

Candida auris:

Epidemiology, surveillance, and prevention

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Disclosures

- I have nothing to disclose.

Acknowledgement

- Many of today's slides come from presentations previously given in New Jersey.
- Some content was adapted from presentations given by Dr. Sharon Tsay and CDC Mycotic Diseases Branch.

Learning Objectives

1. Review the emergence, identification, resistance, and transmission of *Candida auris*
2. Identify key prevention and control activities for *Candida auris*

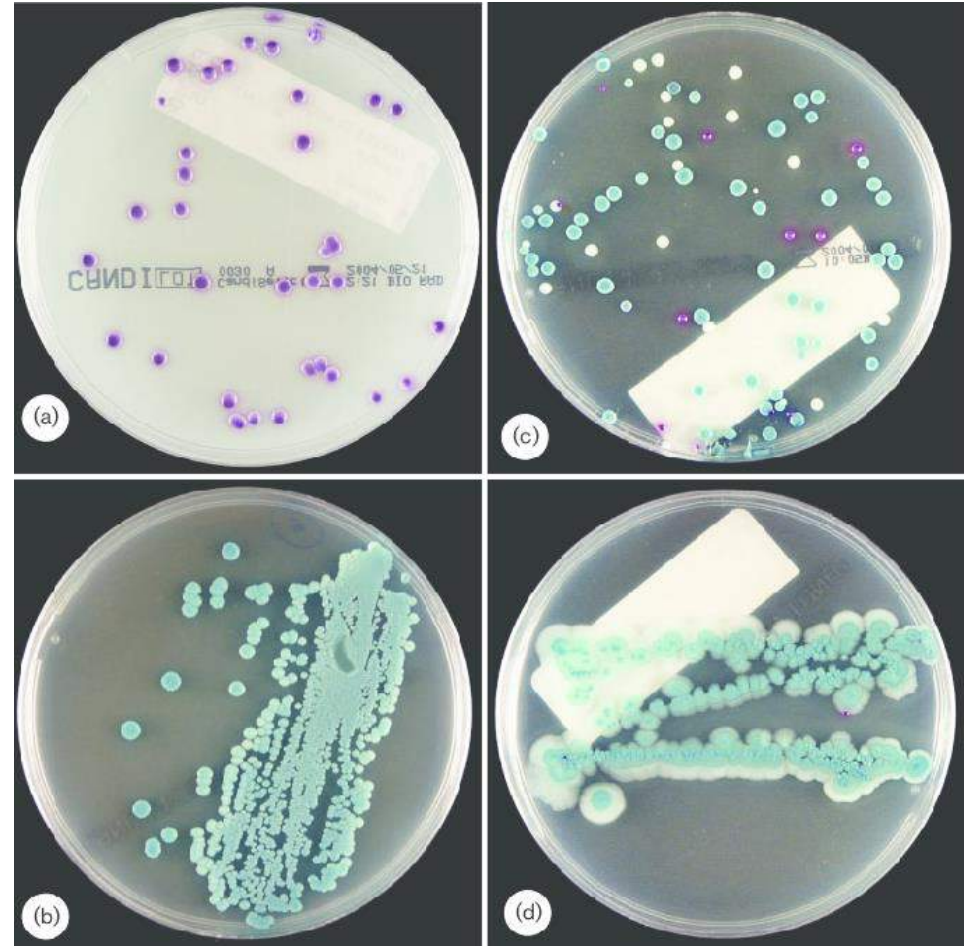
Agenda

- Rethinking '*Candida*'
 - Emergence
 - Identification
 - Resistance
 - Transmission
- Prevention
- Response
- New Jersey experiences
- Takeaways

Let's talk *Candida*.

Candida

- Catch-all for asexual yeast
- Includes hundreds of unrelated species
- More added each year



Candidemia

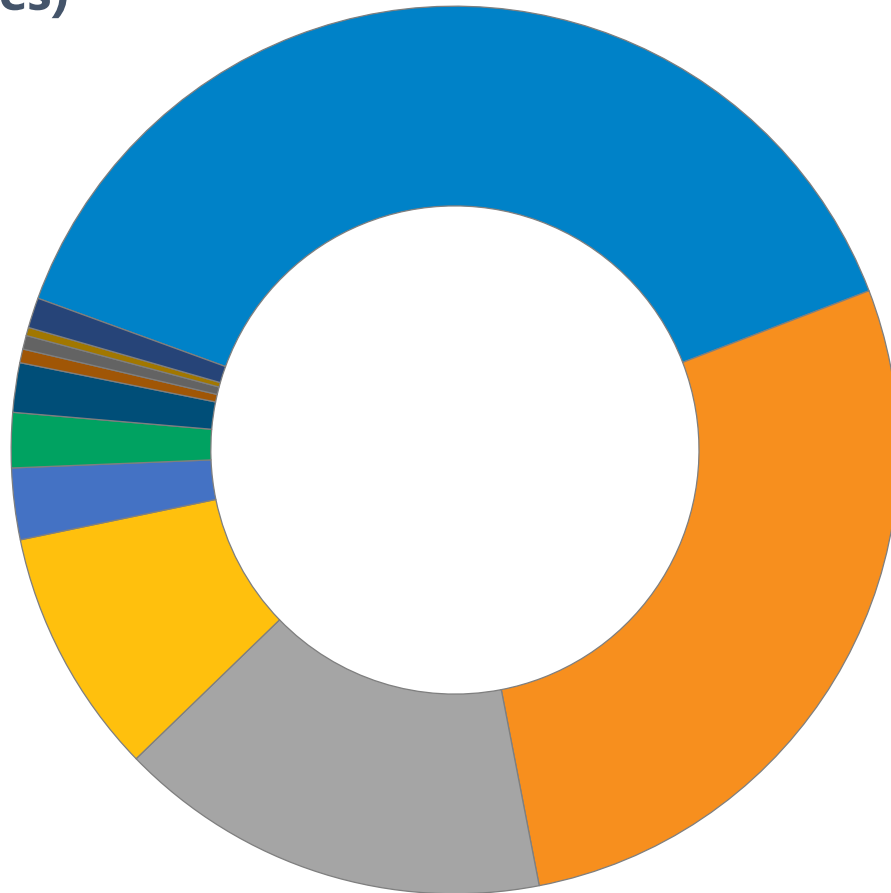
- Bloodstream infections (BSIs) caused by *Candida* spp.
- *Candida* is the most common organism causing healthcare-associated BSIs
- Incidence ~10-14 per 100,000
- Mortality 30-50%



Candida albicans

Candida species distribution in bloodstream isolates

Emerging Infections Program Surveillance, US 2008-2016 (n = ~7,000 isolates)



- *Candida albicans* (38.6%)
- *Candida glabrata* (27.8%)
- *Candida parapsilosis* (15.8%)
- *Candida tropicalis* (9.0%)
- *Candida dubliniensis* (2.6%)
- *Candida krusei* (2.0%)
- *Candida lusitaniae* (1.8%)
- *Candida guilliermondii* (0.5%)
- *Candida orthopsilosis* (0.5%)
- *Candida metapsilosis* (0.3%)
- Other species (1.1%)

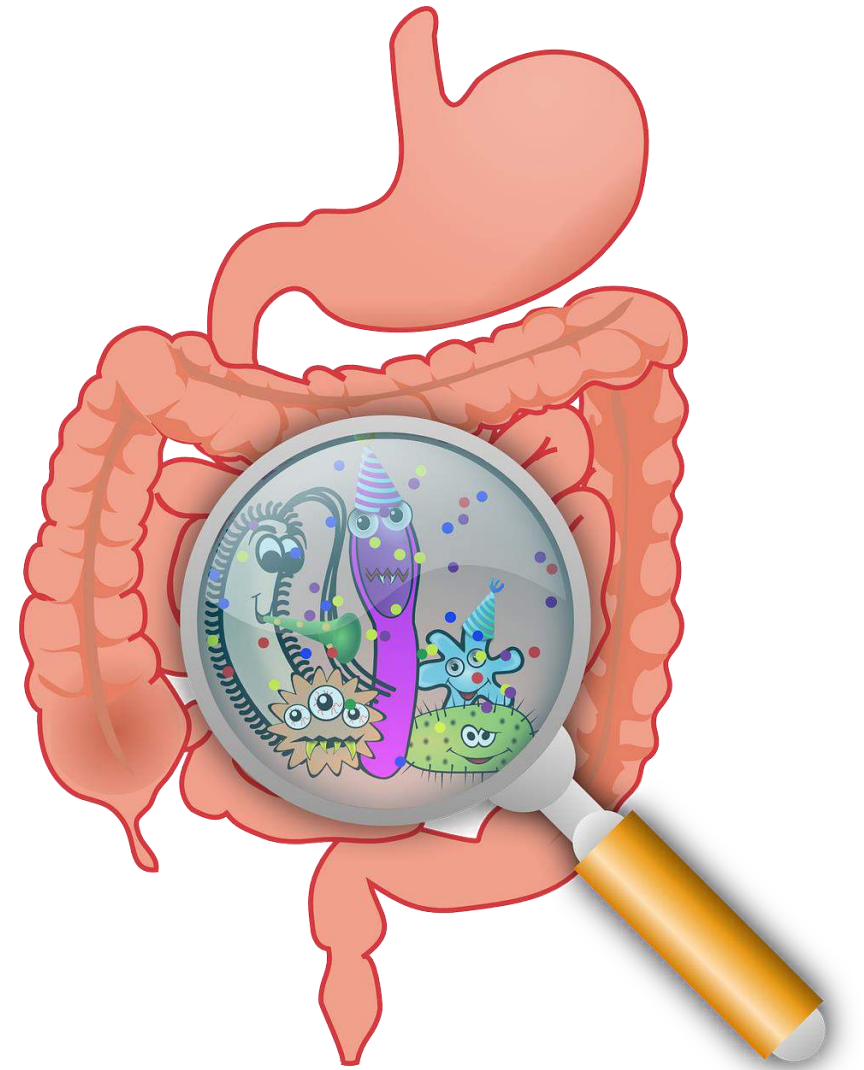
Who gets candidemia?

- Broad-spectrum antibiotic use
- Immunocompromised
- Central lines
- Prolonged ICU stay
- Surgical patients (abdominal surgery)

