Introduction to Priority Multidrug-Resistant Organisms (MDROs)

September 27, 2024

Presented at Beyond the Basics IP Training
Mercy Medical Center, Redding, CA

Healthcare-Associated Infections (HAI) Program
Center for Health Care Quality
California Department of Public Health

Implicit Bias

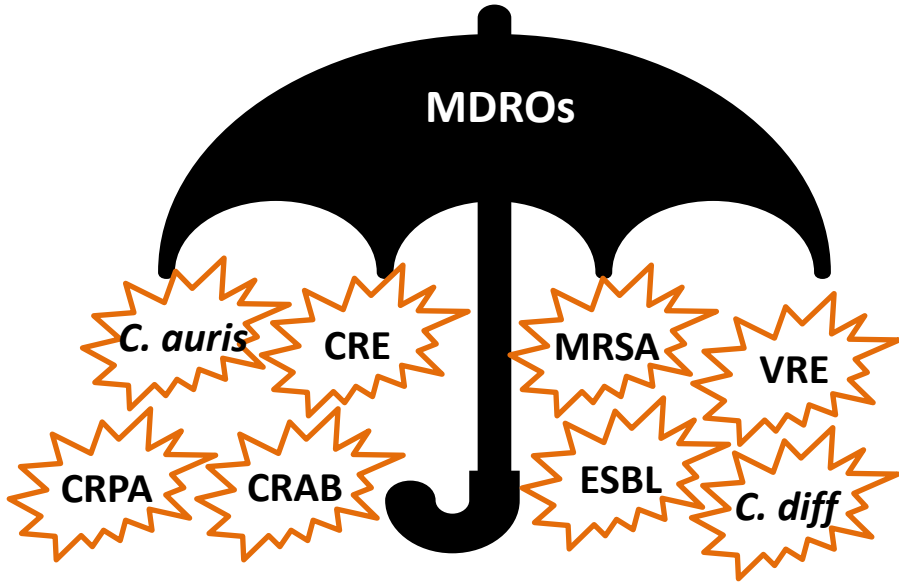
- Describes how our unconscious attitudes or judgements can influence our thoughts, decisions or actions
- Includes involuntary, unintentional perceptions made without awareness
- Occurs as our brains sort information and perceive data to understand our world
- Affects our decisions, contributing to 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 priority multidrug-resistant organisms (MDROs) including *Candida auris and* Carbapenemase-producing organisms (CPOs)
- Understand *C. auris* and CPO epidemiology in California

What are MDROs?

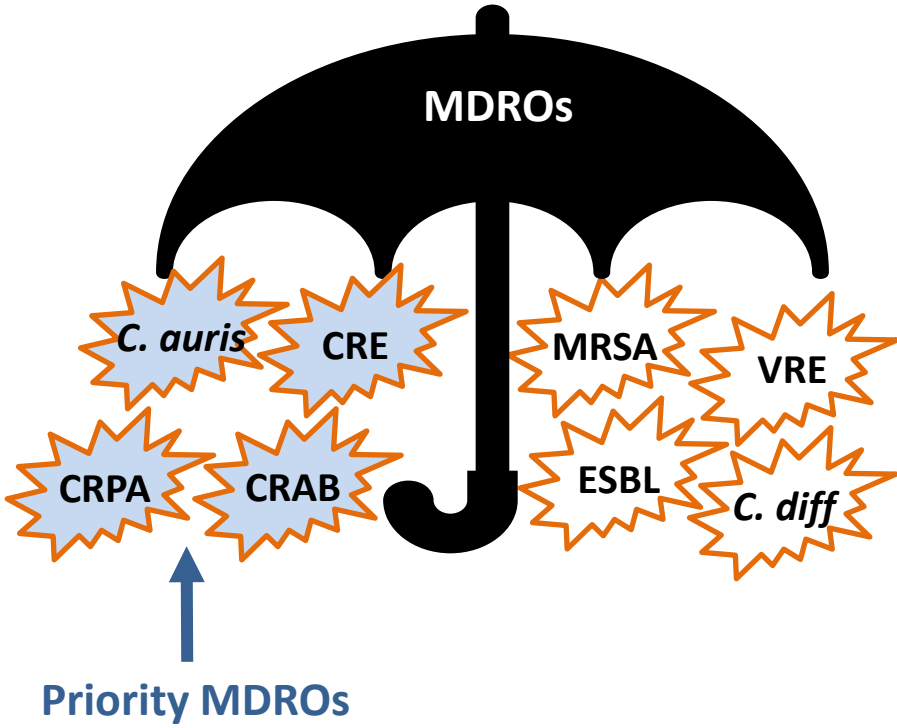
- Bacteria and fungi resistant to many or all antimicrobials (antibiotics, antifungals)
- Infections caused by MDROs can be more difficult and expensive to treat
  - Can result in increased morbidity and mortality
- Can cause outbreaks in healthcare settings



MRSA=methicillin-resistant *Staphylcoccus aureus*; VRE=vancomycin-resistant *Enterococci*; ESBL=extended-spectrum beta-lactamase; *C.* diff=*Clostridiodes difficile*; CRE=carbapenem-resistant Enterobacterales; CRPA=carbapenem-resistant *Pseudomonas aeruginosa*; CRAB=carbapenem-resistant *Acinetobacter baumannii*

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 *Staphylcoccus aureus*; VRE=vancomycin-resistant *Enterococci*; ESBL=extended-spectrum beta-lactamase; *C.* diff=*Clostridiodes difficile*; CRE=carbapenem-resistant Enterobacterales; CRPA=carbapenem-resistant *Pseudomonas aeruginosa*; CRAB=carbapenem-resistant *Acinetobacter baumannii*

What are the Risk Factors for Acquiring a Priority MDRO?

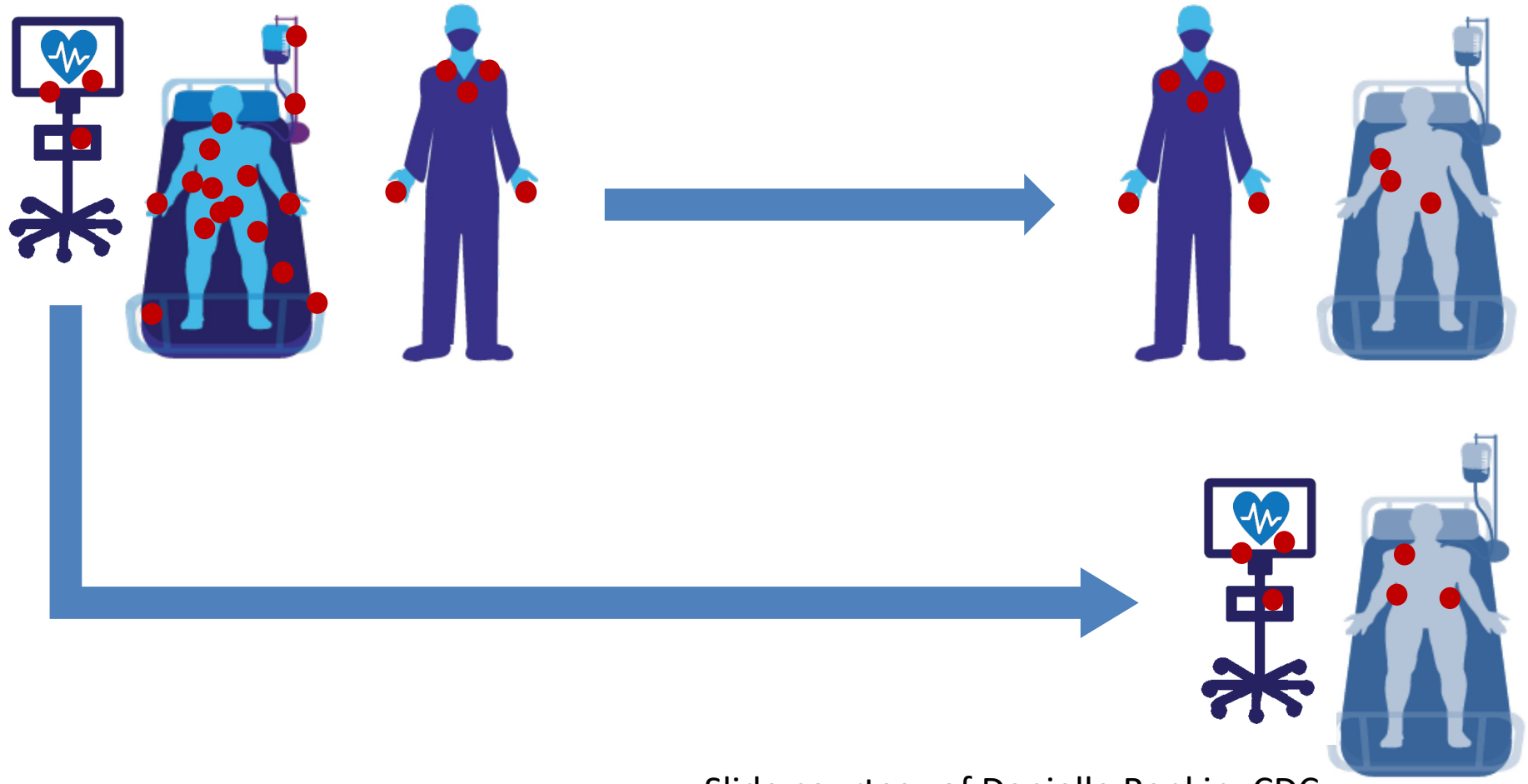
- Exposure to long-term acute care hospitals (LTACHs) and ventilator units in skilled nursing facilities (vSNFs)
- Indwelling medical devices (e.g., urinary catheter, endotracheal tube)
- Mechanical ventilation
- Open/draining wounds
- Recent or frequent antimicrobial use (i.e., antibiotics, antifungals)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

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 CPOs or *C. auris* to assess for "clearance" or to discontinue infection prevention and control (IPC) measures (e.g., Contact Precautions)
- Colonized patients can go on to develop clinical infections

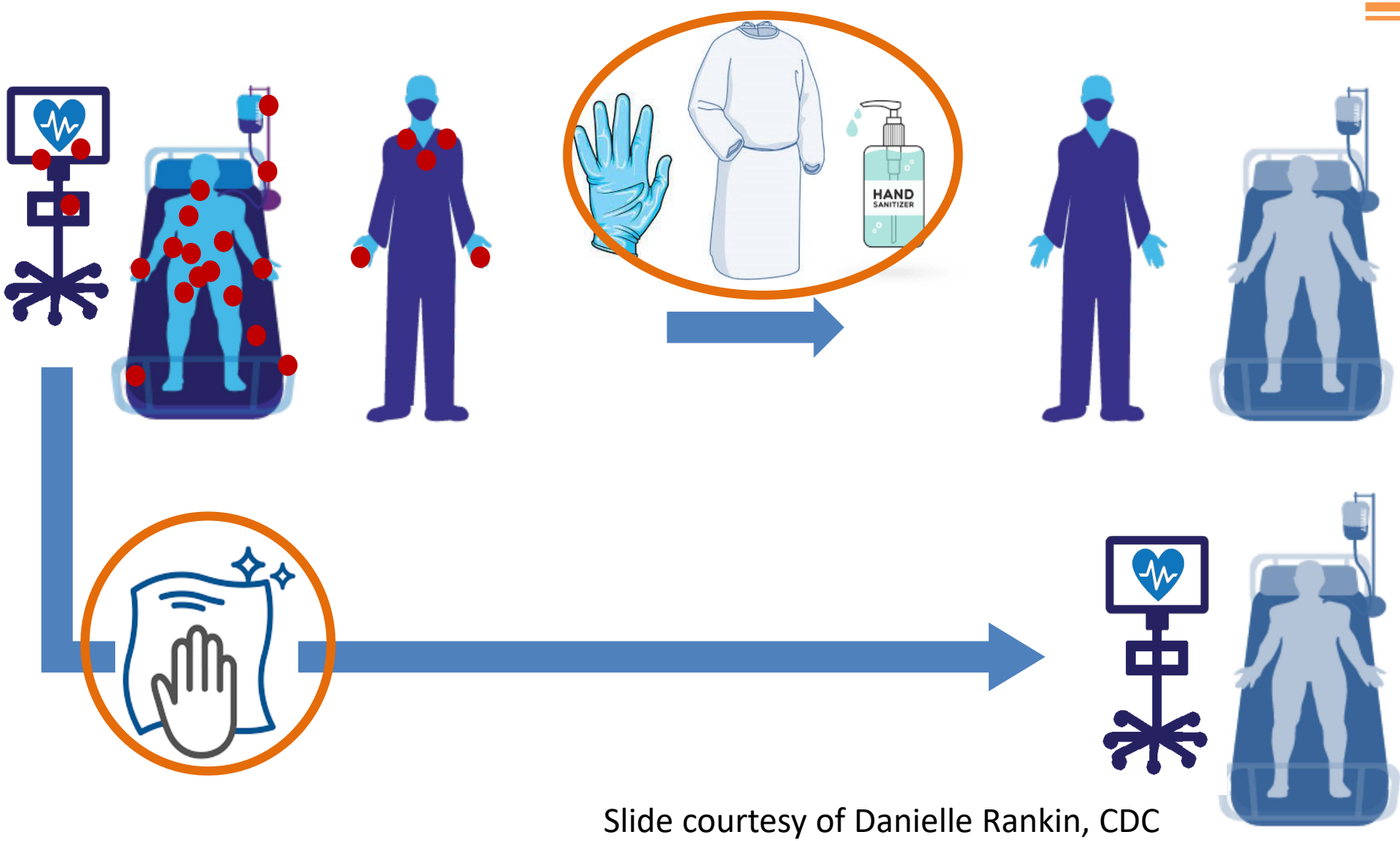
See CDC Preventing MDROs: FAQs (www.cdc.gov/healthcare-associated-infections/php/preventing-mdros/preventing-mdros-faqs.html)

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

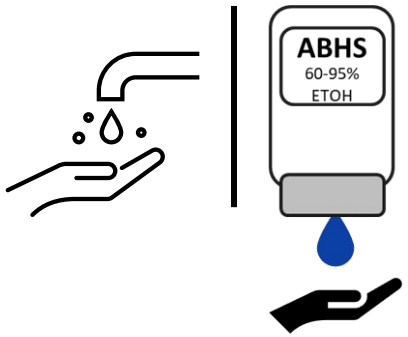
Core IPC practices can prevent spread



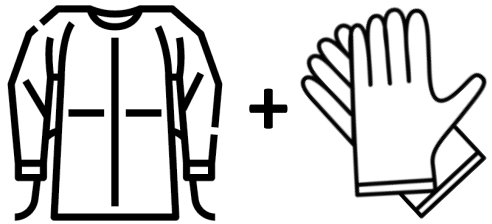
Slide courtesy of Danielle Rankin, CDC

What are Core IPC Practices?

