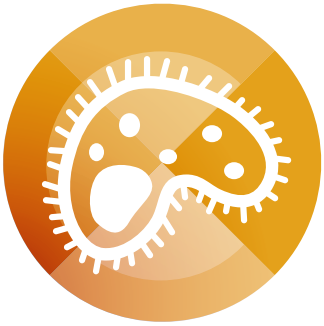
AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

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

A guide for acute care health service organisations

November 2021



Published by the Australian Commission on Safety and Quality in Health Care

Level 5, 255 Elizabeth Street, Sydney NSW 2000
Phone: (02) 9126 3600
Email: **mail@safetyandquality.gov.au**
Website: **www.safetyandquality.gov.au**

ISBN: 978-1-925948-69-1

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

Australian Commission on Safety and Quality in Health Care. Recommendations for the control of carbapenemase-producing *Enterobacterales* (CPE). A guide for acute care health service organisations. Sydney: ACSQHC, 2021.

Disclaimer

The content of this document is published in good faith by Australian Commission on Safety and Quality in Health Care (the Commission) for information purposes. The document is not intended to provide guidance on particular health care choices. You should contact your health care provider on particular health care choices.

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

Contents

Executive summary

Background

Carbapenemase-producing *Enterobacterales* (CPE) are an ongoing threat to public health. Outbreaks of CPE in Australia and overseas[1–9] have demonstrated the need for a timely, well-coordinated response that includes a multi-disciplinary, multi-level approach for containment and management. In some Australian states and territories, CPE colonisation or infection is formally notifiable to assist in outbreak detection and response.

The Australian Commission on Safety and Quality in Health Care (the Commission) produced the *Recommendations for the control of carbapenemase-producing* Enterobacteriaceae *(CPE). A guide for acute care health facilities* (CPE Guide) in 2017 to support health service organisations in responding to CPE and meeting the requirements of the National Safety and Quality Health Service (NSQHS) Standards (second edition).[10] The recommendations in the CPE Guide are grouped into five topic areas:

- Planning, prevention and preparation
- CPE screening and surveillance
- Strategies to reduce CPE transmission
- Outbreak management
- Laboratory screening and confirmation methods.

These recommendations were generated through a consultation process involving a clinical expert taskforce, Australian state and territory health departments, professional groups and healthcare organisations.

Since 2017, the prevalence of CPE has continued to increase across Australia.[11] As a result, the CPE Guide has been updated to ensure that it reflects contemporary clinical practice and scientific evidence, and is consistent with the latest revision of the ***Australian Guidelines for the Prevention and Control of Infection in Healthcare***.[12] The 2021 CPE Guide was developed following a review of current clinical context and guidance, and consultation involving clinical experts in infectious diseases, clinical microbiology, infection prevention and control, as well as representatives from Australian state and territory health departments.

Changes to the 2021 CPE Guide

The main changes included in the 2021 CPE Guide are:

- The inclusion of additional recommendations for
  - use of standard precautions at all times
  - appropriate waste disposal
  - documentation of CPE status for a CPE contact at transfer or discharge
- Modifications to the recommendations relating to
  - provision of patient information on CPE
  - processes for following up CPE contacts after discharge
  - timing and frequency of specimen collection from CPE contacts
  - transfer of patients to other health service organisations, or aged care facilities, after CPE exposure
  - inclusion of CPE in organisational outbreak planning
  - timely access to microbiology results in an outbreak
- Repeated prevalence surveys in high risk unit(s) are no longer recommended as a screening strategy for situations where local transmission is established or CPE is endemic. The use of other screening strategies is considered more appropriate for this situation.
- Screening requirements for CPE contacts has been clarified to specify that screening should include at least three suitable specimens taken at least 24 hours apart.
- Reference to recent data on CPE from the Australian Group on Antimicrobial Resistance (AGAR) and the National Alert System for Critical Antimicrobial Resistances (CARAlert)
- Additional emphasis on environmental cleaning, including reference to the *Australasian Health Facility Guidelines*[13]
- Clarification that the recommendations regarding laboratory screening and confirmation methods are a minimum requirement.

The following recommendations have been rescinded in the 2021 CPE Guide:

1. Following identification of a CPE-positive patient within a health service organisation, the microbiology laboratory servicing the hospital should be asked to review susceptibility testing results for the previous 12 months to identify any previously unrecognised cases of CPE – **meeting this recommendation is resource intensive for health service organisations and may be impractical to apply if historical testing results are not available**
2. All CPE contacts should be identified and screened – **this recommendation duplicates another recommendation that has been maintained in the Guide (see recommendation 2.5.1)**
3. 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 – **this recommendation duplicates another recommendation that has been maintained in the Guide (see section 2.8.1)**.

A number of the recommendations included across the various sections of the 2021 CPE Guide are linked, and are intended to reinforce each other.

2021 CPE Guide recommendations

1 Planning, prevention and preparation

Topic	Recommendation
1.1 Health service organisation governance and management	**1.1.1** Health service organisations should have a governance framework and plan for responding to organisms of significance, such as CPE. The framework should ensure implementation, monitoring and oversight of measures to establish and maintain CPE control. Health service organisation executives should be engaged in support of the plan. **1.1.2** Health service organisations should have systems in place for effective patient screening; including a system to allow screening and identification of patients at risk of CPE carriage on admission to the health service organisation. **1.1.3** Health service organisations should have systems in place 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** Health service organisations should develop a CPE outbreak action plan that identifies specific actions to be implemented in the event of an outbreak including allocation of staff and resources and transfer of patients. **1.1.5** Health service organisations should provide education to clinical and non-clinical staff on how to respond to cases of CPE. This includes provision of information on the nature of CPE and the requirements of standard and transmission-based precautions (contact precautions). **1.1.6** Health service organisations should have an alert system in place for patients colonised or infected with CPE to ensure that transmission-based precautions are used for subsequent admissions. **1.1.7** Microbiology laboratories should have processes in place to allow timely notification of CPE results to clinical and infection prevention and control staff.

Topic	Recommendation
1.2 Strategies to prevent transmission of infection	**1.2.1** Standard precautions should be applied at all times, as per the guidance provided in the current edition of the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12], and according to jurisdictional requirements. **1.2.2** Health service organisations should have an overarching infection prevention and control program, guided by the requirements of the NSQHS Standards[10], that incorporates hand hygiene as part of standard precautions. The organisation should implement a hand hygiene program that is consistent with the current *National Hand Hygiene Initiative*[14], and jurisdictional requirements. **1.2.3** Patients and visitors should be provided with information about the importance of hand hygiene, especially handwashing after toileting. Patients should also be provided with appropriate access to hand hygiene facilities. Particular consideration should be given to enabling patients with limited mobility, including those confined to bed, to perform hand hygiene. **1.2.4** Frequently touched surfaces in health service organisations 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.[12] **1.2.5** All reusable patient equipment should be cleaned and reprocessed between every patient use. **1.2.6** The disposal of faecal, antimicrobial and other clinical waste should be addressed as part of the health service organisation's waste management policy.
1.3 Environmental cleaning	**1.3.1** Health service organisations should implement policies and procedures for environmental cleaning, in accordance with the NSQHS Standards[10] and the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12] **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. A risk-based cleaning schedule and regular cleaning audits should be implemented.[12,15]
1.4 Reprocessing of endoscopes and bronchoscopes	**1.4.1** Health service organisations 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.[16–18] **1.4.2** Health service organisations should implement quality control measures to ensure that reprocessing is undertaken in line with the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12] This may involve regular microbiological testing of endoscopes, evaluation or biological marker testing, such as adenosine triphosphate (ATP) testing.[16,19–22]

Topic	Recommendation
1.5 Antimicrobial stewardship	**1.5.1** Health service organisations should implement antimicrobial stewardship (AMS) programs consistent with local needs, which are, at a minimum, consistent with the requirements of the NSQHS Standards.[10] **1.5.2** To minimise the impact of antimicrobial resistance in gram-negative bacteria, AMS programs should: ▪ Monitor the use of antimicrobials that are commonly used to treat gram-negative infections, including cephalosporins, fluoroquinolones, carbapenems, ß-lactam/ß-lactamase inhibitor combinations, and aminoglycosides ▪ Use audit systems to identify inappropriate empirical, directed or prophylactic use of all antimicrobials, especially cephalosporins, fluoroquinolones, carbapenems, ß-lactam/ß-lactamase inhibitor combinations, and aminoglycosides. Therapy requirements should be referenced against the most recent version of *Therapeutic Guidelines: Antibiotic*[23] ▪ Introduce strategies to promote appropriate antimicrobial use. For example, participation in the annual National Antimicrobial Prescribing Survey (NAPS) and the National Antimicrobial Utilisation Surveillance Program (NAUSP), or in the paediatric setting, through feedback from Antimicrobial Resistance and Prescribing in European Children (ARPEC) ▪ Monitor antimicrobial resistance at a facility level for key gram-negative bacteria that commonly cause infection, and use resistance data to inform local antibiograms.[24]

2 CPE screening and surveillance

Topic	Recommendation
2.1 Key risk factors for CPE	See page 23 for an overview of key risk factors for CPE.
2.2 CPE screening and tracking	**2.2.1** Every health service organisation, state or territory, should select an appropriate active CPE surveillance strategy, based on their current CPE epidemiology. 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 CPE colonisation or infection (e.g. recent admission to a hospital with a known CPE outbreak, or endemic transmission) should be actively screened for CPE colonisation or infection upon hospital admission. **2.2.3** Prior to screening for CPE, patients (and/or their carers) should be provided with information on the need for screening, and implications of a positive result. Patients (and/or their carers) who are colonised or infected with CPE should also be provided with information on strategies to help minimise the spread of CPE in the hospital and after discharge. **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 CARAlert have been from urine specimens. Specimens from open wounds, or aspirates from any tubes or drains should also be considered for screening. Perianal swabs are not generally recommended because they may not give accurate results, unless they are visibly stained by faecal material. However, they may be necessary in some situations, such as anal pathology or in some neutropenic patients. **2.2.5** Health service organisations should have a system in place for effective communication between the microbiology laboratory and the infection prevention and control teams to enable rapid notification and isolation of patients, as necessary.
2.3 Screening strategies	See page 25 for an overview of CPE screening strategies.
2.4 CPE infections in infants and children	See page 28 for guidance on CPE infections in infants and children.
2.5 Identification of CPE contacts	**2.5.1** All CPE contacts that are inpatients at the time of CPE identification should be identified and screened. **2.5.2** It is essential that health service organisations have a process in place to allow follow up of CPE contacts who have been discharged prior to screening.
2.6 Timing and frequency of CPE contact screening	**2.6.1** Screening of CPE contacts should include at least three suitable specimens taken at least 24 hours apart. Refer to relevant jurisdictional guidelines for specific screening requirements for CPE contacts. For patients who are hospitalised for extended periods or have had repeated exposure to a CPE-positive patient, advice on the frequency of screening should be sought from the infection prevention and control team.

Topic	Recommendation
2.7 Screening to determine clearance of CPE carriage	**2.7.1** Contact precautions should be used for patients with a history of CPE colonisation or infection for all subsequent hospital admissions, unless cleared. **2.7.2** The health service organisation may consider ceasing contact precautions for patients with no risk factors who are readmitted more than 12 months since a positive result of CPE colonisation. This requires three negative screening swabs taken at least 24 hours apart. **2.7.3** CPE clearance should follow review of relevant state and territory policies, and be issued in consultation with infection prevention and control professionals, clinical microbiologists and/or infectious disease physicians. **2.7.4** All patients who have been deemed cleared should be rescreened at every subsequent overnight admission to detect potential relapse in CPE colonisation. Day-only admissions do not require rescreening. **2.7.5** A patient colonised with CPE cannot be considered cleared within 12 months of a positive result.
2.8 Environmental screening in non-outbreak settings	**2.8.1** Environmental screening in non-outbreak settings is not recommended.

3 Strategies to reduce CPE transmission

Topic	Recommendation
3.1 Management of CPE-positive patients	**3.1.1** Standard and contact precautions should be used in the management of all patients with suspected or confirmed CPE. These patients should be placed in single rooms, with access to their own toilet facilities. If single rooms are not available for every confirmed 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 – patients with medical devices in situ ▪ CPE-positive patients should not be placed in the same room without prior approval by the infection prevention and control team ▪ Toilets should not be shared; if a CPE-positive patient cannot have their own toileting facilities, a bedpan or commode should be used. **3.1.2** Contact precautions should remain in place for the length of the patient's hospital stay. **3.1.3** Compliance of health service organisation staff with standard and contact precautions should be monitored, and feedback should be provided to staff in line with the NSQHS Standards.[10] **3.1.4** Environmental controls, including facility redesign where possible, should be used to minimise the risks associated with environmental reservoirs of CPE.