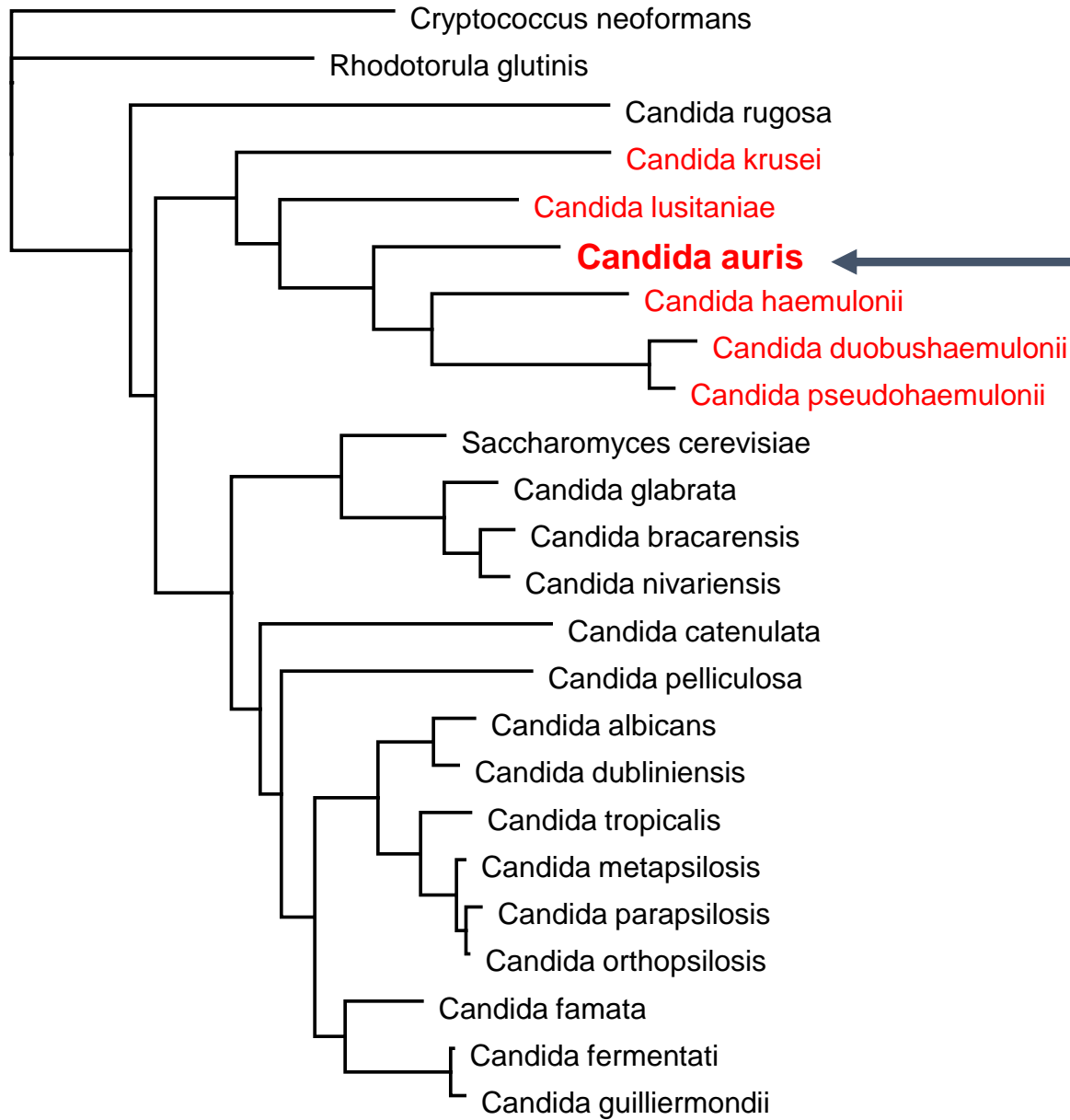


Source of infection

- **Conventional wisdom:** autoinfection with host flora
- Transmission in hospital environments not thought to be common
- Outbreaks rare, but reported with *Candida parapsilosis*

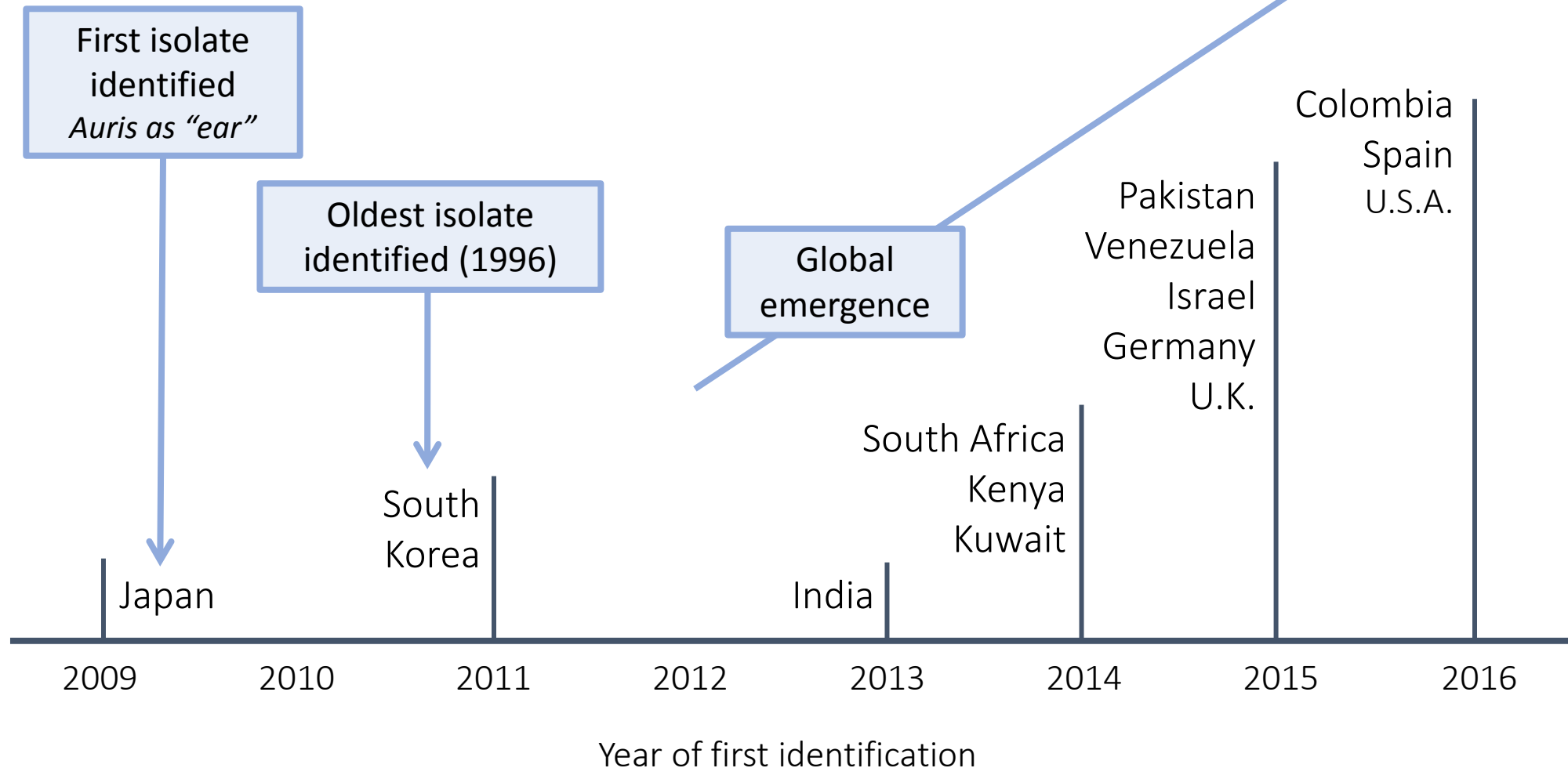


**Conventional wisdom does
not apply to *Candida auris*.**



Closely related to other *Candida* species known for antifungal resistance

Global emergence of *C. auris*

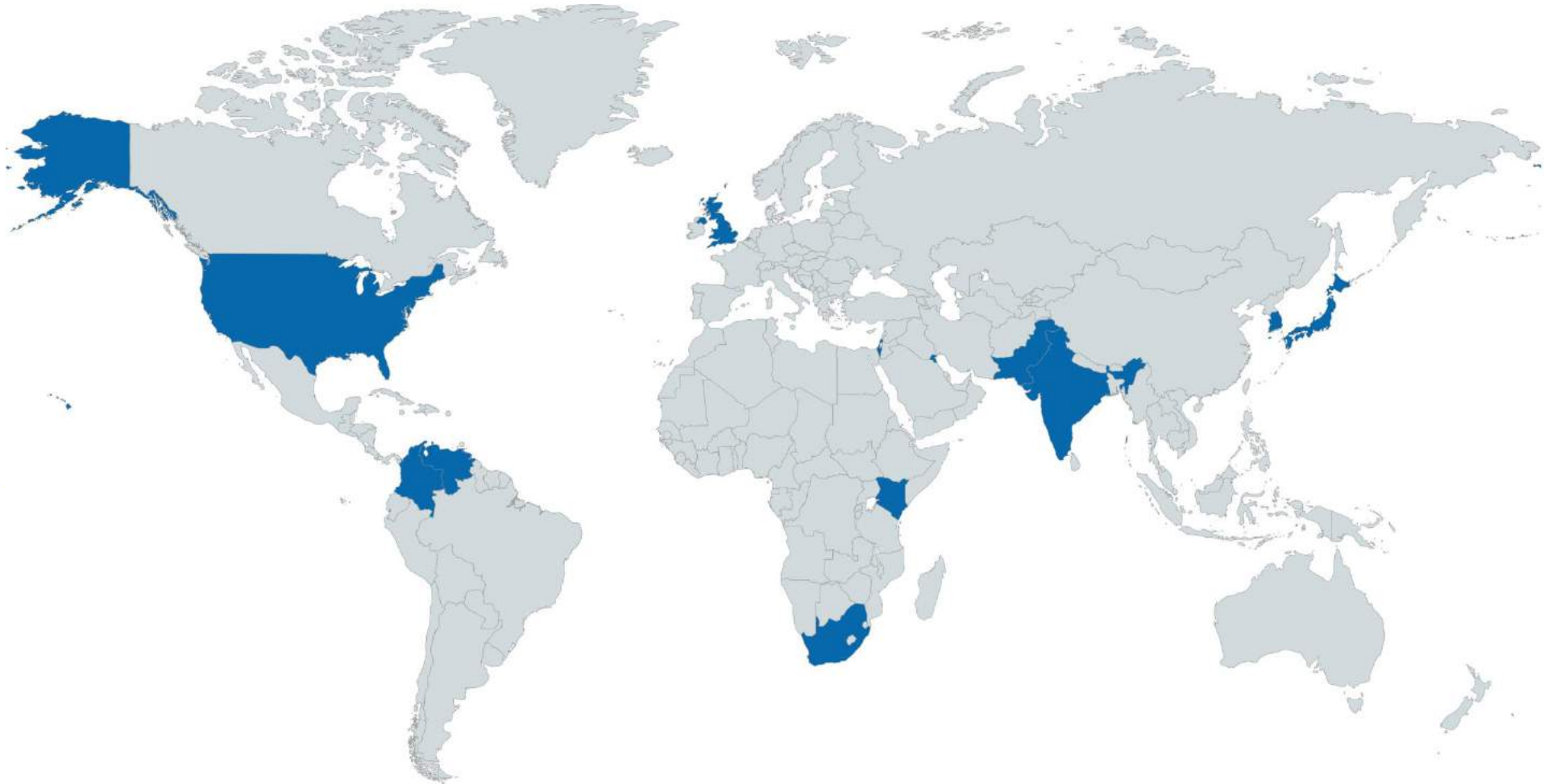


Healthy skepticism

- Was *C. auris* with us all along?
- Maybe newer diagnostic methods responsible for supposed emergence?
 - MALDI-TOF
 - DNA sequencing
- Most systems misidentify as *Candida haemulonii* or other species



