Guidance Relating to Carbapenemase Producing Enterobacterales[1] (CPE): Interventions for Control of Transmission of CPE in the Acute Hospital Sector

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 (April, 2019).

Footnote[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*".

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Glossary of Terms

AMAU = Acute Medical Assessment Unit

Cohorting = Cohorting refers to accommodation of two or more patients in a space that they share with each other, but which is separate from space used by other patient

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 most common variant)

VIM: Verona Integron-encoded metallo-beta-lactamase

ED = Emergency Department

Isolation = Isolation refers to accommodation of one patient in a single room

***Note:** 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*".

Background

Managing transmission of antimicrobial resistant bacteria in an acute hospital setting is very challenging**.** This document is intended to support hospitals in focusing on those measures likely to be necessary to control spread of CPE and other antimicrobial resistant bacteria, accepting that in some cases they may be very challenging to implement and may impact on continuity of overall service.

Infection prevention and control activities, particularly in the context of an outbreak are usually multi-faceted or delivered as a bundle, making it difficult to determine which components of a response are most important. As in many other areas of healthcare, practice may be based, of necessity, on consensus and expert opinion; because formal research studies to evaluate the evidence as to the relative importance of individual components of a bundle of interventions is often not available.

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

The documents are available at the following link:

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

The challenges with CPE

CPE is not a homogenous group of organisms. Although sub-classification of CPEs may be confusing, the distinctions are important. The more common categories of CPE are IMP, KPC, OXA-48, NDM and VIM as listed above in the Glossary of Terms. Two of these, NDM and VIM, are metallo-beta-lactamases. This means the enzyme has a metal ion at the active site. The other three enzymes do not have a metal enzyme at the active site. Although treatment options are limited for all CPE, including IMP, KPC, OXA-48, the treatment options are frequently even more limited for metallo-beta-lactamase-producing *Enterobacterales,* such as NDM and VIM. This means that cohorting patients who are suspected to be, or are confirmed to be, carrying different categories of CPE must be avoided to prevent spread of different categories of CPE between patients.

Note: 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.

What is meant by isolation?

Isolation refers to accommodation of one patient in a single room, ideally with an *en-suite* toilet.

If a single room does not have access to a dedicated toilet, a commode should be dedicated to that room and decontaminated after each patient use. The commode must be in good condition so that it can be effectively cleaned.

Note: Wherever possible, the equipment to be used for the care of the patient should be single-use or dedicated for that patient's use only, for example, blood pressure cuff, stethoscope.

What is meant by cohorting?

Cohorting refers to accommodation of two or more patients in a space that they share with each other, but which is separate from space used by other patients.

In the context of CPE, effective cohorting means

- Cohorted patients have separate toilet facilities restricted to their use. One toilet per four cohorted patients should be the minimum acceptable. If practical, each patient should be assigned a preferred use toilet (colour code) to minimise mixing.
- Toilet facilities used by cohorted patients are cleaned at least hourly between 7am and midnight and contact surfaces are wiped by trained staff with disinfectant wipe after every patient use.
- If a cohort area does not have access to a dedicated toilet, a commode is dedicated to the cohort area and decontaminated after each patient use.
- Cohort areas have good spacing between beds (2.4 metres between bed centres). When choosing a cohort area, where possible, the multi-bedded area should use the minimum number of beds, for example, two, rather than four or six-beds.

Note: Equipment used for cohorted patients should be single-use, or named patient use only, for example, blood pressure cuff and stethoscope. If this is not feasible, for example, for larger items, equipment should be dedicated to the cohort area and decontaminated after each patient use.

Patient Accommodation

In all acute hospitals, clinical areas used to accommodate patients, including areas for isolation or cohorting, should undergo periodic formal audit of the environment including of the toilet facilities by the Infection Prevention and Control Team (IPCT), with regard to the number of toilets and the general standard of available facilities.

One toilet per four patients should be considered the minimal acceptable standard.

If toilet facilities are lacking, the provision of additional toilet facilities should be addressed as a matter of urgency.

The quality of environmental cleaning should also be audited regularly.

What CPE scenarios does this guidance cover?

