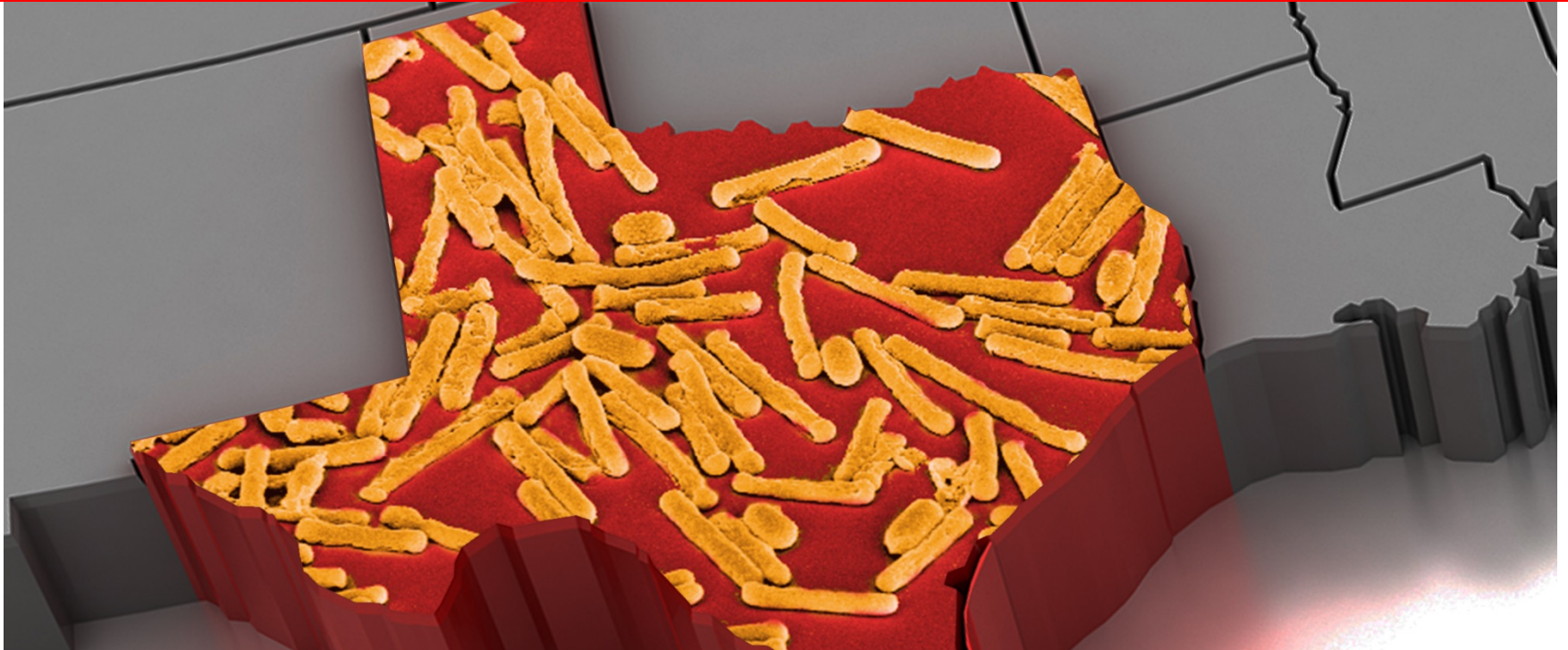


Active surveillance for C. diff and Candida auris in Texas

If your name starts with a “C”, we are looking for you!!