International collaboration to assess emergence

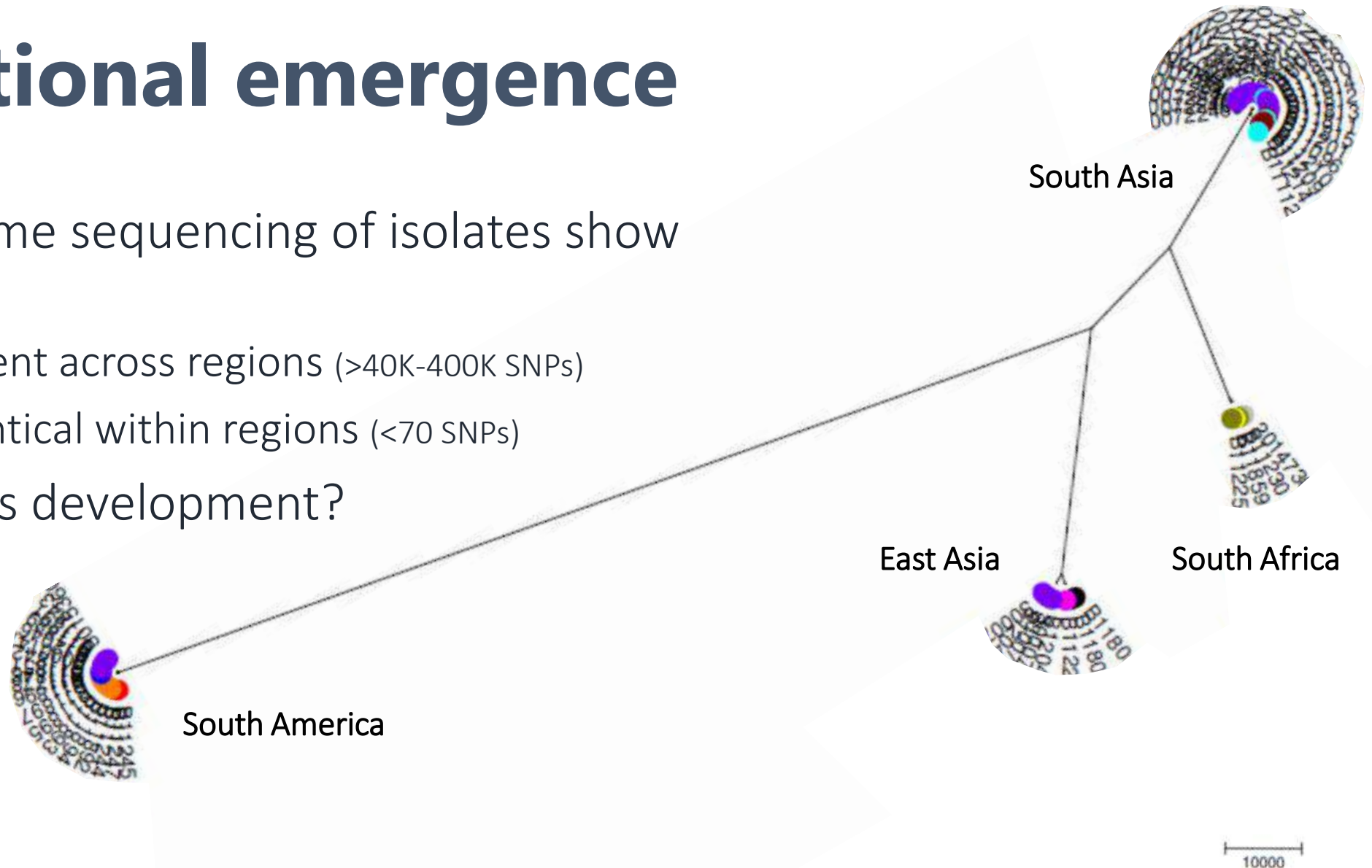


Emergence is not just improved detection

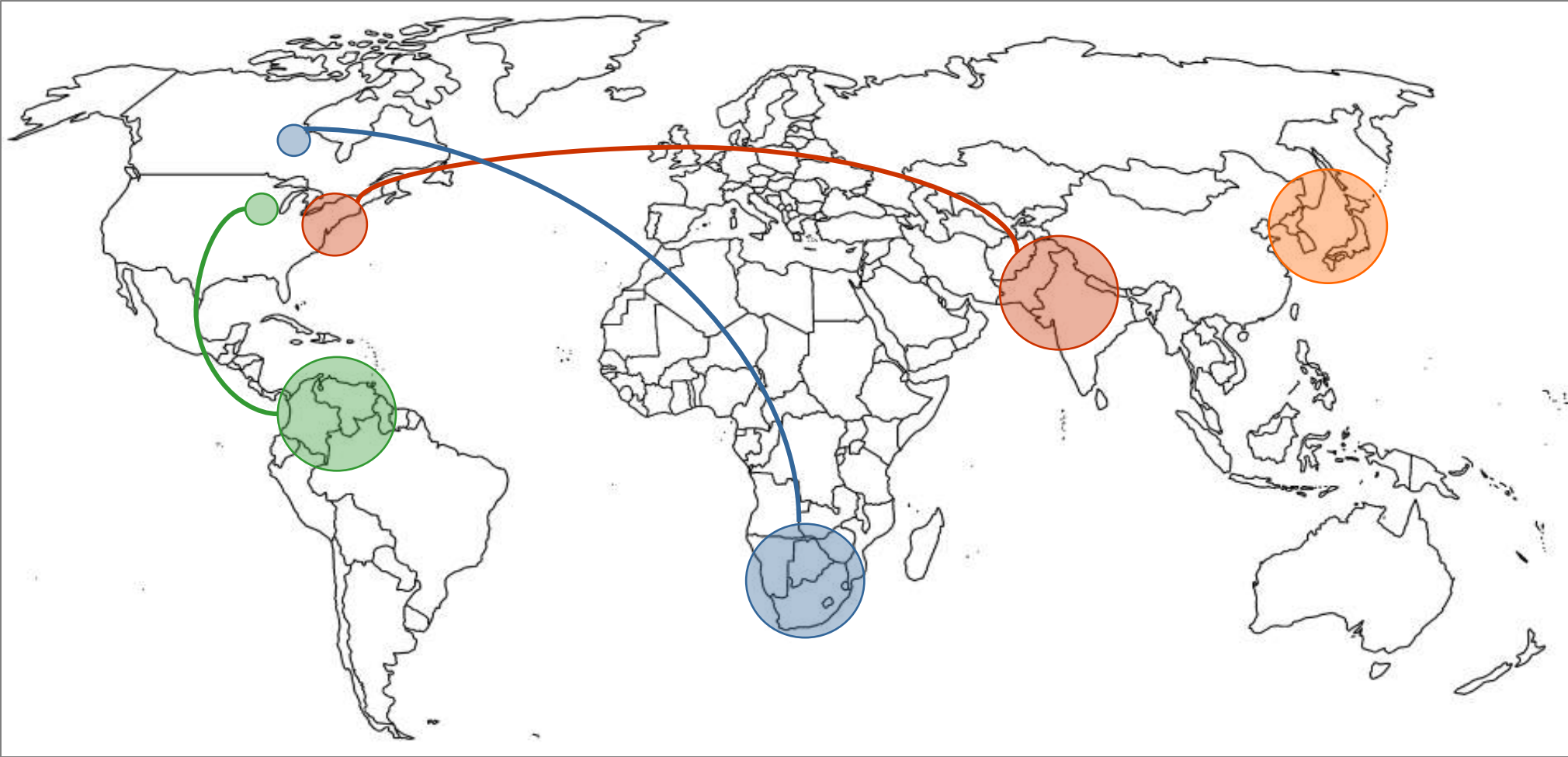
- EIP Candidemia Surveillance Program
 - >7000 *Candida* isolates collected in U.S. 2008 –2016
 - No *C. auris* found
- SENTRY and ARTEMIS programs (private collections from 4 continents)
 - >30,000 *Candida* isolates from 1996-2015
 - No *C. auris* before 2009

International emergence

- Whole genome sequencing of isolates show four clades
 - Very different across regions (>40K-400K SNPs)
 - Nearly identical within regions (<70 SNPs)
- Simultaneous development?

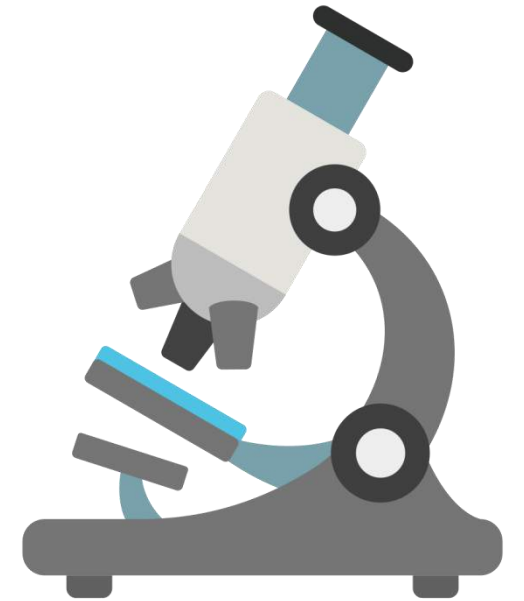


Introduction to North America



Data and concept provided courtesy of CDC Mycotic Diseases Branch

Identifying *C. auris*



Challenges with identification

- Identification varies by laboratory method.
- *C. auris* can be **misidentified** as:
 - *Candida haemulonii*
 - *Candida duobushaemulonii*
 - *Candida catenulate*
 - *Candida famata*
 - *Candida guilliermondii*
 - *Candida lusitanae*
 - *Candida parapsilosis*
 - *Candida sake*
 - *Rhodotorula glutinis*
 - *Candida* spp. after a validated method of *Candida* identification attempted

Misidentifications of *C. auris* (1)

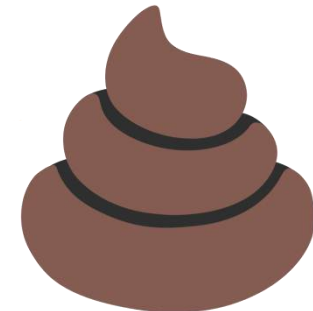
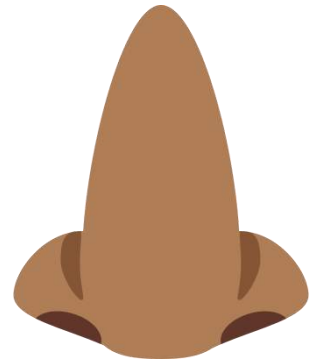
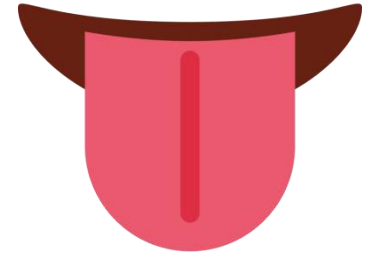
Identification Method	% NJ Labs	Organism <i>C. auris</i> can be misidentified as
Vitek 2 YST Proper ID possible with v.8.01	57%	<i>Candida haemulonii</i> <i>Candida duobushaemulonii</i>
API 20C	32%	<i>Rhodotorula glutinis</i> (characteristic red color not present) <i>Candida sake</i>
BD Phoenix yeast identification system	4%	<i>Candida haemulonii</i> <i>Candida catenulata</i>
Microscan	8%	<i>Candida famata</i> <i>Candida guilliermondii</i> (no hyphae/pseudohyphae present on cornmeal agar) <i>Candida lusitanae</i> (no hyphae/pseudohyphae present on cornmeal agar) <i>Candida parapsilosis</i> (no hyphae/pseudohyphae present on cornmeal agar)

Misidentifications of *C. auris* (2)

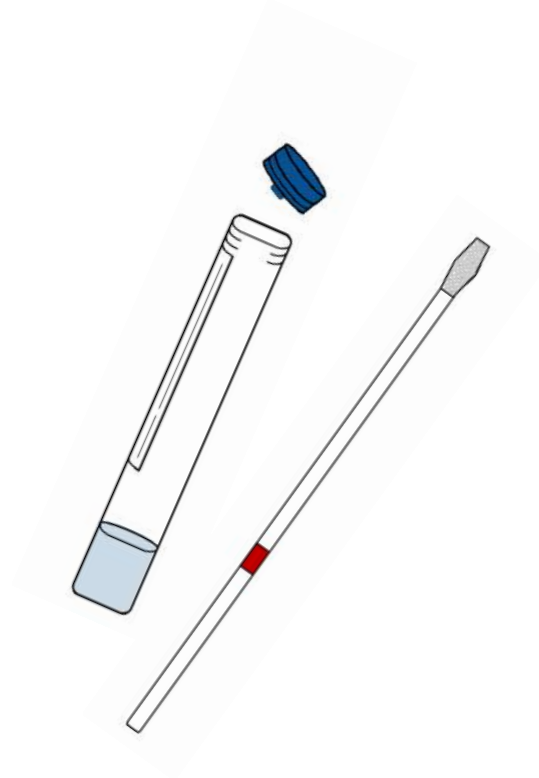
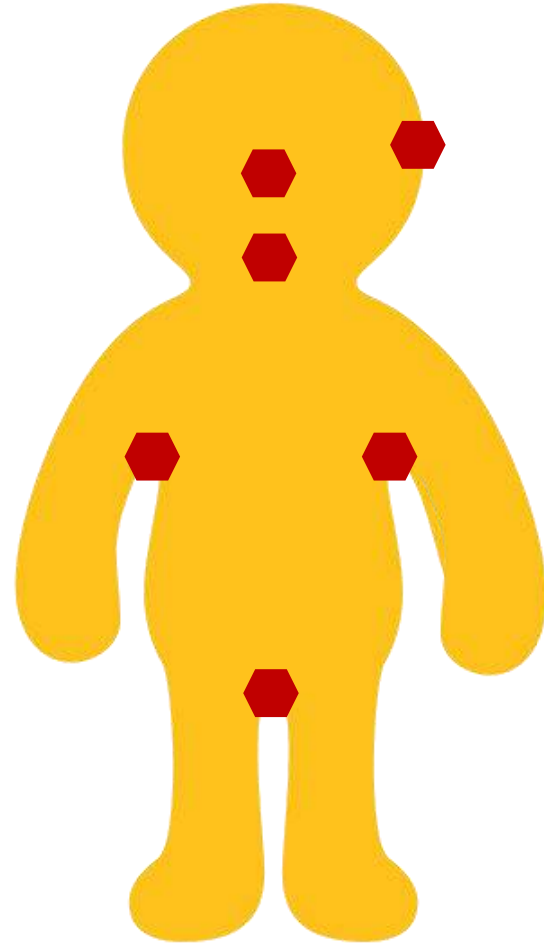
Identification Method	% NJ Labs	Databases needed to identify <i>C. auris</i>
MALDI-TOF	25%	
Bruker Biotyper	--	Research use only database
VITEK MS	--	Saramis Ver 4.14 database and Saccharomycetaceae update
Molecular methods	--	Sequencing the D1-D2 region of the 28s rDNA or the Internal Transcribed Region (ITS) of rDNA

