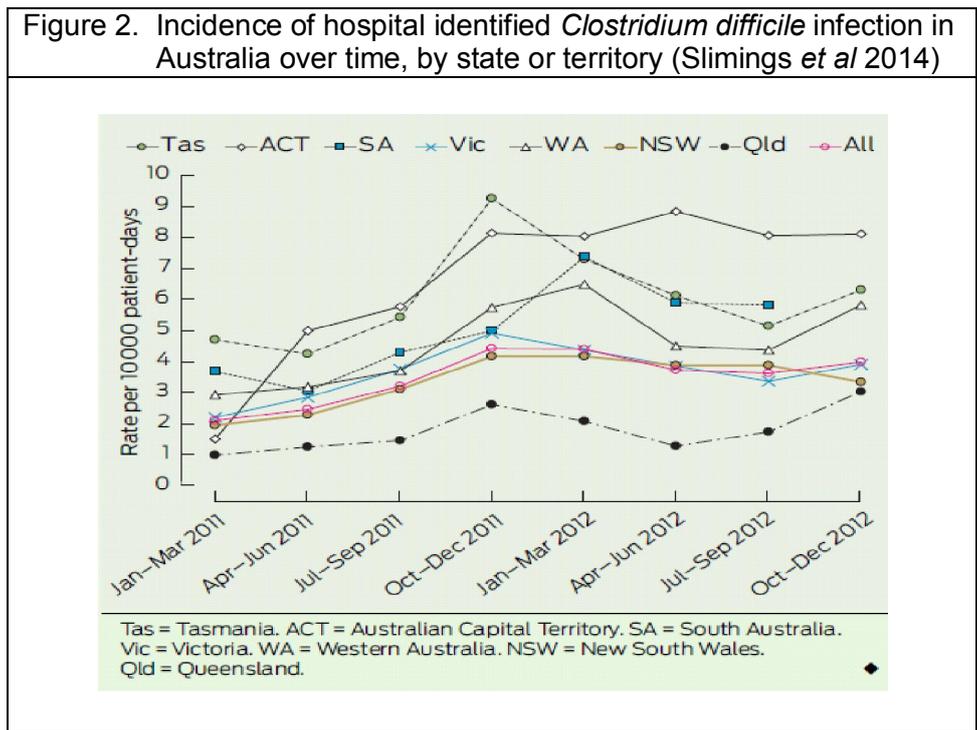
This paper builds on a CDI symposium led by the Commission in Sydney in 2010 and the identification of CDI as a key organism of importance by Australian infection control professionals.³⁰ In addition, the work undertaken by the Communicable Diseases Network Australia (CDNA), investigating the potential of foodborne transmission of community acquired *C. difficile* has been considered. Following consideration of commentary received on the issues and options of this discussion paper, recommendations will be developed for consideration by the states and territories and the Commonwealth on national strategies to address the burden of CDI in Australia.

The epidemiology of CDI in Australia will be the first element of this paper to provide a sound foundation to consider issues identified by clinical experts. Discussion questions have been included after each section; each response to the discussion questions provided to the Commission will be reviewed. Many of the issues raised in this paper are linked and overlap. Linkages between the issues are explored in Section 8.

3 CDI IN AUSTRALIA

3.1 Epidemiology of CDI in Australia

Reports on CDI across the world suggest that the incidence has increased significantly over the past 10 years.^{31–33} During the same period, there have been outbreaks of CDI in North America and Europe that were associated with increased morbidity and mortality. These increases occurred at the same time as the emergence of fluoroquinolone-resistant *C. difficile* RT-027. In more recent years, Australia has witnessed an increase in hospital-identified CDI. In a study undertaken by Slimings *et al.* (2014), data from 450 public hospitals in New South Wales, Queensland, South Australia, Tasmania, Victoria, Western Australia and the Australian Capital Territory collected between 2011 and 2012 were analysed.¹⁵ During this period, there were 12 683 cases of hospital-identified CDI, giving an aggregate incidence of 3.65 per 10 000 patient days. The annual incidence between 2011 and 2012 rose by 24% from 3.25 to 4.03 per 10 000 patient days. The aggregate incidence of community associated CDI during the study period was 1.08 per 10 000 patient days, increasing by 24% between 2011 and 2012. Since early 2012 the incidence of CDI has remained above the 2011 level.² Of the hospital-identified cases, 26% were community associated CDI cases with rates substantially increasing. There have also been other Australian reports describing an increase in hospital-identified and community associated CDI.^{34, 35} Figure 2 illustrates that compared to the 2010 baseline; there has been an upward trend in the rate of CDI reported.