Kevin W. Garey, PharmD, MS, FASHP
Professor and Chair

Dept of Pharmacy Practice and Translational Research

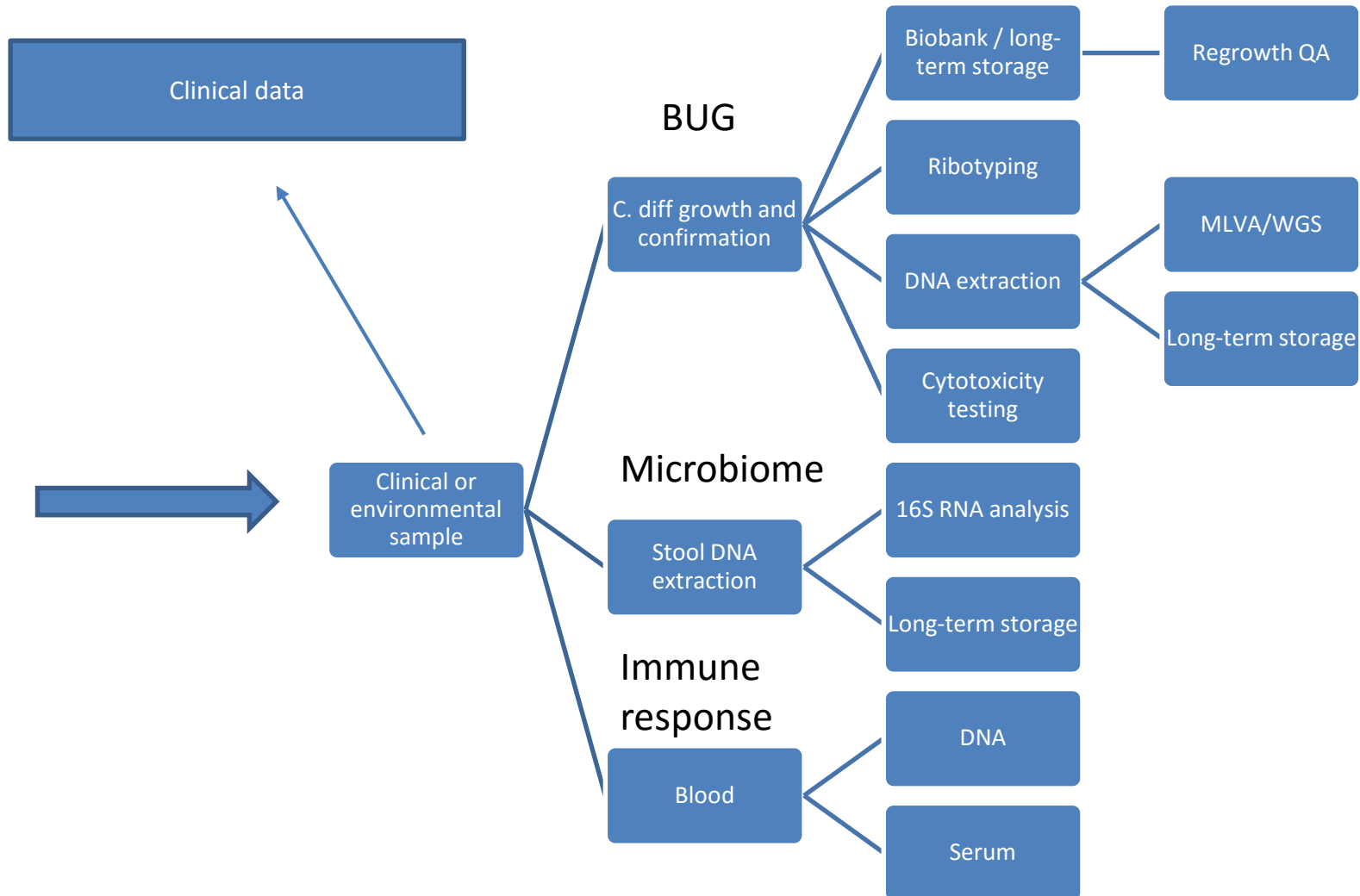
UNIVERSITY of **HOUSTON** | COLLEGE OF PHARMACY

