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New Zealand Government

Infection Prevention and Control and Management of Carbapenemase-producing Enterobacteriaceae

Guidelines for health care providers in New Zealand acute and residential care facilities

Released 2018

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Abbreviations

AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
ARRC	Age-related residential care
ASID-NZ	Australasian Society for Infectious Diseases, Inc, New Zealand subcommittee
AST	Antimicrobial susceptibility testing
CLSI	Clinical and Laboratory Standards Institute
CPE	Carbapenemase-producing Enterobacteriaceae
CRE	Carbapenem-resistant Enterobacteriaceae
CRO	Carbapenem-resistant organism
DHB	District health board
DST	Direct susceptibility testing
ESBL	Extended-spectrum beta-lactamase
ESR	Institute of Environmental Science and Research
EUCAST	European Committee on Antimicrobial Susceptibility Testing
HARC	Health Antimicrobial Resistance Coordination Committee
HQSC	Health Quality & Safety Commission New Zealand
ICU	Intensive care unit
IPC	Infection prevention and control
IPCNC	Infection Prevention and Control Nurses College
MDRO	Multi-drug resistant organism
NHI	National Health Index
non-CP CRE	non-carbapenemase-producing, carbapenem-resistant Enterobacteriaceae
NZMN	The New Zealand Microbiology Network
PPE	Personal protective equipment
PPS	Point prevalence screen
TAG	Technical advisory group
TRA	Transmission risk area

Definitions

Carbapenemase-producing Enterobacteriaceae (CPE)	CPE are bacteria that are members of the family Enterobacteriaceae that are identified to carry a carbapenemase gene. Enterobacteriaceae are the largest family of gram-negative bacteria causing human infection.
Carbapenem-resistant Enterobacteriaceae (CRE)	CRE are bacteria from the Enterobacteriaceae that have been found to have resistance to carbapenem antibiotics by any mechanism.
Case	A case is a person who has had a clinical or screening specimen that has tested positive for the presence of a species of Enterobacteriaceae identified as carrying a carbapenemase gene.
Cohorting	In this instance, cohorting is placing together, in the same room, patients who are infected or colonised with the same pathogen and are suitable roommates.
Contact	A contact is a person who has shared a room, bathroom or toilet facility with a confirmed CPE case for more than 24 hours.
Colonisation	Colonisation is when a microorganism is present on a person without causing signs or symptoms of disease. Someone who is colonised still has the potential to spread the organism to other people.
Frequently touched surfaces	Frequently touched surfaces are surfaces that experience frequent hand contact, including but not limited to doorknobs, bedrails, over-bed tables, light switches, table tops and wall areas around a toilet.
Infection	This term is used when microorganisms invade the body's tissues, causing damage to the tissues with subsequent signs and symptoms of disease.

Outbreak	An outbreak is more cases of infection than typically expected in a given area, among a specific group of people, over a particular period of time, for example: • two or more units experience related CPE cases within 12 months • single cases with the same CPE molecular epidemiology are found in more than one unit • two or more patients in a defined clinical area with positive CPE colonisation • several epidemiologically-linked CPE isolates, or an increase in numbers of cases over a baseline, are detected.
Point prevalence screen	Point prevalence screening is when a consensus point in time is chosen to screen a cohort of patients (for example, all patients on a ward on a particular date) at risk of being infected or colonised with CPE.
Residential care facility	This includes age-related residential care, which could be hospital or rest home; dementia units; or residential care for people younger than 65 years of age who require long-term care.
Transmission risk area (TRA)	A TRA is a distinct geographical area (such as a ward) in which local transmission has been determined to have occurred.

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Purpose

These guidelines are intended for health care providers. They set out recommendations, requirements and response actions for the prevention, management, and control of health care-associated infections due to carbapenemase-producing Enterobacteriaceae (CPE) in health care facilities in New Zealand, including:

- acute care facilities (tertiary and secondary-level hospitals, including public and private surgical hospitals)
- residential[1] care facilities, including dementia units, rest homes and hospitals and other residential facilities providing long-term care for people with disabilities.

The guidelines build on work already undertaken by the Ministry of Health (the Ministry) and other relevant New Zealand professional bodies and organisations.

- **Section 1** includes background information as well as details about roles and responsibilities and the epidemiology of CPE.
- **Section 2** provides an operational framework for health care workers who are managing CPE and outbreak response measures.

The guidelines consider recommendations from the Australasian Society for Infectious Diseases Inc. (ASID), the ASID New Zealand subcommittee (ASID-NZ) and Infection Prevention & Control Nurses College (IPCNC) joint 2018 position statement: Minimum specifications for New Zealand's national response plan for carbapenemase-producing Enterobacteriaceae (CPE) (ASID et al 2018).

This is a 'living document' and will be updated as appropriate to reflect the changing epidemiology of CPE internationally and in New Zealand. Please refer to the latest electronic version available at: health.govt.nz/search/results/amr

[1] The term 'residential care facility' applies to a range of facilities dealing with residents or patients with differing health needs. For example, residential care facilities that provide hospital-level care may have similar practices to those outlined for acute hospitals, while rest homes where the residents are mobile will present different challenges.

Section 1

> Carbapenemase-producing Enterobacteriaceae (CPE) is the newest in a long line of 'superbugs' ... and [is] a particular problem in hospital settings. Of all the superbugs, CPE is the most difficult to kill with antibiotics.
>
> The World Health Organization (WHO), Centre for Disease Control [CDC] and the European Centre for Disease Prevention and Control (ECDC) all identify that infections with CPE are a serious threat to patient safety due to their resistance to multiple antimicrobials, meaning that there are very few treatment options for infected patients. Patients with CPE experience poorer patient outcomes, increased morbidity, mortality and have higher associated hospital costs.
>
> An Roinn Sláinte Department of Health, 2017a, page 4

Introduction

Antimicrobial resistance (AMR) is a growing threat to the entire New Zealand population and globally because it hinders our ability to manage infections. Without effective antimicrobials to prevent and treat infections, routine surgeries and medical and cancer treatments (such as chemotherapy) will become increasingly less safe. In response to the growing global threat of AMR, in August 2017, the Ministry of Health and Ministry for Primary Industries released the *New Zealand Antimicrobial Resistance Action Plan* (Ministry of Health and Ministry for Primary Industries 2017).

Additionally, spread of multi-drug resistant Enterobacteriaceae in long-term care facilities indicates that these facilities are increasingly identified as reservoirs of antibiotic resistance, particularly associated with microorganisms that colonise the human host without currently causing active infection. The literature includes numerous analyses, showing that a previous stay in a long-term care facility is a risk factor for the subsequent onset of infection with multi-drug resistant gram-negative bacteria, including those with carbapenemases (Wilson et al 2016).

Enterobacteriaceae

Enterobacteriaceae are part of a large and diverse family of gram-negative bacteria *(Enterobacterales*) and, although they generally exist as commensal organisms in the human gastrointestinal tract, they can be responsible for a variety of infections, including: urinary tract infections, wound infections, gastroenteritis, meningitis, septicemia and pneumonia.

Enterobacteriaceae are the most frequent cause of both community-acquired and health care-acquired infections. They are easily transmitted, allowing for the spread of strains via the food chain, and they readily colonise in all individuals. Additionally, antimicrobial-resistance genes are frequently transmitted between the different genera and species of the Enterobacteriaceae family.

Carbapenems

For more than 30 years, carbapenems have been used to prevent and treat infections caused by gram-negative bacteria, including the Enterobacteriaceae family. Carbapenems possess the broadest spectrum of activity within the group of β-lactam antibiotics. They have their greatest activity against gram-negative bacteria, and therefore they are often reserved for serious infections and prescribed as a 'last resort' treatment for infections caused by antibiotic-resistant gram-negative bacteria (Public Health England 2013; Yagoubat et al 2017).

There are different types of carbapenemases, of which the New Delhi metallo-β-lactamase-1, Oxacillinase-48-like, *Klebsiella pneumoniae* carbapenemase, imipenem metallo-β-lactamases and Verona integron-encoded metallo-β-lactamase enzymes are currently the most common.

Carbapenemase-producing Enterobacteriaceae

Carbapenemase-producing Enterobacteriaceae (CPE) are defined as any of the Enterobacteriaceae that harbour a gene encoding carbapenemase (a β-lactamase). CPE are resistant to carbapenem antibiotics and often also to many other classes of antimicrobial agents. It has been estimated that CPE have the greatest potential to contribute to the overall problem of antimicrobial resistance (CDC 2018; Doi & Paterson 2015). The resistance of CPE to carbapenems is due to production of a carbapenemase, an enzyme that hydrolyses and thereby inactivates carbapenems and most other β-lactam antibiotics (Doi & Paterson 2015; Public Health England 2013).

CPE are (typically) resistant to nearly all known antibiotics, with very few antibiotics in the development pipeline likely to have activity against them (ASID et al 2018). Infections caused by CPE are of significant concern because they are not only resistant to the usual antimicrobial therapy but also increase patient morbidity and mortality, add to the cost of treatment and have the potential to spread and act as a reservoir of resistant genes for transmission to other organisms.

CPE pose a threat for the dissemination of AMR within health care facilities because they colonise patients' gastrointestinal tracts, and these colonised patients can then act as a reservoir for ongoing transmission to other patients. The colonisation or infection of patients with CPE is emerging as a significant global public health threat. The Irish An Roinn Sláinte Department of Health (2017a, page 5) explains that "[t]he spread of this superbug in hospitals can lead to the closure of beds, wards and units removing thereby, essential capacity to provide services, to admit patients from Emergency Departments and to address waiting lists effectively".

The international situation

Internationally, mortality rates associated with infections caused by CPE and carbapenem-resistant Enterobacteriaceae (CRE) range from 38–57% (Singapore Ministry of Health 2013). The mortality rate associated with the first documented outbreak of CPE in Australia, involving 10 cases identified in the seven months to December 2012, was 40% (Australian Commission on Safety and Quality in Health Care 2017).

While the majority of cases of infection or colonisation by CPE are detected via active surveillance at admission to health care facilities, there is international evidence of an increasing trend of community carriers, particularly in areas where CPE are endemic, such as the Indian subcontinent. Since 2016, CPE have spread rapidly due to global movements, including medical tourism, and through transmission of plasmids carrying the gene from one bacterium to another. Sporadic cases of colonised or infected patients have been reported in a range of countries across most continents. Typically, these patients had recently received health care in a high CPE-burden country.