There are several potential causes for the observed overall increase in CDI, including:

- changes and or variations of circulating strains of *C. difficile*;
- changes in laboratory practice and therefore ascertainment bias;
- changes in patterns of antimicrobial use or other risk factors;
- differences in, or compliance with, infection control practices; and
- an increased risk of transmission in the environment, including community transmission pathways.

It is difficult to obtain a clear picture of antimicrobial usage across the country; and although the Commission is currently establishing a national antimicrobial resistance and usage surveillance system (the AURA project) and *C. difficile* is an organism of interest in that project, establishing formal surveillance for CDI is not part of its remit.

The Commission has funded two voluntary snapshot surveys examining circulating strains of *C. difficile* in 2010 and 2012. The objective of these surveys was to determine the current molecular epidemiology of CDI in Australia, the relative frequency of epidemic *C. difficile* strains within Australia and to determine the frequency of severe disease. In the last survey, isolates obtained from 19 laboratories/hospitals were polymerase chain reaction (PCR) RT. RT-014 group (25%), RT-002 (10%), RT-056 (6%) were the most common. Compared to the 2010 snapshot survey, a number of 'new' RTs appeared. The survey identified RT-056. This RT has been isolated from Australian cattle and a single poultry isolate in a Dutch study.³⁶ It represented the first report of RT 056 in cattle.³⁷ RT 056 has been identified as among the most frequent types of toxigenic isolates found in a European hospital survey, associated with complicated disease outcome.³⁶ The survey also identified RT244, which has been associated with more severe disease and a higher mortality rate.³⁸ It is important to note that the CDI situation in Australia is continuously evolving, as illustrated by this snapshot survey. Hence, it is important for Australia to have a surveillance system that is able to identify important epidemiological changes and respond accordingly.

The impact CDI has on patients varies, depending on the country and circulating strains.⁸ In Australia, there are limited published data describing the clinical impact of CDI. One Australian study including over 60 000 admissions examined mortality and CDI in Australia, and results indicated significantly higher all-cause mortality in persons with CDI compared to matched controls. Those with CDI were twice as likely to die compared to matched controls without CDI, after adjusting for co-morbidities, length of hospital stay and antibiotic exposure.²⁷ The current CDI surveillance system in Australia, which focuses on cases of CDI identified in Australian hospitals, does not reliably capture patient-outcome data or identify cases of CDI that occur in the community — only those patients that present to hospital. Therefore, in Australia, the burden of community associated CDI – and definitive data regarding any transmission in these settings – remains largely unknown.

3.2 Available resources to reduce the incidence of CDI in Australia

A number of Australian resources are available for healthcare workers and service providers to reduce the incidence and management of CDI. These resources include:

- *Australian Guidelines for the Prevention and Control of Infection in Healthcare* (National Health and Medical Research Council, 2010);¹⁴

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- *ASID/ACIPC position statement: infection control guidelines for patients with Clostridium difficile infection in healthcare settings* (2011);⁵
- *Clostridium difficile laboratory testing in Australia and New Zealand: national survey results and Australasian Society for Infectious Diseases recommendations for best practice* (2011);³⁹
- *Australasian Society for Infectious Diseases: guidelines for the diagnosis and treatment of Clostridium difficile infection* (2011);⁴⁰
- *Implementation Guide for Surveillance of Clostridium difficile Infection* (2013)⁴¹
- State-based protocols and resources.^{42–47}

Internationally, additional resources have been developed to reduce the incidence of CDI in hospitals. These include trigger tools, investigation of severe cases, high-impact interventions and root-cause analysis tools.^{48–51}

3.3 Consultation questions for this section

- Is any additional guidance or supporting documentation required for the prevention and control of CDI in Australia, over and above those currently being undertaken?

The full list of numbered consultation questions for this discussion paper is detailed in section 9.

4 OVERVIEW OF CURRENT ISSUES

There are Australian and international guidelines for the prevention and control of CDI in healthcare settings.^{5, 52} Nonetheless, an improved understanding of CDI transmission indicates there are knowledge gaps about the transmission of this disease.⁵³ To assist in the development of this discussion paper, advice was sought from members of the Healthcare Associated Infection Advisory Committee, Healthcare Associated Infection Technical Working Group, Information Strategy and Commonwealth Programs team. The advice on the pertinent issues of CDI in Australia forms the basis of this current consultation and discussion paper. The questions posed on each section were endorsed by the Commission's Healthcare Associated Infection Advisory Committee.

Through this process, the following themes (issues) were identified:

- laboratory testing methods (section 5)
- CDI surveillance in Australia (section 6)
 - in hospitals
 - in the community setting
- priorities for research (section 7)
- communication and oversight (section 8).