Topic	Recommendation
3.2 Management of CPE contacts	**3.2.1** All CPE contacts should be isolated and/or cohorted, and contact precautions should be initiated. **3.2.2** Rooms, baths/showers and frequently touched items should be cleaned and disinfected at least daily for the duration of the patient's admission, or until contact precautions are ceased. Toilets should be cleaned at least twice daily. **3.2.3** Dedicated equipment should be used for the care of CPE contacts. When it is not possible to dedicate equipment, reusable non-dedicated equipment should be cleaned and disinfected before it is used with another patient.[12,25] **3.2.4** CPE contacts should be managed in accordance with Figure 2 (page 38) until three negative screening swabs taken at least 24 hours apart are received, or as otherwise advised by the infection prevention and control team. **3.2.5** All CPE contacts to be transferred or discharged should have their CPE status recorded in the transfer or discharge summary.
3.3 Patient movement	**Transfer of patients within a facility** **3.3.1** Transfer of CPE-positive patients within a facility should be avoided. If a transfer does occur, CPE status should be communicated to the receiving ward/unit ideally prior to the transfer. **Transfer of patients between health service organisations** **3.3.2** CPE infection or colonisation should not preclude the transfer of a patient from one health service organisation to another, where required for optimal care. The transferring health service organisation should notify the receiving health service organisation before transfer of a CPE-positive patient to ensure appropriate bed management. **3.3.3** Patient transfer to another health service organisation or an aged care home should not be delayed by CPE status or the availability of screening results. Where screening results are available prior to transfer, these results should be provided to the transfer/transport agency and the receiving facility prior to the patient being transported and transferred. **3.3.4** An infection prevention and control management plan should be discussed by the infection prevention and control team at the transferring facility and staff at the receiving facility. **3.3.5** If a patient has been transferred prior to screening results being made available, the results should be provided to the receiving facility as soon as possible. Where a receiving facility has screened a CPE contact, the facility should inform the transferring facility of the results of the screening. **Discharge of patients** **3.3.6** CPE-positive patients and/or their carers should be provided with relevant information on how to manage CPE after discharge. **3.3.7** CPE status should be recorded in the discharge summary to the transferring facility and the general practitioner.

Topic	Recommendation
3.4 Cleaning and disinfection as part of contact precautions	**3.4.1** Rooms, baths/showers and frequently touched surfaces and items should be cleaned and disinfected at least daily for the duration of the patient's admission. Toilets should be cleaned at least twice daily. **3.4.2** Dedicated equipment should be used for the care of CPE-positive patients. The equipment should be cleaned and disinfected before it is used with another patient. **3.4.3** Following discharge or transfer of the patient, the room, toilet and all frequently touched surfaces and items should be cleaned and disinfected in accordance with the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12,15] **3.4.4** Health service organisations should monitor and audit cleaning according to relevant state or territory policies.

4 Outbreak management

Topic	Recommendation
4.1 Outbreak recognition	**4.1.1** The infection prevention and control team should assess the risk of potential outbreaks by regularly reviewing source surveillance data to identify an increase in the number of CPE cases in the health service organisation. **4.1.2** The infection prevention and control team, the health service organisation executive, and other relevant individuals and groups (clinicians, laboratory, state or territory health department, and state or territory public health unit) should be notified of any increase in the number of CPE cases. **4.1.3** An outbreak management team should be established, led by the health service organisation 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.[4,12,26] **4.1.4** As part of the health service organisation's outbreak action plan, a CPE action plan should be developed and implemented. This plan should include the use of standard and contact precautions for all suspected or confirmed cases of CPE and CPE contacts, monitoring staff compliance with contact precautions, and provision of relevant feedback.
4.2 Identification of CPE cases to confirm an outbreak	**4.2.1** The outbreak management team should develop a strategy to identify CPE cases within the health service organisation. This should include guidance on what constitutes a high-risk area during an outbreak and which patient groups are considered to be high risk. **4.2.2** Health service organisations should have systems in place to ensure that outbreak management teams have timely access to microbiology results.

Topic	Recommendation
4.3 Patient screening during an outbreak	**4.3.1** Health service organisations should consider additional screening for patients with a high risk of CPE acquisition and transmission. These include patients with: ▪ Faecal or urinary incontinence ▪ Indwelling urinary catheters ▪ Uncontained wound drainage or respiratory secretions ▪ Cognitive or intellectual impairment and have difficulty complying with infection prevention and control precautions. **4.3.2** Health service organisations should consider implementing additional screening practices to reduce the risk of transmission to susceptible patients receiving care in high-risk units including intensive care, haematology/oncology, burns, transplant, renal haemodialysis, aged care, and gastroenterology/gastrointestinal surgery units.
4.4 Timeframe for contact tracing during an outbreak	See page 45 for guidance on contact tracing during an outbreak of CPE.
4.5 Additional screening	See page 46 for guidance on staff and environmental screening during an outbreak of CPE.
4.6 Staff education	**4.6.1** Education and training updates should be provided to all staff, as relevant to their role, including medical, nursing, allied health 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 service organisation, hospital-wide education may be required.
4.7 Staff allocation	**4.7.1** The outbreak control team should consider allocating separate, dedicated staff to CPE-positive patients and contacts, taking into account patient acuity, staff knowledge, experience and availability; and resources.
4.8 Cleaning and disinfection during outbreaks	See page 47 for guidance on cleaning and disinfection during an outbreak of CPE.

5 Laboratory screening and confirmation methods

Topic	Recommendation
5.1 Laboratory testing for CPE	See page 49 for an overview of laboratory testing methods for CPE.
5.2 Recommended screening for asymptomatic carriage in high-risk patients	**5.2.1** Screening specimens should include rectal swabs or faeces. Urine from catheterised patients should also be included in screening. Specimens from open wounds, or aspirates from any tubes or drains should also be considered for screening. Perianal swabs are not generally recommended because they may not give accurate results. However, they may be necessary in some situations, such as anal pathology or in some neutropenic patients.
5.3 Detection of CPE with 'routine' susceptibility testing of clinical isolates	**5.3.1** As a minimum standard, laboratories should test meropenem susceptibility of all isolates of *Enterobacterales* with the extended-spectrum ß-lactamase (ESBL) phenotype or that are non-susceptible to gentamicin. **5.3.2** Suspected CPE (as defined by the breakpoints documented for the susceptibility testing system being used) should always undergo confirmatory testing.[27] **5.3.3** Laboratories using semi-automated methods for susceptibility testing should also undertake, or seek, molecular confirmation of all *Enterobacterales* where meropenem MIC is > 0.125 mg/L or > 0.25 mg/L depending on the species and method used, especially from high-risk patients or units.
5.4 CPE confirmation	**5.4.1** All suspected CPE isolates should undergo molecular screening for at least the suite of carbapenemase gene families that have so far been seen in *Enterobacterales* 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 carbapenem inactivation method (CIM)[28,29] or modified CIM (mCIM)[30,31], the Carba NP test[32] or enhanced Carba NP test[33], or the Carb Blue test[34], 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 Blue Kit [Rosco]). The mCIM/CIM methods 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.[35]
5.5 Reporting of suspected CPE	**5.5.1** For inpatients, all suspected CPE isolates should be notified to infection prevention and control staff and treating clinicians. Notification should not be delayed while awaiting confirmation in a confirming laboratory.

Role of state and territory health departments

To support health service organisations in responding to the threat of CPE, state and territory health departments should oversee a range of actions, including coordinating risk assessments, undertaking epidemiological and microbiological investigations, determining the requirement for control measures, and coordinating risk-communication activities.

Coordinated responses from state and territory health departments should take into account advice from experts in infectious diseases, microbiology, infection prevention and control, public health as well as epidemiologists, health service organisation executives and policy advisors. Communication expertise is also advisable to assist with the development of effective communication of relevant issues.

State and territory health departments should also ensure:

- CPE is addressed as part of jurisdictional outbreak management plans
- There is a nominated contact within the department responsible for receiving CPE notifications and communicating relevant information to designated branches and directorates (e.g. public health, communicable diseases and population health)
- Confirmatory results about CPE provided through the CARAlert system are regularly reviewed
- Communication is established with outbreak management teams in health service organisations, and guidance and appropriate expertise are provided to the health service(s) affected by the outbreak. 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
- Health service organisations affected by an outbreak of CPE have the necessary capability and capacity to manage the outbreak. This may include ensuring adequate supply of personal protective equipment or other equipment and consumables, and laboratory capacity for testing
- Specific additional CPE control measures are implemented if ongoing transmission is identified
- Responsibility for declaring de-escalation or stand-down of outbreak management.

A number of state, territory and local health networks have developed detailed policies and procedures on the prevention, detection and containment of CPE. The recommendations provided in this Guide should be read in conjunction with these resources.

The Commission will update the recommendations provided in this Guide, as appropriate, as new information about CPE and its epidemiology in Australia becomes available.

Introduction

The proliferation of carbapenemase-producing *Enterobacterales* (CPE) is a continuing issue for public health in Australia. Given the ongoing paucity of therapeutic options, early detection, adherence to infection prevention and control measures and antimicrobial stewardship (AMS) are vital to containing the spread of CPE within, and between, health service organisations. Local surveillance is required to determine appropriate prevention and containment approaches.[2]

Aim and scope of this guide

This guide aims to:

- Alert healthcare workers, health departments and health service organisation executives to the threat of CPE in Australia
- Provide information and resources for health service organisation executives, healthcare workers and consumers about CPE
- Provide recommendations on strategies to prevent, detect and contain CPE
- Provide recommendations on laboratory screening and confirmation methods for CPE.

This guide is specific to the prevention and management of CPE in acute health service organisations – that is, hospitals and day procedure units. It includes information on the prevention and management of CPE in specific areas and for patient populations, such as intensive care, neonatal and paediatric units. A number of elements of this guide may be applicable to, or adapted for, use in other settings.

Non-acute settings

Because of the complexities and individual requirements, this guide does not address identification and management strategies for CPE colonisation and infection for people receiving care outside of acute care settings, or for residents of aged care homes.

There are documented reports of multidrug-resistant gram-negative bacteria among residents of aged care homes in Australia and overseas.[1,36–38] These reports are of concern, and have implications for the potential amplification and transmission of CPE in the broader community, and during transfers between care settings.

Nature and importance of CPE

What are *Enterobacterales*?

Enterobacterales is the largest order of gram-negative bacteria causing human infection. This includes common pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae complex* and *Proteus mirabilis*. Taxonomic studies have narrowed the definition of the family *Enterobacteriaceae*.[39] Some previous members of this family are now included in other families within the order *Enterobacterales*, and this term is now used across the Commission's publications.

Enterobacterales colonise the normal human gastrointestinal tract, generally without causing disease. However, they can also cause common infections, including urinary tract, abdominal and bloodstream infections. *Enterobacterales* are important human pathogens and 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 *Enterobacterales* family.

What are CPE?

CPE are members of the *Enterobacterales* that are resistant to carbapenems through the expression of one or more degrading enzymes called carbapenemases. Carbapenems are a class of 'last resort' antimicrobials for treating serious infections. Carbapenemases are of great concern because the genes that encode them are frequently found on mobile genetic elements and are therefore readily transmissible to other *Enterobacterales* and other gram-negative bacteria affecting human health.

Gram-negative bacteria – including members of *Enterobacterales* – that are resistant to most, or even all, types of antimicrobials 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.

Why a change from carbapenem-resistant *Enterobacterales* (CRE) to CPE?

This guide refers to the control of CPE, and enhances the scope of the 2017 guide that referred to the control of carbapenem-resistant *Enterobacterales* (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 service organisations. This guide does not use 'carbapenem resistance', as defined by routine susceptibility testing, to define *Enterobacterales* 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 service organisations 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 *Enterobacterales* that are known to harbour a gene encoding a carbapenemase enzyme.

What are carbapenemases?

The most common way that *Enterobacterales* become resistant to carbapenems is by producing an enzyme called a carbapenemase. Such bacteria are referred to as carbapenemase-producing *Enterobacterales* (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 antimicrobials. Furthermore, bacteria that produce carbapenemase enzymes are almost always resistant to other important antimicrobial classes, such as other ß-lactams, ß-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%.[2]

There have been a number of CPE cases in Australia since 2012, most of which have been associated with international travel or outbreaks in health service organisations. A number of outbreaks in Australia have identified clusters of CPE-positive patients with clear relationships with individual health service organisations and more broadly across multiple health service organisations in Victoria[40], where transmission was primarily healthcare-associated.[2]

Since the establishment by the Commission of **the National Alert System for Critical Antimicrobial Resistances (CARAlert)** in 2016, approximately half of the critical antimicrobial resistances reported in the CARAlert system have been CPE. For the period 2016 to December 2020, CPE were the most common critical antimicrobial resistance reported.[11]

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 *Klebsiella pneumoniae* (*K. pneumoniae*) (a common CPE); AMS programs; and, a limited number of medical transfers from high-risk continents where carbapenemase-producing isolates are common.[12] This position creates an opportunity to prevent and contain CPE in Australia, and thereby limit their impact on human health. Data on CPE is also captured and analysed by the Australian Group on Antimicrobial Resistance (AGAR) as part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System[41] **and also is included in reports on data submitted to CARAlert**.[42] 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.

Structure of the guide

Section	Description
Section 1: Planning, prevention and preparation	This section outlines the recommended minimum requirements for planning and preparing for CPE by health service organisations where no cases of CPE have been identified. Strategies include governance and management, standard and transmission-based precautions, and AMS.
Section 2: CPE screening and surveillance	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 service organisations 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.
Section 3: Strategies to reduce CPE transmission	This section provides recommendations for health service organisations 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.
Section 4: Outbreak management	This section provides recommendations for the management of an outbreak of CPE, 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.
Section 5: Laboratory screening and confirmation methods	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 the process for reporting to the National Alert System for Critical Antimicrobial Resistances (CARAlert).

Section 1:

Planning, prevention and preparation

This section outlines the recommended minimum requirements for planning and preparing for carbapenemase-producing *Enterobacterales* (CPE) by all health service organisations. It focuses on key infection prevention and control strategies that are incorporated into infection prevention and 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.[43] In Australia, this model should operate under the auspice of a governance approach that is informed by the requirements of the National Safety and Quality Health Service (NSQHS) Clinical Governance Standard.[10]

An effective risk management system for CPE prevention and control involves the identification of hazards and assessment and control of risks so far as is reasonably practicable (what can be done and what is possible in the circumstances to ensure patient health and safety and continuity of health service delivery). This approach requires consultation, cooperation and coordination between the health service organisations, their staff and patients and visitors.

