# Assessing Evidence of Transmission and End of Transmission of Carbapenemase Producing Enterobacterales[1] (CPE)

**CPE Expert Group**

**National Guidance Document, Version 1.0**

**Scope of this Guidance**

This guidance is intended for infection control specialists working in the acute hospital sector. Additional guidance or to confirm that you are using the most current version of this guidance, please go to www.hse.ie/hcai and www.hpsc.ie

**Next review of this guidance document**

This guidance document will be reviewed in 12 months (May, 2019).

[1] Recent changes in microbial nomenclature have altered the meaning of the term "*Enterobacteriaceae*" and mean that the term "Enterobacterales" now corresponds more closely to the former meaning of "*Enterobacteriaceae*".

# Table of Contents

## Glossary of Terms

**CPE** = Carbapenemase Producing *Enterobacterales*

The following in alphabetical order are some of the more common carbapenemase enzymes. There are a number of other carbapenemase enzymes.

**IMP:** Imipenemase

**KPC:** *Klebsiella pneumoniae* carbapenemase

**NDM:** New Delhi metallo-beta-lactamase

**OXA:** Oxacillinase-type carbapenemase (OXA-48 is the common variant)

**VIM:** Verona Integron-encoded metallo-beta-lactamase

**ED** = Emergency Department

**IPC** = Infection Prevention and Control

**NCPERL** = National CPE Reference Laboratory

**OCT** = Outbreak control team

## Scope

In some cases it is readily apparent that CPE transmission has occurred in a hospital because two or more patients clearly linked in space and time, for example patients in adjacent beds in the same ward, are identified as having the same type of CPE. However the nature of CPE is such that transmission is not always easy to recognise. This document is intended to support Infection Prevention and Control (IPC) and Public Health practitioners in assessing evidence of possible CPE transmission in an acute hospital or other healthcare facility providing a similar intensity of care.

What follows in each section applies equally to hospitals and to other healthcare facilities providing a similar intensity of care.

Haemodialysis facilities should be considered as providing an intensity of care similar to an acute hospital.

This document is also intended to assist in determining when transmission can be considered to have ceased.

## Definition of CPE

For the purpose of this document CPE is a member of the family *Enterobacterales* in which one of the recognised carbapenemase genes or enzymes, such as IMP, KPC, OXA-48, NDM or VIM, has been confirmed by a validated laboratory method.

Isolates of Enterobacterales with resistance to a member of the carbapenem family of antimicrobial agents **by other mechanisms or by an unconfirmed mechanism** do **NOT** meet the definition of CPE for this purpose. Such organisms may however require transmission based precautions as multi-drug resistant organisms.

The document should be considered in association with related HSE policy documents concerning CPE specifically "*Requirements for Screening of Patients for Carbapenemase Producing Enterobacterales (CPE) in the acute hospital sector, Version 1.0, February 2018*"; "*Acute Hospital Carbapenemase Producing Enterobacterales (CPE) Outbreak Control Checklist, Version 1.0, March 2018*"; and "*Interventions for Control of Transmission of CPE in the Acute Hospital Sector, Version 1.0, April 2018*".

The documents are available at the following link:

http://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/strategyforthecontrolofantimicrobialresistanceinirelandsari/carbapenemresistantenterobacteriaceaecre/guidanceandpublications/

## Introduction

The term Enterobacterales is used to describe families of bacteria normally found in the human bowel/enteric tract. The sharing of mobile genes (generally on plasmids) between Enterobacterales enables them to make enzymes, called carbapenemases such as IMP, KPC, OXA-48, NDM and VIM. When this happens, they are called carbapenemase producing Enterobacterales (CPE). CPE are generally resistant not only to a critical family of antimicrobials, known as carbapenems, but usually to many other antimicrobial agents also.

It is important to note that the mobile genes that convert bacteria into CPE can spread not only between bacteria of the same species (for example, from one *Escherichia coli* to another *Escherichia coli*) but also between different species of Enterobacterales (for example, from *E. coli* to *Klebsiella pneumoniae*). This is the basis of a fundamental difference between CPE outbreaks and most other outbreaks. In most outbreaks all the affected patients have the same species of bacteria or virus (for example, all patients involved in an outbreak of methicillin-resistant *Staphylococcus aureus*) but in CPE outbreaks multiple different species of bacteria can be involved.