Hand Hygiene



Personal Protective Equipment



Environmental Cleaning & Disinfection

+ observe and monitor compliance

See [CDPH Core Infection Prevention and Control Practices](www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CoreIPCPractices.aspx)
(www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CoreIPCPractices.aspx)

California Department of PublicHealth

Candida auris

C. auris

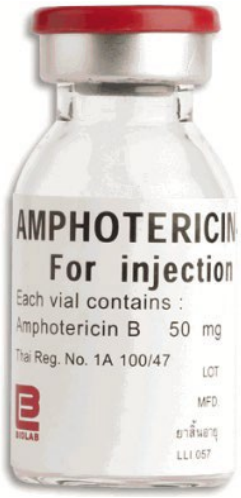
- Drug-resistant yeast, can be resistant to all 3 antifungal classes
- Invasive infections can lead to 30-60% mortality
- Persistence in the environment contributes to rapid spread in healthcare settings
  - Cleaning and disinfection requires agents effective against *C. auris*
    - Regular disinfecting 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

First-line treatment

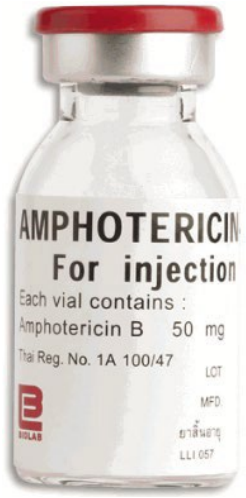


	Fluconazole	Amphotericin B	Echinocandins
United States	86%	21%	1%

US-subset of isolates submitted to CDC AR Lab Network, 2017–2022 (www.cdc.gov/antimicrobial-resistance-laboratory-networks/php/about/domestic.html)

California Department of PublicHealth

In California, Almost All Isolates are Fluconazole-resistant
Very Few are Amphotericin B- or Echinocandin-resistant

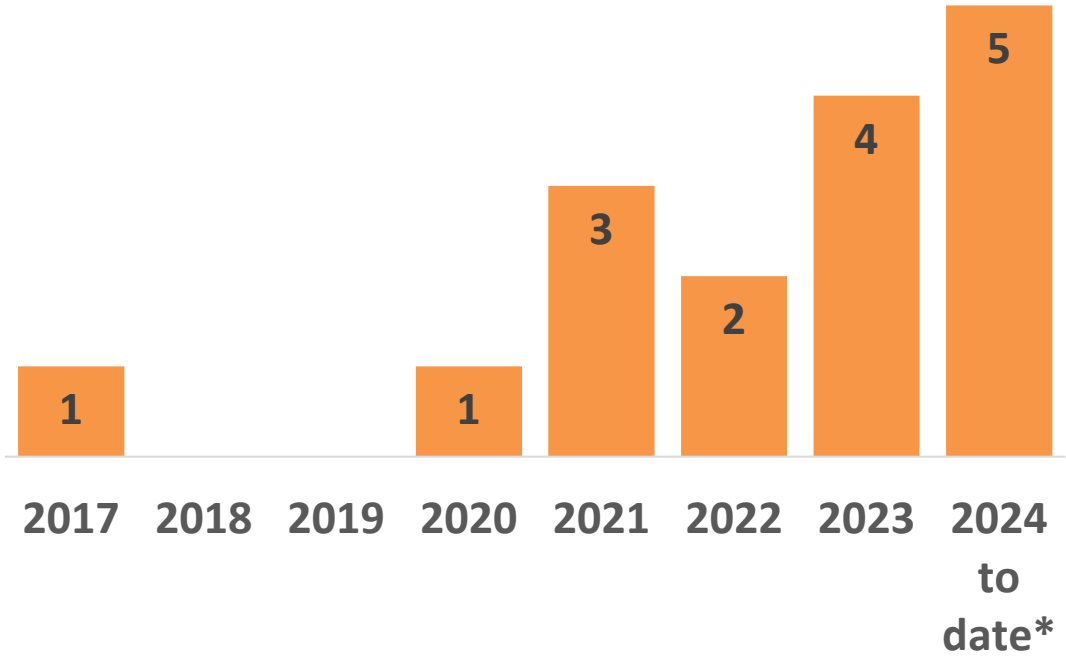


	Fluconazole	Amphotericin B	Echinocandins
United States	86%	21%	1%
California	99%	2%	<1%

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)

California Department of PublicHealth

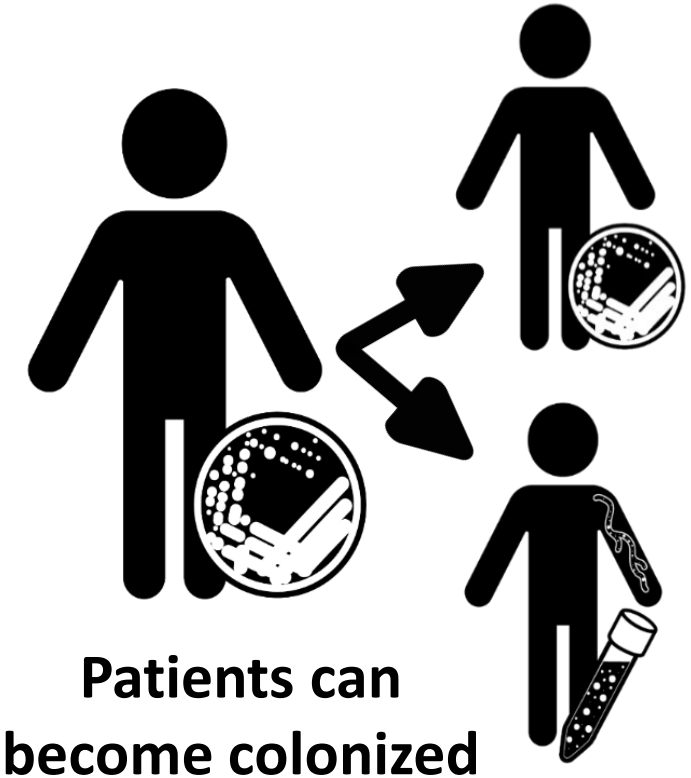
However, in California, We are Identifying More Fluconazole+echinocandin-resistant *C. auris* Cases



*Data reported as of September 9, 2024

Why are We Concerned About *C. auris?*

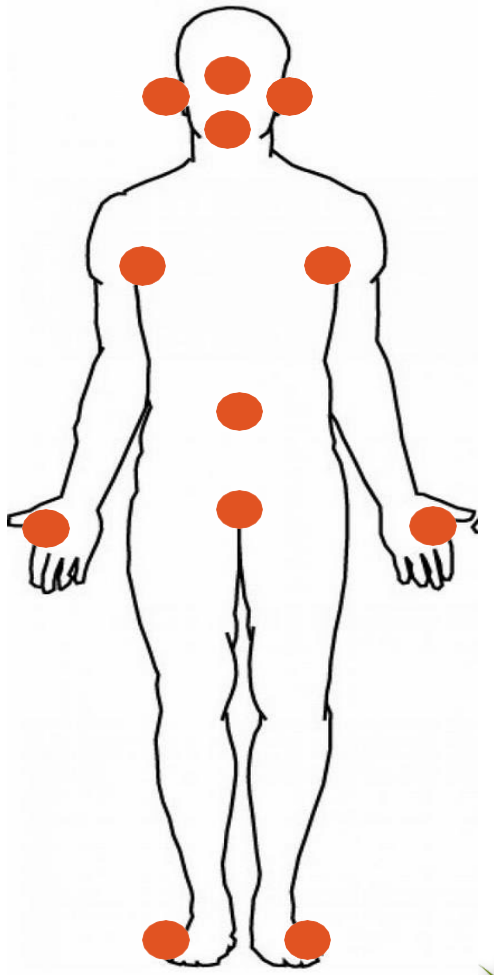
Highly drug-resistant



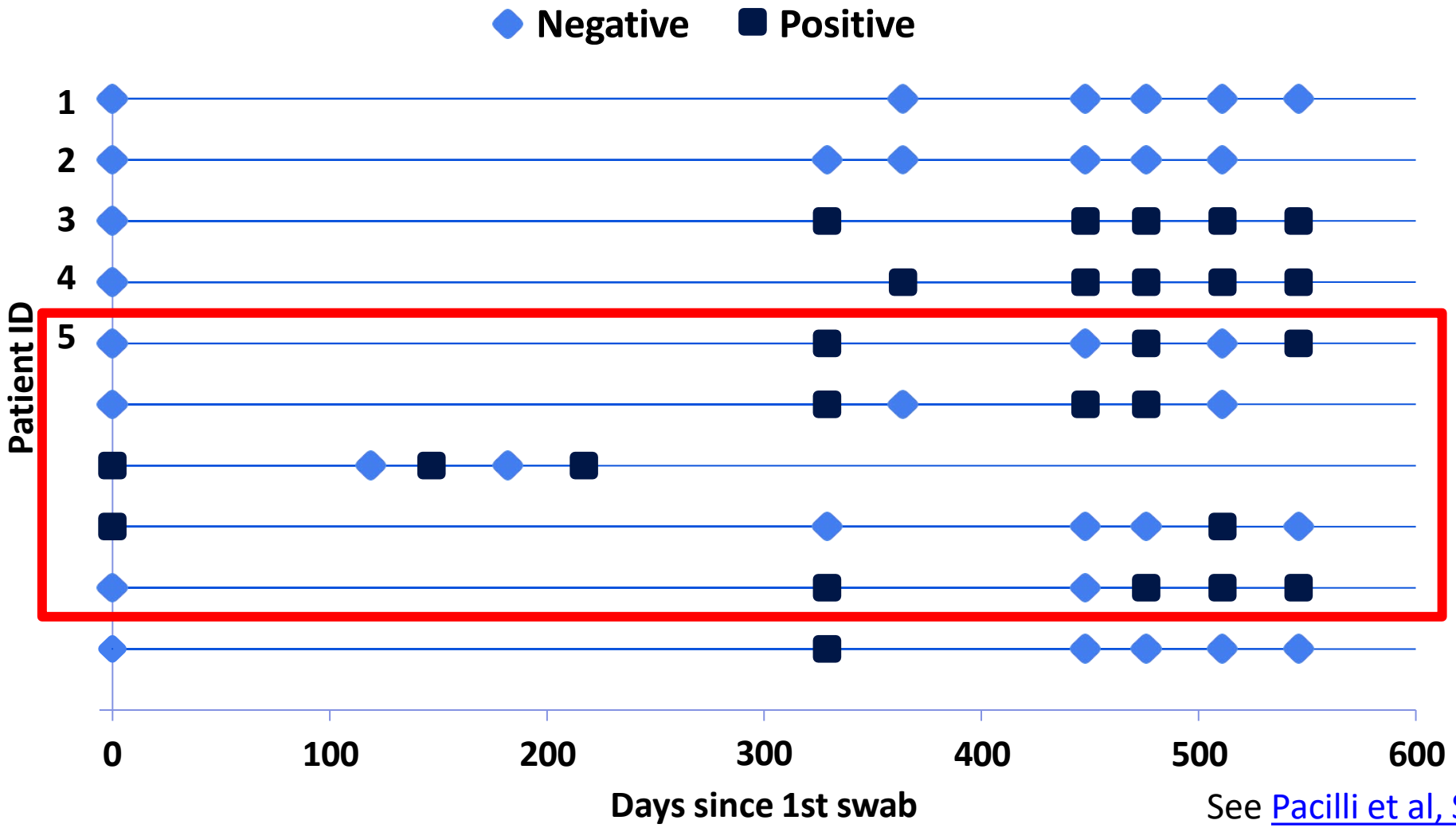
Patients can become colonized and develop invasive infections

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



C. auris Colonization Can be Long-term



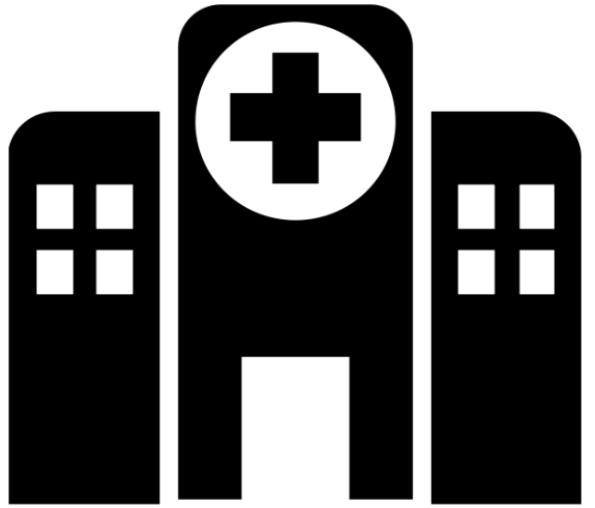
See Pacilli et al, SHEA 2019 (academic.oup.com/cid/article/71/11/e718/5820113)

California Department of PublicHealth

Why are We Concerned About *C. auris?*

Highly drug-resistant

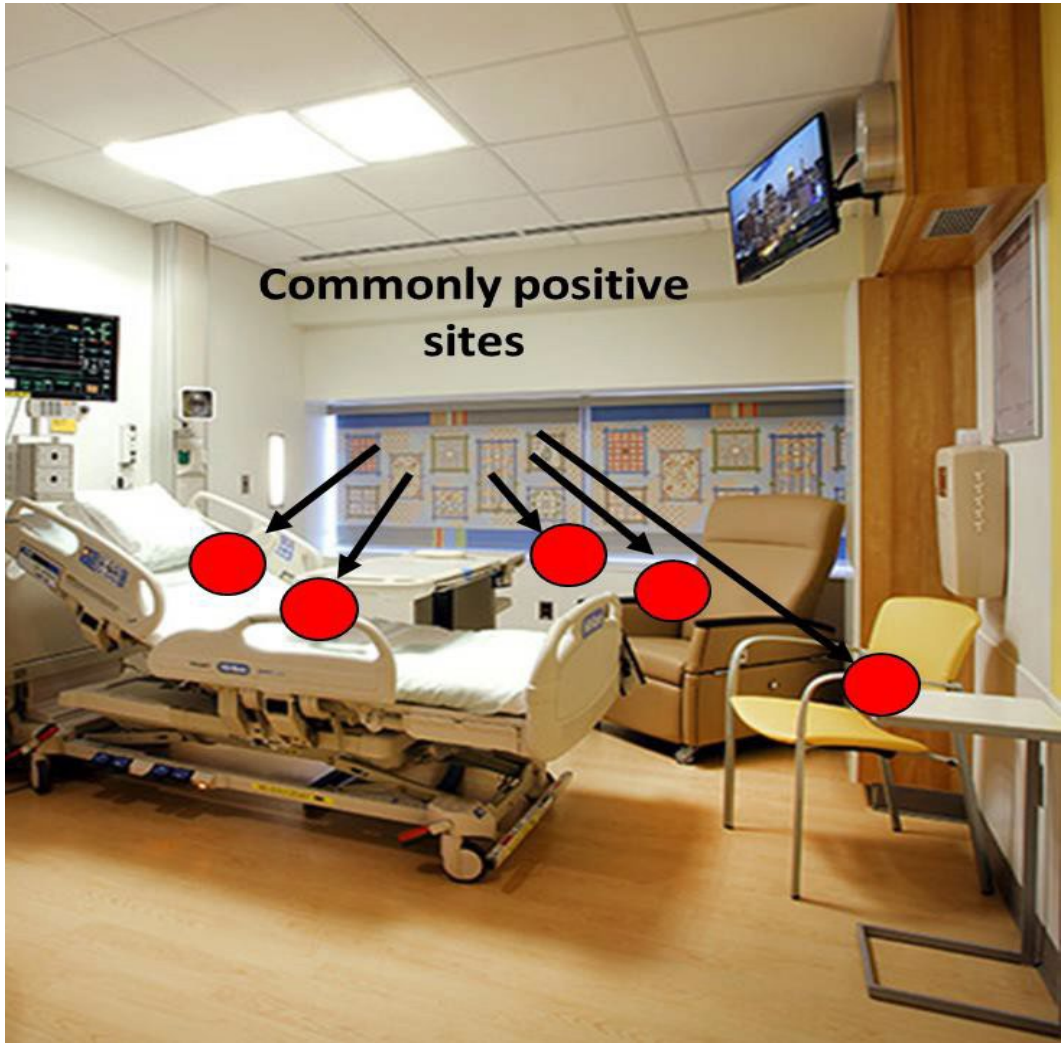
Patients can become colonized and develop invasive infections