There are different scenarios in a patient's healthcare journey. This guidance will consider three of the most common CPE scenarios encountered in the acute hospital:

1. CPE contact
2. CPE cases: suspected or confirmed
3. CPE Outbreak. See also the CPE Outbreak Checklist

The distinction between the different carbapenemase categories and the different CPE clinical scenarios has practical implications for patient management in the hospital setting, as outlined below.

1. CPE Cases: suspected or confirmed

What is meant by the term CPE case?

A **CPE case** is a patient from whom CPE has been detected from a diagnostic specimen (invasive, non-invasive infection or colonisation) or from a CPE screening specimen (rectal swab or faeces).

Depending on local microbiology laboratory resources, once the presence of a carbapenemase is suspected, further confirmation that a carbapenemase is present is required using validated molecular or immunological techniques:

- In the event that laboratory confirmation can be performed on-site, the suspected carbapenemase may be rapidly confirmed, with the patient categorised as a **confirmed CPE case**.

- In the event that the suspected CPE isolate cannot be confirmed on site, there may be an interval while awaiting confirmation whereby a patient is a **suspected CPE case** for some time.

Recommended inpatient accommodation for a suspected CPE case

To stop the onward spread of CPE, it is recommended that an inpatient **suspected CPE case** is accommodated in an isolation room or designated cohort ward, along with other suspected CPE cases of the same CPE category while they remain in the acute hospital setting.

Suspected CPE cases, pending confirmation, should **NOT** be cohorted with **confirmed CPE** cases**.**

Recommended inpatient accommodation for a confirmed CPE case

To stop the onward spread of CPE, it is recommended that an inpatient **confirmed CPE case** is accommodated in an isolation room or designated cohort ward, along with other confirmed CPE cases that have the same category of carbapenemase, for example, OXA-48 with OXA-48, while they remain in the acute hospital setting.

Confirmed CPE cases should **NOT** be cohorted with other confirmed CPE cases **if their carbapenemases are of different categories,** for example, OXA-48 with NDM.

Recommended nurse/healthcare worker allocations for the care of CPE cases

It is recommended that CPE cases be cared for by nursing and healthcare assistant staff who are **not** engaged with care of non-CPE cases for the duration of their duty shift.

2. CPE Contact

What is meant by the term CPE Contact?

For the purposes of this guidance document, a **CPE contact** is a person who

1. Has shared a multi-bed area and/or shared toilet facilities with a person identified as colonised or infected with CPE. This includes time spent in the Emergency Department (ED) and Acute Medical Assessment Units (AMAUs). In general, consideration of a patient as a contact should mean that they have shared an in-patient clinical space or with a CPE patient **for at least four hours**, but it is not possible to apply a simple rule in all cases. For the purpose of this document trolleys or chairs in Emergency Departments used by patients undergoing active clinical treatment or evaluation should be regarded as in-patient clinical space.
2. Has been cared for in an inpatient area (including ED and AMAU) by nursing staff who were simultaneously caring for one or more patients colonised with CPE in the absence of Contact Precautions. This might arise in relation to a patient who was not known to be colonised with CPE at the time in question.
3. A person who has shared a waiting area, for example in out-patients or ED waiting areas or other spaces not related to treatment or evaluation, need not normally be considered as contacts however infection prevention and control practitioners may consider that under particular circumstances it may be appropriate to use a broader definition of contacts.

Being a CPE contact does **NOT** mean that the person has acquired CPE. Being a CPE contact **increases the chance** that a person has acquired CPE, so there is a need to

- Inform the patient
- Test them multiple times for CPE while they remain an inpatient or if they present again to the acute hospital services (see national requirements for screening)
- Take particular precautions with the patient, particularly with those who remain inpatients or have frequent attendance at hospital

Experience to date suggests that among those CPE contacts who have acquired CPE colonisation it may take several weeks from the time of contact until CPE is detectable from a rectal swab/faeces specimen. This has important implications for control of transmission. For example, a CPE contact who is reported as 'CPE not detected' on sequential screening specimens taken within one or two weeks after exposure to a CPE case, but who becomes positive on the third week after exposure will most likely have been shedding CPE for some days during the interval between the second and third swab. Experience suggests that this may be a key vulnerability in efforts to control CPE transmission.

Recommended inpatient accommodation for a CPE contact

To stop the onward spread of undetected CPE, inpatient CPE contacts should be accommodated in an **isolation room** or **designated cohort ward** along with other CPE contacts while they remain in the acute hospital setting. These measures should apply throughout the period during which they are considered a CPE contact (see document on requirements for screening).