# The challenges in identifying potential CPE transmission in an acute hospital

## Screening

Because CPE are mostly carried asymptomatically in the bowel, it may not be known that a person is carrying CPE unless a rectal swab or faeces specimen is taken to screen or check for CPE (See HSE policy "Requirements for Screening of Patients for carbapenemase producing Enterobacterales (CPE) in the Acute Hospital Sector, Version 1.0, February 2018"). If the national CPE screening policy is not implemented in an acute hospital, this increases the risk that CPE carriers will not be detected and that CPE may therefore be more likely to spread and evidence of transmission more difficult to detect.

## Patient movement

For many reasons, patients will move from place to place when they are admitted to a hospital and may spend varying amounts of time in each place, from hours to days or weeks. Journeys include: From the emergency department (ED) to a ward; from ward to ward; between rooms on a ward; and from the ward to other departments such as the operating theatre, radiology, endoscopy etc.. Therefore, the epidemiological links between CPE cases may be difficult to identify even with careful review of patient journeys. In many cases, association with the hospital or haemodialysis unit alone is sufficient to declare a potential CPE outbreak.

## Hospital length of stay

The length of stay in hospital is getting shorter. Some patients may have been discharged before a potential contact with a CPE case or link to a CPE outbreak is identifiable.

### Undetected CPE

Transmission of CPE from patients with undetected CPE colonisation or from contamination of the patient environment may explain cases of CPE in settings where the source of CPE is not apparent.

### First case not necessarily the first patient

The first CPE case identified may not be the first patient with CPE in the hospital. Without careful review of a patient's journey prior to CPE detection, other cases might be missed.

### Different microorganisms with the same type of carbapenemase

A highly transmissible plasmid is often involved, for example, a plasmid carrying OXA-48, which is readily exchanged between different Enterobacterales. This means that two patients with different species of Enterobacterales producing the same type of carbapenemase (for example, one OXA-48 producing *E. coli* and one OXA-48 producing *Klebsiella pneumoniae*) and with different antimicrobial susceptibility patterns might indicate a CPE outbreak.

### Robust laboratory testing protocol required

A robust local microbiology laboratory testing protocol is essential to ensure that CPE can be picked up from screening and clinical specimens and reported rapidly to the infection prevention and control team and confirmed as quickly as possible (either local confirmation or confirmation by the national reference laboratory service). Timely confirmation of a suspected CPE case is important, because the carbapenemase type, such as IMP, KPC, OXA-48, NDM or VIM, may be the key to identifying a potential link between CPE cases.

## Robust local surveillance system required

A robust local surveillance system is vital to ensure that all new suspected and confirmed CPE cases are carefully reviewed by the Infection Prevention and Control Team (IPCT) in a timely manner. This allows the team to determine quickly any potential association with the hospital or haemodialysis unit. This process is vital to early identification of potential increased CPE incidence, which may warrant further investigation.

## Comparison of isolates required

Patients in whom CPE is detected by validated direct molecular methods should be considered in the same way for infection prevention and control purposes as patients from whom CPE has been detected by conventional culture. Laboratories should attempt to culture the organism from such patients to facilitate comparison of isolates.

## The challenges in associating a newly-detected CPE patient with the acute hospital

Many of the challenges in identifying potential CPE transmission outlined in the previous section are also challenges to identifying potential association between a newly detected patient with CPE and a particular hospital.

### First case not necessarily the first patient

Sometimes a microbiology specimen taken from a patient in the context of investigating suspected infection (for example, urine, wound swab or blood culture) might be the first specimen found to contain CPE. If there are no previous microbiology specimens from that patient during the hospital stay, it may be difficult to determine exactly where the patient acquired the CPE.

### Low levels of CPE (CPE not detected)

A patient could be admitted to hospital carrying CPE at very low levels, which might be below the threshold of detection of the CPE screening test in use and therefore be reported as “CPE not detected” on admission screen. Subsequent antimicrobial exposure confers a survival advantage for CPE, enabling them to multiply and become more readily detectable on a subsequent CPE screen. Thus a patient may appear to have acquired CPE recently whereas in fact they have carried CPE for some time but it has only recently become apparent.