Spreads in healthcare settings and networks

C. auris is Persistent in the Healthcare Environment

- Environmental cleaning and disinfection of *C. auris* requires **List P** agents with claims against *C. auris*
  - If List P is unavailable, **List K** or bleach
  - "Quats" don't work
- Greater environmental contamination associated with higher patient colonization burden

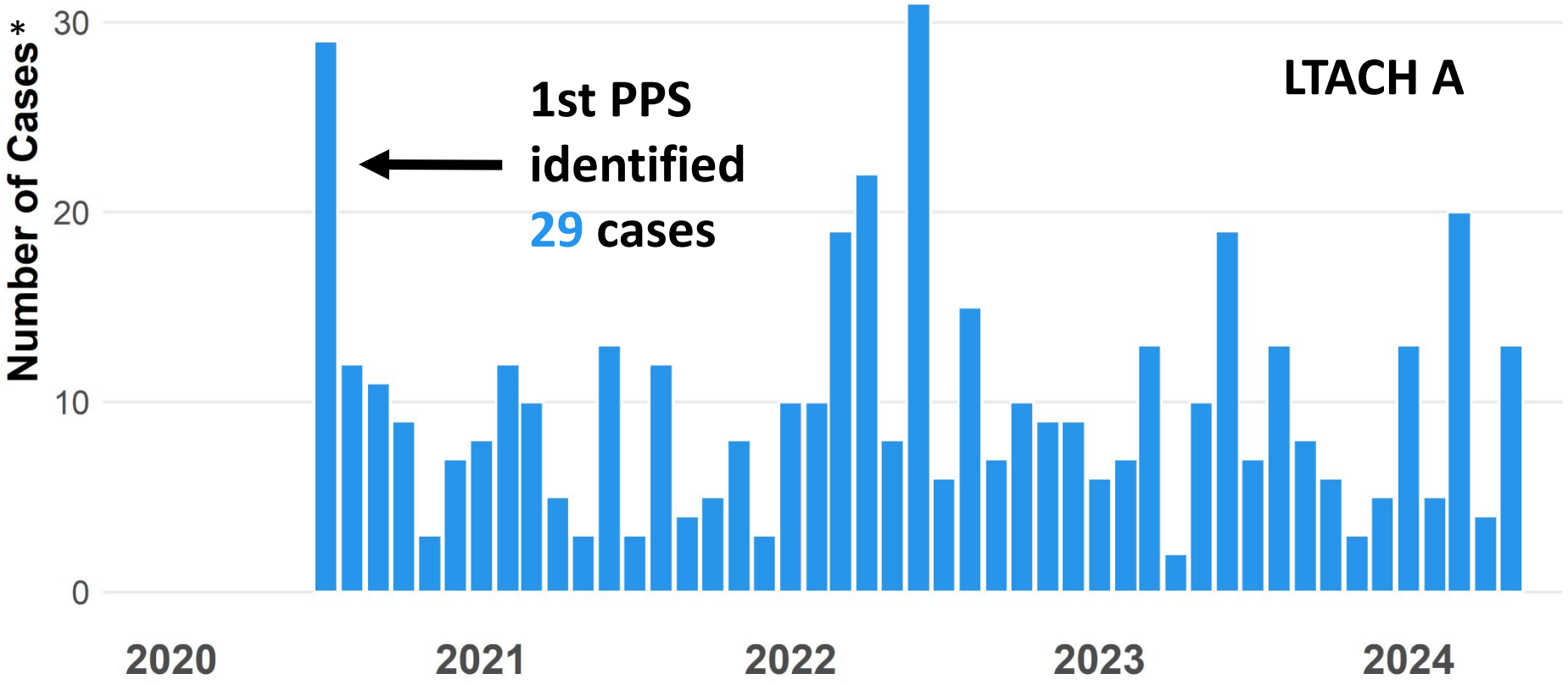


See EPA's Registered Antimicrobial Products Effective Against Candida auris [List P] (www.epa.gov/pesticide-registration/epas-registered-antimicrobial-products-effective-against-candida-auris-list)

See Yadav et al., *J. Fungi* (2021) (DOI.org/10.3390/jof7020081)

See Sexton et al., *Clin Infect Dis*. (2021) (DOI.org/10.1093/cid/ciab327)

Once *C. auris* is In a Facility, it can Spread Rapidly

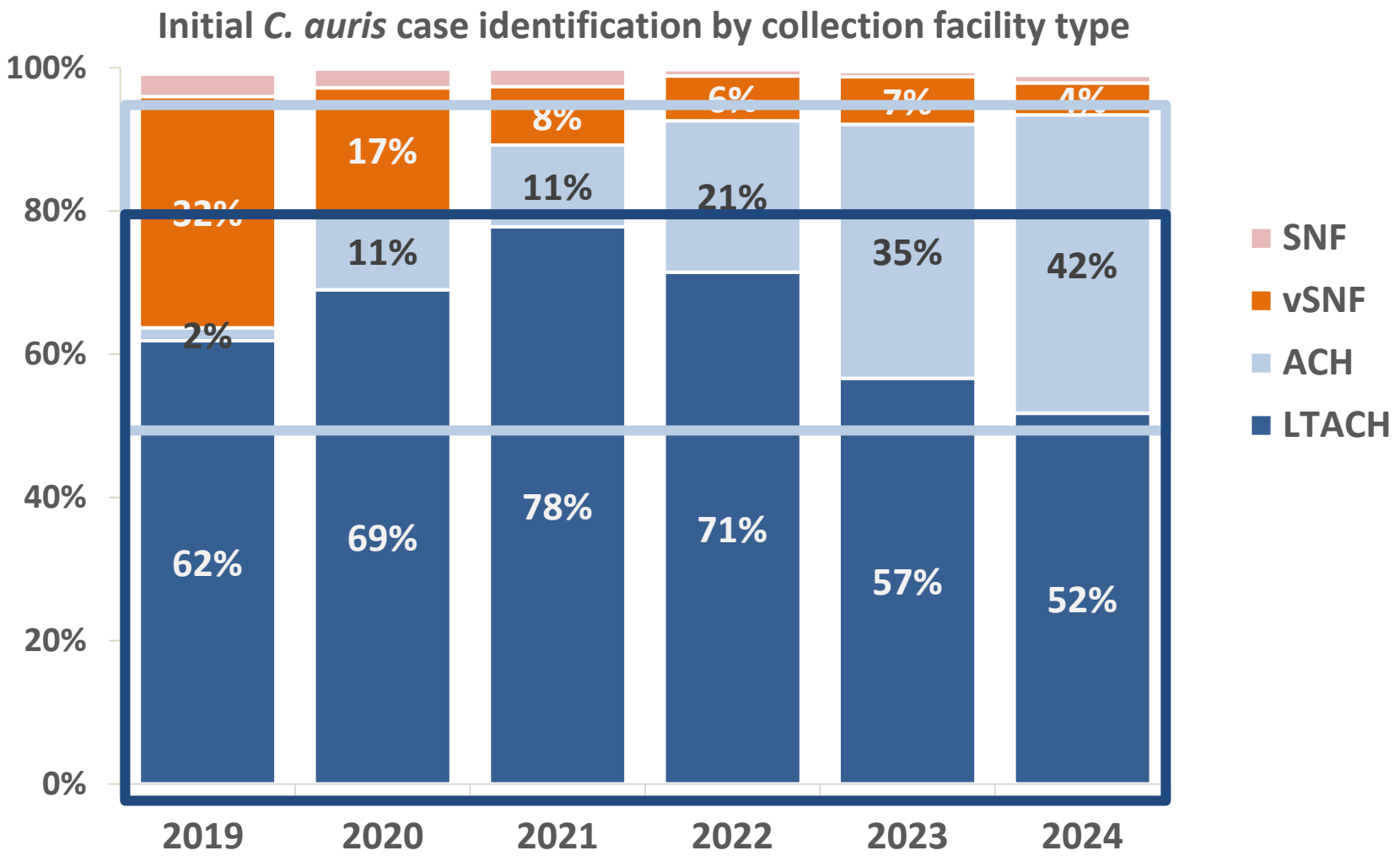


The **high burden of *C. auris*** identified during the first point prevalence survey (PPS) at LTACH A likely contributed to internal spread in the facility

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

California Department of PublicHealth

C. auris is Being Identified in High-risk Facilities (LTACHs, vSNFs) and Increasingly in Short-stay Acute Care Hospitals

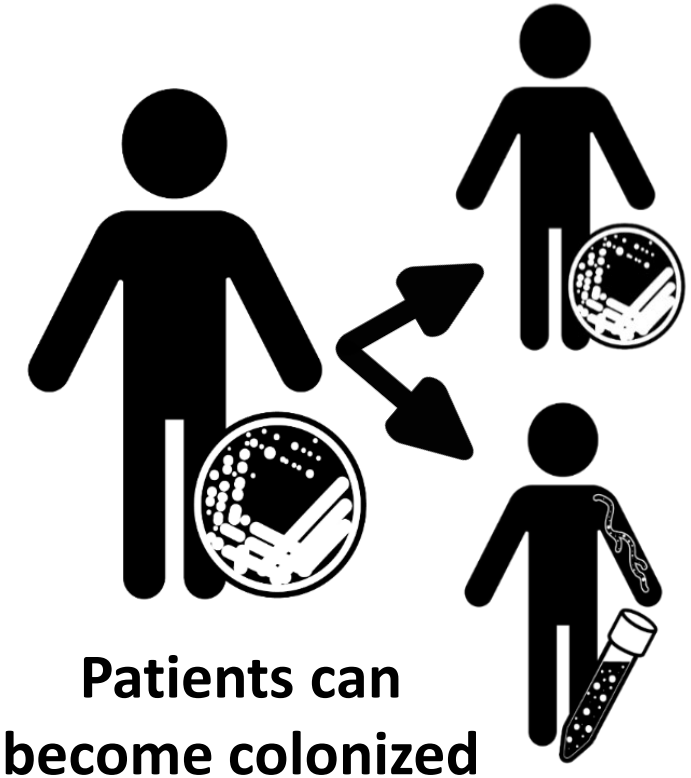


*preliminary data

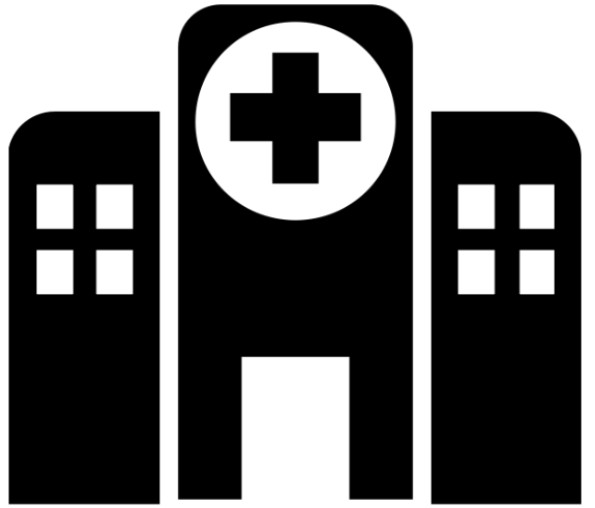
Why are We Concerned about *C. auris*?

All the makings of a fungal superbug!