Candida auris speciation

- *Candida auris* identification requires speciation of *Candida* isolates
- ~30% of clinical cases in the U.S. have been from non-bloodstream isolates (urine, bile, wounds, etc.)
 - Isolates from non-sterile sites may not be worked up to species level
- 68% of surveyed clinical labs in New Jersey speciated isolates onsite

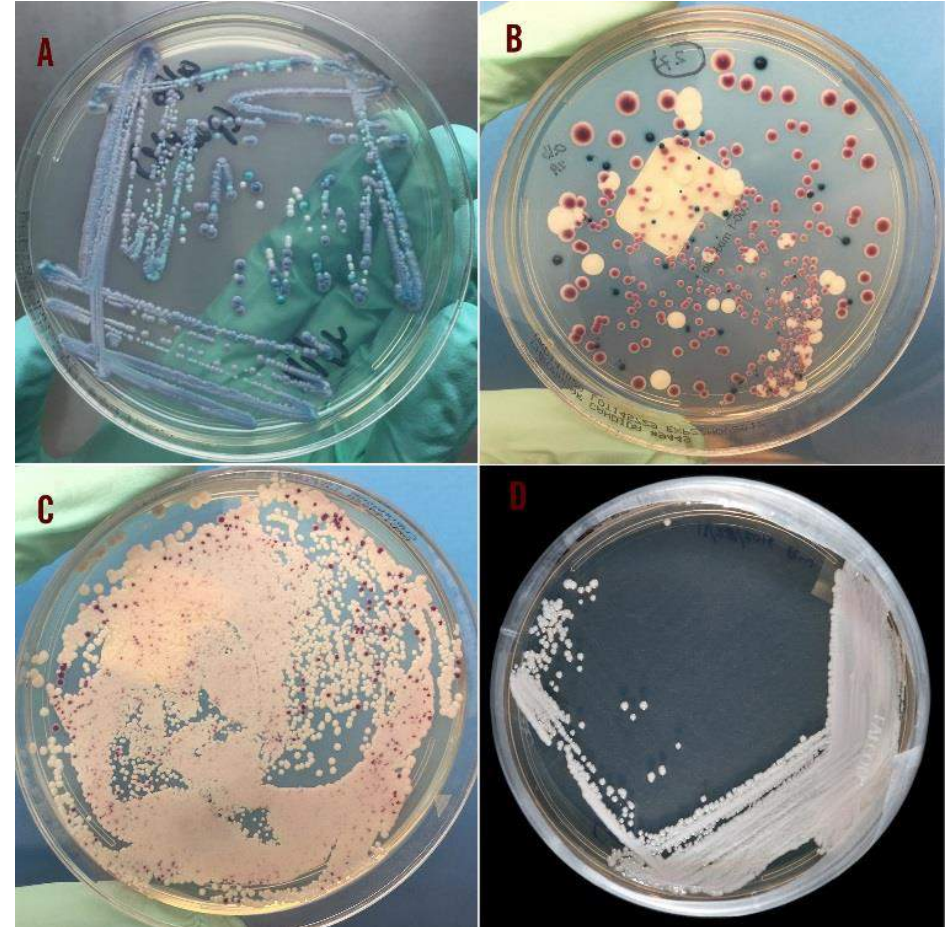


Challenges to detecting colonization

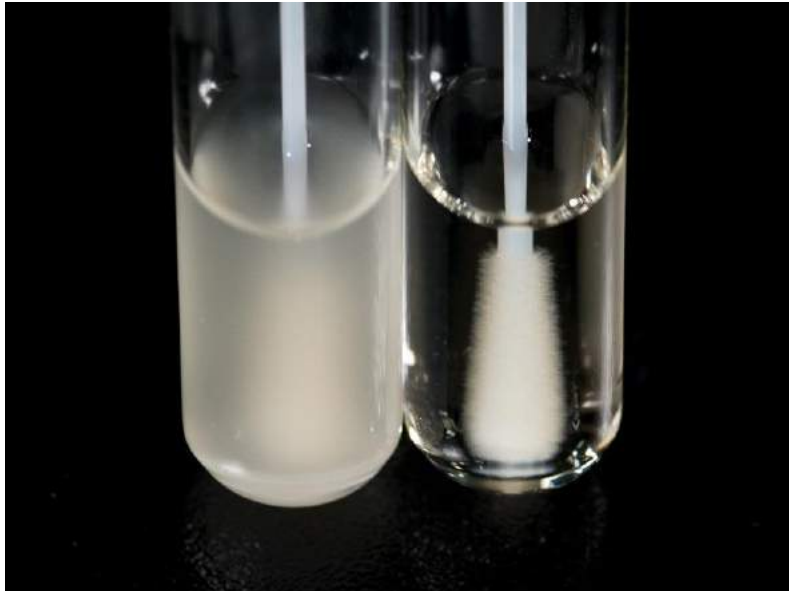


Establishing methods to culture and isolate *C. auris*

- Enrichment broth procedure
- Combination of high salt media (10% w/v) and high temperature (40°C) incubation
- Simple procedure readily adopted by advanced and resource limited laboratories



Enrichment broth



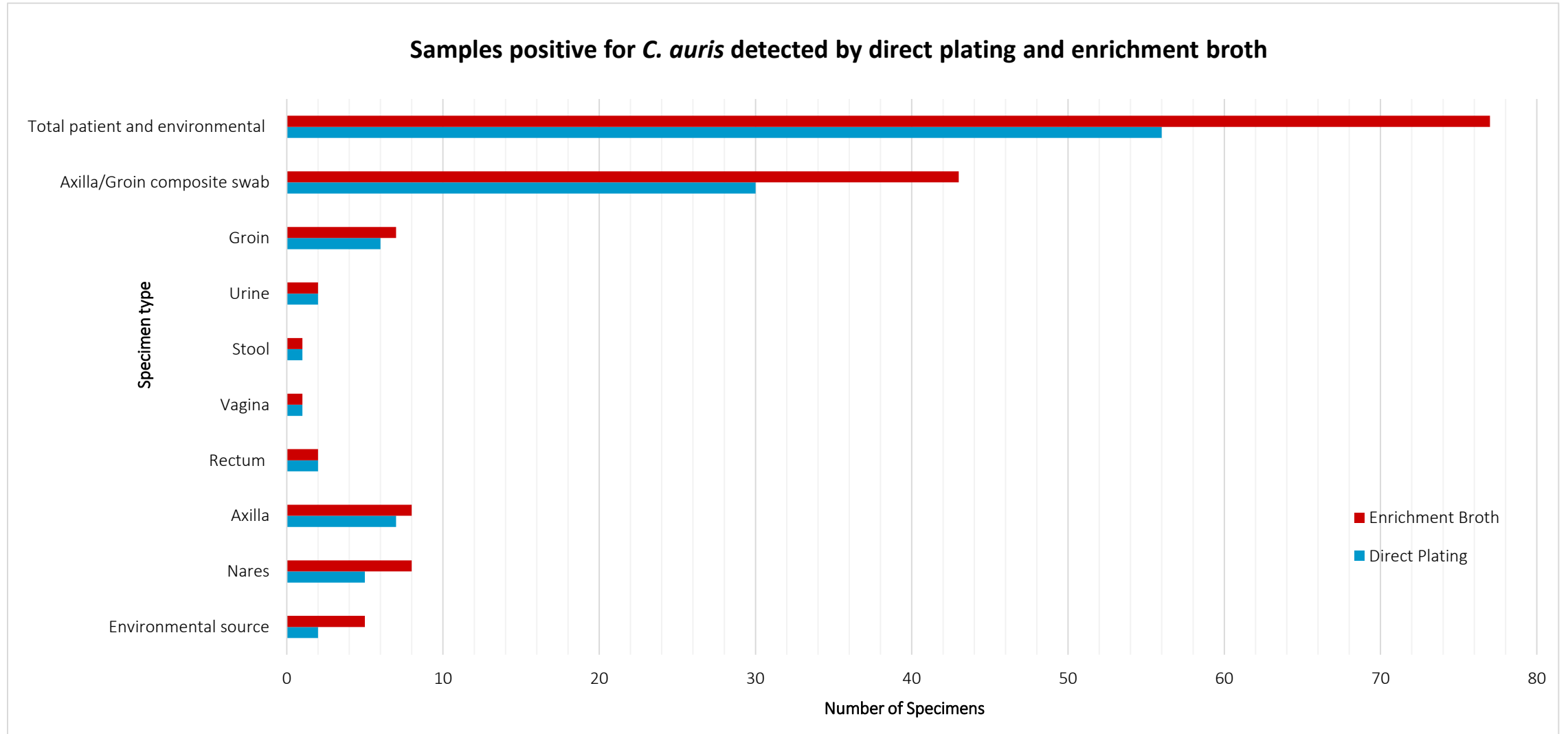
*Cloudy (left) =
positive*

CHROMagar



*Candida auris
appears pink*

Establishing methods to culture and isolate *C. auris*



Culture independent diagnostic

- Culture dependent diagnostics take ~14 days
- CDC assisting the development of rapid diagnostics
 - Cepheid
 - T2
- PCR developments underway:
 - Rutgers contract with CDC to develop a rapid PCR assay
 - NYSDOH Wadsworth Laboratories

Antifungal resistance of *C. auris*



Antifungal susceptibility testing

- Susceptibility breakpoints for *C. auris* have not been established, but CDC developed the following as a general guide:

Class/Drug	Tentative MIC Breakpoints (µg/mL)
Fluconazole	≥32
Amphotericin B	≥2
Anidulafungin	≥ 4

Class/Drug	Tentative MIC Breakpoints (µg/mL)
Caspofungin	≥ 2
Micafungin	≥ 4

*Reference updated CDC guidance for more information and comments on interpretation.