The situation for New Zealand

In New Zealand, multidrug-resistant gram-negative bacteria, including CPE, increase a patient's risk of developing potentially untreatable infections, and patients with comorbidities are at increased risk of developing an infection and dying as a consequence.

While CPE are not currently considered to be endemic in either New Zealand health care facilities or the wider community, their transmission here is considered to be evolving rapidly, with the window of opportunity to minimise the risk of spread in health care facilities likely to be narrow.

In New Zealand, the rate of CPE carriage and infection has increased sharply in recent years, and while, until very recently, nearly all CPE have been imported from overseas, there is now evidence of secondary spread in the community and in health care facilities.

The consequences of CPE spreading between patients within the New Zealand health care system are very serious. Patients at highest risk would be those most reliant on antibiotics for survival, including those in intensive care units (ICUs); those undergoing treatment for cancers; those undergoing bone marrow and solid organ transplantation; those with complex urological problems and those undergoing major surgery (ASID et al 2018).

Without appropriate active surveillance and infection prevention measures, there is a high likelihood that CPE will spread within residential care facilities in New Zealand. The prospects of CPE spreading in age-related residential care (ARRC) poses a risk, not only to ARRC residents themselves but also to patients in acute care hospitals (due to the frequent movement of patients between these two types of facilities) (ASID et al 2018).

The first appearance of CPE in New Zealand occurred in 2009, with the number of reported cases increasing from 2015 (ESR 2017). This increase can be attributed in part to active surveillance in district health board (DHB) hospitals.

Predominantly, CPE cases in New Zealand have occurred in travellers or repatriated patients from the Indian subcontinent and South East Asia where CPE are likely to have become established in the community as well as in health care facilities. Worryingly, CPE have also been isolated from travellers to high-prevalence areas who have had no health care contact during their trip. And more recently, there have been cases originating from contacts within New Zealand.

The Institute of Environmental Science and Research (ESR) publishes data on CPE on their website monthly and produce comprehensive annual reports.[2] Some key features of the current epidemiology of CPE in New Zealand are as follows.

- The majority (89% in 2017) of CPE identified in New Zealand are isolated from patients who have recently been overseas.
- About two-thirds of these patients had been hospitalised while overseas.
- The Indian subcontinent is the most common source of CPE acquired overseas and appears to be the origin of about two-thirds of the CPE being identified in New Zealand.
- Most CPE are isolated from high-risk patients being screened for multi-drug resistant organisms (MDROs) rather than from patients with infections caused by CPE.
- The most common carbapenemase types identified in New Zealand are the New Delhi metallo-β-lactamase and OXA-48-like carbapenemases, which have, respectively, accounted for 59% and 31% of all carbapenemases identified in Enterobacteriaceae in New Zealand.

There have been a small number of documented episodes of CPE transmission in New Zealand health care facilities. These transmission events have occurred following the admission of an index case who had been overseas, and all events to date have involved only a small number of secondary cases.

[2] Reports are published at: **surv.esr.cri.nz/antimicrobial/AccqEnterobacteriaceae.php**

Roles and responsibilities

Ministry of Health

The Ministry has a key strategic leadership role in managing CPE transmission events.

It is important that the Ministry is informed of any actual or suspected CPE transmissions as soon as possible after such transmissions have been identified. The infection prevention and control (IPC) committee, infectious diseases specialist, clinical microbiologist or ESR must inform the Ministry's Communicable Diseases team at **notifycommdiseases@moh.govt.nz**

The Ministry has overall responsibility for communicating relevant information to the wider health sector and stakeholders.

As required in the event of a novel or serious transmission event, the Ministry will assemble a technical advisory group (TAG) to advise on the specific issue or event. The composition of the group will vary depending on the particulars of the case and would likely include representation from the Ministry's Communicable Diseases team, ESR, the IPCNC, the ARRC sector, the health care facility affected, The New Zealand Microbiology Network (NZMN) and ASID-NZ, as required.

The role of the TAG is to, as required:

- provide advice and guidance on IPC to assist in effectively responding to the transmission event and prevent further transmission[3]
- help communicate information related to transmission event(s)
- help identify and declare a transmission risk area (TRA) (see **Transmission risk area on page 23**)
- support affected health care facility as required.

The Ministry will also be responsible for:

- ensuring that these guidelines are updated regularly
- communicating updated and e-changes to relevant stakeholders (including but not limited to: health care providers, the NZMN, the IPCNC and ASID-NZ
- managing national-level communications in relation to a transmission event
- informing the Minister of Health of CPE situations of concern if appropriate.

[3] This is likely to be minimal for larger health care facilities with access to high-level, in-house IPC expertise, whereas greater input, guidance, support and oversight will be needed for smaller health care facilities or residential care facilities.

Institute for Environmental Science and Research

The Ministry of Health contracts ESR to undertake national AMR surveillance using data from various surveillance systems and sources.

The level of surveillance depends on the pathogen, the prevalence and the extent to which current and/or anticipated levels of AMR threaten human health. The National AMR surveillance programme covers community and hospital AMR.

CPE, as an emerging threat, is an important focus for ESR, and ESR is responsible for collecting, processing and reporting CPE data.[4]

ESR identifies and characterises CPE from samples sent from laboratories, (including hospital and community laboratories), conducts continuous surveillance and reports monthly and annually on the number, characteristics and epidemiology of isolates identified.

This is important to provide a real-time and accurate view of the epidemiology. ESR performs confirmatory testing and molecular epidemiology testing on the isolate to determine the subtype. Basic epidemiological data, including overseas travel and hospitalisation history, is collected for patients with confirmed CPE. Once confirmed, ESR notifies the referring laboratory of the result.

ESR will also send an alert to members of the NZMN and the Ministry's Communicable Diseases team when any of the following triggers are met:

- suspected or confirmed transmission in a health care facility
- identification of identical isolates that are not linked to a single facility
- identification of a novel resistance pattern.

New Zealand Microbiology Network

In 2014, the Ministry contracted ESR to establish and facilitate the NZMN in order to enable a timely and consistent response to issues relating to laboratory testing and to ensure regular communication between microbiology laboratories.[5] ESR provides the secretariat role for the NZMN. The membership includes clinical microbiologists from all DHBs, along with representatives from the Ministry, public health, the Ministry for Primary Industries and ESR.

The NZMN plays an important role in promoting best practice in clinical and public health microbiology, providing support and advice on the surveillance, investigation and management of outbreaks and sharing information across the country on identifying cases of CPE colonisation or infection and the response to them.

[4] The data is held at: https://surv.esr.cri.nz/antimicrobial/AccqEnterobacteriaceae.php

[5] For more information about NZMN, see: www.nzmn.org.nz

District health boards

DHBs are required to take overall leadership and operational responsibility for preventing, managing and controlling CPE in their region. In addition to adhering to the recommendations, requirements and response actions in these guidelines, each DHB should have in place a CPE response plan that identifies the key triggers for regional action, wider reporting and response escalation.

Triggers for implementing the DHB CPE response plan should include identifying:

- an obvious index case
- colonisation or infection in someone who has no known risk factors (for example, a patient who has not travelled overseas to a high-risk country within the last 12 months)
- a patient in an ARRC facility
- a cluster of cases in one facility.

The response plan should include documenting roles and responsibilities for further investigating the source of the infection, tracing and screening known contacts and placing critical resistance alerts into the system. The incident management team should coordinate the response, and this should involve the IPC committee, the clinical microbiologist and the public health unit.

In addition, DHBs should assist and advise residential care facilities in their region as required, on ways to prevent, manage and control CPE. This can include providing:

- access to the DHB's IPC personnel for specific support and advice to residential care facilities if the facility admits a patient who is either colonised or infected with a CPE or who has been identified as a contact of a colonised or infected person
- advice on contact tracing and screening
- advice on environmental screening requirements following the discharge of a patient or resident
- advice on communications for local health practitioner awareness and reporting specific cases or alerts to inform health providers in the district, such as primary health care providers, hospitals and residential care facilities, about the detection and identification of CPE isolates in the district.

Residential care facilities

Residential care facilities need to ensure they:

- know who, how and when to contact IPC services at a regional level for advice when required
- have access to relevant laboratories for testing, surveillance and screening and that results are provided in a timely manner to the facility.

Clinical governance

All health care facilities are required to have clearly identified delegated responsibilities for infection prevention and control. The requirements for an IPC committee or equivalent is set out in the New Zealand Standard, Health and Disability Services (Infection Prevention and Control) Standards: 8134.3.

Membership of the IPC committee or its equivalent should include, but is not limited to, representatives from the relevant clinical disciplines, including IPC specialists, physicians and nurses, antimicrobial stewardship pharmacists, clinical microbiologists, cleaning services, quality improvement teams and senior management. It is also relevant and appropriate to include representatives from, public health units, medical officers of health, residential care facilities or community groups and consumers.

The role of the IPC committee or equivalent is to provide direction and oversight of the organisation's IPC programme. This includes but is not limited to:

- endorsing associated policies and procedures to manage patients colonised or infected with CPE
- establishing and monitoring an active surveillance programme
- enabling the use of transmission-based precautions during the care of the patient
- providing current information about each CPE case to identify the likely source of acquisition and the need for further patient screening
- ensuring that alerts are linked to the patient's National Health Index (NHI) and notifications are sent back to relevant community health providers
- providing strong links with the laboratory to support timely notification to the clinical and IPC committee when CPE are suspected
- providing advice on the management of individual cases and contacts
- auditing and monitoring compliance and reporting to management.

Residential care facilities

In residential care facilities, the clinical governance oversight role may be the responsibility of the clinical nurse manager, but facilities should ensure that formal responsibility for IPC is assigned to an appropriately qualified and prepared nurse (with specialist understanding of IPC), who is supported and provided with the resources to undertake the role.

Transmission and risk factors

Transmission

The most common mode of CPE transmission in the health care setting is through contact with a contaminated environment or contaminated hands (infected or colonised patients or contaminated environmental surfaces being the reservoir). The Australian Commission on Safety and Quality in Health Care guide on CPE (2017) cites evidence that pathogenic organisms have been detected on the hands of 40% of acute care patients 48 hours after admission. This emphasises the critical importance of hand hygiene for patients and staff in preventing transmission.

