

**Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae (CP-CRE):
Updated Laboratory Reporting Requirements
and Recommendations for Healthcare Facilities**
December 11, 2019

**California Antimicrobial Resistance Lab-Epi Alliance
Webinar**

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Objectives

1. Provide background information on CRE and CP-CRE
2. Review the new CP-CRE reporting requirements
3. Describe facility-based surveillance, investigation, and infection control actions
4. Present facility thresholds for initiating an investigation and notifying public health

Background



Carbapenem-resistant Enterobacteriaceae (CRE)

- Gram-negative bacteria
- Enterobacteriaceae family
 - E.g., *Klebsiella pneumoniae*, *E. coli*, *Enterobacter cloacae*
- Normally inhabit the gut
- Resistant to carbapenem antibiotics
 - Doripenem, ertapenem, imipenem, and meropenem

Carbapenemase-producing CRE (CP-CRE)

Carbapenemases are beta-lactamase enzymes

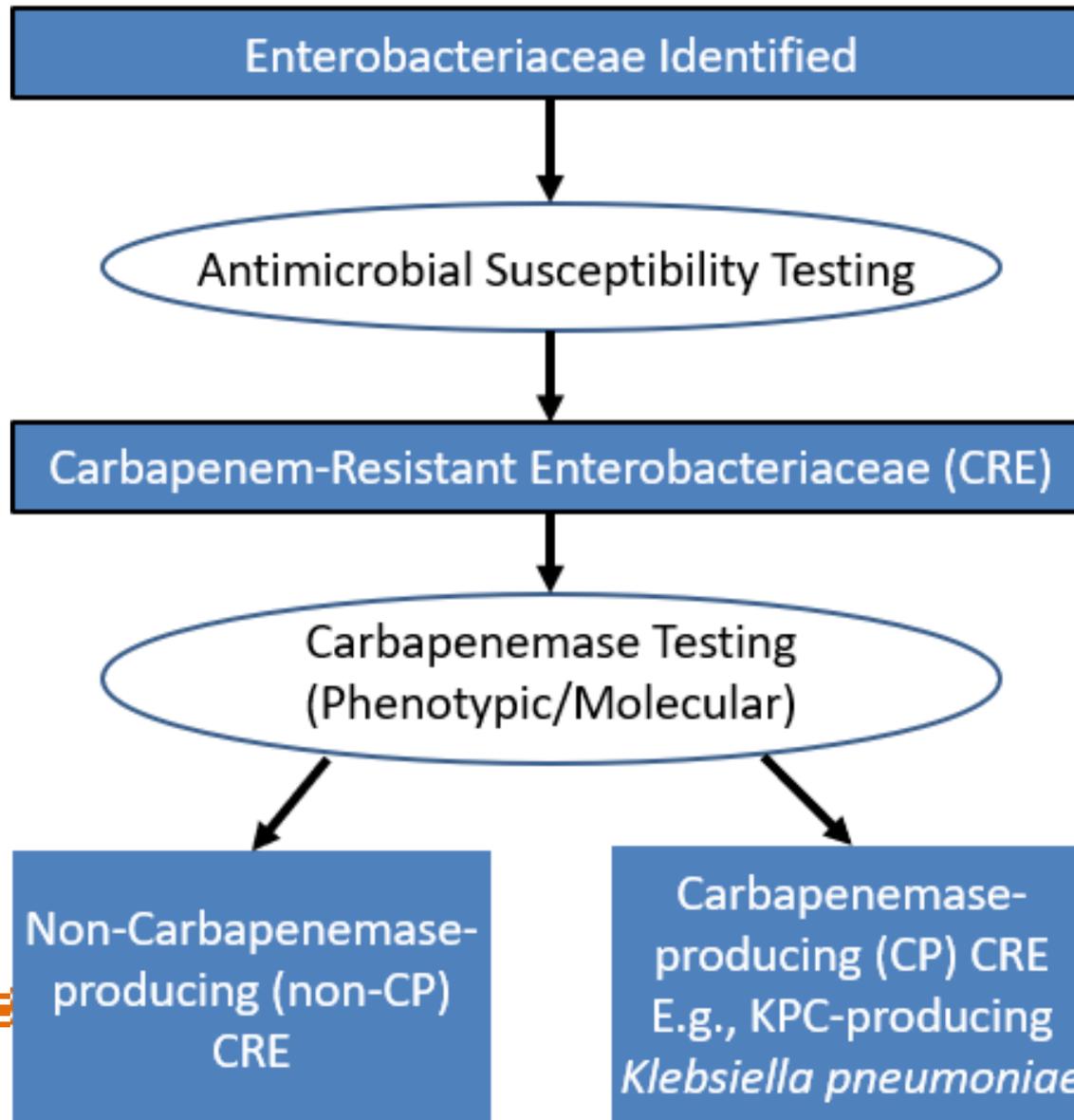
- Inactivate carbapenems, other beta-lactam antibiotics (e.g., penicillins, cephalosporins)
- On mobile genetic elements (plasmids), enabling transfer across bacterial species
- Examples include:
 - *Klebsiella pneumoniae* carbapenemase (KPC), most common in U.S. but also found in other genera/species
 - NDM, IMP, VIM, OXA-48-like