Drug resistance of *C. auris*

Polyenes



35% resistant to amphotericin B

Azoles



93% resistant to fluconazole
54% resistant to voriconazole

Echinocandins



7% resistant to echinocandins

41% multi-drug resistant
4% resistant to all three major antifungal classes

Drug resistance of *C. glabrata*

Polyenes



<1% resistant to amphotericin B

Azoles



11% resistant to fluconazole

Echinocandins



Up to 12% resistant to echinocandins

Resistance mechanisms

- A significant portion of the *C. auris* genome encodes
 - ATP-binding cassette (ABC)
 - Major facilitator superfamily (MFS) transporter families
 - Drug transporters
- ABC-type efflux activity by Rhodamine 6G transport was significantly greater among *C. auris* than *C. glabrata* isolates
- ERG-11 hotspot mutations
 - Different mutations in different clades

Transmission of *C. auris*

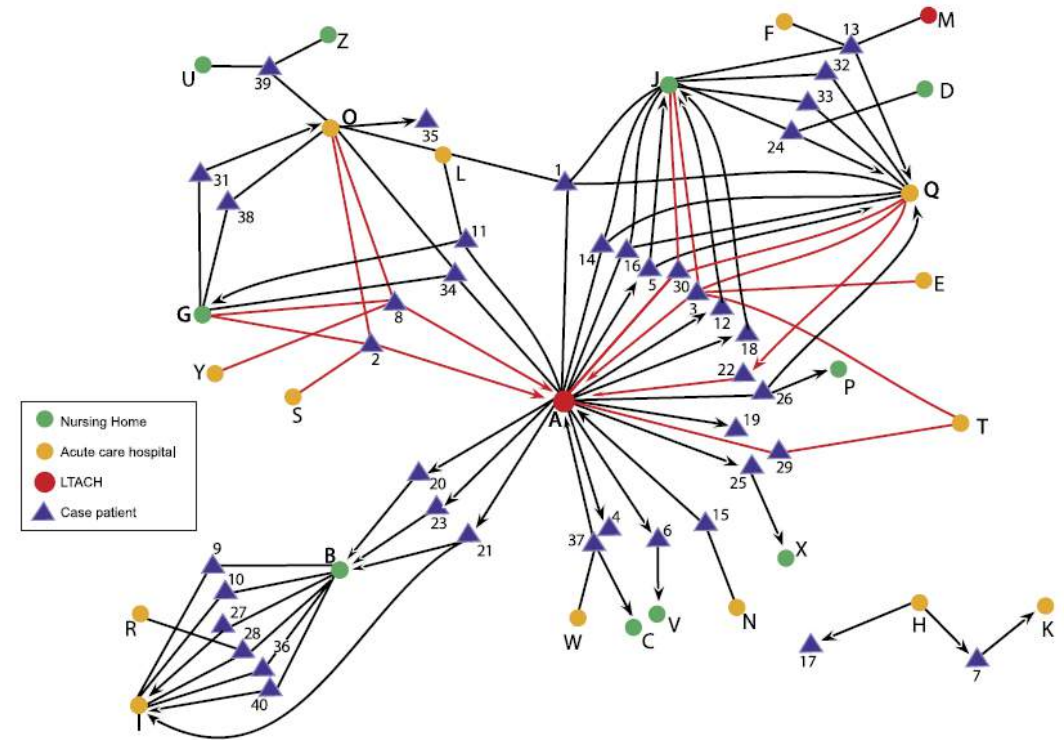


C. auris transmission: what we know

- Environmental surfaces, equipment
 - Piedrahita et al. (2017), *Infection Control & Hospital Epidemiology*
 - New York State and CDC investigation
- Patients and healthcare workers
 - Selenchez et al. (2016), *Antimicrobial Resistance and Infection Control*
- Donor-derived
 - Azar et al. (2017), *Clinical Infectious Diseases*

C. auris transmission

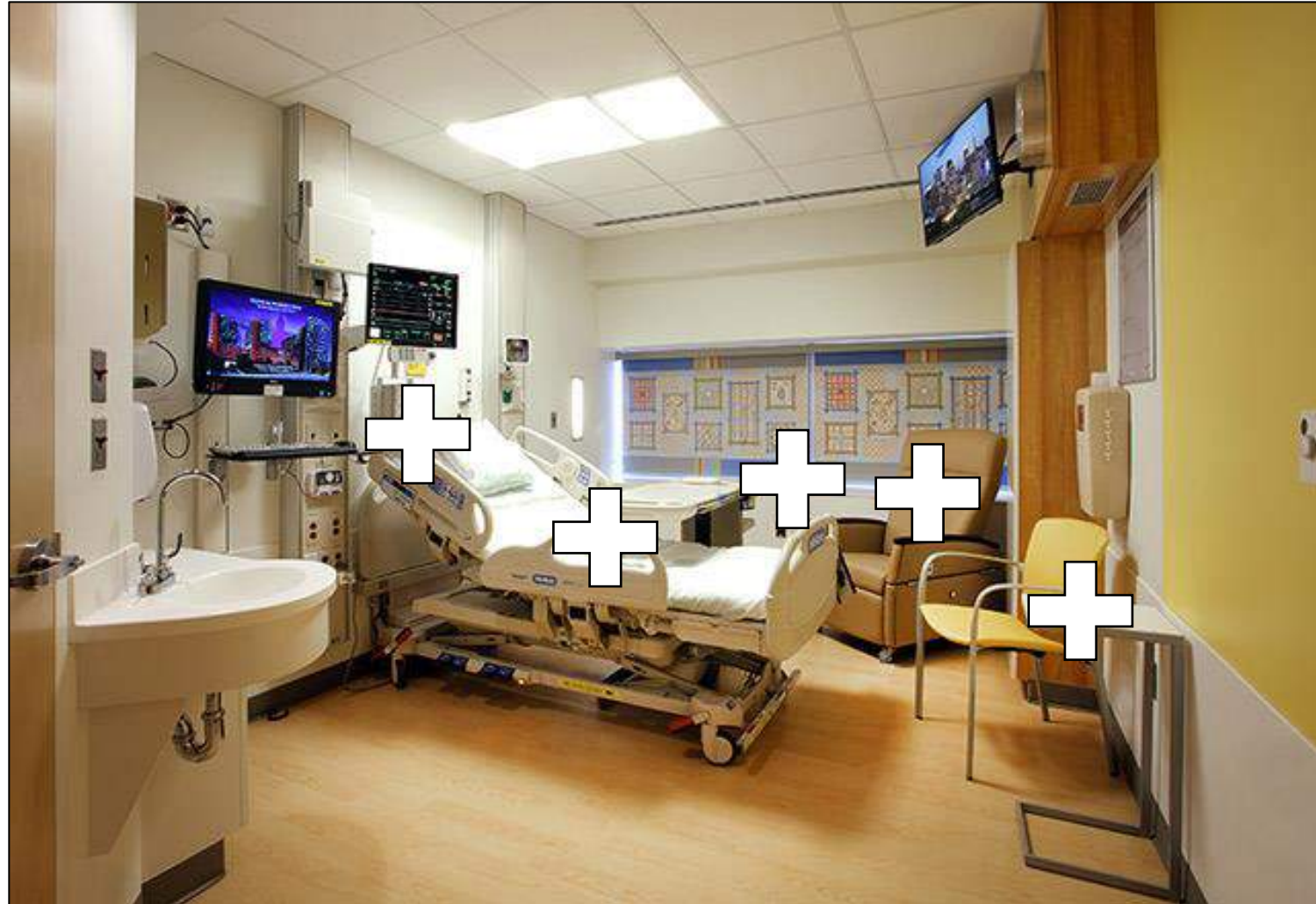
- More research is needed to better understand *C. auris* transmission
- Currently, the majority of public health response and recommendations assume transmission is similar to CRE
- Various studies are ongoing