The hierarchy of controls is a model used in work health and safety risk management.[44] It is a step-by-step approach to eliminating or reducing risks that ranks risk controls from the highest level of protection and reliability through to the lowest and least reliable protection. The hierarchy should be used in conjunction with infection prevention and control systems to design CPE prevention and control programs. The levels of the hierarchy of controls, from most to least protective and reliable, are as follows:

- Risk elimination – e.g. using telemedicine or outpatient settings for patient encounters, where possible
- Risk reduction
  - substitution – e.g. switching from intravenous to oral administration of antimicrobial therapy, using narrow spectrum antimicrobials instead of broader spectrum antimicrobials
  - engineering controls – e.g. redesign of sinks and other plumbing, redesign of waste management and cleaning areas
- Administrative controls – e.g. reduce patient movement within the facility, establishment of local antimicrobial formularies, implementing local policies and procedures for environmental cleaning
- Personal protective equipment – e.g. using gloves, gowns, masks, protective eyewear.

Internationally, organisations familiar with the management of CPE emphasise the importance of rigorously applying infection prevention and control strategies to prevent and/or limit the transmission and impact of the bacteria.[45,46]

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 *Klebsiella 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.[4]

A number of studies have examined the prevalence of CPE in healthcare and aged care facilities in Australia and internationally.[6] These studies identified that CPE is not widespread and that screening efforts should be focused on high-risk patients and high-risk units within healthcare facilities.[6,47–51] Examples of units considered to be high-risk for CPE transmission include intensive care, haematology/oncology, severe burn, transplant, renal haemodialysis, aged care, rehabilitation and gastroenterology/gastrointestinal surgery units.

1.1 Health service organisation governance and management

Statement of intent

The focus of planning, prevention and preparation for the control of organisms of significance, such as CPE, requires an effective infection prevention and 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 health service organisation staff.

These recommendations are consistent with information on organisational governance in the *Australian Guidelines for the Prevention and Control of infection in Healthcare*[12] (Section 4.1 Management and clinical governance), and the NSQHS Standards.[10]

Recommendations

1.1.1 Health service organisations should have a governance framework and plan for responding to organisms of significance, such as CPE. The framework should ensure implementation, monitoring and oversight of measures to establish and maintain CPE control. Health service organisation executives should be engaged in support of the plan.

1.1.2 Health service organisations should have systems in place for effective patient screening; including a system to allow screening and identification of patients at risk of CPE carriage on admission to the health service organisation.

1.1.3 Health service organisations should have systems in place 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 Health service organisations should develop a CPE outbreak action plan that identifies specific actions to be implemented in the event of an outbreak including allocation of staff and resources and transfer of patients.

1.1.5 Health service organisations should provide education to clinical and non-clinical staff on how to respond to cases of CPE. This includes provision of information on the nature of CPE and the requirements of standard and transmission-based precautions (contact precautions).

1.1.6 Health service organisations should have an alert system in place for patients colonised or infected with CPE to ensure that transmission-based precautions are used for subsequent admissions.

1.1.7 Microbiology laboratories should have processes in place to allow timely notification of CPE results to clinical and infection prevention and control staff.

Rationale and commentary

- The NSQHS Standards[10] 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 (see recommendations 1.2.1 and 3.1.1). Staff should be provided with education on how to implement standard and transmission-based precautions, including education on the correct use of personal protective equipment (PPE).
- To minimise the risk of further transmission, **appropriate patient placement** should be implemented as part of transmission-based precautions. To minimise the risk of further transmission, patients who are known to have a CPE infection or are colonised with CPE, as well as those who are suspected to have a CPE infection and are awaiting screening results, should be cared for in single rooms with ensuite facilities, where available.
- All healthcare staff should have an understanding of the nature of multidrug-resistant organisms, such as CPE, in order to maximise compliance with standard and contact precautions and ensure appropriate management.
- Additional information on management and clinical governance is provided in the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12] (Section 4 Organisational Support).

1.2 Strategies to prevent transmission of infection

Statement of intent

The recommendations in this section are intended to assist health service organisations with preventing or reducing 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 should be used for all patients, regardless of their infection status. Transmission-based precautions should be used in addition to standard precautions when standard precautions are insufficient to interrupt the mode of transmission of certain pathogens.

These recommendations are consistent with information on standard precautions outlined in the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12] (Section 3.1 Standard precautions).

Recommendations

1.2.1 Standard precautions are applied at all times, as per the guidance provided in the current edition of the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12], and according to jurisdictional requirements.

1.2.2 Health service organisations should have an overarching infection prevention and control program, guided by the requirements of the NSQHS Standards[10], that incorporates hand hygiene as part of standard precautions. The organisation should implement a hand hygiene program that is consistent with the current National Hand Hygiene Initiative[14], and jurisdictional requirements.

1.2.3 Patients and visitors should be provided with information about the importance of hand hygiene, especially handwashing after toileting. Patients should also be provided with appropriate access to hand hygiene facilities. Particular consideration should be given to enabling patients with limited mobility, including those confined to bed, to perform hand hygiene.

1.2.4 Frequently touched surfaces in health service organisations 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.[12]

1.2.5 All reusable patient equipment should be cleaned and reprocessed between every patient use.[12]

1.2.6 The disposal of faecal, antimicrobial and other clinical waste should be addressed as part of the health service organisation's waste management policy.

Rationale and commentary

- Standard precautions are work practices that should be used at all times by all staff when providing patient care and working in healthcare settings. Standard precautions are the primary strategy for minimising the transmission of microorganisms.[12]
- Most of the individual elements of infection prevention and control strategies, such as hand hygiene[14,52], aseptic technique, and environmental cleaning and disinfection[53], can limit the impact of CPE by reducing transmission in healthcare settings.
- CPE is usually transmitted by indirect contact, either through contact with contaminated hands or via contact with contaminated environmental surfaces or shared equipment.[54]
- Pathogenic organisms have been detected on the hands of 40% of acute care patients 48 hours after admission.[54] A high level of compliance with hand hygiene, environmental cleaning and reprocessing of medical equipment is essential to prevent the transmission of CPE.
- Studies have demonstrated that the disposal of antimicrobial and other clinical waste, such as faecal matter, in sinks in patient rooms may contribute to the proliferation of environmental CPE reservoirs.[55,56]
- 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 provided in the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12] (Section 3.1 Standard precautions and Section 3.1.3 Reducing infections spread through the physical environment).

1.3 Environmental cleaning

Statement of intent

The recommendations in this section are intended to ensure that health service organisations maintain a clean environment, consistent with the NSQHS Standards[10], national guidelines and state and territory policies, irrespective of patients' infection status. Recommendations for cleaning and disinfection when patients are suspected of, or confirmed as, being infected or colonised with CPE are provided 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*.[12]

Recommendations

1.3.1 Health service organisations should implement policies and procedures for environmental cleaning, in accordance with the NSQHS Standards[10] and the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12]

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. A risk-based cleaning schedule and regular cleaning audits should be implemented.[12,15]

Rationale and commentary

- Environmental reservoirs are important risk factors for healthcare-associated transmission of gram-negative bacteria, such as CPE. Patients colonised or infected with CPE widely contaminate their immediate patient environment.[57]
- Environmental contamination may be exacerbated through inadequate environmental cleaning and disinfection of environmental surfaces and systems, including plumbing systems.
- Inadequate environmental cleaning may lead to ongoing bacterial growth and biofilm development that may extend beyond the initial location of contamination[58] (See Section 3.4).
- 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.
- Some studies have highlighted an environmental risk associated with poor placement and design of sinks and the use of drains for the disposal of contaminated body fluids.[55,58–60] The ***Australasian Health Facility Guidelines***[13] provide guidance on appropriate sink type and placement for different clinical environments. Once installed, regular cleaning and maintenance of sinks and associated plumbing should be performed to minimise the risk of transmission associated with these environmental reservoirs.[61,62]
- For additional information on environmental controls for infection prevention, refer to the ***Australasian Health Facility Guidelines***[13] and the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12] (Section 3.1.3 Routine management of the physical environment and Section 3.4.1 Core strategies for MRO [multi-resistant organism] prevention and control).
- For additional information on storage requirements for patient equipment, sterile stock and linen, refer to the relevant Australian Standard.

As part of standard precautions for every patient, routine environmental cleaning should include cleaning of the patient environment on a daily basis.

1.4 Reprocessing of endoscopes and bronchoscopes

Statement of intent

The recommendations in this section are intended to ensure that health service organisations have processes 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 NSQHS Standards[10], *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12], *GESA Infection Control in Endoscopy Consensus Statements on Carbapenemase-Producing Enterobacteriaceae*[63] and *GESA GENCA Infection Control in Endoscopy*.[19]

Recommendations

1.4.1 Health service organisations 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.[16–18]

1.4.2 Health services should implement quality control measures to ensure that reprocessing is undertaken in line with the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12] This may involve regular microbiological testing of endoscopes, evaluation or biological marker testing, such as adenosine triphosphate (ATP) testing.[16,19–22]

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.
- All endoscopic instruments present a risk of CPE – transmission of CPE has been predominantly associated with instruments with complex tips (duodenoscopes and linear echoendoscopes).[63]
- There have been a number of documented outbreaks of CPE linked to endoscopic retrograde cholangiopancreatography.[16–18]
- Automated flexible endoscope reprocessors approved by the Therapeutic Goods Administration should be used for reprocessing in accordance with the manufacturer's instructions.[63] Protocols should be in place for regular cleaning, maintenance and microbiological monitoring of the machines.
- Health service organisations should conduct regular quality reviews of reprocessing procedures, particularly for difficult-to-clean parts of endoscopes.
- Quality checking for cleaning may take the form of regular microbiological testing, as recommended by the Gastroenterological Society of Australia (GESA), process tracking, or newer methods such as ATP monitoring pre- and post-reprocessing.[19–22]
- For additional advice regarding endoscopes, refer to the *GESA Infection Control in Endoscopy Consensus Statements on Carbapenemase-Producing Enterobacteriaceae*.[63]

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

1.5 Antimicrobial stewardship

Statement of intent

The recommendations in this section are intended to ensure that health service organisations have measures in place to support appropriate prescribing and use of antimicrobials, as part of a broader plan to reduce the development of resistant bacteria, and to ensure that antimicrobial use and resistance within the health service organisation are monitored.

These recommendations are consistent with information on antimicrobial stewardship (AMS) outlined in *Antimicrobial Stewardship in Australian Health Care*[64], the NSQHS Standards[10] and the Antimicrobial Stewardship Clinical Care Standard[65], which requires all health service organisations to have an appropriate AMS program in place.

Recommendations

1.5.1 Health service organisations should implement antimicrobial stewardship (AMS) programs consistent with local needs, which are, at a minimum, consistent with the requirements of the NSQHS Standards.[10]

1.5.2 To minimise the impact of antimicrobial resistance in gram-negative bacteria, AMS programs should:

- Monitor the use of antimicrobials that are commonly used to treat gram-negative infections, including cephalosporins, fluoroquinolones, carbapenems, ß-lactam/ß-lactamase inhibitor combinations, and aminoglycosides
- Use audit systems to identify inappropriate empirical, directed or prophylactic use of all antimicrobials, especially cephalosporins, fluoroquinolones, carbapenems, ß-lactam/ß-lactamase inhibitor combinations, and aminoglycosides. Therapy requirements should be referenced against the most recent version of *Therapeutic Guidelines: Antibiotic*[23]
- Introduce strategies to promote appropriate antimicrobial use. For example, participation in the annual National Antimicrobial Prescribing Survey (NAPS) and the National Antimicrobial Utilisation Surveillance Program (NAUSP), or in the paediatric setting, through feedback from Antimicrobial Resistance and Prescribing in European Children (ARPEC)
- Monitor antimicrobial resistance at a facility level for key gram-negative bacteria that commonly cause infection, and use resistance data to inform local antibiograms.