Objectives

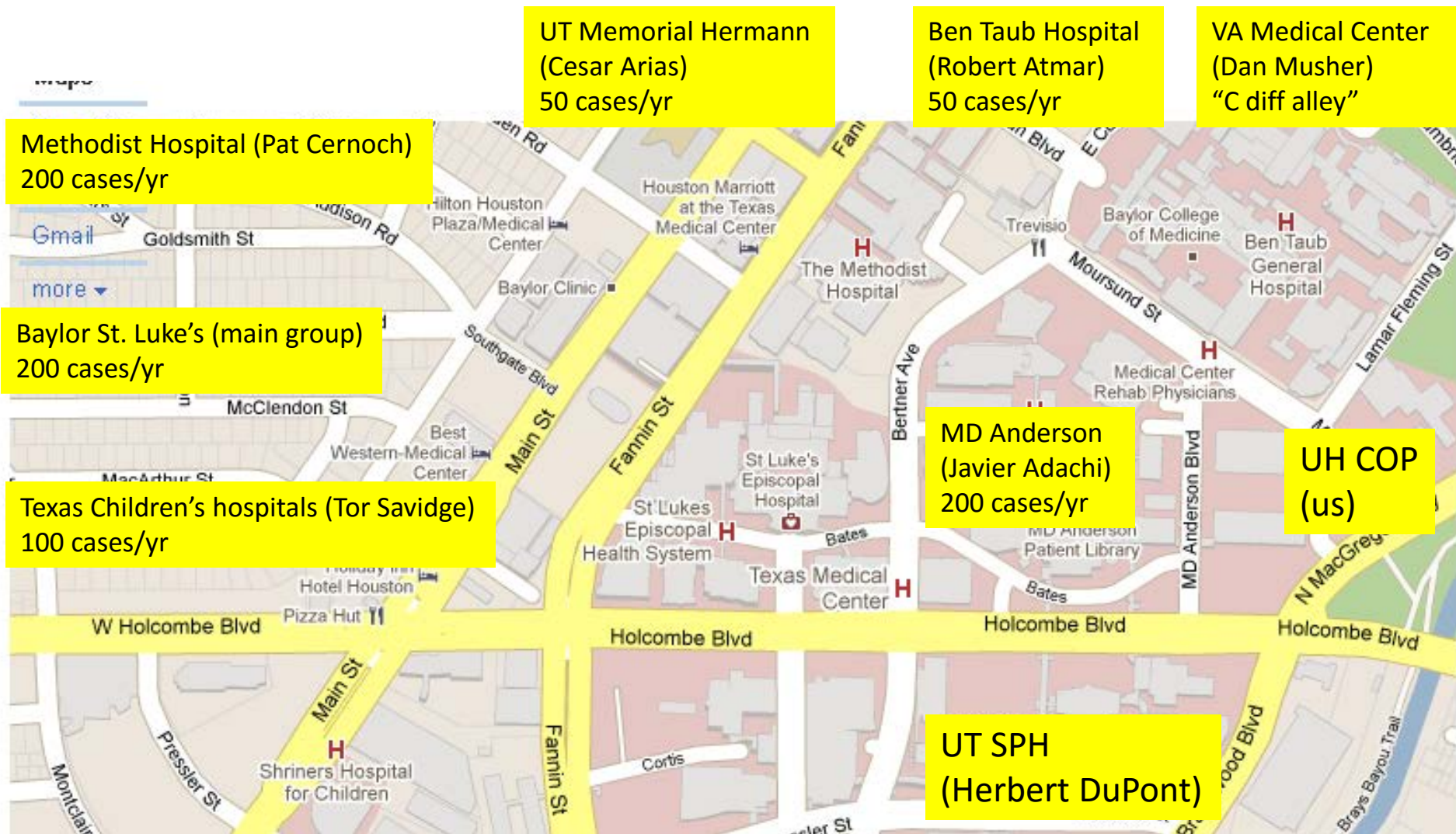
- Defend the need for increased surveillance of MDRO organisms.
- Explain the importance of the emergence and antifungal resistance in *Candida auris*
- Create the shell of a registry to identify MDRO organisms

Components of an active surveillance system:

C difficile

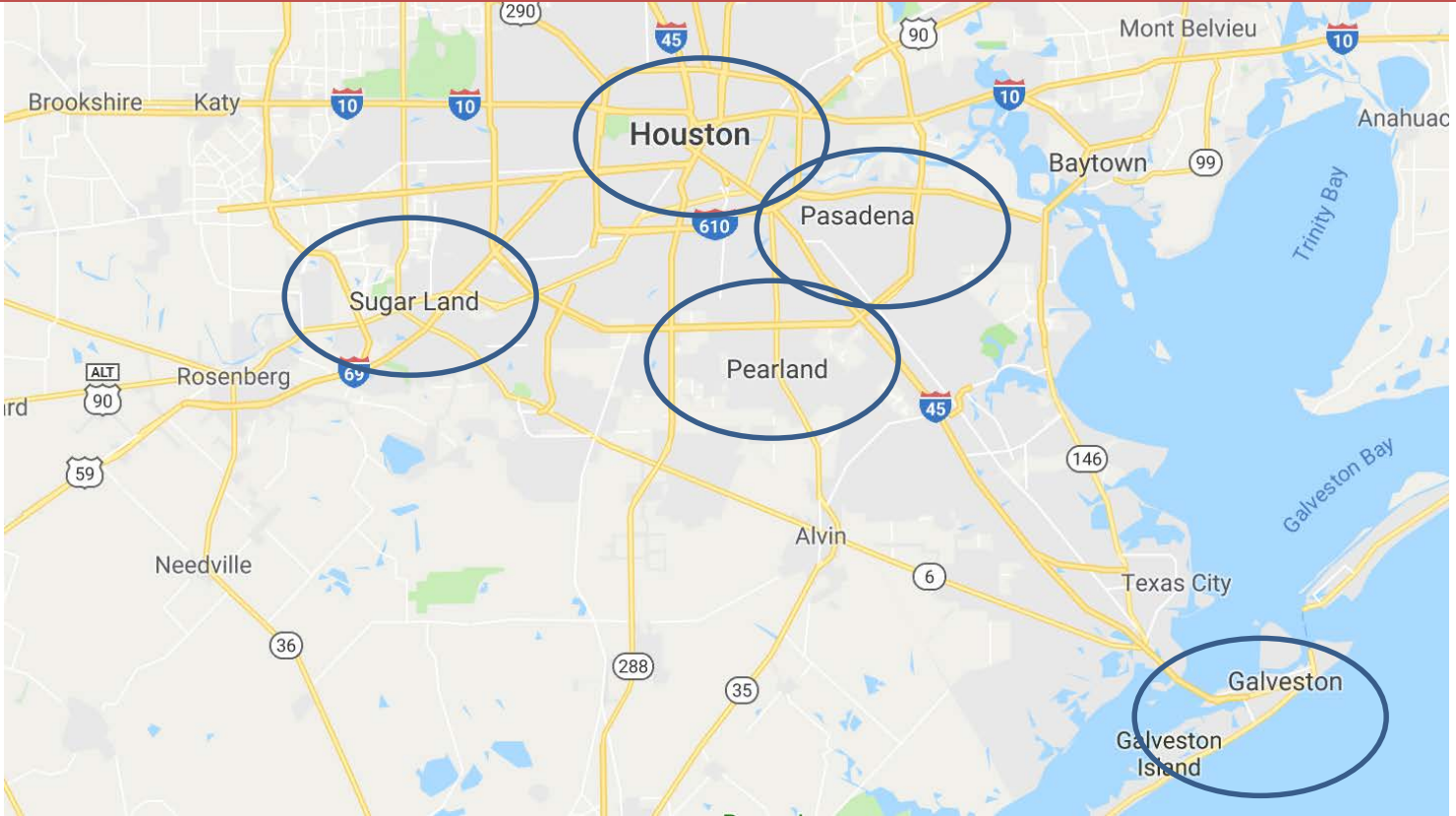


TMC C. diff surveillance network

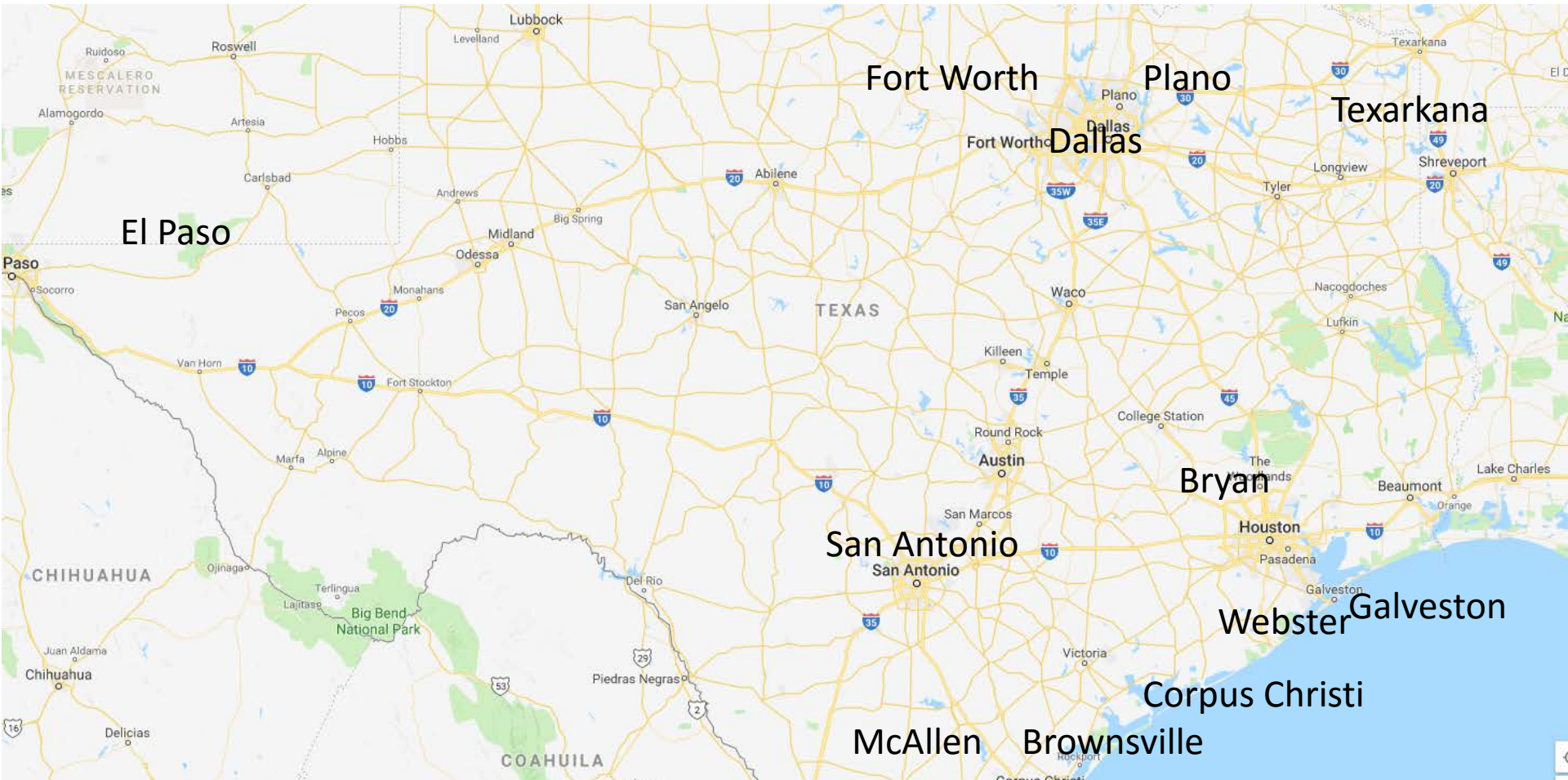




Thanks to the systemization of health-systems, HCA, and some buddies, we have an active surveillance system that covers Houston



...and thanks from funding from the TX Dept of State Health Services we have a network of hospitals all over TX sending us samples