C. auris in the environment

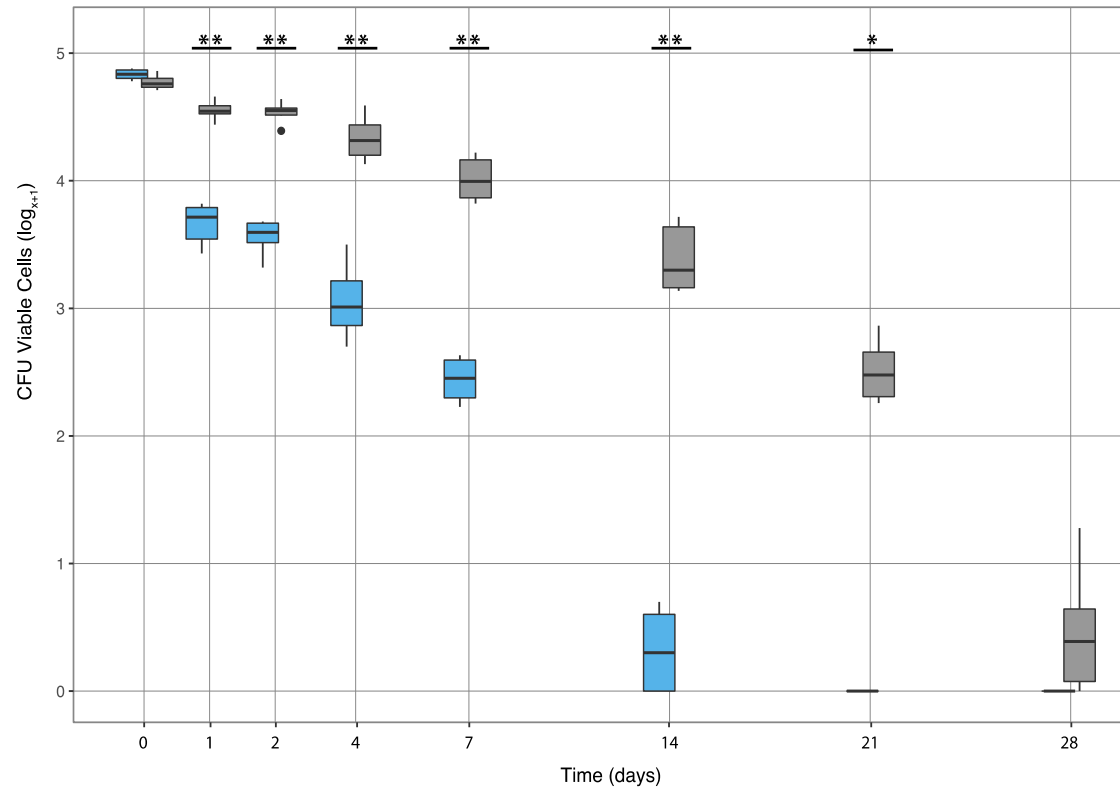


Environmental contamination

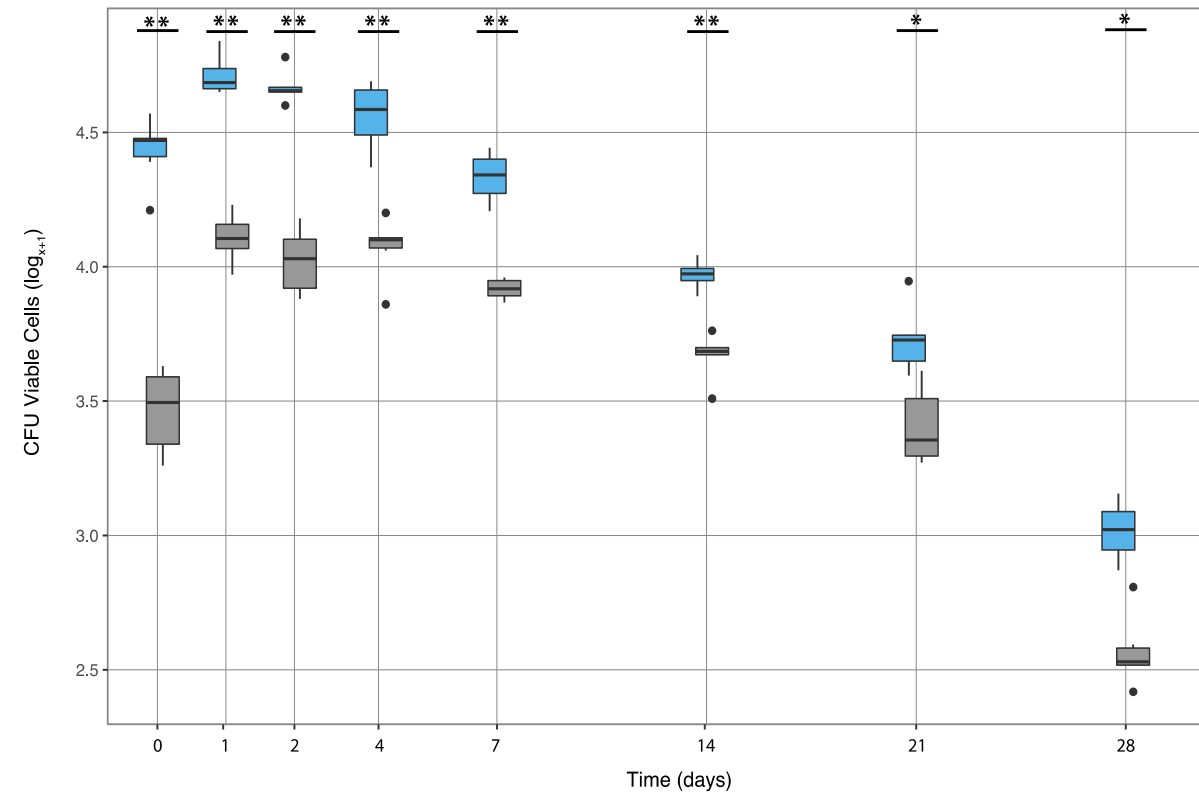


Survival and persistence

Remains viable by culture for at least **two weeks**

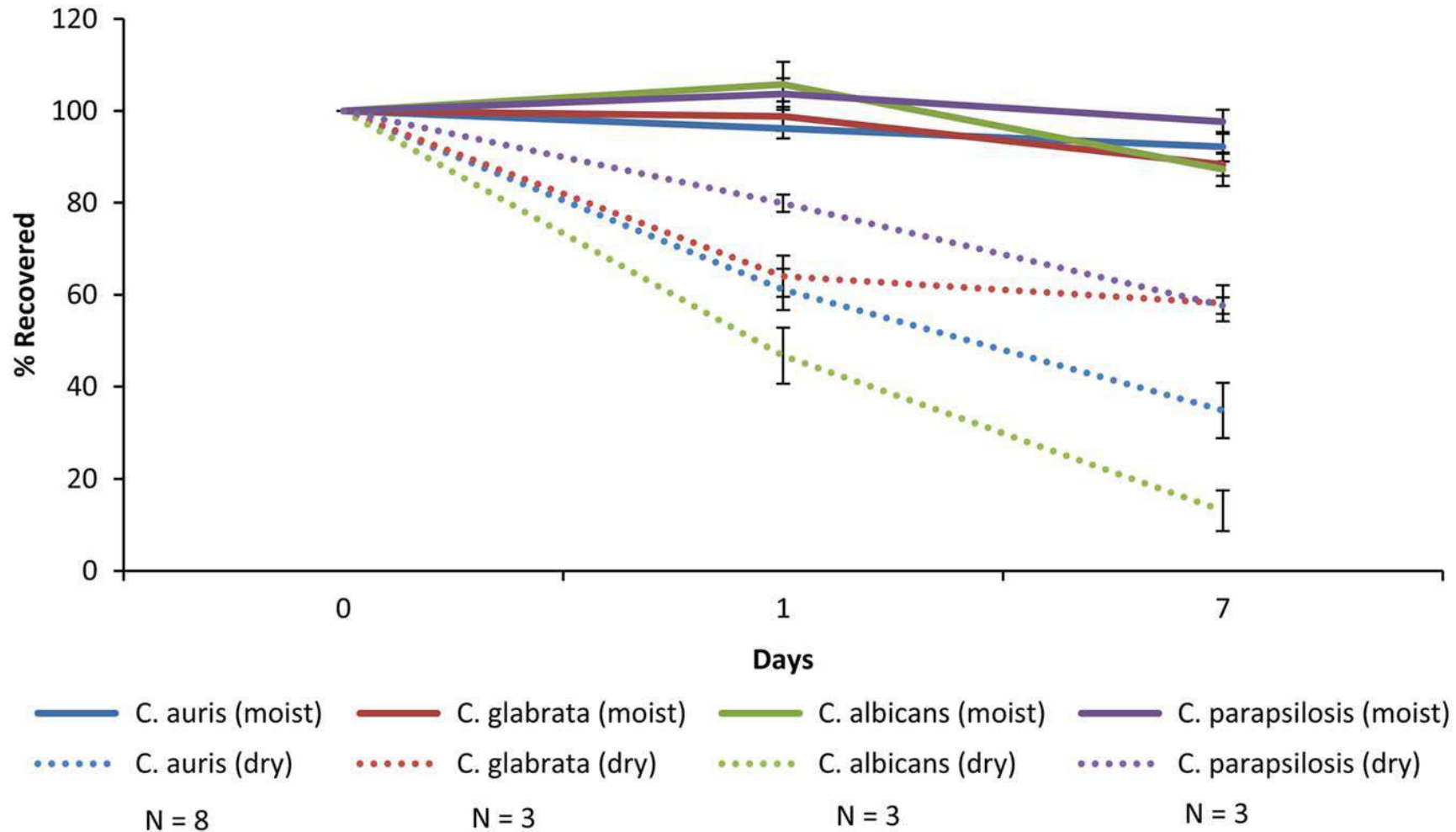


Remains viable by esterase activity for at least **four weeks**

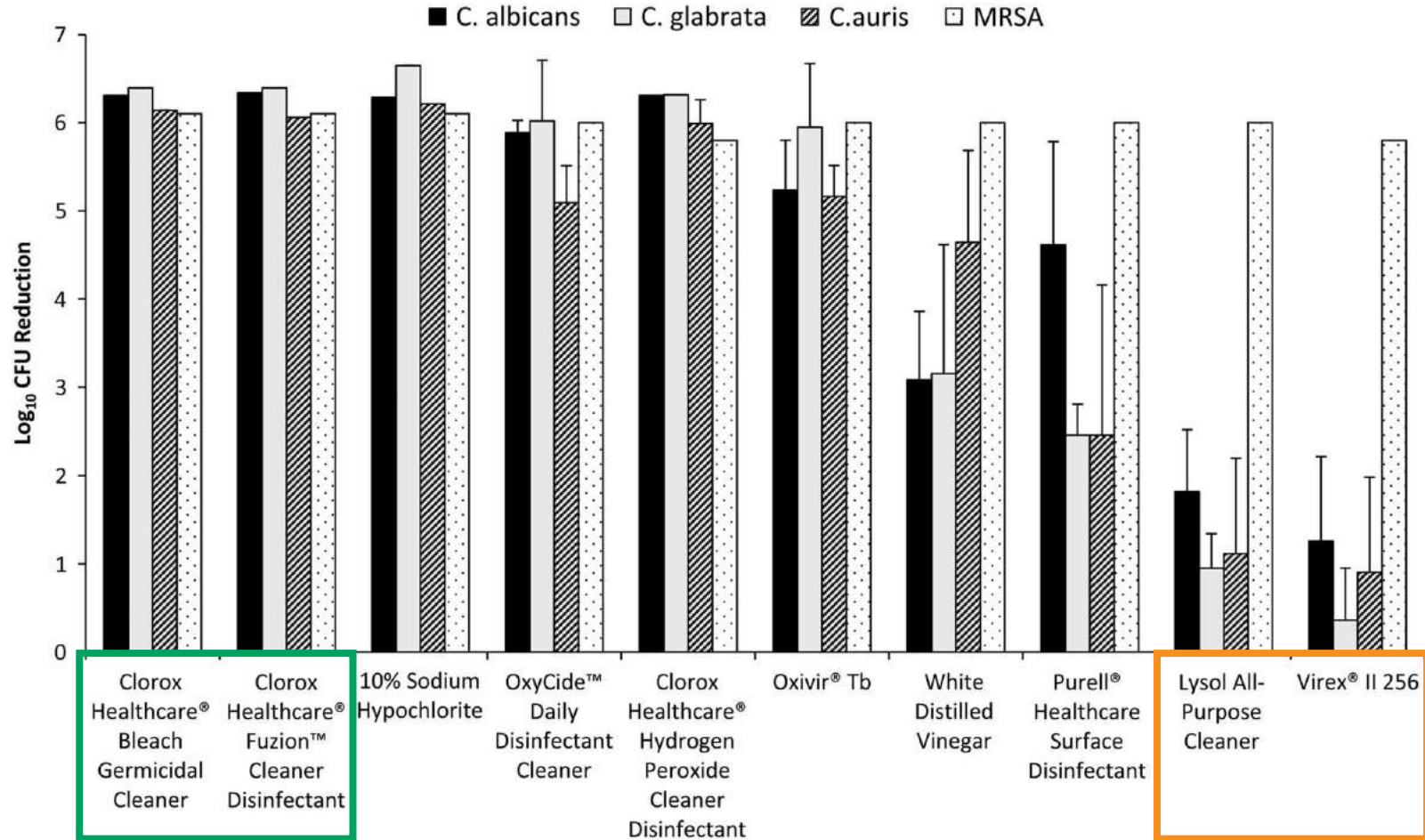


 *C. auris*  *C. parapsilosis*

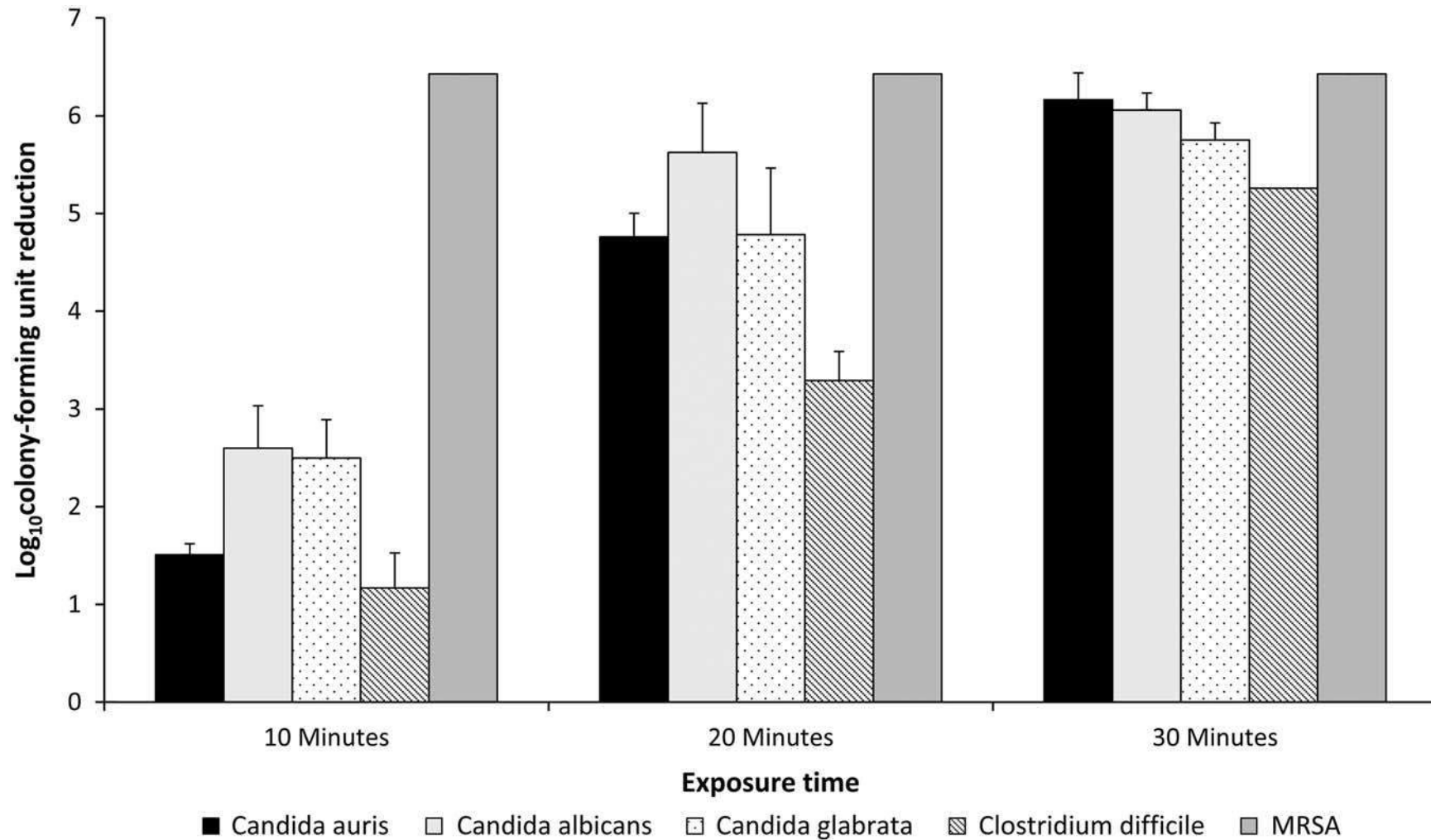
Survival and persistence



Cleaning and disinfection



Ultraviolet light



Patient + healthcare worker transmission



Findings from a European hospital

- Minimal contact with a case is needed for *C. auris* acquisition
 - Root cause analysis found acquisition required ≥ 4 hour contact period with a known case or contaminated environment
- Transient carriage of *C. auris* by a healthcare worker
 - 1 of 285 HCWs had a positive nares swab
 - The positive staff had extensive care with a colonized patient