Transmission can occur from moist environmental sources, and viable organisms have also been found persisting on dry surfaces, such as hospital linen and floors for a long period after contamination. CPE are known to be transmitted by either direct or indirect exposure to contaminated:

- equipment
- solutions
- food and/or water.

Risk factors

International evidence shows that sharing a room with a colonised patient is a risk factor for acquisition of CPE (Wilson et al 2016) and that patients colonised or infected with CPE widely contaminate their immediate patient environment (Australian Commission on Safety and Quality in Health Care 2017).

The risk of infection with CPE is heightened in patients who:

- have recently travelled to areas of high CPE prevalence (especially if hospitalisation occurred), particularly the Indian subcontinent and South East Asia
- are placed in close proximity to other patients who are infected or colonised with CPE
- are more susceptible to infection, particularly if they are immune compromised. These include:
  - patients who have had long periods of hospitalisation, particularly in ICUs, haematology/oncology, severe burns units, renal haemodialysis units and gastroenterology units
  - patients with compromised immune systems requiring intensive and frequent medical care
  - chronically infected patients
  - patients recovering from recent major surgery or interventions (especially solid organ, bone marrow or stem cell transplants)
  - patients with a history of previous multiple, recent or extensive antimicrobial use

- patients with in-dwelling medical devices (eg, vascular and urinary catheters, wound drains)
- residents of long-term ARRC facilities who, due to their age and medical conditions are likely to have experienced frequent episodes of acute health service care (Victoria State Government 2018).

The risk of transmission is increased if carriers of CPE have diarrhoea or incontinence.

Managing transmission of CPE in health care facilities

The specifics of managing transmission of CPE will vary depending on factors such as: local risk and incidence and the nature and level of care provided.

All health care facilities must have an IPC programme in place to prevent, manage or control the spread of health care associated infections, including CPE, all staff should be familiar with these programmes and comply with the requirements of the Health and Disability Services (Safety) Act 2001 and the New Zealand Standard *Health and Disability Services (Infection Prevention and Control) Standards*, NZS 8134.3:2008 – or any subsequent revisions.

Infection prevention and control of CPE should include:

- designating roles and responsibilities
- implementing, monitoring and overseeing measures to establish and maintain CPE control.

Measures to maintain control of the CPE include:

- surveillance:
  - effective active surveillance and screening of patients identified as at risk of CPE colonisation/infection (see **Section 2: Patient assessment: Surveillance**)
  - access to diagnostic laboratory services
- policies and procedures:
  - a process for timely internal reporting to clinical and IPC staff when CPE are suspected/confirmed
  - a process for managing patients with suspected or confirmed infection or colonisation with CPE, including placing the relevant medical warning alerts on the patient's NHI electronic record to manage subsequent admissions
  - documented procedures for conducting periodic audits to ensure that processes are followed
  - communication processes for reporting the colonisation or infection with CPE to other relevant clinicians, such as primary health care providers, other health care facilities or residential care providers to which these patients are being transferred, or when such patients are discharged from an acute care facility

  - an outbreak management plan that incorporates specific actions, including the allocation of staff and resources that is required to respond to an outbreak of CPE
- antimicrobial stewardship (see **below**):
  - access to antimicrobial stewardship expertise
- education:
  - educating all staff about CPE, standard and contact precautions, use of personal protective equipment (PPE), cleaning and disinfection and available resources, such as single rooms and dedicated patient equipment (see Appendix 6).

Antimicrobial stewardship

Acute health care facilities

Acute health care facilities should have an antimicrobial stewardship (AMS) programme in place, as required in the New Zealand Health and Disability Services Standards 2008 (Standards New Zealand Infection Prevention and Control) and as indicated in the *New Zealand Antimicrobial Resistance Action Plan* (Ministry of Health and Ministry for Primary Industries 2017).[6] The AMS plays an important role by limiting exposure of bacteria to antibiotics and thereby reducing the development of resistance. The AMS should include clinical guidelines and protocols for using antibiotics, antifungals and antivirals to ensure that health professionals optimise the use of antimicrobial medicines.

Residential care facilities

Residents of long-term care facilities can act as reservoirs for CPE and can transmit CPE organisms to acute care facilities when patients are transferred between facilities. Preventing transmission in residential facilities such as rest homes can also be challenging.

Residential care facilities should ensure that they have a documented policy on AMS that outlines the responsibility of clinical staff to ensure good stewardship. The policy should cover the points listed under **Managing transmission of CPE in health care facilities above** and also include arrangements for auditing the use of antibiotics in the facility at regular intervals. Community prescribers should seek the advice of clinical microbiologists and/or infectious diseases physicians in their DHBs if they think they need to use one of the last-line broad-spectrum antibiotics, such as fluoroquinolones, and third-generation cephalosporins and carbapenems.

Regional support for residential care facilities should be fostered to encourage staff to access AMS for advice and laboratories for culturing samples to identify the most effective antibiotic treatment.

[6] **www.health.govt.nz/publication/new-zealand-antimicrobial-resistance-action-plan**

Section 2

Patient assessment

All patients in all types of health care facilities that are assessed as requiring CPE screening should be managed in a single room with an en-suite bathroom. If this is not possible, talk with IPC staff to confirm appropriate management. See **Figure 1** below for an example of a patient assessment process.

Standard and contact precautions should be used at all times, with visible signs outside the room until the results of the testing are known.

Patients with a suspected or known CPE should not be placed in a room with high-risk patients, including patients with open wounds, patients with in-dwelling devices, immune compromised patients and long-term patients, however, it may be necessary to group patients who have the same strain of CPE as cohorts. This should only be done following consultation with IPC staff.

Figure 2 provides a flow chart outlining the steps to follow in cohorting patients appropriately.

Figure 1: Patient assessment flow chart

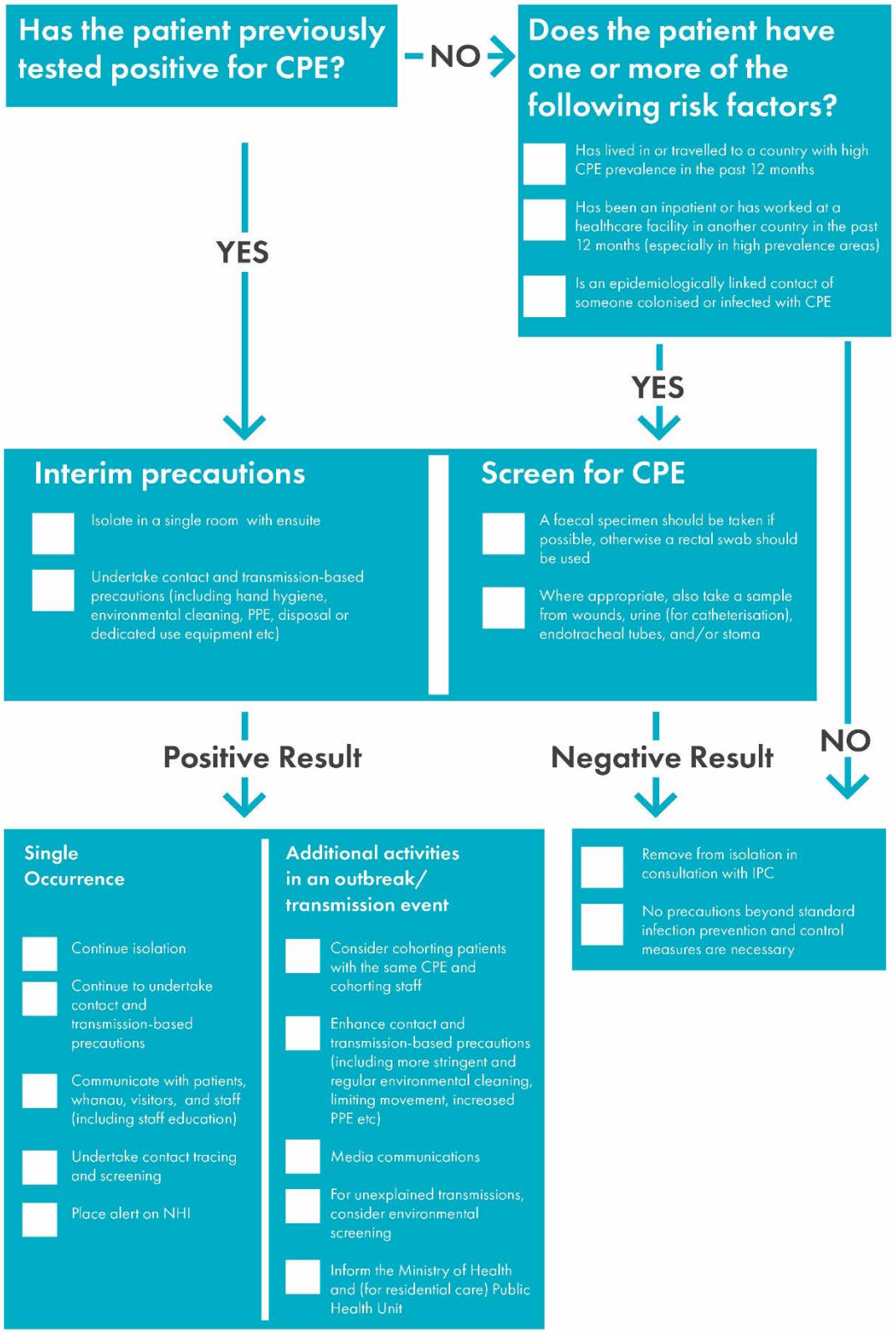
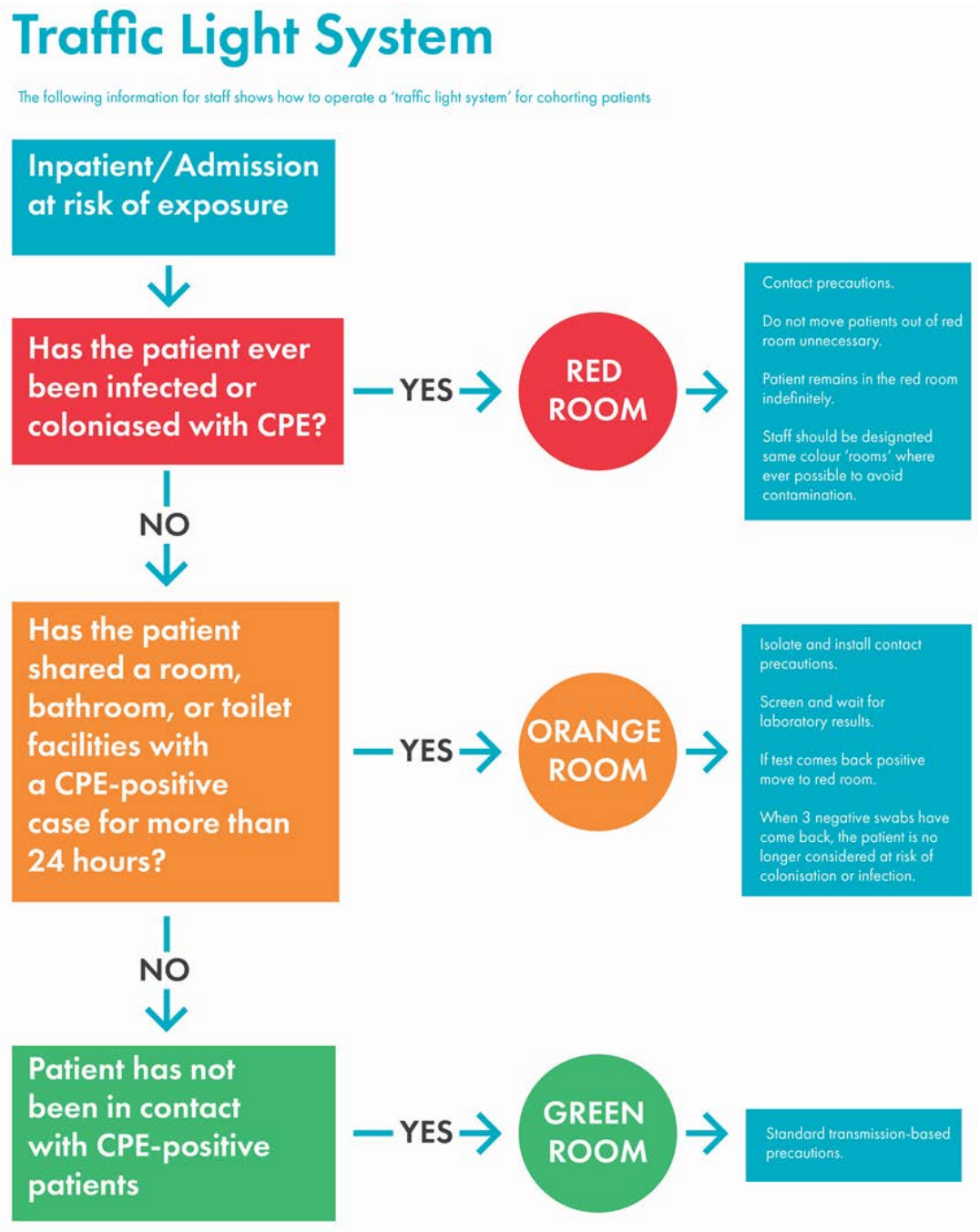