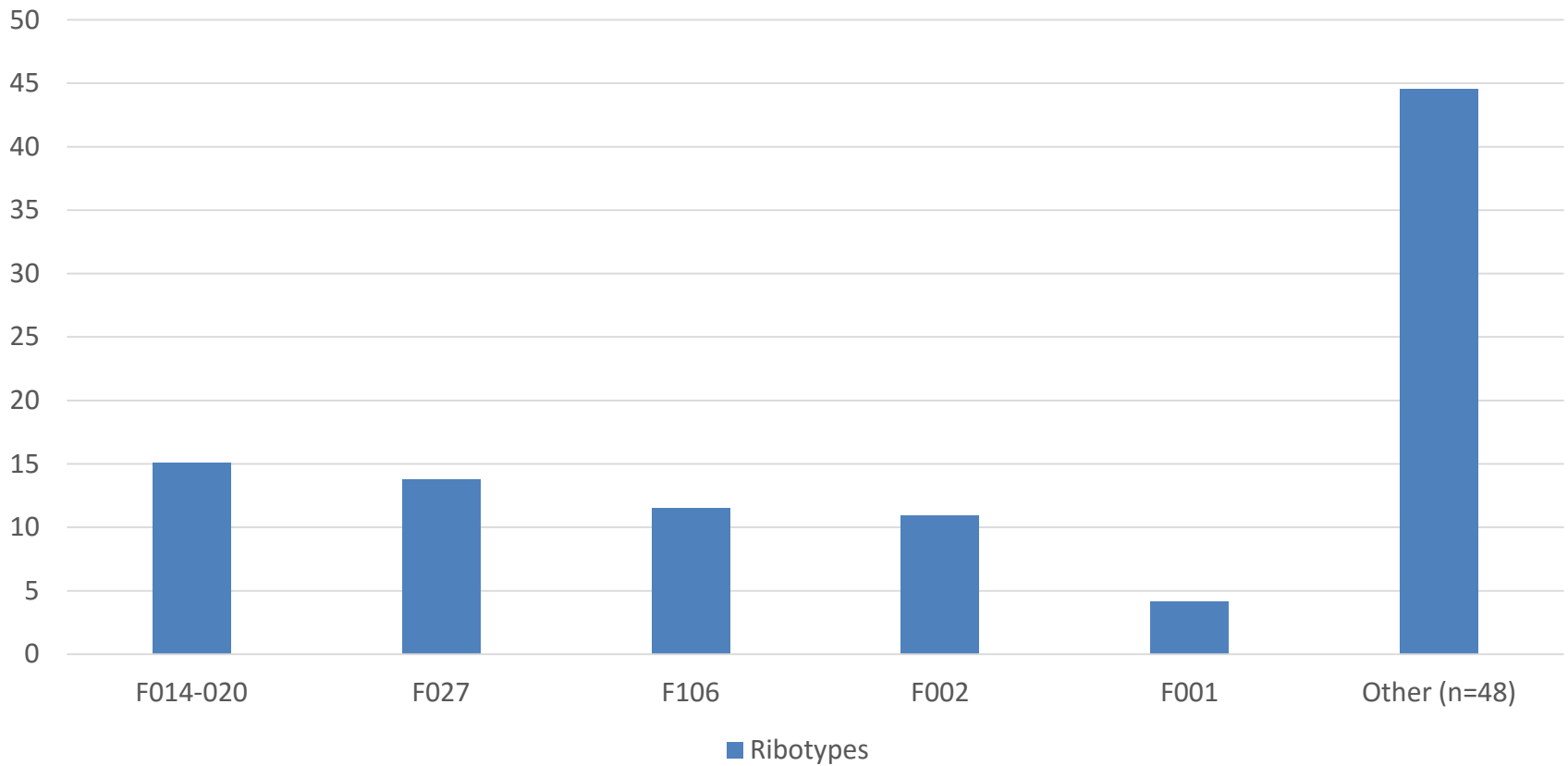


We have been able to collect a lot of C
diff samples around Texas!

City	Total
Amarillo	195
Austin	194
Corpus Christi	187
Dallas	180
El Paso	194
Fort Worth	190
Galveston	162
Laredo	192
Lubbock	175
San Antonio	185
Total	1896

Active surveillance of C. diff in Texas

Ribotypes



PCR ribotyping is commonly used worldwide

Ribotype	Houston	Australia	Belgium	Europe
014/020	15%	26%	20%	12%
002	11%	11%	8%	3%
106	12%	NR	6%	2.5%
027	14%	1.6%	4.2%	12%
001	4%	NR	NR	9%

Congratulations, Houston! We have our own unique *C. difficile* ribotype!!

Collins et al. Pathology 2017:309-13

Neely et al. J Hosp Infect 2017; 394-9

Freeman et al. Clin Microbiol Infect 2015:248e9-e16

We can likely detect the next emerging strain

	2011		2012		2013		2014		2015		2016		2017		2018	
RT027	28	22%	63	28%	91	27%	12	22%	49	20%	266	15%	226	14%	22	14%
RT014-020	23	18%	42	19%	56	17%	16	29%	39	16%	301	17%	265	16%	22	14%
RT106	16	12%	21	9%	36	11%	5	9%	33	13%	175	10%	236	15%	18	12%
RT002	12	9%	22	10%	37	11%	5	9%	20	8%	149	9%	139	9%	16	10%
RT001	13	10%	8	4%	14	4%	1	2%	11	4%	57	3%	54	3%	5	3%
RT078-126	9	7%	13	6%	21	6%	3	6%	12	5%	40	2%	23	1%	0	0%
RT255	0	0%	0	0%	0	0%	0	0%	2	1%	77	5%	80	5%	10	7%
RT054	2	2%	7	3%	10	3%	4	7%	11	4%	45	3%	37	2%	9	6%
RT053-163	4	3%	6	3%	4	1%	2	4%	12	5%	43	3%	26	2%	3	2%
RT017	3	2%	10	4%	10	3%	1	2%	7	3%	44	3%	34	2%	1	1%

We can then link these findings back to the rest of the world

PubMed ▾ ribotype 255 |
Create RSS Create alert Advanced

Format: Summary ▾ Sort by: Most Recent ▾ Per page: 20 ▾

Send to ▾

Search results

Items: 11

- [Circulation of Highly Drug-Resistant Clostridium difficile Ribotypes 027 and 001 in Two Tertiary-Care Hospitals in Mexico.](#)
 1. Martínez-Meléndez A, Tijerina-Rodríguez L, Morfin-Otero R, Camacho-Ortiz A, Villarreal-Treviño L, Sánchez-Alanís H, Rodríguez-Noriega E, Baines SD, Flores-Treviño S, Maldonado-Garza HJ, Garza-González E.
Microb Drug Resist. 2018 May;24(4):386-392. doi: 10.1089/mdr.2017.0323. Epub 2018 Feb 27.
PMID: 29485939
[Similar articles](#)

- [Clostridium difficile PCR ribotypes 001 and 176 - the common denominator of C. difficile infection epidemiology in the Czech Republic, 2014.](#)
 2. Krutova M, Matejkova J, Kuijper EJ, Drevinek P, Nyc O; Czech Clostridium difficile study group.
Euro Surveill. 2016 Jul 21;21(29). doi: 10.2807/1560-7917.ES.2016.21.29.30296.
PMID: 27484171 **Free Article**
[Similar articles](#)