Highly drug-resistant

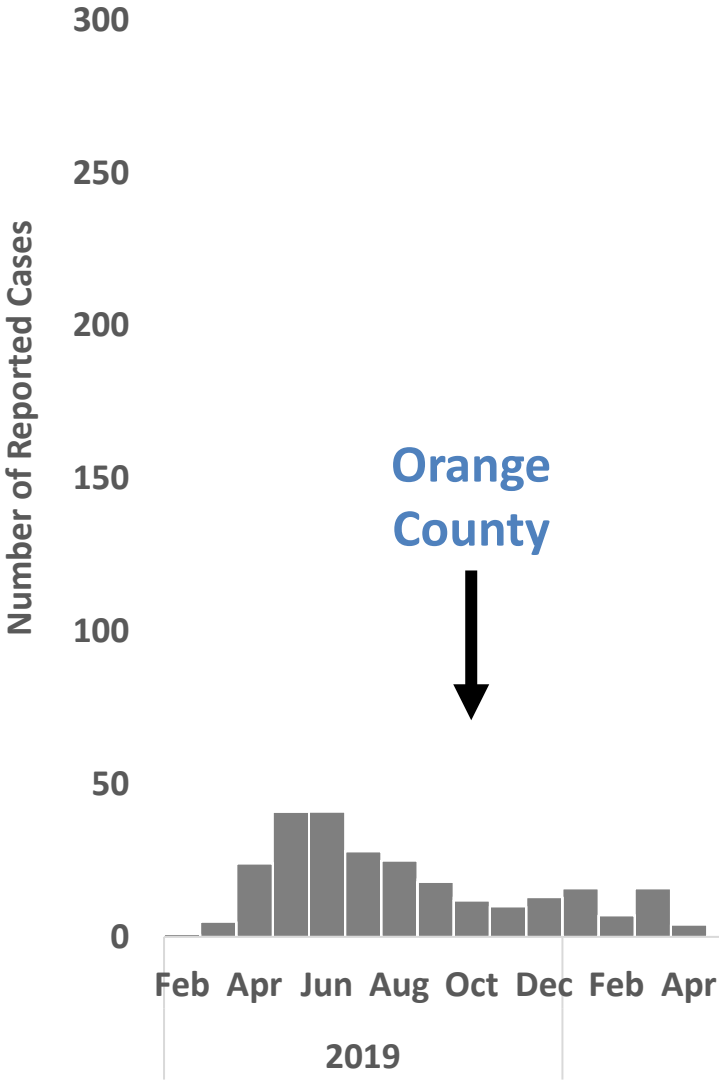


Patients can become colonized and develop invasive infections



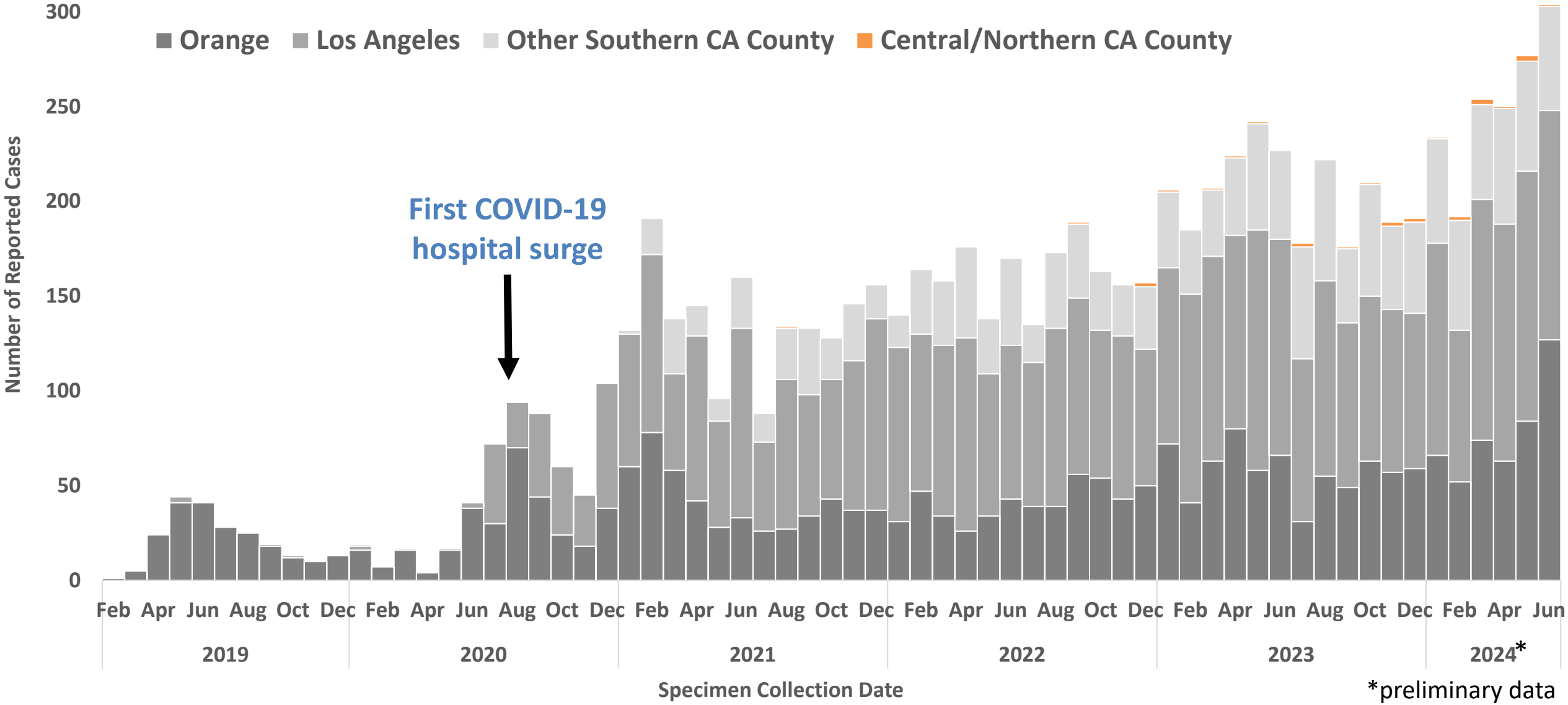
Spreads in healthcare settings and networks

Aggressive Response to our First *C. auris* Outbreak was Successful



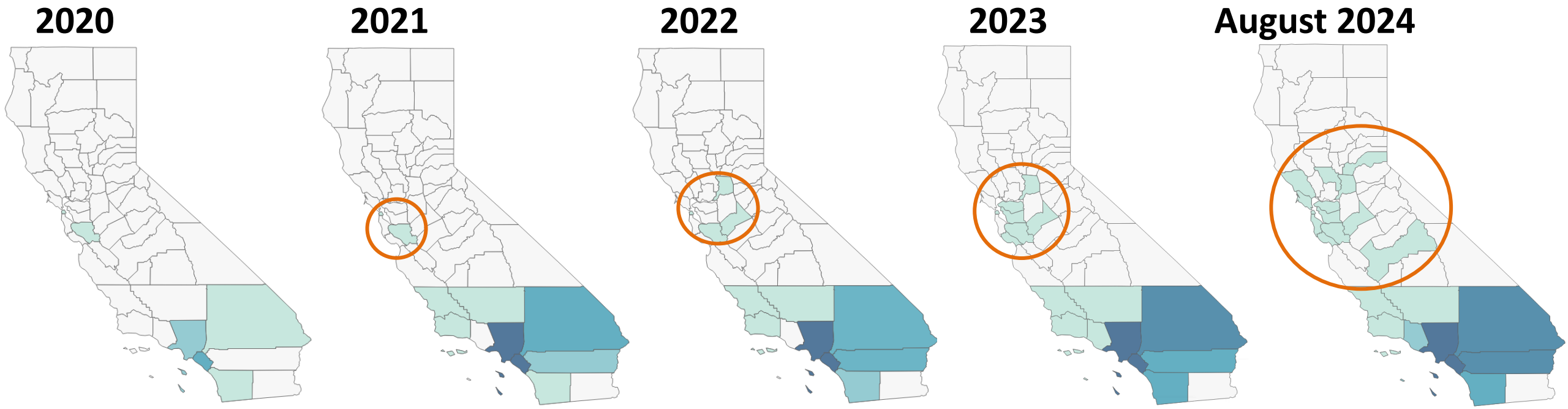
See [Karmarkar et al. 2021](www.acpjournals.org/doi/10.7326/M21-2013) (www.acpjournals.org/doi/10.7326/M21-2013)

The Pandemic Contributed to Widespread and Sustained Spread of *C. auris*



*preliminary data

We are Seeing More *C. auris* in Central and Northern California



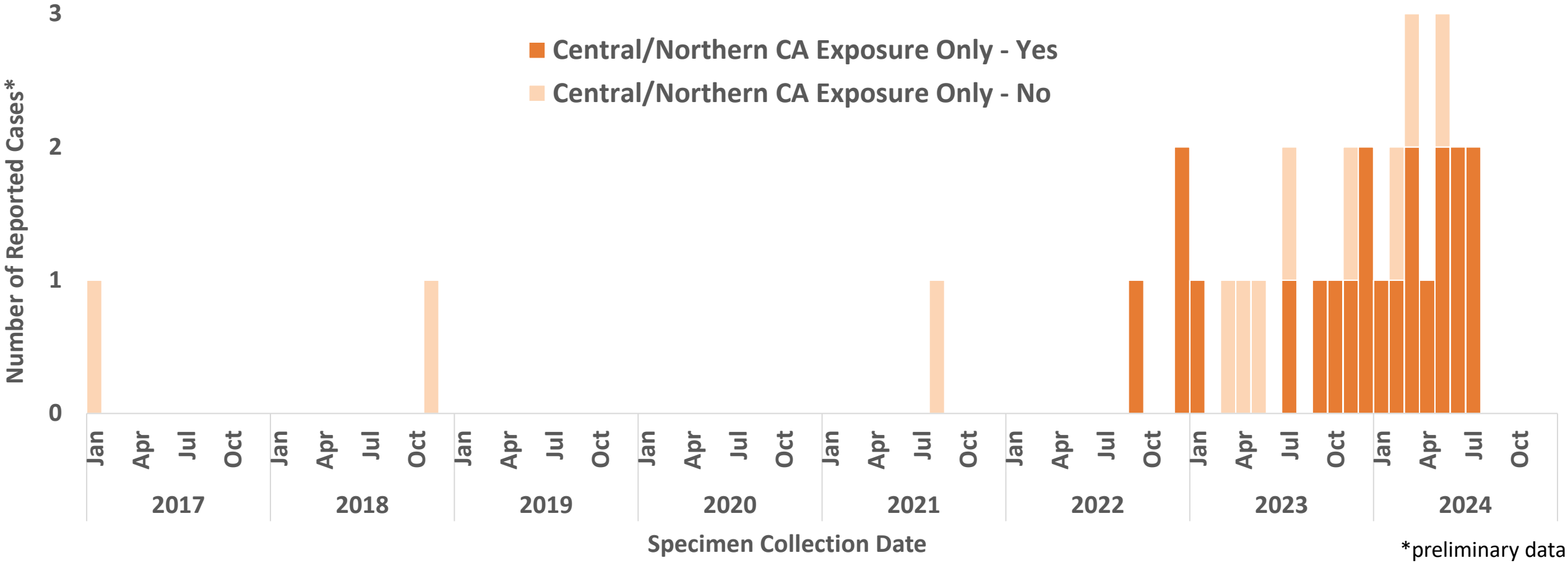
*preliminary data

Number of cumulative reported cases 0 1-10 11-100 101-500 501-1000 >1000

See CDPH *C. auris* website (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Candida-auris.aspx)

California Department of PublicHealth

From September 2022, Most Central/Northern California Cases* had No Exposure Outside the Region



*preliminary data

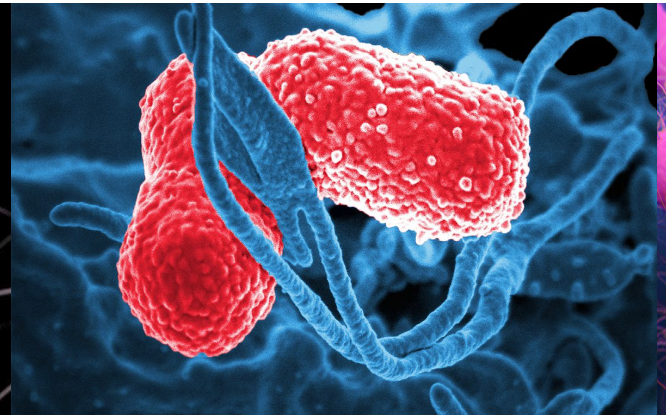
California Department of PublicHealth

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

Carbapenem-Resistant Organisms (CROs) and Carbapenemase-Producing Organisms (CPOs)

Acronyms

- **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 US)

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

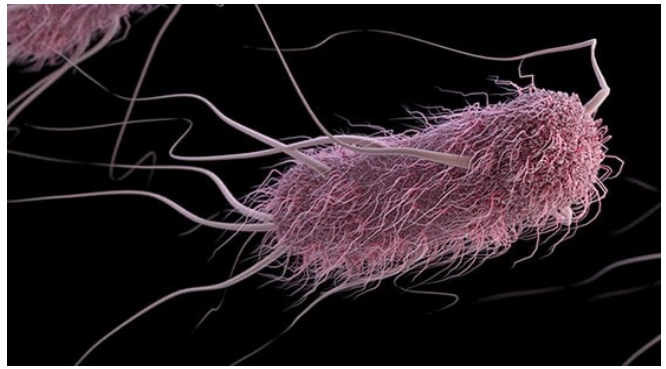
+= Deduced drug *= AES modified **= User modified

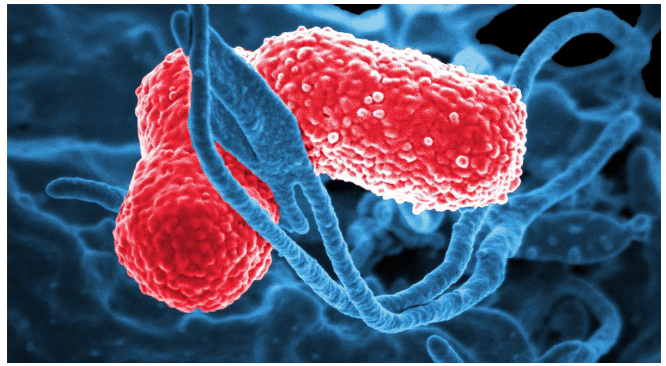
O is for Organism

Gram-negative bacteria

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

Carbapenem-resistant Enterobacterales (CRE)





- 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

See CDC CRE Information for Facilities (PDF)
(www.cdc.gov/healthcare-associated-infections/media/pdfs/CRE-handout-V7-508.pdf)

O is for Organism

Gram-negative bacteria

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

Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)

- *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
  - 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

See CDC CRPA Information for Facilities (PDF) (www.cdc.gov/healthcare-associated-infections/media/pdfs/CRPA-handout-V7-508.pdf)

See 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/)

O is for Organism

Gram-negative bacteria

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

Carbapenem-resistant *Acinetobacter baumannii* (CRAB)

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

See CDC CRAB Information for Facilities (PDF)
(www.cdc.gov/healthcare-associated-infections/media/pdfs/CRAB-handout-V7-508.pdf)

Acronyms

CROs

- CRE
- CRPA
- CRAB

Carbapenemase-producing organisms (CPOs)

Carbapenemases:

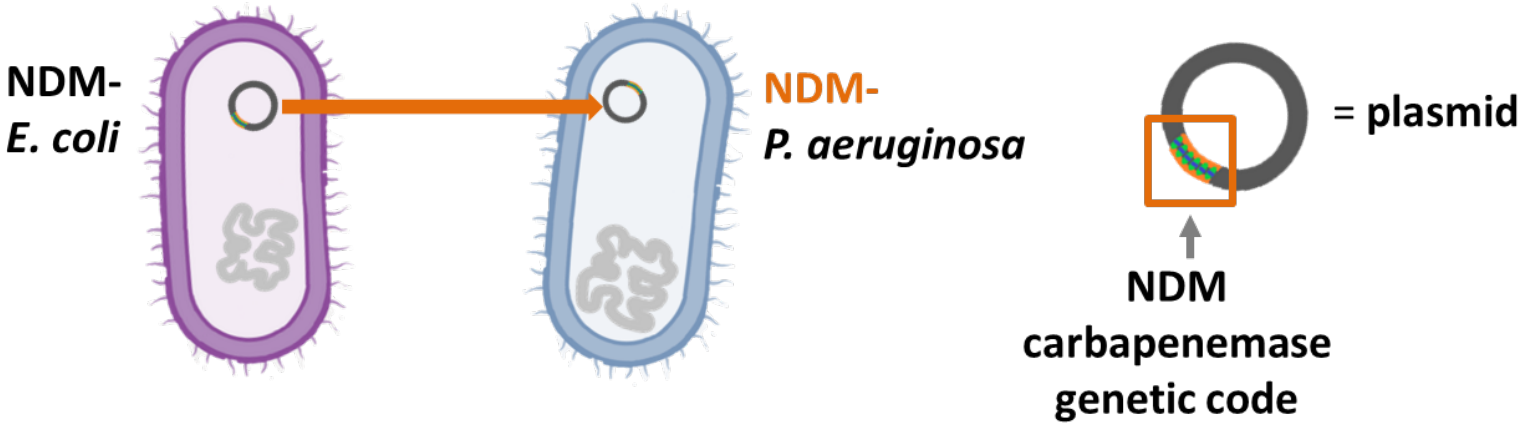
- **KPC**
- **NDM**
- **VIM**
- **OXA-48**
- **IMP**

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
  - e.g., 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**
  - e.g., NDM in *E. coli* → NDM in *Pseudomonas aeruginosa*



P is for Producing

Detection of carbapenemase production (phenotypic tests)

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

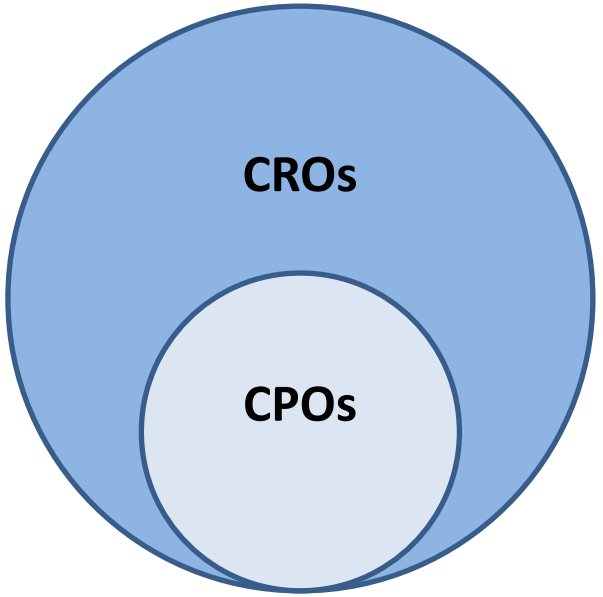
Detection of carbapenemase type (genotypic, other tests)

