



# The role of the PHL in Antimicrobial Resistance Surveillance

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*APHL*

# Objectives

- Understand the roles played by clinical labs, state and local public health labs, and the regional AR Lab Network Labs in antimicrobial resistance surveillance
- Understand the primary functions of the Antimicrobial Resistance Laboratory Network
- Understand the importance of screening in mitigating the transmission in health care facilities



# Outline

- History and structure of the AR Laboratory Network
- Overview of testing and screening activities
- The purpose of whole genome sequencing
- Expanded antimicrobial susceptibility testing
- Patient Safety Portal
- Case Studies

The image features the Kahoot! logo in a bold, purple, sans-serif font. The text is centered within a white rectangular area that is framed by a teal border. To the left of this frame is a teal rectangular shape that appears to be a page tab or a decorative element, extending from the top and bottom edges of the frame.

**Kahoot!**

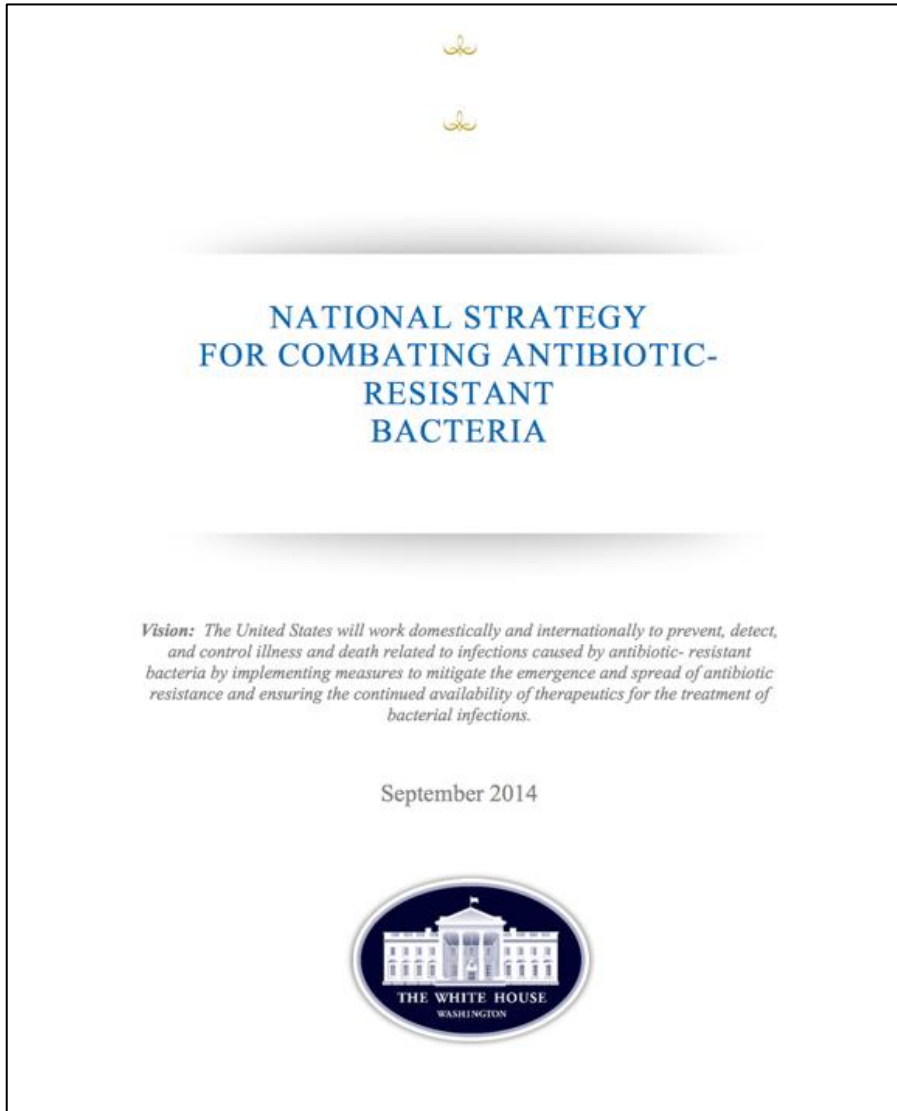


# AR Laboratory Network-History

- Antibiotic Resistance Threats in the US
- First published in 2013, updated in 2019
  - Urgent Threats
    - C. difficile
    - Carbapenem Resistant Enterobacterales,
    - Drug resistant *Neisseria gonorrhoea*
  - Serious Threats
  - Concerning Threats



# National Strategy for Combating Antibiotic Resistant Bacteria 2014



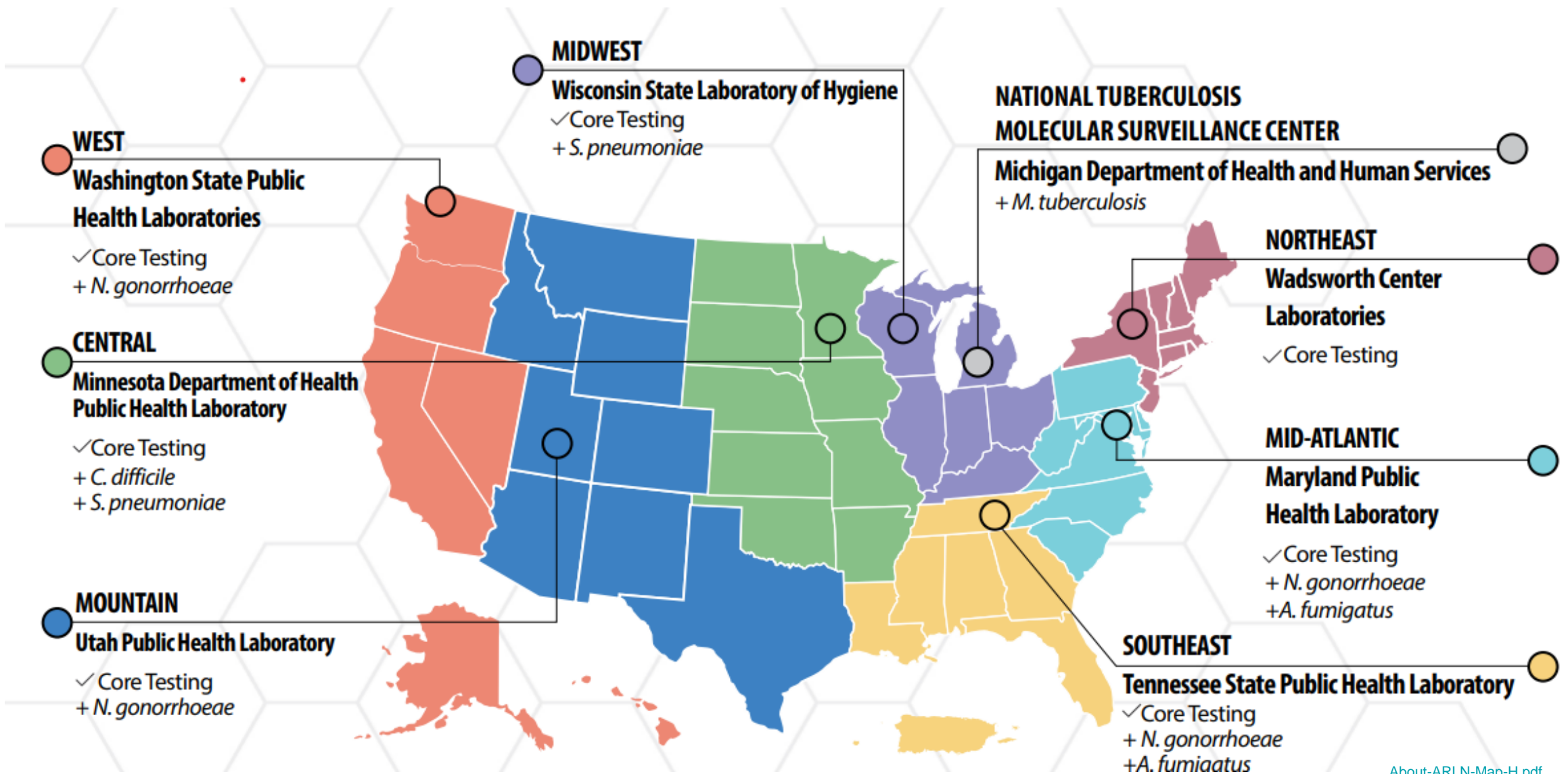
## Objectives:

- Create a regional laboratory network that uses standardized testing platforms
  - Link this data to existing PH surveillance networks so that AST data is readily available during investigations of outbreaks
- Create a repository of resistant bacterial strains, including a database that describes the characteristics of the strains
- Develop and maintain a national sequence database of resistant pathogens

# Significant Investments

- 2015: Congress provided \$160 million to CDC to implement [2014 National Strategy](#)
- 2016: CDC established the Antibiotic Resistance (AR) Laboratory Network, including seven regional labs
- 2021: American Rescue Plan Act of 2021, ['Strengthening HAI/AR Program Capacity' \(SHARP\) supplement](#)
  - Additional \$385M additional critical support to recipients as they continue to address COVID-19 within their communities

# AR Lab Network



[About-ARLN-Map-H.pdf](#)  
(cdc.gov)



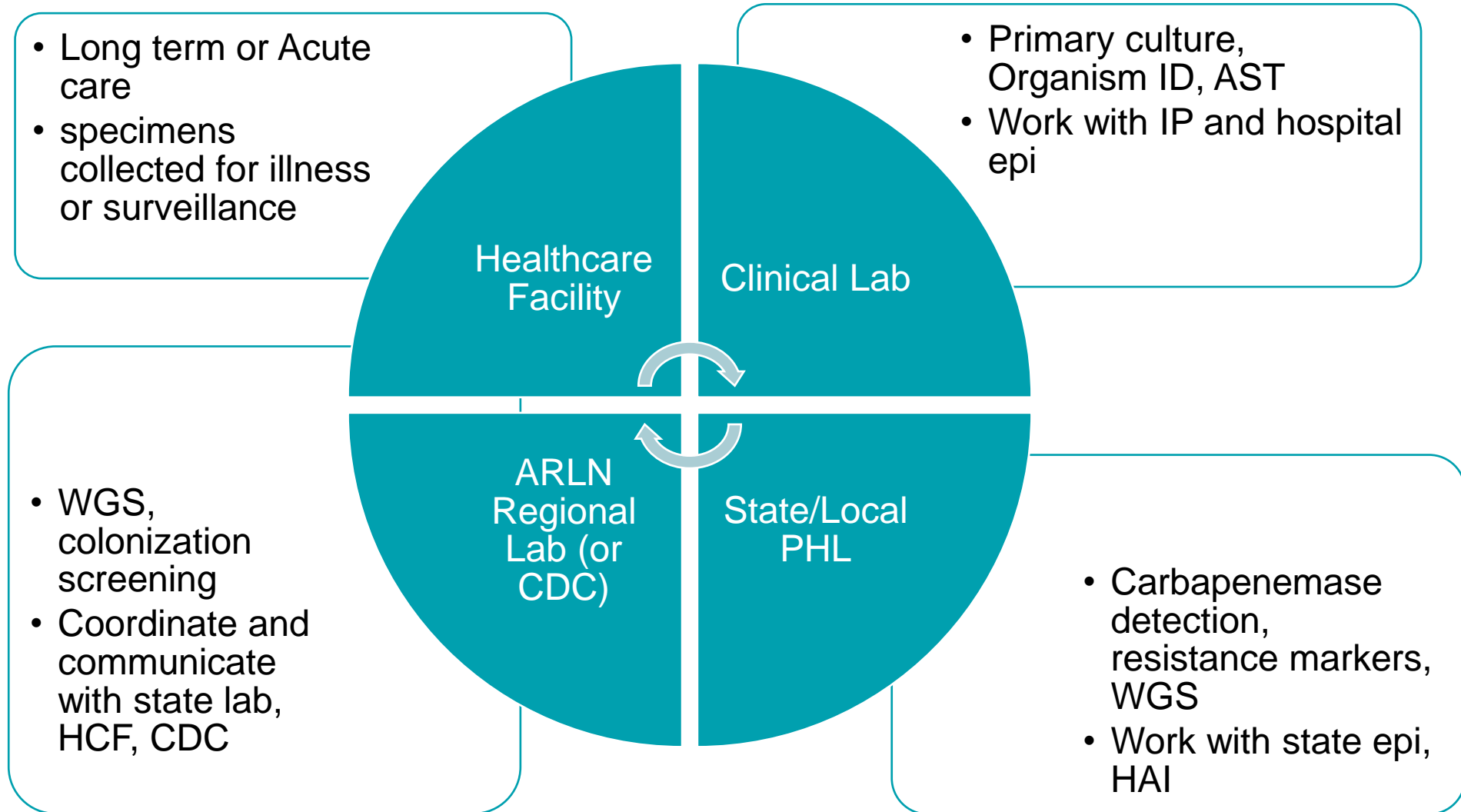


# Core testing by all regional labs

## Core Testing by all regional labs:

- ✓ Molecular testing to detect colonization of carbapenem-resistant Enterobacterales (CRE).
- ✓ Detection of new and emerging threats, like novel carbapenemase genes, and ability to detect changes in known threats, like methicillin-resistant *Staphylococcus aureus*.
- ✓ Fungal susceptibility of *Candida* species to identify emerging resistance.
- ✓ Identification and colonization screening to detect and help prevent spread of *Candida auris* (*C. auris*).
- ✓ Perform expanded susceptibility testing to determine if new drugs or drug combinations will be effective to treat patients infected with especially rare resistant pathogens.
- ✓ Isolates may be used for the CDC and FDA AR Isolate Bank and WGS projects.