One Health meets *C. diff*



Fig. 1: Isolation of *Clostridium difficile* from park tree leaves

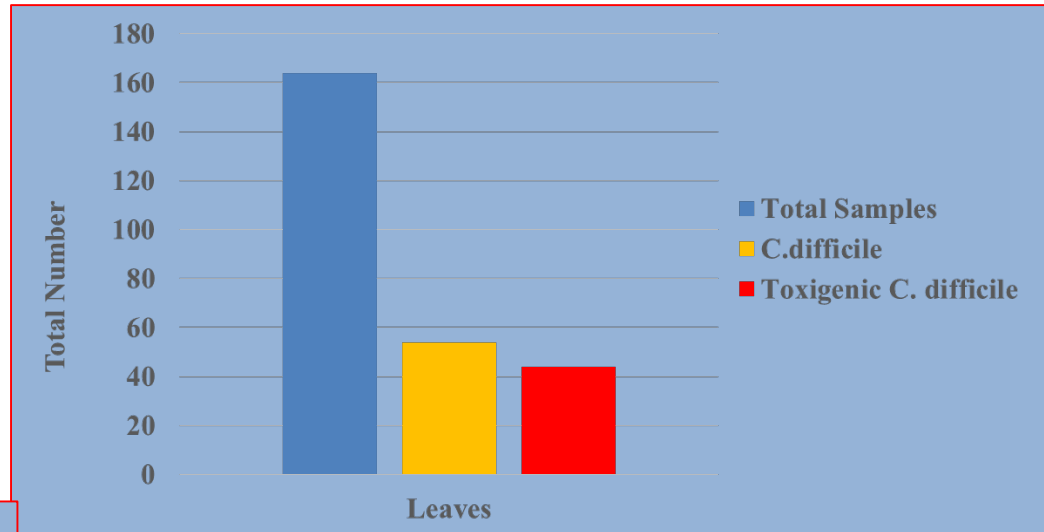
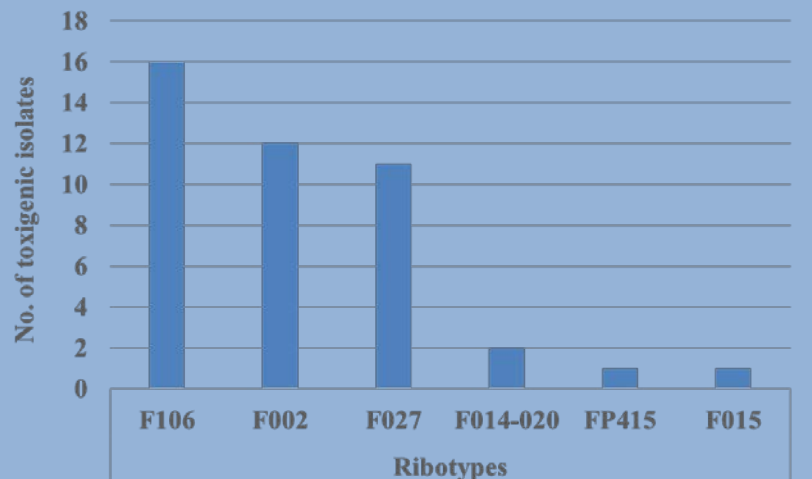