Detecting CP-CRE

2 types of carbapenemase testing

- **Phenotypic**
 - Detects presence of carbapenemase (yes/no)
- **Molecular**
 - Identifies specific carbapenemase (e.g., KPC, NDM)

CRE Identification Algorithm



Dispelling Some Common Misconceptions

- Not all CRE are carbapenemase-producing
 - Distinguishing CP-CRE from non-CP-CRE informs clinical, infection prevention and public health actions
- CRE are carbapenem-resistant, not carbapenemase-resistant
- KPC = *Klebsiella pneumoniae* carbapenemase
 - Originally discovered in *K. pneumoniae*, but can be found in *E. coli*, *Enterobacter* spp. and other organisms
- KPC is not synonymous with CRE

Reporting Requirements

CP-CRE Reporting Requirements

- Title 17, Section 2505, Subsection (e)(2) **laboratory reportable** conditions list, effective October 1, 2019
- [CDC case definition](https://wwwn.cdc.gov/nndss/conditions/carbapenemase-producing-carbapenem-resistant-enterobacteriaceae/)
(<https://wwwn.cdc.gov/nndss/conditions/carbapenemase-producing-carbapenem-resistant-enterobacteriaceae/>)
- No clinical criteria, no submission requirements
- Local reporting requirements do **not** change

CP-CRE Reporting Requirements

1. Laboratories that perform carbapenemase testing, or use a public health or reference laboratory to obtain carbapenemase testing, will report the following:

Any Enterobacter spp., E. coli, or Klebsiella spp. where the isolate is:

- Positive for carbapenemase production by a **phenotypic** method

-OR-

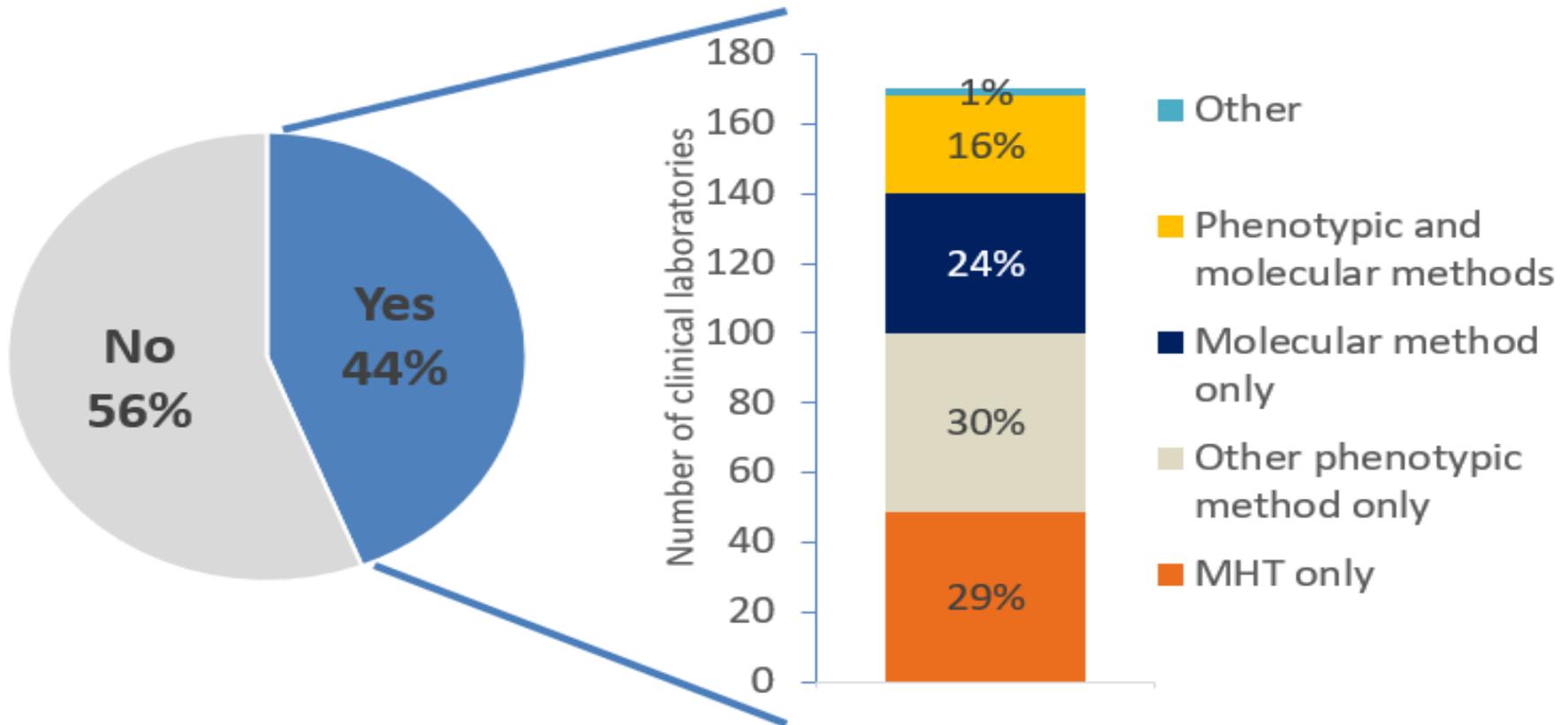
- Positive for a known carbapenemase resistance mechanism (KPC, NDM, IMP, VIM, OXA-48, novel carbapenemase) by a recognized **molecular** test