# AR Lab Network: The System in Action



The image features the Kahoot! logo, which consists of the word "Kahoot!" in a bold, purple, sans-serif font. The logo is centered within a white rectangular area that is framed by a teal border. To the left of this frame is a teal rectangular shape that appears to be a tab or a page edge, extending from the left side of the frame.

# Molecular detection of resistance

## THE BIG FIVE

### 1. *Klebsiella pneumoniae carbapenemase (KPC)*

- Most common carbapenemase in the United States
- Confers resistance to ALL  $\beta$ -lactam agents

### 2. *New Delhi Metallo- $\beta$ -lactamase (NDM)*

- First detected in 2009; rapid global spread, primarily among Enterobacteriaceae
- Previously associated with travel, now with domestic transmission

### 3. *OXA-48- like enzymes*

- Inefficient carbapenemases, don't hydrolyze cephalosporins well
- Commonly travel with other  $\beta$ -lactamases

### 4. *Verona Integron-encoded Metallo- $\beta$ -lactamase (VIM)*

- Relatively slow global spread; mostly in *P. aeruginosa*

### 5. *Active on Imipenem Metallo- $\beta$ -lactamase (IMP)*

- Relatively slow global spread; mostly in *P. aeruginosa*

# Whole Genome Sequencing



## **SURVEILLANCE**

- Detection of novel resistance mechanisms which could represent new or emerging HAI/AR threats



## **RESPONSE**

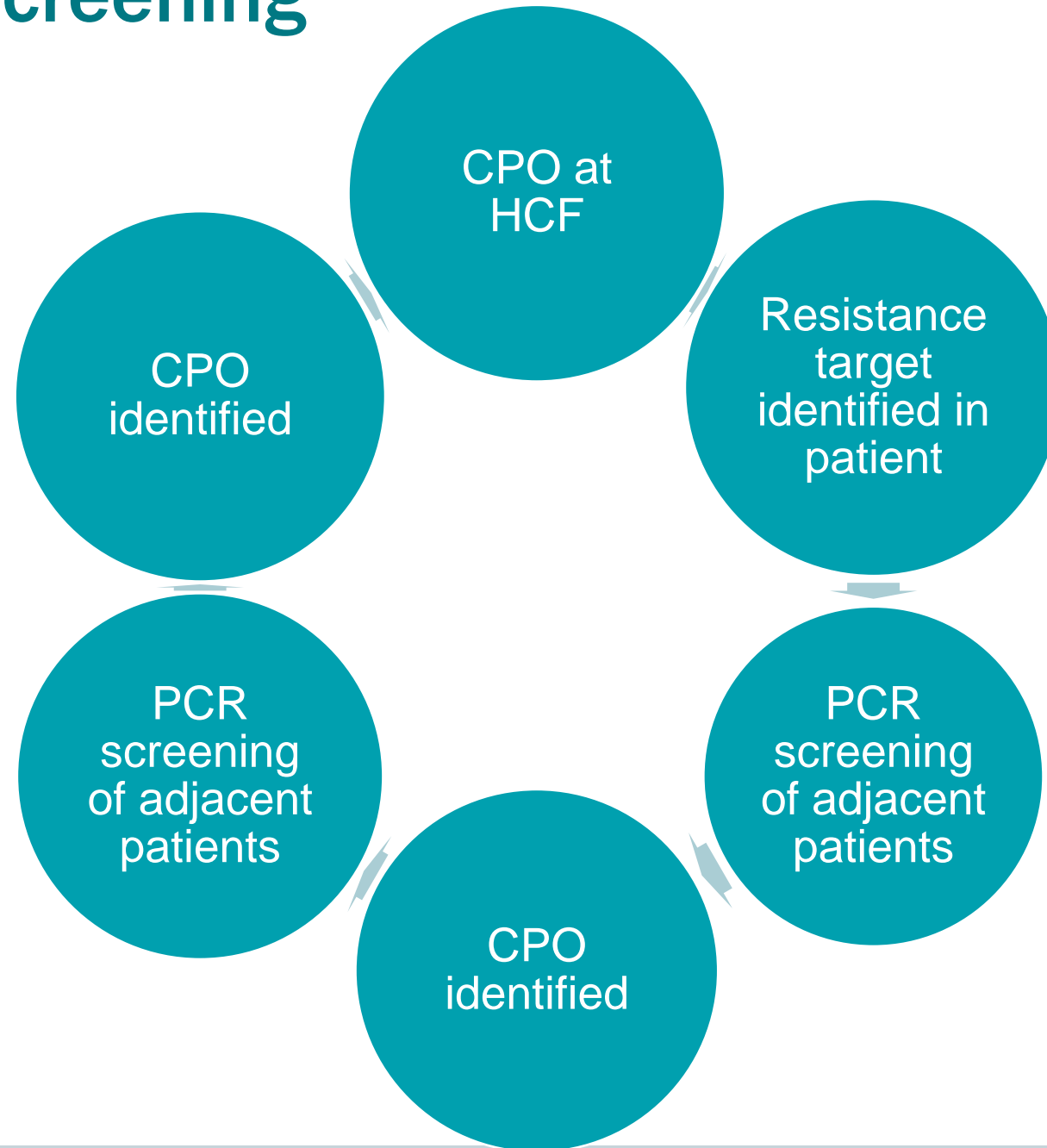
- Genomic epidemiology; use to determine relatedness between cases
- Can determine if transmission occurred in a facility or even between facilities



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**Kahoot!**

# Colonization screening





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# Expanded AST (ExAST)

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**Kahoot!**

# Expanded Antimicrobial Susceptibility Testing (ExAST)



## Expanded Antimicrobial Susceptibility Testing for Hard-to-Treat Infections

### Antimicrobial susceptibility testing for Enterobacteriales producing a metallo-beta-lactamase (MBL)

Clinicians and clinical and public health laboratories can request expanded antimicrobial susceptibility testing (ExAST) from CDC's Antibiotic Resistance Lab Network (AR Lab Network) to find potentially effective treatment options for their patients' most resistant infections.

- Resistance to new drugs used for treatment of carbapenem-resistant Enterobacteriales (CRE) has been identified, specifically to ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-relebactam. However, these bacteria may be susceptible to the combination therapy ceftazidime-avibactam plus aztreonam, a combination of drugs that is an option in current IDSA guidance for treatment of serious infections caused by MBL-producing Enterobacteriales.\*
- Susceptibility testing is CLIA-compliant and is performed at no cost. MIC results will be reported within 3 business days for treatment of ceftazidime-avibactam, aztreonam, and aztreonam-avibactam to help assess utility of combination therapy.

**1. Isolates to submit:**

Hospital laboratories and clinicians are encouraged to submit Enterobacteriales isolates that:

- Test "not susceptible" to all beta lactams tested, including ceftazidime-avibactam, meropenem-vaborbactam, or imipenem-relebactam. These may be MBL-producing isolates with few treatment options.

