

# Recommendations for the control of carbapenemase-producing *Enterobacteriaceae* (CPE)

A guide for acute care  
health facilities

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# Acronyms

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<b>AMS</b>	antimicrobial stewardship
<b>AGAR</b>	Australian Group on Antimicrobial Resistance
<b>AURA</b>	Antimicrobial Use and Resistance in Australia
<b>CARAlert</b>	National Alert System for Critical Antimicrobial Resistances
<b>CLSI</b>	Clinical and Laboratory Standards Institute
<b>CRE</b>	carbapenem-resistant <i>Enterobacteriaceae</i>
<b>CPE</b>	carbapenemase-producing <i>Enterobacteriaceae</i>
<b>ESBL</b>	extended-spectrum $\beta$ -lactamase
<b>EUCAST</b>	European Committee on Antimicrobial Susceptibility Testing
<b>KPC</b>	<i>Klebsiella pneumoniae</i> carbapenemase
<b>NSQHS</b>	National Safety and Quality Health Service

# Introduction

The Australian Commission on Safety and Quality in Health Care (the Commission), working with policy advisors and clinical and laboratory experts, has developed this guide to provide advice to governments, health professionals and consumers on the response to carbapenemase-producing *Enterobacteriaceae* (CPE).

## Aim and scope of this guide

This guide aims to:

- Alert healthcare professionals, health departments and hospital executives to the emerging threat of CPE in Australia
- Recommend strategies to prevent, detect and contain CPE
- Provide information and resources for hospital executive, healthcare professionals and consumers
- Recommend laboratory screening and confirmation methods.

The guide provides recommendations for patient management in health facilities to prepare and respond to CPE. The recommendations are based on the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup>, and are consistent with the systems outlined in the National Safety and Quality Health Service (NSQHS) Standards – Standard 3: Preventing and Controlling Healthcare Associated Infections.<sup>2</sup> The guide also incorporates the principles and recommendations from the Antimicrobial Stewardship Clinical Care Standard<sup>3</sup>, especially in relation to consumer engagement.

The scope of this guide is to provide information on the prevention and management of CPE in acute health facilities – that is, hospitals and day procedure units. The guide includes information on the prevention and management of CPE in specific areas and patient populations, such as intensive care, neonatal and paediatrics units. Elements of this guide may be applicable or adapted for use in other settings.

State, territory and local health networks may also develop more detailed procedures. A number have already put in place such arrangements, based on consultation during the development of this guide.

## Aged care homes

This guide does not address identification and management strategies for CPE infection for patients outside acute care or for residents of aged care homes. Because of the complexities and the level of detail required, the CPE Working Group recommends development of a separate document for non-acute or aged care homes, if required.

There are documented reports of multidrug-resistant gram-negative bacteria among residents of aged care homes in Australia and overseas.<sup>4,5,6,7</sup> These reports are of concern, and have implications for the potential amplification and transmission of CPE.

“The proliferation of carbapenem-resistant *Enterobacteriaceae* (CRE) represents a rising public health threat in Australia. Given the paucity of therapeutic options, early detection, meticulous adherence to infection control measures and antimicrobial stewardship (AMS) are vital to containing spread of CRE within individual institutions. Continued local surveillance will be required to determine the extent of the problem.”<sup>8</sup>

# Introduction

## Nature and importance of CPE

### What are *Enterobacteriaceae*?

*Enterobacteriaceae* are the largest family of gram-negative bacteria causing human infection. This family includes common pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae* and *Proteus species*. *Enterobacteriaceae* colonise the normal human gastrointestinal tract, generally without causing disease. However, they can also cause common infections, including urinary tract infection, abdominal infection and bloodstream infection. *Enterobacteriaceae* are of key importance as human pathogens and as vehicles for the dissemination of antimicrobial resistance because:

- Some are normal flora of the gastrointestinal tract
- Most have the potential to colonise all people
- They are the most frequent gram-negative bacteria to cause human infections in the community and in healthcare settings
- They are easily spread between patients
- Antimicrobial resistance genes can easily spread between different species and strains within the *Enterobacteriaceae* family.

### What are CPE?

CPE are members of the *Enterobacteriaceae* that are resistant to carbapenems, a class of 'last resort' antibiotics for treating serious infections.

Gram-negative bacteria – including members of the *Enterobacteriaceae* – that are resistant to most, or even all, types of antibiotics have emerged as a significant global public health threat. Resistance to carbapenems is of particular concern. Multidrug-resistant gram-negative bacteria, including CPE, place Australian patients at greater risk of potentially untreatable infection. Vulnerable patients with comorbidities are at increased risk of developing an infection and dying as a consequence.

### What are carbapenemases?

The most common way that *Enterobacteriaceae* become resistant to carbapenems is by producing an enzyme called a carbapenemase. Such bacteria are referred to as carbapenemase-producing *Enterobacteriaceae* (CPE). Carbapenemases

inactivate all the common members of the carbapenem antimicrobial class. There are many different types of carbapenemases. Carbapenemase enzymes commonly identified in clinical isolates in Australia include IMP, NDM, VIM, KPC and OXA-48-like. This list is constantly evolving because of changing local and global epidemiology.

Each carbapenemase has a slightly different spectrum of activity against different antibiotics. Furthermore, bacteria that produce carbapenemase enzymes are almost always resistant to other important antibiotic classes, such as other  $\beta$ -lactams,  $\beta$ -lactamase inhibitor combinations, fluoroquinolones and aminoglycosides.

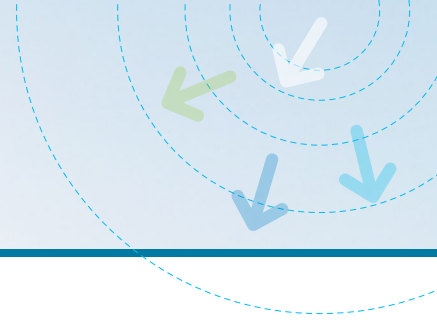
### What is the occurrence of CPE in Australia?

The first documented outbreak of CPE in Australia, in which 10 cases were identified in the seven months to December 2012, had a mortality rate of 40%.<sup>8</sup>

An increasing number of CPE cases have been identified in Australia since 2012.<sup>9</sup> It has been reported that approximately half of the critical antimicrobial resistances reported by CARAlert have been CPE.<sup>10</sup> More than half the cases identified in an enhanced surveillance program in Victoria in 2015 had a history of overseas travel in the previous 12 months.<sup>11</sup> Obtaining a clear account of the number of cases nationally is complicated by a lack of uniformity in methods for laboratory detection of CPE, a lack of a coordinated communication network within and between states and territories, and inconsistent reporting.

An outbreak reported in 2014 identified clusters of CPE-positive patients who appeared to have a strong relationship with individual health facilities. This suggests that transmission was primarily healthcare associated rather than within the community.<sup>8</sup>

Australia has not seen a significant number of CPE cases compared with Europe, North America or the Middle East. This is partly attributed to good infection control for multi-drug resistant *K. pneumoniae*, AMS in ICU's and a limited number of medical transfers from high risk continents where KPC is common.<sup>12</sup> This creates an opportunity to prevent and contain CPE, and thereby limit their impact on human health.



## Recommendations for states and territories

CPE presents a threat to public health. Outbreaks of CPE in Australia and overseas<sup>7,8,12,13,14</sup> have demonstrated the need for a coordinated response that includes a multi-disciplinary, multi-agency approach to contain and manage CPE. In some Australian states and territories, CPE infection is a notifiable condition.

State and territory health departments should oversee a range of actions, including coordinating a risk assessment, undertaking epidemiological and microbiological investigations, determining the requirement for control measures, and coordinating risk communication activities. It is essential that there are formal communication links, standardised microbiological testing, and reporting within and between each of the states and territories.

In responding to outbreaks of CPE, state and territory health departments need a coordinated response. This should take into account advice from health professionals, including experts in infectious diseases, microbiology, public health, and infection prevention and control, epidemiologists, executives from health facilities, and policy advisors. Media and public relations expertise is also advisable to assist with the development of effective communication.

State and territory health departments should ensure:

- A jurisdictional outbreak management plan that incorporates CPE
- A point of contact is nominated within the department to receive notifications of CPE (see Section 5.5), and to communicate information to designated branches and directorates, such as public health, communicable diseases and population health
- Communication is established with outbreak management teams in health facilities, and guidance and external expertise are provided to the outbreak health facility. This may include support for clinical governance, public health, microbiology (including a reference laboratory), infection prevention and control, infectious diseases, epidemiology, communications, and safety and quality

- The outbreak health facility has the necessary capability and capacity to manage the outbreak; this may include personal protective equipment, other equipment, consumables and laboratory capacity for testing
- Specific additional control measures are undertaken for CPE where ongoing transmission is identified
- Responsibility for declaring de-escalation or stand-down of outbreak management.

## Australian Government response

### Antimicrobial Use and Resistance in Australia project

The Commission has established CARAlert as part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System. CARAlert is supported by a network of laboratories to enable timely communication of critical antimicrobial resistances (CARs) in Australia. The data and reports on antimicrobial resistance, antimicrobial use and appropriateness of antimicrobial prescribing from AURA provides clinicians, policy and program developers, and states and territories with the information needed to inform prevention and containment strategies for antimicrobial resistance.

### National Health Emergency Response arrangements

The Australian Health Protection Principal Committee oversees the National Health Emergency Response Arrangements (NatHealth), which provide coordination of the health sector in response to emergencies of national consequence. The NatHealth arrangements may be used in response to a domestic or international event that affects, or threatens to affect, two or more states or territories. These can include emergent and re-emergent diseases for which emergency preparedness and planning are essential components in minimising threats to the public.

# Introduction

## Why a change from CRE to CPE?

This guide refers to the control of CPE, and enhances the scope of the 2013 guide that referred to the control of CRE. The change from CRE to CPE was made after consideration of contemporary data and the potential risks posed by antibiotic-resistant gram-negative bacteria in Australian health facilities. This guide does not use 'carbapenem resistance', as defined by routine susceptibility testing, to define *Enterobacteriaceae* that require control. The change was made because some CPE do not meet the formal definition of resistant (or non-susceptible) to carbapenems in a clinical laboratory.

CPE that do not meet a clinical definition of resistant (or non-susceptible) still pose a significant threat for the dissemination of antimicrobial resistance within health facilities because:

- All CPE contain the genetic information required to produce carbapenemase enzymes. These genes are carried on mobile genetic elements, and can be easily spread to other strains and species
- The measured level of resistance may vary between different laboratories and testing episodes, depending on the methods used.

For the purpose of this guide, CPE is defined as any *Enterobacteriaceae* that are known to harbour a gene encoding a carbapenemase enzyme.

## Development of the guide

This document was developed in consultation with the Australian states and territories, learned societies, healthcare institutions and expert individuals. Grading of evidence for each of the recommendations is not provided because higher levels of evidence are not available.

Information on the surveillance, identification and control of CPE was obtained from assessment of peer-reviewed literature (obtained via PubMed); local, state and territory guidelines, and fact sheets; and international guidelines and recommendations. Examples include:

- *Guidance for tackling carbapenem-resistant Enterobacteriaceae from the Centers for Disease Control and Prevention in the United States*<sup>15</sup>
- *Guidance: infection prevention and control measures for health workers in all health settings – carbapenem-resistant gram-negative bacilli from the Public Health Agency of Canada*<sup>16</sup>
- The article 'An ongoing national intervention to contain the spread of carbapenem-resistant *Enterobacteriaceae*'<sup>17</sup>

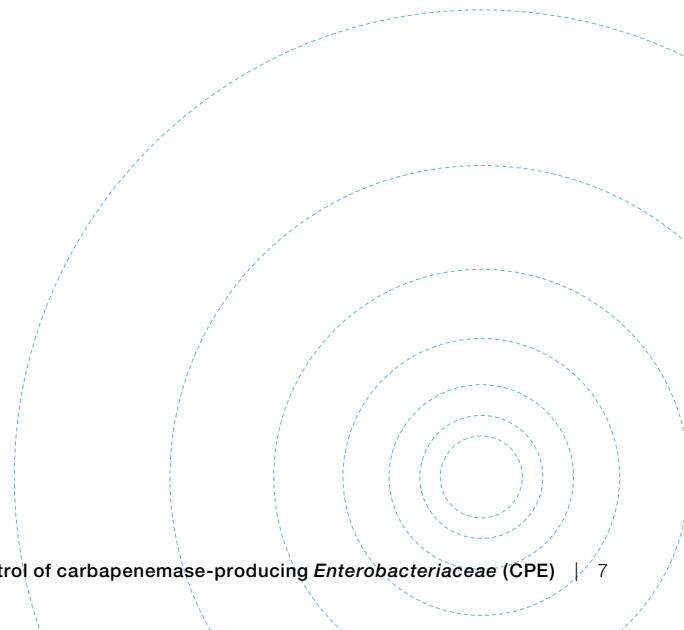
A collaborative process was used in which policymakers, infectious diseases physicians, clinical microbiologists and infection control professionals met initially to develop an outline of the current guide. Regular teleconferences to generate recommendations based on the available evidence were held with leaders for each section of the guide, individual section groups and the CPE Working Group convened by the Commission, which included policy leaders, and clinical and laboratory experts.

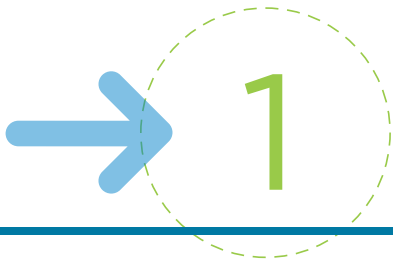




## Structure of the guide

<b>Section 1: Planning, preparing and prevention</b>	This section outlines the recommended minimum requirements in planning and preparing for CPE by all health facilities where no cases of CPE have been identified. Strategies include governance and management, standard precautions, and AMS.
<b>Section 2: CPE screening and surveillance</b>	This section relates to screening and surveillance when no cases of CPE have been identified; or following the identification of sporadic cases, local transmission or an outbreak. It outlines the recommended minimum requirements for surveillance in health facilities to ensure that patients with CPE are identified. The section includes recommendations for identification of CPE contacts, timing and frequency of screening, determination of CPE clearance, and environmental screening.
<b>Section 3: Strategies to reduce CPE transmission</b>	This section provides recommendations for health facilities to manage a small number of CPE cases that are not epidemiologically linked or where limited local transmission is occurring. It includes recommendations on the management of CPE-positive patients, CPE contacts, patient movement, and cleaning and disinfection.
<b>Section 4: Outbreak management</b>	This section provides recommendations for health facilities to manage an outbreak of CPE cases where widespread transmission is occurring and cases may be epidemiologically linked. It includes recommendations on identification of an outbreak, contact tracing, staffing considerations, and cleaning and disinfection.
<b>Section 5: Laboratory screening and confirmation methods</b>	This section addresses laboratory procedures for screening patient specimens or cultures for CPE. It provides advice and recommendations on the detection of CPE, and outlines mechanisms for reporting to CARAlert.