Rationale and commentary

- A number of studies have identified that previous antimicrobial use is a significant risk factor for colonisation or infection with multidrug-resistant bacteria, including CPE. A number of classes of antimicrobials have been associated with CPE colonisation or infection including cephalosporins, fluoroquinolones and carbapenems. Control strategies should include AMS measures that aim to minimise overall antimicrobial use and ensure that key antimicrobials such as cephalosporins, fluoroquinolones and carbapenems are only used when necessary.[49,51,66,67]
- Carbapenems are a group of antimicrobials with a broad-spectrum of activity. They belong to the class of antimicrobials known as ß-lactams, along with penicillins, cephalosporins and monobactams. Carbapenems are of vital importance because they are considered as last-line antimicrobials, used for the treatment of serious infections that do not respond to other antimicrobials. Limited options are available for the treatment of infections caused by bacteria that are resistant to carbapenems, as these bacteria are usually resistant to multiple antimicrobial classes.
- Reduction in hospital or community antimicrobial use may lead to decreased bacterial resistance rates, even within communities that have high rates of colonisation with multidrug-resistant bacteria.[68]
- Local prophylaxis, empirical and treatment guidelines should address strategies that reduce the use of antimicrobial classes that are more likely to contribute to the emergence and spread of multidrug-resistant pathogens. For multidrug-resistant gram-negative bacteria such as CPE, reports strongly implicate fluoroquinolones, extended-spectrum cephalosporins and carbapenems.[51,68–70]
- AMS programs aim to reduce overall antimicrobial exposure and target treatment more effectively, through mechanisms such as restricting access to broad-spectrum antimicrobials, providing clear direction on indications for use of approved antimicrobials and reducing the duration of prophylaxis/treatment wherever possible. 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.[71]

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.[72]

Section 2:

CPE screening and surveillance

This section outlines the recommended minimum requirements for surveillance in health service organisations to ensure that patients with carbapenemase-producing *Enterobacterales* (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 *Enterobacterales* increase the risk of morbidity and mortality. Patients with significant comorbidities have a greater risk of CPE infection.[46,48,53,67,73–76] Studies have demonstrated that CPE are more likely to affect patients who:

- Have been hospitalised for a long time[77–79]
- Have been hospitalised or have undergone surgery overseas[79–81]
- Have been recently admitted to a hospital with a known CPE outbreak or endemic transmission[79]
- Have had multiple or recent exposures to different antimicrobial agents, especially cephalosporins, fluoroquinolones and carbapenems[46,49,53,77,82–84]
- Have received chemotherapy within the previous 12 months[74]
- Have diabetes mellitus[46,53]
- Are using mechanical ventilation[77,85]
- Are admitted to the intensive care unit[46,82–84]
- Have an indwelling medical device (central venous catheter, urinary catheter or biliary catheter)[46]
- Are recipients of an organ or stem cell transplant.[67,75–77]

2.2 CPE screening and tracking

Statement of intent

The recommendations in this section are intended to ensure that patients with CPE infection or colonisation in a health service organisation are promptly identified to allow implementation of measures to prevent onwards transmission to other patients. The recommendations also aim to support health service organisations in maintaining an accurate picture of the current epidemiology of CPE in their institution and informing appropriate prevention and control policies.

Recommendations

2.2.1 Every health service organisation, state or territory, should select an appropriate active CPE surveillance strategy, based on their current CPE epidemiology. 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 CPE colonisation or infection (e.g. recent admission to a hospital with a known CPE outbreak or endemic transmission) should be actively screened for CPE colonisation or infection upon hospital admission.

2.2.3 Prior to screening for CPE, patients (and/or their carers) should be provided with information on the need for screening, and implications of a positive result. Patients (and/or their carers) who are colonised or infected with CPE should also be provided with information on strategies to help minimise the spread of CPE in the hospital and after discharge.

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 the National Alert System for Critical Antimicrobial Resistances (CARAlert) have been from urine specimens. Specimens from open wounds, or aspirates from any tubes or drains should also be considered for screening. Perianal swabs are not generally recommended because they may not give accurate results, unless they are visibly stained by faecal material. However, they may be necessary in some situations, such as anal pathology or in some neutropenic patients.

2.2.5 Health service organisations should have a system in place for effective communication between the microbiology laboratory and the infection prevention and control teams to enable rapid notification and isolation of patients, as necessary.

Rationale and commentary

- Identification of patients colonised with CPE on entry to the health service organisation 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.[86] Cross-border transfer of patients from countries with high rates of CPE has resulted in the introduction of CPE into countries that had previously detected few or no CPE isolates.
- A number of risk factors for infection or colonisation with CPE have been identified. 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 service organisation with endemic CPE to another health service organisation in the same country, has also been reported to result in the introduction of CPE in the receiving health service organisation.[66]
- A number of studies have reported on the incidence and prevalence of CPE in hospitals to inform the development of a risk assessment for CPE screening. These studies support the use of focussed screening strategies that target high-risk patients and units rather than hospital-wide screening programs.[6,48,74,87]

Patients who are to be screened for CPE should be provided with information on the need for screening, and implications of a positive result.

2.3 Screening strategy options

Health service organisations should develop a screening strategy to identify patients with CPE, based on current epidemiology.[6,48,74] Many patients with CPE are colonised and are asymptomatic[48]; therefore, the screening strategy cannot solely rely on the collection of clinical specimens from patients who are clinically symptomatic.

Health service organisations may implement different screening strategies, depending on the burden of CPE and level of local risk. Screening strategies should also be in line with jurisdictional screening policies. Table 1 provides a summary of screening strategies according to CPE burden, and Table 2 outlines the rationale for active screening strategies. Strategies are categorised according to settings where:

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

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

Screening strategy	CPE burden		
	No cases	Sporadic cases	Local transmission established or CPE endemic
Admission **from** high-risk settings*	Y	Y	Y
Admission **to** high-risk units†	Y	Y	Y
Single or periodic point prevalence surveys	C	C	Y
Screening of contacts‡ of confirmed cases	n/a	Y	Y
Opportunistic screening (e.g. all faecal specimens)	C	C	Y

Y = Screen. C = Consult infection prevention and control team. n/a = Not applicable.

Table 2: Description and rationale for active screening strategies

Screening strategy	CPE burden	Screening required?	Rationale
Admission from high-risk settings*	No cases	Y	▪ Establish processes to identify risk groups (e.g. a questionnaire to obtain information about recent medical care and treatment overseas). This strategy is only feasible if risk groups are easily identified by direct questioning. ▪ A high-risk group might include readmissions from particular units. ▪ 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 – e.g. patients who have been recently admitted to or directly transferred from an overseas hospital, or an Australian hospital with a known outbreak of CPE. Overseas travel (without contact with a health service organisation) appears to be a risk factor for colonisation with some resistant gram-negative bacteria, but less commonly with CPE.[88]
	Sporadic cases	Y	
	Transmission established or endemic	Y	

Y = Screen. C = Consult infection prevention and control team. n/a = Not applicable.

Note: Content is based on clinical experience and expert opinion by members of the Commission's 2017 clinical expert taskforce.

* High-risk settings are settings where there is an elevated risk of exposure and transmission of CPE due to local epidemiology and individual risk factors.

† High-risk units are units where there is an elevated risk that transmission and subsequent CPE infection would cause severe clinical disease in the patient cohort receiving care in that unit.

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

Screening strategy	CPE burden	Screening required?	Rationale
Admission to high-risk units*	No cases	Y	▪ High-risk units include intensive care units, oncology units and gastroenterology/gastrointestinal surgery units. ▪ Identify patients with CPE in areas where there are vulnerable patients. This strategy is most useful when the major source of CPE is from patients who are admitted to the health service organisation (i.e. there is little known transmission within the high-risk unit). ▪ 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 with CPE outside the defined high-risk areas may be missed.
	Sporadic cases	Y	
	Transmission established or endemic	Y	
Single or periodic point prevalence surveys	No cases	C	▪ Perform single or periodic (e.g. annual) point prevalence surveys of all patients and/or high-risk areas to define the current epidemiology of CPE and detect changes in the burden. This may define the focus of future surveillance – e.g. whether to identify patients with CPE before or after admission.
	Sporadic cases	C	
	Transmission established or endemic	Y	
Screening of contacts† of confirmed cases	No cases	n/a	▪ Screen patients who have been in the same room, unit or area as CPE-positive patients for a period of 24 hours or longer. ▪ This strategy is not likely to be sensitive, because the length of the infectious period prior to the identification of the index patient is not generally clear. The frequency of patient movement (to other rooms or units, or outside the hospital) may also make patient follow-up difficult.
	Sporadic cases	Y	
	Transmission established or endemic	Y	
Opportunistic screening (e.g. all faecal specimens)	No cases	C	▪ In health service organisations with limited resources for active patient screening, opportunistic screening of specimens received by the laboratory should be considered. ▪ This might include screening of all faecal samples received, or faecal samples received from specific units or from all inpatients. ▪ 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 of the health service organisation (e.g. aged care units, where the frequency of clinical specimens may be lower). It may also be resource intensive for the laboratory and could lead to overtreatment of patients colonised with CPE if mistaken for infection. ▪ Other specimens and techniques may also be suitable for CPE detection – e.g. susceptibility testing on urine mixed growth.
	Sporadic cases	C	
	Transmission established or endemic	Y	

Y = Screen. C = Consult infection prevention and control team. n/a = Not applicable.

Note: Content is based on clinical experience and expert opinion by members of the Commission's 2017 clinical expert taskforce.

* High-risk units are units where there is an elevated risk that transmission and subsequent CPE infection would cause severe clinical disease in the patient cohort receiving care in that unit.

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

2.4 CPE infections in infants and children

Despite increasing CPE prevalence, infection in infants and children remains rare. Evidence is limited, however one case series report has indicated that while mortality is lower in children with CPE compared to adult cases, there are fewer effective therapies available for children.[89]

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

- Intensive care admission
- Immunosuppression
- Prematurity
- Presence of indwelling devices
- History of surgery
- Prior antimicrobial use.[90]

Screening in neonatal ICU

Neonatal patients born to mothers who are known to be colonised or infected with CPE, or who have a high risk of CPE carriage, should be considered as close contacts for screening purposes. These neonatal patients should always be screened prior to admission to a neonatal ICU as this is a high-risk setting for CPE transmission. 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 National Alert System for Critical Antimicrobial Resistances have come from urine specimens.[11] Perianal swabs are not recommended. Consideration could also be given to screening oral/nasal/pharyngeal swabs, skin/ear swabs and gastric aspirates.[90] Refer to Table 3 for suggested screening strategies during outbreaks in neonatal areas of the health service organisation.

2.5 Identification of CPE contacts

Statement of intent

The recommendations in this section are intended to assist health service organisations with identifying and screening 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 a confirmed CPE-positive patient for more than 24 hours.

Additional patient groups to be considered in a CPE screening strategy

A health service organisation may consider screening patients who have had less than 24 hours of contact with a confirmed case of CPE, but who may have an increased risk of CPE transmission or acquisition. These may include: patients with intellectual or cognitive impairment and who have difficulty complying with infection prevention and control precautions; patients who have participated in group activities; patients with 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.

2.5.2 It is essential that health service organisations have a process in place to allow follow up of CPE contacts who have been discharged prior to screening.

Rationale and commentary

- In the absence of ongoing exposure to a CPE-positive patient, a CPE contact is considered cleared after three negative swabs, taken at least 24 hours apart, have been obtained.
- Some jurisdictions have specific guidelines regarding the screening of CPE contacts. This guidance may include the number of screening swabs required, or the timeframe for screening. Refer to specific jurisdictional guidelines for specific CPE-contact screening requirements.
- Patients who have shared a room, bathroom or toilet facilities with a CPE-positive patient should be screened to determine CPE status. A key consideration in the identification of CPE contacts is 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 contacts 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 contacts who have had the most contact with the CPE-positive patient, followed by further screening if colonisation is detected in these contacts. If a high proportion of contacts have already been discharged, these contacts may need to be screened on readmission.
- Although transmission to household contacts and carriage of CPE in healthcare workers has been confirmed, studies have not examined whether screening of these groups provides additional benefit in controlling the spread of CPE.[91,92]

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*	Y	N	N	C	Y	Y	Mother and child
Single or periodic point prevalence surveys	Y	N	N	N	C	C	N
Repeated prevalence surveys	N	N	N	N	N	N	N
Screening of contacts† of confirmed cases	n/a	n/a	n/a	n/a	Y	Y	Child to be screened if mother is a confirmed case
Opportunistic screening (e.g. all faecal specimens)	C	C	N	C	N	C	N

Y = Screen. C = Consult infection prevention and control team. N = Do not screen. n/a = Not applicable.

* High-risk settings are settings where there is an elevated risk of exposure and transmission of CPE due to local epidemiology and individual risk factors.

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

2.6 Timing and frequency of screening of contacts

Statement of intent

The recommendations in this section are intended to ensure that health service organisations develop a screening strategy that considers patient and environmental factors that may affect screening sensitivity.

Recommendations

2.6.1 Screening for CPE contacts should include at least three suitable specimens taken at least 24 hours apart. Refer to relevant jurisdictional guidelines for specific screening requirements for CPE contacts.

For patients who are hospitalised for extended periods or have repeated exposure to a CPE-positive patient, advice on the frequency of screening should be sought from the infection prevention and control team.

Rationale and commentary

- In non-outbreak situations, where there are no CPE-positive patients (or 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. This decision should be made in accordance with relevant jurisdictional policies and in consultation with the infection prevention and control team.
- The sensitivity of screening is uncertain, and is likely to vary with specimen quality and the density of CPE carriage.[93] Although some studies have identified 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.[94]
- Studies of patients known to be colonised with CPE have identified that 15–25% of patients with two or more negative screening swabs, subsequently returned a positive screening swab, suggesting that the sensitivity of screening could be as low as 50%.[95] 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 recommendations in this section are intended to provide guidance for health service organisations 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 Contact precautions should be used for patients with a history of CPE colonisation or infection for all subsequent hospital admissions, unless cleared.

2.7.2 The health service organisation may consider ceasing contact precautions for patients with no risk factors who are readmitted more than 12 months since a positive result of CPE colonisation. This requires three negative screening swabs taken at least 24 hours apart.

2.7.3 CPE clearance should follow review of relevant state and territory policies, and be issued in consultation with infection prevention and control professionals, clinical microbiologists and/or infectious disease physicians.

2.7.4 All patients who have been deemed cleared should be rescreened at every subsequent overnight admission to detect potential relapse in CPE colonisation. Day-only admissions do not require rescreening.