-OR-

- Enterobacteriales that test positive for NDM, VIM, or IMP genes.

**2. What is the testing process?**

- Isolates will be tested to confirm carbapenem resistance, carbapenemase production, and to identify the presence of specific carbapenemase genes.
- Isolates meeting the inclusion criteria will be tested against ceftazidime-avibactam, aztreonam, and avibactam-aztreonam.
- AST turn-around time is 3 business days after receipt of isolate.

**3. How do I request ExAST and receive results?**

- Please email your AR Lab Network Regional Laboratory (see map) to request testing and submission instructions.
- Please provide prior laboratory testing results, including organism identification and AST.
- Please confirm that Infection Prevention and Infectious Diseases services are aware of this patient and isolate.



- Southeast:** Tennessee Public Health Laboratory | [ARLN.health@tn.gov](mailto:ARLN.health@tn.gov)
- Mid-Atlantic:** Maryland Public Health Laboratory | [MDPH\\_arn@maryland.gov](mailto:MDPH_arn@maryland.gov)
- Northeast:** Wadsworth Center Labs | [ARLNcoreNY@health.ny.gov](mailto:ARLNcoreNY@health.ny.gov)
- Midwest:** Wisconsin State Lab of Hygiene | [wARN@slh.wisc.edu](mailto:wARN@slh.wisc.edu)
- West:** Washington State Public Health Labs | [ARLN@doh.wa.gov](mailto:ARLN@doh.wa.gov)
- Central:** Minnesota Dept. of Health Public Health Lab | [ARLNMN@state.mn.us](mailto:ARLNMN@state.mn.us)
- Mountain:** Utah Public Health Lab | [ARLNuh@utah.gov](mailto:ARLNuh@utah.gov)

\*Tamma PD, Aiken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of Extended-Spectrum  $\beta$ -lactamase Producing Enterobacteriales (ESBL-E), Carbapenem-Resistant Enterobacteriales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-R aeruginosa). Clin Infect Dis. 2021 Apr 8;72(7):1019-1031. doi: 10.1093/cid/ciaa787. PMID: 33308864.

For more information on CDC's AR Lab Network, visit: [www.cdc.gov/drugresistance/laboratories.html](http://www.cdc.gov/drugresistance/laboratories.html)



CS125608-A

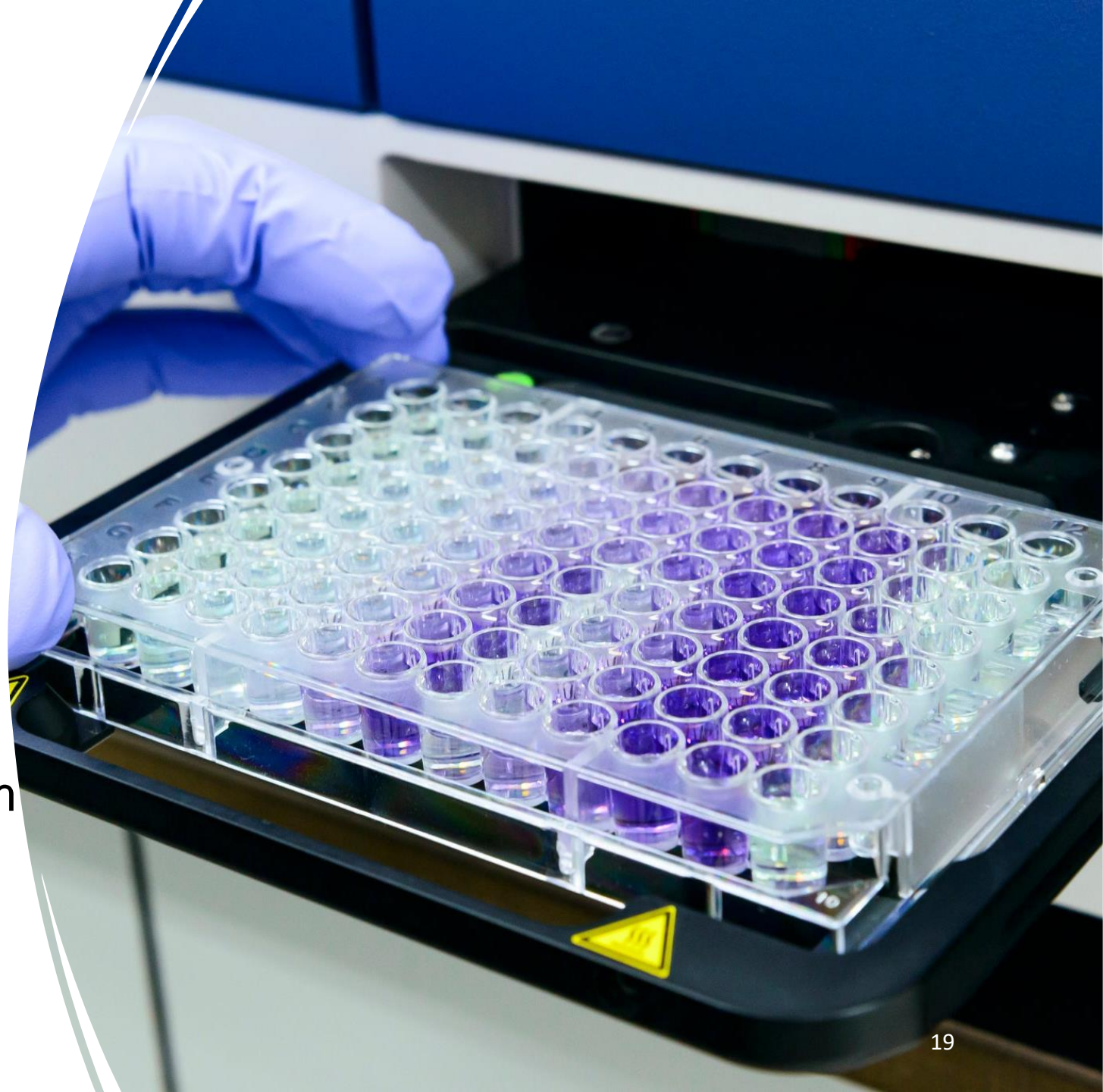
- CLIA compliant testing
- At no cost to clinical labs
- Performed at Regional labs
- Antimicrobial Resistance Laboratory Network | New York State Department of Health, Wadsworth Center
- By request and prior approval
- [ARLNcoreNY@health.ny.gov](mailto:ARLNcoreNY@health.ny.gov)



# ExAST Drugs Tested

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- Drug/ Drug combinations tested
  - Ceftazidime/avibactam
  - Aztreonam
  - Aztreonam/avibactam
  - Aztreonam/ceftazidime/avibactam



## CDC & FDA Antibiotic Resistance Isolate Bank

[AR Isolate Bank Home](#)[About the Bank](#) +[All Isolate Panels](#)[Isolate Search](#)[Contact Us](#)

### All Isolate Panels

[Download this page](#)[Download all MIC & gene data](#)

Order pre-assembled resistance panels from CDC's isolate collection below.