Figure 2: Cohorting flow chart



Patient movement

Unnecessary transfer of CPE-positive patients should be avoided as much as possible, and patients with a suspected or known CPE should be encouraged to stay in their rooms. In acute care, patients with a suspected or known CPE should be kept away from communal areas where possible. It may be necessary for these patients to attend facilities such as an X-ray room or physiotherapy clinic. In this case, the facility should be informed of the patient's status before the visit occurs so that full infection contact precautions can be applied. Following such visits, thorough environmental cleaning and disinfection must be undertaken before any other patients are allowed access to the facility.

CPE-status should not preclude patients from being transferred, but strict contact precautions should be maintained if they do need to be transferred.

It is important to provide information to colonised or infected patients to help them understand why they are in isolation and why their movements is limited.

Additional information for residential care facilities

In residential care, complete social isolation may have harmful psychological effects. Patients with suspected or confirmed colonisation or infection with CPE should be allowed to attend meals and activities provided hand hygiene is observed and any wounds are covered. If the CPE infection is present in the respiratory tract, then the patient should be situated at least 1 metre away from others in the day room. Infected patients who are positive for respiratory CPE may need to wear a mask for activities if unable to perform good cough etiquette.[7]

Screening

Who should be screened?

Patients and their support people should be informed about CPE, the required screening procedures and the implications of a positive result before any screening tests are performed. Patients must give consent for screening. The consent can be verbal and documented in the patient's notes. This applies to all health care facilities.

It is important that the history taken on admission includes the travel history of the patient and their family as well as any hospitalisations.

All patients in the following high-risk patient groups should be screened on admission.

- Patients directly transferred from a health care facility overseas
- Patients who have been hospitalised overseas in the 12 months before admission
- Patients who have travelled within the past 12 months in a high-risk area (currently the Indian subcontinent and South East Asia) even if they have not been hospitalised
- Patients with a history of admission as an inpatient in facilities with known cases of CPE, either in New Zealand or another country
- Patients epidemiologically linked to other cases of CPE (ie, contacts of confirmed cases or those with previous CPE colonisation or infections)
- Patients admitted to acute care from long-term residential care.

The criteria for screening patients should be tailored to maximise the detection of colonised and infected patients while at the same time minimising unnecessary testing. The criteria will be reviewed and modified in response to changes in CPE epidemiology at the local, national and international levels.

[7] If this is not possible due to cognitive impairment or other issues, staff and others in close proximity to the patient should don a mask during the activity.

Additional information for residential care facilities

It is important that the initial assessment of patients or residents in a residential care facility include collecting and recording information relating to the risk factors. The facility's registered nurse must ensure that there are no alerts or information for patients or residents being admitted to the facility that might require further action.

Screening contacts

It is important to ensure that all contacts of identified colonised and infected cases are traced and screened to prevent transmission of CPE. Contacts may include:

- other patients or residents in the health care facility
- family members
- close friends in the community.

Discuss with the IPC team for guidance on how best to approach the matter with people identified in the community.

Acute care facilities

People identified as 'contact cases' in an acute care facility should be individually assessed and a decision to follow up should be made on the potential for ongoing risk of transmission to others. In general, a contact is a person who has shared a room, bathroom or toilet facility with a confirmed CPE case. While the evidence shows a variation in the contact exposure time favouring transmission, an average is 24 hours (Queensland Health 2017).

If the contact has been discharged, then an alert should be attached to their NHI via the national medical warning system to ensure that they are screened upon re-admission to hospital. Reports should be sent to the discharged contact's primary health care provider(s). If the contact is to be transferred to a residential care facility, then the receiving facility needs to be given adequate notice and arrangements must be made for relevant screening. If the contact has already been transferred, then the receiving facility needs to be notified immediately so that they can arrange appropriate screening.

Outpatient screening will vary, depending on an assessment of risk. Outpatient appointments for patients known to be colonised or infected with CPE should be managed in a way that limits contact with others as much as possible, for example, scheduling their appointment for the end of the day.

Residential care facilities

Identification of contacts in residential care facilities requires individual risk assessment. All identified contacts should be screened as outlined above. It is not always necessary to screen all the residents in a wing of a facility where the contact resident or patient is mobile, but someone who shared a room with that person should be screened. In facilities that have shared bathrooms, all residents who used that bathroom should be screened.

Clinical specimens for screening

. The highest sensitivity and specificity for detecting CPE in an asymptomatic patient is a faeces specimen. Where this is not practically or clinically possible, a rectal swab (with evidence of faecal matter on the swab) should be taken. A peri-anal swab is not acceptable because of lower sensitivity and specificity.

In addition, the following samples should be considered.

- For patients with discharging wounds, a single wound swab placed in transport medium should be collected.
- For patients with intermittent or continuous urinary catheterisation, a urine sample should be collected.
- For patients who are intubated, a tracheal aspirate sample should be collected.
- For patients with enterostomies, a stomal specimen should be collected.

Frequency of screening[8]

This information applies to all health care facilities.

High-risk patients should be screened on admission. The IPC service will provide guidance on additional screening depending on the local epidemiology of the CPE. Confirmed cases of CPE are potentially infectious indefinitely.

Environmental screening

Environmental screening (eg, taking samples from equipment, furniture and walls) should be discussed with the IPC team where there is unexplained transmission of a CPE or a possible common source for an outbreak (Wilson et al 2016).

[8] Colonisation has been observed for an average of 144 days (range 41–349 days) in a study of 233 residents of a care home with spontaneous cure being found in only three residents (Mattner et al 2012). Residents who have been identified as colonised or infected with CPE should be re-screened on admission to an acute care facility, but otherwise, re-screening should be done at least annually, followed by a further screen if the initial screen was negative to ensure clearance.

Surveillance

Surveillance will enable the facility to monitor and respond to changes in CPE epidemiology. It will contribute to an accurate picture of the CPE epidemiology at a local, regional and national level and, most importantly, will enable patients colonised or infected with CPE to be managed appropriately. Surveillance is closely linked with screening, which is sometimes referred to as 'active surveillance'.

Systems for effective communication between the microbiology laboratory, the IPC service and the public health unit should be in place to enable prompt identification and management of CPE cases.

Each DHB and residential care facility is required to develop an appropriate surveillance strategy, based on their current epidemiology of CPE colonisation. Further details are presented below. This strategy must include the screening of patients at risk of colonisation on admission and/or following contact with other colonised or infected patients. Documented processes should include:

- identification of the people to be screened
- the type of screening specimen required and when and by whom the specimen should be taken
- the management of the patient(s) whilst the screening results are pending
- monitoring of trends in incidence of CPE in the facility over time to determine if rates are changing and if additional interventions are needed.