# Planning, preparation and prevention

This section outlines the recommended minimum requirements for planning and preparing for CPE by all health facilities where no cases of CPE have been identified. It focuses on key infection prevention strategies that are incorporated into infection control programs for the day-to-day management of all patients, regardless of whether or not cases of CPE are suspected.

There is evidence that a high-level, coordinated model is required for effective control of an outbreak of CPE.<sup>18</sup> A well-coordinated model will include appropriate governance, effective AMS, and cleaning and infection control precautions to prevent CPE infection and transmission.

Internationally, organisations where CPE have existed for some time recommend rigorous application of infection control strategies to limit the impact of the bacteria.<sup>19</sup> The objectives are to prevent both transmission of, and infections with CPE.<sup>20</sup>

Prior to an outbreak involving *Klebsiella pneumoniae* carbapenemase (KPC) in 2006, CPE cases were extremely rare in Israel. The rapid spread of a clone of carbapenem-resistant *K. pneumoniae* that was not controlled by local measures resulted in more than 1,200 patients being infected in 27 hospitals across the country. The pathogen displayed an exceptional combination of multi-drug resistance, virulence and efficiency of spread, and threatened the country's entire hospital system. A centrally coordinated, nationwide intervention was launched to contain the outbreak and control further transmission. The measures that were imposed, although successful, had a high impact on resources, clinical staff and patients, and placed a financial burden on the healthcare system.<sup>13</sup>

## 1.1 Health facility governance and management

### Statement of intent

The focus of planning, preparation and prevention for the control of organisms of significance, such as CPE, requires an effective infection control program. The intent of the recommendations in this section is to ensure the presence of a governance framework that incorporates executive responsibility and commitment to a risk management approach in minimising infection risk to patients and the workforce.

These recommendations are consistent with information on organisational governance in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section C1: Management and clinical governance), and the NSQHS Standards – Standard 1: Governance for Safety and Quality in Health Service Organisations<sup>21</sup> and Standard 3: Preventing and Controlling Healthcare Associated Infections.<sup>2</sup>

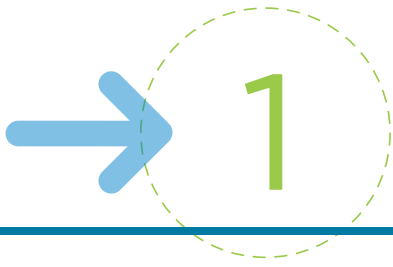


## Recommendations

- 1.1.1** The health facility should have a governance framework and plan to respond to organisms of significance, such as CPE. The framework should ensure implementation, monitoring and oversight of measures to establish and maintain CPE control. The executive of the health facility should be engaged in support of the plan.
- 1.1.2** The health facility should have in place systems for effective patient screening; including a system to screen and identify patients at risk for CPE carriage on admission to the health facility (see Section 2).
- 1.1.3** The health facility should have in place systems that detect and manage clusters or outbreaks of CPE, including:
  - Access to a laboratory that can provide accurate testing and a rapid turnaround time for results
  - An epidemiological evaluation of every new CPE case to identify the likely source of acquisition and the need for further patient screening.
- 1.1.4** The health facility should develop an outbreak action plan that incorporates specific actions, and allocation of staff and resources to respond to an outbreak of CPE, including the transfer of patients.
- 1.1.5** The health facility should have in place an alert system for colonised or infected patients to ensure that transmission-based precautions are used for subsequent admissions.
- 1.1.6** The health facility should educate staff on how to respond to cases of CPE. This would include information on the nature of CPE, standard and transmission-based precautions (contact precautions), use of personal protective equipment, cleaning and disinfection, and available resources, such as single rooms or dedicated patient equipment.
- 1.1.7** Microbiology laboratories should have in place processes for timely notification to clinical and infection prevention staff when CPE is suspected, while awaiting confirmation.

## Rationale and commentary

- The NSQHS Standards on Governance (Standard 1)<sup>21</sup> and Infection Prevention and Control (Standard 3)<sup>2</sup> require organisations to demonstrate governance mechanisms and risk management for infection prevention and control.
- Standard and transmission-based (contact) precautions should be used for all patients suspected or confirmed of being colonised or infected with CPE.
- Electronic alerts are a flag on a patient's medical record that signals a patient's previous or current CPE colonisation or infection status.
- Increased awareness and knowledge about multidrug-resistant organisms such as CPE are required by all healthcare staff to maximise compliance and ensure appropriate management.
- Additional information on management and clinical governance is given in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section C1).



# Planning, preparation and prevention

## 1.2 Strategies to prevent transmission of infection

### Statement of intent

The intent of the recommendations in this section is to prevent or reduce the transmission of infectious agents from one person to another through the use of existing infection prevention and control strategies. Standard precautions are a primary strategy for preventing infection by direct or indirect routes and are used for all patients, regardless of their infection status.

These recommendations are consistent with information on standard precautions outlined in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B1: Standard precautions).



### Recommendations

- 1.2.1** Staff in healthcare settings should undertake hand hygiene in accordance with the 5 Moments for Hand Hygiene and implement a hand hygiene program consistent with the National Hand Hygiene Initiative.<sup>22</sup>
- 1.2.2** Patients and visitors should be educated about the importance of hand hygiene, especially handwashing after toileting. Patients should be provided with access to hand hygiene facilities. Consideration should be given to enabling patients with limited mobility, including those confined to bed, to perform hand hygiene.
- 1.2.3** In health facilities, frequently touched surfaces should be cleaned when visibly soiled, after every known contamination or spill, and at least daily. Frequently touched surfaces in high-risk units should be cleaned twice daily (Sections B1.4, B3 and B5.1 of the *Australian guidelines for the prevention and control of infection in healthcare*).<sup>1</sup>
- 1.2.4** All reusable patient equipment should be cleaned and reprocessed between every patient use (Section B1.5 of the *Australian guidelines for the prevention and control of infection in healthcare*).<sup>1</sup>

### Rationale and commentary

- Standard precautions provide safe work practices that should be observed at all times by all staff working in healthcare settings. Standard precautions are the primary strategy for minimising the transmission of microorganisms.<sup>1</sup>
- There is strong evidence that most of the individual elements of infection control strategies, such as hand hygiene<sup>22,23</sup>, aseptic technique, and environmental cleaning and disinfection<sup>24</sup>, can limit the impact of multidrug-resistant gram-negative organisms by reducing transmission in healthcare settings.
- The routes of transmission of CPE from patient to patient are either by direct contact through carriage of CPE on the hands of healthcare workers, or indirectly via contaminated environmental surfaces or shared equipment.<sup>25</sup>
- Pathogenic organisms have been detected on the hands of 40% of acute care patients 48 hours after admission.<sup>25</sup> A high level of compliance with hand hygiene, environmental cleaning and reprocessing of medical equipment is essential to prevent the transmission of CPE.
- Transmission-based precautions are additional measures that further reduce the risk of spread of CPE; these measures are indicated for management of individual cases of CPE (see Section 3.1).
- Further information on standard precautions is given in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B1: Standard precautions, Section B2: Transmission based precautions, and Section C6.2.2: Reducing infections spread through the physical environment).



## 1.3 Environmental cleaning

### Statement of intent

The intent of the recommendations in this section is to ensure that the health facility maintains a clean environment, consistent with national guidelines and state and territory policies, regardless of patient infection status. Recommendations for cleaning and disinfection where patients are suspected of, or confirmed as, being infected or colonised with CPE are in Section 3.4.

These recommendations are consistent with the information on environmental cleaning outlined in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Sections B1.4 and B5.1).



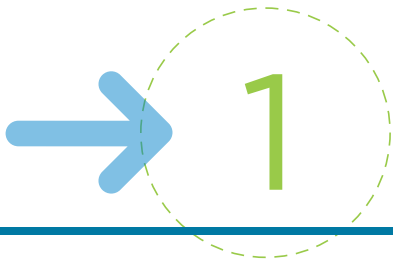
### Recommendations

- 1.3.1** Health facilities should implement policies and procedures for environmental cleaning, in accordance with the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> and the NSQHS Standards.<sup>26</sup>
- 1.3.2** Routine environmental cleaning should include cleaning of the patient environment on a daily basis; this includes frequently touched surfaces and patient care equipment. Frequently touched surfaces in high-risk units should be cleaned at least twice daily. A cleaning schedule and regular cleaning audits should be implemented.<sup>1</sup>

### Rationale and commentary

- Environmental cleaning is essential in decreasing the spread of resistant bacteria. For cleaning to be effective, audits of schedules and cleaning need to be undertaken regularly, with prompt feedback to key stakeholders.
- Environmental reservoirs for multidrug-resistant gram-negative bacteria are an important factor in healthcare-associated transmission. Patients colonised or infected with CPE widely contaminate their immediate patient environment.<sup>27</sup>
- For additional information, refer to the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B1.4: Routine management of the physical environment, and Section B3.1.2: Core strategies for MRO [multi-resistant organism] prevention and control).

“Routine environmental cleaning should include cleaning of the patient environment on a daily basis.”



# Planning, preparation and prevention

## 1.4 Reprocessing of endoscopes and bronchoscopes

### Statement of intent

The intent of the recommendations in this section is to ensure that processes are in place for appropriate reprocessing of endoscopes (duodenoscopes and colonoscopes) and bronchoscopes. These recommendations are consistent with the information on reprocessing of medical devices outlined in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B1.5) and *Infection control in endoscopy*.<sup>28</sup>

### Recommendations

- 1.4.1** Health facilities should implement policies and procedures for reprocessing of all endoscopes and bronchoscopes. Particular attention should be given to duodenoscopes used for endoscopic retrograde cholangiopancreatography procedures, which have been linked to CPE outbreaks internationally.<sup>29,30,31</sup>
- 1.4.2** Health facilities should implement quality control measures to ensure that reprocessing is undertaken in line with in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B1.5). This may take the form of regular microbiological testing of endoscopes, evaluation or biological marker testing, such as adenosine triphosphate (ATP) testing.<sup>28,32,33,34</sup>

### Rationale and commentary

- Flexible endoscopes are complex medical equipment. Knowledge and expertise are required to ensure that they are cleaned and reprocessed correctly between every patient use.
- Recent reports have documented outbreaks of CPE linked to endoscopic retrograde cholangiopancreatography.<sup>29,30,31</sup> Outbreaks have been associated with bacterial contamination of duodenoscopes, even though reprocessing lapses have not been recognised.
- Facilities should conduct regular quality reviews of the reprocessing procedure, particularly for difficult-to-clean parts of the endoscope.
- Quality checking for cleaning may take the form of regular microbiological testing, as recommended by the Gastroenterological Society of Australia; process tracking; or newer methods, such as ATP monitoring pre- and post-reprocessing.<sup>28,32,33,34</sup>
- Automated flexible endoscope reprocessors have been implicated in potential transmission of CPE. If these are used, protocols should be in place for regular cleaning, maintenance and microbiological monitoring of the machines.

Health facilities should implement policies and procedures for reprocessing of all endoscopes and bronchoscopes.



## 1.5 Antimicrobial stewardship

### Statement of intent

The intent of the recommendations in this section is to ensure that appropriate prescribing and use of antimicrobials are in place, as part of a broader plan to reduce the development of resistant bacteria, and to ensure that antimicrobial use and resistance within health facilities are monitored.

These recommendations are consistent with information on AMS outlined in Antimicrobial stewardship in Australian hospitals<sup>36</sup> and NSQHS Standard 3: Preventing and Controlling Healthcare Associated Infections<sup>2</sup>, which require all health facilities to have an appropriate AMS program.



### Recommendations

- 1.5.1** Facilities should implement AMS programs, consistent with the requirements of NSQHS Standard 3: Preventing and Controlling Healthcare Associated Infections.<sup>2</sup>
- 1.5.2** To minimise the impact of antibiotic resistance in gram-negative bacteria, AMS programs should:
  - Monitor the use of antibiotics that are commonly used to treat gram-negative infections, including cephalosporins, fluoroquinolones, carbapenems,  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations, and aminoglycosides
  - Use audit systems to identify inappropriate empirical, directed or prophylactic use of all antibiotics, especially cephalosporins, fluoroquinolones, carbapenems,  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations, and aminoglycosides. Therapy requirements should be referenced against the most recent version of *Therapeutic guidelines: antibiotic*<sup>37</sup>
  - Introduce strategies to reduce antibiotic use – for example, participation in the annual National Antimicrobial Prescribing Survey (NAPS) and the National Antimicrobial Utilisation Surveillance Program (NAUSP), or in paediatrics through feedback from Antimicrobial Resistance and Prescribing in European Children (ARPEC)
  - Monitor antimicrobial resistance at a facility level for key gram-negative bacteria commonly causing infection.

