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California Department of Public Health

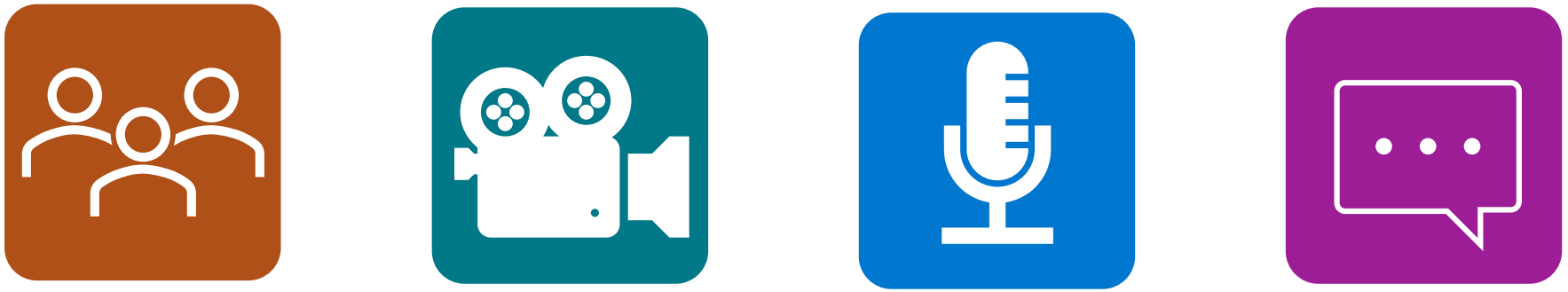
Introduction to Priority Multidrug-Resistant Organisms (MDROs)

Healthcare-Associated Infections Program

February 20, 2025

Presented via Webinar

Housekeeping



Questions? Email us at HAIProgram@cdph.ca.gov or visit our website to learn about additional resources for public health partners (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/LHD_Resources_and_Trainings.aspx)

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Reminder

To receive 1 continuing credit offered by CA-BRN, you must:

- Register on Absorb (replaced Learning Stream)
- Complete the post-evaluation survey

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Implicit bias

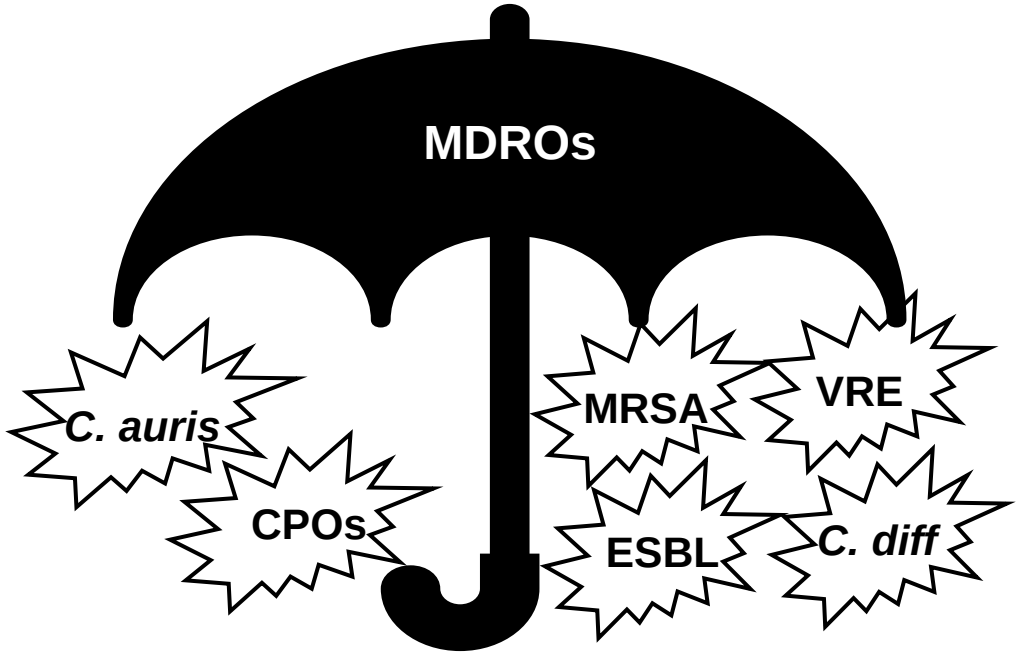
- Describes how our unconscious attitudes or judgements can influence our thoughts, decisions, or actions
- Includes involuntary, unintentional perceptions made without awareness
- Occurs as our brains sort information and perceive data to understand our world
- Affects our decisions, contributing to societal disparities
  - Self awareness about implicit bias can promote healthcare diversity and equality
- Learn more about your own implicit bias at Project Implicit (implicit.harvard.edu/implicit/)

Objectives

- Describe *Candida auris* and carbapenemase-producing organisms (CPOs)
- Discuss risk factors for acquiring these priority multidrug-resistant organisms (MDROs)
- List how MDROs are transmitted in healthcare settings
- Explain how the epidemiology of *C. auris* and CPOs has changed in California since 2019

What are MDROs?

- Bacteria and fungi resistant to many or all antimicrobials (antibiotics, antifungals)
- Infections caused by MDROs can be more difficult and expensive to treat
  - Can result in increased morbidity and mortality
- Can cause outbreaks in healthcare settings



MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant *Enterococci*;
ESBL= extended-spectrum beta-lactamase; *C. diff* = *Clostridiodes difficile*;
CPO = carbapenemase-producing organisms

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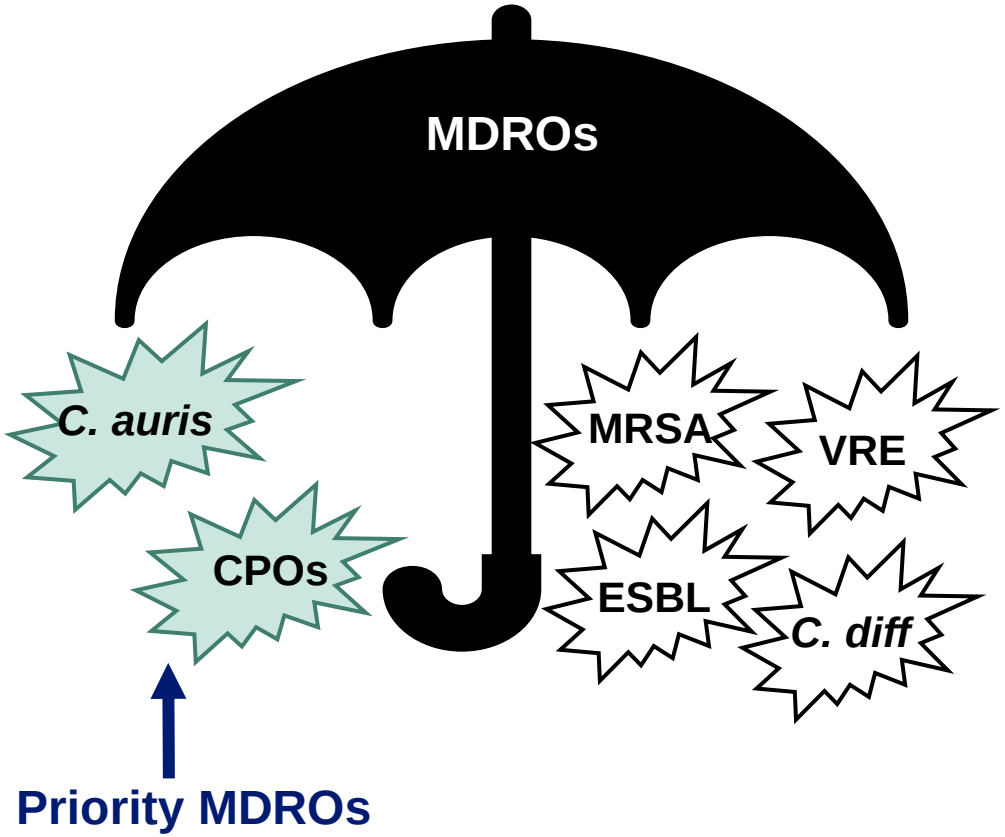
What are priority MDROs?

- Novel or emerging MDROs
- Can spread more rapidly within and among healthcare facilities
- We do not want these pathogens to become common in healthcare facilities!
  - Early and aggressive facility and public health containment efforts can limit spread



MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant *Enterococci*; ESBL= extended-spectrum beta-lactamase; *C. diff* = *Clostridiodes difficile*; CPO = carbapenemase-producing organisms

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What are the risk factors for acquiring a priority MDRO?

- Exposure to long-term acute care hospitals (LTACHs) and ventilator units in skilled nursing facilities (vSNFs)
- Indwelling medical devices (e.g., urinary catheter, endotracheal tube)
- Mechanical ventilation
- Open/draining wounds
- Recent or frequent antimicrobial use (i.e., antibiotics, antifungals)
- Overnight healthcare exposure outside of California or the US

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What is colonization?

- Colonization is when a patient or resident is carrying a pathogen but is not showing signs or symptoms of infection
- Patients or residents colonized with MDROs can still spread the pathogen to other patients or residents
- Patients/residents can be colonized for many months, sometimes indefinitely; patients/residents can be colonized intermittently
  - Do not recommend rescreening patients with the same CPO or *C. auris* to assess for “clearance” or to discontinue infection prevention and control (IPC) measures (e.g., Contact Precautions)[1]
- Colonized patients can go on to develop clinical infections

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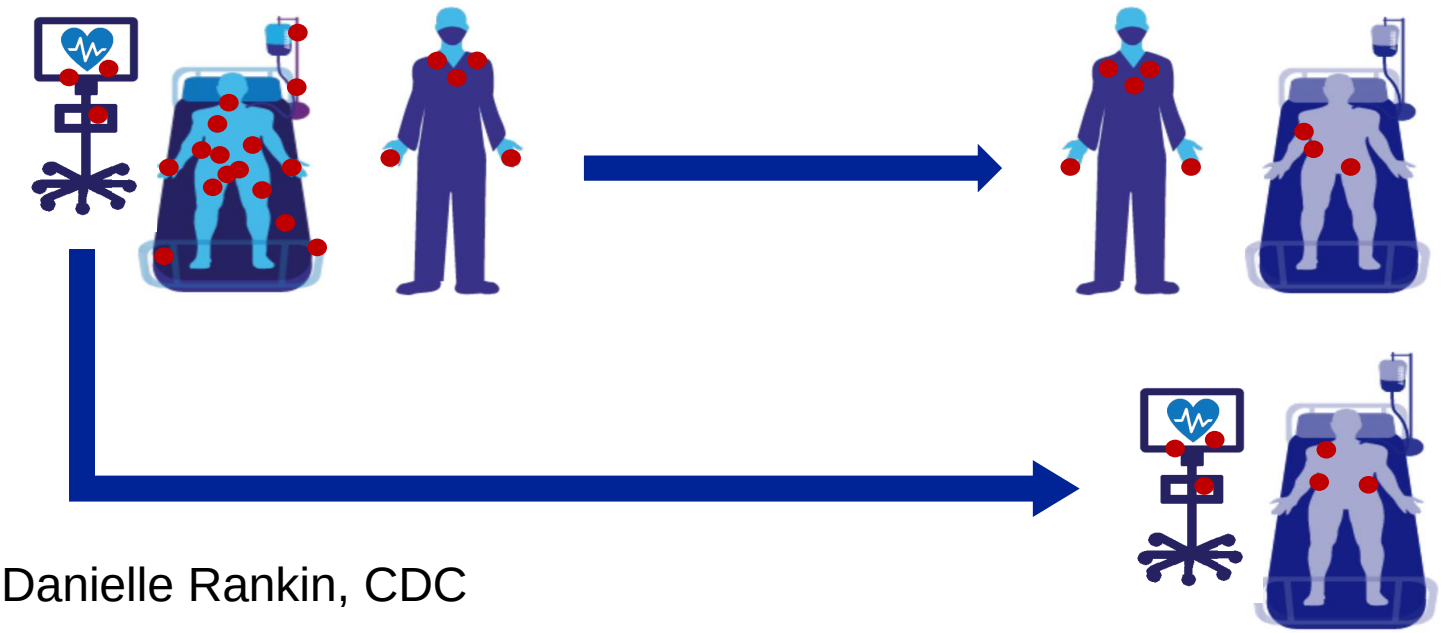
MDROs spread from person to person, via the hands and clothing of healthcare personnel or contaminated equipment or surfaces when there are gaps in core IPC practices