2.7.5 A patient colonised with CPE cannot be considered cleared within 12 months of a positive result.

Rationale and commentary

- In the absence of high-quality evidence to show that clearance of CPE colonisation will occur, a cautious approach to determining clearance is required. In a study of returned travellers, 39% of patients colonised with CPE still had detectable colonisation after 12 months.[96] Some bacterial clones appear to be better adapted to prolonged colonisation than others. Antimicrobial use, recurrent admissions to health service organisations and the presence of foreign bodies have also been associated with prolonged duration of colonisation.[97]
- The sustainability of instituting contact precautions with increasing case numbers, and the potential impact on patient care and patient flow[98] should be considered as part of planning and preparation strategies.
- Some health service organisations may choose to 'clear' a low-risk patient with previous CPE infection or colonisation, by screening the patient on readmission.
- Screening to determine clearance should be based on three negative screening swabs, taken at least 24 hours apart.
- Patients with a history of CPE should be monitored for recurrence. CPE recurrence has been identified in patients with CPE-negative results following the administration of antimicrobials.[99]
- Currently, there is insufficient evidence to support attempts to decolonise CPE-positive patients. As the bacteria generally colonise the gut, decolonisation through the use of non-absorbable antimicrobials is not generally advised.

2.8 Environmental screening in a non-outbreak setting

Statement of intent

This section aims to provide guidance to health service organisations that are considering environmental screening in non-outbreak situations.

Recommendation

2.8.1 Environmental screening in non-outbreak settings is not recommended.

Rationale and commentary

- Environmental screening in non-outbreak situations is not recommended because there is no standardised method to collect specimens. Environmental screening also requires considerable resources and provides results that can be difficult to interpret.
- 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 prevention and control team. See Section 4.5 for information on environmental screening in outbreak situations.

Section 3:

Strategies to reduce CPE transmission

This section provides recommendations to support health service organisations in managing a small number of carbapenemase-producing *Enterobacterales* (CPE) cases, that are not epidemiologically linked, or where there is limited local transmission. It includes recommendations on the management of CPE-positive patients, CPE contacts, patient movement, cleaning and disinfection, and environmental controls.

3.1 Management of CPE-positive patients

Statement of intent

The recommendations in this section are intended to support health service organisations with implementing strategies to reduce CPE transmission to patients and healthcare workers.

Section 1 provides health service organisations with key strategies that should be part of the facility's infection prevention and control program to minimise risk and respond to organisms of significance, such as CPE. This section builds upon Section 1 by utilising the hierarchy of controls to reduce and minimise infection risk using specific strategies that have been identified to assist health service organisations in responding to local CPE transmission within a facility.

These recommendations are consistent with the information on contact precautions in the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12]

Recommendations

3.1.1 Standard and contact precautions should be used in the management of all patients with suspected or confirmed CPE. These patients should be placed in single rooms, with access to their own toilet facilities. If single rooms are not available for every confirmed 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
  - patients with medical devices in situ
- CPE-positive patients should not be placed in the same room without prior approval by the infection prevention and control team
- Toilets should not be shared; if a CPE-positive patient cannot have their own toileting facilities, a bedpan or commode should be used.

3.1.2 Contact precautions should remain in place for the length of the patient's hospital stay.

3.1.3 Compliance of health service organisation staff with standard and contact precautions should be monitored, and feedback should be provided to staff in line with the National Safety and Quality Health Service (NSQHS) Standards.[10]

3.1.4 Environmental controls, including facility redesign where possible, should be used to minimise the risks associated with environmental reservoirs of CPE.

Rationale and commentary

- A number of strategies have been demonstrated to reduce transmission of multidrug-resistant gram-negative organisms (Figure 1). These include the use of standard and transmission-based precautions (including hand hygiene, appropriate patient placement 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 address the potential psychological effects of isolation.
- The environment may act as a reservoir for CPE where appropriate cleaning has not occurred. There are reports of CPE acquisition linked to the environment.[6,8,9,58,60,100,101] (See Section 1.3 Environmental Cleaning). The design of plumbing and sink facilities is also an important consideration in the management of environmental reservoirs of CPE.
- Information on contact precautions and patient placement is provided in the Australian Guidelines for the Prevention and Control of Infection in Healthcare[12] (Section 3.2.2 Contact precautions and Section 3.4.1 Core strategies for MRO [multi-resistant organism] prevention and control).

Figure 1: Management of patient with CPE

CPE-positive result from laboratory

Infection control notified of CPE-positive laboratory result

Infection control

- Infection control team notifies ward/unit and clinical team
- Infection control team identifies all patient contacts
- Alert placed in patient's medical record
- Identify most likely place of CPE acquisition
  - previous exposure to a CPE patient
  - accommodated in a room previously occupied by a patient with CPE
  - transferred from another health facility.

Ward/unit

- Isolate patient in single room (see recommendation 3.1.1 for guidance on prioritisation)
- Use contact precautions
- Inform patient and provide with information on CPE
- Room and equipment cleaning and disinfection (see Section 3.4)
- Restrict non-essential patient movement within the facility (see Section 3.3)
- If patient has been discharged or transferred to another facility, ensure the receiving facility or general practitioner is notified.

Note: Some of these actions may occur concurrently.

3.2 Management of CPE contacts

Statement of intent

The recommendations in this section are intended to assist health service organisations with responding to local CPE transmission. 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 isolated and/or cohorted, and contact precautions should be initiated.

3.2.2 Rooms, baths/showers and frequently touched items should be cleaned and disinfected at least daily for the duration of the patient's admission, or until contact precautions are ceased. Toilets should be cleaned at least twice daily.[12,102,103]

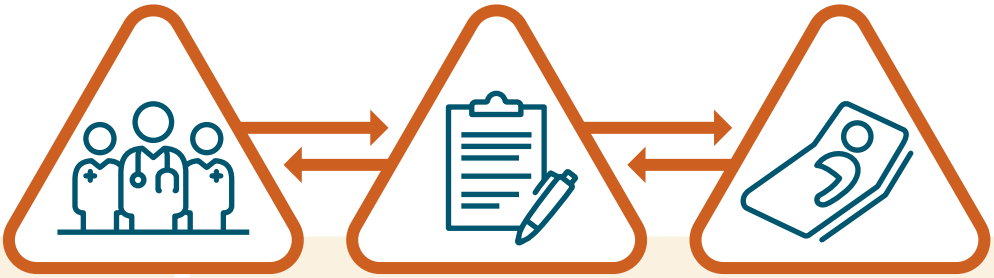
3.2.3 Dedicated equipment should be used for the care of CPE contacts. When it is not possible to dedicate equipment, reusable non-dedicated equipment should be cleaned and disinfected before it is used with another patient.[12,25]

3.2.4 CPE contacts should be managed in accordance with Figure 2 until three negative screening swabs taken at least 24 hours apart are received, or as otherwise advised by the infection prevention and control team.

3.2.5 All CPE contacts to be transferred or discharged should have their CPE status recorded in the transfer or discharge summary.

Figure 2: Management of the contacts of a patient with CPE

Following identification of CPE-positive patient



Infection control

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

Ward/unit

Patient-level precautions:

- Isolate or cohort contacts (see Section 3.2)
- Use contact precautions
- Inform patient and provide with information on CPE
- Undertake screening of patient contacts (see Section 2.5)
- Room and equipment cleaning and disinfection (see Section 3.4).

Ward-level precaution:

- Restrict non-essential patient movement within the facility (see Section 3.3).

Out-of-hospital precaution:

- If patient has been discharged or transferred to another facility, ensure the receiving facility or general practitioner is notified.

Screening precautions:

- Positive CPE laboratory result — follow Figure 1
- Negative CPE laboratory result — screen until three negative screening swabs, taken at least 24 hours apart, are received, or as otherwise advised by the infection prevention and control team.

3.3 Patient movement

Statement of intent

The recommendations in this section are intended to assist health service organisations with responding to local CPE transmission and ensuring that a patient's CPE status is communicated before transfer between or within health services.

These recommendations are consistent with the information on patient management in the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12]

Recommendations

Transfer of patients within a facility

3.3.1 Transfer of CPE-positive patients within a facility should be avoided. If a transfer does occur, CPE status should be communicated to the receiving ward/unit ideally prior to the transfer.

Transfer of patients between health service organisations

3.3.2 CPE infection or colonisation should not preclude the transfer of a patient from one health service organisation to another, where required for optimal care. The transferring health service organisation should notify the receiving health service organisation before transfer of a CPE-positive patient to ensure appropriate bed management.

3.3.3 Patient transfer to another health service organisation or an aged care home should not be delayed by CPE status or the availability of screening results. Where screening results are available prior to transfer, these results should be provided to the transfer/transport agency and the receiving facility prior to the patient being transported and transferred.

3.3.4 An infection prevention and control management plan should be discussed by the infection prevention and control team at the transferring facility and staff at the receiving facility.

3.3.5 If a patient has been transferred prior to screening results being made available, the results should be provided to the receiving facility as soon as possible. Where a receiving facility has screened a CPE contact, the facility should inform the transferring facility of the results of the screening.

Discharge of patients

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

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

Rationale and commentary

- Information on a patient's CPE status should be communicated verbally and in written form within and/or between health service organisations and the patient's health practitioners.[74] Inclusion of the dates and results of any relevant clinical and/or surveillance cultures should also be considered. An assessment of the risk of secondary transmission should be undertaken by the receiving health service organisation and should take into account risk factors 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 health services, refer to the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[1] (Section 3.2.2 How should contact precautions be applied?).

3.4 Cleaning and disinfection as part of contact precautions

Statement of intent

The recommendations in this section are intended to provide guidance on the importance of health service organisations maintaining a clean and hygienic environment, to minimise the risk of CPE transmission to patients and staff. These recommendations are consistent with the information on cleaning and disinfection in the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12] and NSQHS Standards.[10] For guidance on routine environmental cleaning, see Section 1.3.

Cleaning and disinfection of environmental surfaces and equipment are important risk management strategies used as part of standard and contact precautions for CPE-positive patients. Disinfection can be achieved using thermal or chemical agents following cleaning to destroy any remaining infectious agents.

What is the difference between cleaning and disinfection?

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

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

Recommendations

3.4.1 Rooms, baths/showers and frequently touched surfaces and items should be cleaned and disinfected at least daily for the duration of the patient's admission. Toilets should be cleaned at least twice daily.[12,102,103]

3.4.2 Dedicated equipment should be used for the care of CPE-positive patients. The equipment should be cleaned and disinfected before it is used with another patient.[12,25]

3.4.3 Following discharge or transfer of the patient, the room, toilet and all frequently touched surfaces and items should be cleaned and disinfected in accordance with the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*.[12,15]

3.4.4 Health service organisations should monitor and audit cleaning according to relevant state or territory policies.[26]

Rationale and commentary

- A relationship exists between the environment and transmission of multidrug-resistant gram-negative bacteria[58–60,100,104] (see Section 1.3).
- Patients colonised or infected with CPE widely contaminate their immediate environment.[54,57,58,100,105]
- Strategies to reduce environmental reservoirs should include consideration of the potential contamination of items or equipment as a result of their storage (e.g. storage of items near sinks).[58–60]
- For additional information, refer to the *Australian Guidelines for the Prevention and Control of Infection in Healthcare*[12] (Section 3.1.3 Routine management of the physical environment, Section 3.2.2 How should contact precautions be applied? and Section 3.2 Core strategies for MRO [multi-resistant organism] prevention and control).
- The Commission has also developed a number of **resources** to support effective environmental cleaning in health service organisations.[15]

Section 4:

Outbreak management

This section provides recommendations for the management of an outbreak of carabapenemase-producing *Enterobacterales* (CPE), 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.

4.1 Outbreak recognition

Statement of intent

The recommendations in this section are intended to assist health service organisations with identifying and managing a CPE outbreak where widespread transmission is occurring and cases may be epidemiologically linked. Recommendations relate to the 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.[106] In the context of CPE, this means two or more cases which can be linked epidemiologically and which are the same species and carbapenemase gene as determined by polymerase chain reaction and/or whole genome sequencing.

However, due to high incidence of asymptomatic transmission and the ability for carbapenemase genes to move between bacteria of different species on mobile genetic elements such as plasmids, the following should be considered as a potential CPE outbreak:

- **two or more cases without a direct epidemiological link, but where whole genome sequencing analysis is indicative of recent transmission; or**
- **two or more cases which can be linked epidemiologically and which are the same carbapenemase gene, in different species.**

Recommendations

4.1.1 The infection prevention and control team should assess the risk of potential outbreaks by regularly reviewing source surveillance data to identify an increase in the number of CPE cases in the health service organisation.

4.1.2 The infection prevention and control team, the health service organisation executive, and other relevant individuals and groups (clinicians, laboratory, state or territory health department, and state or territory public health unit) should be notified of any increase in the number of CPE cases.

4.1.3 An outbreak management team should be established, led by the health service organisation 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.[4,12,26]

4.1.4 As part of the health service organisation's outbreak action plan, a CPE action plan should be developed and implemented. This plan should include the use of standard and contact precautions for all suspected or confirmed cases of CPE and CPE contacts, monitoring staff compliance with contact precautions, and provision of relevant feedback.

Rationale and commentary

- Healthcare-associated outbreaks of multidrug-resistant gram-negative organisms are well documented.[98,102,107]
- The establishment of an outbreak management team is an important component of best practice management for responding to CPE within a health service organisation.[4,74,104,108] The outbreak management team may be activated at the discretion of the relevant lead within the health service organisation.
- The membership of the outbreak management team can be discussed with the state or territory health department at the time of identification of the CPE outbreak. Appointed external experts may include infectious diseases physicians and infection prevention and control practitioners, microbiologists from an off-site laboratory, or public health physicians and medical epidemiologists. For smaller health service organisations, multidisciplinary involvement is essential.