All acute hospitals are required to have either laboratories with the capacity to perform testing or access to independent laboratories equipped to undertake testing. They should also provide community-based practitioners with access to their laboratories for diagnostic purposes, for example, general practitioners or residential care facilities. The microbiology laboratory should ensure that:

- their testing meets the minimum standards for laboratory testing as set out in **Appendix 1: Minimum laboratory standards**
- routine laboratory-based procedures to detect organisms from screening and clinical specimens are in place
- a system is in place to ensure that the laboratory communicates evidence of CPE in clinical isolates to the IPC service, the referring clinician and the NZMN in a timely manner
- relevant isolates are referred to ESR for molecular characterisation and typing to maintain a high quality of national reporting and surveillance
- relevant metadata on the case is forwarded to ESR including specimen type from which the organism was recovered and patient travel history in the last 12 months (places travelled and details of health care exposure overseas); if no travel history exists, then provide the travel history of household members

It is recommended that facilities document strategies for following-up findings, including:

- informing relevant people of positive findings: the patient and their family, primary caregivers and health care staff

- investigating the aetiology of the infection after a positive culture has been found, including the travel history of the patient and their family, particularly all the countries visited within the last year
- re-testing the index patient if more than three months have passed since the initial infection was identified
- identifying contacts of the CPE case for follow up with relevant screening.

Infection prevention and control measures

There is strong evidence that most of the individual elements of correctly applied infection control strategies can limit the impact of multi-drug resistant gram-negative organisms by reducing their transmission in health care settings (Australian Commission on Safety and Quality in Health Care 2017).

Standard precautions should be used for the care of all patients all of the time. Such precautions include:

- hand hygiene
- the use of PPE
- the safe use and disposal of sharps
- routine environmental cleaning and disinfection
- reprocessing of reusable medical equipment and instruments
- respiratory hygiene and cough etiquette
- the use of aseptic non-touch techniques
- waste management
- appropriate handling of linen.

Staff education

Education for the prevention and control of CPE should be considered and should always be provided in an outbreak situation. Education may include (but is not limited to):

- the nature of CPE
- the clinical implications of resistant organisms
- risk factors, and how to perform an effective risk assessment
- the importance of good hand hygiene
- the proper use of PPE to prevent transmission
- proper cleaning and disinfection of the environment and equipment
- isolation and cohorting.

See the appendices listed for further information on:

- transmission-based precautions, including contact precautions (**Appendix 2**)
- hand hygiene (**Appendix 3**)
- PPE (**Appendix 4**)
- environmental cleaning and disinfection (**Appendix 5**)
- equipment (**Appendix 6**)
- endoscopes (**Appendix 7**)
- appropriate handling of linen (**Appendix 8**)
- waste management (**Appendix 9**).

Communication

Communication with patients, families, primary caregivers and visitors

Organisations need robust systems for facility-wide reporting and, in particular, for placing alerts in the notes of a patient found to be colonised or infected with CPE. It is important that there is timely, open and effective communication with patients, families, primary caregivers and visitors. At a minimum, these people need to understand:

- the nature of the infection
- what this means for them
- how this will affect the patient's care
- what transmission-based precautions should be undertaken.

Signs and/or information sheets should be placed in appropriate places to ensure that everyone follows appropriate hand hygiene and other contact precautions.

Communication between transferring and receiving facilities

If a patient is transferred from an acute-care facility to a residential care facility, then the receiving facility should undertake admission screening.

If a transferring patient has a suspected or known CPE, the transferring facility should inform the receiving facility of this before the transfer (and with sufficient time for the receiving facility to make necessary arrangements). Communication between facilities and health practitioners should be both verbal and written and include information on the patient's CPE status. Reports should include the dates and results of any relevant clinical and/or surveillance cultures. The receiving health facility should undertake an

assessment of the risk of secondary transmission, taking into account conditions such as diarrhoea, urine or faeces incontinence, wounds with uncontrolled drainage or medical devices that the patient may have.

If a patient is diagnosed with CPE infection or colonisation, the facility should immediately notify any subsequent healthcare facilities that this person may either be attending or being transferred to. All contacts should be appropriately followed up.

If CPE-positive patients are to be transferred to a non-inpatient setting or aged residential care facility, an IPC management plan should be in place beforehand. Before discharge into the community, the patient's primary health care provider and the public health unit needs to be informed of the patient's status, and the patient and any relevant care giver(s) should be provided with relevant information on how to manage the CPE infection.

It is important to note that not all residential care providers can access NHI data on patients that they admit, therefore DHBs cannot assume that alerts entered on the patient's NHI record will necessarily be picked up by wider community providers.

Media communications

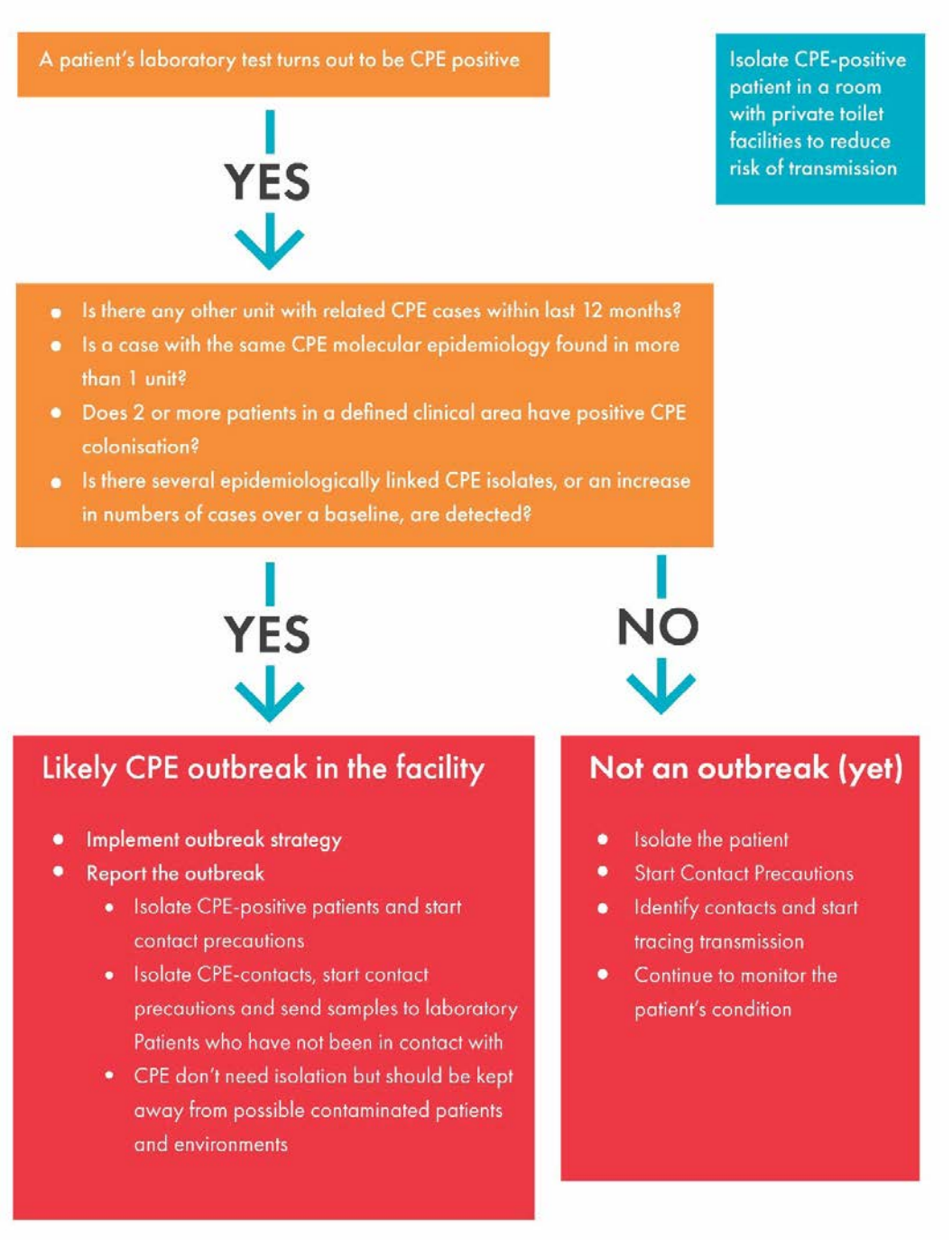
All health care facilities should have a clearly articulated policy on handling media communications. Media communications should come from the DHB, which takes overall responsibility for local leadership and operational management of any outbreak in its district. The DHB communications staff should work with the IPC committee, public health unit (if the outbreak is not within the DHB) and the Ministry's Communicable Diseases team in ensuring the quality and timeliness of all communications.

The Ministry, in its national leadership role, will help with media communications regarding outbreaks in order to ensure that all communications are aligned.

CPE outbreaks

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, for example, two or more linked cases of CPE with the same molecular epidemiology. In some cases, a single case of CPE may be classified as an outbreak. Figure 3 below outlines the process for discerning if an outbreak has occurred.

Figure 3: Flow chart for determining whether there is an outbreak or not



Transmission risk area

A transmission risk area (TRA) is an area (a distinct geographical area or ward) in which local transmission has been determined to have occurred. An area should be declared a TRA if:

- there are two or more confirmed cases of the same CPE, and
- at least one case is a locally acquired case, and
- there is a plausible epidemiological connection between the cases

or

- where acquisition from an environmental source is hypothesised, clustering in time and place without a direct patient-to-patient epidemiological link.

Outbreak management plan

All health care facilities should have outbreak management plan suitable for use if a CPE outbreak occurs. The IPC committee and TAG should ensure a facility's plan is fit for purpose.

The plan must be implemented as soon as an outbreak is confirmed. At a minimum, the plan should involve:

- declaring a TRA
- identifying a nominated point of contact (in an acute health care facility, this is usually the IPC clinical nurse specialist) to receive reports and manage communications with other relevant departments
- intensifying surveillance, screening and reporting processes
- ensuring that the microbiology department is adequately resourced to manage the additional testing
- implementing processes and resources for communicating with staff, patients and visitors
- activating processes for enhancing transmission-based precautions, including hand hygiene, environmental cleaning, the use of PPE and disinfection procedures
- mobilising provisions to ensure suitable expertise, capability and capacity are available to respond to the outbreak
- ensuring processes are in place for de-escalating the outbreak management measures.

Additional information for residential care facilities

The entire residential care facility should be considered a TRA in most cases. Exceptions may occur if residents are located in separate buildings or geographically distinct areas and there is limited resident movement between these locations.