Slide courtesy of Danielle Rankin, CDC

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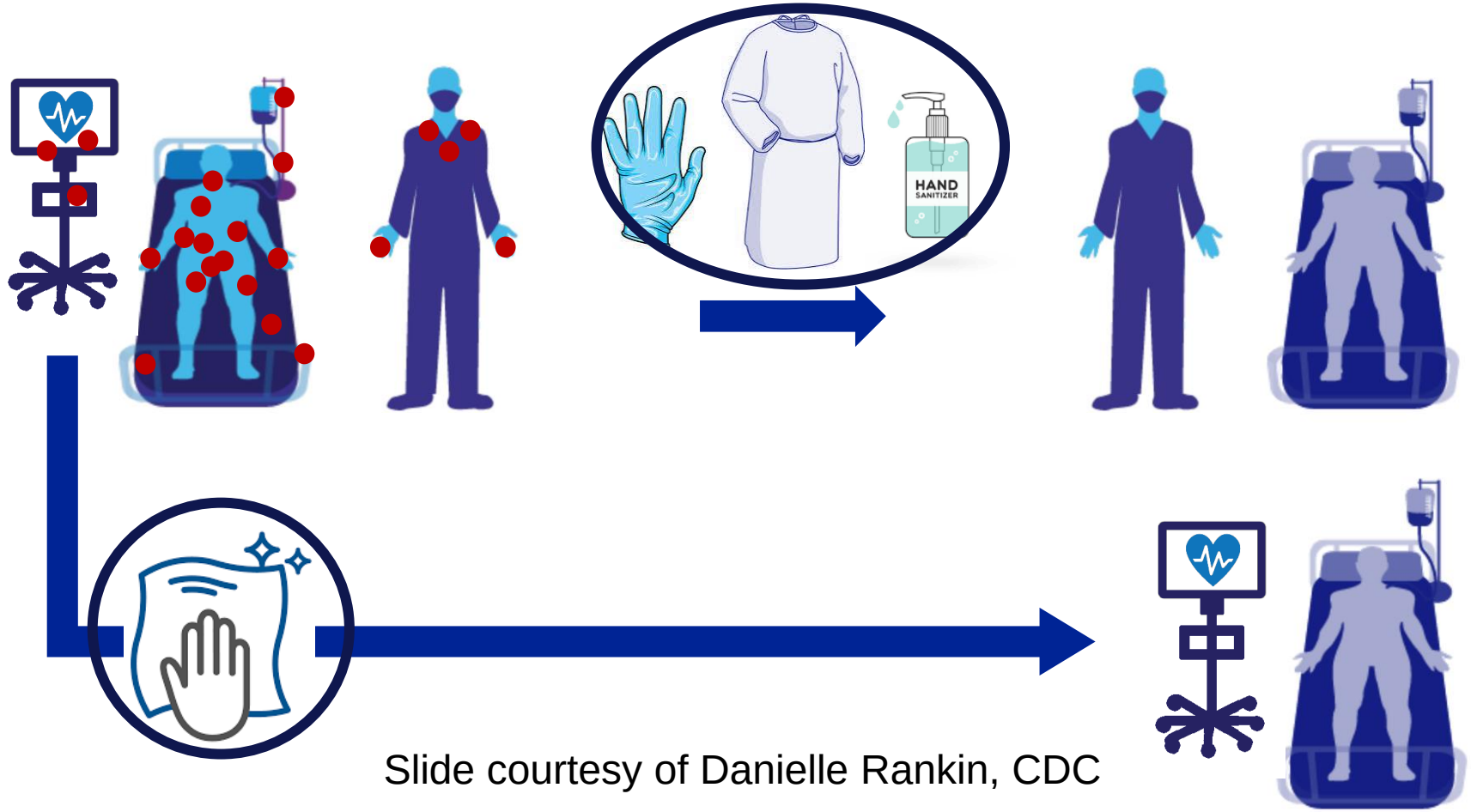
Core IPC practices can prevent spread



Slide courtesy of Danielle Rankin, CDC

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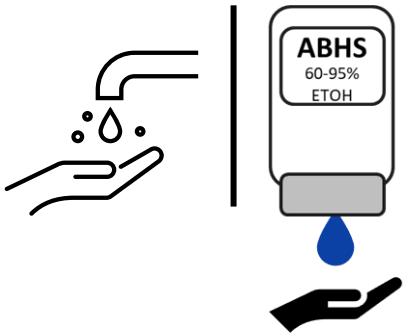
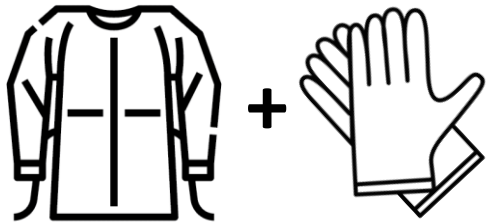
What are Core IPC practices?[2]

Hand Hygiene



Personal Protective Equipment



Environmental Cleaning & Disinfection

+ observe and monitor compliance

CDC's Core Infection Prevention and Control Practices for Safe Healthcare Delivery in All Settings | Infection Control | CDC
(www.cdc.gov/infection-control/hcp/core-practices/index.html)

Candida auris

Candida auris (C. auris)

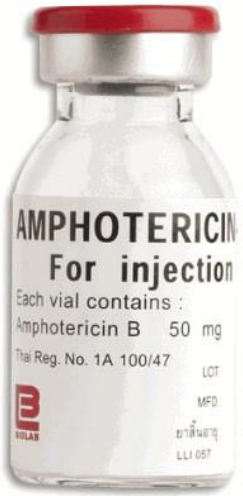
- Drug-resistant yeast, can be resistant to all 3 antifungal classes
- Invasive infections can lead to 30-60% mortality
- Persistence in the environment contributes to rapid spread in healthcare settings
  - Cleaning and disinfection requires agents effective against *C. auris* (regular disinfecting agents such as “quats” are not effective)
- Title 17 requirements as of September 2022
  - Reportable by laboratories and providers
  - Laboratories submit specimens from sterile sites (e.g., blood)

Why are we concerned about *C. auris*?

Highly drug-resistant

C. auris antifungal resistance in the United States[3]

First-line treatment



	Fluconazole	Amphotericin B	Echinocandins
United States	86%	21%	1%

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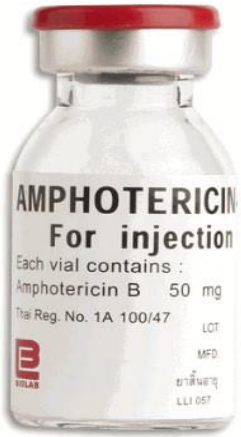
In California, almost all isolates are fluconazole-resistant; very few are amphotericin B- or echinocandin-resistant[4]



	Fluconazole	Amphotericin B	Echinocandins
United States	86%	21%	1%
California	99%	2%	<1%

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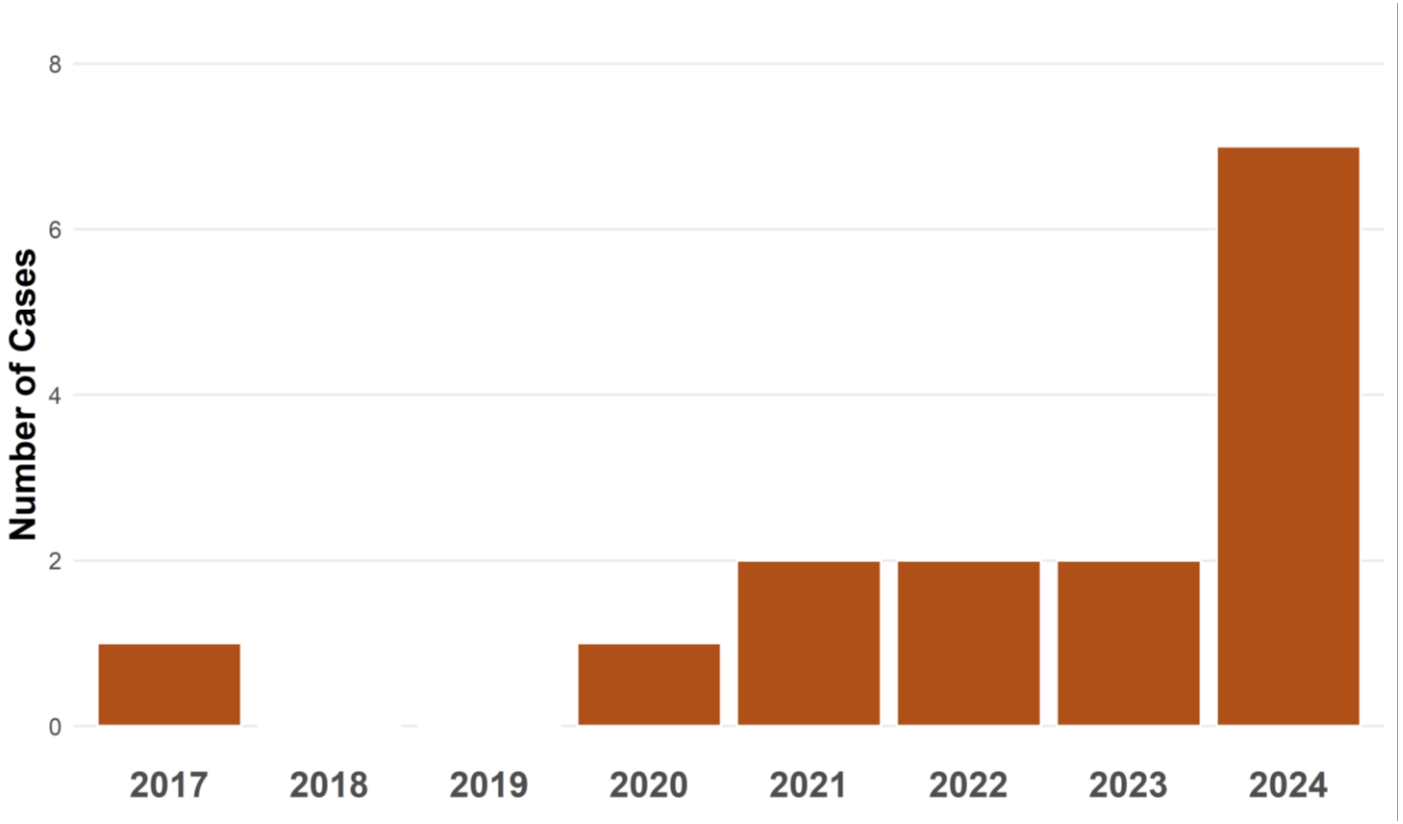
However, in California, we are identifying more fluconazole+echinocandin-resistant *C. auris* cases*



*preliminary data

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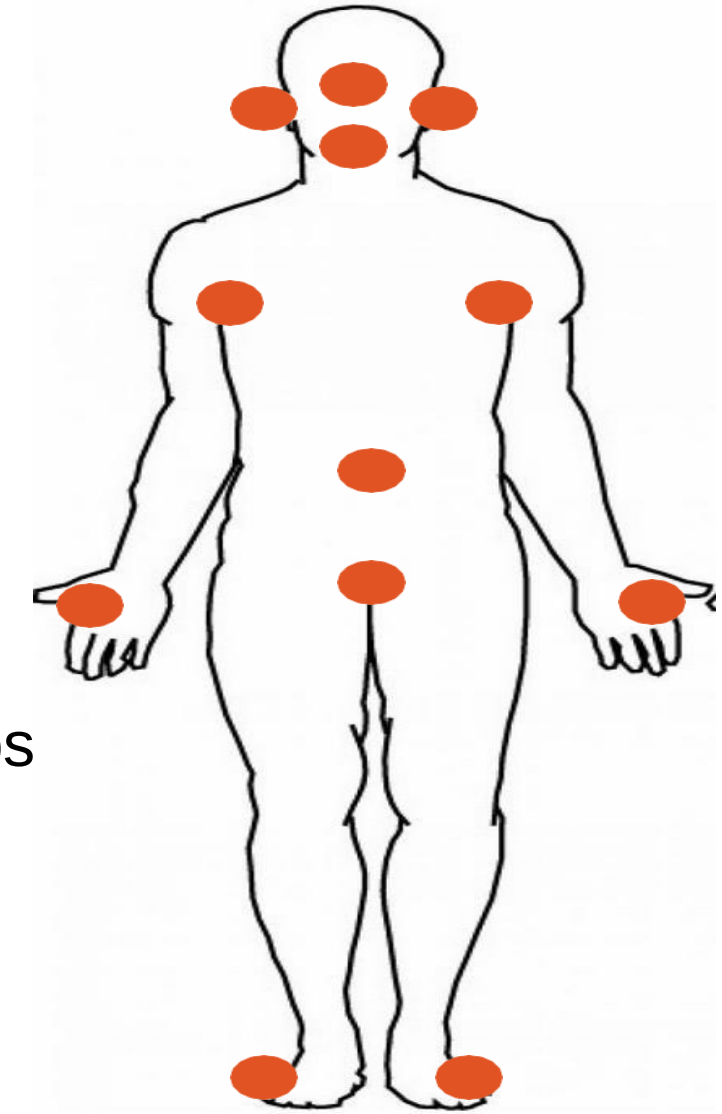
More reasons we are concerned about *C. auris*

Highly drug-resistant

Patients can become colonized and develop invasive infections

C. auris colonization

- *C. auris* can colonize the skin and other body sites
  - Axilla
  - Inguinal creases
  - Nares
  - Hands
  - Toes
  - Other skin sites
- Screening recommendation: Composite axilla/groin swabs



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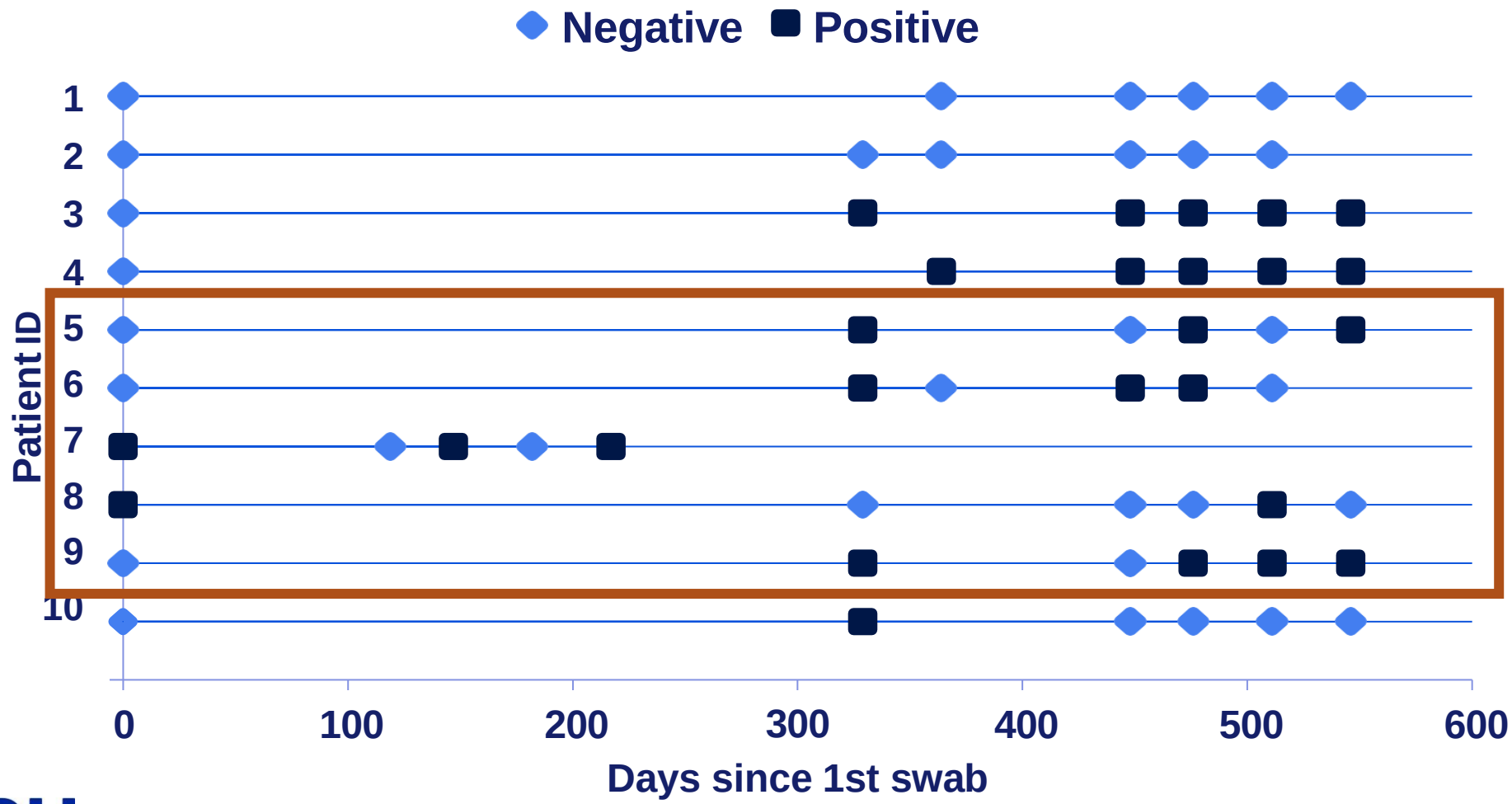
C. auris colonization can be long-term[5]