- 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, OXA-23)

See CRO Primer Test for Carbapenemases (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CRO_PrimerTests_for_Carbapenemases.pdf)

O is for Organism

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

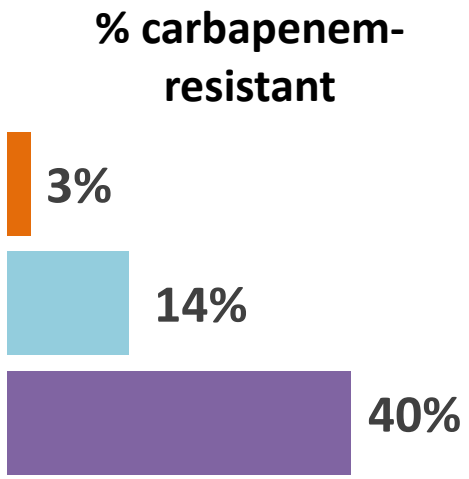


Examples include:

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

Percent Carbapenem Resistance in Isolates from HAIs in US Hospitals

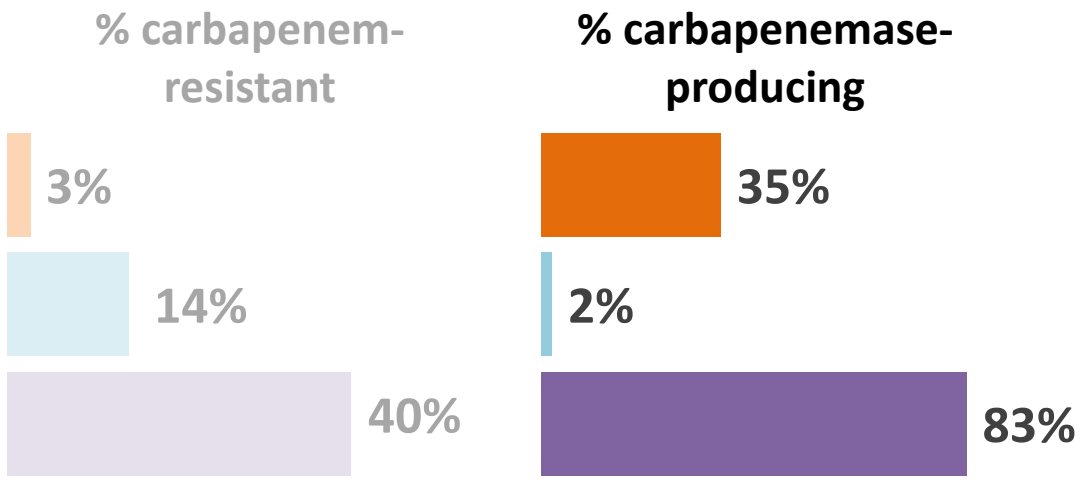
- **Enterobacterales (CRE)**
- ***Pseudomonas aeruginosa* (CRPA)**
- ***Acinetobacter baumannii* (CRAB)**



See National Healthcare Safety Network 2021 Hospital Data (arpsp.cdc.gov/profile/antibiotic-resistance?tab=antibiotic-resistance)

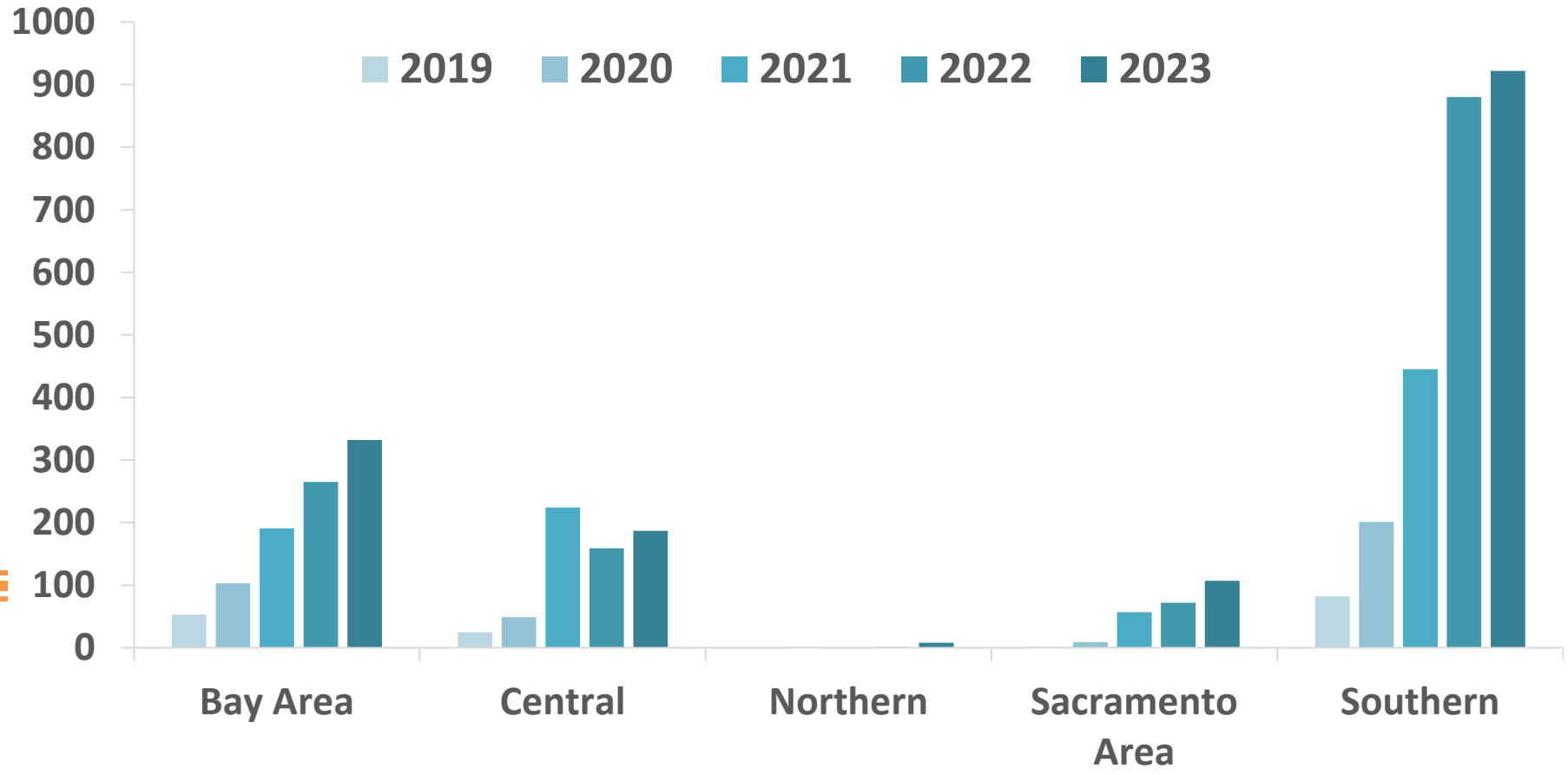
Percent CRE, CRPA, CRAB That are Carbapenemase-producing in the US

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



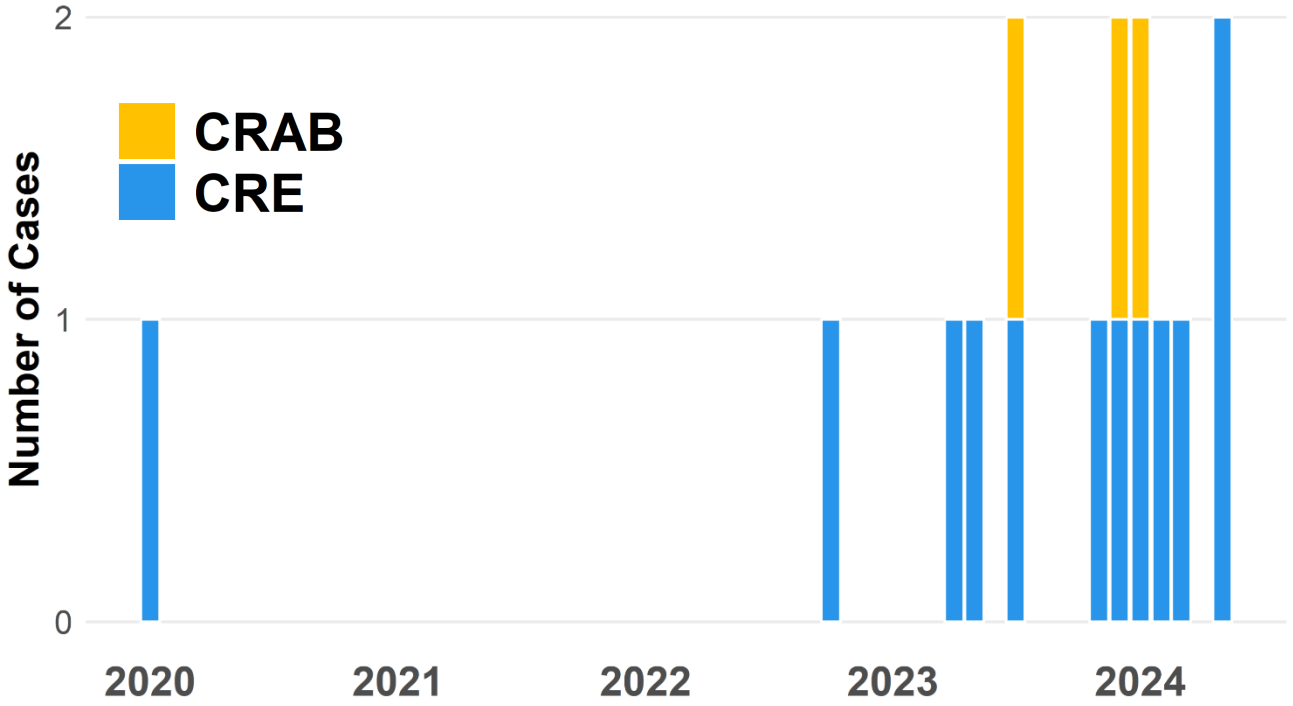
See National Healthcare Safety Network 2021 Hospital Data (arpsp.cdc.gov/profile/antibiotic-resistance?tab=antibiotic-resistance)

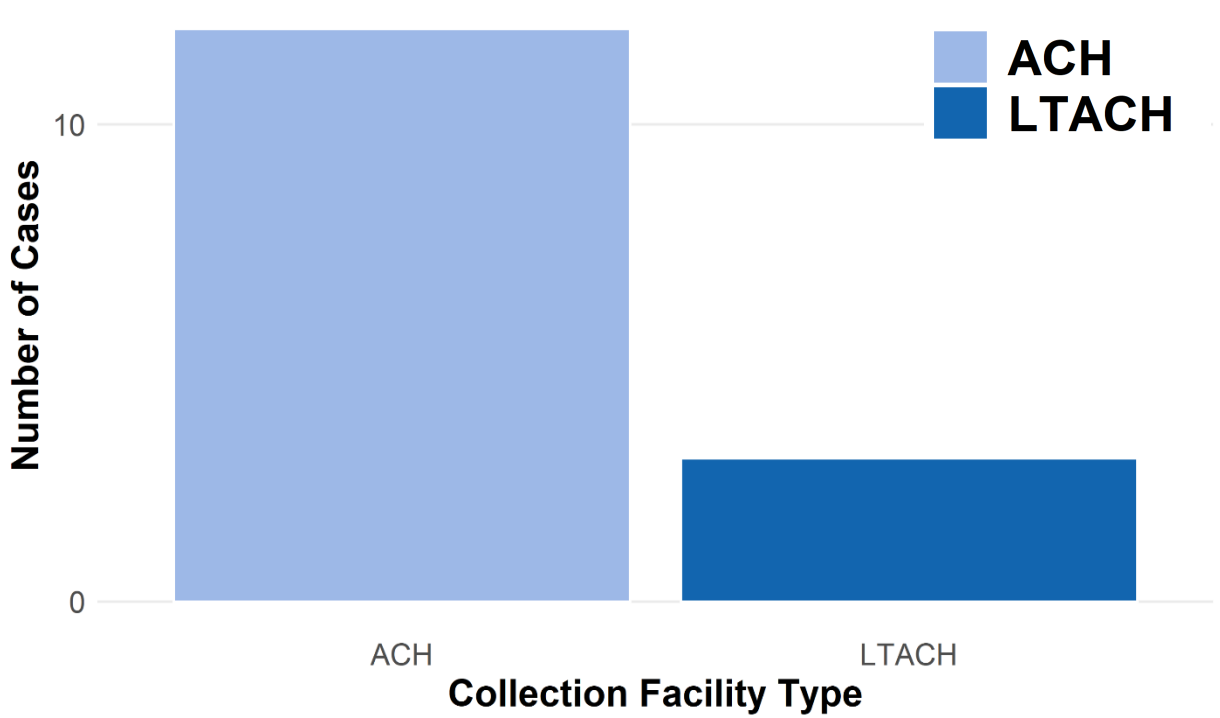
Since 2019, Reported CPO Cases* have Risen in All Regions