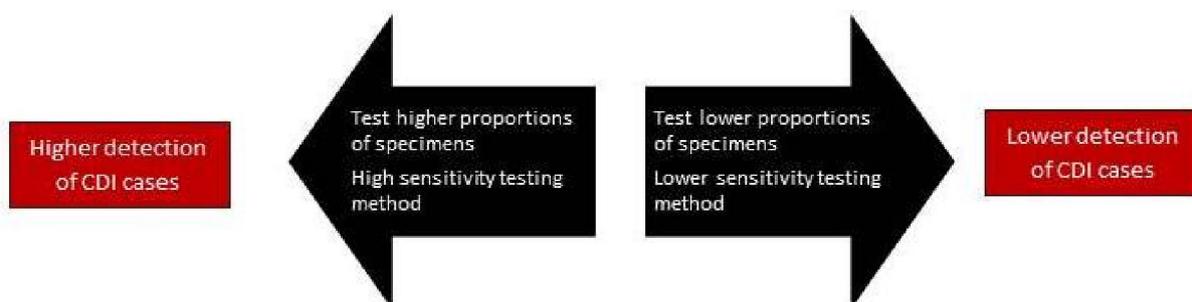
Each of these issues will now be explored in more detail, through which it becomes clear that there is some overlap between the identified issues.

5 ISSUE 1: LABORATORY TESTING METHODS

5.1 Diagnosis of CDI

The diagnosis of CDI is based on a combination of signs and symptoms, and laboratory findings and/or the demonstration of pseudomembranous colitis by colonoscopy or histopathology. There is a range of laboratory tests used to detect the presence of toxin producing *C. difficile*, or its toxins alone, in stools. These include bacterial culture, immunoassays to detect enzymes present in the organism cell wall (glutamate dehydrogenase - GDH), immuno and cytotoxin assays to detect *C. difficile* toxins A and/or B and various molecular assays to detect toxin genes of *C. difficile*.^{54, 55} A survey in Western Australia in 2008 identified significant variation in methods for detecting *C. difficile* in diagnostic laboratories within that state.³⁴ Variation in laboratory testing has the potential to impact the quality of surveillance data. The Australian Society for Infectious Diseases (ASID) *C. difficile* Working Party conducted a review of methodologies and testing recommendations, resulting in ASID-endorsed evidence-based recommendations for best practice in diagnosis of *C. difficile*.³⁹ Two issues addressed that are relevant to this section of the discussion paper were: sample selection (which samples should be tested); and laboratory diagnosis (the methods used to detect *C. difficile*). Standardisation of testing methods creates a level playing field and improves epidemiological data.⁵⁶ Figure 2 summarises the potential effect of laboratory testing methods on CDI detection and surveillance.

Figure 2. Potential effect of testing methods on detection of CDI and surveillance data



It has been suggested that the overall increased number of cases of CDI identified recently in Australia may, in part, reflect changes in diagnostics, sample submission, test-requesting practice, testing policies and increased awareness. The degree to which increases in CDI can be ascribed to changes in laboratory practice remain unknown and will continue to do so until there is standardised practice.

5.2 Recommendations for *C. difficile* laboratory practice

Table 1 provides an overview of ASID recommendations produced in 2011. The recommendations are largely supported by recently released CDI guidelines from the Society of Healthcare Epidemiology of America;⁵² and updated guidance on the diagnosis of CDI from the Department of Health in the United Kingdom.⁵⁷ However, the science around

C. difficile laboratory testing and diagnoses is quickly evolving and the recommendations below do not necessarily reflect current laboratory practice.

Table 1. Recommendations for *C. difficile* laboratory practice (Developed by the Australasian Society for Infectious Diseases)