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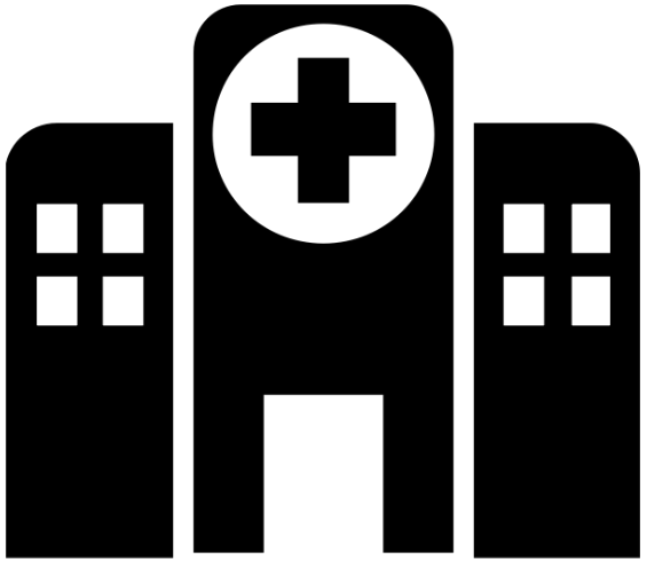
Additional concern about *C. auris*

Highly drug-resistant

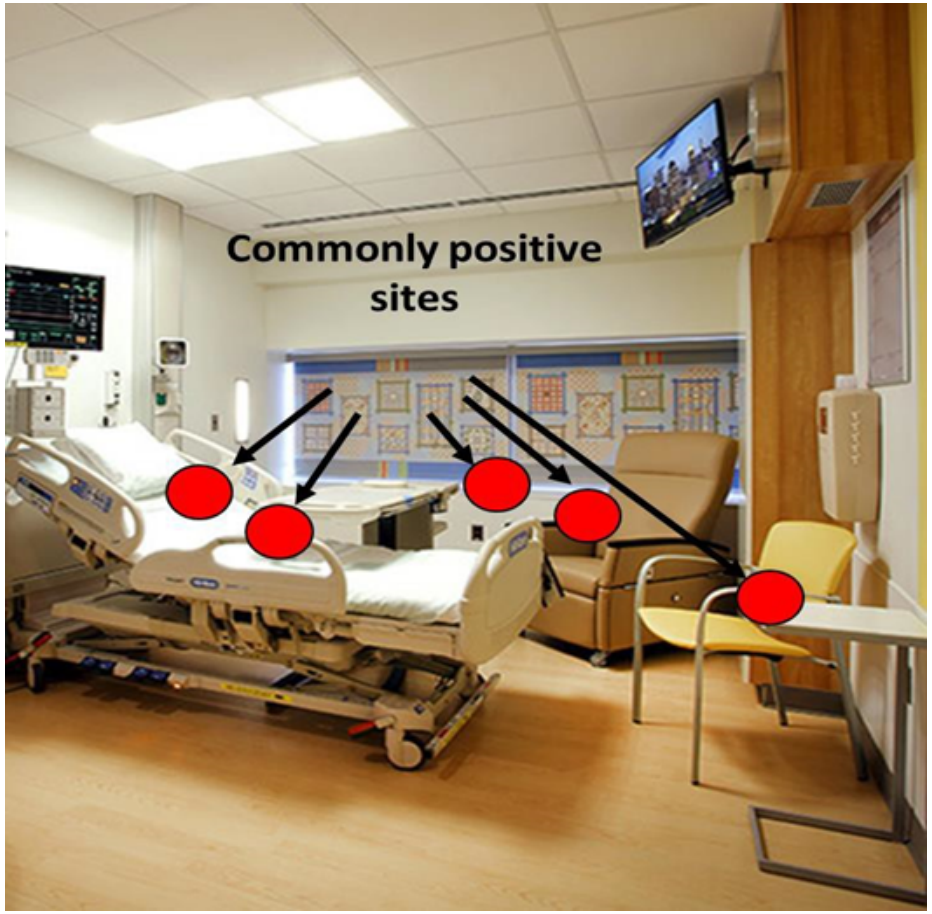
Patients can become colonized and develop invasive infections



Spreads in healthcare settings and networks

C. auris is persistent in the healthcare environment

- Persistent on high-touch surfaces (e.g., bedrails, doorknobs, windowsills, medical equipment)
- Environmental cleaning and disinfection of *C. auris* requires List P[6] agents with claims against *C. auris*
  - If List P is unavailable, List K or bleach
  - Quaternary ammonium chloride products or “Quats” don’t work
- Higher patient colonization burden associated with greater environmental contamination[7, 8]



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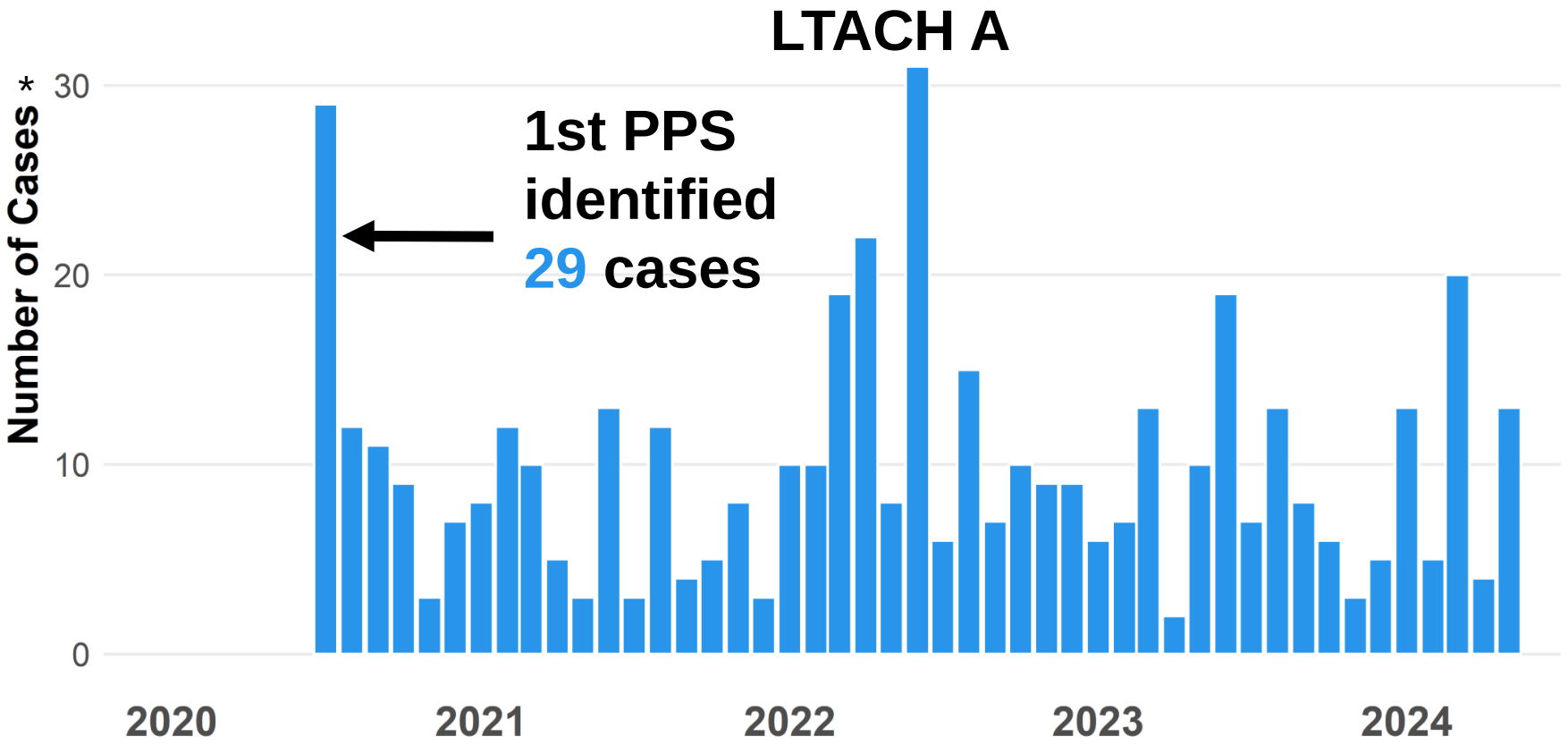
Once *C. auris* is in a facility, it can spread rapidly



The **high burden of *C. auris*** identified during the first point prevalence survey (PPS) at LTACH A likely contributed to internal spread in the facility

*preliminary data from an LTACH with a high burden of *C. auris*

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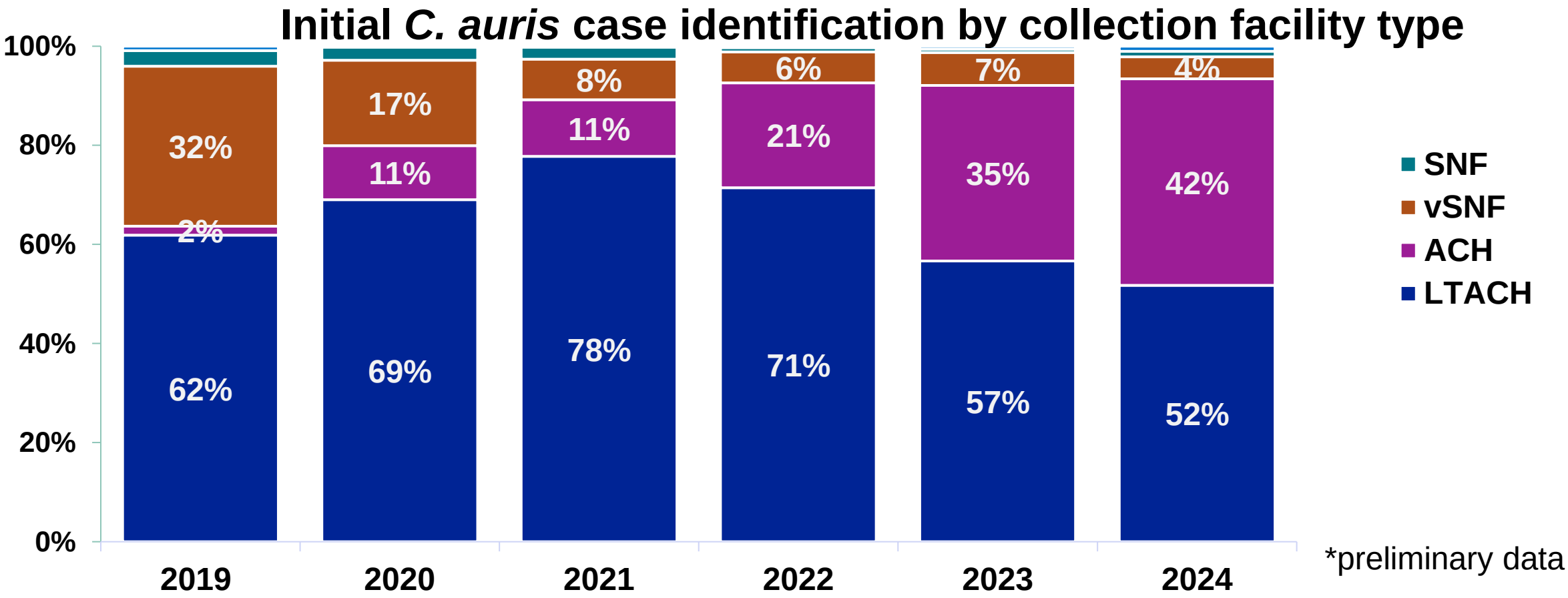
C. auris has mainly been identified in LTACHs and vSNFs