Isolates are gathered through CDC's outbreak response and surveillance programs, validated and sequenced for testing, and then thoughtfully curated to increase lab efficiencies and public health innovations. The isolates represent samples from healthcare-associated, foodborne, gonorrhea, and community-associated infections.

Showing 1 - 25 of 32 records

Search:

Panel	Action
<a href="#">Acinetobacter baumannii</a> (41) This panel of <i>Acinetobacter baumannii</i> isolates were chosen to represent a diversity of antimicrobial susceptibility results for drugs that are used to treat infections. Panel ID: ACI**THIS PANEL IS CURRENTLY OUT OF STOCK	<a href="#">Add Panel to Cart</a>

# Antimicrobial Resistance and Patient Safety Portal



Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives, Protecting People™



## Antibiotic Resistance & Patient Safety Portal



Home > Carbapenem-resistant Enterobacterales (CRE): An urgent public health threat

JULY 2021

## Carbapenem-resistant Enterobacterales (CRE): An urgent public health threat

AR THREAT LEVEL: URGENT



CRE, which stands for carbapenem-resistant Enterobacterales, are a family of germs that are difficult to treat because they are resistant to nearly all antibiotics, including carbapenems, some of our most powerful drugs. Often called “nightmare bacteria”, there were 13,100 estimated cases of CRE in hospitalized patients in 2017, with an estimated 1,100 deaths (Antibiotic Resistance Threats in the United States, 2019). The two most common types of CRE in the United States are carbapenem-resistant *Klebsiella* species and carbapenem-

[Carbapenem-resistant Enterobacterales \(CRE\): An urgent public health threat | A.R. & Patient Safety Portal \(cdc.gov\)](#)



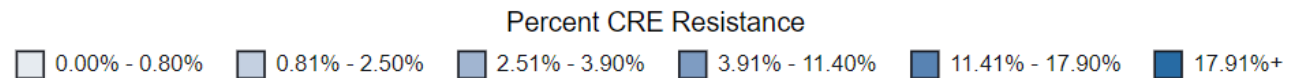
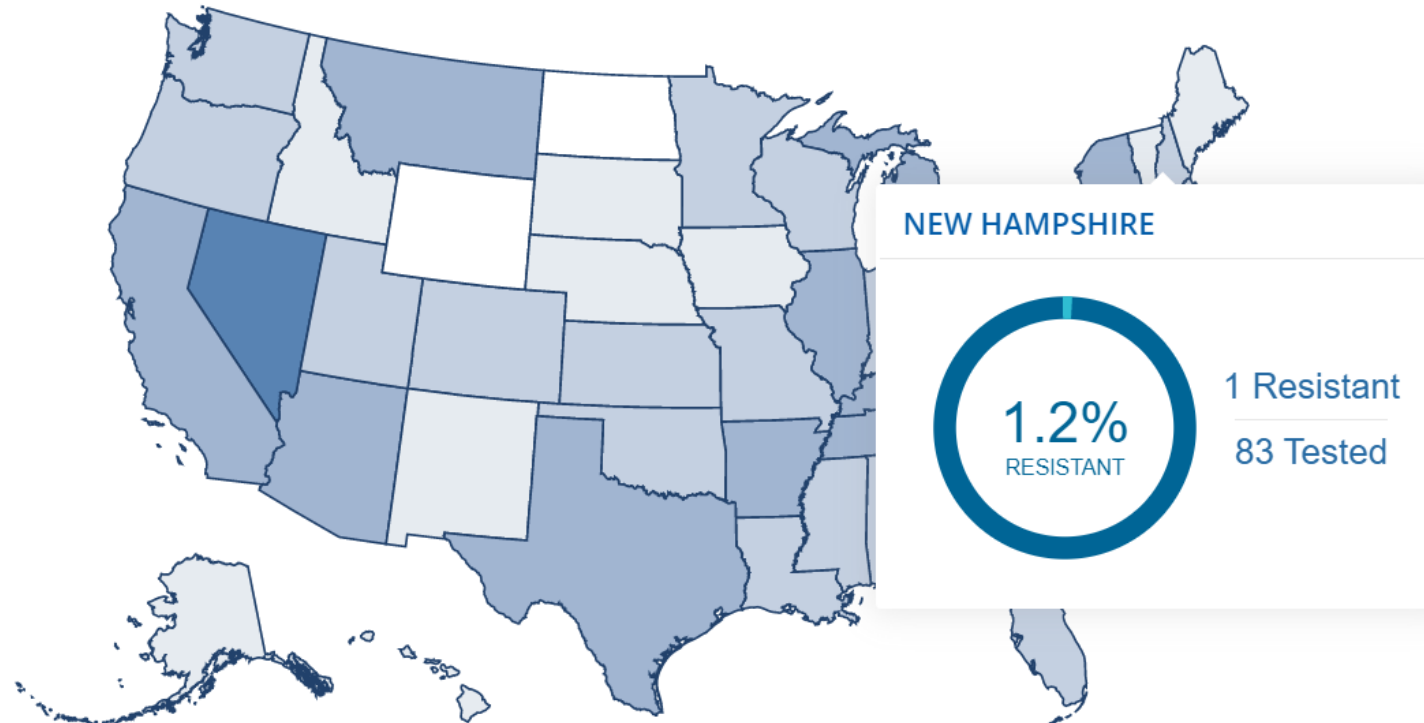
Analysis. Answers. Action

[www.aphl.org](http://www.aphl.org)