Table 1: Summary of outbreak measures

	Acute care	Residential care
Surveillance	• Increase monitoring and reporting of trends. • Ensure all cases are thoroughly investigated – including the aetiology of the infection.	• Increase monitoring and reporting of trends. • Ensure all cases are thoroughly investigated – including the aetiology of the infection.

	Acute care	Residential care
Screening	• If any colonised or infected patients remain as inpatients in a TRA, or were discharged within the past four weeks, a weekly point prevalence screen (PPS) for CPE should be performed on ward patients until there have been two consecutive weeks of negative screens. If all colonised or infected patients have been discharged for at least four weeks, a one-off PPS should be performed. • Where an environmental source is identified or suspected, environmental screening may be appropriate.	• All residents should be screened as soon as an outbreak has been identified. • While the facility remains a TRA and there are residents colonised or infected with CPE, a weekly point prevalence screen (PPS) for CPE should be performed on residents until there have been two consecutive weeks of negative screens. If all colonised or infected patients have been discharged for at least four weeks, a one-off PPS should be performed. • Where an environmental source is identified or suspected, environmental screening may be appropriate.
Contacts	• All TRA contacts discharged before clearance criteria are met should be screened and have alerts placed on their medical record. • All contacts who are discharged before clearance criteria are met, should be screened and be informed either electronically or via post or given of their status and risk factors. This includes TRA contacts who were discharged before the transmission was identified. • Report to any health care or residential care facilities where contacts have been transferred before clearance to enable the receiving facility to screen those contacts, place alerts and consider further action if required.	• All residents discharged before clearance criteria are met should be screened and have alerts placed on their medical record (through the public health unit). • All contacts who are discharged before clearance criteria are met, should be screened and be informed either electronically or via post or given of their status and risk factors. This includes TRA residents who were discharged before the transmission was identified. • Report to any health care or other residential care facilities where contacts have been transferred before clearance to enable the receiving facility to screen those contacts, place alerts and consider further action if required.
Transfer within or between health care facilities	• When transferring within or between facilities, screen contacts on discharge or within 24 hours of transfer. • Inform the receiving ward or facility in writing that the patient is a contact and must be placed in contact precautions until cleared. • Avoid unnecessary transfers within and between facilities.	• When transferring within or between facilities, screen contacts on discharge or within 24 hours of transfer. • Inform the receiving ward or facility in writing that the patient is a contact and must be placed in contact precautions until cleared. • Avoid unnecessary transfers within and between facilities.

	Acute care	Residential care
Movement within facilities	• Movement within the facility should be limited.	• Movement within the facility should be limited. • Residents colonised or infected with CPE should have limited interaction with other residents and communal areas while the facility remains a TRA.
Communication	• Situational reports should be provided to the relevant public health unit and the Ministry's Communicable Diseases team with agreed frequency or need. • Staff education on transmission-based and contact precautions, the nature of CPE and CPE risk factors should be increased in an outbreak. • All patients and visitors in the TRA should receive information on CPE, their risks and effective hand hygiene. • The TRA should be clearly identified, with clear signs that provide key information on transmission prevention requirements. • Liaise with the Ministry on media matters.	• Reports should be sent to the relevant public health unit, NZMN and the Ministry's Communicable Diseases team. • Staff education on transmission-based and contact precautions, the nature of CPE and CPE risk factors should be increased in an outbreak. • All residents and visitors should receive education on CPE, their risks and effective hand hygiene. • The TRA should be clearly identified, with clear signs that provide key information on transmission prevention requirements. • The Ministry will liaise and coordinate media responses as required.
Patient/ resident placement	• Patients colonised or infected with CPE should be isolated in a single room with en-suite where possible. • When single rooms are not available, patients who are infected or colonised with the same CPE (and no additional CPE or MDROs) may be grouped in the same room. • If cohorting is undertaken, consider increasing the space between patient beds. • PPE should be changed between interactions with patients. • If bathrooms are shared, then residents colonised or infected with CPE should shower last in the day. Enhance cleaning regimes, especially toilets and frequently touched surfaces. • In an outbreak, consider grouping staff to prevent the transmission of CPE within the TRA or to other units or wards.	• Residents colonised or infected with CPE should be isolated in a single room with en-suite where possible. • When single rooms are not available, residents who are infected or colonised with the same CPE (and no additional CPE or MDROs) may be grouped in the same room. • If cohorting is undertaken, consider increasing the space between resident beds. • PPE should be changed between interactions with patients. • If bathrooms are shared, then residents colonised or infected with CPE should shower last in the day. Enhance cleaning regimes, especially toilets and frequently touched surfaces. • In an outbreak, consider grouping staff to prevent the transmission of CPE within the facility.

	Acute care	Residential care
Endoscopes	• Endoscopes should be screened/microbiologically tested if more than one patient with confirmed CPE is found to have had a common exposure to an endoscope.	

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Appendix 1: Minimum laboratory standards

All diagnostic microbiology laboratories must have in place minimum laboratory standards for detecting CPE from clinical samples and active surveillance specimens. Diagnostic laboratories are expected to follow the *Minimum Laboratory Requirements for the Detection of Carbapenemase-producing Enterobacteriaceae from Clinical Samples and Screening Specimens,* which were published by the New Zealand National Antimicrobial Susceptibility Testing Committee (NZNAC) and endorsed by The New Zealand Microbiology Network (NZMN) (NZNAC 2018).

Aim

The aim of the *Minimum Laboratory Requirements for the Detection of Carbapenemase-producing Enterobacteriaceae from Clinical Samples and Screening Specimens* is to provide a minimum requirement for the laboratory detection of carbapenemase-producing Enterobacteriaceae (CPE) in New Zealand and to ensure laboratories can identify when confirmatory testing, referral of isolates and notification to clinical and infection prevention teams is required.

Background

There are several different mechanisms by which Enterobacteriaceae can develop resistance to carbapenem antibiotics.

Acquired carbapenemases (carbapenem-hydrolysing enzymes) are of most concern because their genetic determinants are mainly carried on plasmids and therefore can transfer between strains, species and genera.

It can be difficult to detect CPE because:

- not all carbapenem resistance is due to carbapenemase production, and
- not all carbapenemase producers are phenotypically resistant to carbapenems using standard antimicrobial susceptibility testing (AST) breakpoints.

Other mechanisms of carbapenem resistance, such as extended-spectrum beta-lactamase (ESBL) or AmpC beta-lactamase production, combined with porin loss (commonly seen in *Enterobacter* spp) or efflux mechanisms, are not readily transferable between strains. Such non-carbapenemase-producing, carbapenem-resistant Enterobacteriaceae (non-CP CRE) do not pose the same infection prevention and control risk. Laboratories must therefore be able to identify organisms with acquired carbapenemases and differentiate them from isolates with other mechanisms of carbapenem resistance in order to help clinicians make appropriate treatment decisions and implement appropriate infection prevention measures. Also key to improving the patient's outcome is the timely provision of accurate susceptibility data to support directive therapy.

Laboratories should maintain a high index of suspicion for CPE based on clinical presentation, epidemiological risk factors (such as overseas travel and hospitalisation) and susceptibility testing results. A low threshold for further confirmatory testing of suspect isolates, either locally or by referral to another laboratory, should be maintained.

These laboratory requirements outline procedures for detecting CPE in clinical specimens (see **Clinical isolates** below) and CPE screening samples (see **CPE screening samples** below). Laboratories may need to modify their testing processes or increase their testing capacity in order to meet these standards.

Scope

Laboratory detection of acquired carbapenemases in Enterobacteriaceae.[9]

Not included

- Carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*
- Organisms with intrinsic carbapenemases, such as *Stenotrophomonas maltophilia* and *Aeromonas* spp
- ESBL or AmpC beta-lactamase detection in Enterobacteriaceae
- Environmental and veterinary samples

[9] The authors acknowledge the recent changes in taxonomy that have resulted in several genera formerly included in the family Enterobacteriaceae now being included in other families in the order *Enterobacterales*. However, the term Enterobacteriaceae is used in this document but should be considered to cover all genera now included in the order *Enterobacterales*.

Clinical isolates

Antimicrobial susceptibility testing and using an indicator antimicrobial for CPE

All diagnostic laboratories should have the capability to perform antimicrobial susceptibility testing (AST) in accordance with methods recommended by either the European Committee on Antimicrobial Susceptibility Testing (EUCAST) or the Clinical and Laboratory Standards Institute (CLSI). The most recent versions of these methods should be used.

All clinically significant Enterobacteriaceae isolates should be screened for the presence of a carbapenemase, using an indicator antimicrobial as part of routine AST. Subsequent additional confirmatory testing should be performed where the indicator antibiotic indicates it is necessary.

The suggested indicator carbapenem is meropenem since it offers the best balance of sensitivity and specificity for the detection of CPE.

Recommended CPE screening method for all hospital and community specimens

Test an indicator carbapenem (meropenem) against all clinically significant Enterobacteriaceae isolates

or

Test an indicator carbapenem (meropenem) against all clinically significant Enterobacteriaceae isolates that have decreased susceptibility to cefpodoxime, ceftriaxone or ceftazidime

or

Test an indicator carbapenem (meropenem) against all clinically significant Enterobacteriaceae isolates that are resistant to cephalexin. (This is the least specific option for detection of CPE, but may be considered where a carbapenem or third-generation cephalosporin is not tested as part of first-line AST.)

Where there are epidemiological risk factors for CPE (such as overseas travel or hospitalisation, previous-known CPE colonisation or a household member with CPE), Enterobacteriaceae isolates resistant to amoxicillin-clavulanate, should also be considered for meropenem susceptibility testing.

Urine direct susceptibility testing

Laboratories performing direct susceptibility testing (DST) on urine samples should ensure that a valid inoculum is achieved before reading and reporting susceptibility results. Any invalid results should be repeated using a controlled inoculum to avoid inaccurate susceptibility results. This has particular relevance when reading the indicator antimicrobial zone diameters.

Indicator carbapenem interpretive criteria

Laboratories are advised to use the EUCAST carbapenemase screening criteria, which offers sufficient sensitivity for CPE detection in low-prevalence settings such as New Zealand. Organism identification to species level is required for valid interpretation of AST, including CPE screening criteria.