Outbreak management team roles

- 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 health service organisations are advised to screen any CPE contacts that have been discharged
- Ensure that wards and units implement standard and contact precautions (see Sections 3.1, 3.2, 3.3 and 3.4), entry signage, designated equipment and limits on patient movement
- Ensure that information is provided to staff and patients (see Recommendation 1.1.5, 2.2.3 and 3.3.6)
- Review and address results from compliance audits for standard and transmission-based precautions, hand hygiene, and environmental cleaning procedures
- Where there is ongoing transmission of CPE with no clearly identified source, consider
  - review and re-audit of environmental cleaning procedures
  - review of patient placement
  - closure of the unit to admissions
  - expansion of screening strategies (see Section 2.3).

What is ongoing transmission?

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 that occur in more than one unit.**

In these circumstances, the health service organisation is at risk of CPE becoming widespread, and specific additional control measures should be considered (see Section 1). Refer to the relevant jurisdictional guidelines for additional information.

4.2 Identification of CPE cases to confirm an outbreak

Statement of intent

The recommendations in this section are intended to assist health service organisations with the identification of CPE cases.

Recommendations

4.2.1 The outbreak management team should develop a strategy to identify CPE cases within the health service organisation. This should include guidance on what constitutes a high-risk area during an outbreak and which patient groups are considered to be high risk.

4.2.2 Health service organisations should have systems in place to ensure that outbreak management teams have timely access to microbiology results.

4.3 Screening of patients during an outbreak

Statement of intent

The recommendations in this section are intended to provide health service organisations with guidance on additional screening for high-risk patients and units during an outbreak.

Recommendations

4.3.1 Health service organisations should consider additional screening for patients with a high risk of CPE acquisition and transmission. These include patients with:

- Faecal or urinary incontinence
- Indwelling urinary catheters
- Uncontained wound drainage or respiratory secretions
- Cognitive or intellectual impairment and have difficulty complying with infection prevention and control precautions.

4.3.2 Health service organisations should consider implementing additional screening practices to reduce the risk of transmission to susceptible patients receiving care in high-risk units including intensive care, haematology/oncology, burns, transplant, renal haemodialysis, aged care, and gastroenterology/gastrointestinal surgery units.

Suggested screening strategies for certain clinical areas during outbreaks, if patients are known to be colonised or infected with CPE, are described in Table 3.

4.4 Timeframe for contact tracing during an outbreak

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

- 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 service organisation.

Where this information is unclear or unavailable, health service organisations are suggested to undertake contact tracing for a period of one month prior to the implementation of contact precautions within the organisation.[61]

CPE contacts should be screened within 48 hours before transfer from an outbreak area.

Antimicrobial stewardship (AMS) in an outbreak situation

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

- **Review recent local antimicrobial audits or conduct a point prevalence audit to identify areas of high broad-spectrum and inappropriate antimicrobial use. Feed these data back to the units to engage them in the issue and request their involvement in addressing the inappropriate antimicrobial use and explain how it is related to the outbreak situation.**
- **Promote, and audit compliance with, the approval process for broad-spectrum antimicrobials (phone or electronic approval systems).**
- **Improve the post-prescription review service, with the aim of providing an earlier review (e.g. within 24–48 hours) of patients who are prescribed broad-spectrum antimicrobials such as carbapenems and fluoroquinolones. To ensure that use is appropriate, review national and local guidelines to identify alternatives to broad-spectrum agents, where possible.**
- **Review microbiology laboratory reports to ensure that they promote narrower-spectrum antimicrobial options when clinically appropriate.**
- **Review local guidelines for management of severe sepsis to guide clinicians on when to consider empirical antimicrobial 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 may include advice on when to discuss patients with sepsis with infectious diseases experts.**
- **Keep records of the antimicrobial 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 antimicrobial 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.[12]

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

Environmental screening

Health service organisations may consider environmental screening where there is confirmed local transmission of CPE. If environmental screening is considered necessary by the health service organisation, processes for specimen collection, specimen processing and results interpretation should be developed in conjunction with the health service organisation's microbiology laboratory. Environmental screening should be coordinated by the infection prevention and control team.

There is evidence to indicate that environmental reservoirs exist for CPE. CPE has been found in sinks and wastewater drainage and is thought to be associated with contamination following the disposal of body fluids, particularly in areas where CPE-positive patients have been accommodated.[58–60,100,109] These areas may be considered as part of environmental screening.

Examples of environmental screening:

- Shared patient equipment[110] – blood glucose monitors, blood pressure monitors, patient lifting devices
- 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.[103]

Environmental screening is not recommended in non-outbreak situations (see Section 2.8).

4.6 Staff education

Statement of intent

The recommendations in this section are intended to ensure that relevant information and education is provided to staff during an outbreak. See recommendation 1.1.5 for staff education requirements.

Recommendations

4.6.1 Education and training updates should be provided to all staff, as relevant to their role, including medical, nursing, allied health, 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 service organisation, hospital-wide education may be required.

4.7 Staff allocation

Statement of intent

The recommendation in this section is intended to provide guidance on the allocation of staff to minimise the transmission of CPE within a health service organisation during an outbreak.

During an outbreak, 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 service organisation to target training and education activities to those staff initially. Rostering should be considered, to prevent staff fatigue and burnout during outbreaks.

Recommendation

4.7.1 The outbreak control team should consider allocating separate, dedicated staff to CPE-positive patients and contacts, taking into account patient acuity, staff knowledge, experience and availability; and resources.

4.8 Cleaning and disinfection during outbreaks

Cleaning and disinfection of environmental surfaces and equipment for CPE-positive 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) and Section 3.4 (Cleaning as part of contact precautions).

Endoscopes have been linked to outbreaks of CPE.[17,18,57] Health service organisations should review cleaning and disinfection practices for endoscopes (see Section 1.4).

Section 5:

Laboratory screening and methods

This section addresses laboratory procedures for screening patient carbapenemase-producing *Enterobacterales* (CPE) specimens or cultures. 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:

- *Enterobacterales* that are carbapenem-resistant (non-susceptible) without producing a carbapenemase enzyme. These bacteria use a combination of other resistance mechanisms. In general, such bacteria have a lower risk of transmission and dissemination within health service organisations than CPE
- A number of carbapenem-resistant gram-negative bacilli other than *Enterobacterales* 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 associated with 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 service organisation 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, advise on appropriate patient management.

5.1 Laboratory testing for CPE

Laboratory testing for CPE and genes encoding carbapenemase enzymes is an evolving field; therefore, recommendations will require review in the light of new evidence. The recommendations included in this section are provided as a minimum for laboratories. 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.[27] CARAlert is a program that is part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, established to provide timely communication of the presence of CARs, and facilitate appropriate response.

Whole genome sequencing is playing an increasing role in tracking outbreaks of CPE. It is conducted in suitably equipped laboratories and used mainly: (i) to confirm true clusters of cases; and (ii) to link CPE cases that may not have appeared to be initially linked, triggering public health services to investigate and recommend cross-facility actions if needed. The results of whole genome sequencing are not immediately available and therefore, it plays a supplementary role to the procedures described in this section.

5.2 Recommended screening for asymptomatic carriage in high-risk patients

Statement of intent

The recommendation in this section is intended to provide guidance on procedures for screening patient specimens or cultures for *Enterobacterales*-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. Specimens from open wounds, or aspirates from any tubes or drains should also be considered for screening. Perianal swabs are not generally recommended because they may not give accurate results. However, they may be necessary in some situations, such as anal pathology or in some neutropenic patients.

Rationale and commentary

- This recommendation is 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 CARAlert have come from urine specimens.[11] A recent survey in Victoria, Australia, found that most CPE isolates were cultured from urine (42.1%) or screening samples (34.8%).[40]
- There is currently no internationally accepted 'gold standard' laboratory screening method for carbapenemases in *Enterobacterales*. 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.[45,111–113]
- 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 have been developed[114], 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
  - Brilliance CRE (Oxoid)[115]
  - ChromID® Carba, ChromID® OXA-48[116], ChromID® CARBA SMART (bioMérieux)[117]
  - CHROMagar™ KPC, CHROMagar™ mSuperCARBA™ (Chromagar, Paris)[118,119]
  - Chromatic CRE (Liofilchem®)[120]
- These media have undergone limited trialling in at least two sites in Australia.[121,122] 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.[123]
- 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.[117]
- Extended-spectrum ß-lactamase (ESBL) screening media (e.g. Brilliance ESBL, ChromID ESBL) may be used; however, they lack specificity.[120]

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

Statement of intent

The recommendations in this section are intended to provide microbiology laboratories in Australia with guidance on procedures for detecting 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 *Enterobacterales* with the ESBL phenotype or that are non-susceptible to gentamicin.

5.3.2 Suspected CPE (as defined by the breakpoints documented for the susceptibility testing system being used) should always undergo confirmatory testing.[27]

5.3.3 Laboratories using semi-automated methods for susceptibility testing should also undertake, or seek, molecular confirmation of all *Enterobacterales* where meropenem MIC is > 0.125 mg/L or > 0.25 mg/L depending on the species and method used, especially from high-risk patients or units.

Rationale and commentary

- The aim of laboratory screening is to provide early detection of carbapenemase genes in *Enterobacterales*, 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 has been made in recent years about screening methods, including
  - using specifically designed screening media (see Section 5.2)[124,125]
  - using the susceptibility testing results on positive cultures.[126,127]
- Some carbapenemase-producing strains may test as susceptible to meropenem in routine testing using current breakpoints, especially those harbouring OXA-48 or OXA-48-like enzymes. Laboratories ideally should seek to identify these carbapenemase producers (resources permitting). These strains can be detected with the current Australian

configurations Phoenix™ gram-negative panels using the criterion noted above. The meropenem concentration on the current configuration of Vitek™ cards is not low enough to accurately detect some species of *Enterobacterales*.

- 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 Australian Group on Antimicrobial Resistance (AGAR) studies (2013–2020)[128–132] indicate that CPE usually show an ESBL phenotype (89%) (either ceftazidime or ceftriaxone non-susceptibility, or cefepime MIC > 1 mg/L), or gentamicin resistance (78%). However, this is often not true for strains harbouring OXA-48 or OXA-48-like enzymes.

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 the CARAlert system[11] 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 clinical 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 or 0.25 mg/L, depending on the species. 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 *Enterobacterales* are known.[126,133] Strains with a zone diameter of < 28 mm on Mueller-Hinton agar should then undergo confirmation testing. Note that this method is intended 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 *Enterobacterales*.[134]

5.4 CPE confirmation

Statement of intent

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

Recommendations

5.4.1 All suspected CPE isolates should undergo molecular screening for at least the suite of carbapenemase gene families that have so far been seen in *Enterobacterales* 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 carbapenem inactivation method (CIM)[28,29] or modified CIM (mCIM)[30,31], the Carba NP test[32] or enhanced Carba NP test[33], or the Carb Blue test[34], 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 Blue Kit [Rosco]). The mCIM/CIM methods 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.[35]

Rationale and commentary

- Published evidence indicates that the CIM and Carba NP tests and their variations are reliable and 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.[11]

5.5 Reporting of suspected CPE

Statement of intent

The recommendation in this section is intended 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 prevention and control staff and treating clinicians should be notified of suspected (e.g. Carba NP or CIM/mCIM 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 "I" breakpoint of 2 mg/L (CLSI) or the "R" breakpoint of 8 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 prevention and control staff of the health service organisation 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.

Recommendation

5.5.1 For inpatients, all suspected CPE isolates should be notified to infection prevention and 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 prevention and 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.[135] 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 service organisation.[136] Current evidence suggests that patients carrying such isolates present a lower infection control risk and do not warrant attention unless cross-transmission is demonstrated.