*preliminary data

CPO Cases* in Northern California, January 2020—June 2024

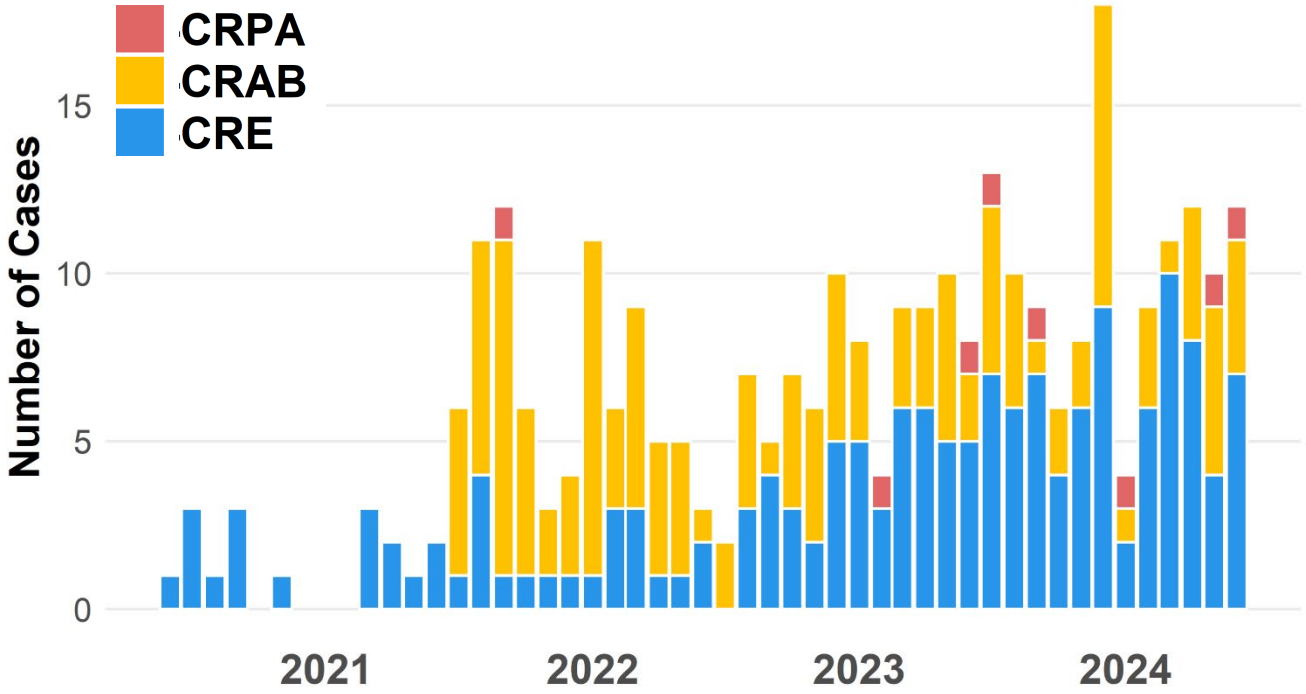


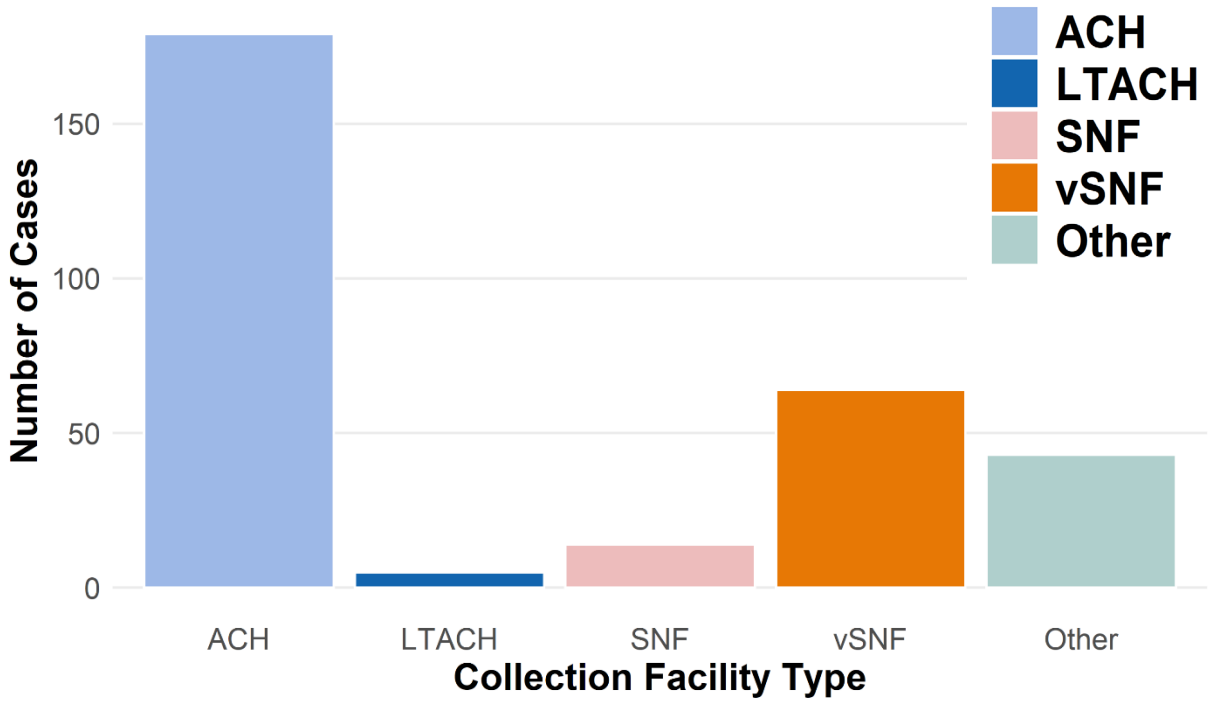


*preliminary data, including CPO cases from Del Norte, Glenn, Humboldt, Lake, Lassen, Mendocino, Modoc, Shasta, Siskiyou, Tehama, Trinity

California Department of PublicHealth

CPO Cases* in Sacramento Area, January 2020—June 2024

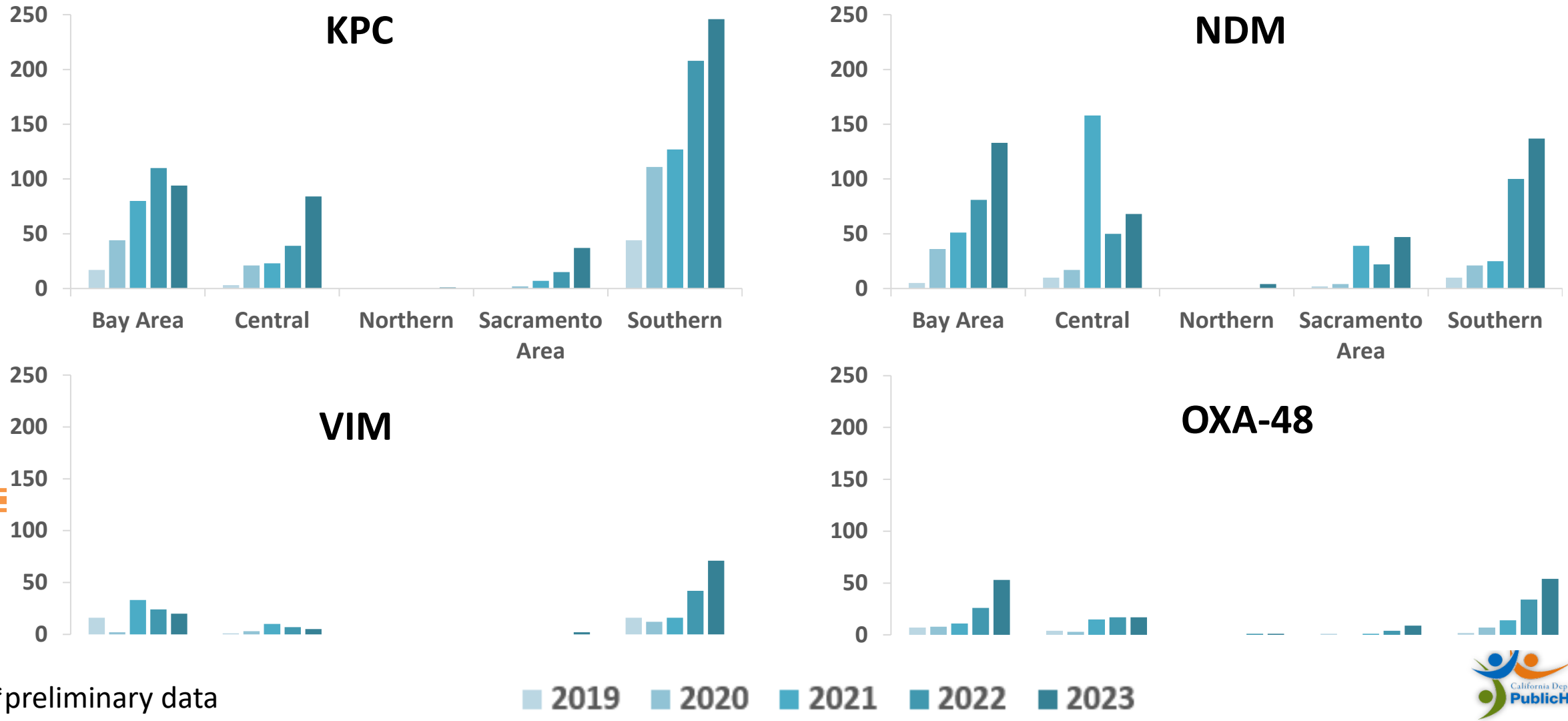




*preliminary data, including CPO cases from Amador, Butte, Colusa, El Dorado, Nevada, Placer, Plumas, Sacramento, Sierra, Solano, Sutter, Yolo, Yuba

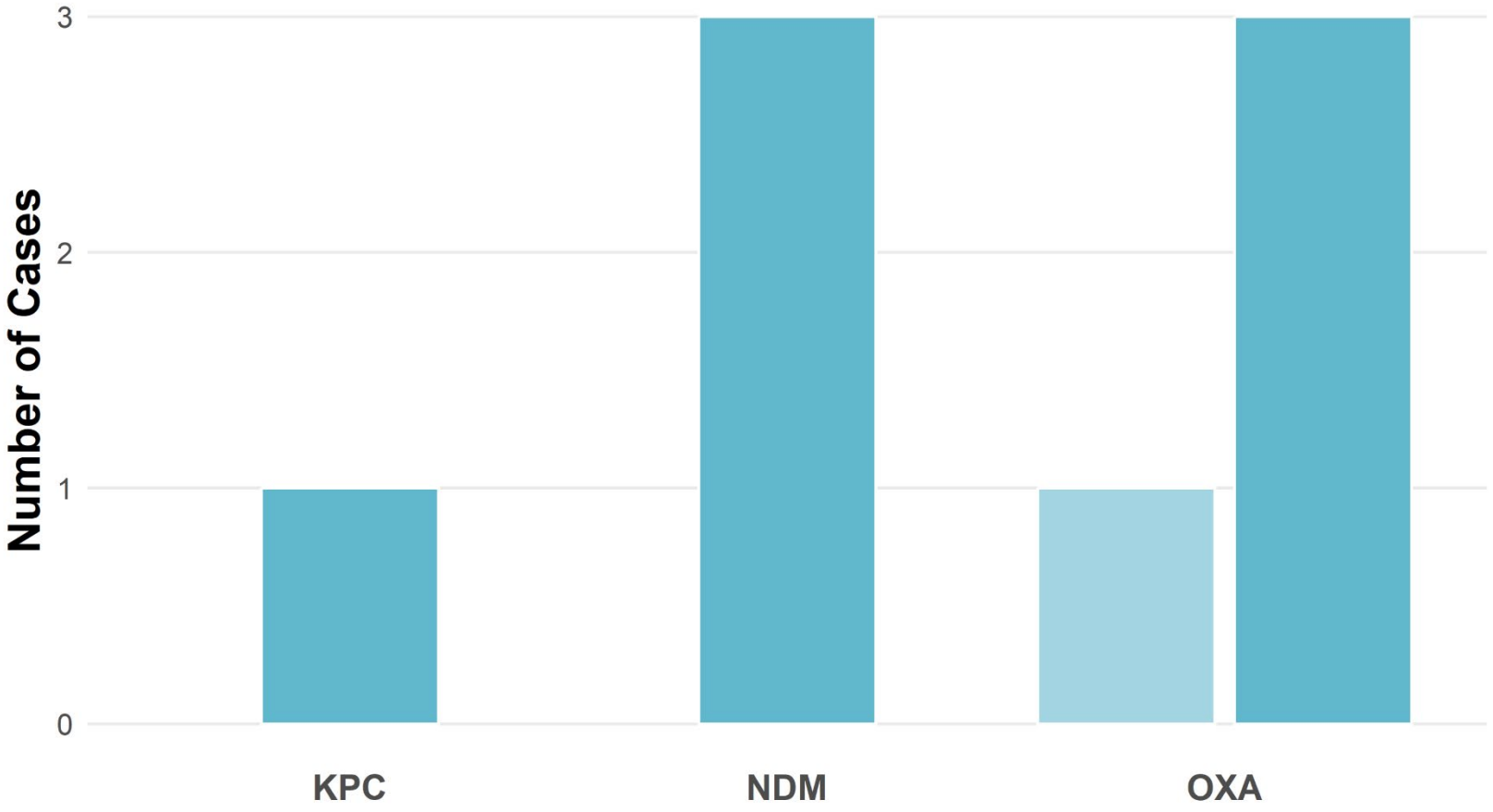
California Department of PublicHealth

We have Seen Increases Across all Carbapenemase Types* in all Regions



*preliminary data

Carbapenemase Types* in Northern California



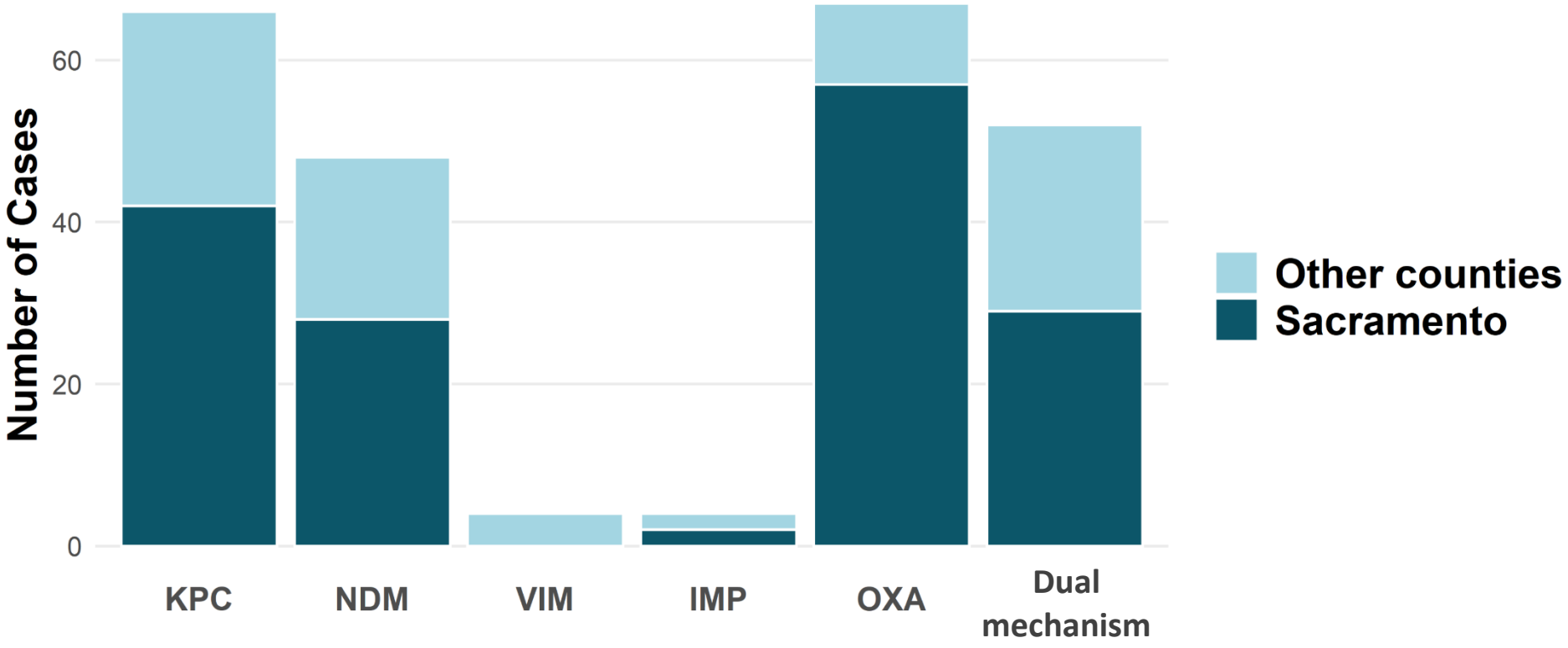
OXA variants include:

- 1 OXA-23
- 2 OXA-48
- 1 OXA-235

*preliminary data, including CPO cases from Del Norte, Glenn, Humboldt, Lake, Lassen, Mendocino, Modoc, Shasta, Siskiyou, Tehama, Trinity