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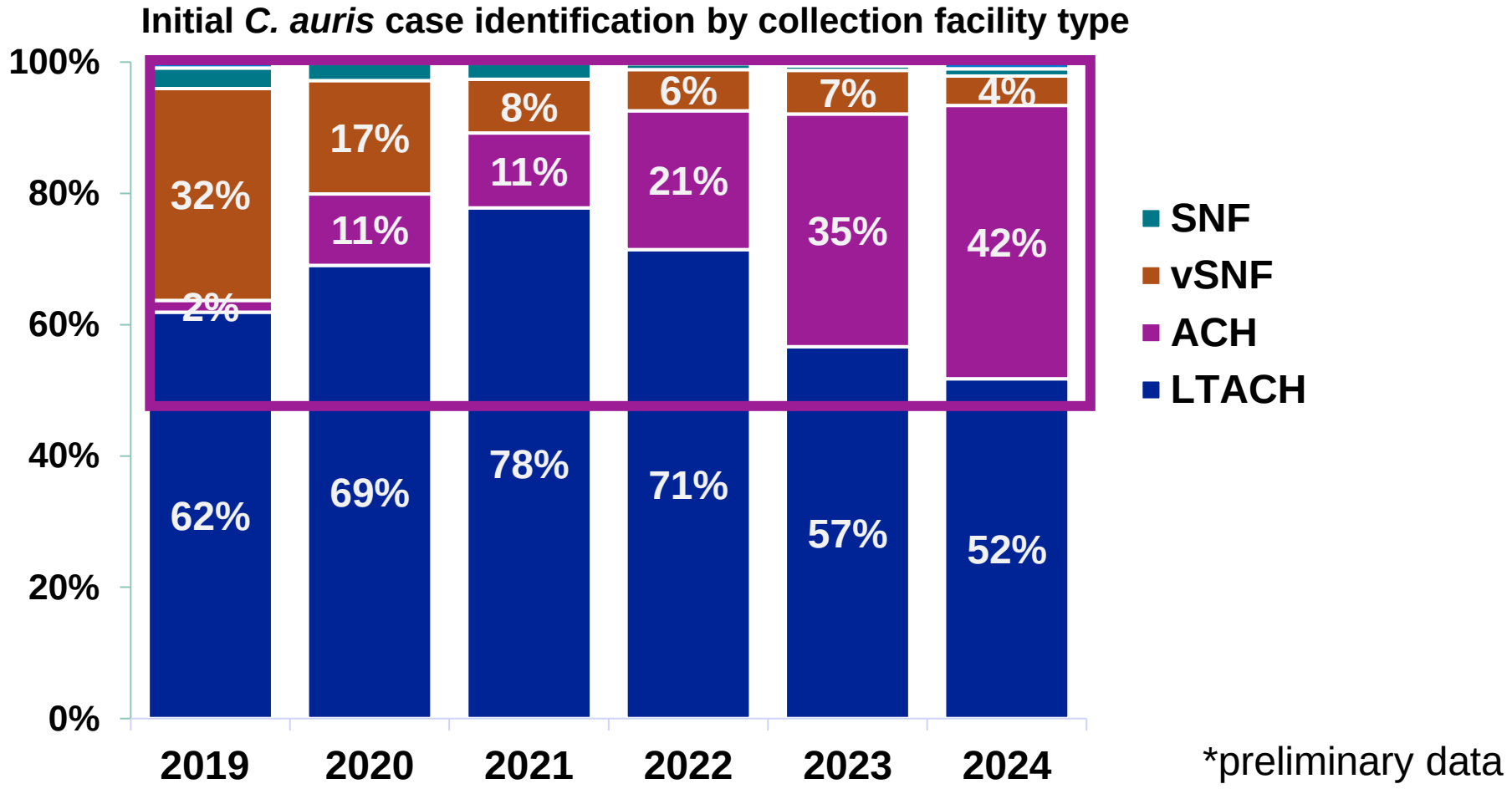
C. auris is increasingly being identified in short-stay acute care hospitals



*preliminary data

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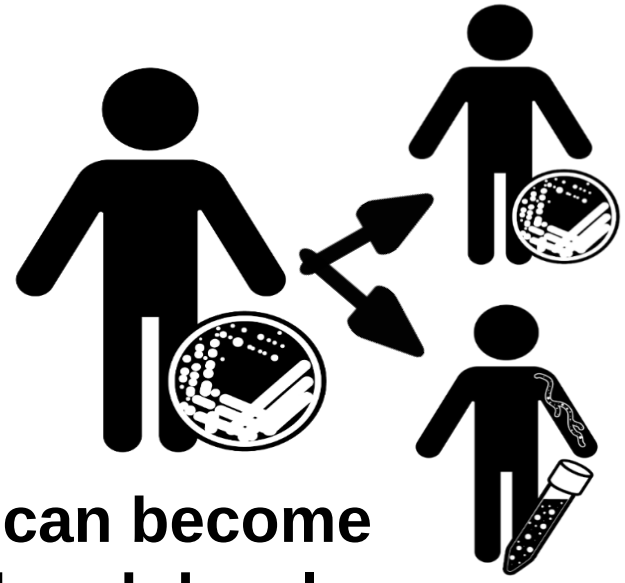
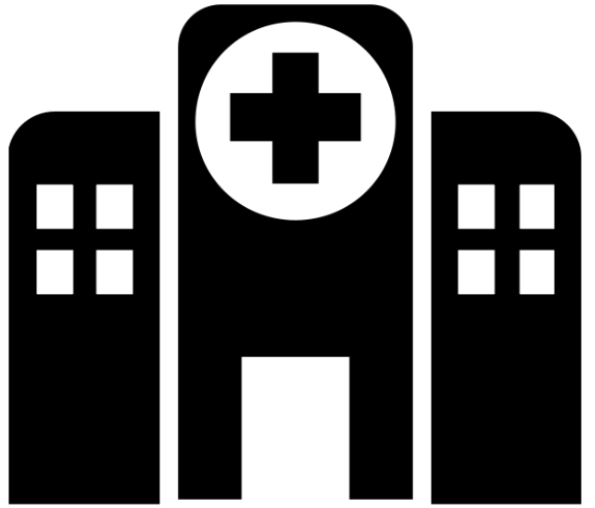
C. auris has the makings of a fungal superbug

Highly drug-resistant



Patients can become colonized and develop invasive infections



Spreads in healthcare settings and networks

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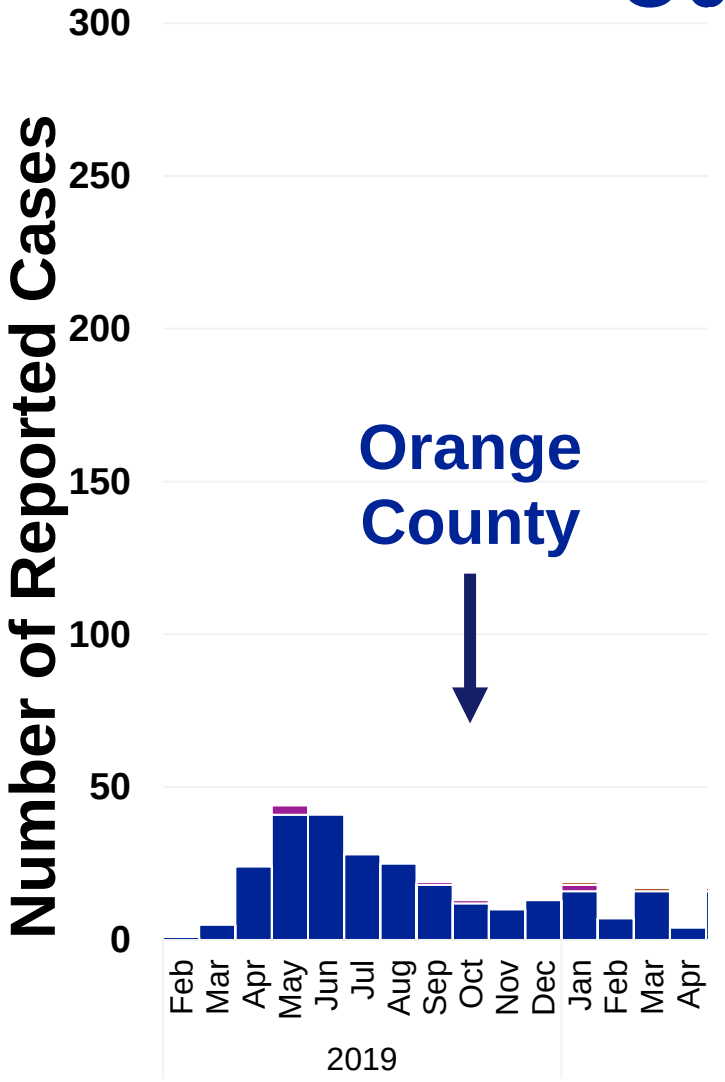
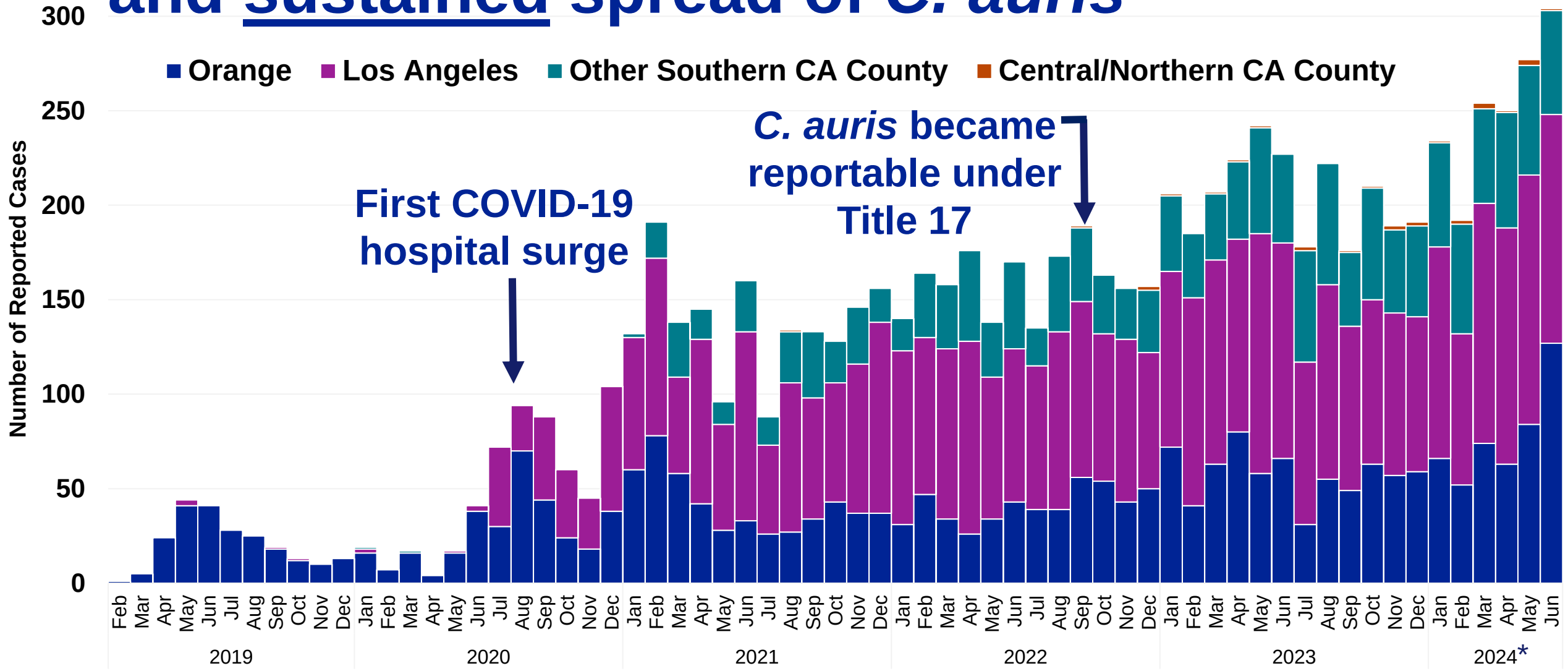
Aggressive response to our first *C. auris* outbreak was successful[9]

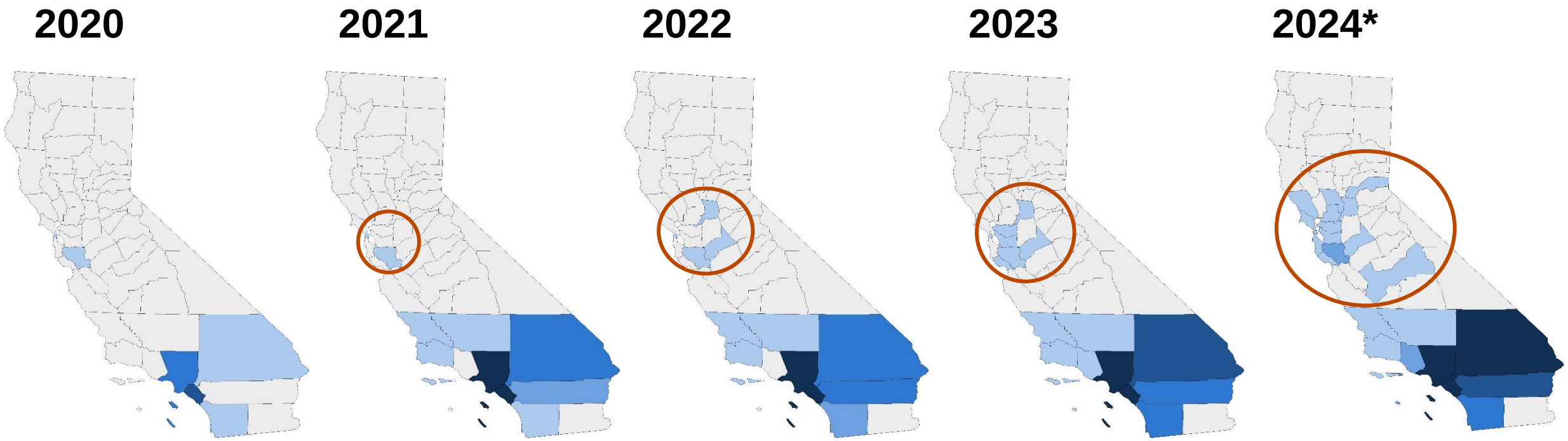


The pandemic contributed to widespread and sustained spread of *C. auris*



*preliminary data

We are seeing more *C. auris* in Central and Northern California



*preliminary data

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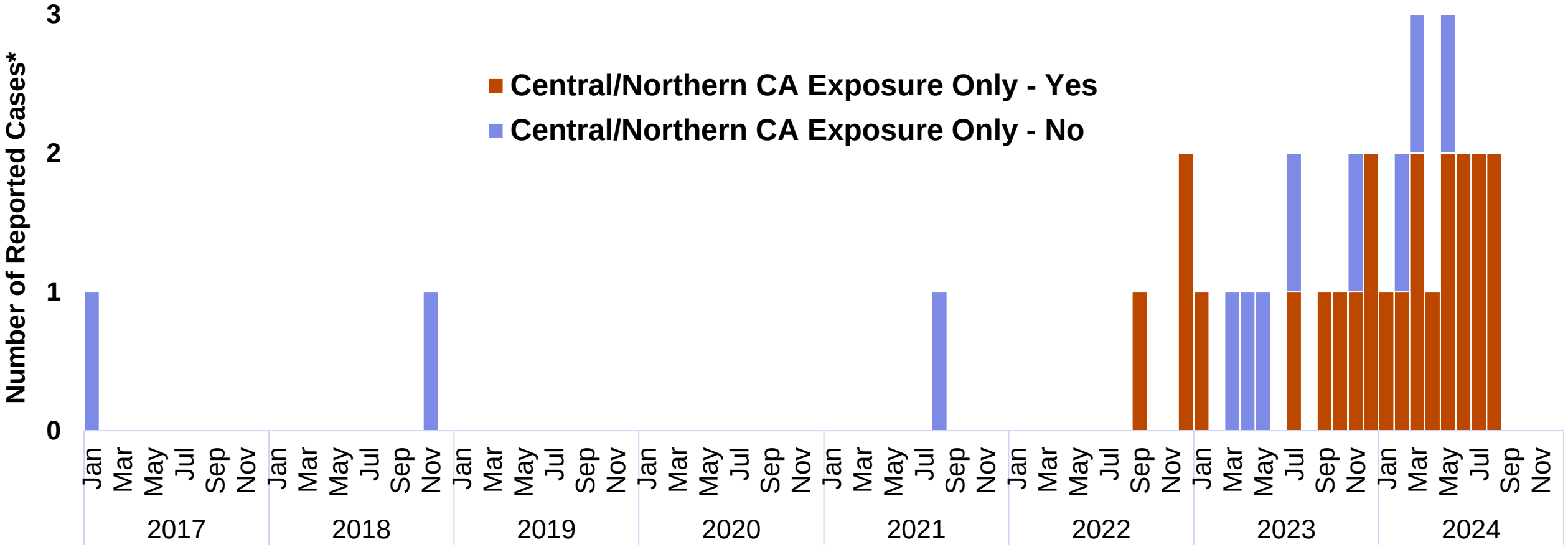
From September 2022, most Central/Northern CA cases* had no exposure outside the region