Acronyms

AMS: antimicrobial stewardship

AGAR: Australian Group on Antimicrobial Resistance

AURA: Antimicrobial Use and Resistance in Australia

CAR: critical antimicrobial resistance

CARAlert: National Alert System for Critical Antimicrobial Resistances

CLSI: Clinical and Laboratory Standards Institute

CRE: carbapenem-resistant *Enterobacterales*

CPE: carbapenemase-producing *Enterobacterales*

ESBL: extended-spectrum ß-lactamase

EUCAST: European Committee on Antimicrobial Susceptibility Testing

GESA: Gastroenterological Society of Australia

KPC: *Klebsiella pneumoniae* carbapenemase

NSQHS: National Safety and Quality Health Service

References

1. Ben-David D, Masarwa S, Adler A, Mishali H, Carmeli Y, Schwaber MJ, et al. A National Intervention to Prevent the Spread of carbapenem-resistant Enterobacteriae in Isreaeli Post-Acute Care Hospitals. Infect Control Hosp Epidemiol. 2014;35(7):802–809.
2. Chang LW, Buising 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. Internal Medicine Journal. 2015 October;45(10):1037–1043.
3. 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 Sep;13(9):785–796.
4. 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 Apr 1;52(7):848–855.
5. 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 Oct 30;19(43).
6. Brett JA, Johnson SA, Cameron DRM, Lane CR, Easton M, van Diemen A, et al. Carbapenemase-producing Enterobacteriaceae in Australian hospitals: outcome of point-prevalence screening in high-risk wards. J Hosp Infect. 2019 Feb;101(2):163–166.
7. Bearman M, Palermo C, Allen LM, Williams B. Learning Empathy Through Simulation: A Systematic Literature Review. Simul Healthc. 2015 Oct;10(5):308–319.
8. Marmor A, Daveson K, Harley D, Coatsworth N, Kennedy K. Two carbapenemase-producing Enterobacteriaceae outbreaks detected retrospectively by whole-genome sequencing at an Australian tertiary hospital. Infection, Disease & Health. 2020 2020/02/01/;25(1):30–33.
9. Sidjabat HE, Townell N, Nimmo GR, George NM, Robson J, Vohra R, et al. Dominance of IMP-4-producing enterobacter cloacae among carbapenemase-producing Enterobacteriaceae in Australia. Antimicrob Agents Chemother. 2015 Jul;59(7):4059–4066.
10. Australian Commission on Safety and Quality in Health Care. National Safety and Quality Health Service Standards. 2021. Available from: **https://www.safetyandquality.gov.au/standards/nsqhs-standards**.
11. Australian Commission on Safety and Quality in Health Care. CARAlert Annual Report: 2020. In press.
12. National Health and Medical Research Council, Australian Commission on Safety and Quality in Health Care. Australian Guidelines for the Prevention and Control of Infection in Healthcare. [Internet] Canberra: NHMRC; 2019. Available from: **https://www.nhmrc.gov.au/about-us/publications/australian-guidelines-prevention-and-control-infection-healthcare-2019**.
13. Australasian Health Facility Guidelines. Part D: Infection Prevention and Control. [Internet] 2016. Available from: **https://healthfacilityguidelines.com.au/full-guidelines**.
14. Australian Commission on Quality and Safety in Health Care. National Hand Hygiene Initiative Manual. Sydney: ACSQHC; 2019.
15. Australian Commission on Quality and Safety in Health Care. Environmental Cleaning and Infection Prevention and Control. [Internet] Sydney: ACSQHC; 2020. Available from: **https://www.safetyandquality.gov.au/our-work/infection-prevention-and-control/environmental-cleaning-and-infection-prevention-and-control**.
16. Muscarella LF. Risk of transmission of carbapenem-resistant Enterobacteriaceae and related "superbugs" during gastrointestinal endoscopy. World J Gastrointest Endosc. 2014 Oct 16;6(10):457–474.
17. Kola A, Piening B, Pape UF, Veltzke-Schlieker W, Kaase M, Geffers C, et al. An outbreak of carbapenem-resistant OXA-48 – producing Klebsiella pneumonia associated to duodenoscopy. Antimicrob Resist Infect Control. 2015 March;4:8.
18. Epstein L, Hunter JC, Arwady MA, Tsai V, Stein L, Gribogiannis M, et al. New Delhi metallo-beta-lactamase-producing carbapenem-resistant Escherichia coli associated with exposure to duodenoscopes. JAMA. 2014 Oct 8;312(14):1447–1455.
19. Gastroenterological Society of Australia and Gastroenterological Society of Australia. Infection Control in Endoscopy. Melbourne: GESA GENCA; 2010.
20. Gillespie EE, Kotsanas D, Stuart RL. Microbiological monitoring of endoscopes: 5-year review. J Gastroenterol Hepatol. 2008 Jul;23(7 Pt 1):1069–1074.
21. Fernando G, Collignon P, Beckingham W. ATP bioluminescence to validate the decontamination process of gastrointestinal endoscopes. Healthcare infection. 2014;19(2):59–64.
22. 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(3):249–253.
23. Therapeutic Guidelines Antibiotic Expert Group. Therapeutic Guidelines: Antibiotic. Version 16. Melbourne: Therapeutic Guidelines Limited; 2019.
24. Australian Commission on Quality and Safety in Health Care. Specification for a Hospital Cumulative Antibiogram. Sydney: ACSQHC; 2019.

25. Munoz-Price LS, Quinn JP. Deconstructing the infection control bundles for the containment of carbapenem-resistant Enterobacteriaceae. Curr Opin Infect Dis. 2013 Aug;26(4):378–387.
26. Schwaber MJ, Carmeli Y. An ongoing national intervention to contain the spread of carbapenem-resistant enterobacteriaceae. Clin Infect Dis. 2014 Mar;58(5): 697–703.
27. Australian Commission on Safety and Quality in Health Care. CARAlert Laboratory Handbook. [Internet] Sydney: ACSQHC; 2019. Available from: **https://www.safetyandquality.gov.au/publications-and-resources/resource-library/caralert-laboratory-handbook**.
28. 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. 2016 Jan;71(1):274–276.
29. 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(3):e0123690.
30. Beresford RW, Maley M. Reduced Incubation Time of the Modified Carbapenem Inactivation Test and Performance of Carbapenem Inactivation in a Set of Carbapenemase-Producing Enterobacteriaceae with a High Proportion of bla IMP Isolates. J Clin Microbiol. 2019 Jul;57(7).
31. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. CLSI supplement M100. [Internet] Wayne, PA: Clinical and Laboratory Standards Institute; 2020. Available from: **https://clsi.org/standards/products/microbiology/documents/m100/**.
32. 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 May;63(Pt 5):772–776.
33. Dortet L, Agathine A, Naas T, Cuzon G, Poirel L, Nordmann P. Evaluation of the RAPIDEC(R) CARBA NP, the Rapid CARB Screen(R) and the Carba NP test for biochemical detection of carbapenemase-producing Enterobacteriaceae. J Antimicrob Chemother. 2015 Nov;70(11):3014–3022.
34. 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 Sep;53(9):3105–3107.
35. Doyle D, Peirano G, Lascols C, Lloyd T, Church DL, Pitout JD. Laboratory detection of Enterobacteriaceae that produce carbapenemases. J Clin Microbiol. 2012 Dec;50(12):3877–3880.
36. 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 Jan;64(1):138–141.
37. Centres for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services; 2019.
38. 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 Nov 7;195(9):530–533.
39. Adeolu M, Alnajar S, Naushad S, R SG. Genome-based phylogeny and taxonomy of the 'Enterobacteriales': proposal for Enterobacterales ord. nov. divided into the families Enterobacteriaceae, Erwiniaceae fam. nov., Pectobacteriaceae fam. nov., Yersiniaceae fam. nov., Hafniaceae fam. nov., Morganellaceae fam. nov., and Budviciaceae fam. nov. Int J Syst Evol Microbiol. 2016 Dec;66(12):5575–5599.
40. Sherry NL, Lane CR, Kwong JC, Schultz M, Sait M, Stevens K, et al. Genomics for Molecular Epidemiology and Detecting Transmission of Carbapenemase-Producing Enterobacterales in Victoria, Australia, 2012 to 2016. J Clin Microbiol. 2019 Sep;57(9).
41. Australian Commission on Safety and Quality in Health Care. AURA 2019: Antimicrobial Resistance. [Internet] 2019. Available from: **https://www.safetyandquality.gov.au/sites/default/files/2019-06/AURA-2019-Information-Sheet-AMR%20%281%29.pdf**.
42. Australian Commission on Safety and Quality in Health Care. CARAlert annual report: 2019. [Internet] 2020. Available from: **https://www.safetyandquality.gov.au/publications-and-resources/resource-library/caralert-annual-report-2019**.
43. Slayton RB, Toth D, Lee BY, Tanner W, Bartsch SM, Khader K, et al. Vital Signs: Estimated effects of a coordinated approach for action to reduce antibiotic-resistant infections in health care facilities – United States. MMWR Morbidity and Mortality Weekly Report. 2015;64(30):826–831.
44. Safe Work Australia. Identify, assess and control hazards. [Internet] 2020. Available from: **https://www.safeworkaustralia.gov.au/risk#controlling-risks-using-the-hierarchy**.
45. Poirel L, Walsh TR, Cuvillier V, Nordmann P. Multiplex PCR for detection of acquired carbapenemase genes. Diagn Microbiol Infect Dis. 2011 May;70(1):119–123.
46. 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. 2013 May;19(5):451–456.
47. Campbell AJ, Daley DA, Bell JM, Pang S, Coombs GW, Carapetis JR, et al. Progress towards a coordinated, national paediatric antimicrobial resistance surveillance programme: Staphylococcus aureus, enterococcal and Gram-negative bacteraemia in Australia. J Antimicrob Chemother. 2020 Jun 1;75(6):1639–1644.

48. Wilson HJ, Khokhar F, Enoch DA, Brown NM, Ahluwalia J, Dougan G, et al. Point-prevalence survey of carbapenemase-producing Enterobacteriaceae and vancomycin-resistant enterococci in adult inpatients in a university teaching hospital in the UK. J Hosp Infect. 2018 Sep;100(1):35–39.

49. Marimuthu K, Venkatachalam I, Khong WX, Koh TH, Cherng BP, Van La M, et al. Clinical and Molecular Epidemiology of Carbapenem-Resistant Enterobacteriaceae Among Adult Inpatients in Singapore. Clin Infect Dis. 2017;64(suppl_2):S68–S75.

50. Trepanier P, Mallard K, Meunier D, Pike R, Brown D, Ashby JP, et al. Carbapenemase-producing Enterobacteriaceae in the UK: a national study (EuSCAPE-UK) on prevalence, incidence, laboratory detection methods and infection control measures. J Antimicrob Chemother. 2017 Feb;72(2):596–603.

51. Wilson H, Torok ME. Extended-spectrum beta-lactamase-producing and carbapenemase-producing Enterobacteriaceae. Microb Genom. 2018 Jul;4(7).

52. World Health Organization. WHO Guidelines on Hand Hygiene in Health Care. Geneva: World Health Organization; 2009.

53. Chitnis AS, 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 Oct;33(10):984–992.

54. 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 Infect Control. 2013 Sep;41(9):793–798.

55. De Geyter D, Blommaert L, Verbraeken N, Sevenois M, Huyghens L, Martini H, et al. The sink as a potential source of transmission of carbapenemase-producing Enterobacteriaceae in the intensive care unit. Antimicrobial Resistance & Infection Control. 2017 2017/02/16;6(1):24.

56. Park SC, Parikh H, Vegesana K, Stoesser N, Barry KE, Kotay SM, et al. Risk Factors Associated with Carbapenemase-Producing Enterobacterales (CPE) Positivity in the Hospital Wastewater Environment. Applied and Environmental Microbiology. 2020;86(24):e01715–01720.

57. Lerner A, Adler A, Abu-Hanna J, Meitus I, Navon-Venezia S, Carmeli Y. Environmental contamination by carbapenem-resistant Enterobacteriaceae. J Clin Microbiol. 2013 Jan;51(1):177–181.

58. Kizny Gordon AE, Mathers AJ, Cheong EYL, Gottlieb T, Kotay S, Walker AS, et al. The Hospital Water Environment as a Reservoir for Carbapenem-Resistant Organisms Causing Hospital-Acquired Infections: A Systematic Review of the Literature. Clin Infect Dis. 2017;64(10):1435–1444.

59. Aranega-Bou P, George RP, Verlander NQ, Paton S, Bennett A, Moore G, et al. Carbapenem-resistant Enterobacteriaceae dispersal from sinks is linked to drain position and drainage rates in a laboratory model system. J Hosp Infect. 2019 May;102(1):63–69.

60. Smolders D, Hendriks B, Rogiers P, Mul M, Gordts B. Acetic acid as a decontamination method for ICU sink drains colonized by carbapenemase-producing Enterobacteriaceae and its effect on CPE infections. J Hosp Infect. 2019 May;102(1):82–88.

61. Hopman J, Meijer C, Kenters N, Coolen JPM, Ghamati MR, Mehtar S, et al. Risk Assessment After a Severe Hospital-Acquired Infection Associated With Carbapenemase-Producing Pseudomonas aeruginosa. JAMA Netw Open. 2019;2(2):e187665–e187665.

62. Decraene V, Phan HTT, George R, Wyllie DH, Akinremi O, Aiken Z, et al. A Large, Refractory Nosocomial Outbreak of Klebsiella pneumoniae Carbapenemase-Producing Escherichia coli Demonstrates Carbapenemase Gene Outbreaks Involving Sink Sites Require Novel Approaches to Infection Control. Antimicrobial agents and chemotherapy. 2018;62(12):e01689–01618.

63. Gastroenterological Society of Australia and Gastroenterological Society of Australia. Infection Control in Endoscopy Consensus Statements on Carbapenemase-Producing Enterobacteriaceae. Melbourne: GESA GENCA; 2017.

64. Australian Commission on Quality and Safety in Health Care. Antimicrobial Stewardship in Australian Health Care. [Internet] Sydney: ACSQHC; 2018. Available from: **https://www.safetyandquality.gov.au/publications-and-resources/resource-library/antimicrobial-stewardship-australian-health-care**.

65. Australian Commission on Safety and Quality in Health Care. Antimicrobial Stewardship Clinical Care Standard. Sydney: ACSQHC; 2014.

66. Kohler PP, Melano RG, Patel SN, Shafinaz S, Faheem A, Coleman BL, et al. Emergence of Carbapenemase-Producing Enterobacteriaceae, South-Central Ontario, Canada. Emerg Infect Dis. 2018 Sep;24(9):1674–1682.

67. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. Clin Infect Dis. 2011 Jul 1;53(1):60–67.

68. Canton R, Bryan J. Global antimicrobial resistance: from surveillance to stewardship. Part 2: stewardship initiatives. Expert Rev Anti Infect Ther. 2012 Dec;10(12):1375–1377.

69. 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 June;7(6):e38719.

70. Legeay C, Thepot-Seegers V, Pailhories H, Hilliquin D, Zahar JR. Is cohorting the only solution to control carbapenemase-producing Enterobacteriaceae outbreaks? A single-centre experience. J Hosp Infect. 2018 Aug;99(4):390–395.