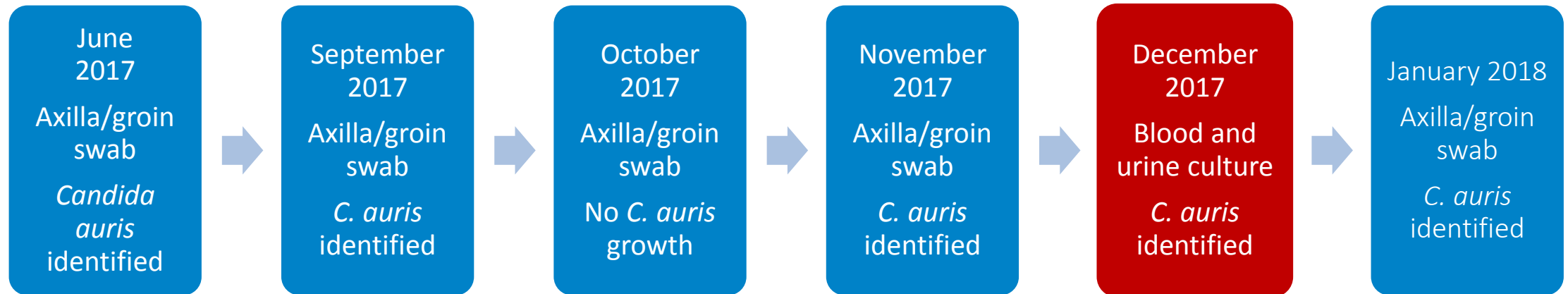
C. auris colonization

- Little is known about *C. auris* colonization.
- Axilla and groin appear to be the highest-yield sites to identify *C. auris* colonization, per CDC
- CDC continues to offer re-screening of *C. auris* colonization, however few patients have met basic requirements to be considered 'decolonized'

C. auris colonization example

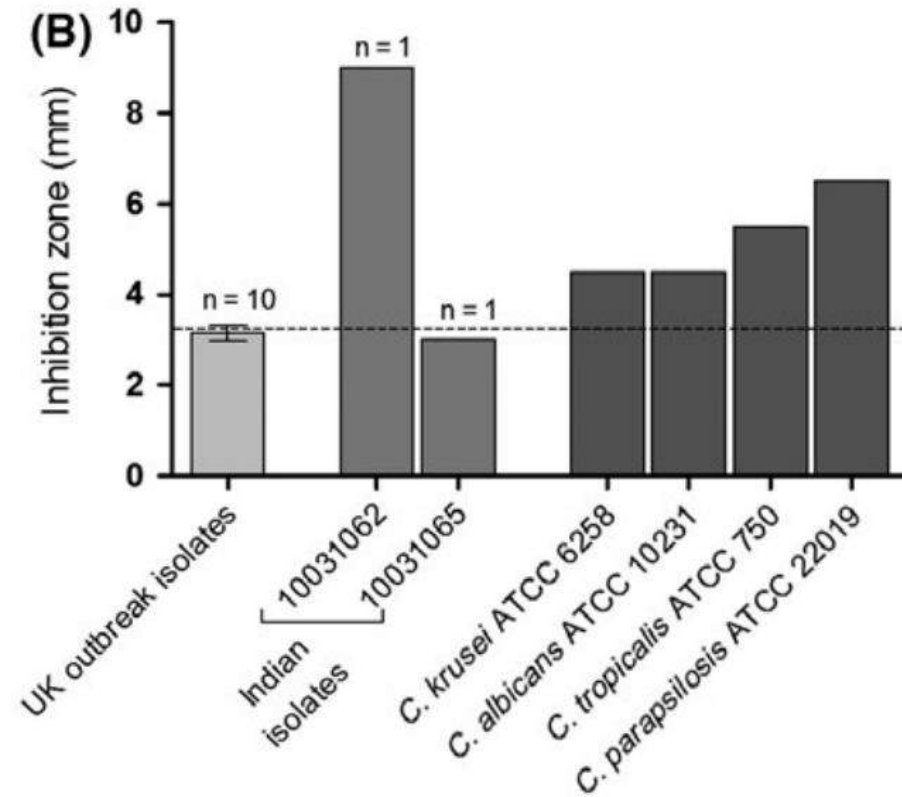
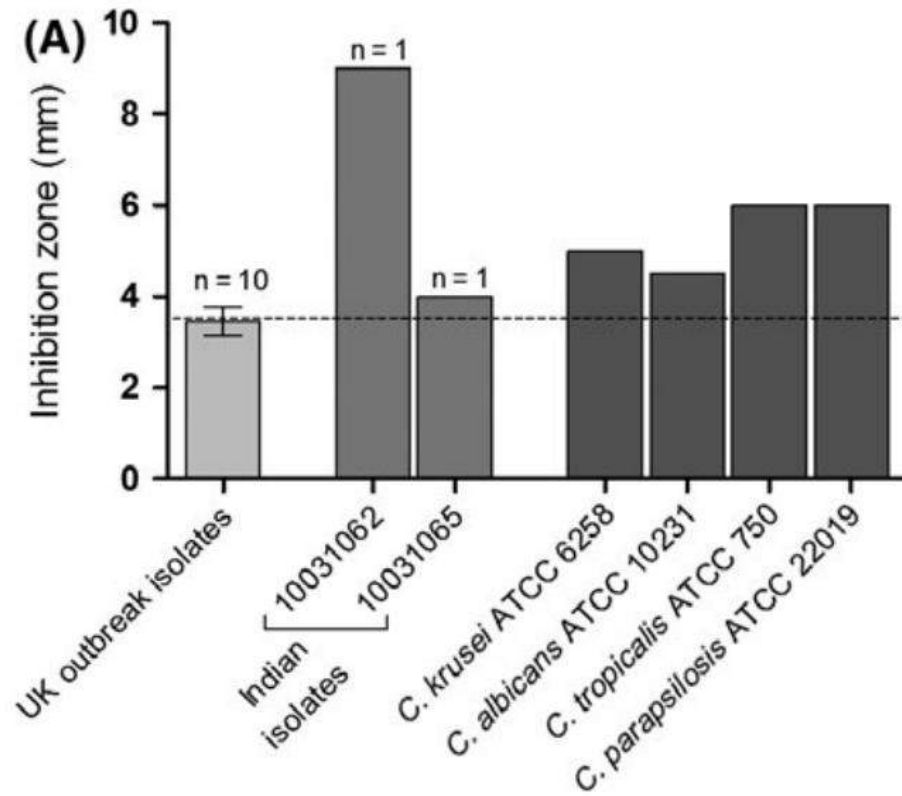
***Candida auris* colonization**

Infection



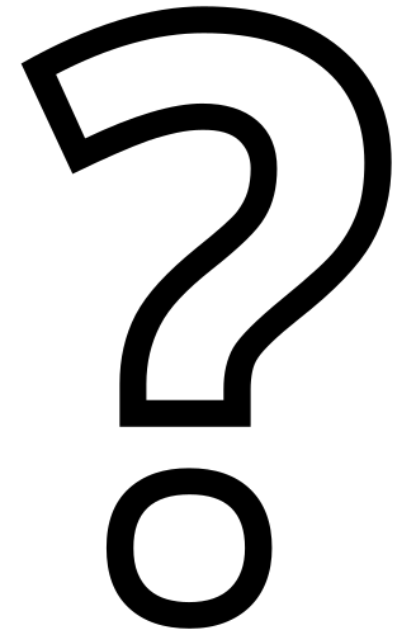
***Candida auris* shed into environment**

Decolonization regimens?



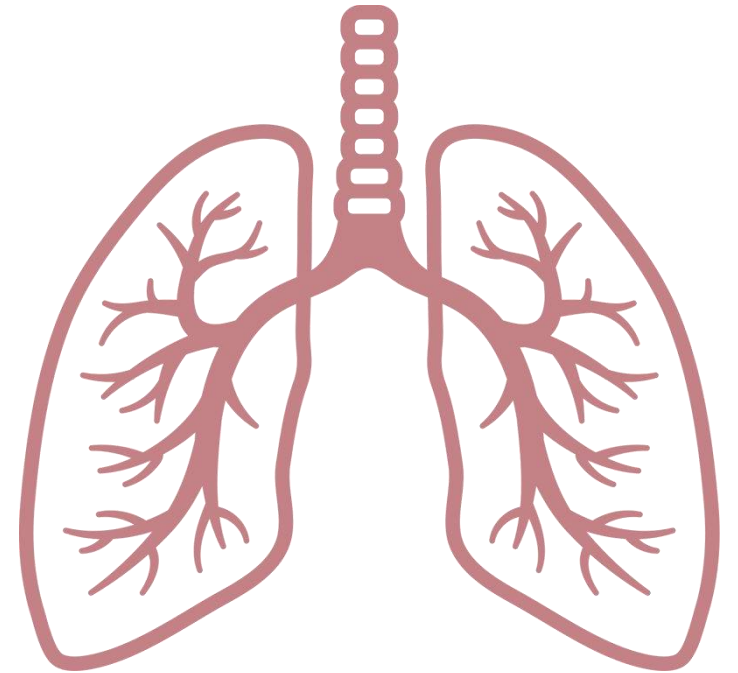
Unknowns of *C. auris* colonization

- Length of colonization
 - Possibly indefinite
- Colonization dynamics
 - Skin recolonization from gut or oral cavity?
- True risk of *C. auris* infection after colonization
- No public health recommendations for *C. auris* decolonization



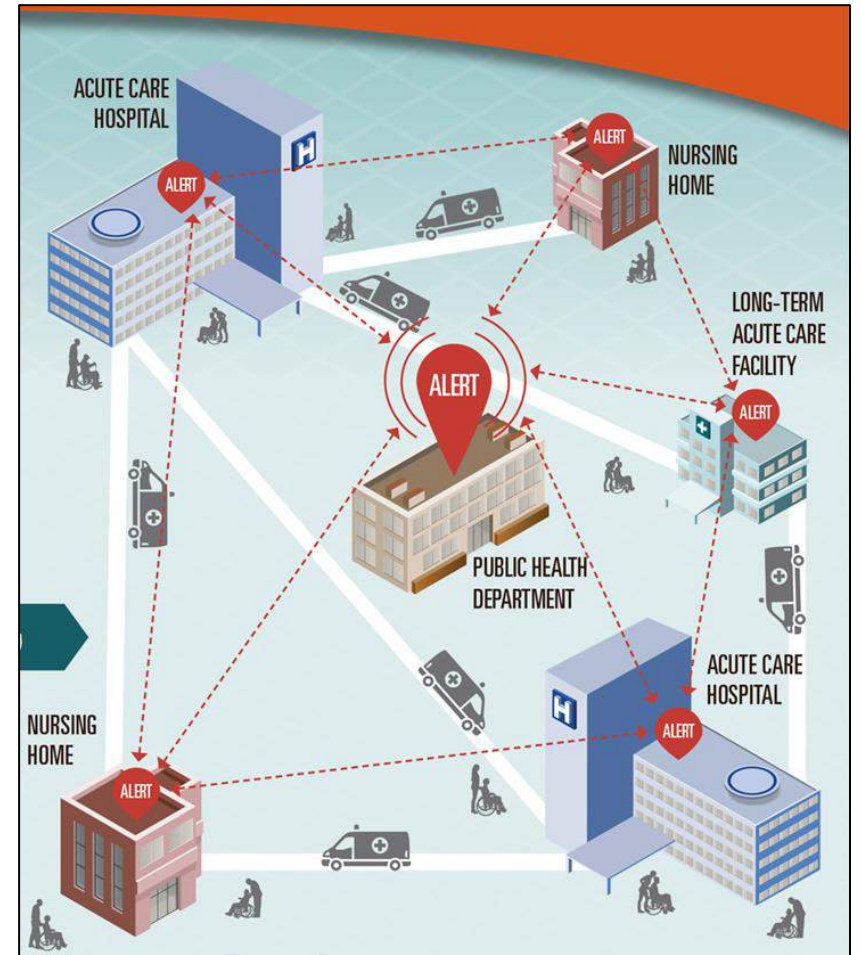
Donor-derived transmission

- Illinois organ donor had premortem respiratory culture that grew *C. haemulonii* (misidentification)
- Lung from this donor went to a Massachusetts patient
 - Pre and post-transplant cultures grew *C. auris*
- These isolates were closely related to IL isolates by whole genome sequencing (WGS)



Transmission in New Jersey

- No 'smoking gun'
 - Multiple overlaps in units, staff, equipment, specialty care, etc.
- Patient movement within a healthcare transfer network
 - High-acuity units, facilities
- Little information derived from WGS
 - Per CDC, NJ isolates are ~99.9% related



Preventing *C. auris*



Antimicrobial stewardship

- Many *C. auris* patients received broad-spectrum antimicrobials in the weeks before first culture yielding *C. auris*.
- >50% of patients in a NJ long-term acute care hospital (LTACH) with an ongoing *C. auris* outbreak received antifungals
- Antimicrobial therapies may *create* an opportunity for *C. auris* acquisition or infection

Who receives antifungals?