Effective antimicrobial stewardship programs have been shown to improve the appropriateness of antimicrobial use, reduce patient morbidity and mortality, and reduce institutional bacterial resistance rates and healthcare costs<sup>36</sup>

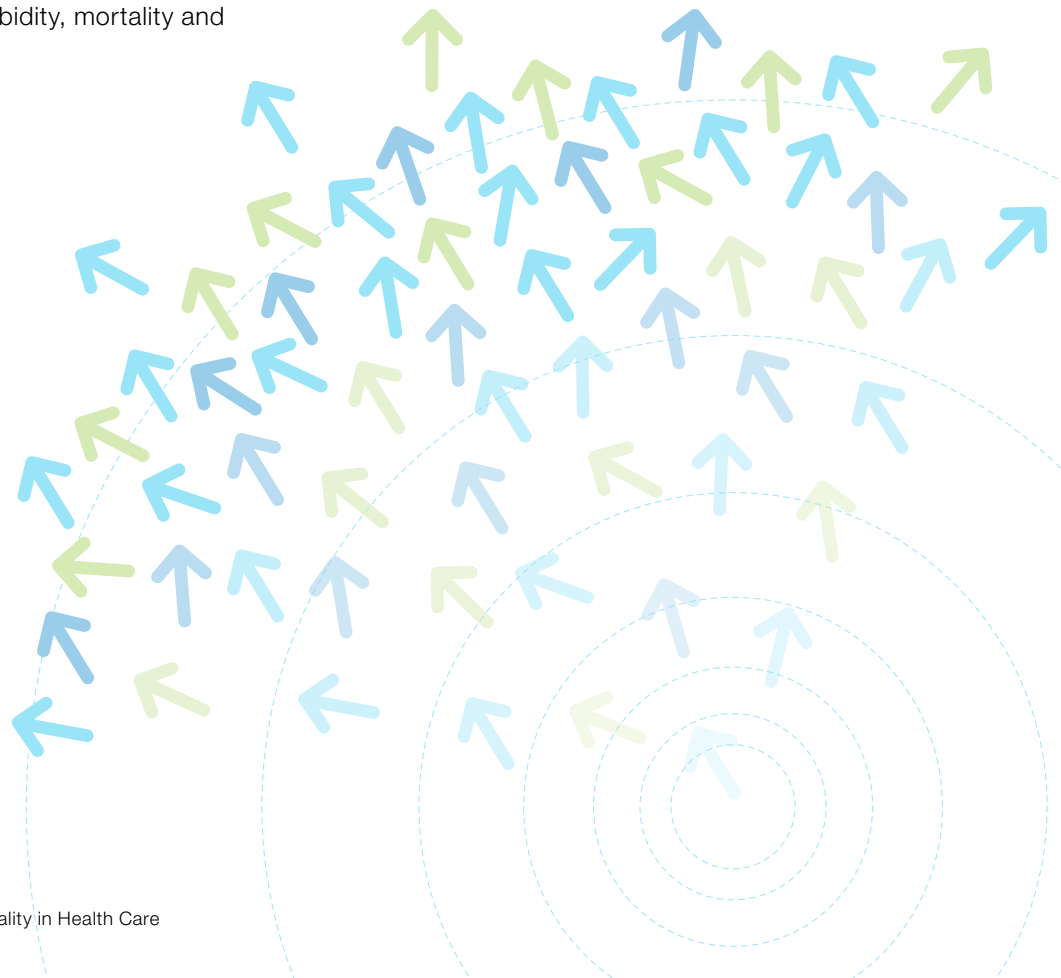


# 1

## Planning, preparation and prevention

### Rationale and commentary

- Carbapenems are a group of antibiotics with a broad spectrum of activity. They belong to the class of antibiotics known as  $\beta$ -lactams, along with penicillins, cephalosporins and monobactams. Carbapenems are of vital importance because they are considered as the antibiotics of 'last resort' for the treatment of patients with serious infections caused by bacteria that are resistant to other common antibiotics. Few good options exist for treating infections caused by bacteria that are resistant to carbapenems because these bacteria are usually resistant to multiple classes of antimicrobials. For further information on antibiotic classes, see *Principles of antibiotic pharmacotherapy, Part 2*<sup>35</sup>, on the Commission's website.
- AMS programs aim to reduce overall antimicrobial exposure and target treatment more effectively, through mechanisms such as restricting access to broad-spectrum antimicrobials and providing clear direction on indications for use of approved antimicrobials. Access to clinical microbiologists and infectious diseases experts can provide guidance for complex situations. Although antimicrobial resistance is a worldwide problem, AMS programs that operate locally or at a national level have demonstrated a decrease in resistance, morbidity, mortality and healthcare costs.<sup>36</sup>
- Many studies show that previous antimicrobial use is a significant risk factor for individual patients to acquire multidrug-resistant bacteria, including CPE. A number of classes of antibiotics have been associated with colonisation of, or infection by, CPE, including cephalosporins, fluoroquinolones and carbapenems. Control strategies should include AMS measures that aim to minimise overall antimicrobial use and ensure that any use of key antibiotics such as cephalosporins, fluoroquinolones and carbapenems is necessary.<sup>38</sup>
- Local prophylaxis, empirical and treatment guidelines need to consider strategies that reduce the use of antimicrobial classes that are more likely to drive emergence and spread of multidrug-resistant pathogens. In the case of multidrug-resistant gram-negative bacteria such as CPE, reports strongly implicate fluoroquinolones, extended-spectrum cephalosporins and carbapenems.<sup>39,40</sup>
- Reduction in hospital or community antimicrobial use may be followed by decreased bacterial resistance rates, even where patients or communities have high levels of colonisation with multidrug-resistant bacteria.<sup>40</sup>







This section outlines the recommended minimum requirements for surveillance in health facilities to ensure that patients with CPE are identified. It includes recommendations for surveillance screening to identify CPE contacts, timing and frequency of screening, determination of CPE clearance, and environmental screening.

## 2.1 Key risk factors for CPE

Infections caused by resistant *Enterobacteriaceae* increase the risk of morbidity and mortality. Patients with significant comorbidities have a greater risk of CPE infection.<sup>20,38,41,42</sup> Studies have demonstrated that CPE are more likely to affect patients who:

- Are hospitalised for a long time
- Have been hospitalised or had surgery overseas
- Have had multiple or recent exposures to different antibiotic agents, especially cephalosporins, fluoroquinolones and carbapenems
- Have diabetes mellitus
- Are on mechanical ventilation
- Are admitted to the intensive care unit
- Have an indwelling medical device (central venous catheter, urinary catheter or biliary catheter)
- Are recipients of an organ or stem cell transplant.

## 2.2 Screening for, and tracking of, CPE

### Statement of intent

The intent of the recommendations in this section is to ensure that patients with CPE infection or colonisation are identified; to ensure that measures are taken to prevent onwards transmission to other patients; to provide an accurate picture of the current epidemiology of CPE at each institution; and to inform appropriate control policies.

“Patients who are to be screened should be given information regarding the need for screening, and implications of a positive result.”

# 2

## CPE screening and surveillance



### Recommendations

- 2.2.1** Each health facility, or state or territory should select an appropriate active surveillance strategy, based on their current epidemiology of CPE colonisation. This may include screening of patients at risk of colonisation on admission and/or following contact with other colonised or infected patients in the hospital environment.
- 2.2.2** Patients at high risk of colonisation or infection (e.g. patients who have received treatment in an overseas hospital in the previous 12 months) should be actively screened for CPE colonisation or infection upon hospital admission.
- 2.2.3** Patients who are to be screened should be given information regarding the need for screening, and implications of a positive result. Patients should also be given general information on CPE.
- 2.2.4** Screening specimens should include rectal swabs or faeces. Urine from catheterised patients should also be included in screening, since the majority of CPE detected in surveillance studies by the Australian Group on Antimicrobial Resistance (AGAR) have come from urine specimens. Perianal swabs are not recommended generally because they may not give accurate results. However, perianal swabs may be necessary in some situations, such as anal pathology or in some neutropenic patients. Specimens from open wounds, or aspirates from any tubes or drains should also be considered for screening.
- 2.2.5** Following identification of a CPE-positive patient within a health facility, the microbiology laboratory servicing the facility should be asked to review susceptibility testing results for the past 12 months to identify any previously unrecognised cases of CPE.
- 2.2.6** A system for effective communication between the microbiology laboratory and the infection control team should be in place to enable rapid notification and isolation of patients, as necessary (see Section 1.1).

### Rationale and commentary

- Identification of colonised patients on entry to the health facility is important, because transfer of colonised patients has been identified as a major risk factor for the introduction and spread of CPE. This has been clearly documented at a global level.<sup>43</sup> Cross-border transfer of patients from countries with high rates of CPE has resulted in the introduction of CPE into countries that previously had detected few or no CPE isolates.
- A number of less well defined risk factors for infection or colonisation with CPE have been identified (see Section 2.5). These factors may increase the risk of acquiring CPE or the risk of infection once a patient has been colonised.
- Transfer of patients from a health facility with endemic CPE to another health facility in the same country has also been reported to result in the introduction of CPE into the receiving health facility.
- Reports of transmission associated with cross-border transfer from hospitals in endemic countries to non-endemic countries consistently demonstrate the risk of secondary transmission within the receiving health facility. However, national and global data on the incidence and prevalence of CPE in hospitals, to inform risk assessment of patients, are currently lacking.



## 2.3 Screening strategy options

Health facilities need to develop a screening strategy to identify patients with CPE, based on current epidemiology. Many patients with CPE are colonised and asymptomatic; therefore, a screening strategy cannot rely only on the collection of clinical specimens.

Health facilities may implement different screening strategies, depending on the burden of CPE. Table 1 provides a summary of screening strategies, and Table 2 indicates the rationale for active screening strategies. Strategies are based on whether:

- No cases have been identified
- Sporadic cases have been identified (single, epidemiologically unrelated cases)
- Localised transmission is established (two or more epidemiologically related cases in a localised area)
- CPE is endemic, with evidence of widespread transmission across the health facility, and possible or known transmission to other healthcare settings.

**Table 1 Summary of screening strategies, by burden of CPE**

Screening strategy	Outbreak phase		
	No cases	Sporadic cases	Local transmission established or CPE endemic
Admission from high-risk settings	Yes	Yes	Yes
Admission to high-risk unit(s)	Yes	Yes	Yes
Single or periodic point prevalence surveys	Consider	Consider	Yes
Repeated prevalence surveys in high-risk unit(s)	No	Consider	Yes
Screening of contacts of confirmed cases	na	Yes	Yes
Opportunistic screening (e.g. all diarrhoeal specimens)	Consider	Consider	Yes

CPE = carbapenemase-producing *Enterobacteriaceae*; na = not applicable; yes = screen; no = do not screen; consider = consult infection control team.

Note: Content is based on clinical experience and expert opinion by members of the Commission’s CPE Working Group.

In health facilities, screening strategies will vary according to risk. Examples of units that might be considered to be high-risk units are intensive care, haematology/oncology, severe burn, transplant, renal haemodialysis, aged care, and gastroenterology/gastrointestinal surgery units.

## CPE screening and surveillance

**Table 2 Description and rationale for active screening strategies**

Screening strategy			Admission <b>from</b> high-risk settings
Outbreak phase	No cases	Y	<p><b>Rationale</b></p> <p>Establish processes to identify risk groups (e.g. a questionnaire seeking information about recent medical care and treatment overseas). This strategy is only feasible if risk groups are easily identified by direct questioning.</p> <p>A high-risk group might include readmissions from particular units.</p> <p>Screening of admissions from high-risk settings is most useful when the major sources of patients with CPE are external to the institution, and this risk group can be identified based on risk factors – for example, patients who have been directly transferred from an overseas hospital, or who were recently in an overseas hospital or an Australian hospital with a known outbreak of CPE. Overseas travel (without contact with a health facility) appears to be a risk factor for colonisation with some resistant gram-negative bacteria, but less commonly with CPE.<sup>44</sup></p>
	Sporadic cases	Y	
	Transmission established or endemic	Y	
Screening strategy			Admission <b>to</b> high-risk units
Outbreak phase	No cases	Y	<p><b>Rationale</b></p> <p>Identify patients with CPE in areas where there are vulnerable patients. This strategy is most useful when the major CPE sources are patients who are admitted to the health facility (i.e. there is little known transmission within the high-risk unit). High-risk units include intensive care units, haematology/ oncology units and gastroenterology/gastrointestinal surgery units. Although this strategy is relatively simple to implement, it requires resources for the laboratory to process specimens. A limitation of this strategy is that patients outside the defined high-risk areas may be missed.</p>
	Sporadic cases	Y	
	Transmission established or endemic	Y	
Screening strategy			Single or periodic point prevalence surveys
Outbreak phase	No cases	C	<p><b>Rationale</b></p> <p>Perform single or periodic (e.g. annual) point prevalence surveys in all patients or high-risk areas to define the current epidemiology of CPE. This might define the focus of future surveillance – for example, whether to identify patients with CPE on admission or after admission.</p>
	Sporadic cases	C	
	Transmission established or endemic	Y	
Screening strategy			Repeated prevalence surveys in high-risk units
Outbreak phase	No cases	N	<p><b>Rationale</b></p> <p>Where transmission within units has been established, perform regular screening to detect new acquisition of colonisation after admission. The frequency of screening will depend on the rate of transmission and the average length of stay on each unit. This strategy is resource intensive for both infection prevention staff and the laboratory.</p>
	Sporadic cases	C	
	Transmission established or endemic	Y	

**KEY**



Yes = screen



Consider = consult infection control team



No = do not screen



Screening strategy			Screening of contacts of confirmed cases
Outbreak phase	No cases	N	<b>Rationale</b> Screen close-contact patients who are in the same room, unit or area as CPE-positive patients. Consider the duration of exposure (whether cohabitation was for 24 hours or longer, and whether exposure was in a shared room or open unit).  This strategy is not likely to be sensitive, because the period of infectiousness before the index patient is identified is not generally clear, and the frequency of patient movements (to other rooms or units, or outside the hospital) may make patient follow-up difficult.
	Sporadic cases	Y	
	Transmission established or endemic	Y	
Screening strategy			Opportunistic screening (e.g. all diarrhoeal specimens)
Outbreak phase	No cases	C	<b>Rationale</b> Where few resources are available to actively screen patients, opportunistically screen specimens received by the laboratory. This might include all faecal samples received, or faecal samples received from specific units or from all inpatients. Other specimens may also be suitable for techniques to detect CPE – for example, susceptibility testing on urine mixed growth. Although this strategy has the advantage of sampling specimens that are most likely to be infectious (e.g. diarrhoea), it may fail to detect significant transmission in specific areas (e.g. aged care units, where the frequency of clinical specimens may be lower). It may also be resource intensive for the laboratory and may drive overtreatment of CPE-colonised patients by clinicians, because colonisation could be confused with infection.
	Sporadic cases	C	
	Transmission established or endemic	Y	

Note: Content is based on clinical experience and expert opinion by members of the Commission's CPE Working Group.

<b>KEY</b> Y Yes = screen      C Consider = consult infection control team      N No= do not screen
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## 2.4 CPE infections in infants and children

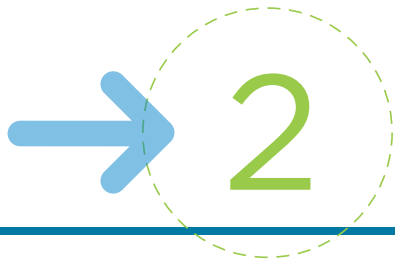
Despite increasing CPE prevalence, infection in infants and children remains rare. In limited reported case series, mortality is lower than in adult cases but still significant (10%). Effective therapy is even more limited than for adult patients.<sup>45</sup>

Potential risk factors for CPE infection in children are similar to those in adults. They include:

- Intensive care
- Immunosuppression
- Prematurity
- Presence of indwelling devices
- History of surgery
- Prior antibiotic use.<sup>46</sup>

### Screening in neonatal ICU

Special considerations apply for neonatal patients born to mothers who are known to be colonised with CPE. Screening specimens should include rectal swabs or faeces. Urine from catheterised patients should also be included in screening, since the majority of CPE detected in AGAR surveillance studies have come from urine specimens. Perianal swabs are not recommended. Consideration could be given to screening oral/nasal/pharyngeal swabs, skin/ear swabs and gastric aspirates.<sup>46</sup> Refer to Table 3 for suggested screening strategies during outbreaks in neonatal areas.



# CPE screening and surveillance

## 2.5 Identification of CPE contacts

### Statement of intent

The intent of the recommendations in this section is to identify and screen patients who have been in contact with a CPE-positive patient, to reduce the risk of further transmission.

A CPE contact is a person who has shared a room, bathroom or toilet facilities with confirmed CPE cases for more than 24 hours.

