Proposed Investigation/Reporting Thresholds and Outbreak Definition for Carbapenem-Resistant Enterobacteriaceae (CRE)
Version 2, August 2019

A. Background

The thresholds and outbreak definition presented below are based on available scientific resources and expert opinion and intended only as guidance, reflecting the local epidemiology of carbapenem-resistant Enterobacteriaceae (CRE); states and localities may have their own outbreak definitions and reporting requirements. For example, the information provided here does not replace reporting of carbapemase-producing (CP)-CRE\(^1\) as part of the Nationally Notifiable Disease Surveillance System.

Suggested thresholds are intended to expedite facilities’ investigation of CRE cases and reporting to public health authorities, thus ensuring early detection of possible outbreaks and timely intervention to prevent the microbes’ spread. Detailed guidance for investigation of CRE cases is available from CDC.\(^2,3\) Healthcare facilities should consult public health authorities if they have questions.

NOTE: Case numbers presented below include both cases of colonization and cases of infection, identified in patients not previously known to have CRE.

B. Outbreak Detection and Reporting

1. Proposed Investigation/Reporting Thresholds and Outbreak Definition for Carbapenem-resistant Enterobacteriaceae

   For Long-Term Care Facilities (LTCFs), Critical Access Hospitals, Dialysis Facilities, and Outpatient Facilities:
   - Threshold for investigation and public health reporting:
     - 1 case CRE (CP, non-CP, or unknown CP\(^4\))
   - Outbreak\(^5\) Definition:
     - \(\geq 2\) cases CRE with same organism (or mechanism, if mechanism testing performed) in a 4-week period in patients who are epidemiologically-linked\(^6\) or determined to be genetically related\(^7\) by laboratory testing.

   For Acute Care Hospitals, Long-Term Acute Care Hospitals and High-Acuity Long-Term Care Facilities\(^8\):

   The suggested thresholds for starting an investigation and reporting to public health are dependent on CRE prevalence, which varies from region to region and even from facility to facility within a region.\(^9\) Facilities should consult with state or local public health authorities for guidance about the appropriate prevalence category for their facility; if the category is uncertain, consider beginning with the thresholds for low CRE prevalence and modifying as more information becomes available.
Thresholds:

**Very Low Prevalence** – CRE cases are rarely identified; facilities typically experience one to a few cases per year

- Threshold for investigation and public health reporting: 1 case CRE (CP, non-CP, or unknown CP)

**Low Prevalence** – CRE cases are identified with some regularity; facilities might average one case per month

- Thresholds for investigation:
  - 1 case CP-CRE (KPC, NDM, VIM, IMP, OXA-48 type, or positive by phenotypic test)
  - 2 cases CRE (non-CP or mechanism testing not performed) of same organism in a 4-week period in patients on the same unit

- Thresholds for public health reporting:
  - 1 case CP-CRE (KPC, NDM, VIM, IMP, OXA-48 type, or positive by phenotypic test)
  - 2 cases CRE (non-CP or mechanism testing not performed) of same organism in a 4-week period in patients who are epidemiologically-linked, with confirmatory laboratory testing

**High/Endemic Prevalence** – CRE cases are routinely identified; facilities might average several cases per month, trending to one or more cases per week in endemic sites

- Thresholds for investigation:
  - 1 case non-KPC CP-CRE (NDM, VIM, IMP, OXA-48 type)
  - 2 cases KPC-CRE, 2 cases CP-CRE (unknown mechanism), or 2 cases CRE (non-CP or mechanism testing not performed) of same organism in a 4-week period in patients on the same unit

- Thresholds for public health reporting:
  - 1 case non-KPC CP-CRE (NDM, VIM, IMP, OXA-48 type)
  - 2 cases KPC-CRE, 2 cases CP-CRE (unknown mechanism), or 2 cases CRE (non-CP or mechanism testing not performed) of same organism in a 4-week period in patients who are epidemiologically-linked

**Outbreak Definition:** ≥ 2 cases CRE involving the same organism (or mechanism, if mechanism testing performed) in a 4-week period in patients who are epidemiologically-linked or determined to be genetically-related by laboratory testing.

C. **Notes:**

1. Acronyms: CP=carbapenemase-producing; non-CP = non carbapenemase-producing; KPC=Klebsiella pneumoniae carbapenemase; NDM = New Delhi Metallo-β-Lactamase; OXA-48-type = oxacillinase; VIM = Verona-Integron encoded carbapenemase; IMP = active-on-Imipenem Metallo-β-lactamase

2. CDC. Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs). Available at: [https://www.cdc.gov/hai/containment/guidelines.html](https://www.cdc.gov/hai/containment/guidelines.html)
3. CDC. Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE). Available at: https://www.cdc.gov/hai/organisms/cre/index.html

4. When CP mechanism is unknown, facilities should consider arranging testing via the closest public health laboratory that participates in the Antibiotic Resistance Laboratory Network (AR Lab Network). (All state public health laboratories are members, plus laboratories in 5 cities and Puerto Rico.) Note that screening tests to identify asymptomatic carriers are also available at no cost through the AR Lab Network. Additional information is available at: https://www.cdc.gov/drugresistance/laboratories/AR-lab-network-testing-details.html

5. Facilities in high prevalence or endemic areas whose baseline exceeds this level should work with public health authorities to consider adjusting these parameters.

6. Examples of epidemiologic links include (but are not limited to) patients who resided on the same unit (or within the same facility if the facility is small), were transferred from or seen at the same outside facility, were assigned to the same primary or consultative service, had facility staff in common, or had the same procedure.

7. Laboratory testing methods commonly used for assessing genetic relatedness include pulsed field gel electrophoresis (PFGE) and whole genome sequencing (WGS).

8. The term high acuity long term care facilities is used here to refer to nursing homes and skilled nursing facilities that provide care to residents requiring mechanical ventilation or complex wound care.

9. Prevalence of CRE cases may vary among facilities within a region due to facility bed size, patient population, whether admission screening or active surveillance is conducted, and other factors, such as patient transfer patterns. Facilities whose prevalence differs from the regional average might consider using a different threshold. Of note, some facilities might fall into one prevalence group for CP-CRE and a different prevalence group for CRE.

10. Patients do not need to have overlapping stays to meet the threshold for investigation. In addition to admission on a common unit, consider additional factors that might indicate a common exposure, such as invasive procedures, as triggers for additional investigation.

11. Non-KPC CRE cases remain rare throughout the U.S. Identification of any non-KPC CP-CRE infection/colonization (or KPC CRE infection/colonization in non-endemic areas) should trigger a public health investigation as described in the CDC Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (See #2 above).

12. In high prevalence or endemic areas, the threshold of 2 CRE cases was selected for greatest sensitivity. For some facilities (e.g., in KPC endemic settings), this threshold might be too sensitive and burdensome. In this case, facilities should document their baseline CRE prevalence and collaborate with public health authorities to determine appropriate thresholds that represent a rise above baseline and carefully balance sensitivity with specificity. Facilities in these regions might have a lower threshold for investigating and reporting non-K. pneumoniae CRE cases, which could carry rarer carbapenemases, compared with carbapenem-resistant K. pneumoniae.

Disclaimer: The positions and views expressed in this guidance do not necessarily represent the official positions of CORHA’s member organizations.