Carbapenemase Testing Methods

Phenotypic tests for carbapenemase production	Molecular tests for resistance mechanism
Carba NP	BioFire
Carbapenem inactivation method (CIM)	Polymerase chain reaction (PCR)
Metallo- β -lactamase test (e.g., E-test)	Verigene
Modified carbapenem inactivation method (mCIM)	Whole-genome sequencing (WGS)
Modified Hodge test (MHT)*	Xpert Carba-R

*A positive MHT can be used to confirm CP-CRE for *Klebsiella* spp and *E. coli* but **not *Enterobacter* spp.** An isolate that tests positive on MHT but negative by PCR for KPC, NDM, OXA-48, VIM and IMP should have additional characterization performed with another phenotypic test for carbapenemase such as mCIM.

Carbapenemase Testing Capacity among Hospital Labs in California (N=386)



Source: NHSN 2018 Annual Hospital Survey

CP-CRE Reporting Requirements

2. Laboratories that do not perform or obtain carbapenemase testing, will report the following:

Enterobacter spp., *E. coli*, or *Klebsiella* spp. from any site, resistant to at least one carbapenem.

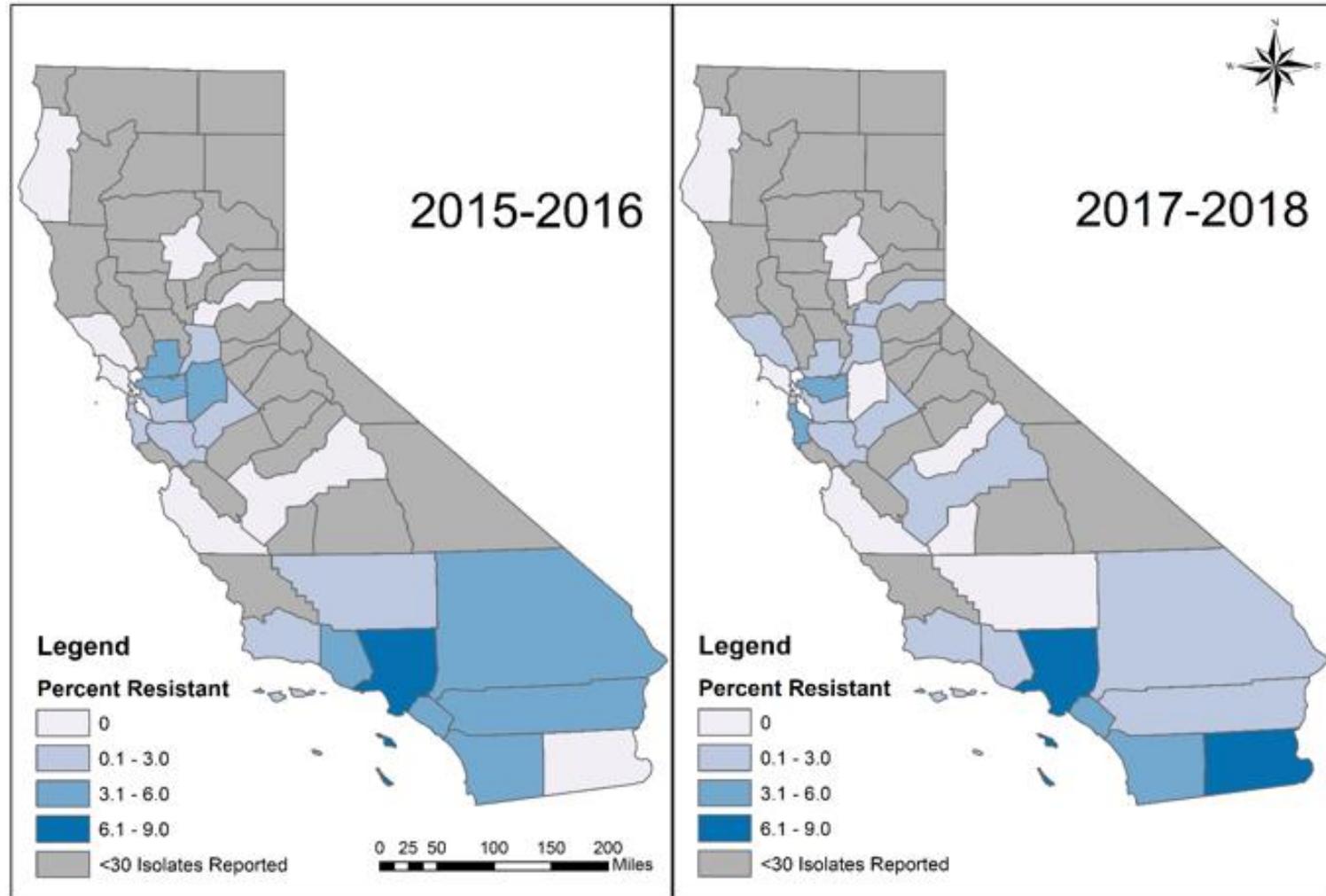
- All labs report AST results
- Labs performing or obtaining multiple tests wait until final results available before reporting
- CDPH Microbial Diseases Lab (MDL) can do phenotypic and molecular testing