### Additional patient groups to be considered in a CPE screening strategy

A health facility may consider screening patients who have had less than 24 hours contact with a confirmed case of CPE but where there may be increased risk of transmission or acquisition of CPE. Examples of this group are patients with intellectual or cognitive impairment, participation in group activities, or immunosuppression; and patients in haematology/oncology, transplant and intensive care units.



### Recommendations

- 2.5.1** All CPE contacts that are inpatients at the time of CPE identification should be identified and screened (see Recommendation 2.6.1 for timing and frequency of screening; also see Table 3 Suggested screening strategies and Section 5).
- 2.5.2** CPE contacts discharged before screening should be flagged, and screened if readmitted within four weeks.
- 2.5.3** CPE contacts discharged to an aged care home or transferred to another hospital should be screened for CPE before discharge or transfer. The results of the screening should be provided to the receiving facility.
- 2.5.4** Where a receiving facility has screened a CPE contact, the facility should inform the transferring facility of the results of the screening.

### Rationale and commentary

- Because of the potential delay between exposure and infection, weekly screening of all inpatient CPE contacts is suggested. However, weekly screening may be modified in consultation with the infection control team for patients hospitalised for a prolonged period.
- In the absence of ongoing exposure to a CPE-positive patient, an inpatient CPE contact is no longer considered a CPE contact after three negative swabs.
- Patients who have shared a room, bathroom or toilet facilities with a CPE-positive patient should be screened to determine CPE status. A key issue to identify CPE contacts includes the proximity with a confirmed CPE case (shared room and toilet facilities) and the duration of exposure (e.g. cohabitation for 24 hours or longer).
- Screening of patients who have been discharged should be considered, where possible, either by the general practitioner or on subsequent readmission of the patient to hospital. A common strategy is to screen the closest contacts, then proceed with further screening if colonisation is detected in close contacts (termed 'concentric' or 'ripple' screening). A high proportion of contacts may have been discharged.
- There is no evidence that screening of household contacts or healthcare workers provides additional benefit in controlling spread of CPE within the healthcare setting (see Figure 2 in Section 3.2).

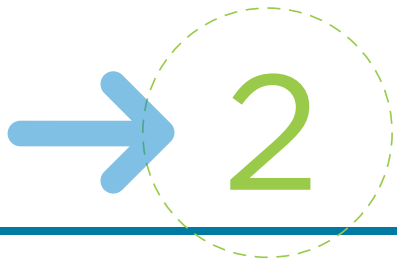


**Table 3 Suggested screening strategies for selected hospital areas during outbreaks, if patients are known to be colonised or infected with CPE**

Screening strategy	Setting						
	Renal haemodialysis	Hospital in the home	Outpatient clinic or emergency department	Day oncology	Rehabilitation or subacute	Inpatient aged care unit	Neonatal
Admission from high-risk settings	Yes	No	No	Consider	Yes	Yes	Mother and child
Single or periodic point prevalence surveys	Yes	No	No	No	Consider	Consider	No
Repeated prevalence surveys	No	No	No	No	No	No	No
Screening of contacts of confirmed cases	Yes	na	na	No	Consider	Consider	Yes
Opportunistic screening (e.g. all diarrhoeal specimens)	Consider	Consider	No	Consider	No	Consider	No

CPE = carbapenemase-producing *Enterobacteriaceae*; na = not applicable; yes = screen; no = do not screen; consider = consult infection control team.

Note: Content is based on clinical experience and expert opinion by members of the Commission's CPE Working Group.



## CPE screening and surveillance

### 2.6 Timing and frequency of screening of contacts

#### Statement of intent

The intent of the recommendation in this section is to ensure that health facilities develop a screening strategy that considers patient and environmental factors that affect screening sensitivity.



- 2.6.1** CPE contacts should be screened once a week for the duration of the admission. For patients who are hospitalised for extended periods, advice on the frequency of screening should be sought from the infection control team.

#### Rationale and commentary

- Repeat screening is warranted in known CPE contacts to confirm negative results in high-risk patients.
- Weekly screening should be undertaken for all CPE contacts. Where an outbreak has not been identified, there are no CPE-positive patients (i.e. they have been discharged or transferred), and no new cases have been identified in the unit for at least seven days, consideration could be given to ceasing screening of CPE contacts, in consultation with the infection control team.
- The sensitivity of screening is uncertain, and is likely to vary with specimen quality and the density of CPE carriage. Although some studies have found that newer chromogenic agars are sensitive and rapid, they have generally been evaluated only in comparison with other culture media, which are also of unknown sensitivity.<sup>47</sup>
- Studies of patients known to be colonised have found that 15–25% of patients with two or more negative screening swabs had a positive subsequent screening swab, suggesting that the sensitivity of screening could be as low as 50%.<sup>48</sup> In the presence of certain antimicrobial agents, false negative results from CPE screening tests may occur early after acquisition of CPE.





## 2.7 Screening to determine clearance of CPE carriage

### Statement of intent

The intent of the recommendations in this section is to provide guidance for health facilities that elect to undertake screening to determine clearance of CPE. The duration of CPE colonisation is uncertain and is likely to vary between individuals.



### Recommendations

- 2.7.1** A patient colonised with CPE cannot be considered cleared within 12 months of a positive result.
- 2.7.2** Contact precautions should be used for patients with a history of CPE colonisation or infection for all subsequent hospital admissions, unless cleared.
- 2.7.3** The hospital may consider ceasing contact precautions for patients with no risk factors who are readmitted to a hospital more than 12 months since a positive result of CPE colonisation. This requires three negative screening swabs at least 24 hours apart.
- 2.7.4** Any patient who is deemed cleared should be rescreened at every subsequent overnight admission to identify any relapse in detectable CPE colonisation. Day-only admissions do not require rescreening.
- 2.7.5** CPE clearance should only be assessed after relevant state and territory policies have been consulted, and in consultation with infection prevention and control professionals, and a clinical microbiologist or infectious diseases physician.

### Rationale and commentary

- In the absence of high-quality evidence to show that clearance of colonisation will occur, a cautious approach to determining clearance is required. In a study of returned travellers, 39% of patients colonised with CPE had detectable colonisation after 12 months.<sup>49</sup> Some bacterial clones appear to be better adapted to prolonged colonisation than others. Antimicrobial use, recurrent admissions to health facilities and the presence of foreign bodies have also been associated with prolonged duration of colonisation.<sup>50</sup>
- The sustainability of instituting contact precautions with increasing case numbers, and the potential impact on patient care and patient flow should be considered as part of planning and preparation strategies.
- Some health facilities may aim to ‘clear’ a low-risk patient with previous CPE infection or colonisation, by screening the patient on readmission.

# → 2

## CPE screening and surveillance

### 2.8 Environmental screening in a non-outbreak setting

#### Statement of intent

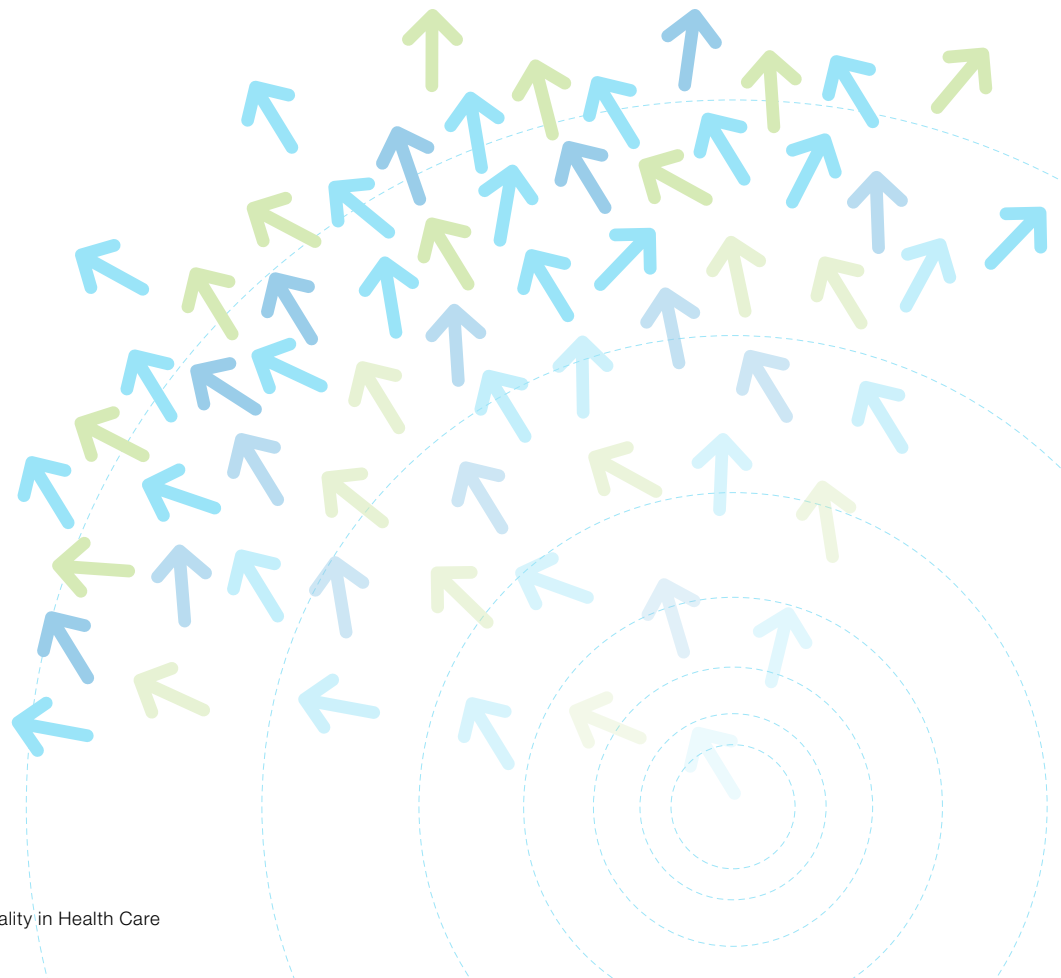
The intent of the recommendations in this section is to provide guidance to health facilities that are considering environmental screening in a non-outbreak setting.

#### → Recommendations

- 2.8.1** Environmental screening in non-outbreak situations is not recommended.
- 2.8.2** Targeted environmental screening should only be considered as part of an outbreak investigation where specific environmental foci are suspected. This should be coordinated by the infection control team.

#### Rationale and commentary

- Environmental screening in non-outbreak situations is not recommended because there is no standardised method to collect specimens. Environmental screening takes considerable resources and provides results that are not easily interpreted.
- See Section 4.5 for information on environmental screening in outbreak situations.





This section provides recommendations for health facilities to manage a small number of CPE cases that are not epidemiologically linked or where limited local transmission is occurring. It includes recommendations on the management of CPE-positive patients, CPE contacts, patient movement, and cleaning and disinfection.

## 3.1 Management of CPE-positive patients

### Statement of intent

The intent of the recommendations in this section is to implement and prioritise strategies to reduce CPE transmission to patients and healthcare workers.

Section 1 provides health facilities with key strategies that should be part of the facility's infection control program to minimise risk and respond to organisms of significance, such as CPE. This section builds upon Section 1, but specifically focuses on strategies that have been identified as important in assisting health facilities to respond where there is local transmission of CPE within the facility.

These recommendations are consistent with the information on contact precautions in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section A1.2.2).



### Recommendations

- 3.1.1** All patients with suspected or confirmed CPE should be managed using contact precautions in a single room with their own toilet facilities. If single rooms are not available for every known or suspected CPE-positive patient:
- Single rooms should be prioritised for those at highest risk of secondary transmission, such as patients who have diarrhoea or are incontinent (urine or faeces), patients who have wounds with uncontrolled drainage, and patients with medical devices in situ
  - CPE-positive patients should not be grouped together without previous approval by the infection control team
  - Toilets should not be shared; if a CPE-positive patient cannot have their own toileting facilities, a bedpan or commode is required.
- 3.1.2** Contact precautions should remain in place for the length of the patient's hospital stay (the admission during which CPE was isolated).
- 3.1.3** Compliance of the health workforce with the use of contact precautions should be monitored, and feedback of results should be provided to staff (NSQHS Standard 3: Preventing and Controlling Healthcare Associated Infections).<sup>2</sup>

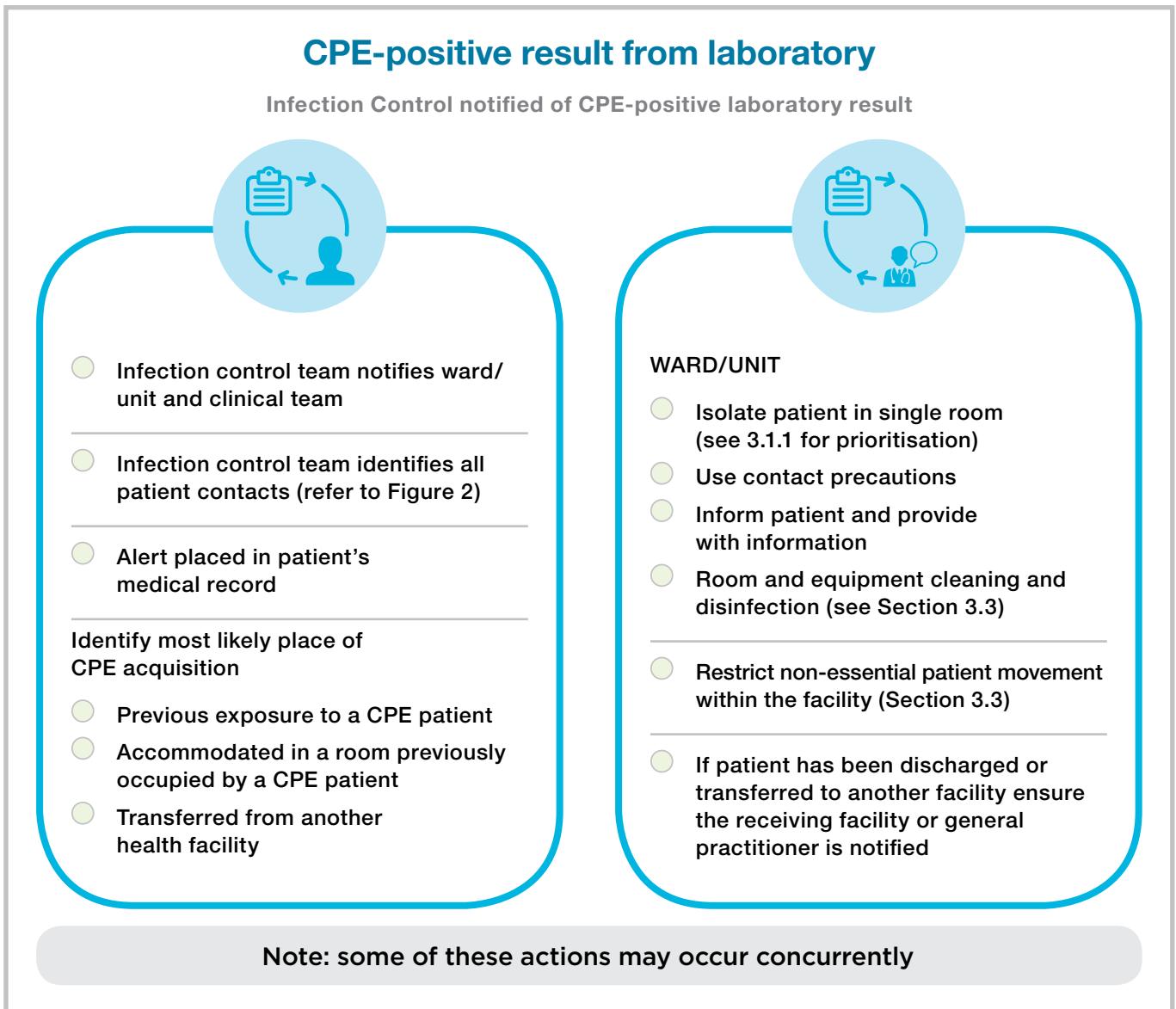
# 3

## Strategies to reduce CPE transmission

### Rationale and commentary

- A number of successful strategies have been identified to reduce transmission of multidrug-resistant gram-negative organisms (Figure 1). These include the use of standard and transmission-based precautions (including hand hygiene, patient isolation and use of personal protective equipment), increased patient screening, and environmental cleaning and disinfection.
- When contact precautions are used for patients colonised or infected with CPE, efforts should be made to ensure that the patients continue to receive appropriate care and treatment, and to counteract the potential psychological effects of isolation.
- Information on contact precautions and patient placement is provided in the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B2.2: Contact precautions, and Section B3.1.2: Core strategies for MRO [multi-resistant organism] prevention and control). Currently, there is insufficient evidence to support attempts to decolonise CPE-positive patients. Because the bacteria generally colonise the gut, decolonisation (by prescribing non-absorbable antimicrobials) is not generally advised.<sup>51</sup>