Contacts of CPE cases with different categories of carbapenemases should **NOT** be cohorted together. For example, the contact of a known OXA-48 CPE case should not be cohorted with the contact of a known NDM CPE case.

If a CPE contact accommodated in a cohort area develops diarrhoea or becomes incontinent, it is advised the patient is moved from the cohort to an isolation room and investigated for diarrhoea. A 'CPE Contact' isolated for diarrhoea should remain in the isolation room until they have formed stool for more than 48 hours. When diarrhoea has resolved they may return to the cohort area but should not return to the general in-patient area (non-cohort area) while still considered a contact.

Recommended action in the event a CPE contact subsequently has a positive test result

1. The patient is no longer considered as a CPE contact but as a CPE case and should be managed as per the recommendations for a CPE case.

2. If the patient who is now a CPE case had been cohorted with other CPE contacts, the patient should be promptly transferred out of the cohort area and accommodated in accordance with the guidance for a confirmed CPE case.

Recommended nurse/healthcare worker allocations for the care of CPE contacts

It is recommended that patients categorised as CPE contacts who are being cohorted are cared for by nursing and healthcare assistant staff who are **not** engaged with care of non-cohort patients for the duration of their duty shift.

CPE Outbreak

What is the definition of a CPE outbreak?

A **CPE outbreak** is considered as **two or more** linked cases of CPE (infection and/or colonisation).

CPE outbreaks can be difficult to recognise early. Please see relevant guidance document on assessing if transmission of CPE has occurred in a hospital and on assessing whether transmission has ceased.

Recommended action in the event a CPE outbreak is suspected or confirmed

1. Outbreaks of infectious diseases **MUST** be notified to the local Department of Public Health under Irish Infectious Diseases Regulations. For guidance, refer to http://www.hpsc.ie/notifiablediseases/whotonotify/

2. In addition to notifying the Department of Public Health of the CPE outbreak, the hospital should also inform the following: **National Lead for HCAI/AMR** and the **Consultant Clinical Microbiologist at the HPSC**.

3. An outbreak control team should be convened by the by the most senior manager (CEO or GM) to assess what further action is required.

IMPORTANT

Cohorting of patients who fall into different clinical scenarios, for example, CPE contact, suspected CPE case or confirmed CPE case, or patients with differing confirmed carbapenemases, for example, OXA-48 and KPC, should be avoided.

What are key considerations for CPE outbreak control?

The following are required for effective control of ongoing CPE transmission in the context of an outbreak in an acute hospital setting.

This list of measures is not exhaustive and additional measures may be required depending on the setting and extent of the outbreak. See also the separate document: Acute Hospital CPE Outbreak Control Checklist.

Communications

1. Frequent meetings of an outbreak control team lead by the most senior manager (CEO or GM) and with active participation by the Clinical Director and Director of Nursing.
2. Regular, open and effective communication with staff, patients, the hospital group, other hospitals and healthcare facilities, including nursing homes, the relevant Department of Public Health, general practitioners and the wider community to ensure full support for efforts to control the outbreak.
3. Ensuring that patients already known to be colonised or infected with CPE are readily identified on readmission. If possible this process should be based on use of information technology systems.
4. Control access to the ward (or hospital) and ensure reasonable control of visiting consistent with respect for the patients need for partner/family/close friend/pastoral support. Provide information and support for visitors to adhere to practices that reduce their risk of acquiring CPE or of spreading CPE especially hand hygiene before visiting and after leaving the patient's bedside.

Infection Prevention and Control

1. An adequately resourced IPC and antimicrobial stewardship service.
2. Effective implementation of Standard Precautions for all clinical care, in particular, for high compliance with the five moments of hand hygiene, using alcohol-based hand

rub.