*preliminary data

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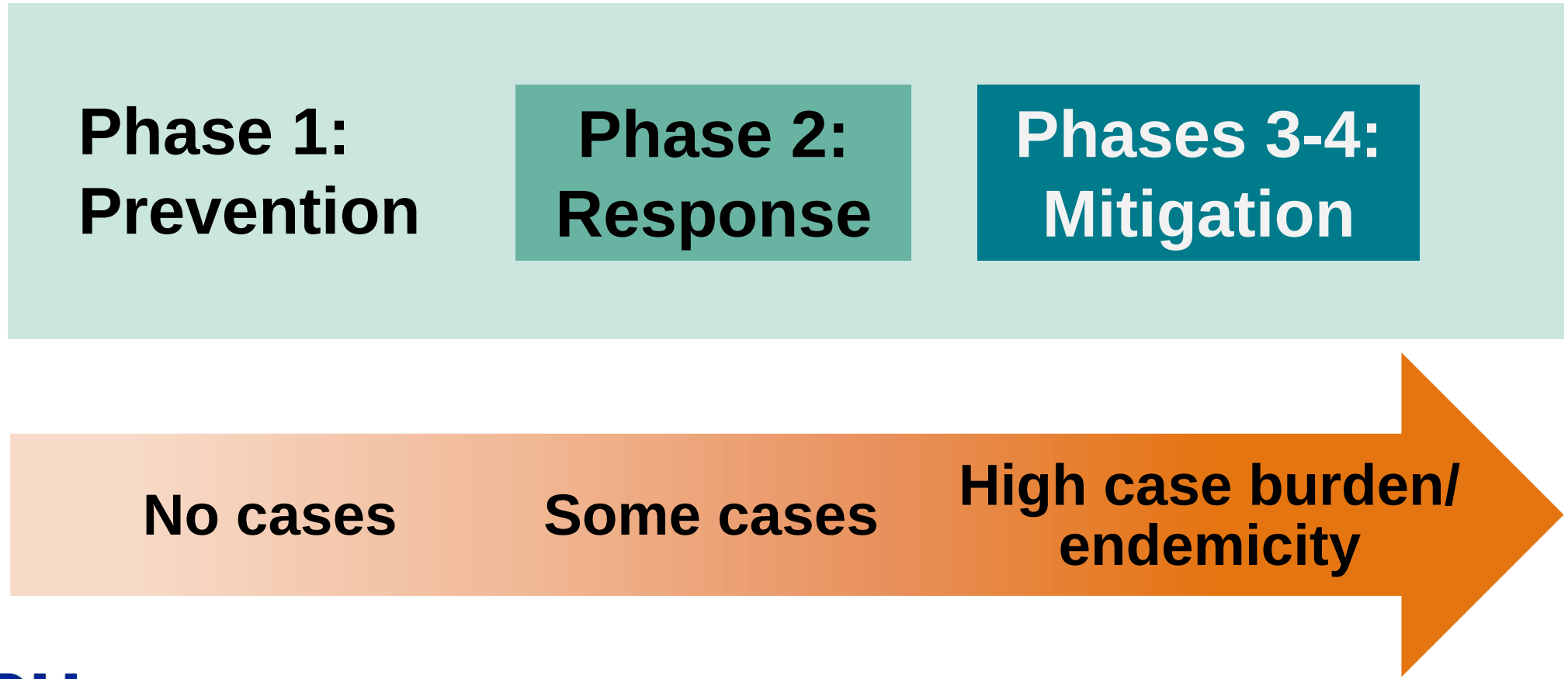
Regional MDRO prevention and response strategy: a phased approach based on local epidemiology[10]

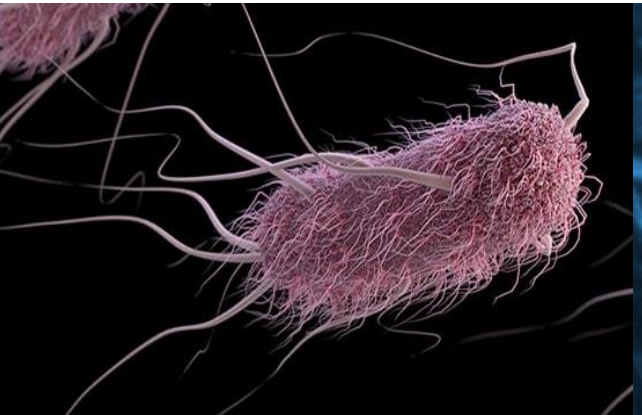
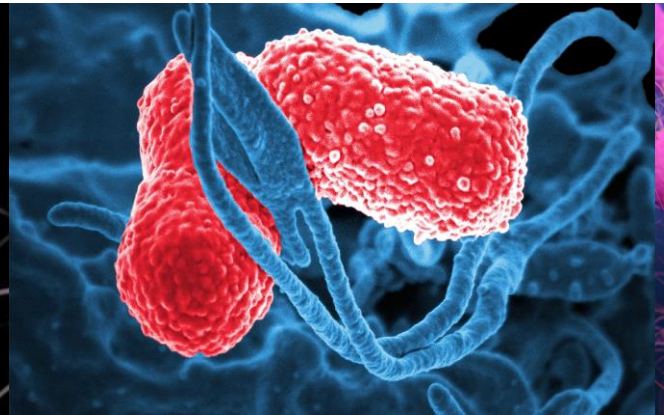


Let’s prevent further spread of *C. auris* in Central and Northern California!

Carbapenem-resistant organisms (CROs) and carbapenemase-producing organisms (CPOs)

Acronyms for carbapenem resistance

- **Carbapenem-resistant organisms (CROs)** include:
  - Carbapenem-resistant Enterobacterales (CRE)
  - Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)
  - Carbapenem-resistant *Acinetobacter baumannii* (CRAB)

C is for carbapenem

- Class of beta-lactam antibiotics (others include penicillin, cephalosporins)
- Broad spectrum
  - Imipenem
  - Meropenem
  - Ertapenem
  - Doripenem (not used in the United States)

R is for resistant

- Resistant to at least 1 **carbapenem** antibiotic
- Treatment options for infections can be more limited, expensive, and toxic, and less effective

Selected Organism: Acinetobacter baumannii complex

Susceptibility Information	Card:		Status: Final	Analysis Time: 7.30 hours	
	Completed:				
Antimicrobial	**MIC**	**Interpretation**	**Antimicrobial**	**MIC**	**Interpretation**
Ampicillin			Meropenem	>= 16	R
Amoxicillin/Clavulanic Acid			Amikacin		
Piperacillin/Tazobactam	>= 128	R	Gentamicin	>= 16	R
Cefazolin	>= 64	R	Tobramycin	>= 16	R
Cefoxitin			Ciprofloxacin	>= 4	R
Ceftazidime	>= 64	R	Levofloxacin	>= 8	R
Ceftriaxone	>= 64	R	Tetracycline	>= 16	R
Cefepime	>= 64	R	Nitrofurantoin		
Ertapenem			Trimethoprim/Sulfamethoxazole	>= 320	R

+= Deduced drug *= AES modified **= User modified

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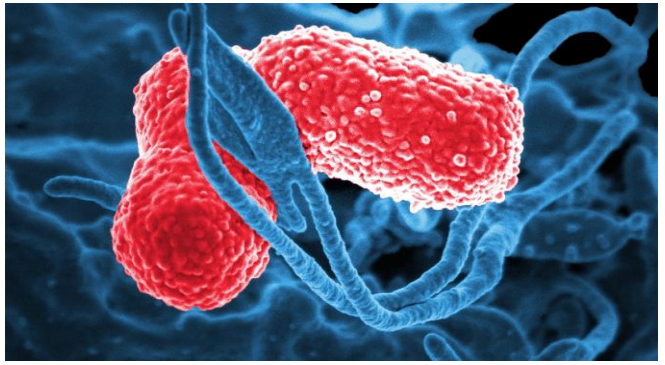
O is for organism

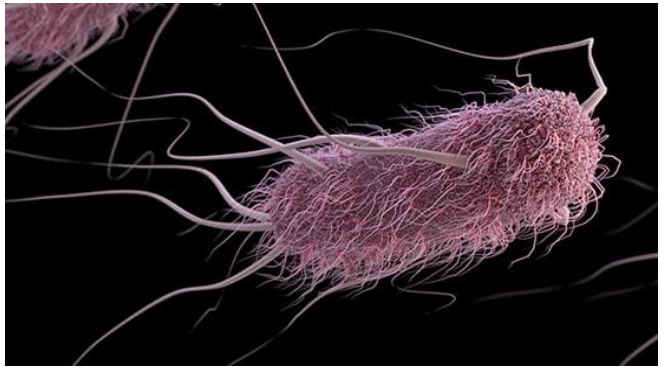
Gram-negative bacteria

- **Enterobacterales (formerly Enterobacteriaceae) (CRE)**

Carbapenem-resistant Enterobacterales (CRE)[11]

- Commonly identified organisms include:
  - *E. coli*
  - *Klebsiella* spp.
  - *Enterobacter* spp.
  - 50+ other genera
- Naturally inhabit the gut
- Cause infections in wounds, bloodstream, urinary tract, and other sites





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O is for organism

Gram-negative bacteria

- Enterobacterales (CRE)
- ***Pseudomonas aeruginosa* (CRPA)**

Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)[12]

- *P. aeruginosa* is commonly found in the environment, particularly water sources
  - Some outbreaks in healthcare settings found to be associated with drains, sinks, and faucets[13]
  - Other CROs also found in these water sources
- CRPA are naturally resistant to many antibiotics, some pan-resistant
- CRPA can cause serious infections in patients with chronic lung disease

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O is for organism

Gram-negative bacteria

- Enterobacterales (CRE)
- *Pseudomonas aeruginosa* (CRPA)
- ***Acinetobacter baumannii* (CRAB)**

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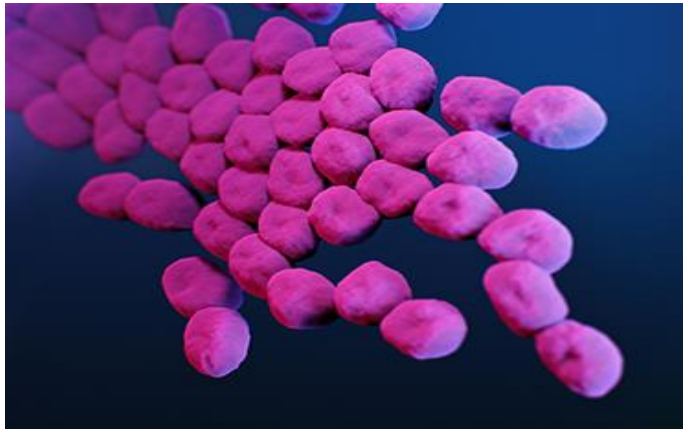
Carbapenem-resistant *Acinetobacter baumannii* (CRAB)[14]

- *A. baumannii are* often found in the environment, particularly soil and water
- Naturally resistant to many antibiotics, some pan-resistant
- CRAB can cause infections in blood, wound, urinary and respiratory tract, other sites
- *A. baumannii* can be persistent in the healthcare environment
  - Outbreaks of CRAB associated with contaminated healthcare environment, healthcare worker hands and clothing, medical equipment



More acronyms

CROs

- CRE
- CRPA
- CRAB

Carbapenemase-producing organisms (CPOs)

Carbapenemases:

- **KPC**
- **NDM**
- **VIM**
- **OXA-48**
- **IMP**

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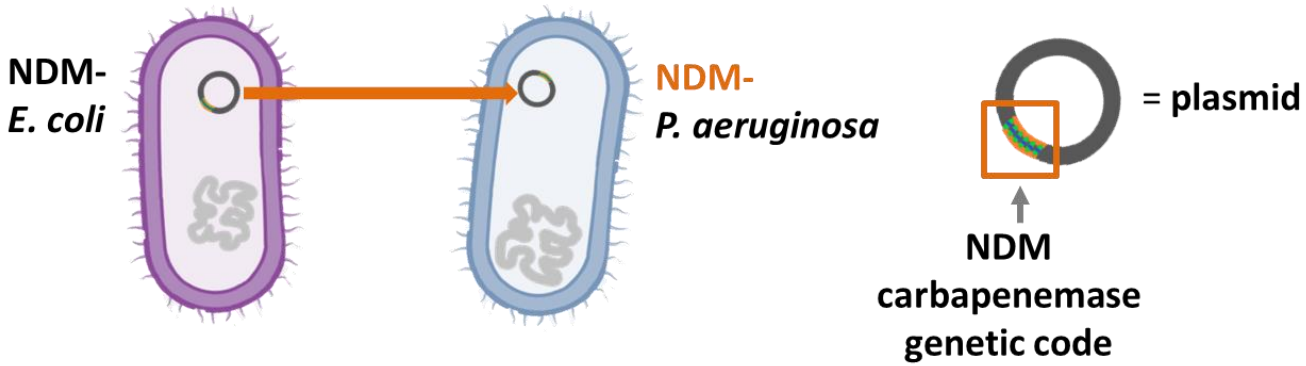
C is for carbapenemase