Figure 1 Management of CPE-positive patient





## 3.2 Management of CPE contacts

### Statement of intent

The intent of the recommendations in this section is to assist health facilities to respond where local CPE transmission is occurring. The recommendations relate to managing patients who have been in contact with a CPE-positive patient, and reducing the risk of further transmission.

#### What is a CPE contact?

A CPE contact is a person who has shared a room, bathroom, or toilet facilities with a confirmed CPE-positive case for more than 24 hours.



### Recommendations

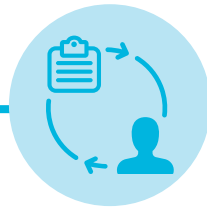
- 3.2.1** All CPE contacts should be identified and screened (see Table 3 in Section 2, and Section 5).
- 3.2.2** All CPE contacts should be isolated and/or cohorted, and contact precautions should be initiated.
- 3.2.3** Rooms, bathrooms and toilets, and frequently touched items should be cleaned and disinfected at least twice per day for the duration of the patient's admission or until contact precautions are ceased.<sup>1,52,53</sup>
- 3.2.4** Dedicated medical equipment should be used for patient care. All equipment, including non-dedicated equipment used for CPE contacts, should be cleaned and disinfected before it is used with another patient.<sup>54,55</sup>
- 3.2.5** CPE contacts should be managed in accordance with Figure 2 until advised by the infection control team.



## Strategies to reduce CPE transmission

Figure 2 Management of CPE contacts

### Following identification of CPE-positive patient



#### INFECTION CONTROL

- Identifies all patient contacts (Section 2.3)
- Notifies ward/unit and clinical team of patient contacts

#### WARD

- Isolate or cohort contacts (Section 3.2)
- Use contact precautions
- Inform patient and provide with information
- Undertake screening of patient contacts (refer to Section 2.5)
- Room and equipment cleaning and disinfection (see Section 3.4)
- Restrict non-essential patient movement within the facility (Section 3.3)
- If patient has been discharged or transferred to another facility ensure the receiving facility or General Practitioner is notified
- **Positive CPE laboratory result**  
Follow Figure 1
- **Negative CPE laboratory result**  
Screened once a week until discharged

## 3.3 Patient movement

### Statement of intent

The intent of the recommendations in this section is to assist health facilities to respond where local transmission of CPE is occurring and to ensure that a patient's CPE status is communicated before transfer between or within health facilities.

These recommendations are consistent with the information on patient management in the *Australian guidelines for the prevention and control of infection in healthcare*.<sup>1</sup>



### Recommendations

#### Transfer of patients within a facility

**3.3.1** Unnecessary transfer of CPE-positive patients within a facility should be avoided.

#### Transfer of patients between facilities

**3.3.2** The presence of CPE infection or colonisation should not preclude transfer of a patient from one health facility to another.

**3.3.3** The transferring health facility should notify the receiving health facility before transfer of a CPE-positive patient, to ensure appropriate bed management.

**3.3.4** If a patient is being transferred to a non-inpatient setting or aged care home, before transfer, an infection control management plan should be discussed by infection control at the transferring facility and staff at the receiving facility.

#### Discharge of patients

**3.3.5** CPE-positive patients and/or their carers should be provided with relevant information on how to manage CPE after discharge.

**3.3.6** CPE status should be recorded in the discharge summary to the transferring facility and the general practitioner.

### Rationale and commentary

- Communication between facilities and health practitioners should be both verbal and written, and include information on the patient's CPE status. Inclusion of the dates and results of any relevant clinical and/or surveillance cultures should be considered. An assessment of the risk of secondary transmission should be undertaken by the receiving health facility (taking into account conditions such as diarrhoea, incontinence of urine or faeces, wounds with uncontrolled drainage, or medical devices in situ).
- For additional information on the application of contact precautions when moving patients within or between facilities, refer to the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B2.2.3: How should contact precautions be applied?).



## Strategies to reduce CPE transmission

### 3.4 Cleaning and disinfection as part of contact precautions

#### Statement of intent

The intent of the recommendations in this section is to provide a clean and hygienic environment, to minimise the risk of transmission of CPE to patients and the workforce. These recommendations are consistent with the information on cleaning and disinfection in the *Australian guidelines for the prevention and control of infection in healthcare*.<sup>1</sup>

Recommendations 1.3.1 and 1.3.2 provide an overview for a health facility cleaning program. The implementation of contact precautions for CPE-positive patients means that cleaning and disinfection of environmental surfaces and equipment are important risk management strategies. Disinfection can be achieved using thermal or chemical agents following cleaning, to destroy any remaining infectious agents.

#### What is cleaning and disinfection?

**Cleaning:** Removal of visible or identifiable contamination from devices or a surface, using either mechanical or physical action with a detergent and water, or with appropriate chemical agents.

**Disinfection:** Destruction of microorganisms (but not spores) by thermal or chemical means.



#### Recommendations

- 3.4.1** Rooms, toilets, and frequently touched surfaces and items should be cleaned and disinfected at least twice per day for the duration of the patient's admission.<sup>1,52,53</sup>
- 3.4.2** Dedicated medical equipment should be used for care of CPE-positive patients. The equipment should be cleaned and disinfected before it is used with another patient.<sup>54,55</sup>
- 3.4.3** Following discharge or transfer of the patient, the room, toilet and all other items should be cleaned and disinfected in accordance with the *Australian guidelines for the prevention and control of infection in healthcare*.<sup>1</sup>
- 3.4.4** Health facilities should monitor and audit cleaning according to state or territory policy.<sup>26</sup>

Note: Standard precautions apply for the management of linen and waste from CPE-positive patients.

#### Rationale and commentary

- Environmental reservoirs for multidrug-resistant gram-negative bacteria are potentially an important factor in healthcare-associated transmission. Patients colonised or infected with CPE widely contaminate their immediate patient environment.<sup>25,27</sup>
- A relationship exists between the environment and transmission of multidrug-resistant gram-negative bacteria<sup>56</sup> (see Section 1.3).
- For additional information, refer to the *Australian guidelines for the prevention and control of infection in healthcare*<sup>1</sup> (Section B1.4: Routine management of the physical environment, Section B2.2.3: How should contact precautions be applied?, and Section B3.1.2: Core strategies for MRO [multi-resistant organism] prevention and control).



## 4.1 Outbreak recognition

### Statement of intent

The intent of the recommendations in this section is to provide health facilities with information to identify and manage an outbreak of CPE where widespread transmission is occurring and cases may be epidemiologically linked. Recommendations include identification of an outbreak, contact tracing, staffing considerations, and cleaning and disinfection.

#### What is an outbreak?

An outbreak is the occurrence of more cases of disease than expected in a given area among a specific group of people, over a particular period of time.<sup>57</sup> This would include two or more linked cases of CPE with the same molecular epidemiology.



### Recommendations

- 4.1.1** The infection control team should identify a potential outbreak by reviewing surveillance data to identify an increase in the number of cases in a health facility.
- 4.1.2** The infection control team, health facility executive, and other relevant individuals and groups (clinicians, laboratory, state or territory department of health, and state or territory public health unit) should be notified of any increase in the number of cases.
- 4.1.3** An outbreak management team should be established, led by a health facility executive, with representatives from bed management, infection prevention and control, infectious diseases and/or microbiology, unit/unit manager(s), relevant clinical team(s), and cleaning/environmental services.<sup>1,13,41,58</sup>
- 4.1.4** The CPE action plan developed as part of the outbreak action plan should be implemented (see Recommendation 1.1.4), including the use of contact precautions for all suspected or confirmed cases of CPE (see Recommendation 3.1.1), monitoring of compliance of the health workforce with contact precautions and provision of feedback (see Recommendation 3.1.3).

### Rationale and commentary

- Healthcare-associated outbreaks of multidrug-resistant gram-negative organisms are well documented.<sup>53,59,60</sup>
- The establishment of an outbreak management team provides best practice for responding to CPE within a health facility.<sup>4,13,26,58</sup> An outbreak management team may be activated at the discretion of the relevant lead within the health facility.
- The membership of the team can be discussed with the state or territory health department at the time of identification of the CPE outbreak (see 'Introduction'). Appointed external experts may include infectious diseases physicians and infection control practitioners, microbiologists from an off-site laboratory, or public health physicians and medical epidemiologists. For smaller facilities, multidisciplinary involvement is essential.



# Outbreak management

## The outbreak management team should:

- Ensure timely notification of suspected cases as per the CPE action plan
- Ensure that data are collected and provided to the state or territory health department
- Ensure that recommendations in the outbreak action plan (see Section 1) are implemented, and communication systems are established to inform hospital managers of the outbreak and the resources required
- Ensure that a communication strategy is developed for patients, family, staff, the state or territory health department, and the media
- Ensure that CPE contacts are screened (see Section 2). Consideration should be given to screening patients in high-risk units
- Ensure that, where possible, general practitioners and receiving facilities are advised to screen any CPE contacts that have been discharged
- Ensure that wards and units implement contact precautions (see Sections 3.1, 3.3 and 3.4), entry signage, designated equipment and limits on patient movement
- Ensure that education are provided to staff and patients (see Recommendation 1.1.6 for education of staff, Recommendation 2.2.3 for education of patients on screening, and Recommendation 3.3.5 patient and carer information on managing CPE on discharge)
- Review compliance audits for standard and transmission-based precautions, hand hygiene, and environmental cleaning and disinfection procedures
- Where there is ongoing transmission of CPE with no clearly identified source, consider
  - Review and re-audit of cleaning and disinfection procedures
  - Review of patient placement
  - Closure of the unit to admissions
  - Expansion of screening strategies (see Section 2.3).

## 4.2 Identification of CPE cases to confirm an outbreak

### Statement of intent

The intent of the recommendations in this section is to assist the health facility with the identification of CPE cases.



- 4.2.1** The outbreak management team should develop a strategy to identify CPE cases within the health facility. This includes the identification of what constitutes a high-risk area, and high-risk patient groups for the outbreak (see Section 2).
- 4.2.2** The outbreak management team should ensure access to timely microbiology results (see Recommendation 1.1.7).

Ongoing transmission of CPE can be defined as either of the following:

- Within a 12-month period, two or more units are affected by related CPE, as identified using appropriate molecular epidemiological analysis.

- Single cases with the same molecular epidemiology occur in more than one unit.

In these circumstances, the health facility is at risk of CPE becoming widespread, and specific additional control measures should be considered.



## 4.3 Screening of patients during an outbreak

### Statement of intent

The intent of the recommendations in this section is to provide health facilities with recommendations for additional screening of high-risk patients and units during an outbreak.



### Recommendations

- 4.3.1** Health facilities should consider additional screening in patients at high risk of CPE acquisition and transmission. Examples of patients in this category are patients with faecal or urinary incontinence, indwelling urinary catheters, uncontained wound drainage or respiratory secretions; and patients with cognitive or intellectual impairment who have difficulty complying with infection control precautions.
- 4.3.2** Health facilities should consider additional screening practices in patients in high-risk units, including intensive care, haematology/oncology, burns, transplant, renal haemodialysis, aged care, and gastroenterology/gastrointestinal surgery units.

The following actions were developed by Victorian health authorities for use during a CPE outbreak,<sup>61</sup> and are provided as an example for consideration in developing a local response:

- Initiate weekly screening of all patients in the designated unit.
- Close the unit to admissions and transfers to other units or departments, unless medically necessary.
- Conduct weekly screening of patients in affected units until 4–8 weeks after the last positive test on that unit. If all screened specimens are negative, conduct monthly screening for six months and then screening every three months until 12 months after the last positive test.
- Consider screening patients at high risk of sepsis (e.g. haematology, transplant, intensive care units) or patients receiving broad-spectrum antibiotics for more than two weeks.

For patients being transferred:

- Screening should take place as close as possible to transfer (ideally within 24–48 hours)
- Ideally, long-term aged care homes should have a screening result before transfer
- Receiving facilities should use contact precautions until screening results are known.



# Outbreak management

## 4.4 Timeframe for contact tracing during an outbreak

It is not always possible to determine the date of CPE acquisition, which needs to be considered on a case-by-case basis, in consultation with infection control and infectious diseases/microbiology. The following timeframes should be considered before contact precautions are implemented:

- The date of discharge from an overseas hospital (e.g. whether this was within the past 12 months)
- The date of admission to an affected unit
- The date of contact with a CPE case with the same molecular epidemiology in a health facility.

In the absence of admission, discharge or placement information, it is suggested that health facilities undertake contact tracing for one month before contact precautions are implemented.<sup>61</sup>

A CPE contact should be screened within the 48 hours before transfer from an outbreak area.