# Percentage of Carbapenem Resistance Among Enterobacteriaceae

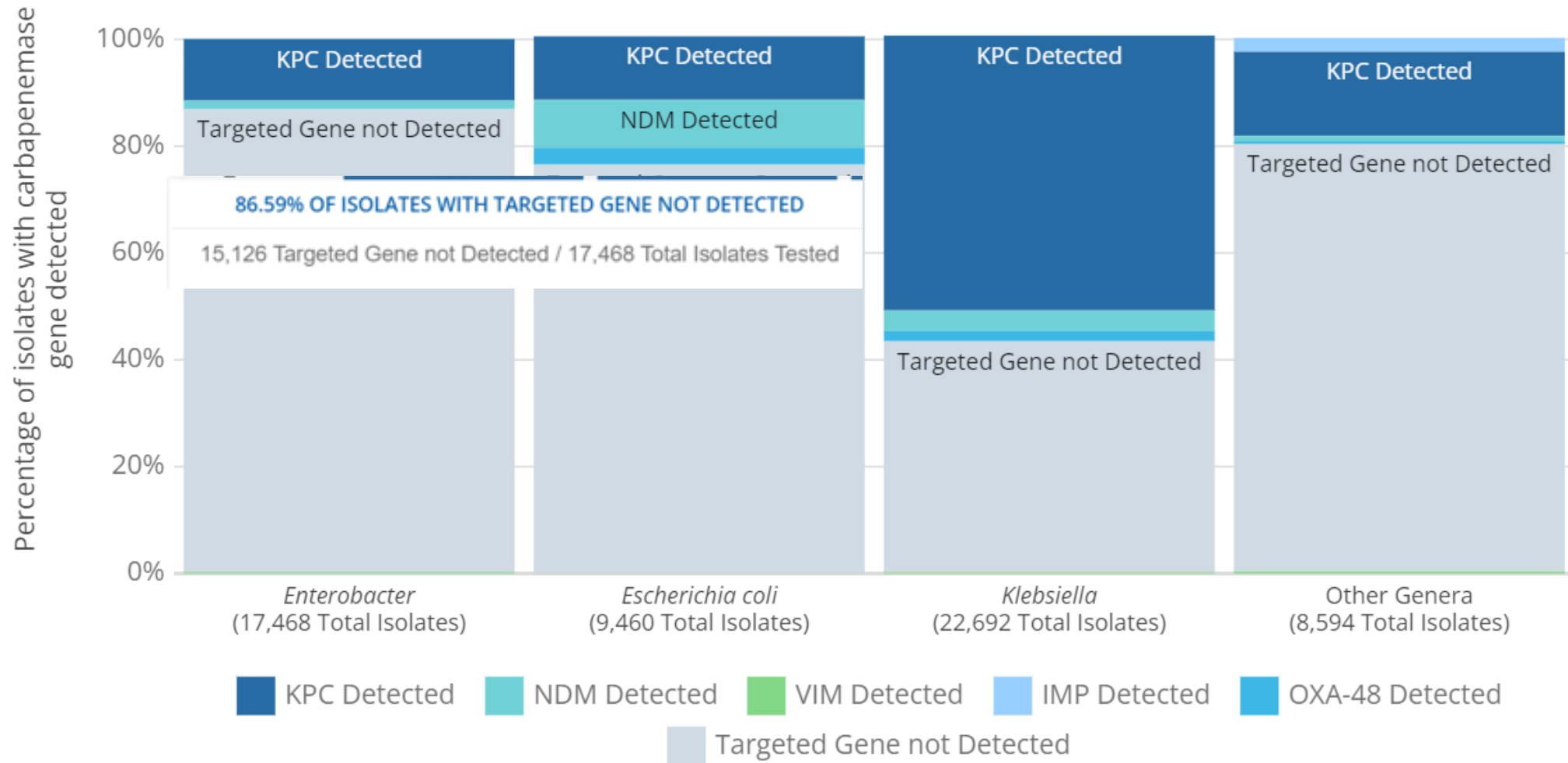
Percentage Carbapenem Resistance Among Enterobacteriaceae by State (NHSN PSC 2019)

[VIEW DATA](#) [SAVE IMAGE](#) [SHARE](#)



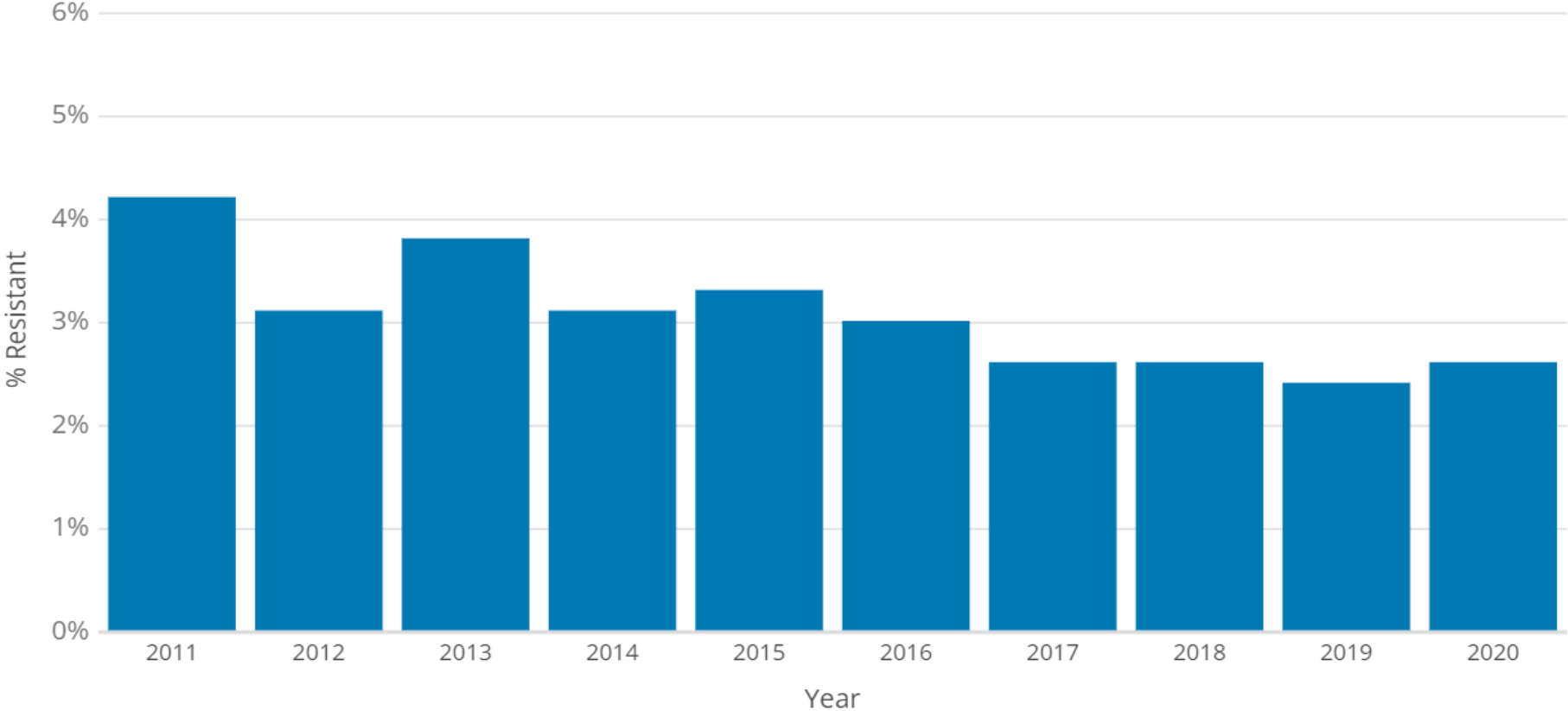
# Carbapenemase Genes Detected in CRE, by Genus, 2017-2020 (AR Lab Network)

[VIEW DATA](#) [SAVE IMAGE](#) [SHARE](#)