Other Reporting Requirements

- Unusual infectious disease occurrence
 - Other carbapenemase-producing organisms
 - *Pseudomonas aeruginosa*
 - *Acinetobacter baumannii*
 - Other Enterobacteriaceae (e.g., *Citrobacter freundii*)
- No organism identified (e.g., rectal swab)
- Outbreaks

CRE Epidemiology

CRE among isolates reported to NHSN* (2015-2018)



*National Healthcare Safety Network SSI, CAUTI, and CLABSI *Klebsiella* and *Enterobacter* spp. and *E. coli* isolates in hospitals

Regional CRE Prevalence Definitions

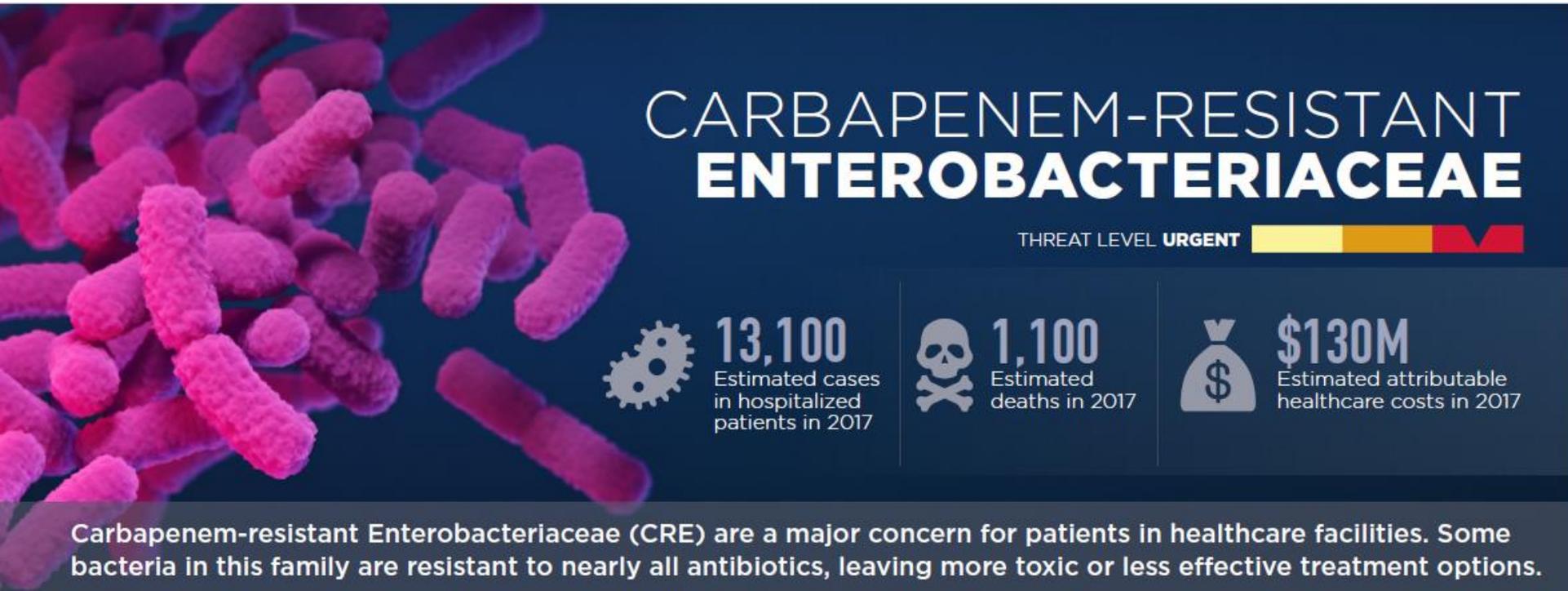
Prevalence	Definition
High or endemic	CRE are routinely identified; e.g., hospitals have >1 case a month
Lower prevalence	CRE identified with regularity; e.g., hospitals have 3-12 cases a year
Very low prevalence	CRE rarely identified; e.g., hospitals have 1 or 2 cases a year

- Highest prevalence facilities: Long-term acute care hospitals (LTACH), ventilator-equipped skilled nursing facilities (vSNF)

Sources: [CORHA Proposed Definitions](https://corha.org/resources-and-products/) (https://corha.org/resources-and-products/)

McKinnell JA, Singh RD, Miller LG, et al. SHIELD Orange County Project: MDRO Prevalence in 21 Nursing Homes and Long-term Acute Care Facilities in Southern California, Clin Infect Dis 2019.