### An example of antimicrobial stewardship in an outbreak situation

The following AMS strategies should be considered by hospitals during a CPE outbreak:

- Review recent local antibiotic audits or conduct a point prevalence audit to identify areas of high broad-spectrum and inappropriate antibiotic use. Feed these data back to the units to engage them in the issue and request their help in addressing the inappropriate antibiotic use.
- Promote, and audit compliance with, the pre-prescription approval process for broad-spectrum antibiotics (phone or electronic approval systems).
- Improve the post-prescription review service, with the aim of providing an earlier (e.g. within 24–48 hours) review of patients who are prescribed broad-spectrum antibiotics such as carbapenems and fluoroquinolones. To ensure that use is appropriate, review national and local guidelines to look for alternatives to broad-spectrum agents, where possible – for example, the ‘carbapenem sparing guidelines’ promoted in Scotland.<sup>62</sup>
- Review microbiology laboratory reports to ensure that they promote narrower-spectrum antibiotic options.
- Review local guidelines for management of severe sepsis to guide clinicians on when to consider empirical antibiotic therapy for CPE; this might include empirical stat doses of aminoglycosides for patients in septic shock (if local CPE isolates are aminoglycoside susceptible). The case may be related to a particular patient group if the outbreak is isolated (e.g. within an intensive care unit or haematology unit). The review will often include advice on when to discuss patients with sepsis with infectious diseases experts.
- Keep records of the antibiotic susceptibility profiles of the local CPE isolates, so that the infectious diseases experts know how to adjust empirical therapies accordingly.
- Ensure that the clinical teams are aware of admitted patients who are CPE colonised, so that empirical antibiotic recommendations can be adjusted accordingly if the patients develop severe sepsis.



## 4.5 Additional screening

### Staff screening

In the absence of evidence to support screening of staff during an outbreak of CPE, routine screening is not required.<sup>1</sup>

Health facilities may consider screening staff who have worked in overseas hospitals in the previous 12 months.

### Environmental screening

Environmental screening is generally not recommended (see Section 2.8). Health facilities may consider environmental screening where there is confirmed local transmission of CPE. If environmental screening is considered necessary, it should be coordinated by the infection control team.

Examples of environmental screening:

- Shared patient equipment.<sup>56</sup>
- Frequently touched surfaces – trolleys, bedside commodes, bedrails, doorknobs, light switches, tap handles, ensuite facilities, drains, sinks, toilets, mobile computer workstations and other shared electronic devices such as tablet computers.<sup>53</sup>

## 4.6 Staff education

### Statement of intent

The intent of the recommendations in this section is to ensure staff education and awareness during an outbreak. See Recommendation 1.1.6 for staff education requirements.



### Recommendations

- 4.6.1** Education and training updates should be provided to the entire health workforce, relevant to their role, including medical, nursing, allied health, patient care assistant, and environmental services staff.
- 4.6.2** In-service education should be conducted for the affected unit and other departments, as necessary.
- 4.6.3** If an outbreak affects more than one area of the health facility, hospital-wide education may be required.



# 4

## Outbreak management

### 4.7 Staff allocation

#### Statement of intent

The intent of the recommendation in this section is to provide advice on the allocation of staff to minimise the transmission of CPE within a health facility during an outbreak.

During an outbreak, the cohorting of nursing, medical and allied health staff to care for CPE patients may reduce the risk of transmission to other staff. It may also allow the health facility to target training and education to those staff initially. Rostering should be considered, to prevent fatigue and burn-out of staff during outbreaks.



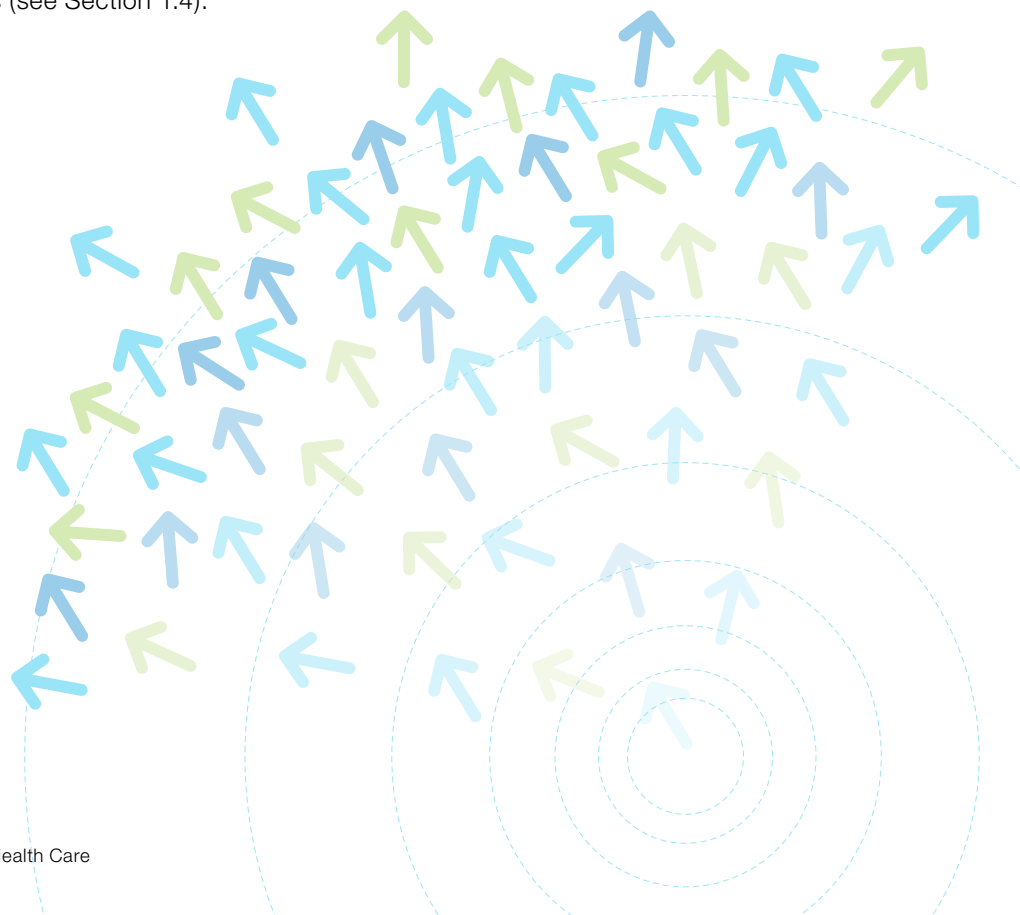
#### Recommendation

**4.7.1** The health facility outbreak control team should consider allocating separate, dedicated staff to CPE-positive patients and contacts, taking into account patient acuity; staff knowledge, experience (see Recommendation 1.1.6 for staff education) and availability; and resources.

### 4.8 Cleaning and disinfection during outbreaks

Cleaning and disinfection of environmental surfaces and equipment for CPE patients is the same for individual or multiple cases of CPE. The recommendations for cleaning and disinfection are outlined in Section 1.3 Environmental cleaning (Recommendation 1.3.1 and 1.3.2) and Section 3.4 cleaning as part of contact precautions.

Endoscopes have been linked to outbreaks of CPE.<sup>29,30,31</sup> Health facilities should review cleaning and disinfection practices for endoscopes (see Section 1.4).





This section addresses laboratory procedures for screening patient specimens or cultures for CPE. It provides advice and recommendations on the detection of CPE for all medical diagnostic microbiology laboratories in Australia.

## Carbapenem-resistant gram-negative bacteria not included in this guide

The following carbapenem resistant gram-negative bacteria are not included in this guide:

- *Enterobacteriaceae* that are carbapenem resistant (non-susceptible) without producing a carbapenemase enzyme. These bacteria use a combination of other resistance mechanisms. In general, such bacteria pose a lower risk of transmission and dissemination within health facilities than CPE
- A number of carbapenem-resistant gram-negative bacilli other than *Enterobacteriaceae* that are implicated in transmission and outbreaks of infection within healthcare settings, including *Pseudomonas aeruginosa*, *Acinetobacter species* and *Stenotrophomonas maltophilia*.

Although these gram-negative pathogens can be highly problematic, they are usually confined to healthcare-associated infection in selected patient groups, such as those with a compromised immune system, critical illness or chronic disease. Most often, the epidemiology of these pathogens within a hospital is well defined and restricted to a particular patient group(s), geographic location or service that manages a risk group (e.g. severe burn units, intensive care units or cystic fibrosis services). The risks associated with transmission of these pathogens are therefore lower than for CPE.

However, many reports in the literature describe transmission and/or broader outbreaks of such bacteria. In circumstances where there is a reasonable risk of transmission or evidence of transmission, it is appropriate to use the recommendations in this guide. If a health facility identifies a patient who is colonised or infected with one of these bacteria, expert advice should be sought to ascertain whether the instance is of concern and, if so, advice on appropriate management of the patient.

## 5.1 Laboratory testing for CPE

Laboratory testing for CPE and genes encoding carbapenemase enzymes is a rapidly developing field; therefore, recommendations will require review in the light of new evidence. CPE are one of the critical antimicrobial resistances (CARs) in Australia, and many of the laboratory processes described in this section are considered usual practice. They are also documented in the handbook for the national alert system for CARs, known as CARAlert.<sup>62</sup> CARAlert is a program in the AURA Surveillance System to provide more timely communication of the presence of CARs, and facilitate appropriate response.



# 5

## Laboratory screening and confirmation methods

### 5.2 Recommended screening for asymptomatic carriage in high-risk patients

#### Statement of intent

The intent of the recommendation in this section is to provide microbiology laboratories in Australia with guidance on procedures for screening patient specimens or cultures for *Enterobacteriaceae* harbouring transmissible carbapenemase genes and on the detection of CPE.



#### Recommendation

- 5.2.1** Screening specimens should include rectal swabs or faeces. Urine from catheterised patients should also be included in screening, since the majority of CPE detected in AGAR surveillance studies have come from urine specimens. Perianal swabs are not recommended generally because they may not give accurate results. However, they may be necessary in some situations, such as anal pathology or in some neutropenic patients. Specimens from open wounds, or aspirates from any tubes or drains should also be considered for screening.

#### Rationale and commentary

- These recommendations are consistent with current evidence on laboratory methods for screening, detection, confirmation, reporting and notification of CPE.
- Most colonised people carry CPE in their faeces. Screening specimens should include rectal swabs or faeces. Urine from catheterised patients should also be included in screening, since the majority of CPE detected in AGAR surveillance studies have come from urine specimens. Isolated urinary carriage of KPC-producing strains has been demonstrated in 24% of colonised patients.<sup>63</sup>
- There is currently no internationally accepted 'gold standard' laboratory screening method for carbapenemases in *Enterobacteriaceae*. Highly sensitive and specific molecular methods for detection of carbapenemase genes are well described, but not yet widely in use for direct detection from patient specimens.<sup>64</sup>
- A range of carbapenem-specific primary screening media is available in Australia. The manufacturer's instructions should be followed on the procedures for cultures suspected to be positive. The choice of medium is defined by the local, regional and national epidemiology of CPE.
- Commercial screening media<sup>65</sup> have been developed, but their suitability to Australian circumstances has not been fully evaluated. Their utility, including sensitivity and specificity, are strongly dependent on national, regional and local prevalence. No screening medium with adequate sensitivity and specificity for all CPE has yet been developed. At the time of preparation of this guide, commercially available media are
  - ChromID® Carba, ChromID® OXA-48<sup>66</sup>, ChromID® CARBA SMART (bioMérieux)<sup>67</sup>
  - Brilliance CRE (Oxoid)<sup>68</sup>
  - CHROMagar KPC (Chromagar, Paris)<sup>69</sup>
  - Chromatic CRE (Liofilchem®).
- These media have undergone limited trialling in at least one site in Australia.<sup>70</sup> A recent study from the United Kingdom showed poorer performance of Brilliance CRE than ChromID Carba, in a setting where the NDM and KPC carbapenemase classes predominated.<sup>71</sup>
- The use of two chromogenic agars may increase sensitivity and specificity. Recently, a biplate formulation (ChromID CARBA SMART) was released that contains both ChromID Carba and ChromID OXA-48.
- Extended-spectrum β-lactamase (ESBL) screening media (e.g. Brilliance ESBL, ChromID ESBL) may be used; however, they lack specificity.



## 5.3 Detection of CPE with 'routine' susceptibility testing of clinical isolates

### Statement of intent

The intent of the recommendations in this section is to provide microbiology laboratories in Australia with guidance on procedures for recognition of possible CPE as part of routine susceptibility testing.



### Recommendations

- 5.3.1** As a minimum standard, laboratories should test meropenem susceptibility of all isolates of *Enterobacteriaceae* with the ESBL phenotype or that are non-susceptible to gentamicin.
- 5.3.2** CPE (as defined by the breakpoints documented for the susceptibility testing system being used) should always undergo confirmatory testing.<sup>62</sup>
- 5.3.3** Laboratories using semi-automated methods for susceptibility testing should also undertake, or seek, molecular confirmation of all *Enterobacteriaceae* with a meropenem of MIC is  $\geq 0.25$ mg/L, especially from high-risk patients or units.

### Rationale and commentary

- The aim of laboratory screening is to provide early detection of carbapenemase genes in *Enterobacteriaceae*, and thereby prevent the dissemination and establishment of CPE. CPE carrying the KPC or NDM carbapenemase types are a particular problem, because the great majority of these bacteria are resistant to multiple other drug classes.
- A range of suggestions have been made in recent years about screening methods, including:
  - Using specifically designed screening media (see Section 5.3)<sup>72</sup>
  - Using the susceptibility testing results on positive cultures.<sup>73</sup>
- Some carbapenemase-producing strains may test as susceptible to meropenem in routine testing using current breakpoints, and laboratories ideally should seek to identify these carbapenemase producers (resources permitting). These strains can be detected with the current Australian configurations of Vitek™ cards and Phoenix™ gram-negative panels using the criterion noted above.
- Current experience suggests that ertapenem has the highest sensitivity to the presence of carbapenemases, but specificity remains a major issue. Using the ertapenem susceptibility test result as the first screen will result in a day's delay in detecting possible CPE carriers, and will probably result in a large amount of unnecessary additional laboratory confirmation work. Therefore, this approach is not recommended.
- Data from AGAR indicate that CPE are mostly likely to show a phenotype that includes gentamicin non-susceptibility, or either ceftazidime or ceftriaxone non-susceptibility (i.e. ESBL phenotype).