Recommendation	Rationale
Sample selection	
Testing for <i>C. difficile</i> or its toxins should be performed only on unformed stool unless ileus due to <i>C. difficile</i> is suspected.	The function of testing is to confirm a clinical diagnosis or suspicion of CDI.
All unformed stools submitted from patients (adults and children >2 years) who have been hospitalised 72 h or more should be tested for CDI, irrespective of the physician's request.	Early diagnosis enables early treatment. CDI is often unsuspected, even in severe disease.
Unformed repeat stool samples submitted from patients (adults and children >2 years) with diarrhoea that has persisted for longer than 48 h and in whom initial stool tests were negative for common enteropathogens should be tested for CDI, irrespective of the physician's request.	Presentations of CDI in patients from the community are increasingly prevalent.
<i>C. difficile</i> testing in children under 2 years should be performed and interpreted in consultation with a clinical microbiologist or paediatrician.	<i>C. difficile</i> carriage is common in young children and is often asymptomatic.
Repeat testing during the same episode of CDI is of limited value and should be discouraged within 4 weeks of a positive test, unless a more sensitive method is used.	Repeat testing serves no value as a test of cure in view of prolonged asymptomatic carriage in recovering or immune patients. To assess response to treatment, clinical assessment is required.
Repeat <i>C. difficile</i> testing during the same episode of diarrhoea is of limited value and should be discouraged.	An initial negative test in a low incidence setting has a high negative predictive value for CDI.
Laboratory diagnosis	
The diagnosis of CDI should be based on clinical signs and symptoms in combination with laboratory tests.	Patients may develop diarrhoea that resolves spontaneously. Patients with a positive result will not require treatment unless ongoing symptoms are present.
The primary screening method for <i>C. difficile</i> used by major laboratories should be optimally sensitive (>90%) and preferably offer a rapid turnaround time.	Rapid, sensitive screening allows for prompt detection of potential cases.
If the primary screening method is sensitive but not specific (e.g. a GDH assay of proven sensitivity) then a 2-step approach should be adopted. GDH-positive stools are tested by a secondary method of sufficient sensitivity and specificity.	Use of a secondary method reduces the number of false-positive results. Cost is reduced by confining use of secondary confirmatory methods to those samples that are GDH-positive.
Primary screening by enzyme immunoassay or immunochromatography for toxins A and B (without other testing) is not recommended due to poorer sensitivity of the available assays.	When compared with the gold standard (toxigenic culture), these tests have mean sensitivity of 48–79% across method types.
All (or a sample of) CDI cases should have <i>C. difficile</i> culture performed to allow typing and susceptibility testing.	Certain strains are more likely to cause severe disease and mortality.
Toxigenic culture using optimal methods provides the reference standard against which other tests should be compared.	Previous test evaluations have relied on stool cytotoxicity assays as the reference standard, and this has led to overstatement of the method sensitivity.

Note: Adopted from Ferguson *et al.* ³⁹ (refer to original document for full details).

At present, an ASID working group is currently reviewing the existing recommendations, particularly in light of increasing molecular testing. Once developed, these new recommendations will represent best practice *C. difficile* laboratory testing in Australia. In light of potential differences in governance arrangements in laboratories across the country, the Royal College of Pathologists of Australasia Quality Assurance Program may play a valuable role in facilitating implementation and provide external quality assurance.

5.3 Consultation questions for this section

- How can recommendations for *C. difficile* laboratory practice be best developed and implemented?
- With increasing molecular testing, is there a need to continue culture-based CDI surveillance for typing and antimicrobial resistance purpose?

The full list of numbered consultation questions for this discussion paper is detailed in section 9.

6 ISSUE 2: CLOSTRIDIUM DIFFICILE INFECTION SURVEILLANCE IN AUSTRALIA

6.1 Overview

Surveillance of healthcare associated infections is the cornerstone of infection prevention and control. Surveillance involves identification of an event, data collection, data analysis, interpretation and timely dissemination of findings so that appropriate action can be taken to reduce morbidity and mortality and to improve health.⁵⁸ Effective surveillance serves as an alert system for unusual increases in incidence. Surveillance data for quality improvement must be of high quality, with characteristics including representativeness, timeliness, accuracy, authoritativeness and clarity.^{59, 60}

6.2 Hospital-based CDI surveillance

The issues related to CDI diagnosis and surveillance are important to understand as they have implications for case definitions and ascertainment bias. Consensus criteria for CDI surveillance in Australia have been developed using internationally accepted definitions.⁶¹ More specifically, laboratory detection of *C. difficile* is the most common method of defining a case of CDI.^{62, 63} In 2009, a CDI surveillance definition was developed by the HAI Advisory Committee of the Commission and was endorsed by all Australian health ministers. At a minimum, hospitals undertake surveillance of hospital-identified CDI, which refers to cases of CDI identified in admitted (hospitalised) patients – or those attending the emergency department and outpatients departments at hospital – at the time a specimen was collected.⁴¹

6.3 Advantages and disadvantages of hospital-identified CDI surveillance

The major advantage of hospital-identified CDI surveillance is that it is laboratory based, meaning this is the least resource-intensive CDI surveillance method. It provides a surrogate marker for the epidemiology of CDI in a targeted population – patients receiving care associated with hospitals. It does not, however, distinguish between healthcare-associated (HCA) and community associated cases of CDI. Therefore, it has been suggested that this form of surveillance would be inappropriate as a performance indicator for individual hospitals,⁶⁴ a view supported by the Commission's HAI Advisory Committee. Through the work of the HAI Technical Surveillance Group, there are additional surveillance definitions available to further classify cases of CDI. These classifications reflect international expert consensus on categorisation of CDI cases, and a review of individual cases is required to apply these definitions:

- Healthcare Associated (HCA), Healthcare facility onset (HFO): CDI symptom onset or date stool specimen collection, more than 48 hours after admission to a healthcare facility
 - Healthcare-associated community onset: CDI symptom onset or date of stool specimen collection, in the community or within 48 hours of admission to a
-

healthcare facility, provided that symptom onset was less than 4 weeks after the last discharge from a healthcare facility

- Community associated: CDI symptom onset or date of stool specimen collection in the community or within 48 hours of admission to a healthcare facility, provided that symptom onset was more than 12 weeks after the last discharge from a healthcare facility
- indeterminate onset: patient that does not fit any of the above criteria for exposure setting (e.g. onset in community but within four and 12 weeks of discharge from a healthcare facility)
- unknown: exposure setting cannot be determined because of a lack of data.

These definitions have limitations; international work to further refine these as new epidemiology data becomes available may be required. Regardless, it is important to note that these are surveillance definitions; these are optional for Australian hospitals to use as part of a comprehensive CDI surveillance program. However, the use and implementation of these definitions require varying degrees of additional human resource follow-up.

Comprehensive details of these definitions are provided in the Commission's implementation guide for CDI surveillance. It is also important to note that the current surveillance system in Australia is generally associated with collation of public hospital CDI data and it does robustly identify cases of CDI that occur in the community – only those community patients who present to hospital. By contrast, a laboratory or public health notification type system provides a big-picture view of an entire population.

6.4 Options for CDI surveillance programs in Australian hospitals

There is a range of options available for CDI surveillance in Australia hospitals. These are summarised below and listed in a manner that reflects the anticipated resource burden (with the least demanding options listed first). Interventions might comprise a combination of one or more of these options, and variations thereof. They have been provided to stimulate discussion on this topic. Table 2 explores these options further in terms of the advantages and disadvantages of each. Critically, when attempting to classified CDI cases knowledge of exact patient movements is required. Consequently, this becomes difficult with different models of care, for example, patient movement between public hospitals, private hospitals and residential and aged care facilities (RACFs). In most instances, for people in a hospital undertaking CDI surveillance, access to systems that provide such detailed patient movement data is limited. When considering these options, it is important to consider the purpose of the data collection, noting previous comments regarding the use of CDI data as a performance indicator.

The range of options available for CDI surveillance in Australian hospitals is:

1. continuation with the current hospital-identified CDI surveillance program
 - A challenge with this process is identifying whether perceived increases are genuine. For example, there may be ascertainment bias due to laboratory methods (discussed in section 5.1). Standardisation of laboratory practice and routine data collection on test utilisation would clarify this situation.

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2. surveillance of healthcare associated, healthcare facility onset CDI, i.e. those cases occurring >48 hours after admission to hospital
3. continuous surveillance of severe cases of CDI in hospitals, rather than collecting additional information on all hospital identified and/or HCA HFO CDI
4. collection of additional data for hospital-identified and/or HCA HFO CDI cases
 - Examples include mortality (inpatient mortality at 30 days); the number of cases resulting in a colectomy; the number of cases resulting in admission to an intensive care unit.
5. snapshot surveys exploring *C.difficile* strains and reporting of severe cases
6. classification of each case of CDI identified in hospitals, fully using the available surveillance definitions detailed in the Commission's surveillance implementation guide for CDI. Note previous discussion on requirement to know patient movement
7. root-cause analysis of each case of CDI occurring in hospitals.
 - The aim of the root cause analysis process may include a review the sequence of events leading to the development of CDI in an effort to identify avoidable causes of infection, review management procedures and determine CDI classification (acquisition).
 - Examples of CDI root cause analysis tools are available.^{50, 51, 65}

Table 2. Advantages and disadvantages of options for current methods of CDI surveillance in Australian hospitals.