CRE: An Urgent Threat



Source: [CDC Biggest Threats and Data](https://www.cdc.gov/drugresistance/biggest-threats.html)

(<https://www.cdc.gov/drugresistance/biggest-threats.html>)

CP-CRE Epidemiology

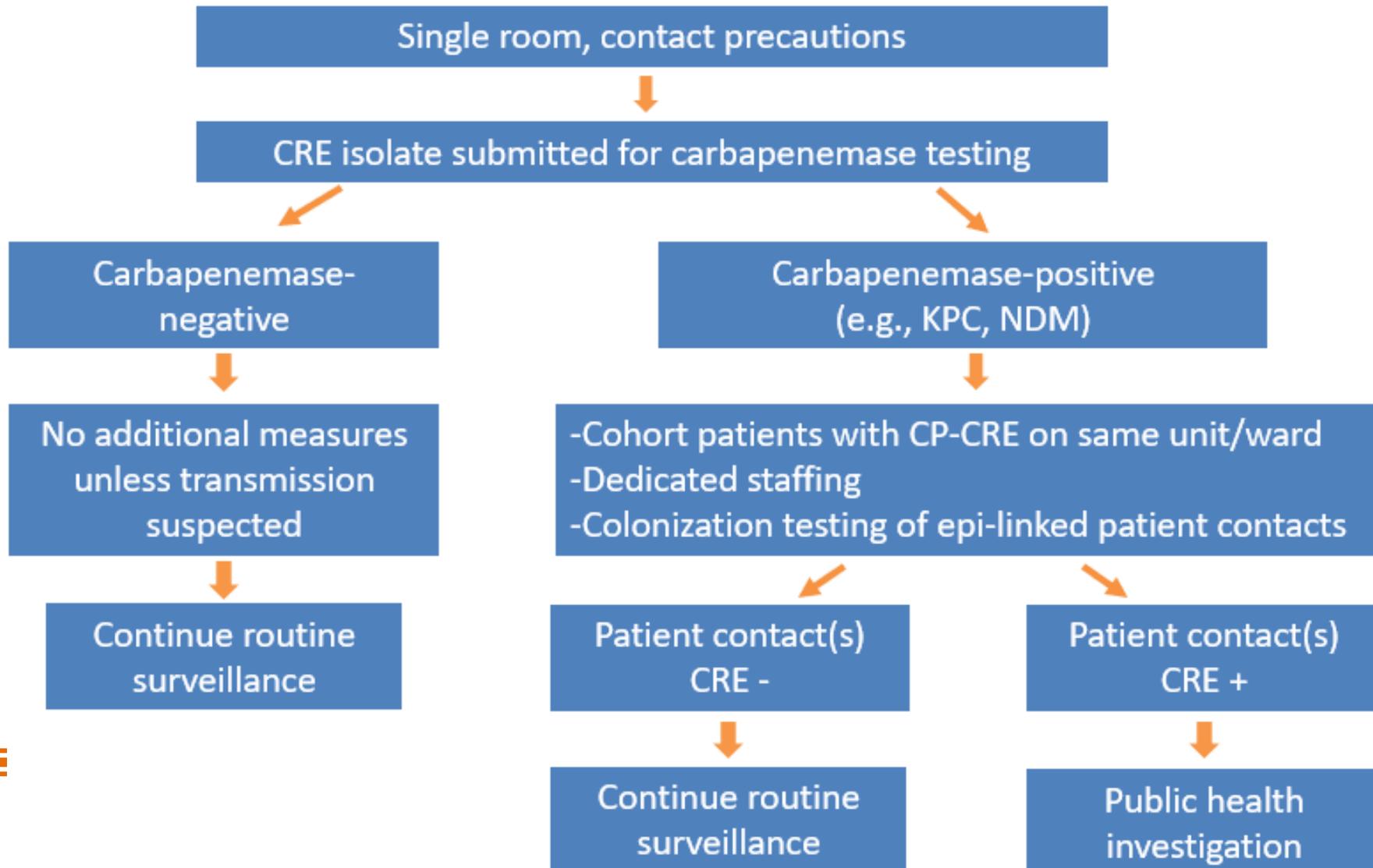
- Highly-transmissible in healthcare settings
- Colonized and infected patients can serve as sources of transmission
- **Risk factors:**
 - International healthcare exposure
 - Antimicrobial treatment
 - Presence of indwelling devices (e.g., urinary catheters, endotracheal tubes)
 - Mechanical ventilation
- Difficult-to-treat infections → high mortality rates

Sources: Guh et al. Epidemiology of CRE in 7 US Communities, 2012-2013. *JAMA* 2015; Tamma et al. Comparing the Outcomes of Patients with Carbapenemase-Producing and Non-Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae Bacteremia. *Clin Infect Dis* 2017.