- Enzyme that confers resistance (inactivates) to:
  - **Carbapenems**
  - Other beta-lactam antibiotics (e.g., penicillins, cephalosporins)
- Examples include:
  - **KPC =** *Klebsiella pneumoniae* carbapenemase (most common in the US)
  - **NDM =** New Delhi metallo-beta-lactamase
  - **IMP =** imipenemase
  - **VIM =** Verona integron-encoded metallo-beta-lactamase
  - **OXA =** oxacillinase (common in CRAB)

P is for producing

- The organism produces the carbapenemase enzyme, the mechanism for carbapenem resistance
- Genes encode for specific carbapenemases
  - Example: NDM gene encodes for NDM carbapenemase
- On mobile genetic elements (e.g., plasmids), enabling transfer within and across bacterial species, **more likely to spread resistance**
  - Example: NDM in *E. coli* → NDM in *P. aeruginosa*



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Testing for carbapenemase production

Detection of carbapenemase production (phenotypic tests)[15]

- Modified Carbapenem Inactivation Method (mCIM), CarbaNP, BD Phoenix
- Results report whether the organism is producing a carbapenemase or not (e.g., yes/no)

Detection of carbapenemase type (genotypic, other tests) [15]

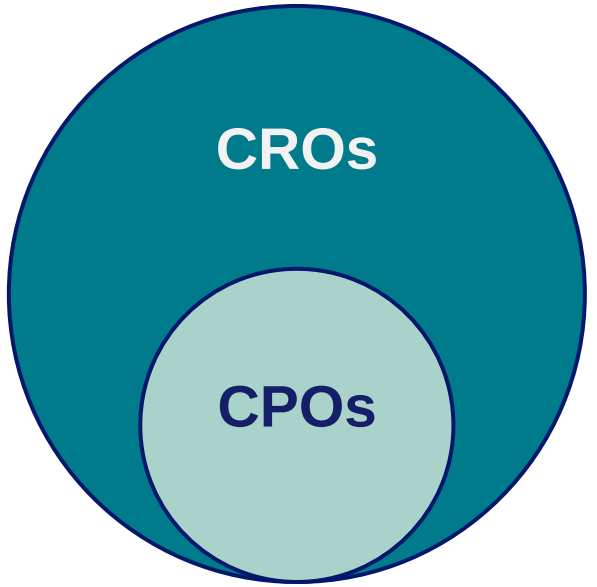
- Polymerase chain reaction (PCR) (e.g., Cepheid Xpert Carba-R), Hardy CARBA 5, whole genome sequencing
- Results report which carbapenemase types are present (e.g., KPC, NDM)

O is for organism

- **CPO = Carbapenemase-producing organism**
  - A subset of CROs are CPOs

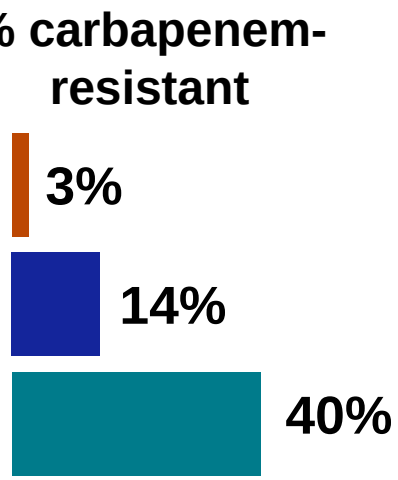
Examples include:

- Enterobacterales
  - NDM-producing *E. coli*
  - KPC-producing *Enterobacter cloacae*
- VIM-producing *Pseudomonas aeruginosa* (VIM-CRPA)
- NDM-producing *Acinetobacter baumannii* (NDM-CRAB)



NHSN* data on percentage of carbapenem resistance in isolates from HAIs[16]

- Enterobacterales (CRE)
- *Pseudomonas aeruginosa* (CRPA)
- *Acinetobacter baumannii* (CRAB)



*National Healthcare Safety Network, 2021

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NHSN* data on percentage of CROs that are carbapenemase-producing[16]

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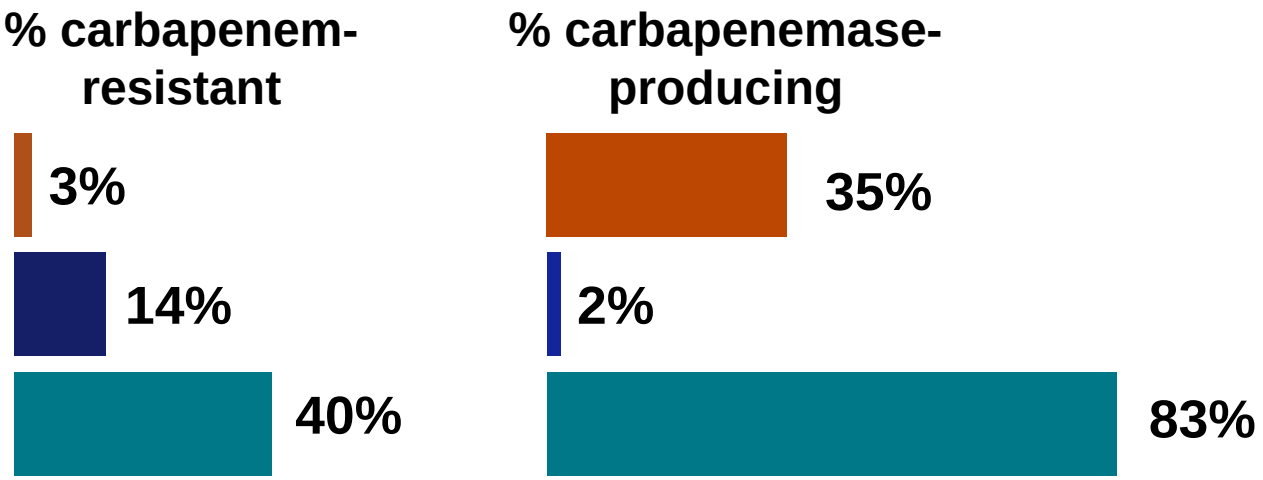
- *Pseudomonas aeruginosa* (CRPA)
- *Acinetobacter baumannii* (CRAB)



*National Healthcare Safety Network, 2021

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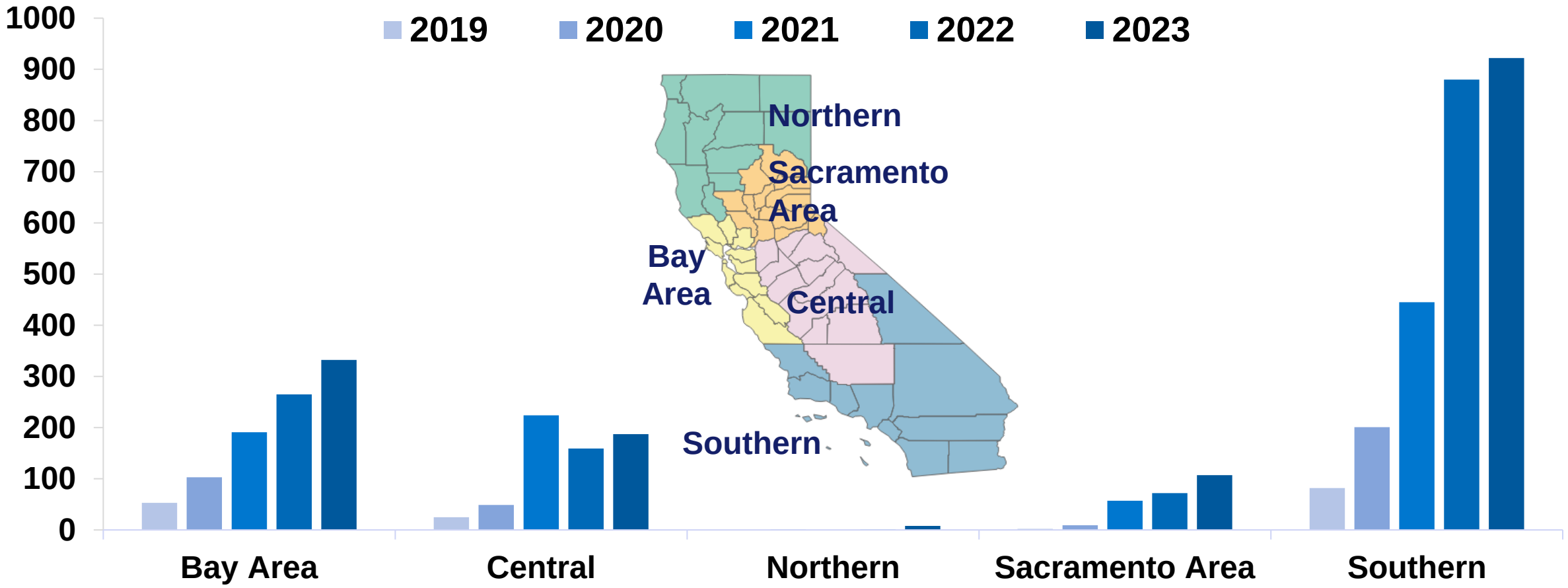
Since 2019, reported CPO cases* have risen in all regions



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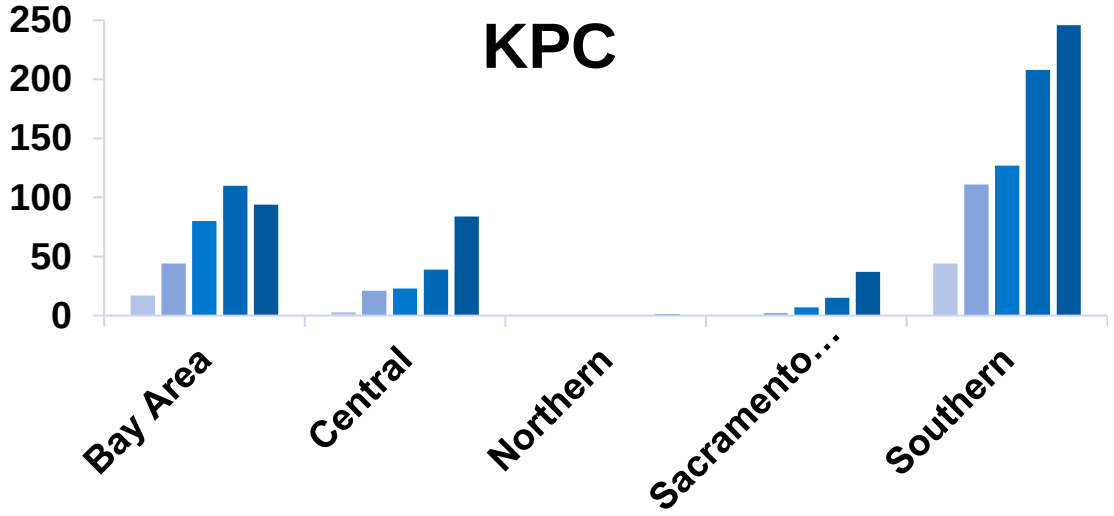
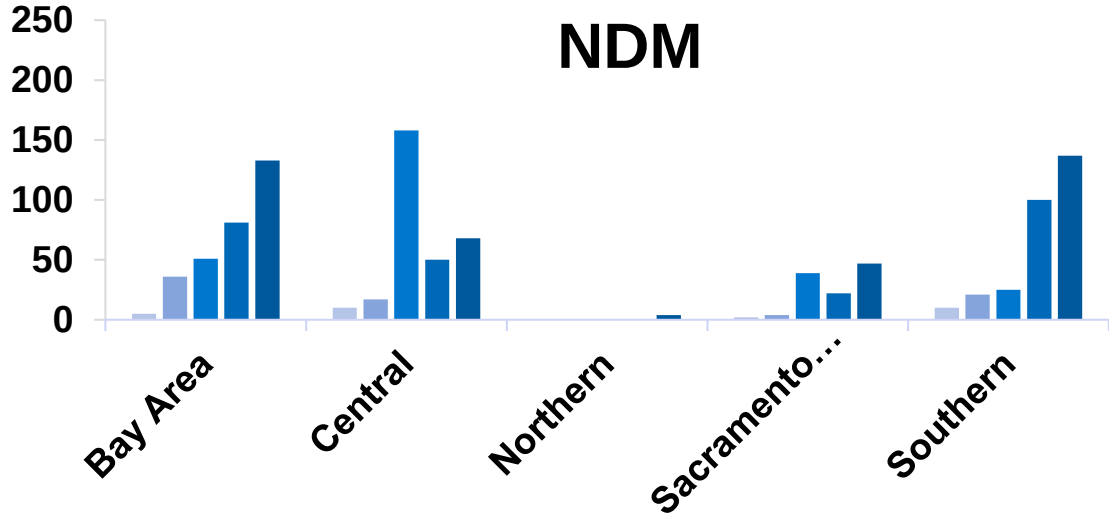
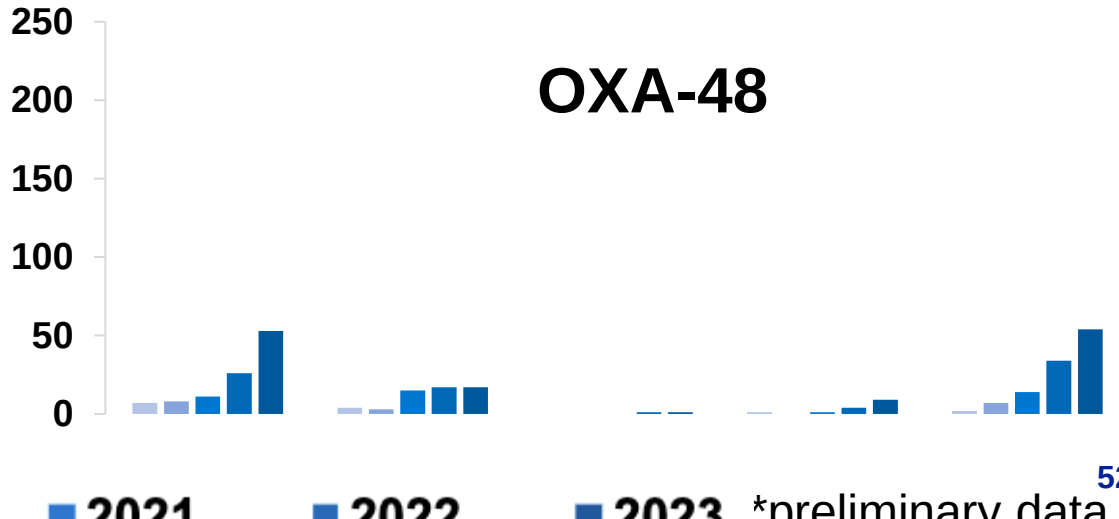
*preliminary data