3. Identification of patients infected with CPE by appropriate diagnostic testing and of those colonised with CPE by performing CPE screening, in accordance with national screening requirements.
4. Ensuring that in-patients considered “CPE contacts” remain isolated or cohorted throughout the period during which they are considered contacts, that is until they have been categorised as CPE negative.
5. A CPE contact who is cohorted with other CPE contacts and who converts to CPE positive is no longer categorised as a contact but as a case. The patient should be promptly transferred out of the contact cohort area and accommodated in accordance to the guidance for a confirmed CPE case.
6. Ensuring that patients in a cohort area who develop diarrhoea or become incontinent are promptly isolated until they have formed stool for more than 48 hours.
7. Ensuring that movement of CPE cases and contacts within the hospital is limited. Transfer of patients from ward to ward should be avoided except where required to facilitate isolation/cohorting or where essential to provide appropriate patient investigation or care. Where movement for investigations, for imaging or surgery for example, is required the receiving department should be informed so that measures to reduce risk of CPE transmission are in place.
8. Ensuring that toilet facilities that are shared by CPE contact patients in the cohort area have contact surfaces wiped with disinfectant wipe after every patient use and are cleaned at least hourly between 7am and midnight.

Stewardship

1. As antimicrobial consumption is likely to be an important factor in sustaining colonisation with and shedding of CPE, antimicrobial stewardship should be enhanced in hospitals with ongoing CPE transmission. Antimicrobial prescribing decisions related to CPE colonised or infected patients should be discussed with a clinical microbiologist or infectious disease physician.

Staffing

1. Ensuring CPE cases are cared for by staff designated to care ONLY for CPE cases during their shift. Staff allocation should take into account healthcare worker staffing, skill-mix, CPE prevalence on a ward and patient needs.
2. Ensuring that isolation and cohort areas have a higher ratio of staff to patients (patient care and cleaning staff) than that which applies in most circumstances, in particular if the patients have high care requirements.

Environment and Infrastructure

1. Ensuring inpatient accommodation of suspected and confirmed CPE cases, and CPE contacts is assigned in accordance with this guidance document.
2. Ensuring cohort areas have adequate spacing between beds (2.4 metres between bed centres) in multi-bed areas and that multi-bed areas are the smallest available units, for example, a two bed rather than a four bed unit.
3. Ensuring that to the greatest extent possible isolation and cohort areas have dedicated patient equipment for each room and bed space. Small portable items (blood pressure cuffs, stethoscopes etc.) should not be taken from bed to bed.
4. Ensuring that all areas used for isolation or cohorting of patients colonised or infected with CPE, or "contacts", should be reviewed to assess if they have adequate numbers and standards of toilet facilities. Where these are lacking, the practicality of retrofitting additional toilet facilities should be assessed as a matter of urgency. One toilet per four patients should be considered the minimum acceptable in this setting and each patient should if practical be assigned a preferred use toilet (colour coded) to minimise mixing.
5. Ensuring effective cleaning and conventional decontamination of surfaces in isolation and cohort areas is performed at least twice daily. Frequent contact surfaces may require more frequent cleaning particularly in toilets.
6. Ensuring that the quality of maintenance and cleaning of isolation and cohort space is audited regularly. Environmental sampling for CPE may be of value as an adjunct to such audits.

Where there are issues implementing these recommendations

Full implementation of these recommendations will be difficult for all hospitals and may be impossible in some hospitals, where physical infrastructure is such that isolation, cohorting and access to designated toilet facilities cannot be undertaken as required.

In situations where these recommendations are not/cannot be fully implemented, control of onward CPE transmission is likely to be less effective, take longer to achieve and there is a higher likelihood of failure. In particular, adequate numbers of and adequate standard of toilet facilities are key requirements.

While adherence to the recommendations of the guidance is strongly advised for control of onward CPE transmission, in the event of insufficient local access to isolation rooms or suitable cohort facilities, prioritisation of patients with CPE for isolation is generally as follows:

1. Patient with confirmed CPE with diarrhoea, incontinence of faeces or behavioural disturbance that may increase likelihood of spread of faeces
2. Patient with confirmed metallo-beta-lactamase-type CPE (NDM, VIM)
3. Patient with confirmed CPE of non-metallo-beta-lactamase type (IMP, KPC, OXA-48)
4. Suspected CPE case awaiting confirmation
5. CPE contacts. There is some reason to consider that contacts with one or more recent screening swabs reported as “CPE not detected” may represent a lower risk for spread of CPE compared to contacts that have not been tested. Such patients may have lower priority for isolation but caution is required because contacts who have acquired CPE frequently are not detected as positive for three weeks or more after the contact.

IMPORTANT

The management of CPE risk cannot be allowed to cause significant delay in patient access to investigations or interventions.

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