71. Duguid M, Cruickshank M, editors. Antimicrobial Stewardship in Australian Hospitals. Sydney: Australian Commission on Safety and Quality in Health Care; 2010.
72. Antimicrobial Stewardship in Australian Health Care. Chapter 1: Evidence for Antimicrobial Stewardship. [Internet] Sydney: ACSQHC; 2018. Available from: **https://www.safetyandquality.gov.au/sites/default/files/migrated/Chapter1-Evidence-for-antimicrobial-stewardship.pdf**
73. Schwaber MJ, Carmeli Y, Harbarth S. Controlling hospital-acquired infection due to carbapenem-resistant Enterobacteriaceae (CRE): Springer New York; 2012.
74. Magiorakos AP, Burns K, Rodriguez Bano J, Borg M, Daikos G, Dumpis U, et al. Infection prevention and control measures and tools for the prevention of entry of carbapenem-resistant Enterobacteriaceae into healthcare settings: guidance from the European Centre for Disease Prevention and Control. Antimicrob Resist Infect Control. 2017 2017/11/15;6(1):113.
75. Errico G, Gagliotti C, Monaco M, Masiero L, Gaibani P, Ambretti S, et al. Colonization and infection due to carbapenemase-producing Enterobacteriaceae in liver and lung transplant recipients and donor-derived transmission: a prospective cohort study conducted in Italy. Clin Microbiol Infect. 2019 Feb;25(2):203–209.
76. Lee KH, Han SH, Yong D, Paik HC, Lee JG, Kim MS, et al. Acquisition of Carbapenemase-Producing Enterobacteriaceae in Solid Organ Transplantation Recipients. Transplant Proc. 2018 Dec;50(10):3748–3755.
77. Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant Klebsiella pneumoniae infection and the impact of antimicrobial and adjunctive therapies. Infect Control Hosp Epidemiol. 2008 Dec;29(12):1099–1106.
78. Wiener-Well Y, Rudensky B, Yinnon AM, Kopuit P, Schlesinger Y, Broide E, et al. Carriage rate of carbapenem-resistant Klebsiella pneumoniae in hospitalised patients during a national outbreak. J Hosp Infect. 2010 Apr;74(4):344–349.
79. Segagni Lusignani L, Presterl E, Zatorska B, Van den Nest M, Diab-Elschahawi M. Infection control and risk factors for acquisition of carbapenemase-producing enterobacteriaceae. A 5 year (2011-2016) case-control study. Antimicrobial resistance and infection control. 2020;9(1):18–18.
80. Otter JA, Dyakova E, Bisnauthsing KN, Querol-Rubiera A, Patel A, Ahanonu C, et al. Universal hospital admission screening for carbapenemase-producing organisms in a low-prevalence setting. Journal of Antimicrobial Chemotherapy. 2016 August 11, 2016.
81. Skjøt-Arkil H, Mogensen CB, Lassen AT, Johansen IS, Chen M, Petersen P, et al. Carrier prevalence and risk factors for colonisation of multiresistant bacteria in Danish emergency departments: a cross-sectional survey. BMJ Open. 2019;9(6):e029000.
82. Schwaber MJ, Klarfeld-Lidji S, Navon-Venezia S, Schwartz D, Leavitt A, Carmeli Y. Predictors of carbapenem-resistant Klebsiella pneumoniae acquisition among hospitalized adults and effect of acquisition on mortality. Antimicrob Agents Chemother. 2008 Mar;52(3):1028–1033.
83. Hussein K, Sprecher H, Mashiach T, Oren I, Kassis I, Finkelstein R. Carbapenem resistance among Klebsiella pneumoniae isolates: risk factors, molecular characteristics, and susceptibility patterns. Infect Control Hosp Epidemiol. 2009 Jul;30(7):666–671.
84. Marimuthu K, Ng O, Cherng B, Fong R, Pada S, De P, et al. Antecedent Carbapenem Exposure as a Risk Factor for Non-Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae (NCPCRE) and Carbapenemase-Producing Enterobacteriaceae (CPE). Antimicrobial Agents and Chemotherapy. 2019 08/05;63.
85. Centers for Disease Control and Prevention. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). [Internet]: U.S. Department of Health and Human Services; 2003. Available from: **https://www.cdc.gov/infectioncontrol/guidelines/environmental/**.
86. 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 Jul 1;53(1):49–56.
87. Vella V, Moore LS, Robotham JV, Davies F, Birgand GJ, Otter JA, et al. Isolation demand from carbapenemase-producing Enterobacteriaceae screening strategies based on a West London hospital network. J Hosp Infect. 2016 Oct;94(2):118–124.
88. Lubbert C, Straube L, Stein C, Makarewicz O, Schubert S, Mossner 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 Jan;305(1):148–156.
89. Logan LK. Carbapenem-resistant enterobacteriaceae: an emerging problem in children. Clin Infect Dis. 2012 Sep;55(6):852–859.
90. Seale J, Millar M. Perinatal vertical transmission of antibiotic-resistant bacteria: a systematic review and proposed research strategy. BJOG. 2014 Jul;121(8): 923–928.
91. van Hattem JM, Arcilla MS, Bootsma MC, van Genderen PJ, Goorhuis A, Grobusch MP, et al. Prolonged carriage and potential onward transmission of carbapenemase-producing Enterobacteriaceae in Dutch travelers. Future Microbiol. 2016 Jul;11:857–864.
92. Yusuf E, Huang TD, Schallier A, Trémérie JM, Mertens R, Jans B, et al. OXA-48 Producing Klebsiella pneumoniae in a Household Contact of a Previously Infected Patient: Person-to-Person Transmission or Coincidental Community Acquisition? Microbial drug resistance. 2016 Mar;22(2):134–136.

93. Savard P, Perl TM. Combating the spread of carbapenemases in Enterobacteriaceae: a battle that infection prevention should not lose. Clin Microbiol Infect. 2014 Sep;20(9):854–861.

94. 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 Jul;34(7):730-739.

95. 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 Jul;36(7):835–837.

96. 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 Mar;41(3):190–194.

97. 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 Aug;36(8):936–941.

98. 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(11):1549–1556.

99. Evain S, Bourigault C, Juvin ME, Corvec S, Lepelletier D. Carbapenemase-producing Enterobacteriaceae digestive carriage at hospital readmission and the role of antibiotic exposure. J Hosp Infect. 2019 May;102(1):25–30.

100. Clarivet B, Pantel A, Morvan M, Jean Pierre H, Parer S, Jumas-Bilak E, et al. Carbapenemase-producing Enterobacteriaceae: use of a dynamic registry of cases and contacts for outbreak management. J Hosp Infect. 2016 Jan;92(1):73–77.

101. Roberts LW, Harris PNA, Forde BM, Ben Zakour NL, Catchpoole E, Stanton-Cook M, et al. Integrating multiple genomic technologies to investigate an outbreak of carbapenemase-producing Enterobacter hormaechei. Nature communications. 2020 Jan 24;11(1):466.

102. Public Health Agency of Canada. Guidance: Infection Prevention and Control Measures for Healthcare Workers in all Healthcare Settings. 2012.

103. 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)(5):267–269.

104. Delory T, Seringe E, Antoniotti 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 Oct 1;43(10):1070–1075.

105. Pirs M, Cerar Kisek T, Krizan Hergouth V, Seme K, Mueller Premru M, Jeverica S, et al. Successful control of the first OXA-48 and/or NDM carbapenemase-producing Klebsiella pneumoniae outbreak in Slovenia 2014–2016. J Hosp Infect. 2019 Feb;101(2):142–149.

106. Grundmann H, Aires-de-Sousa M, Boyce J, Tiemersma E. Emergence and resurgence of meticillin-resistant Staphylococcus aureus as a public-health threat. Lancet. 2006 Sep 2;368(9538):874–885.

107. Kwong J. Victorian KPC Experience. Australian Society for Antimicrobials 16th Annual Scientific Meeting – Antimicrobials 2015; 26-28 February 2015; Brisbane Convention Centre 2015.

108. Coope CM, Verlander NQ, Schneider A, Hopkins S, Welfare W, Johnson AP, et al. An evaluation of a toolkit for the early detection, management, and control of carbapenemase-producing Enterobacteriaceae: a survey of acute hospital trusts in England. J Hosp Infect. 2018 Aug;99(4):381–389.

109. Clinical Excellence Commission. Surveillance and response for carbapenemase producing Enterobacterales (CPE) in NSW Health public facilities. Sydney: NSW Health; 2019.

110. 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 May;36(5):590–593.

111. Ellington MJ, Kistler J, Livermore DM, Woodford N. Multiplex PCR for rapid detection of genes encoding acquired metallo-beta-lactamases. J Antimicrob Chemother. 2007 Feb;59(2):321–322.

112. Mendes RE, Kiyota KA, Monteiro J, Castanheira M, Andrade SS, Gales AC, et al. Rapid detection and identification of metallo-beta-lactamase-encoding genes by multiplex real-time PCR assay and melt curve analysis. J Clin Microbiol. 2007 Feb;45(2):544–547.

113. Meunier D, Woodford N, Hopkins KL. Evaluation of the AusDiagnostics MT CRE EU assay for the detection of carbapenemase genes and transferable colistin resistance determinants mcr-1/-2 in MDR Gram-negative bacteria. J Antimicrob Chemother. 2018 Dec 1;73(12):3355–3358.

114. 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 Feb;75(2):214–217.

115. 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 Jun;61(Pt 6):878–880.

116. 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 Dec;77(4):296–300.

117. Lee SY, Octavia S, Chew KL. Detection of OXA-carbapenemase-producing Enterobacteriaceae with chromID CARBA SMART screening plate. Pathology. 2019 Jan;51(1):108–110.

118. Moubareck CA, Hammoudi Halat D, Sartawi M, Lawlor K, Sarkis DK, Alatoom A. Assessment of the performance of CHROMagar KPC and Xpert Carba-R assay for the detection of carbapenem-resistant bacteria in rectal swabs: First comparative study from Abu Dhabi, United Arab Emirates. J Glob Antimicrob Resist. 2020 Mar;20:147–152.
119. Soria Segarra C, Larrea Vera G, Berrezueta Jara M, Arevalo Mendez M, Cujilema P, Serrano Lino M, et al. Utility of CHROMagar mSuperCARBA for surveillance cultures of carbapenemase-producing Enterobacteriaceae. New Microbes New Infect. 2018 Nov;26:42–48.
120. Gottig S, Walker SV, Saleh A, Koroska F, Sommer J, Stelzer Y, et al. Comparison of nine different selective agars for the detection of carbapenemase-producing Enterobacterales (CPE). Eur J Clin Microbiol Infect Dis. 2020 May;39(5):923–927.
121. 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.
122. Knox J, Gregory C, Prendergast L, Perera C, Robson J, Waring L. Laboratory detection of intestinal carriage of carbapenemase-producing Enterobacteriaceae – A comparison of algorithms using the Carba NP test. Diagn Microbiol Infect Dis. 2017 Jan;87(1):17–21.
123. 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 Sep;50(9):3102–3104.
124. Nordmann P, Poirel L. Strategies for identification of carbapenemase-producing Enterobacteriaceae. J Antimicrob Chemother. 2013 Mar;68(3):487–489.
125. 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 Jun;50(6):1841–1846.
126. European Committee on Antimicrobial Susceptibility Testing. EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance. Version 2.0. [Internet]: EUCAST; 2017 [cited April 2020]. Available from: **https://www.eucast.org/resistance_mechanisms/**.
127. Maurer FP, Castelberg C, Quiblier C, Bloemberg GV, Hombach M. Evaluation of carbapenemase screening and confirmation tests with Enterobacteriaceae and development of a practical diagnostic algorithm. J Clin Microbiol. 2015 Jan;53(1):95–104.
128. Australian Commission on Safety and Quality in Health Care. AGAR: Sepsis Outcome Programs 2015 report. [Internet] Sydney: ACSQHC; 2015. Available from: **https://www.safetyandquality.gov.au/publications-and-resources/resource-library/agar-sepsis-outcome-programs-2015-report-0**.
129. Australian Commission on Safety and Quality in Health Care. AGAR: Sepsis Outcome Programs 2016 report. [Internet] Sydney: ACSQHC; 2016. Available from: **https://www.safetyandquality.gov.au/publications-and-resources/resource-library/agar-sepsis-outcome-programs-2016-report**.
130. Australian Commission on Safety and Quality in Health Care. AGAR Sepsis Outcome Programs 2017 report. [Internet] Sydney: ACSQHC; 2019. Available from: **https://www.safetyandquality.gov.au/publications-and-resources/resource-library/agar-sepsis-outcome-programs-2017-report**.
131. Australian Commission on Safety and Quality in Health Care. AGAR Sepsis Outcome Programs 2018 Report. [Internet]: ACSQHC; 2019. Available from: **https://www.safetyandquality.gov.au/publications-and-resources/resource-library/agar-sepsis-outcome-programs-2018-report**.
132. Australian Group on Antimicrobial Resistance. Australian Enterobacteriaceae Sepsis Outcome Program (EnSOP) Annual Reports. [Internet]: AGAR. Available from: **https://agargroup.org.au/agar-surveys#Gram-Negative-Bacteria**.
133. European Committee on Antimicrobial Susceptibility Testing. Antimicrobial susceptibility testing. [Internet]: EUCAST; [cited April 2020]. Available from: **https://mic.eucast.org/Eucast2/**.
134. Bell SM, Pham JN, Rafferty DL, Allerton JK, James PM. Antibiotic Susceptibility Testing by the CDS Method. A Manual for Medical and Veterinary Laboratories 2018. 9th edition. [Internet] NSW Health Pathology, South Eastern Area Laboratory Services 2018 [cited April 2020]. Available from: **http://cdstest.net**.
135. Garcia-Fernandez 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 Oct;54(10):4178–4184.
136. 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 Feb;41(1):61–67.

AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

Level 5, 255 Elizabeth Street, Sydney NSW 2000
GPO Box 5480, Sydney NSW 2001

Phone: (02) 9126 3600

@ACSQHC

safetyandquality.gov.au