California Department of PublicHealth

Carbapenemase Types* in Sacramento Area January 2020—June 2024



OXA variants include:

- 37 OXA-23
- 6 OXA-24/40
- 11 OXA-48
- 12 OXA-235

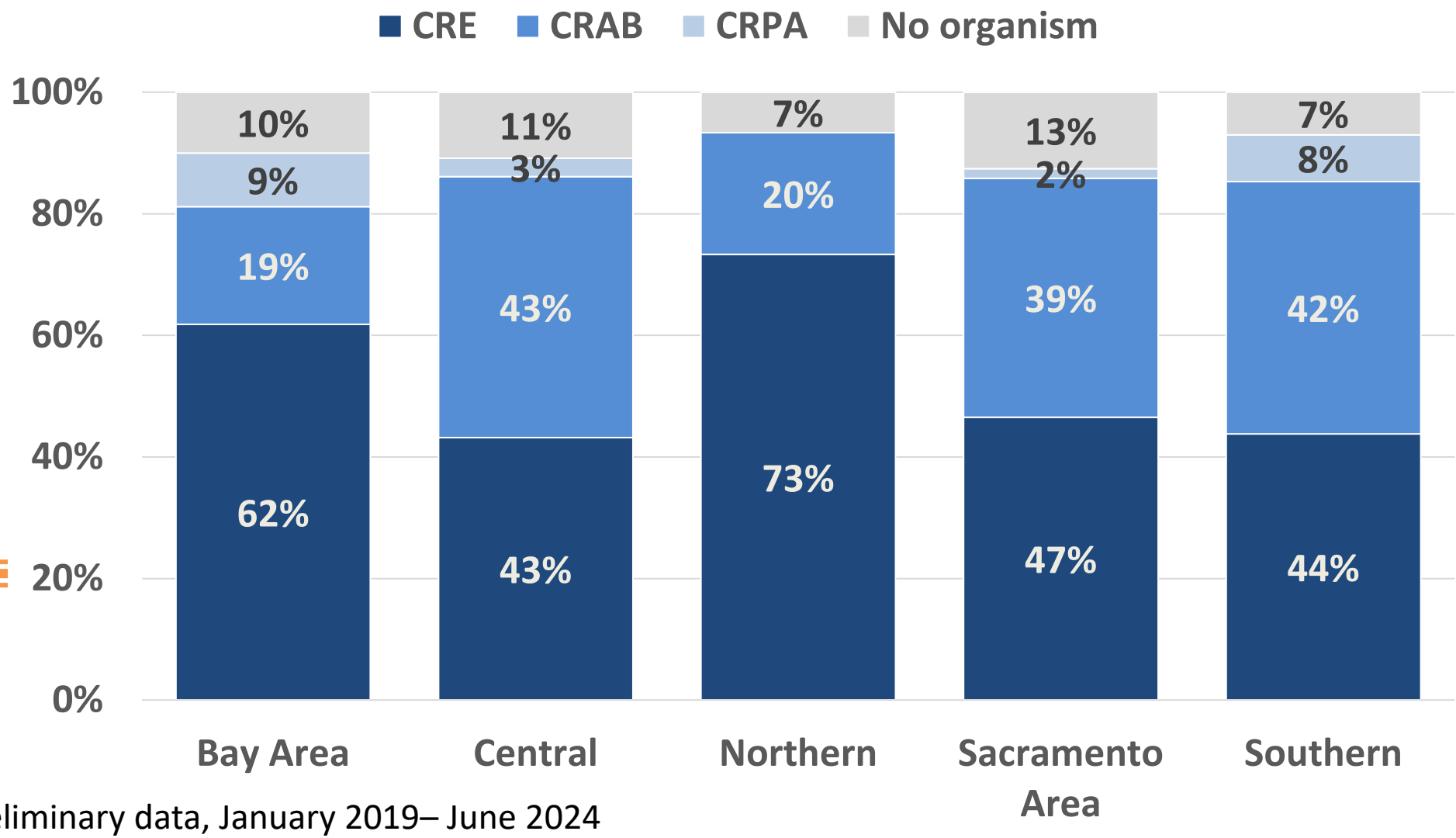
Dual resistance mechanisms include:

- 48 NDM/OXA-23
- 3 NDM/OXA-48
- 1 OXA-23/OXA-58

*preliminary data, including CPO cases from Amador, Butte, Colusa, El Dorado, Nevada, Placer, Plumas, Sacramento, Sierra, Solano, Sutter, Yolo, Yuba

California Department of PublicHealth

The Proportion of CPOs* Varies by Region



*preliminary data, January 2019– June 2024

California Department of PublicHealth

VIM-CRPA

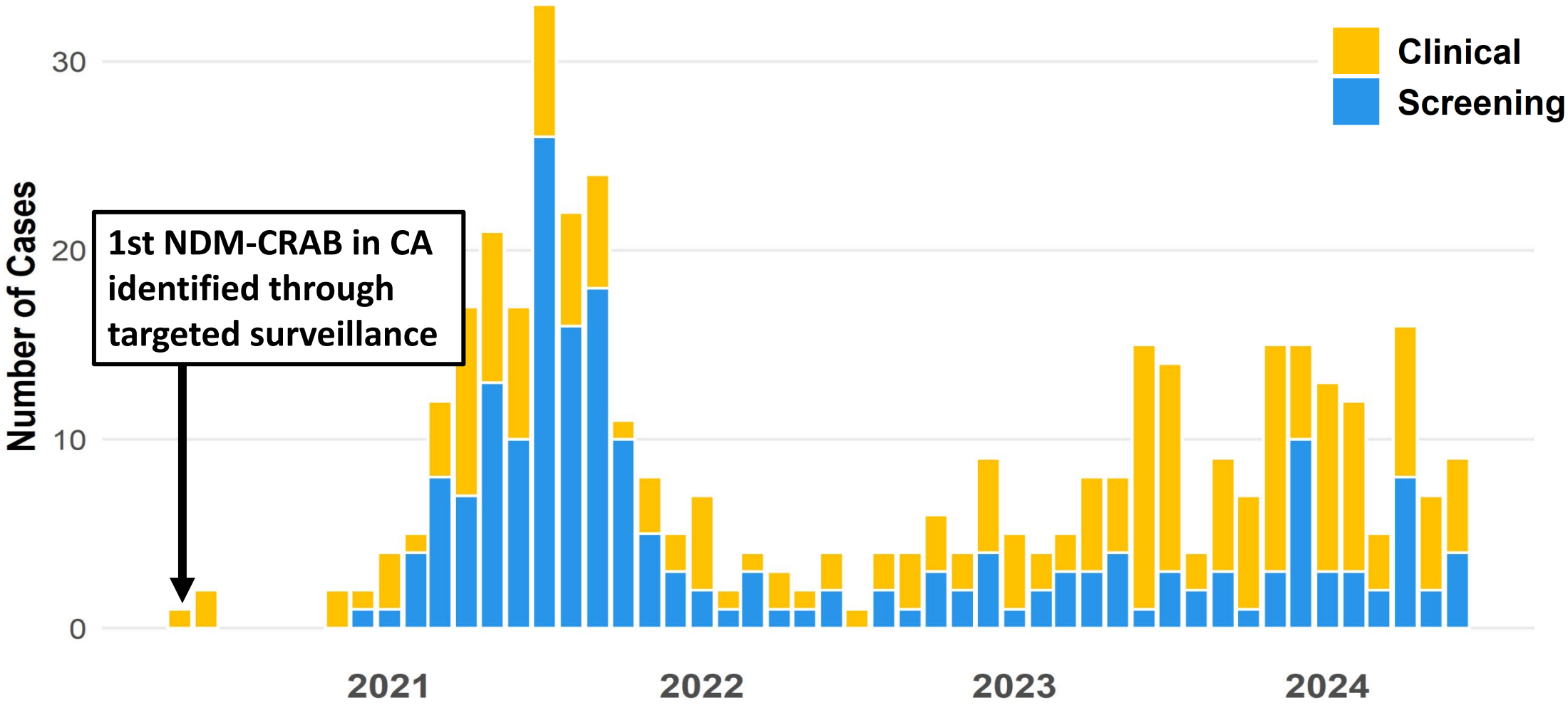
- **VIM** is most common carbapenemase associated with CRPA in California
  - Associated with multiple outbreaks in different healthcare settings
- Since 2018, VIM-CRPA cases have been identified in patients reporting receipt of medical care in Mexico
  - Includes both medical tourism and routine medical care
- National outbreak of VIM-CRPA associated with artificial tears
  - 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

See CDC Outbreak of Extensively Drug-resistant *Pseudomonas aeruginosa* Associated with Artificial Tears (archive.cdc.gov/www_cdc_gov/hai/outbreaks/crpa-artificial-tears.html)