We have seen increases across all carbapenemase types* in all regions







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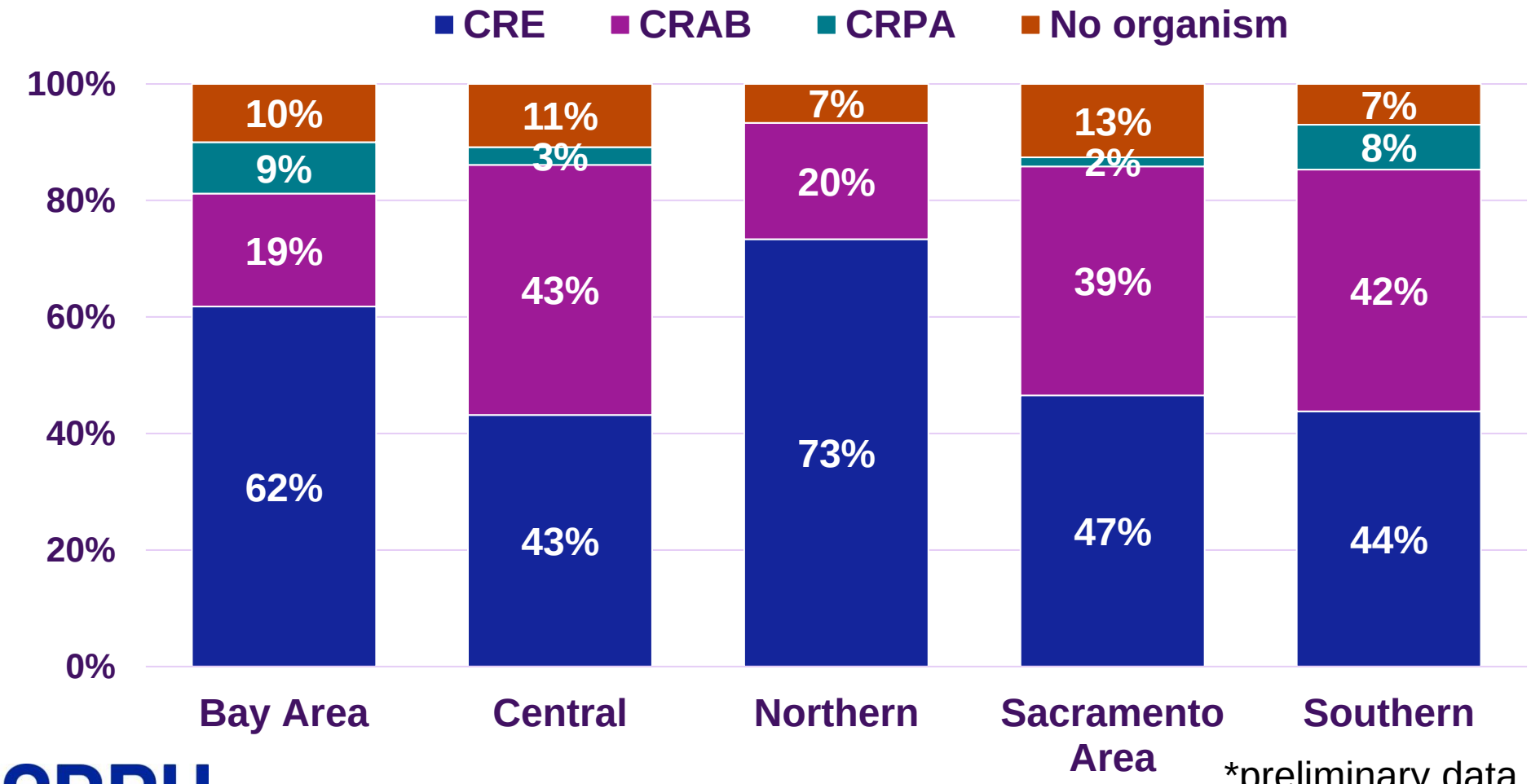
2019 2020 2021 2022 2023 *preliminary data

The proportion of CPOs* varies by region



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*preliminary data, January 2019–June 2024

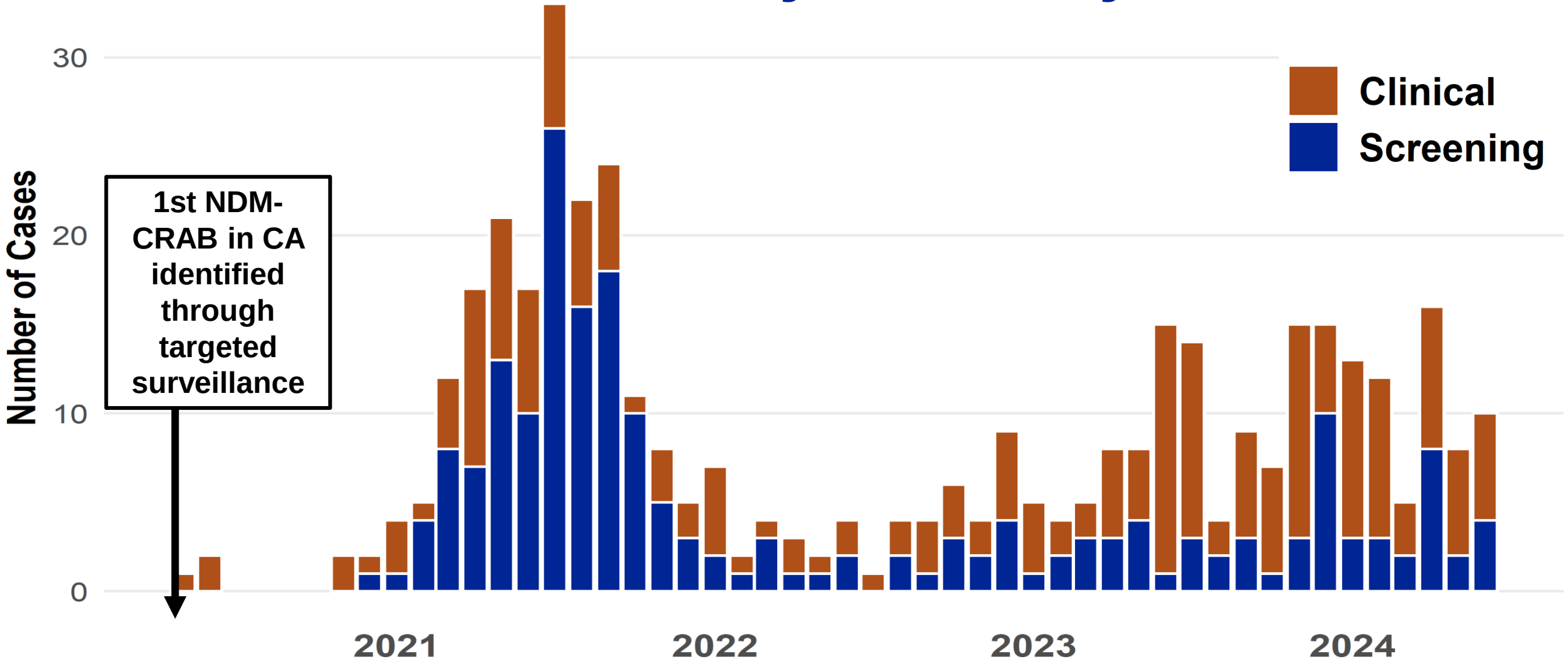
VIM-CRPA

- VIM is most common carbapenemase identified in CRPA in California
  - Associated with multiple outbreaks in different healthcare settings
- Since 2018, VIM-CRPA cases have been identified in patients reporting receipt of medical care in Mexico[17]
  - Includes both medical tourism and routine medical care
- National outbreak of VIM-CRPA associated with artificial tears[18]
  - CDC identified 81 patients in 18 states, May 2022–May 2023
  - 9 cases identified from California, 5 from Southern California were associated with an outpatient eye clinic

Regional NDM-CRAB outbreak

- Prior to 2019, NDM-CRAB had not been identified in the US
  - NDM was mostly identified in CRE (e.g., *Klebsiella pneumoniae*)
  - NDM confers a high level of resistance; infections caused by NDM-CRAB can be very difficult to treat
- Emergence of this highly drug-resistant pathogen in California prompted an aggressive public health response

NDM-CRAB cases, May 2020-May 2024*



*preliminary data

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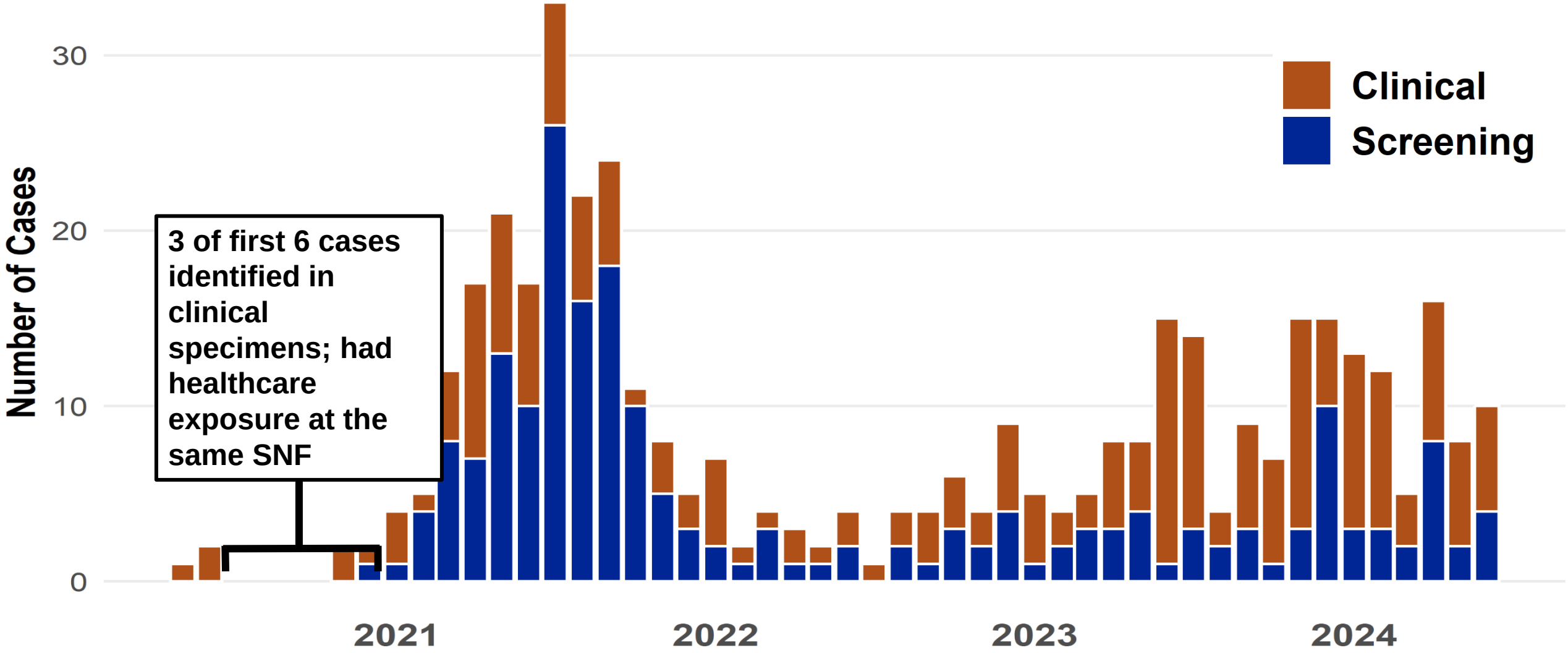
NDM-CRAB cases, May 2020-May 2024*



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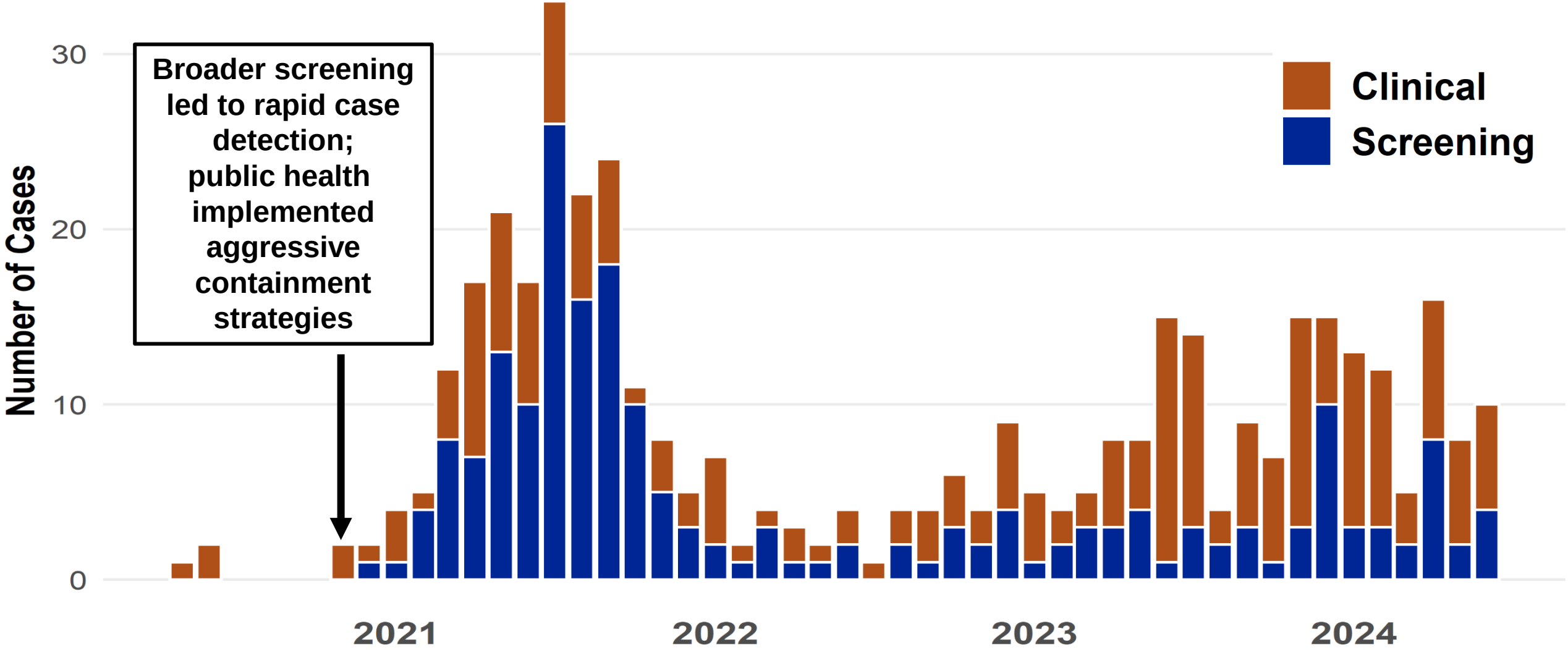
*preliminary data