# Carbapenem Resistance Identified Among Enterobacteriaceae Infections, 2011-2019 (NHSN PSC)



# Key Takeaways

- Communication between partners is crucial
- Submitting CRE and CP-CRE to your state lab quickly can help to identify resistant organisms
- Screening and WGS both work to identify risks and reduce transmission between patients
- AR Isolate Bank is a great service provided by CDC
- Expanded AST (Prior approval needed)
- Visit the patient safety portal to see AR data from your own state



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# Case Studies



# Detection of a novel carbapenemase



- RI DOH
- 65-year-old male with a complicated medical history but no travel
- Foot wound



## *Pseudomonas aeruginosa*

- mCIM and MBL Positive (**carbapenemase production**)
- PCR Negative (**the Big 5**)
- AST testing by BMD at CDC showed resistance to imipenem and meropenem and non-susceptible to most other drugs



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WGS



*bla*<sub>sim-1</sub>



LETTER TO THE EDITOR



Characterization of the First Carbapenem-Resistant *Pseudomonas aeruginosa* Clinical Isolate Harboring *bla*<sub>SIM-1</sub> from the United States

© Catharine Prussing,<sup>a</sup> Theresa Canulla,<sup>b,c,d</sup> Navjot Singh,<sup>a</sup> Patricia McAuley,<sup>a,e</sup> Michael Goscininski,<sup>a,e</sup> Ewa King,<sup>c,d</sup> Utpala Bandy,<sup>a,e</sup> Maria-José Machado,<sup>f</sup> Maria Karlsson,<sup>f</sup> Kimberlee A. Musser,<sup>g</sup> Richard C. Huard,<sup>b,c,d</sup> Elizabeth J. Nazarian<sup>a</sup>

<sup>a</sup>Wadsworth Center, New York State Department of Health, Albany, New York, USA  
<sup>b</sup>Center for Biological Sciences, Providence, Rhode Island, USA  
<sup>c</sup>Rhode Island State Health Laboratory, Providence, Rhode Island, USA  
<sup>d</sup>Rhode Island Department of Health, Providence, Rhode Island, USA  
<sup>e</sup>Center for Acute Infectious Disease Epidemiology, Providence, Rhode Island, USA  
<sup>f</sup>Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA



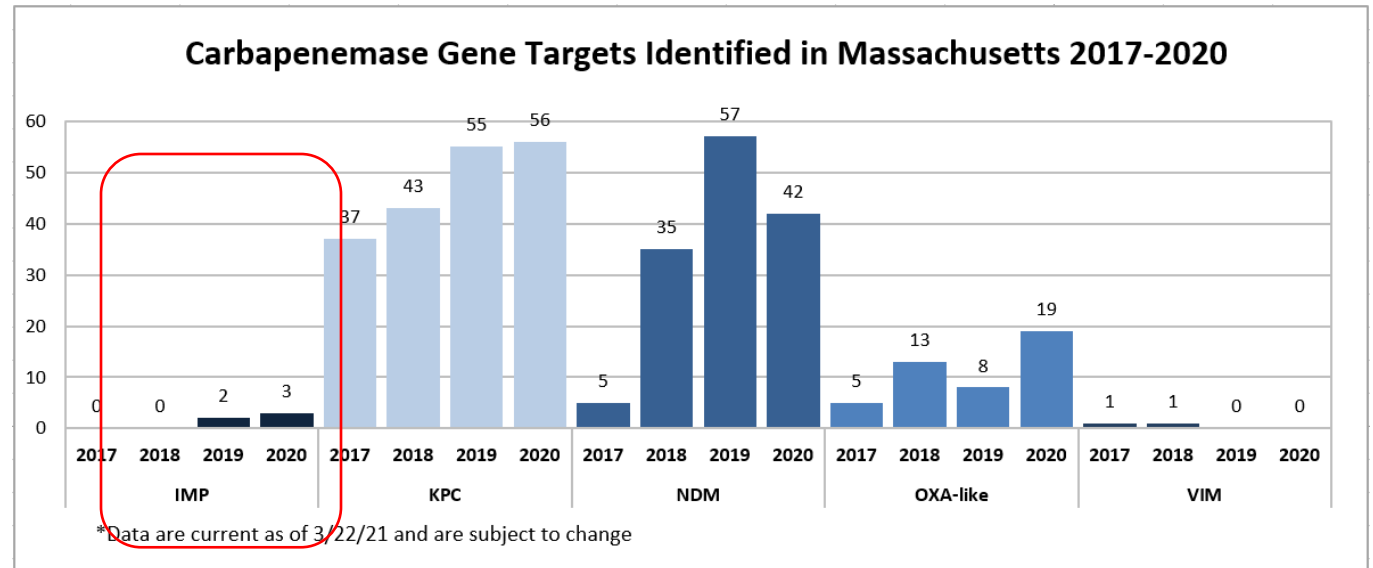
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## NDM-positive *Klebsiella pneumoniae* in a LTCF in MA

# Background

2019 MARCH						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
24	25	26	27	28	1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

- Increasing local transmission of the NDM gene in MA
- Two NDM-positive *K. pneumoniae* identified in LTAC unit
- Follow up investigation and screening revealed **7 additional colonized patients** on the same unit



# Onsite Investigation at LTAC

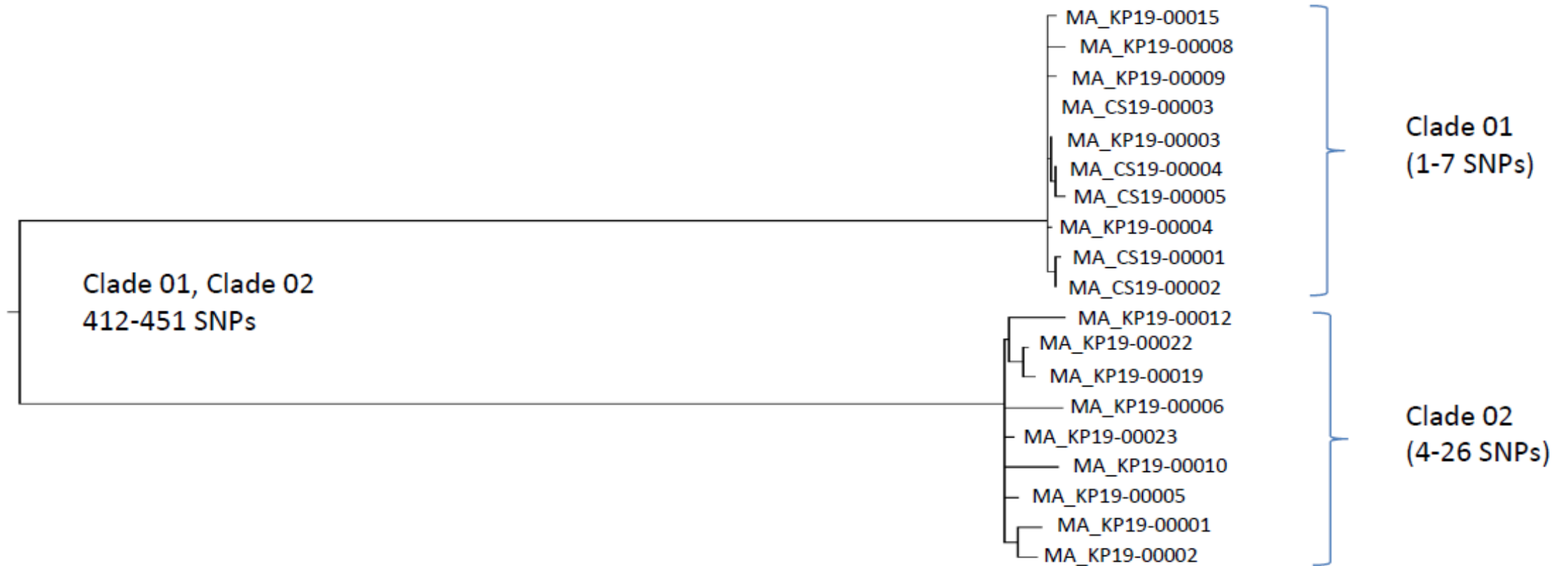
- Most cases associated with a small, 12-bed unit
  - Many ventilator-dependent and had wounds requiring a high level of care
- Non-compliance observed with:
  - PPE use and hand hygiene
  - Cleaning and disinfection of shared medical equipment
- Lack of staff knowledge about carbapenemase-producing organisms