The Case for Carbapenemase Testing

- CP-CRE warrant measures to assess and prevent further transmission in healthcare settings
- Carbapenemase testing to distinguish CP-CRE from non-CP CRE informs
 - Better understanding of hospital CRE epidemiology
 - Immediate infection control interventions
 - Epidemiologic investigation
 - Public health response actions
 - Clinical treatment options

Scenario: Hospitalized Patient Identified with CRE



CP-CRE is a public health priority

Facility Actions



Facility Actions: Routine Surveillance

- Detect CRE and notify clinical and IP staff
- Perform or obtain carbapenemase testing
- Establish baseline

Facility Actions: Active Surveillance

- Screen for CP-CRE, pre-emptive Contact precautions
 - Admitted from LTACH or facility with transmission
 - Epi-linked to new case
 - History of international healthcare exposure in last year

Thresholds for Facility Action and Reporting and Public Health Investigation

Source: [CORHA Proposed Definitions](https://corha.org/resources-and-products/) (https://corha.org/resources-and-products/)

Thresholds*: Higher or Endemic

Prevalence	Definition	Threshold level	Investigate / Notify
Higher or endemic	CRE are routinely identified (> 1 case/month)	1 non-KPC CP-CRE Same organism within 4 weeks: <ul style="list-style-type: none"> • 2 KPC-CRE -OR- • 2 CP-CRE (unknown mechanism) -OR- • 2 CRE (non-CP or CP testing not performed) 	√ √ same unit/ epi-linked
Lower	CRE identified with regularity (3-12 cases/year)	1 CP-CRE 2 CRE (non-CP or CP testing not performed), same organism within 4 weeks	√ √ same unit/ epi-linked
Very low	CRE rarely identified (1-2 cases/year)	1 CRE	√

* All thresholds apply to ACH, LTACH, vSNF; for all other facility types, 1 CRE is the threshold.

Thresholds*: Lower Prevalence

Prevalence	Definition	Threshold level	Investigate / Notify
Higher or endemic	CRE are routinely identified (> 1 case/month)	1 non-KPC CP-CRE Same organism within 4 weeks: <ul style="list-style-type: none"> • 2 KPC-CRE -OR- • 2 CP-CRE (unknown mechanism) -OR- • 2 CRE (non-CP or CP testing not performed) 	√ √ same unit/ epi-linked
Lower	CRE identified with regularity (3-12 cases/year)	1 CP-CRE 2 CRE (non-CP or CP testing not performed), same organism within 4 weeks	√ √ same unit/ epi-linked
Very low	CRE rarely identified (1-2 cases/year)	1 CRE	√

* All thresholds apply to ACH, LTACH, vSNF; for all other facility types, 1 CRE is the threshold

Thresholds*: Low Prevalence

Prevalence	Definition	Threshold level	Investigate / Notify
Higher or endemic	CRE are routinely identified (> 1 case/month)	1 non-KPC CP-CRE Same organism within 4 weeks: <ul style="list-style-type: none"> • 2 KPC-CRE -OR- • 2 CP-CRE (unknown mechanism) -OR- • 2 CRE (non-CP or CP testing not performed) 	√ √ same unit/ epi-linked
Lower	CRE identified with regularity (3-12 cases/year)	1 CP-CRE 2 CRE (non-CP or CP testing not performed), same organism within 4 weeks	√ √ same unit/ epi-linked
Very low	CRE rarely identified (1-2 cases/year)	1 CRE	√

* All thresholds apply to ACH, LTACH, vSNF; for all other facility types, 1 CRE is the threshold.

Facility Actions: Initial Communications

Facility communicates patient's CRE status:

- When transferring patient to another facility, including home healthcare
- During an outbreak
 - Screening, pre-emptive Contact precautions at receiving facility
- Within the facility by flagging the medical record
- To patients, their families and HCP
 - Provide education materials
- Adapt CDPH Infection Control Transfer Form

HEALTHCARE FACILITY TRANSFER FORM (ABBREVIATED)

Use this form for all transfers to an admitting healthcare facility.

Infection Control Transfer Form (PDF)

(<https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/InterfacilityCommunication.aspx>)

Patient Name (Last, First):		
Date of Birth:	MRN:	Transfer Date:
Receiving Facility Name:		
Sending Facility Name:		
Contact Name:	Contact Phone:	

ISOLATION PRECAUTIONS

Patient currently on isolation precautions? <input type="checkbox"/> Yes <input type="checkbox"/> No	Personal Protective equipment (PPE) to consider at receiving facility:		
If yes, check all that apply: <input type="checkbox"/> Contact precautions <input type="checkbox"/> Droplet precautions <input type="checkbox"/> Airborne precautions	 <input type="checkbox"/> Gloves	 <input type="checkbox"/> Gowns	 <input type="checkbox"/> Masks

ORGANISMS

Patient has multidrug-resistant organism (MDRO) or other lab results for which the patient should be in isolation? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, specify organism(s) and include specimen source and collection date.		
Organism	Source	Date
<input type="checkbox"/> <i>C.difficile</i>		
<input type="checkbox"/> Carbapenem-resistant <i>Enterobacteriaceae</i> (CRE) (e.g., <i>Klebsiella</i> , <i>Enterobacter</i> or <i>E.coli</i>)		
<input type="checkbox"/> Extended-spectrum beta lactam-resistant (ESBL) (e.g., <i>E.coli</i> , <i>Klebsiella</i>)		
<input type="checkbox"/> MDR gram negatives (e.g., <i>Acinetobacter</i> , <i>Pseudomonas</i>)		
<input type="checkbox"/> Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)		
<input type="checkbox"/> Vancomycin-resistant <i>Enterococcus</i> (VRE)		
<input type="checkbox"/> Other, specify: (e.g., lice, scabies, disseminated shingles (<i>Herpes zoster</i>), norovirus, influenza, tuberculosis)		

Include copy of **lab results** with organism I.D. and antimicrobial susceptibilities.