Option	Advantages	Disadvantages
1. Continuation of hospital - identified CDI	Currently undertaken Established Least resource intensive	Provides no picture of a change in severity of disease Provides a limited picture of changes in community acquisition or transmission Laboratory-based method, therefore subject to ascertainment bias Provides no additional information about severity of disease
2. Surveillance of HCA HFO CDI	Provides a clearer picture of what is occurring in hospitals	Not necessarily a robust performance indicator; still several limitations Provides no clearer picture of community acquisition, burden or transmission Provides no additional information about severity of disease Laboratory-based method, therefore subject to ascertainment bias
3. Continuous surveillance of severe cases of CDI in hospitals	Provides a method of identifying severe cases in a timely manner (relative to options) Data collected could be analysed for improved understanding and/or evaluation of treatment options	Requires hospital staff to identify severe cases and collect additional data Provides no clearer picture of community acquisition; burden or transmission
4. Collection of additional data	Provides a marker for changes in in-patient mortality Provides a marker for changes in severity	Requires hospital staff to review patient admission record or similar system prior to data being sent to jurisdictional surveillance unit Provides no clearer picture of community acquisition; burden or transmission
5. Snapshot surveys	Have been undertaken twice in the past with positive feedback. Improves understanding of changes in strains and severity	Not continuous, so changes may not be identified for several months or longer Currently voluntary, so may not provide complete picture unless all hospitals participate Requires laboratory to retain stool samples Requires additional data collection for a limited period Provides no clearer picture of community acquisition; burden or transmission
6. Classification of each case of CDI identified in hospitals	Enables data to be collected on community-associated cases of CDI (presenting to hospitals) and thus a marker of potential changes to the epidemiology of CDI in the community	Requires hospital staff to review each case of CDI Provides no additional information about severity of disease Requires detailed information about patient movement across sectors.
7. Root-cause analysis of each case	Provides the gold standard in determining acquisition and identification of severe cases Provides a mechanism for a robust quality improvement process to be put in place locally Optimises opportunity to prevent and control transmission in hospitals, when used in appropriate framework	Most human-resource-intensive option

6.5 Surveillance of CDI in settings other than hospitals

There are other forms of important CDI data captured around the country. These include (but are not limited to): snapshot surveys (described in section 3.1 and section 6.4, Table 2); findings from research including hospital-level quality improvement programs; and surveillance undertaken by private hospitals. As ad hoc surveillance within community settings such as residential and aged care is limited, there is little understanding about what is occurring in these settings. A key gap identified by the Commission's HAI Advisory Committee and Technical Working Group is a lack of data and understanding around the epidemiology of CDI in the Australian community.

6.6 Options for surveillance/ monitoring of CDI in non-hospital settings

Monitoring and/or undertaking surveillance of CDI in non-hospital settings is potentially challenging. Considerations in undertaking CDI surveillance in such settings include: who would undertake the surveillance; and how information collected would feed into a wider network or system. Options available include:

- an expansion of hospital based surveillance systems to include classification of community associated cases (described in section 6.4 and Table 2)
 - A limitation of this approach is that only persons who present to hospital will be captured.
 - For example, the burden of CDI cases treated by general practitioners would remain largely unknown;
- point prevalence surveys in RACFs – options to support this could include funded research or incorporation into accreditations standards;
- population-based studies – options to support this could include funded research, or jurisdictions or organisations that have the ability to integrate laboratory data with patient information systems;
- developing a process whereby outbreaks of CDI in RACFs are required to be reported to public health units;
- using an existing community-based disease surveillance program. For example, ASPREN is a nationally representative network of Australian general practitioners who work together to provide the quality national surveillance data on influenza and other communicable diseases in their communities. ASPREN data provides community level data and aims to detect outbreaks in the community before they reach epidemic proportions;
- a formal education program to increase awareness and testing of CDI in RACFs;
- making CDI a nationally notifiable disease. This would potentially enable a method for all cases of CDI to be identified and classified.

6.7 Consultation questions for this section

- Is additional hospital based CDI surveillance required, over and above what is already occurring?
 - If so, what are the preferred measures?
- What are the best methods and approaches for improving our understanding of the burden of CDI in the community?
 - How are these best coordinated?

The full list of numbered consultation questions for this discussion paper is detailed in section 9.

7 ISSUE 3: PRIORITIES FOR RESEARCH

7.1 Overview

As research creates new knowledge and uses existing knowledge in a new and creative way to generate new concepts, methodologies and understandings⁶⁶ it plays an important role in complementing surveillance-related activities to improve our understanding of CDI in Australia. It also informs interventions and strategies to reduce CDI incidence. The role of surveillance and research is different, and answers to certain questions about CDI in Australia are potentially best sought through research. Research activities related to CDI are being undertaken in Australia; however, there is no efficient method available to robustly identify all these activities.

Through discussion with the clinical experts, the following list provides examples of potential priority areas for CDI research in Australia, in no particular order. This list (Table 3) is not exhaustive, but is intended to stimulate ideas and further discussion.