Additional confirmatory testing (see **Confirmatory testing for CPE** below) should be performed on all Enterobacteriaceae isolates where:

- meropenem MIC >0.12 mg/L, or
- meropenem disc zone diameter <25 mm, or
- meropenem disc zone diameter 25–27 mm, if also resistant to piperacillin-tazobactam (and/or temocillin),[10] or
- automated AST system (eg, Vitek 2, Phoenix) indicates decreased susceptibility to meropenem or that a carbapenemase may be present. Note, where the lowest meropenem concentration tested does not allow interpretation according to the criteria outlined above, an additional step may be required to meet these minimum standards. For example, laboratories using Vitek 2 AST should consider manual meropenem AST and/or additional confirmatory testing for isolates with meropenem MICs ≤0.25 mg/L that are also resistant to a third-generation cephalosporin and piperacillin-tazobactam. Enterobacteriaceae with reduced susceptibility to ertapenem, but remaining fully susceptible to meropenem, do not routinely require further testing for CPE.

[10] For *Enterobacter, Serratia, Citrobacter freundii, Proteus vulgaris, Providencia and Morganella* species, the clinical microbiologist may exercise discretion regarding the need for further testing if resistance is likely to be due to a combination of AmpC de-repression and porin deficiency (eg, when there is no co-resistance to other antibiotic classes and resistance develops progressively during antimicrobial therapy).

CPE screening samples

Clinical selection criteria should be applied in line with local infection prevention procedures and in accordance with national CPE guidance documents.

Recommended samples

A faeces specimen or rectal swab with visible faecal material are the minimum recommended sample types for CPE screening.

Additional samples types should be considered where appropriate, in line with local and national infection prevention guidance documents, that is:

- urine, if symptomatic or urinary catheter/nephrostomy/stent in situ
- swab from wounds and insertion sites of invasive medical devices and catheters
- lower respiratory tract specimens, if intubated.

Laboratory methods for detecting CPE from screening samples

Culture-based methods

Selective culture is the most commonly used methodology for detecting CPE in screening samples. There is currently no consensus best-practice culture medium for this purpose, but the use of a commercially available, selective chromogenic media is recommended. Laboratories should note that these media vary in their performance for detecting the different types of carbapenemases.

Based on the epidemiology of CPE in New Zealand, laboratories should utilise media capable of detecting CPE with low carbapenem MICs (such as OXA-48/OXA-48-like producing isolates). This may require using two different selective media.

MacConkey agar with a carbapenem disc is inferior to screening with chromogenic media and is not recommended as the sole screening method.

Any Enterobacteriaceae growth on CPE screening agar should have AST (including meropenem) performed, followed by confirmatory testing as required (see **Confirmatory testing for CPE** below).

Molecular methods for detecting carbapenemase genes direct from a screening sample

Currently commercially available molecular CPE test panels detect the most common carbapenemase genes. Less common carbapenemase types will not be detected, and therefore, culture-based screening may also be required where there is high clinical suspicion for a CPE genotype not included in the molecular panel available.

Clinical samples in which CPE resistance genes are detected directly should have reflex culture performed to obtain an isolate for identification and susceptibility testing.

Confirmatory testing for CPE

Confirmatory testing for the presence of carbapenemase or a carbapenemase gene may be performed locally or by referral to a second laboratory with the necessary expertise. Accurate organism identification to species level is mandatory for isolates that require CPE confirmatory testing.

Confirmatory testing for isolates from invasive infection should be regarded as urgent, with results available as soon as possible, and within 24 hours. Confirmatory testing for screening or community isolates may be considered less urgent but should still be available promptly and within three working days. Primary diagnostic laboratories should have agreed referral protocols in place to ensure compliance with these requirements.

There are many available methods for confirmatory testing; extensive evaluation studies of the various methods have been undertaken elsewhere and are not included in this document.

Phenotypic methods

Suitable phenotypic methods include:

- colorimetric tests, using pH-related colour change due to hydrolysis of the indicator carbapenem (eg, CarbaNP, BlueCarba)
- carbapenem inactivation method (CIM) or modified CIM (mCIM)
- combination disc testing (eg, MAST D70C)
- immunoassays for detecting carbapenemases (eg, Resist-3 O.K.N for detecting OXA-48-like, KPC and NDM carbapenemases).

The modified Hodge test is no longer recommended due to difficulties in interpretation and lack of sensitivity and specificity.

Isolates with a positive phenotypic carbapenemase test will also require genotypic confirmation by a molecular method, either by local testing or referral to ESR.

Isolates with a negative phenotypic carbapenemase test but with a high clinical suspicion for CPE (due to epidemiological risk factors) may require additional testing using a molecular method.

Molecular methods

Commercially available molecular platforms detect the most common carbapenemase types, which account for more than 95% of CPE. Since less common carbapenemase types will not be detected on these platforms, if a high suspicion for CPE remains despite a negative molecular test, a phenotypic carbapenemase test and/or referral to ESR is advisable.

Notification

All laboratories must have a documented procedure for notifying all suspected and confirmed CPE isolates.

For patients in a health care facility, all confirmed CPE isolates must be notified as soon as possible and on the same day to:

- the treating clinician and
- the supervising clinical microbiologist and
- the infection prevention and control (IPC) team.

For community patients (not in a health care facility), all confirmed CPE isolates must be notified as soon as possible and on the same day to:

- the supervising clinical microbiologist

and by the next working day to:

- the treating clinician and
- the IPC team.

All possible or suspected CPE isolates must be notified on the same day to the supervising clinical microbiologist whilst awaiting confirmation. Onward notification to the clinician and IPC team is at the discretion of the clinical microbiologist and should take into account the likelihood of CPE and potential clinical risk.

Reporting

- Enterobacteriaceae isolates confirmed by molecular methods to carry a carbapenemase gene should be reported as a 'carbapenemase-producing Enterobacteriaceae (CPE)'.
- Carbapenem-resistant isolates with a positive phenotypic test may be reported as a 'probable carbapenemase-producing Enterobacteriaceae (CPE), awaiting confirmation'.
- Non-carbapenemase-producing, carbapenem-resistant Enterobacteriaceae (non-CP CRE) isolates should **not** be reported as 'carbapenemase-producing Enterobacteriaceae (CPE)' in order to maintain differentiation from CPE.
- Similarly, terms such as carbapenemase-producing organism (CPO) and carbapenem-resistant organism (CRO) should **not** be used for confirmed carbapenemase-producing Enterobacteriaceae.

Referring isolates to ESR

All suspected or confirmed CPE isolates should be referred to ESR's Antimicrobial Reference Laboratory, Kenepuru, Porirua, for confirmation and typing, including:

- all isolates confirmed as CPE using a molecular method
- Enterobacteriaceae isolates with a positive phenotypic carbapenemase test but confirmatory molecular testing is negative or not done
- Enterobacteriaceae isolates with decreased carbapenem susceptibility from patients with risk factors for CPE but isolate negative in phenotypic carbapenemase test and molecular test (if done).

Isolates do not require referral to ESR where there is a low index of suspicion and the carbapenemase confirmatory test is negative, such as AmpC beta-lactamase-producing Enterobacteriaceae (eg, *Enterobacter*,) with decreased susceptibility to meropenem and/or ertapenem.

When isolates are referred to ESR for confirmation, in addition to the information requested on the standard ESR referral form (see: **www.esr.cri.nz/assets/Test-Forms/ESR0039-Single-Human-Source-Specimen.pdf**), laboratories should also supply:

- full antimicrobial susceptibility test results for the isolate, including printout from Vitek or similar if available and
- risk factor information, in particular any details of recent overseas travel and hospitalisation for the patient or close household contacts and
- molecular testing results (if available).

ESR should aim to confirm that the isolate is a CPE within three working days of receipt. Any positive results should be reported to the referring laboratory as soon as possible and on the same day that results are available.

Storing isolates

All confirmed CPE isolates will be stored by ESR on referral. Primary diagnostic laboratories are also advised to store isolates for surveillance purposes for a minimum of six months.

Carbapenemases in non-Enterobacteriaceae

Detection of carbapenemases in non-Enterobacteriaceae isolates is beyond the scope of this document. However, laboratories must be aware that transferable carbapenemases do also occur in species such as *P. aeruginosa* and *A. baumannii*. As such, laboratories are advised to follow EUCAST or CLSI guidance to determine when further confirmatory testing or referral to ESR should be performed.

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Appendix 2: Transmission-based precautions

Transmission-based precautions are used in addition to standard precautions for patients who may be infected or colonised with certain infectious agents for which additional precautions are needed to prevent infection transmission. Transmission-based precautions include:

- contact precautions
- droplet precautions
- airborne precautions.

They aim to reduce the risk of transmission of epidemiologically important microorganisms via different routes.

Contact precautions

Are used when there is a risk of direct or indirect contact transmission of infectious agents that are spread by direct or indirect contact with the patient or the patient's environment. Contact precautions include:

- appropriate patient placement
- appropriate use of PPE
- limitations on transport and movement of patients
- use of disposable or dedicated patient-care equipment
- cleaning and disinfection of the rooms used by infected patients.

All patients with suspected or confirmed CPE should be managed using contact precautions for the entire length of their hospital stay.

Residential care facilities

Residential care facilities differ from other health care settings in that the residents, who are often more susceptible to infection anyway, remain in the facility for long periods of time, and many see the facility as their home.

Social interaction is very important for the health and mental well-being of long-term residents, who are encouraged to interact with other residents. It is important that infection control methods in residential care facilities acknowledge the resident's psychosocial needs while limiting transmission.

The use of standard precautions is an essential infection control strategy for successfully preventing and minimising transmission of all infections between residents and will also protect staff from transmitting infection.

Contact precautions for residents who are colonised or infected with CPE are also required, and these should focus on avoiding contamination from care workers hands, shared equipment and the facility's environment.

Appendix 3: Hand hygiene

This information applies to all health care facilities.

Effective hand hygiene is critical for preventing and controlling CPE.

The Health Quality and Safety Commission (HQSC) oversees compliance rates of hand hygiene in acute care settings including running campaigns, publishing information and auditing and reporting on national compliance three times a year. The HQSC statistics show significant improvement since 2012 (Health Quality & Safety Commission New Zealand 2017).