- Sickest of patients tend to receive antifungals
 - Immunocompromised
 - Indwelling devices
 - ICU patients receive more antifungals than general inpatient
- At-risk population is growing
 - Increasing number of transplants and immune-modulating therapies
 - More post-acute care facilities with ICU-like units (LTACHs, vSNF, etc.)

Challenges with fungal infections

- No single syndrome for fungal infections
- Delayed treatment may lead to increased mortality
 - Empiric treatment for invasive infections
- *Candida* colonization vs. infection
 - Is treatment needed from identification in non-sterile specimens?
- Infectious Disease consultation often needed

Challenges in antifungal stewardship

- Fungal ID by culture may be limited
 - Longer turnaround time for certain tests
 - Ancillary diagnostics do not allow for resistance testing
- Clinical data may be limited or unclear
- Staff are less familiar with concepts, compared to antibiotic stewardship

Existing guidelines

Clinical Infectious Diseases

IDSA GUIDELINE



Clinical Practice Guideline for the Management of
Candidiasis: 2016 Update by the Infectious Diseases
Society of America

Bedside
intervention

Implementation
of rapid serological
and molecular
diagnostic tests*

Activities do not significantly differ from antibiotic stewardship.

Think *antimicrobial* stewardship program!

Pre AF Stewardship audit and identification of main AF
prescribers

Creation of a Collaborative Group on Mycosis and Antifungal
treatment

Care of medical devices

- A majority of patients with *C. auris* infection or colonization have various types of invasive lines and tubes.
 - E.g., central venous catheters, urinary catheters and tracheostomy tubes.
- Strict adherence to insertion and maintenance practices of patient devices
- Ensure continued assessment of need for devices and prompt removal when no longer needed
- When *C. auris* patients are identified, review and assess these practices

Surgical procedures

- For patients with *C. auris*, skin preparation should include alcohol-based agent unless contraindicated
- Schedule procedures for *C. auris* patients for the end of the day.

Responding to *C. auris*

“We have a patient with *Candida haemulonii*..... Now what?”



Ideal *C. auris* response

- Suspect and identify early
- Isolate quickly
- Report results
- Remove from the environment
- Communicate moving forward



Identify *C. auris* early

- Speciate all *Candida* isolates from normally sterile sites
- Suspect *C. auris* when there is an increase in infections of unidentified *Candida* spp. in a patient care unit

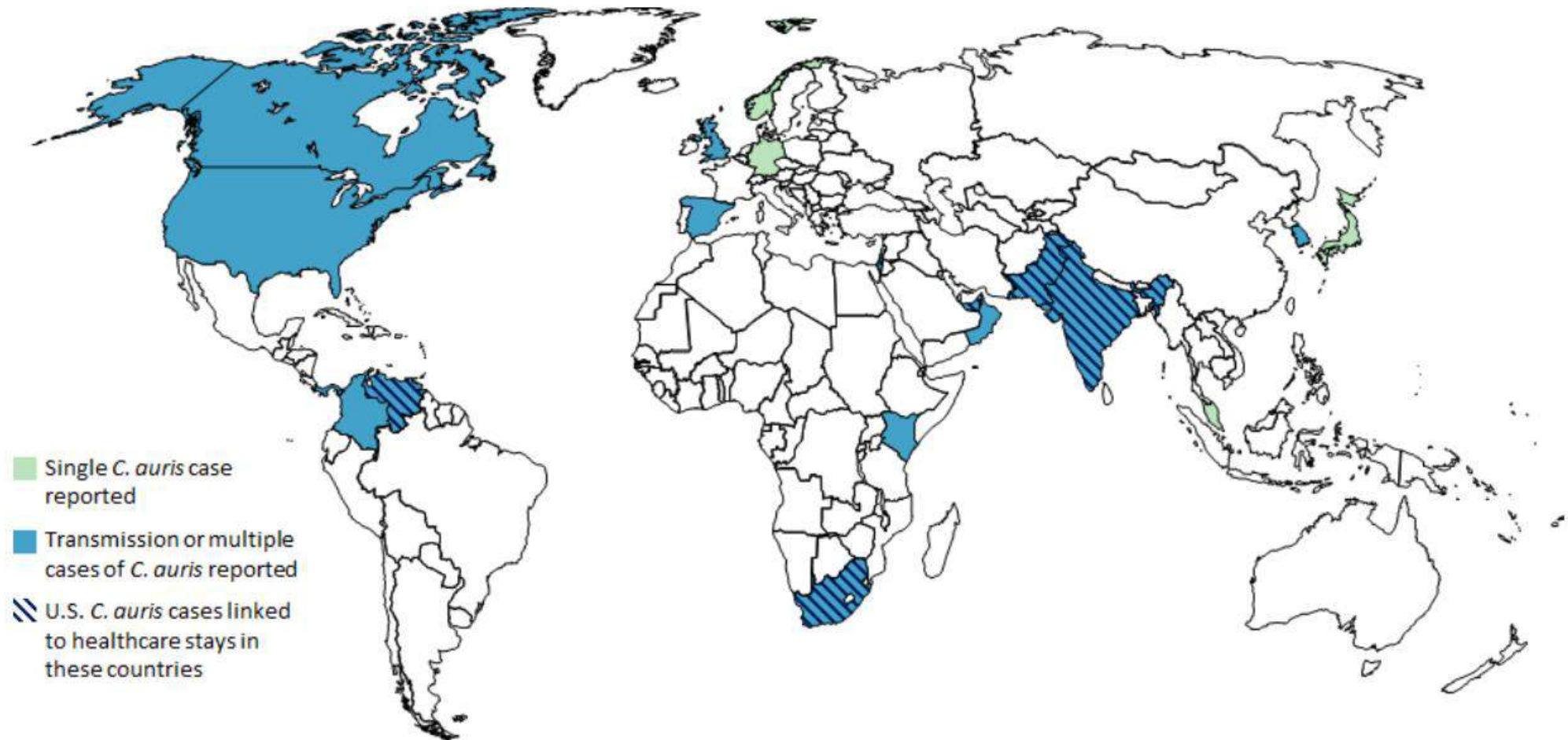


Identify *C. auris* early

- Speciate *Candida* isolates from non-sterile sites when:
 - Clinically indicated (e.g., patient is not responding to therapy)
 - When *C. auris* patients have been identified in the facility or unit
 - During outbreaks
 - When patient had overnight stay at healthcare facility in a country with *C. auris* transmission within 1 year



Countries with *C. auris* transmission



Isolate quickly

- Whenever *C. auris* is suspected, consider preemptive control measures until laboratory confirmation
- Standard and Contact Precautions
- Cohort *C. auris* patients to one area in a facility or unit
 - Minimize number of staff members caring for *C. auris* patients
- Placement in single rooms
 - *C. auris* patients can share rooms
 - If limited rooms, prioritize patients with highest level of care

PDPH *C. auris* isolation requirements

- Hospitals:
 - Contact precautions
 - Private room
- Long-term care:
 - Contact precautions or enhanced standard precautions
 - Private room if available
- Applies to current and future stays
- Dedicate reusable equipment to the patient, when possible



Reporting *C. auris* to PDPH

- *Candida auris* and *Candida haemulonii* from any body site is reportable to PDPH upon receipt of results
 - Applies to both providers and laboratorians
- See the Board of Health regulations: *'Regulations Governing the Control of Communicable and Non-communicable Diseases and Conditions'*



Environmental cleaning and disinfection

- Use Environmental Protection Agency (EPA)-registered hospital-grade disinfectant effective against *Clostridium difficile* spores
 - Ensure contact time, dilution, etc.
- Daily and terminal cleaning of:
 - *C. auris* patient room and any care areas (radiology, physical therapy, etc.)
 - Shared equipment of the unit
 - Common areas (handrails, nurse's stations, etc.)
- Also required by PDPH



Communicate *C. auris* transfer

- Prior to transfer, sending facility should notify the receiving facility of *C. auris* infection or colonization
 - Required by PDPH
- Call ahead to receiving facility whenever possible
- Include *C. auris* in intake or discharge documents
- NJ uses a *C. auris* coversheet and UT form

The New Jersey Department of Health and the Centers for Disease Control and Prevention (CDC) recommend that:

This patient should immediately be placed on **contact precautions.**

This patient has been identified to be colonized or infected with *Candida auris*, an emerging drug-resistant yeast. *Candida auris* has caused long-lasting outbreaks in healthcare facilities and is difficult to remove in the environment. Containment is necessary to prevent an outbreak.

Additional recommendations include:

- This patient should be placed in a private room, if possible*
- Healthcare personnel interacting with this patient or the patient's environment should wear gowns and gloves (PPE)
- Healthcare personnel should conduct diligent hand hygiene during and after contact with this patient.
- All cleaning should be completed with an Environmental Protection Agency (EPA) registered disinfectant effective against *Clostridium difficile*
 - All equipment should be cleaned after contact with this patient (e.g. stethoscopes, X-ray machines, respiratory therapy machines)
 - This patient's room should be cleaned daily and terminally upon discharge
 - Transport vehicles should be terminally cleaned after transfer of this patient using an EPA registered disinfectant effective against *Clostridium difficile*
- Notification of these recommendations to receiving units or healthcare facilities prior to patient transfer or discharge with a phone call

*If a patient cannot be placed in a private room, please ensure their roommates or neighbors are at low risk of developing *Candida* infections. (e.g. are not on antifungal therapies, have no or few indwelling devices)

Note: Patients may be removed from contact precautions following a series of negative surveillance cultures, as recommended by the CDC.

Please call the New Jersey Department of Health at 609-826-5964 to report the patient's admission to your facility and speak with a subject matter expert.

To read the current recommendations for *Candida auris*, visit the CDC website at: <https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html>.

April 10, 2017

New Jersey Department of Health
Communicable Disease Service

Additional recommendations

- Hemodialysis and infusion clinics
- Outpatient settings (physician offices, wound clinic, etc.)
- Home healthcare
- Home and family members
- <https://www.cdc.gov/fungal/diseases/candidiasis/c-auris-infection-control.html>

Summary

- *C. auris*...
 - Is challenging to identify
 - Is multidrug resistant
 - Can be transmitted in healthcare settings
 - Difficult to contain
- Early identification and meticulous infection control is needed to control its spread.
- Philadelphia facilities and providers need to be alert and informed in order to identify and prevent *C. auris* transmission.

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Questions?



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Communicable Disease Service
New Jersey Department of Health

References

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