Table 3. Examples of potential areas for CDI research in Australia

Potential area for research	Examples
1. Improved understanding of CDI transmission in the community	Incidence of CDI in RACFs Potential role of food in spore transmission Improved understanding of incidence of community CDI at population level Enhanced understanding of circulating strains How do antibiotic prescribing practices in the community influence incidence and transmission?
2. Improved understanding of the most effective and efficient prevention measures	What are the most effective antimicrobial stewardship strategies to prevent CDI? What are the most effective transmission prevention strategies (i.e. environmental management and isolation) to prevent CDI in in-patient settings?
3. Improved understanding of the organism	What are the triggers for sporulation and germination of <i>C. difficile</i> in the human gastrointestinal tract? What is the basic relationship of <i>C. difficile</i> to the human gut mucosa and immune system?

7.2 Consultation questions for this section

What are the priorities for CDI research in Australia and how are these best answered?

The full list of numbered consultation questions for this discussion paper are detailed in section 9.

8 ISSUE 4: COMMUNICATION AND OVERSIGHT

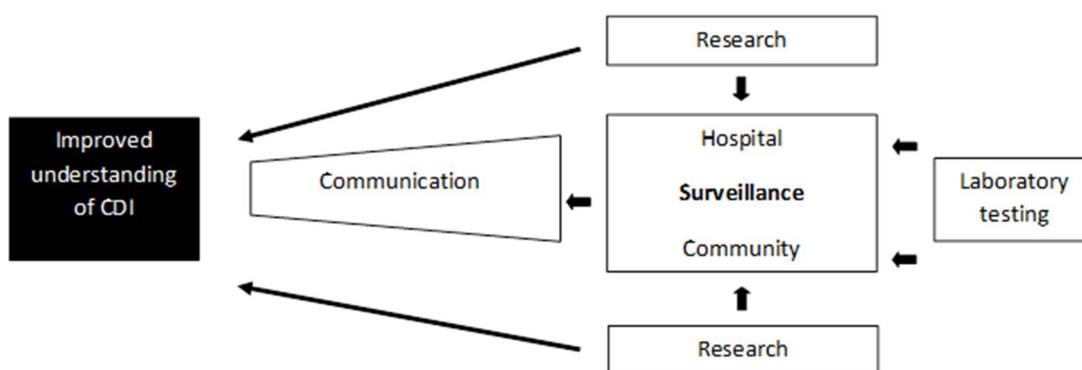
8.1 Overview

A key purpose of improving our understanding of CDI in Australia is to provide high quality data that can act as an effective monitoring and alert system, and to provide an opportunity to design and evaluate strategies to reduce the incidence of CDI. Prevention and control strategies will be enhanced by:

- findings from research and improved data obtained from surveillance systems underpinned by standardised laboratory practice
- a system that enables timely dissemination of information, will enhance.

Figure 3 provides a visual representation of how these issues are linked.

Figure 3. Linkages between issues raised



As the transmission of CDI is complex and involves a range of healthcare workers in a number of settings, various health sectors (and potentially sectors other than health), there is a question of who or which organisation should be responsible for the coordination of CDI-prevention activities in Australia. This particular question is becoming more pertinent as it becomes clearer that healthcare associated infections are issues no longer experienced by hospitals in isolation. There have been recent debates about the need for an overarching organisation or process capable of supporting a multifaceted approach to health.^{67, 68} The issues presented in this discussion paper potentially demonstrate the need for a multifaceted approach and corresponding coordination of strategies in order to reduce the incidence of CDI. It is important for Australia to consider how a nationally coordinated approach to *C.difficile* would work.

8.2 CDI hospital surveillance and communication

The manner in which the incidence of CDI is reported in Australian varies considerably. Some jurisdictions report CDI data in collated healthcare associated infection surveillance reports, whereas others produce documents in other formats (such as internal and external safety and quality or performance reports). In addition, the frequency and timeliness of these

reports and their ease of availability varies. Furthermore, the level of CDI surveillance undertaken at hospital level and reported to jurisdictions varies. For example, some hospitals may only capture data on hospital-identified CDI, whereas others may capture data on HCA HFO CDI and community associated CDI (identified at/by hospitals). Currently, there is no central, national repository for collecting or reporting of CDI surveillance data, nor any formal process for sharing nor aggregating CDI data.

8.3 Other forms of CDI data

There are other forms of important CDI data captured around the country. These include, but are not limited to, snapshot prevalence surveys (described in section 3 and Table 2); findings from research including hospital-level quality improvement programs; and surveillance undertaken by private hospitals. As continuous and ad hoc surveillance within community settings (such as RACFs) there is little understanding about what is occurring in these settings. Should programs exist or be developed in the future, they need to feed into a larger system that enables these data to be placed in context. The same principle applies to all forms of CDI data collection.