Appropriate non-touch techniques should be used for all clinical procedures.

Every health professional should perform hand hygiene in accordance with the Hand Hygiene New Zealand programme (HQSC)[11] and the World Health Organization's (WHO's) hand hygiene guidance[12].

- **before** patient contact
- **before** a procedure
- **after** a procedure or body fluid exposure/risk
- **after** patient contact
- **after** contact with patient surroundings.

Hand hygiene includes hand washing with liquid soap and water and/or the use of alcohol-based hand hygiene products if there is no visible soiling.

The type and length of fingernails and the wearing of jewellery can affect hand hygiene. Artificial fingernails and extenders should be avoided.

Patients should be strongly encouraged to clean their hands after toileting, before eating and before leaving their room. Visitors should clean their hands before and after visiting a patient. If visitors are assisting with patient care, then they should perform hand hygiene in accordance with the Hand Hygiene New Zealand programme guidance (see the **Clean Hands Visitor poster**). If they are visiting more than one patient, then they should visit the CPE infected patient last.

If a patient's cognitive state is impaired, staff caring for them must be responsible for helping with the patient's hand washing.

[11] For more information, visit: www.hqsc.govt.nz/our-programmes/infection-prevention-and-control/projects/hand-hygiene

[12] http://www.who.int/infection-prevention/en/

All health care facilities should regularly audit all staff hand hygiene against the WHO standards.

Hand Hygiene New Zealand programme resources are available at:
https://www.hqsc.govt.nz/our-programmes/infection-prevention-and-control/projects/hand-hygiene/marketing-resources/

World Health Organization hand hygiene tools and resources are available at:
http://www.who.int/infection-prevention/tools/hand-hygiene/en/

Additional information for residential care facilities

All staff in residential care facilities should always comply with the hand hygiene standards. In residential care facilities where residents are in long-term care but are also more independent, the staff need to take extra care to ensure that the residents themselves and their visitors understand the importance and principles of good hand hygiene and each room is supplied with a hand basin, liquid soap and disposable paper towels.

It has been estimated that 50–75% of residents in ARRC facilities have some level of decreased cognitive ability. Therefore, there is more onus on staff in such facilities to supervise or help with hand washing. This is particularly important in specialised dementia units.

The IPC nurse should conduct regular staff audits of hand hygiene practices.

Appendix 4: Personal protective equipment

This information applies to all health care facilities.

Health care workers must wear the appropriate personal protective equipment (PPE), including gloves and gowns whenever they have contact with a patient who is colonised or infected with CPE. Hand hygiene must be performed before donning PPE. (All staff should be educated on how to don and doff PPE).

At a minimum:

- disposable impervious long-sleeved gowns and gloves should be worn by health care workers attending patients with a CPE
- for CPE with a respiratory source of transmission, surgical masks and eye protection should be worn by staff and visitors
- PPE should be put on outside and removed inside the patient's room and placed directly into infectious/medical waste bins
- PPE should be removed in a manner that prevents self-contamination or self-inoculation or environmental contamination with contaminated PPE or hands
- the most heavily contaminated items should be removed first (i.e., gloves)
- hand hygiene must be carried out after removing PPE.

In acute care situations, in line with contact precautions, PPE should always be worn when providing clinical care.

Visitors are not required to wear PPE unless they are assisting patients with activities such as toileting and showering.

Additional information for residential care facilities

In residential care facilities, PPE should be worn if there is a perceived risk of CPE colonisation or infection. At a minimum, PPE should be worn if there is active infection. In ARRC facilities, where many of the residents have cognitive deficiencies, there are extra challenges. PPE should not be kept outside the patient's room but should be provided at point of care.

Appendix 5: Environmental cleaning

The risk of transmission means that it is imperative that equipment and surfaces be cleaned regularly. Health care facilities all need to have well-articulated and detailed cleaning schedules, and all cleaning staff need to be aware of the requirements.

This information applies to all health care facilities.

CPE can spread from a patient to the surrounding environment, which then becomes a vector for transmitting the CPE further within a health care facility. One international study found that the contamination of the hospital environment with resistant organisms was implicated as a source of CPE acquisition in at least five hospital outbreaks in recent years. The contaminated environments were mainly within bathroom and water environments and included contaminated sinks, a wastewater drainage system, patients' toilets and a damaged patient mattress (Victoria State Government 2018).

Cleaning in health care facilities, regardless of whether there are known CPE cases, is essential in preventing and controlling transmission of CPE and resistant bacteria in general. There should be documented policies and procedures for cleaning, disinfection, sterilising and reprocessing reusable medical devices (if applicable) and equipment that comply with the New Zealand Standard *Health and Disability Services (Infection Prevention and Control) Standards*, NZS 8134.3:2008.[13]

Health care facilities should have cleaning schedules. For cleaning to be effective, it is essential that it is undertaken frequently and regularly, and regular cleaning audits are strongly recommended (Lerner et al 2013). The Victorian Cleaning Standards provide a useful audit checklist (Victoria State Government 2011).

Routine environmental cleaning should include:

- cleaning the patient's environment daily (including frequently touched surfaces and patient care equipment)
- cleaning surfaces when visibly soiled
- cleaning surfaces following every known spillage
- giving the room a final clean following the departure of a patient who had a known or suspected CPE (including cleaning and disinfecting mattresses).

[13] See: www.standards.govt.nz/assets/Publication-files/NZS8134.3-2008.pdf

* Unless medically unable to, health care staff should wear a mask.

Cleaning and disinfecting the rooms and furniture of patients on contact precautions need special attention. Frequently-touched surfaces, such as door handles, bedrails, over-bed tables, toilets and commodes, will need to be cleaned and disinfected more often than once a day and before another patient uses the area. Disinfectant should be fit for purpose, effective against a broad range of organisms and procured through appropriate channels.

Terminal cleaning following a patient's discharge needs to follow the same cleaning procedure and should include all room surfaces as well as furniture and bedding. Cleaning staff should receive education and training to undertake a terminal clean and should be familiar with the correct process for donning and doffing PPE.

Additional information for residential care facilities

In residential care facilities, particular care must be given to the regular and thorough cleaning of items such as bedrails, tables and commodes, and when an infected resident is discharged or transferred to another facility.

If the colonised or infected resident uses a shared bathroom, then all surfaces touched need to be cleaned thoroughly after each use and before use by another resident. If shared showers are used, then the infected resident should be showered last, possibly in the evening, and the shower should be thoroughly cleaned afterwards with a suitable product. It can be challenging to clean carpeted areas appropriately, and this task needs to be undertaken with extra care. Carpets should be steam cleaned when necessary and following discharge or patient transfer.

Appendix 6: Equipment

This information applies to all health care facilities.

A minimum amount of equipment should be taken into the room of a patient who has a known or suspected CPE infection.

To eliminate the risk of CPE being transmitted through shared equipment, single use or dedicated-use equipment should be used for patients with a known or suspected CPE where possible.

If this is not possible, equipment should be subject to thorough cleaning and disinfection (for example, using a two-step or 2-in-1 cleaning and disinfection process). Disinfection should occur away from the immediate bed area in designated cleaning sinks and should **not** be done in sinks designed for hand washing. Advice on cleaning specific equipment should be sought from IPC personnel.

The treatment of equipment must meet the New Zealand Standard *Health and Disability Services (Infection Prevention and Control) Standards*, NZS 8134.3:2008; the ISO 15883 (washer disinfectors) standards and the Australian/New Zealand Standard, *Reprocessing of reusable medical devices in health service organizations* AS/NZS 4187:2014.

Appendix 7: Endoscopes

Instruments, such as endoscopes, when used on patients infected with CPE, can become contaminated and serve as vectors for transmitting infection to other patients unless correctly reprocessed. Reported endoscopic transmission of CPE has been predominantly related to instruments with complex tips, such as duodenoscopes and linear echoendoscopes, but all endoscopes can potentially transmit CPE. To prevent these instruments from serving as vectors for infection transmission, health care facilities are required to implement policies and procedures for reprocessing all endoscopes according to guidelines that meet the following standards: *Infection control in Endoscopy Consensus Statements on Carbapenemase-Producing Enterobacteriacea* (GESA et al 2017).

Endoscopic procedures on patients colonised or infected with CPE should be avoided as much as possible. If needed, then they must only be performed in facilities where there is a capacity and capability for staff to reprocess the endoscopes correctly. All endoscopes, except those in sterile packaging, should be stored in TGA-approved forced-air drying cabinets. Following an endoscopic procedure on a known CPE-positive patient, the instrument should undergo microbiological testing and be quarantined until a negative culture result is obtained following incubation for 48 hours.

Additional information for residential care facilities

Where possible, all equipment used for patients with suspected or confirmed colonisation or infection with CPE should be single-use and discarded after use.

Residential care facilities should ensure that all shared equipment, such as patient hoists, wheelchairs and commodes are kept for the sole use of the infected resident and not used for another resident until they have been thoroughly cleaned and disinfected. If equipment cannot be cleaned or disinfected to an adequate standard to eliminate the risk of transmission, it should be disposed of.

Appendix 8: Appropriate handling of linen

This information applies to all health care facilities.

Used linen is potentially contaminated with pathogens. It is important that no linen or bed coverings are shared between patients and that they are kept for the sole use of the infected patient and thoroughly laundered after the patient's discharge or transfer to another facility. Linen must be handled in a way that avoids contamination and stored in a manner that reduces risk of cross-contamination from dirty to clean items. Gloves should be worn when handling infected linen.

Health care facilities should follow their policies/guidelines on handling soiled and infected linen and linen used by a patient who has a known or suspected CPE infection.

Additional information for residential care facilities

In residential care facilities, clothing and linen from an infected or colonised resident should be handled as above and kept separately. Where residents' clothing is synthetic and cannot be washed in hot water, it should be washed on an extra-long cycle. If washing is taken by the resident's relatives to be dealt with at home, the facility should provide the relatives with full information on appropriate washing instructions and how to avoid transmission. All staff should be educated about the correct way to handle potentially infectious linen in order to avoid microbial transmission.

Appendix 9: Waste management

Health care facilities should follow their policy/ guidelines on the appropriate way to dispose of contaminated waste and be familiar with the New Zealand Standard *Management of Healthcare Waste*, NZS 4304:2002.