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

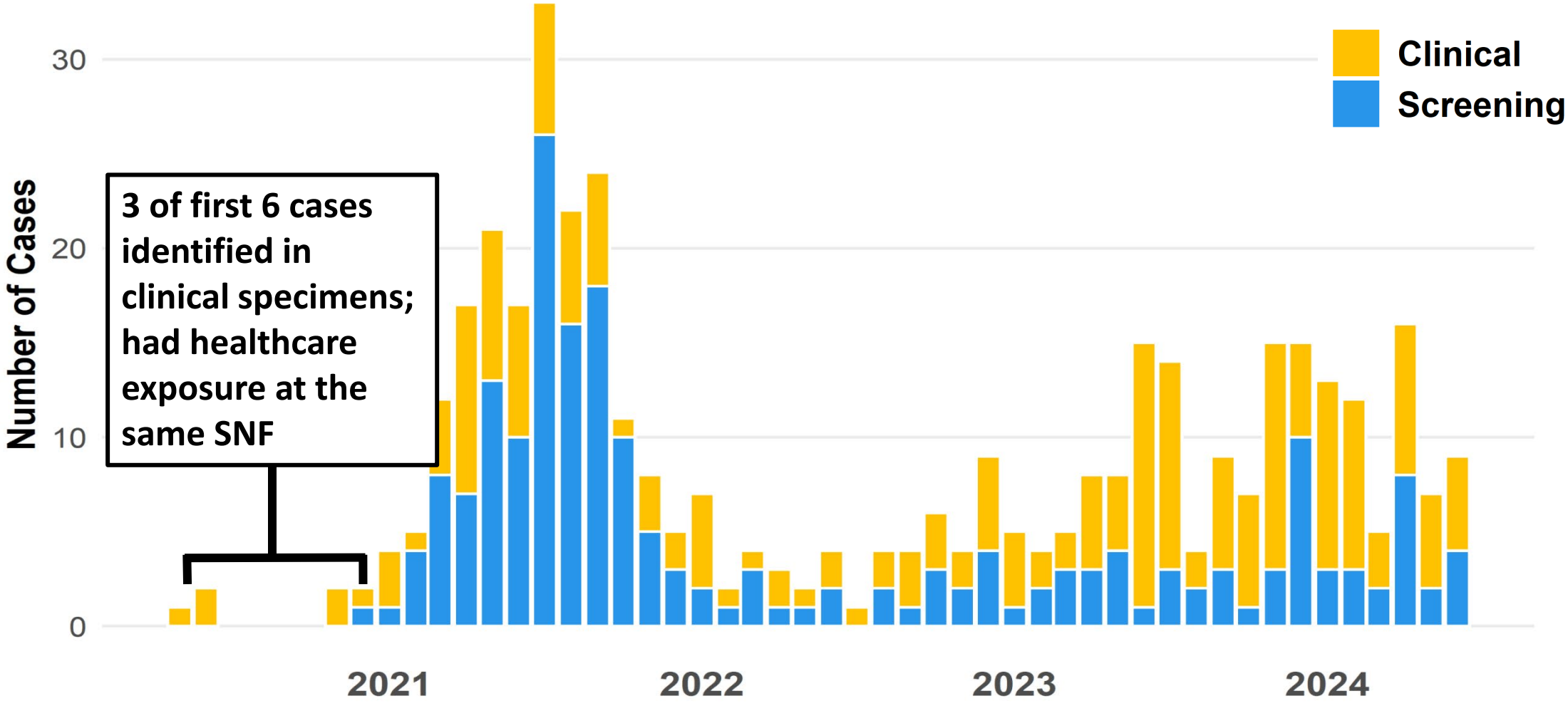
NDM-CRAB Cases, May 2020—May 2024*



*preliminary data

California Department of PublicHealth

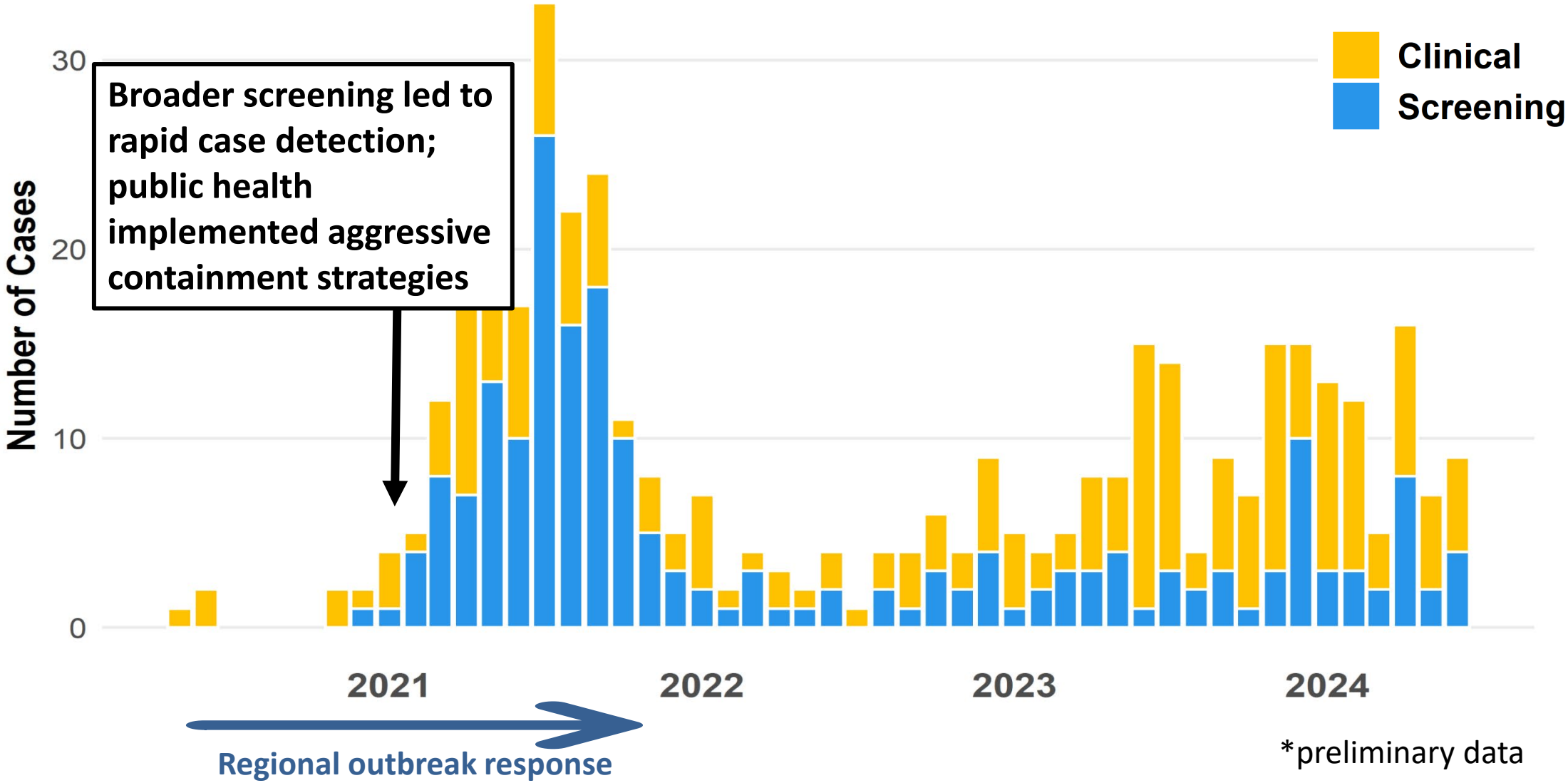
NDM-CRAB Cases, May 2020—May 2024*



*preliminary data

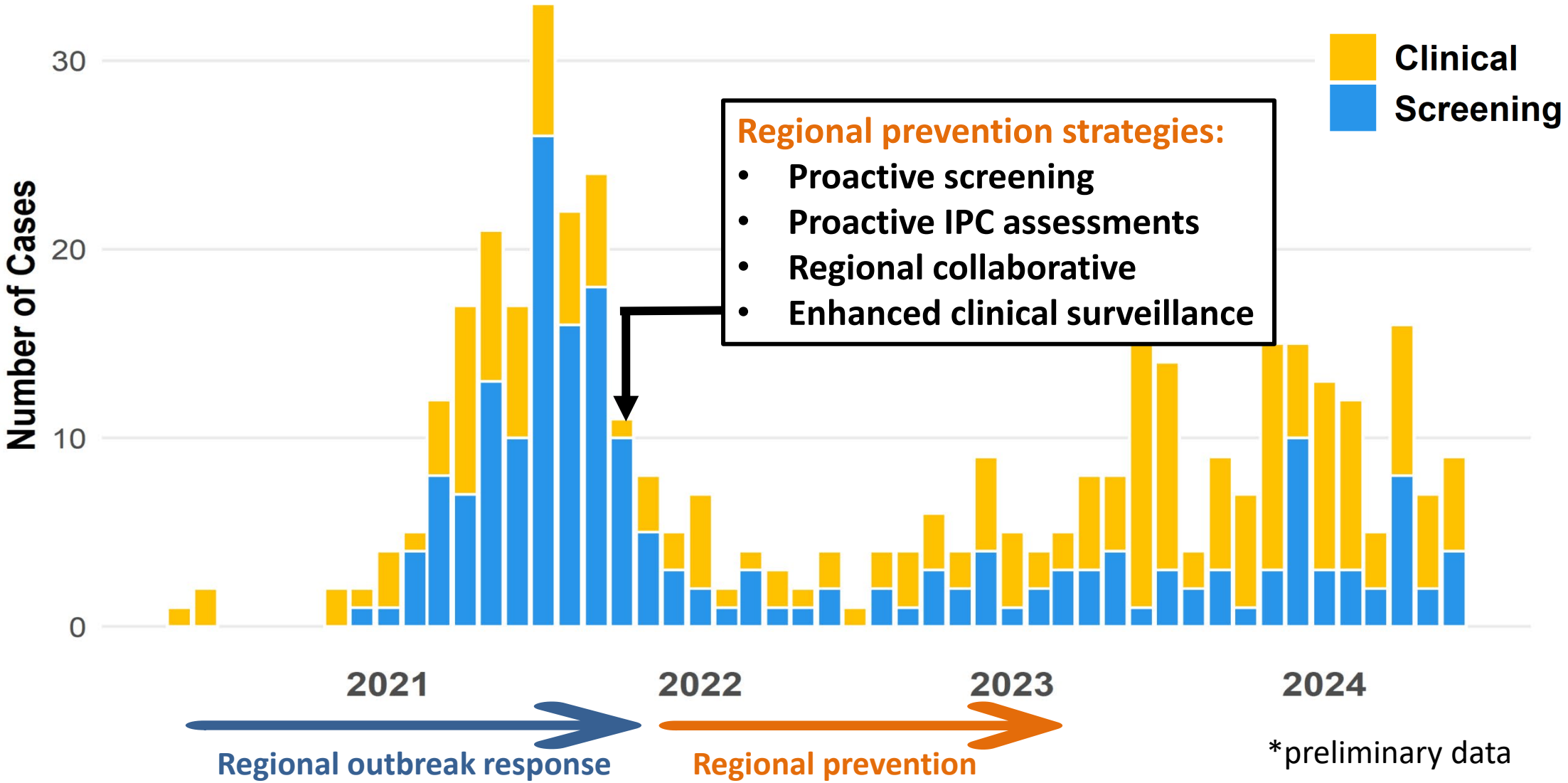
California Department of PublicHealth

NDM-CRAB Cases, May 2020—May 2024*



*preliminary data

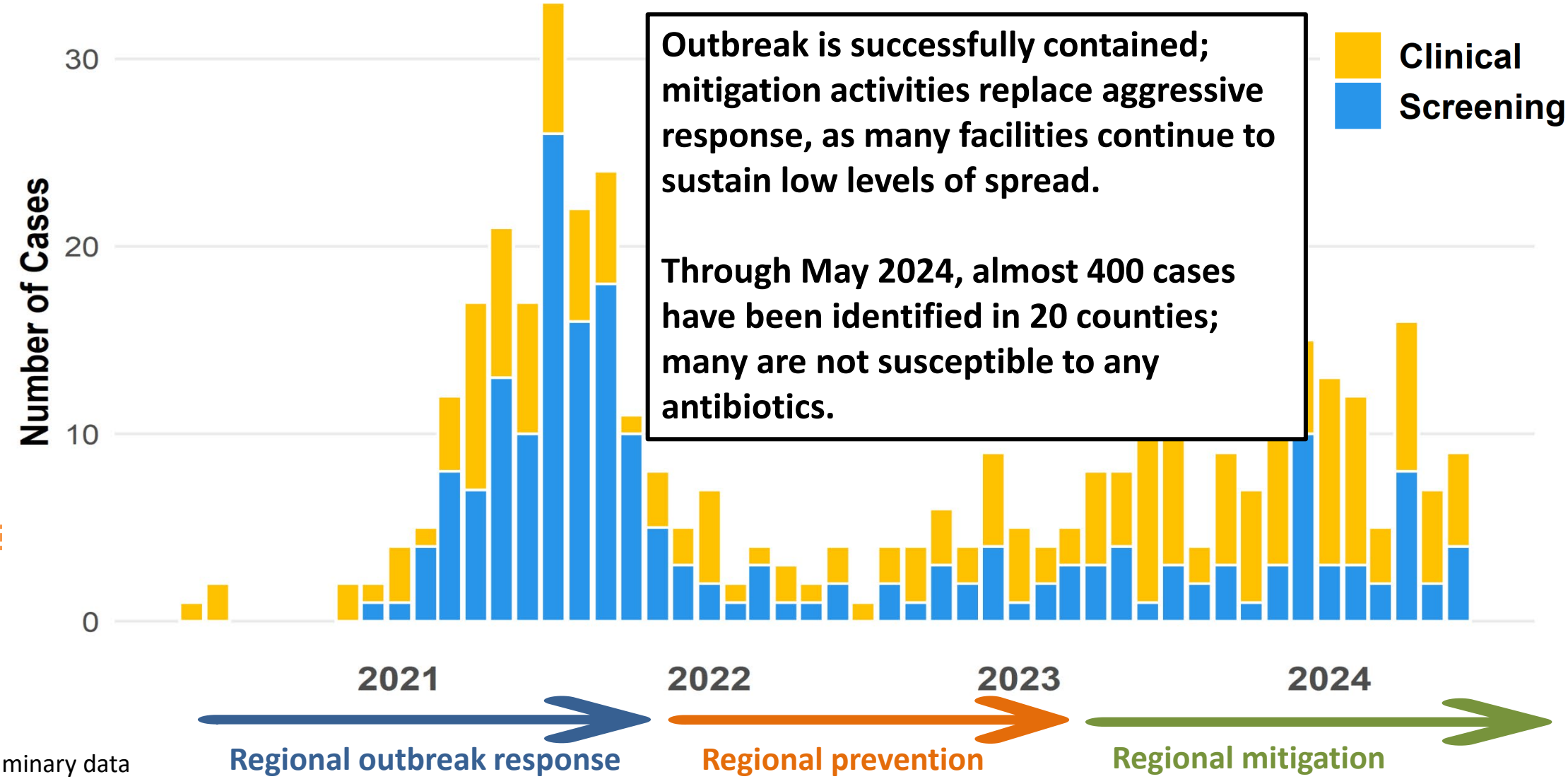
NDM-CRAB Cases, May 2020—May 2024*



*preliminary data

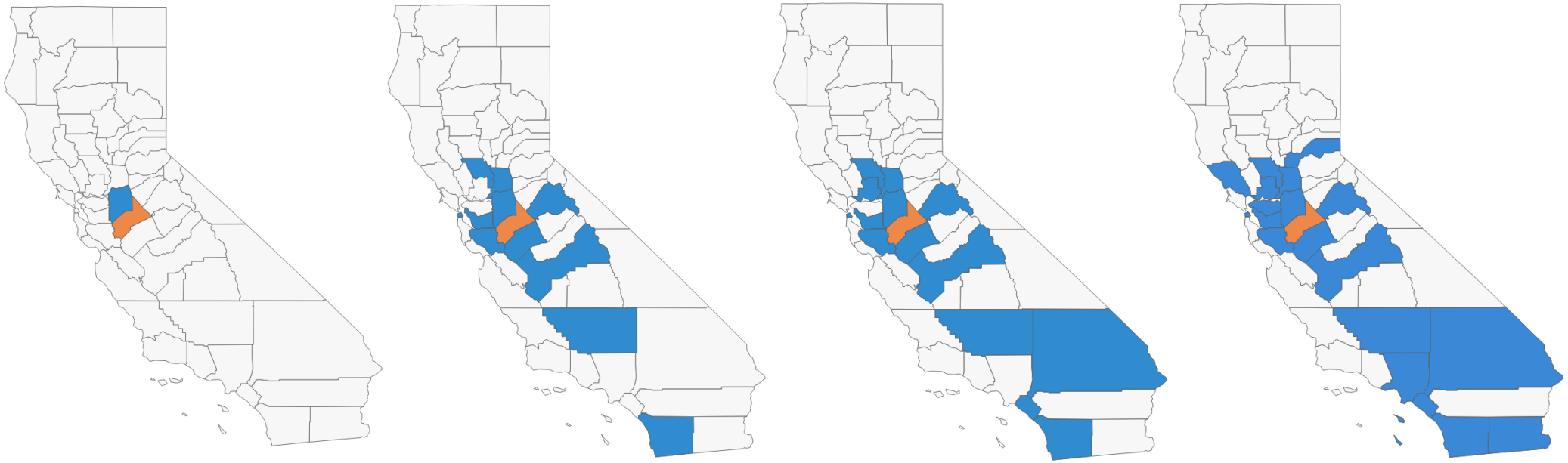
California Department of PublicHealth

NDM-CRAB cases, May 2020—May 2024*



*preliminary data

NDM-CRAB Cases* Continue to Spread Across the State



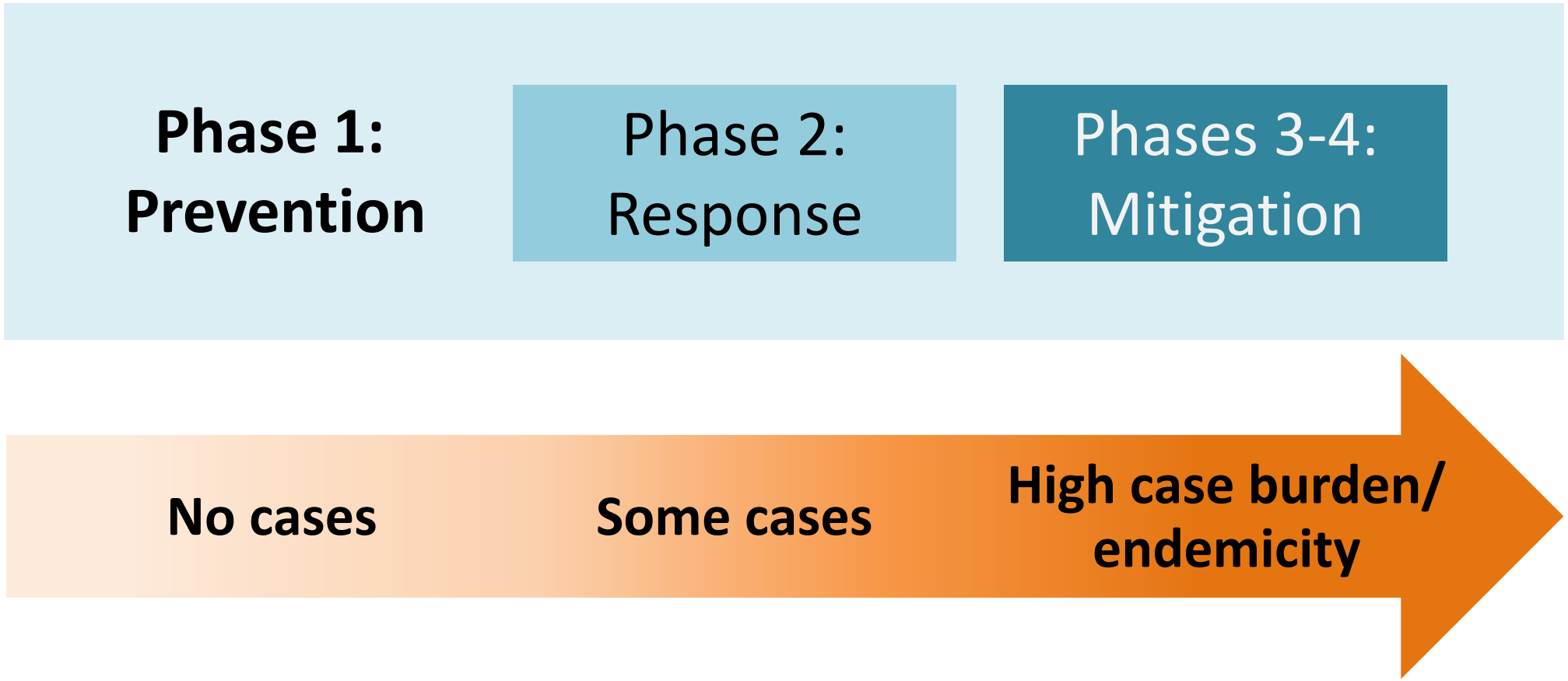
Jan 2021 Jan 2022 Jan 2023 Jan 2024

*preliminary data

See CDPH NDM-CRAB CAHAN (PDF)
(www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CAHAN_NDM_OXA23_CRAB_May2021.pdf)

California Department of PublicHealth

Regional MDRO Prevention and Response Strategy: a Phased Approach Based on Local Epidemiology



See CDPH Regional *C. auris* Prevention and Response Strategy (PDF)
(www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/Cauris_Phases.pdf)

California Department of PublicHealth

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**
- Patients or residents with frequent healthcare exposure, 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!

Thank you!

Questions?

For more information, contact

HAI_AR@cdph.ca.gov