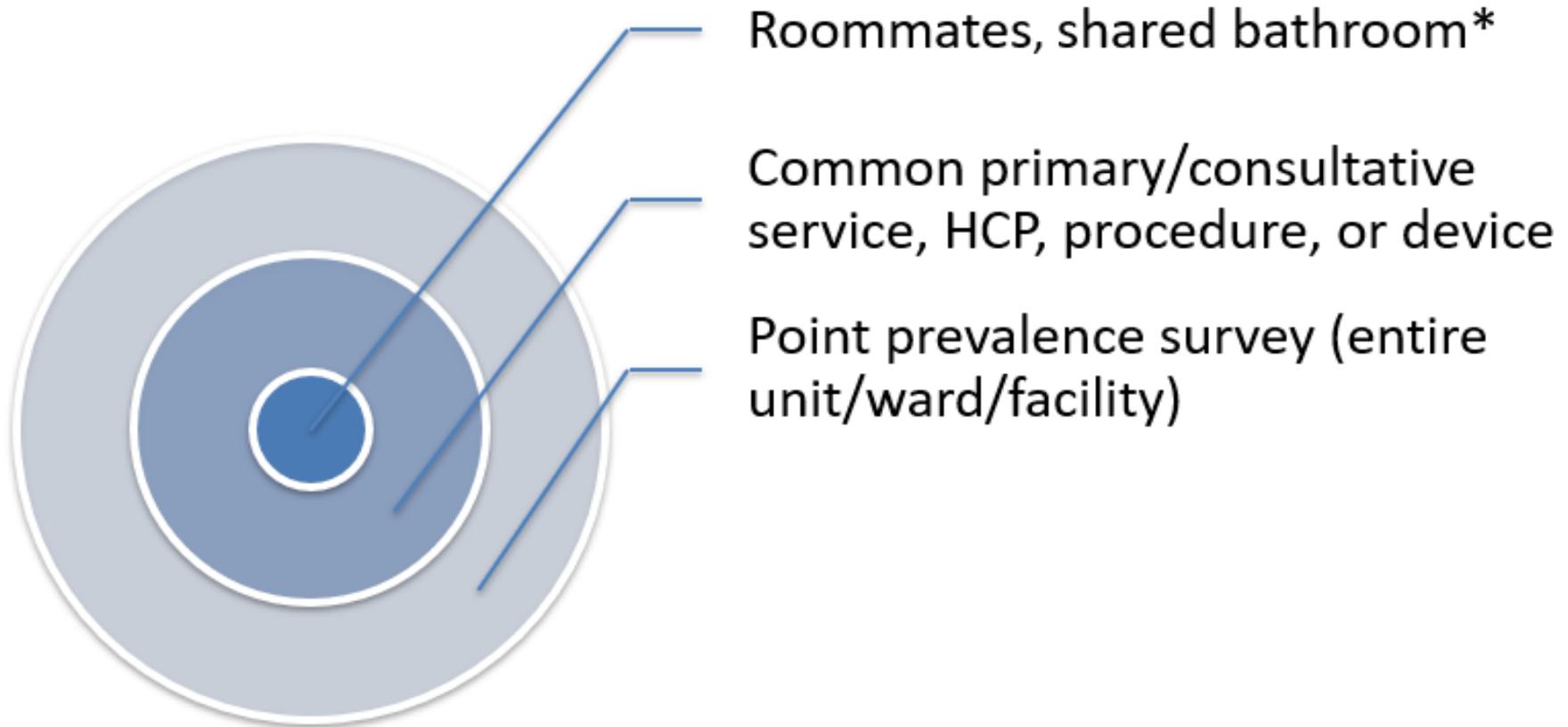
Public Health Response

Public Health Response: Initial Response and Recommendations

- Initial infection control recommendations
 - Room placement (single-bed room, like-with-like)
 - Transmission-based precautions
 - Information gathering
 - Brief medical history
 - Current/previous/subsequent healthcare exposure, including admission/discharge dates and locations (e.g., units, wings)
 - Indwelling devices, invasive procedures, other risk factors
 - International travel, healthcare exposure in prior 12 months
 - Retrospective and prospective lab surveillance
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Public Health Response: Contact Investigation

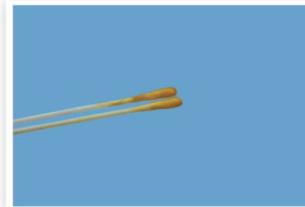
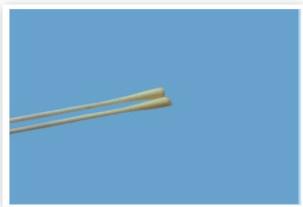
- Colonization testing