### Time lag before CPE becomes detectable

It may be very difficult to determine when a person picked up CPE, because it can take several weeks after contact before CPE becomes detectable from a screening specimen.

### No antimicrobial susceptibility testing performed

A diagnostic specimen with mixed growth (and including Enterobacterales) may not have antimicrobial susceptibility testing performed in the absence of relevant clinical information to support infection. If CPE is detected from a screening or diagnostic specimen taken from the same patient at a later date during the same admission, it may be impossible to determine if one of the bacteria in the earlier sample was CPE.

### CPE contacts

A patient who is identified as a CPE contact of a newly-confirmed CPE case may be screened for the first time as a CPE contact. In the event that the CPE contact is subsequently confirmed to also be a CPE case, a careful review is recommended. The possibility that the CPE contact was actually the source of transmission for the index CPE case needs to be considered.

### The quality of the sample

The quality of the diagnostic or CPE screening specimen will influence the likelihood of recovery of CPE from that specimen and in turn the validity of the test results. If an initial sample is not of good quality, a subsequent correctly-taken specimen that tests positive for CPE may appear to be a newly acquired CPE associated with the specific hospital.

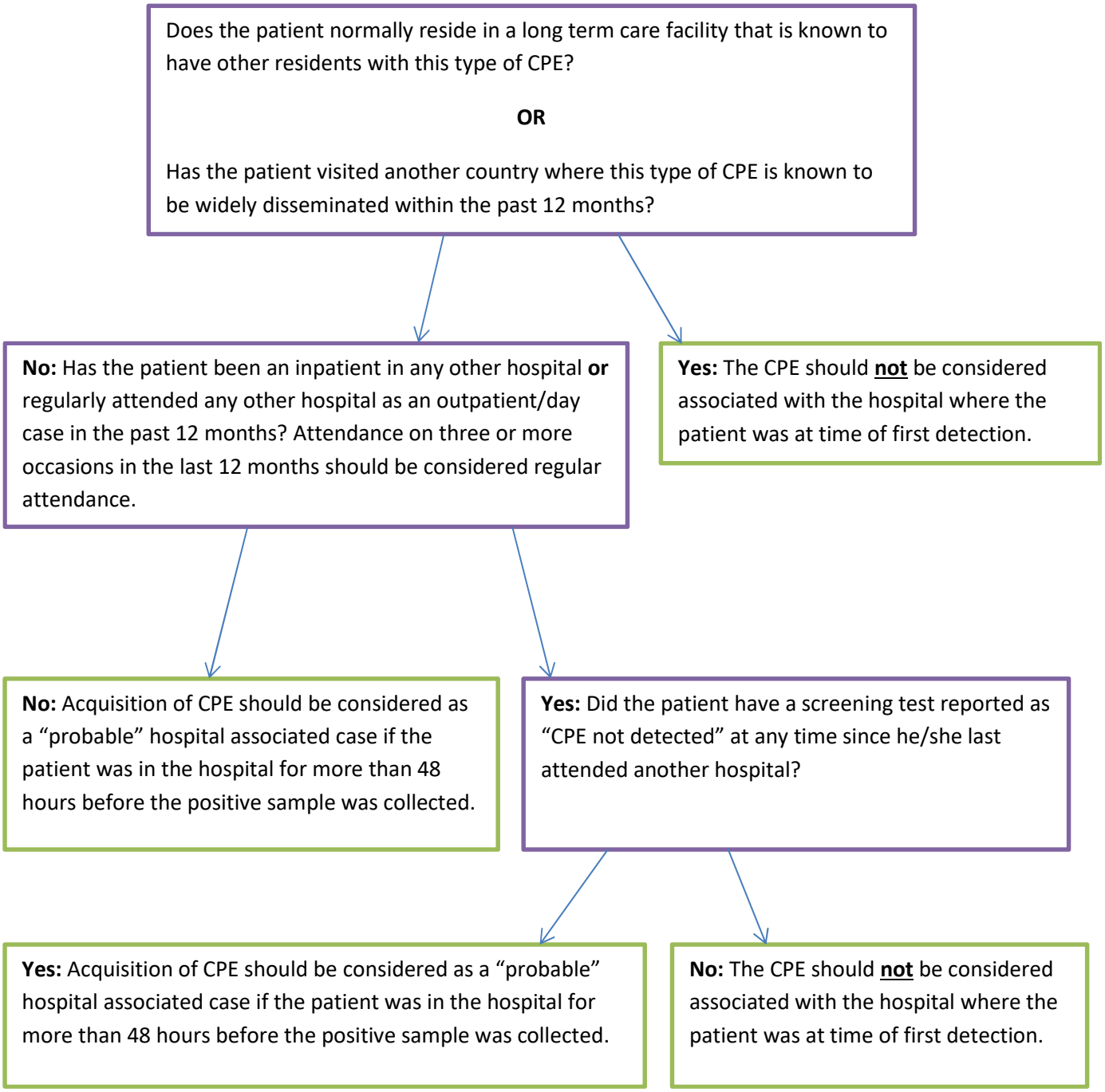
Given these limitations it is very often impossible to say with confidence where or when CPE was acquired. In the context of this uncertainty this document is intended to provide a consistent approach to making a determination about where CPE was acquired to support recognition of transmission (an outbreak).