8.4 Reducing CDI: an international example

The country that has been the most successful at reducing CDI is England. Between 2007/08 and 2013/14, the number of cases of CDI in England has reduced from 148.9 per 100 000 bed days to 30.9 per 100 000 bed days. In addition, 'Trust apportioned cases' – cases occurring on the fourth day of admission to hospital or later, has reduced from 89.7 (or 33 442 cases) to 14.7 (or 5 031 cases) per 100 000 bed days during the same period.⁶⁹ Direct comparison of data should not be made to Australia as the systems and processes vary, however the reduction in CDI achieved is noteworthy. The approach taken by England to date is similar to that taken by Australia in that recommendations on clinical management, laboratory diagnosis, antibiotic stewardship, infection prevention and control activities have been clearly documented. In addition, there was articulation of how to cope with high prevalence in specific hospitals; a proposed approach for CDI in the community and clear governance. This approach, documented in *Clostridium difficile* infection: how to deal with the problem, was adopted in 2008⁷⁰ with refinements, and additional tools and resources developed. In the latest commentary from Public Health England, it is noted that in order to continue to tackle CDIs, additional interventions in the community, primary care and acute Trusts will need to be identified and actioned.⁷¹

8.5 Potential solutions

Solutions for improving communication and providing oversight on issues and options proposed in this paper are required. Potential solutions identified by clinical experts may include one or a combination of the following:

- the Commission's Healthcare Associated Infection Technical Working Group regularly reporting and reviewing hospital CDI rates in their respective jurisdictions
- the Communicable Disease Network of Australia reviewing available community associated CDI data and trends on a regular basis
- a professional organisation taking a lead in the coordination and/or collaboration and/or dissemination of CDI research in Australia

- continued collaboration occurring between jurisdictions through the Commission's Inter-Jurisdictional Committee and other mechanisms
- developing a national CDI plan that includes trigger points and actions, similar to the *National action plan for human influenza pandemic*.⁷² The plan could include parameters for notifying RACFs, hospitals and jurisdictions; and a mechanism for bringing relevant parties together at a national level when needed.

8.6 Consultation questions for this section

- Would the development of a national CDI plan as described in section 8.5 be a useful resource?
 - If so, how should it be integrated into existing systems?
 - Which network should be responsible for the development?
- Do we need additional regulation to support CDI implementation strategies?
 - If so, what might these be?

The full list of numbered consultation questions for this discussion paper is detailed in section 9.

9 LIST OF CONSULTATION QUESTIONS

- 1) Is any additional guidance or supporting documentation required for the prevention and control of *Clostridium difficile* infection in Australia, over and above those currently being undertaken? (refer to section 3)
- 2) How can recommendations for *Clostridium difficile* laboratory practice be best developed and implemented? (refer to section 5)
- 3) With increasing molecular testing, is there a need to continue culture based *Clostridium difficile* surveillance for typing and antimicrobial resistance purpose? (Section 5)
- 4) 4.1) Is additional hospital based *Clostridium difficile* infection surveillance required, over and above what is already occurring? (refer to section 6)
4.2) If so, what are the preferred measures? Please consider the options in Table 2, section 6.4. (refer to section 6)
- 5) 5.1) What are the best methods and approaches for improving our understanding of the burden of *Clostridium difficile* infection in the community? Potential options are presented in section 6.6. (refer to section 6)
5.2) How are these best co-ordinated? (refer to section 6)
- 6) What are the priorities for *Clostridium difficile* infection research in Australia, and how are these best answered? (refer to section 7)
- 7) Would the development of a national *Clostridium difficile* infection plan as described in section 8.5 be a useful resource?
7.1) If so, how should it be integrated into existing systems? (refer to section 8)
7.2) Which network should be responsible for the development? (refer to section 8)
- 8) Do we need additional regulation to support a response to *Clostridium difficile* infection implementation strategies? (refer to section 8)

Responses to the questions and other comments on this discussion paper may be provided by using the www.safetyandquality.gov.au

Written responses may be sent to:

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Sydney NSW 2000

Or email to: HAI@safetyandquality.gov.au

10 ABBREVIATIONS AND ACRONYMS

ACIPC	Australasian College of Infection Prevention and Control
ASID	Australasian College of Infectious Disease
CDI	<i>Clostridium difficile</i> infection
CDNA	Communicable Disease Network Australia
HAI	Healthcare Associated Infection project
HCA	Healthcare associated
HCA HFO	Healthcare associated healthcare facility onset
PCR	Polymerase chain reaction
RACF	Residential and aged care facility
RT	Ribotype
SHEA	Society of Healthcare Epidemiology of America

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