*If already discharged, flag medical record so that patient can be screened if readmitted

Colonization Testing Resources

- Available at West Regional AR Lab in Washington free of charge
 - Rectal swab kits with instructions
 - Requisition form
 - Verbal assent script
- Request and coordinate through Local Health Department and HAI Program



Examples of Acceptable Swabs for
Xpert® Carba-R Assay Testing

Public Health Response: Infection Control

- Transmission-based precautions
 - Transmission-based precautions for duration of hospitalization
 - Enhanced standard precautions (PDF) (skilled nursing facilities) *when transmission has been excluded*
(<https://www.cdph.ca.gov/Programs/CHCQ/LCP/CDPH%20Document%20Library/Enhanced-Standard-Precautions.pdf>)
 - Repeat cultures **not** necessary for “clearance” – patients remain colonized
 - Flag medical record for readmission

Public Health Response: Infection Control

- Dedicated equipment
- Patient and staff cohorting (if > 1 patient; does **not** imply 1:1 nursing ratio)
- Environmental cleaning, particularly of high-touch surfaces and shared equipment
- [Adherence monitoring](http://www.cdph.ca.gov/programs/hai/Pages/AdherenceMonitoringTools.aspx)
(<http://www.cdph.ca.gov/programs/hai/Pages/AdherenceMonitoringTools.aspx>)
- On-site infection control assessment as needed, depending on facility and extent of transmission

Public Health Response: Additional Follow-up

- Point prevalence survey (PPS)
 - Patients not previously identified with CP-CRE on same unit where transmission suspected
 - If 1+ patient identified with CP-CRE, conduct serial PPS at 2-week intervals until 2 consecutive negative PPS
- Follow-up on-site infection control assessment
 - Focus on gaps
 - Ensure implementation of recommendations
- Periodic phone check-in with facility

Public Health Response: Communication

Facility communicates patient's CRE status:

- When transferring patient to another facility, including home healthcare
- During an outbreak
 - Screening, pre-emptive Contact precautions at receiving facility
- Within the facility by flagging the medical record
- To patients, their families and HCP
 - Provide education materials
- Adapt [CDPH Infection Control Transfer Form](#) (PDF)

<https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/InterfacilityCommunication.aspx>

Additional West Regional AR Lab Resources

- Colonization testing for CRE, carbapenem-resistant *P. aeruginosa* (CRPA) and *A. baumannii* (CRAB), and *C. auris* as part of investigation or containment response
- Expanded carbapenemase testing of CRAB (OXA-23, 24/40, 58)
- Expanded antimicrobial susceptibility testing
- Submission for targeted surveillance
 - CR-*Acinetobacter* spp.
 - CRPA
 - Non-*albicans* *Candida* spp. for antifungal susceptibility testing

Resources

- [CDPH CRE Website](https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CRE_InfectionPreventionStrategies.aspx)

(https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CRE_InfectionPreventionStrategies.aspx)

- [CDPH FAQ for CP-CRE Reporting](https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CP-CRE_ReportingFAQ_Approved_10.4.19_ADA.pdf) (PDF)

(https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CP-CRE_ReportingFAQ_Approved_10.4.19_ADA.pdf)

- [CDPH California Antimicrobial Resistance Lab-Epi Alliance](https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CA_ARLN.aspx)

(https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CA_ARLN.aspx)

- [CDPH Adherence Monitoring Tools](https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/MonitoringAdherenceToHCPacticesThatPreventInfection.aspx)

(<https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/MonitoringAdherenceToHCPacticesThatPreventInfection.aspx>)

- [CDPH All Facilities Letter for Reporting Outbreaks and Unusual Infectious Disease Occurrences](https://www.cdph.ca.gov/Programs/CHCQ/LCP/CDPH%20Document%20Library/AFL-19-18.pdf) (PDF)

(<https://www.cdph.ca.gov/Programs/CHCQ/LCP/CDPH%20Document%20Library/AFL-19-18.pdf>)

Resources, cont'd

- [CORHA Proposed Investigation/Reporting Thresholds for CRE \(PDF\)](https://corha.org/wp-content/uploads/2019/06/CORHA-Proposed-CRE-Thresholds-and-Definition-08-19.pdf)
(<https://corha.org/wp-content/uploads/2019/06/CORHA-Proposed-CRE-Thresholds-and-Definition-08-19.pdf>)
- [CDC CRE Website](https://www.cdc.gov/hai/organisms/cre/index.html)
(<https://www.cdc.gov/hai/organisms/cre/index.html>)
- [CDC AR Threats Report](https://www.cdc.gov/drugresistance/biggest-threats.html)
(<https://www.cdc.gov/drugresistance/biggest-threats.html>)
- [CDC Containment Strategy Guidelines](https://www.cdc.gov/hai/containment/guidelines.html)
(<https://www.cdc.gov/hai/containment/guidelines.html>)

Questions?

For more information,
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