## How is association of a CPE isolate with the hospital defined?

1. Have you identified **two or more** patients who have been an inpatient in your hospital or attended your facility in the three months prior to CPE detection with “the same type of CPE”? For this purpose “the same type of CPE” refers to the specific type of CPE such as IMP, KPC, OXA-48, NDM and VIM. Organisms of different species with the same genetic mechanism of resistance should be considered as “the same type of CPE”.

2. To establish for each individual patient whether they should be considered as probably associated with a specific hospital or facility, apply the algorithm on the next page.

## Algorithm to determine if CPE is probably associated with your facility



Bear in mind that other patients who do not fulfil these criteria may possibly be associated with the same hospital. In the context of established evidence of transmission (an outbreak), it is generally preferable to assume that any patient with newly-detected CPE of the outbreak type from a screening or diagnostic specimen taken on day three or later after admission to the hospital/first dialysis is considered as probably associated with the hospital unless there is persuasive evidence to the contrary.

In some cases molecular typing of isolates and or plasmids may provide important evidence that makes a link between particular CPE isolates and particular hospitals or haemodialysis facilities more or less likely and should be discussed with colleagues at the National CPE Reference Laboratory Service (NCPERLS).

## The criteria for possible/probable CPE transmission

**Possible** CPE transmission: Two newly-confirmed CPE cases of the same type, such as IMP, KPC, OXA-48, NDM, VIM, etc., detected within a three month period and deemed to be probably associated with the hospital or haemodialysis unit is considered possible CPE transmission (outbreak).

**Probable** CPE transmission: Three or more newly-confirmed CPE cases of the same type, such as IMP, KPC, OXA-48, NDM, VIM, etc., detected within a three month period and deemed to be probably associated with the hospital or haemodialysis unit is probable CPE transmission (outbreak).

## Next steps when the criteria for possible/probable CPE transmission are not fulfilled

When latest available evidence does not fulfil criteria for possible or probable CPE transmission, the situation should be kept under close review as outlined above.

## Next steps when the criteria for possible/probable CPE transmission are fulfilled

An outbreak control team (OCT) should be convened by the Hospital Manager to assess the evidence and to consider what further action is required. The Medical Officer of Health must be informed in accordance with legislation. Please also inform the National Lead for HCAI/AMR and the Consultant Microbiologist at HPSC and refer to HSE documents guiding the control of transmission as outline above.

## Determining whether CPE transmission in a hospital has abated or ceased

In addition to a generic epidemic curve of all newly-detected CPE patients, a curve limited only to cases assessed as probably associated with the hospital should also be prepared along with measurement of the interval since the last case assessed as "probably" associated with the hospital.

Progress is assessed as a decline in the number of newly-detected CPE patients "probably" associated with the hospital. Given that the interval from CPE exposure to detection may be up to four weeks (or longer), one should anticipate that it may take four weeks from the time of making an intervention to observing a change in detection of new "probable" hospital associated cases.

A period of 90 consecutive days without a newly detected CPE patient assessed as a "probable" hospital associated case should be considered as reasonable evidence that transmission has ceased.

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