# WGS Methods

31 NDM-positive *K. pneumoniae* isolates collected between May 2018- November 2019 were sequenced



# Further analysis

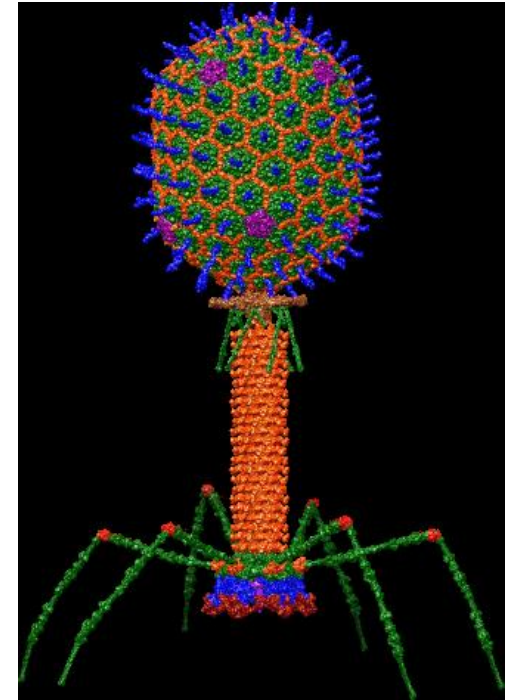






# Results

- The two clades appear to be due to the insertion of a bacteriophage
- When removed, the 2 clades become 1 again
- One patient had both strains
  - October 2018 with organism from Clade 2
  - September of 2019 with organism from Clade 01, the post insertion clade.
  - She remained in the facility during this entire time and crossed two different affected units.



# Conclusions

**WGS data**

**+**

**Epidemiologic data**

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**Better outbreak characterization**



# “Down the Drain”

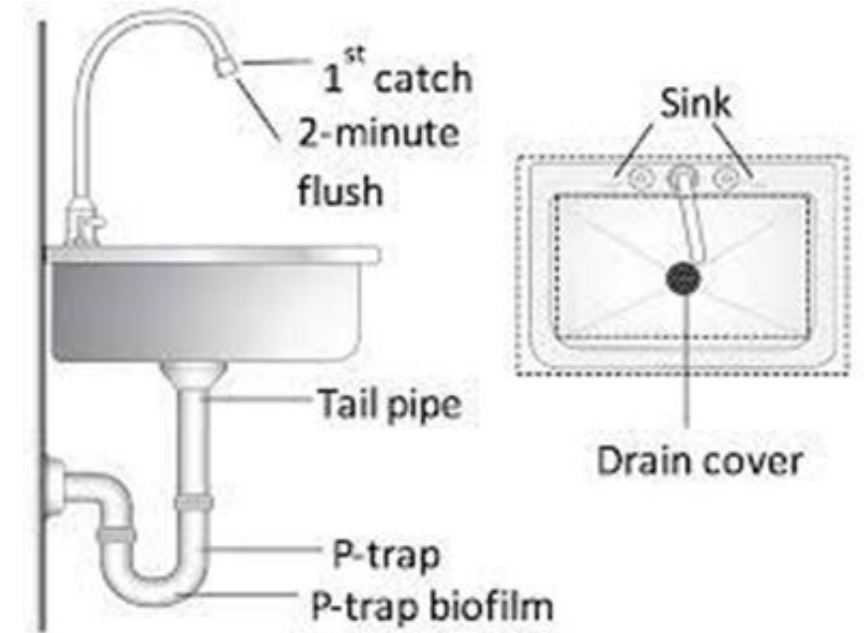
An investigation into a different cluster of NDM+ *Klebsiella pneumoniae* in MA CCU

# Where it all began...

- September 2021
  - Massachusetts State Public Health Laboratory (MASPHL) identified three NDM+ *Klebsiella pneumoniae* isolates that were highly related through whole genome sequencing (WGS).
- Investigation revealed that the isolates were from three patients admitted to the same hospital critical care unit (CCU).

# The Investigation

- Screening
  - Monthly Point prevalence screening (Nov 2021)
  - Discharge screening (Feb 2022)
- 16 CCU drains were sampled from patient rooms in the CCU



<https://microbiologycommunity.nature.com/posts/a-microbiological-survey-of-handwashing-sinks-in-the-hospital-built-environment-reveals-differences-in-patient-room-and-healthcare-personnel-sinks>

- Twelve additional patient isolates identified
- Sixteen patient isolates and one sink drain isolate were determined to be highly related (0-12 SNP differences).
- Additional isolates identified from sink drain cultures included KPC+ *Klebsiella oxytoca* and KPC+ *K. pneumoniae*.
- Investigation identified that, during COVID surges, dialysate and other nutritive materials were disposed of in handwashing sinks to avoid additional instances of PPE donning and doffing.

## But, wait...

- Despite implementation of enhanced infection prevention and control practices, cases continued.





**Kahoot!**



# But, wait...

- Environmental sampling followed by WGS provided evidence that biofilm likely facilitated ongoing transmission by serving as a persistent source of contamination of the environment and the hands of healthcare providers.

# Key Lessons Learned

- Routine water and drain maintenance are key for managing biofilm
- Handwashing sinks in patient rooms should only be use for hand hygiene
- Nutritive materials, such as dialysate, and patient waste should only be disposed of in a toilet (covered) or dirty utility hopper.



<https://sanimag.sanimarc.com/tips-for-a-successful-implementation-of-the-bioassure-process/>

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**Kahoot!**



# Acknowledgements

## Massachusetts SPHL

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## CDC AR Team

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