# 5

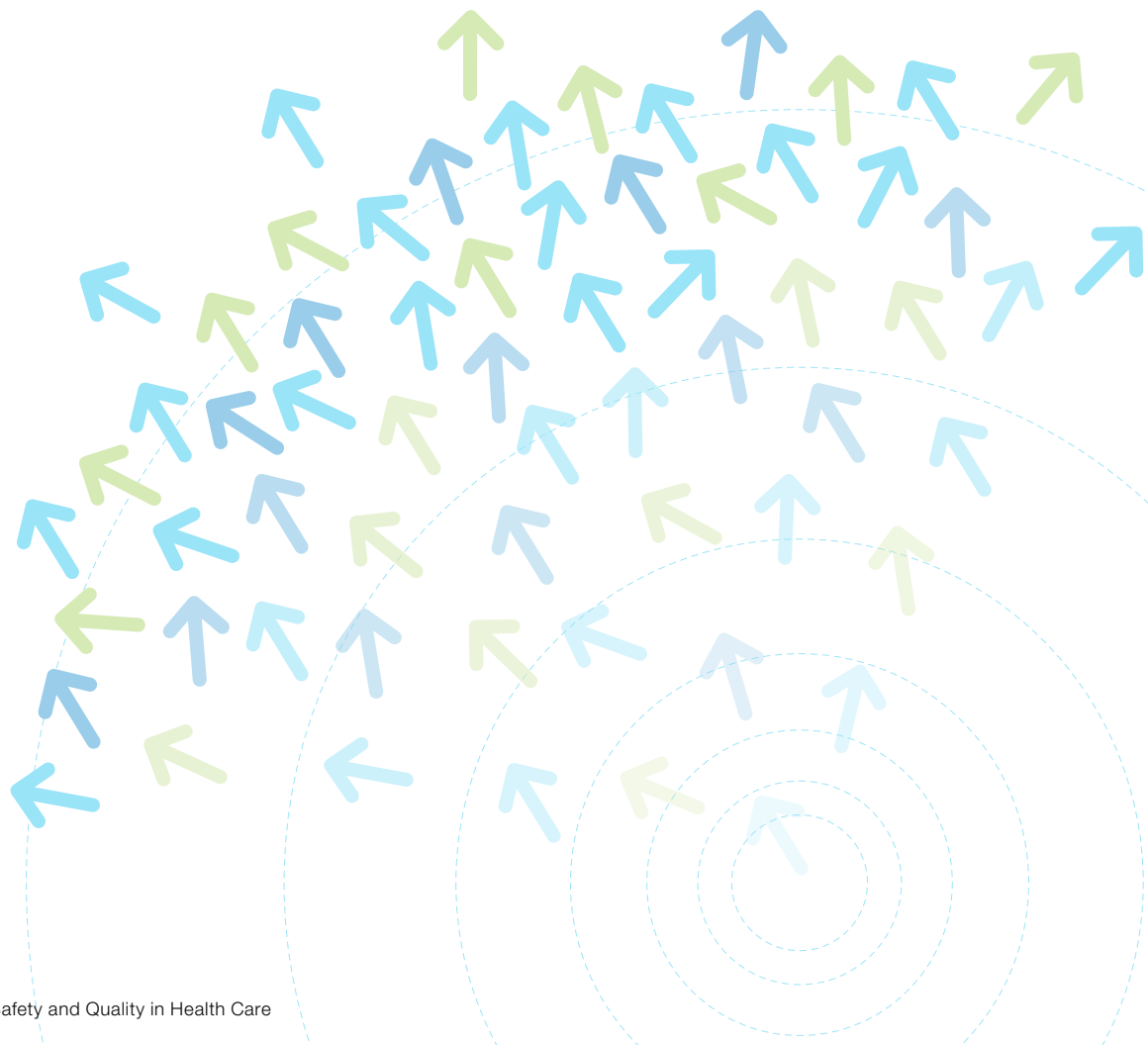
## Laboratory screening and confirmation methods

### Disc testing

Many laboratories perform direct disc susceptibility testing on urine specimens, without repeat testing if the results of direct testing are satisfactory. Few, if any, laboratories routinely include meropenem discs in the range of agents used for direct susceptibility testing. Many smaller laboratories, especially regional laboratories, also use disc susceptibility testing exclusively. Since the majority of CPE detected in AGAR surveillance studies during the past few years have come from urine specimens, the bulk of CPE in Australia could potentially remain undetected if some kind of CPE screening method is not included for disc susceptibility testing. To avoid this problem, laboratories should ideally ensure that urinary isolates are routinely tested against gentamicin and a third-generation cephalosporin, (See Recommendation 5.4.1).

If meropenem is routinely included in urine disc susceptibility testing, for either direct or standard testing, it should be noted that the zone diameter breakpoints for meropenem published by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the Clinical and Laboratory Standards Institute (CLSI) are correlated to the clinical (and pharmacodynamic) breakpoints, and not the lower 'screening' concentration of 0.125 mg/L. In view of this, a suggested option for disc testing in laboratories using Mueller-Hinton agar plates (EUCAST and CLSI methods) is to add meropenem to the routine disc testing range for both direct and standard testing – this has the potential to capture emerging resistance because the wild-type zone diameter distributions of meropenem (using a 10 µg disc) and the *Enterobacteriaceae* are known.<sup>74</sup> Strains with a zone diameter of <25 mm on Mueller-Hinton agar should then undergo confirmation testing. Note that this method is meant to detect non-wild type isolates, and the recommended cut-off is significantly lower than published clinical breakpoints.

Based on early experience, the calibrated dichotomous sensitivity routine disc method appears to be able to detect a range of carbapenemases in *Enterobacteriaceae*.<sup>75</sup>



## 5.4 CPE confirmation

### Statement of intent

The intent of the recommendations in this section is to provide confirming laboratories in Australia with guidance on procedures for confirming a suspected CPE, and originating laboratories with simple tests that can be performed to strengthen the likelihood of a suspected CPE before referral to a confirming laboratory.



### Recommendations

- 5.4.1** All suspected CPE isolates should be subjected to molecular screening for at least the suite of carbapenemase gene families that have so far been seen in *Enterobacteriaceae* in Australia: IMP, VIM, OXA-48 and OXA-48-like, KPC and NDM.
- 5.4.2** The testing laboratory may choose to undertake preliminary phenotypic confirmation on such isolates with the Carba NP test<sup>76,77</sup>, the enhanced Carba NP test II<sup>78</sup>, the Carb Blue test<sup>79,80</sup>, or the carbapenem inactivation method (CIM)<sup>81,82</sup> before referring the isolates for molecular testing. Commercial versions of most of these tests are now available (RAPIDEC® CARBA NP [bioMérieux]; Rapid CARB Screen, Rapid CARB Blue Kit [Rosco]). The CIM method requires no special commercial materials.
- 5.4.3** The modified Hodge test, originally promoted as a phenotypic confirmation test, has now been shown to have poor sensitivity and specificity, and is not recommended.<sup>83</sup>

### Rationale and commentary

- Published evidence indicates that the CIM and Carba NP tests are reliable, rapid phenotypic methods for carbapenemase detection. They detect the presence of a carbapenemase, but do not reveal the genotype.
- At the national level, the most commonly reported carbapenemase is IMP, which is mostly found to be IMP-4 on sequencing. However, all of the carbapenemase classes known to have spread internationally have been seen in Australia since 2009, including VIM, KPC, OXA-48 and OXA-48-like, and NDM types.



# Laboratory screening and confirmation methods

## 5.5 Reporting of suspected CPE

### Statement of intent

The intent of the recommendation in this section is to provide originating microbiology laboratories in Australia with guidance on appropriate notification of suspected CPE, and confirming and originating laboratories with guidance on notification and reporting of confirmed CPE.

For inpatients, infection control staff and treating clinicians should be notified of suspected (e.g. Carba NP or CIM positive) and subsequently proven CPE, so that appropriate precautions can be put in place (see Section 3). In a situation analogous to that of ESBL detection, suspected or proven CPE should only be reported as resistant to meropenem if their minimum inhibitory concentrations are greater than the clinical (pharmacodynamic) breakpoint of 1 mg/L (CLSI) or 2 mg/L (EUCAST). For isolates associated with disease and requiring treatment, this may require discussion with the treating clinician to indicate the possibility of altered response to carbapenem treatment.

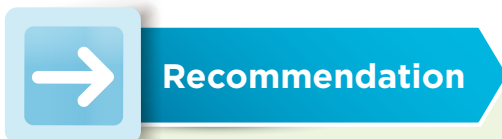
Following confirmation, laboratories should add a comment to the report (either the original or an amended report) about the presence of a transmissible carbapenemase gene (e.g. 'This isolate harbours a proven transmissible carbapenemase with infection control implications. Infection control has been notified').

Strains of CPE that have been confirmed, by molecular means, to have carbapenemase gene(s) should be reported by the confirming laboratory to the originating laboratory, according to usual practice. Subsequently, the confirming laboratory should enter details onto the CARAlert website. The CARAlert system will alert designated individuals in the states and territories, who may take additional action beyond that of the clinicians and infection control staff of the health facility where the patient is an inpatient.

Carbapenem-resistant isolates that do not have carbapenemase genes demonstrated by molecular means are not reported to CARAlert.

Examples of comments that laboratories might consider adding to reports of confirmed CPE are:

- Treatment options are limited.
- Consult infectious diseases or clinical microbiology.
- CPE-colonised patients must be managed with standard and contact precautions.
- An alert has been placed in the patient record.
- For further information, contact infection prevention and control.



**5.5.1** For inpatients, all suspected CPE isolates should be notified to infection control staff and treating clinicians. Notification should not be delayed while awaiting confirmation in a confirming laboratory.

## Rationale and commentary

- Prompt notification provides important information for the clinician and may alter the required patient treatment. Infection control requires prompt notice to ensure that patient isolation and other precautions can be put in place as soon as possible. This also enables surveillance for local clusters or outbreaks.
- National notification provides critical information for public health purposes and informs development of government policy.
- Overseas, there have been many reports of individual cases and a small number of reports of clonal outbreaks of carbapenem-resistant isolates that have non-carbapenemase mediated mechanisms of resistance.<sup>84</sup> On review, these reports appear to be confined to individuals and locations with very high levels of antimicrobial selection pressure – that is, heavy use of carbapenems in the infected individual or health facility.<sup>85</sup> Current evidence suggests that patients carrying such isolates represent a lower infection control risk and do not warrant attention unless cross-transmission is demonstrated.

# References

1. National Health and Medical Research Council. Australian guidelines for the prevention and control of infection in healthcare. Canberra: NHMRC, 2010.
2. Australian Commission on Safety and Quality in Health Care. Standard 3: Preventing and controlling healthcare associated infections – safety and quality improvement guide. Sydney: ACSQHC, 2012.
3. Australian Commission on Safety and Quality in Health Care. Antimicrobial stewardship clinical care standard. Sydney: ACSQHC, 2014.
4. O'Fallon E, Pop-Vicas A, D'Agata E. The emerging threat of multidrug-resistant gram-negative organisms in long-term care facilities. *J Gerontol A Biol Sci Med Sci* 2009;64(1):138.
5. United States Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States. Washington, DC: United States Department of Health and Human Services, 2013.
6. Stuart RL, Kotsanas D, Webb B, Vandergraaf S, Gillespie EE, Hogg GG, et al. Prevalence of antimicrobial-resistant organisms in residential aged care facilities. *Med J Aust* 2011;195:530–3.
7. Ben-David D, Masarwa S, Adler A, Mishali H, Carmeli Y, Schwaber MJ. A national intervention to prevent the spread of carbapenem-resistant *Enterobacteriaceae* in Israeli post-acute care hospitals. *Infect Control Hosp Epidemiol* 2014;35(7):802–9.
8. Chang LW, Busing KL, Jeremiah CJ, Cronin K, Poy Lorenzo YS, Howden BP, et al. Managing a nosocomial outbreak of carbapenem-resistant *Klebsiella pneumoniae*: an early Australian hospital experience. *Intern Med J* 2015;45(10):1037–43.
9. Kwong J. Victorian KPC experience. Proceedings of the Australian Society of Antimicrobials 16th Annual Scientific Meeting: Antimicrobials 2015; 2015 Mar 26–28; Brisbane.
10. Australian Commission on Safety and Quality in Health Care. CARAlert Summary Report: 17 March–31 December 2016. Sydney: ACSQHC, 2017.
11. Lane C. Carbapenemase-producing *Enterobacteriaceae* in Victoria – enhancing surveillance. Proceedings of the Australian Society of Antimicrobials 17th Annual Scientific Meeting: Antimicrobials 2016; 2016 Feb 25–27; Melbourne.
12. Munoz-Price LS, Poirel L, Bonomo RA, Schwaber MJ, Daikos GL, Cormican M, et al. Clinical epidemiology of the global expansion of *Klebsiella pneumoniae* carbapenemases. *Lancet Infect Dis* 2013;13:785–96.
13. Schwaber MJ, Lev B, Israeli A, Solter E, Smollan G, Rubinovitch B, et al. Containment of a country-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* in Israeli hospitals via a nationally implemented intervention. *Clin Infect Dis* 2011;52(7):848–55.
14. Gagliotti C, Cappelli V, Carretto E, Marchi M, Pan A, Ragni P, et al. Control of carbapenemase-producing *Klebsiella pneumoniae*: a region-wide intervention. *Euro Surveill* 2014;19(43).
15. Kallen A, Guh A. United States Centers for Disease Control and Prevention issue updated guidance for tackling carbapenem-resistant *Enterobacteriaceae*. *Euro Surveill* 2012;17.
16. Public Health Agency of Canada. Guidance: infection prevention and control measures for health workers in all health settings – carbapenem-resistant gram-negative bacilli. Ottawa: Public Health Agency of Canada, 2010.
17. Schwaber MJ, Carmeli Y. An ongoing national intervention to contain the spread of carbapenem-resistant *Enterobacteriaceae*. *Clin Infect Dis* 2014;58(5):697–703.
18. United States Centers for Disease Control and Prevention. Vital signs: estimated effects of a coordinated approach for action to reduce antibiotic-resistant infections in health care facilities – United States. *MMWR Morb Mortal Wkly Rep* 2015;826–31.
19. Lledo W, Hernandez M, Lopez E, Molinari OL, Soto RQ, Hernandez E, et al. Guidance for control of infections with carbapenem-resistant or carbapenemase-producing *Enterobacteriaceae* in acute care facilities. *MMWR Morb Mortal Wkly Rep* 2009;256–60.
20. Schechner V, Kotlovsky T, Kazma M, Mishali H, Schwartz D, Navon-Venezia S, et al. Asymptomatic rectal carriage of blaKPC producing carbapenem-resistant *Enterobacteriaceae*: who is prone to become clinically infected? *Clin Microbiol Infect* 2012;19(5):451–6.
21. Australian Commission on Safety and Quality in Health Care. Standard 1: Governance for safety and quality in health service organisations. Sydney: ACSQHC, 2012.
22. Hand Hygiene Australia. The National Hand Hygiene Initiative [Internet]. Melbourne: Hand Hygiene Australia, 2015. Available from: <http://www.hha.org.au>