NDM-CRAB cases, 2020-2024*



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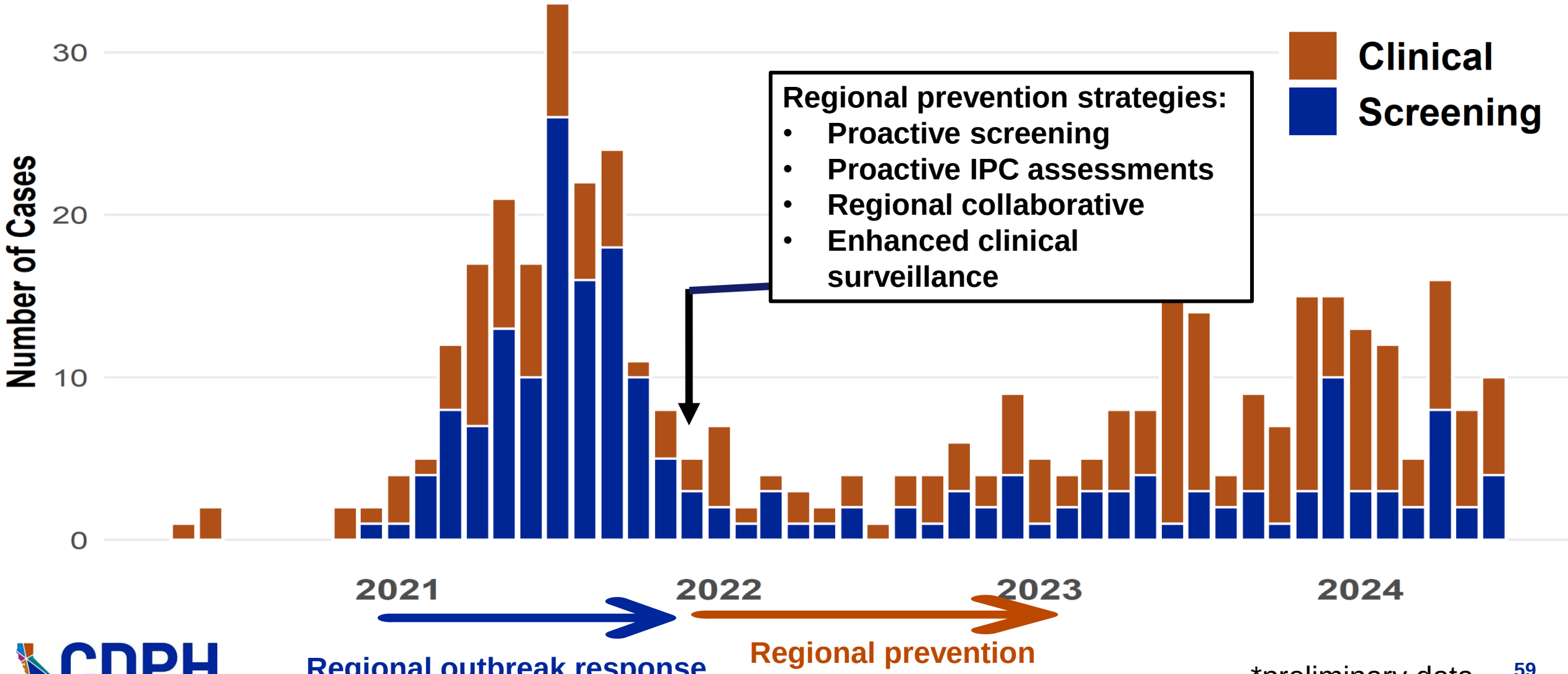
*preliminary data

NDM-CRAB 2020-2024*



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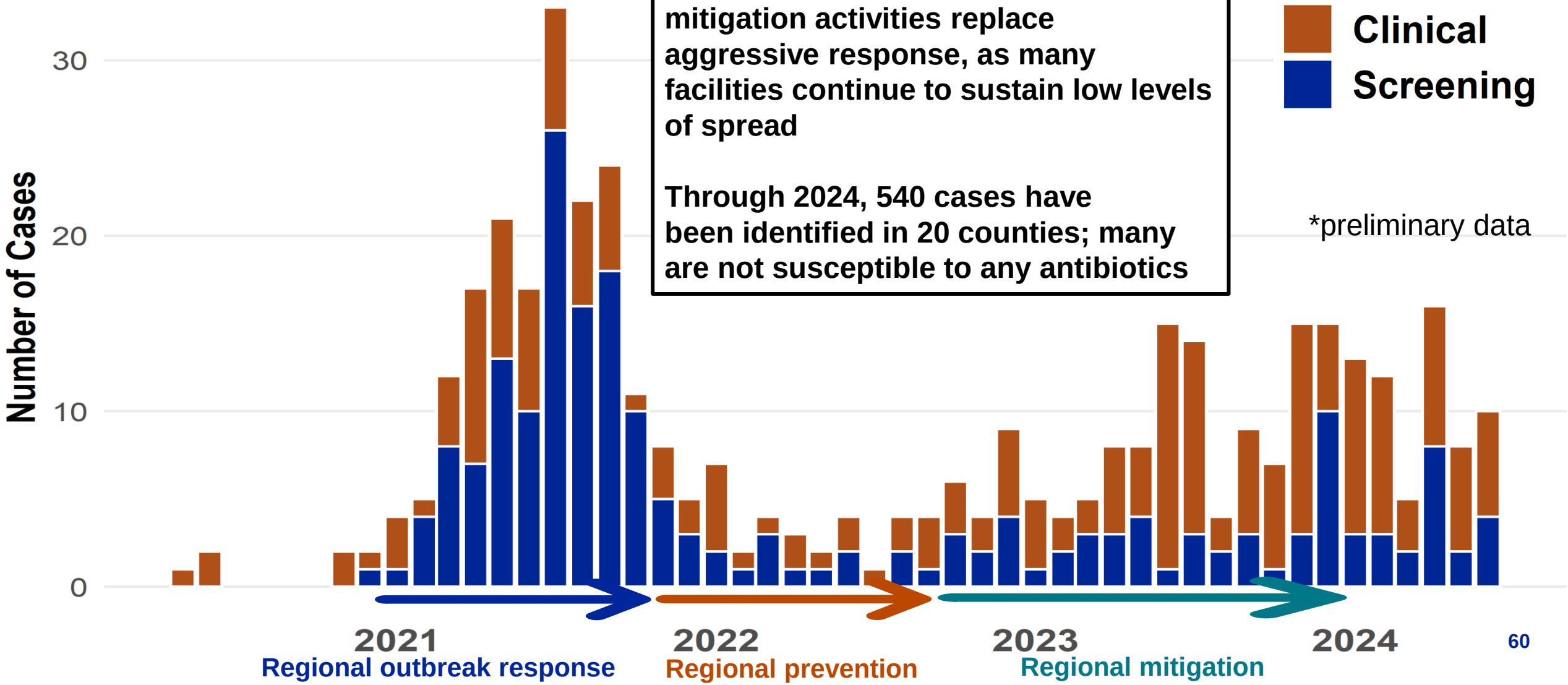
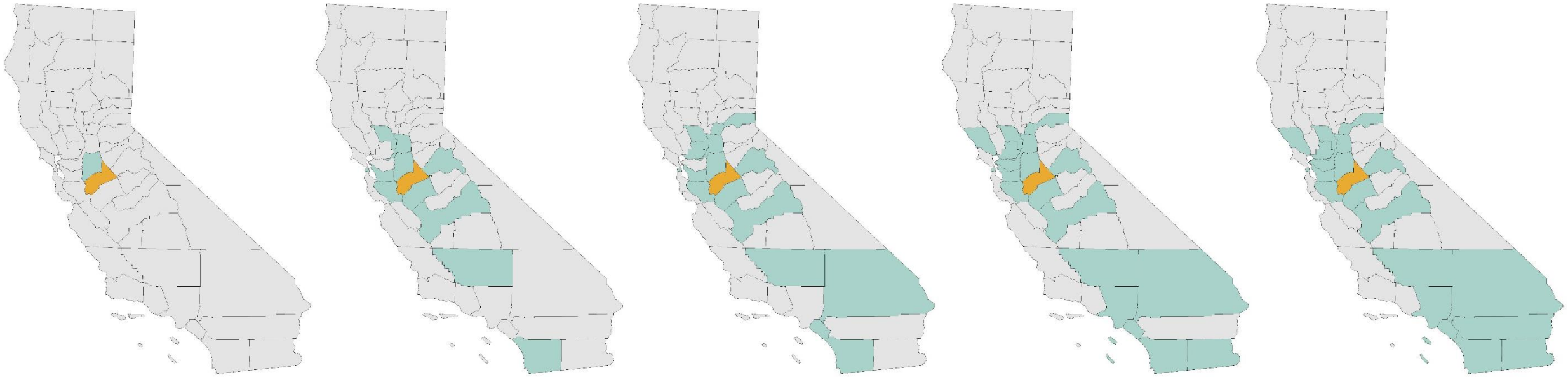
*preliminary data

Cases of NDM-CRAB, May 2020–December 2024*



NDM-CRAB cases continue to increase across the state[19]



Jan 2021 | Jan 2022 | Jan 2023 | Jan 2024* | Jan 2025*

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*preliminary data

Summary

- CPOs and *C. auris* can spread easily in healthcare settings and persist in the environment
  - Core IPC practices can prevent spread in healthcare settings
- Healthcare exposure in LTACHs and vSNFs, high/frequent antimicrobial use, and indwelling devices are at higher risk of colonization; infection is also associated with higher morbidity and mortality
- Reported CPO and *C. auris* cases are increasing throughout California
  - Once rare organisms like NDM-CRAB and *C. auris* are becoming more common
- Cases are not confined within county borders; it's critical to ensure communication of patient's CPO or *C. auris* status during transfer
- Regional prevention and response activities can contain spread!

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2. CDPH Core Infection Prevention and Control Practices (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CoreIPCPractices.aspx)
3. US-subset of isolates submitted to CDC AR Lab Network, 2017–2022 (www.cdc.gov/antimicrobial-resistance-laboratory-networks/php/about/domestic.html)
4. CA-subset of CA isolates submitted to WA regional AR Lab Network lab, 2018–July 2023 (n=1199) (www.doh.wa.gov/ForPublicHealthandHealthcareProviders/PublicHealthLaboratories/ARLNLabTestMenu)

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6. EPA's Registered Antimicrobial Products Effective Against Candida auris [List P] (www.epa.gov/pesticide-registration/epas-registered-antimicrobial-products-effective-against-candida-auris-list#against)
7. Yadav et al., *J. Fungi* (2021) (doi.org/10.3390/jof7020081)
8. Sexton et al., *Clin Infect Dis*. (2021) (doi.org/10.1093/cid/ciab327)
9. Karmarkar et al. 2021 (doi.org/10.7326/m21-2013)
10. CDPH *C. auris* website (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Candida-auris.aspx)

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11. CDC CRE Information for Facilities (PDF) (www.cdc.gov/healthcare-associated-infections/media/pdfs/CRE-handout-V7-508.pdf)
12. CDC CRPA Information for Facilities (PDF) (www.cdc.gov/healthcare-associated-infections/media/pdfs/CRPA-handout-V7-508.pdf)
13. The Hospital Water Environment as a Reservoir for CROs Causing Hospital-Acquired Infections-A Systematic Review of the Literature (pubmed.ncbi.nlm.nih.gov/28200000/)
14. CDC CRAB Information for Facilities (PDF) (www.cdc.gov/healthcare-associated-infections/media/pdfs/CRAB-handout-V7-508.pdf)
15. CRO Primer Test for Carbapenemases (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH Document Library/CRO_PrimerTests_for_Carbapenemases.pdf)

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16. National Healthcare Safety Network 2021 Hospital Data (arpsp.cdc.gov/profile/antibiotic-resistance?tab=antibiotic-resistance)
17. CAHAN Ongoing Risk of Highly Drug-Resistant Infections in Patients Following Hospitalization or Invasive Procedures in Mexico (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CAHAN_VIM-CRPA_Mexico_Feb2021.pdf)
18. Outbreak of Extensively Drug-resistant Pseudomonas aeruginosa Associated with Artificial Tears (archive.cdc.gov/www_cdc_gov/hai/outbreaks/crpa-artificial-tears.html)
19. CDPH NDM-CRAB CAHAN (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH Document Library/CAHAN_NDM_OXA23_CRAB_May2021.pdf)

Resources

- *C. auris* Quicksheet and Prevention and Response Strategy Phases (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CaurisQuicksheet.pdf)
- CPO Quicksheet and Phases (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CPOQuicksheet.pdf)
- MDL Expanded Carbapenemase Testing Services FAQs 2025 (www.cdph.ca.gov/Programs/cls/idld/mdl/Pages/MDL-Expanded-Carbapenemase-Testing-Services-FAQs-2025.aspx)

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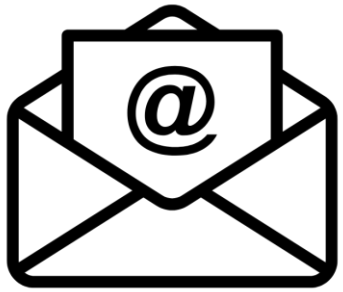
Thank You

Questions?



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