# References

23. World Health Organization. WHO guidelines on hand hygiene in health care (advanced draft). Geneva: WHO, 2006.
24. Otter JA, Yezli S, French GL. The role played by contaminated surfaces in the transmission of nosocomial pathogens. *Infect Control Hosp Epidemiol* 2011;32(7):687–99.
25. Istenes N, Bingham J, Hazelett S, Fleming E, Kirk J. Patients' potential role in the transmission of health care-associated infections: prevalence of contamination with bacterial pathogens and patient attitudes toward hand hygiene. *Am J Infection Control* 2013;41:793–8.
26. Australian Commission on Safety and Quality in Health Care. National safety and quality health service standards. Sydney: ACSQHC, 2012.
27. Lerner A, Adler A, Abu-Hanna J, Meitus I, Navon-Venezia S, Carmeli Y. Environmental contamination by carbapenem-resistant *Enterobacteriaceae*. *J Clin Microbiol* 2013;51:177–81.
28. Gastroenterological Society of Australia, Australian Gastrointestinal Endoscopy Association, Gastroenterological Nurses College of Australia. Infection control in endoscopy. 2nd ed. Melbourne: Gastroenterological Society of Australia, 2010.
29. Muscarella LF. Risk of transmission of carbapenem-resistant *Enterobacteriaceae* and related 'superbugs' during gastrointestinal endoscopy. *World J Gastrointest Endosc* 2014;6:457–74.
30. Kola A, Piening B, Pape UF, Veltzke-Schlieker W, Kaase M, Geffers C, et al. An outbreak of carbapenem-resistant OXA-48 – producing *Klebsiella pneumoniae* associated to duodenoscopy. *Antimicrob Resist Infect Control* 2015;4.
31. Epstein L, Hunter JC, Arwady MA, Tsai V, Stein L, Gribogiannis M, et al. New Delhi metallo-β-lactamase-producing carbapenem-resistant *Escherichia coli* associated with exposure to duodenoscopes. *JAMA* 2014;312:1447–55.
32. Gillespie EE, Kotsanas D, Stuart RL. Microbiological monitoring of endoscopes: 5-year review. *J Gastroenterol Hepatol* 2008;23:1069–74.
33. Fernando G, Collignon P, Beckingham W. ATP bioluminescence to validate the decontamination process of gastrointestinal endoscopes. *Healthc Infect* 2014;19:59–64.
34. Alfa MJ, Fatima I, Olson N. The adenosine triphosphate test is a rapid and reliable audit tool to assess manual cleaning adequacy of flexible endoscope channels. *Am J Infect Control* 2013;41:249–53.
35. Australian Commission on Safety and Quality in Health Care. Principles of antibiotic pharmacotherapy, Part 2. Sydney: ACSQHC, 2015. Available from: <https://www.safetyandquality.gov.au/our-work/healthcare-associated-infection/antimicrobial-stewardship/antibiotic-awareness-week/antimicrobial-stewardship-video-presentations>
36. Duguid M, Cruickshank M. Antimicrobial stewardship in Australian hospitals. Sydney: Australian Commission on Safety and Quality in Health Care, 2010.
37. Antibiotic Expert Group. Therapeutic guidelines: antibiotic. Version 15. Melbourne: Therapeutic Guidelines Limited, 2014.
38. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant *Enterobacteriaceae*: epidemiology and prevention. *Clin Infect Dis* 2011;53(1):60–7.
39. Ginn AN, Wiklendt AM, Gidding HF, George N, O'Driscoll JS, Partridge SR, et al. The ecology of antibiotic use in the ICU: homogeneous prescribing of cefepime but not tazocin selects for antibiotic resistant infection. *PLoS ONE* 2012;7(6):e38719.
40. Cantón R, Bryan J. Global antimicrobial resistance: from surveillance to stewardship. Part 1: surveillance and risk factors for resistance. *Expert Rev Anti Infect Ther* 2012;10(11):1269–71.
41. Schwaber MJ, Carmeli Y, Harbarth S. Controlling hospital-acquired infection due to carbapenem-resistant *Enterobacteriaceae* (CRE). In: Gould IM, van der Meer JWM, editors. Antibiotic policies: controlling hospital acquired infection. Springer: New York, 2012;105–15.
42. Chitnis A, Caruthers PS, Rao AK, Lamb J, Lurvey R, Beau De Rochars V, et al. Outbreak of carbapenem-resistant *Enterobacteriaceae* at a long-term acute care hospital: sustained reductions in transmission through active surveillance and targeted interventions. *Infect Control Hosp Epidemiol* 2012;33(10):984–92.
43. Rogers BA, Aminzadeh Z, Hayashi Y, Paterson DL. Country-to-country transfer of patients and the risk of multi-resistant bacterial infection. *Clin Infect Dis* 2011;53:49–56.
44. Lübbert C, Straube L, Stein C, Makarewicz O, Schubert S, Mössner J, et al. Colonization with extended-spectrum beta-lactamase-producing and carbapenemase-producing *Enterobacteriaceae* in international travelers returning to Germany. *Int J Med Microbiol* 2015;305(1):148–56.

# References

45. Logan LK. Carbapenem-resistant *Enterobacteriaceae*: An emerging problem in children. *Clin Infect Dis* 2012;55:852–9.
46. Seale J, Millar M. Perinatal vertical transmission of antibiotic-resistant bacteria: a systematic review and proposed research strategy. *BJOG* 2014;121:923–8.
47. Savard P, Carroll KC, Wilson LE, Perl TM. The challenges of carbapenemase-producing *Enterobacteriaceae* and infection prevention: protecting patients in the chaos. *Infect Control Hosp Epidemiol* 2013;34:730–9.
48. Lewis JD, Enfield KB, Mathers AJ, Giannetta ET, Sifri CD. The limits of serial surveillance cultures in predicting clearance of colonization with carbapenemase-producing *Enterobacteriaceae*. *Infect Control Hosp Epidemiol* 2015;36:835–7.
49. Zimmerman FS, Assous MV, Bdolah-Abram T, Lachish T, Yinnon AM, Wiener-Well Y. Duration of carriage of carbapenem-resistant *Enterobacteriaceae* following hospital discharge. *Am J Infect Control* 2013;41:190–4.
50. Bart Y, Paul M, Eluk O, Geffen Y, Rabino G, Hussein K. Risk factors for recurrence of carbapenem-resistant *Enterobacteriaceae* carriage: case–control study. *Infect Control Hosp Epidemiol* 2015;36:936–41.
51. Calderdale and Huddersfield NHS Foundation Trust. Section J – Management of patients with multi resistant organisms: carbapenemase-producing *Enterobacteriaceae* (CPE), vancomycin-resistant enterococci (VRE), penicillin-resistant pneumococci (PRP), extended spectrum beta-lactamase producing micro-organisms (ESBL). United Kingdom: Calderdale and Huddersfield NHS Foundation Trust, 2016.
52. Public Health Agency of Canada. Guidance: infection prevention and control measures for healthcare workers in all healthcare settings. Ottawa: Public Health Agency of Canada, 2012.
53. Kotsanas D, Wijesooriya WR, Korman TM, Gillespie EE, Wright L, Snook K, et al. ‘Down the drain’: carbapenem-resistant bacteria in intensive care unit patients and handwashing sinks. *Med J Aust* 2013;198(5):267–9.
54. Provincial Infectious Diseases Advisory Committee. Routine practices and additional precautions in all health care settings. Annex A: Screening, testing and surveillance for antibiotic-resistant organisms (AROs). Toronto: Ontario Agency for Health Protection and Promotion, 2013.
55. Munoz-Price LS, Quinn JP. Deconstructing the infection control bundles for the containment of carbapenem-resistant *Enterobacteriaceae*. *Current Opin Infect Dis* 2013;26(4):378–87.
56. Weber DJ, Rutala WA, Kanamori H, Gergen MF, Sickbert-Bennett EE. Carbapenem-resistant *Enterobacteriaceae*: frequency of hospital room contamination and survival on various inoculated surfaces. *Infect Control Hosp Epidemiol* 2015;36:590–3.
57. Grundmann H, Aires-de-Sousa M, Boyce J, Tiemersma E. Emergence and resurgence of methicillin-resistant *Staphylococcus aureus* as a public-health threat. *Lancet* 2006;368:874–85.
58. Delory T, Seringe E, Antonioti G, Novakova I, Goulenok C, Paysant I, et al. Prolonged delay for controlling KPC-2-producing *Klebsiella pneumoniae* outbreak: the role of clinical management. *Am J Infect Control* 2015;43:1070–5.
59. Peleg AY, Franklin C, Bell JM, Spelman DW. Dissemination of the metallo-beta-lactamase gene blaIMP-4 among gram-negative pathogens in a clinical setting in Australia. *Clin Infect Dis* 2005;41:1549–56.
60. Lowe CF, Kus JV, Salt N, Callery S, Louie L, Khan MA, et al. Nosocomial transmission of New Delhi metallo-β-lactamase-1-producing *Klebsiella pneumoniae* in Toronto, Canada. *Infect Control Hosp Epidemiol* 2013;34(1):49–55.
61. Department of Health and Human Services Victoria. Victorian guidelines on carbapenemase-producing *Enterobacteriaceae* for health services. Melbourne: Department of Health and Human Services, 2015.
62. Australian Commission on Safety and Quality in Health Care. The CARAlert handbook. Sydney: ACSQHC, 2016.
63. Thurlow CJ, Prabaker K, Lin MY, Lolans K, Weinstein RA, Hayden MK. Anatomic sites of patient colonization and environmental contamination with *Klebsiella pneumoniae* carbapenemase-producing *Enterobacteriaceae* at long-term acute care hospitals. *Infect Control Hosp Epidemiol* 2013;34:56–61.
64. Poirel L, Walsh TR, Cuvillier V, Nordmann P. Multiplex PCR for detection of acquired carbapenemase genes. *Diagn Microbiol Infect Dis* 2011;70(1):119–23.
65. Girlich D, Poirel L, Nordmann P. Comparison of the SUPERCARBA, CHROMagar KPC, and Brilliance CRE screening media for detection of *Enterobacteriaceae* with reduced susceptibility to carbapenems. *Diagn Microbiol Infect Dis* 2013;75:214–17.
66. Girlich D, Anglade C, Zambardi G, Nordmann P. Comparative evaluation of a novel chromogenic medium (chromID OXA-48) for detection of OXA-48 producing *Enterobacteriaceae*. *Diagn Microbiol Infect Dis* 2013;77:296–300.



# References

67. Simner PJ, Gilmour MW, DeGagne P, Nichol K, Karlowsky JA. Evaluation of five chromogenic agar media and the Rosco Rapid Carb screen kit for detection and confirmation of carbapenemase production in gram-negative bacilli. *J Clin Microbiol* 2015;53:105-12.
68. d'Humieres C, Birgy A, Doit C, Bidet P, Arlet G, Bingen E. Use of a new screening medium to detect carbapenem-non-susceptible members of the *Enterobacteriaceae*. *J Med Microbiol* 2012;61(6):878-80.
69. Nordmann P, Girlich D, Poirel L. Detection of carbapenemase producers in *Enterobacteriaceae* by use of a novel screening medium. *J Clin Microbiol* 2012;50:2761-6.
70. Huntington PG. Evaluation of CHROMagar ESBL and CHROMagar KPC culture media for detection of carbapenem-resistant *Enterobacteriaceae*. Poster presentation, Australian Society of Antimicrobials 16th Annual Scientific Meeting: Antimicrobials 2015; 2015 Mar 26-28; Brisbane.
71. Wilkinson KM, Winstanley TG, Lanyon C, Cummings SP, Raza MW, Perry JD. Comparison of four chromogenic culture media for carbapenemase-producing *Enterobacteriaceae*. *J Clin Microbiol* 2012;50(9):3102-4.
72. Vrioni G, Daniil I, Voulgari E, Ranellou K, Koumaki V, Ghirardi S, et al. Comparative evaluation of a prototype chromogenic medium (ChromID CARBA) for detecting carbapenemase-producing *Enterobacteriaceae* in surveillance rectal swabs. *J Clin Microbiol* 2012;50(6):1841-6.
73. Nordmann P, Poirel L. Strategies for identification of carbapenemase-producing *Enterobacteriaceae*. *J Antimicrob Chemother* 2013;68(3):487-9.
74. European Committee on Antimicrobial Susceptibility Testing. Antimicrobial wild type distributions of microorganisms [Internet]. EUCAST, 2013. Available from: <https://mic.eucast.org/Eucast2/>
75. Bell SM, Pham JN, Newton PJ, Nguyen TT. Antibiotic susceptibility testing by the CDS method: a manual for medical and veterinary laboratories. 7th edition. Sydney: South Eastern Area Laboratory Services, 2014. Available from: <http://cdstest.net>
76. Dortet L, Brechard L, Poirel L, Nordmann P. Impact of the isolation medium for detection of carbapenemase-producing *Enterobacteriaceae* using an updated version of the Carba NP test. *J Med Microbiol* 2014;63(5):772-6.
77. Nordmann P, Poirel L, Dortet L. Rapid detection of carbapenemase-producing *Enterobacteriaceae*. *Emerg Infect Dis* 2012;18(9):1503-7.
78. Dortet L, Poirel L, Nordmann P. Rapid identification of carbapenemase types in *Enterobacteriaceae* and *Pseudomonas* spp. by using a biochemical test. *Antimicrob Agents Chemother* 2012;56(12):6437-40.
79. Novais A, Brilhante M, Pires J, Peixe L. Evaluation of the recently launched Rapid Carb Blue Kit for detection of carbapenemase-producing gram-negative bacteria. *J Clin Microbiol* 2015;53(9):3105-7.
80. Pires J, Novais A, Peixe L. Blue-carba, an easy biochemical test for detection of diverse carbapenemase producers directly from bacterial cultures. *J Clin Microbiol* 2013;51(12):4281-3.
81. van der Zwaluw K, de Haan A, Pluister GN, Bootsma HJ, de Neeling AJ, Schouls LM. The carbapenem inactivation method (CIM), a simple and low-cost alternative for the Carba NP test to assess phenotypic carbapenemase activity in gram-negative rods. *PLoS ONE* 2015;10.
82. Tijet N, Patel SN, Melano RG. Detection of carbapenemase activity in *Enterobacteriaceae*: comparison of the carbapenem inactivation method versus the Carba NP test. *J Antimicrob Chemother* 2015;71(1):27-6.
83. Doyle D, Peirano G, Lascols C, Lloyd T, Church DL, Pitout JD. Laboratory detection of *Enterobacteriaceae* that produce carbapenemases. *J Clin Microbiol* 2012;50:3877-80.
84. García-Fernández A, Miriagou V, Papagiannitsis CC, Giordano A, Venditti M, Mancini C, et al. An ertapenem-resistant extended-spectrum-beta-lactamase-producing *Klebsiella pneumoniae* clone carries a novel OmpK36 porin variant. *Antimicrob Agents Chemother* 2010;54(10):4178-84.
85. Orsi GB, Bencardino A, Vena A, Carattoli A, Venditti C, Falcone M, et al. Patient risk factors for outer membrane permeability and KPC-producing carbapenem-resistant *Klebsiella pneumoniae* isolation: results of a double case-control study. *Infection* 2013;41(1):61-7.

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