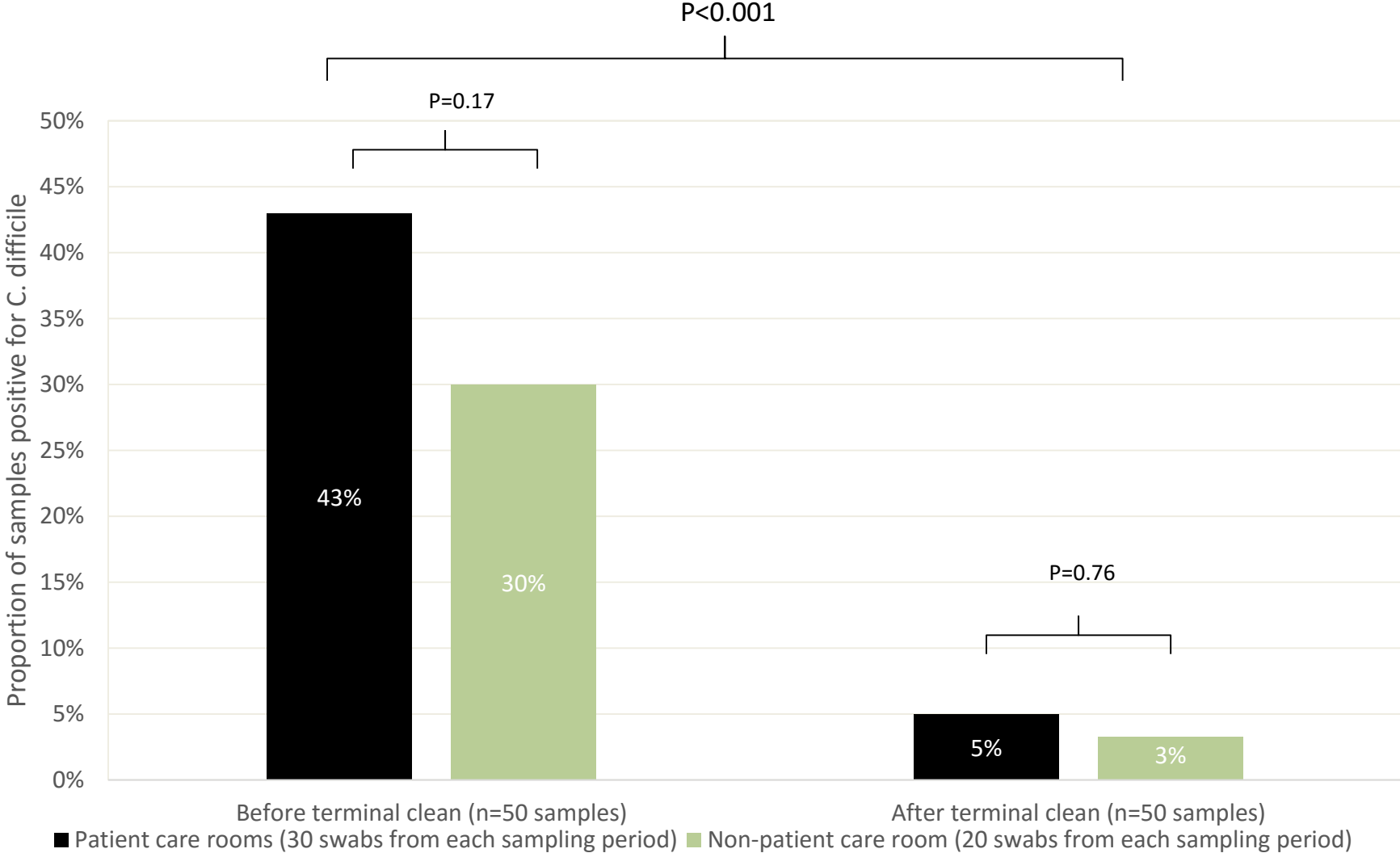
Fig. 2: Ribotypes of *Clostridium difficile* from park tree leaves



We can also use these tool to impact patient care

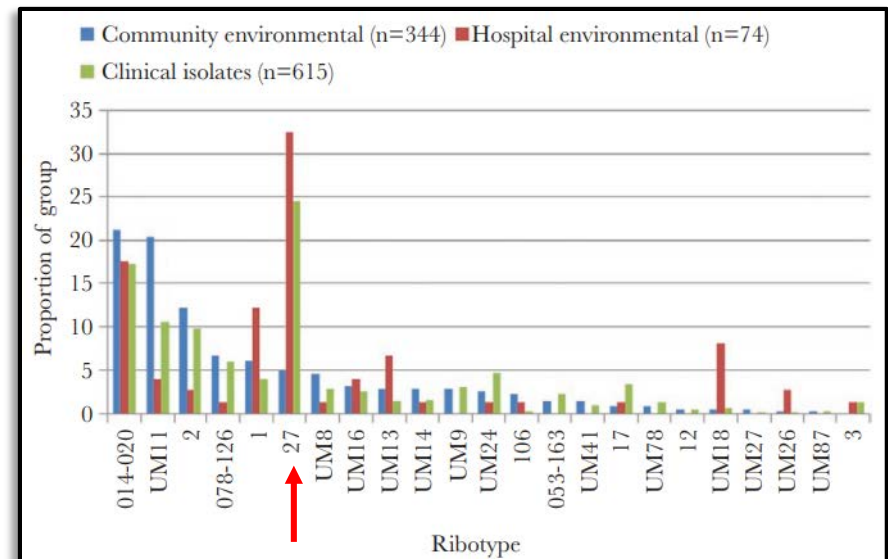
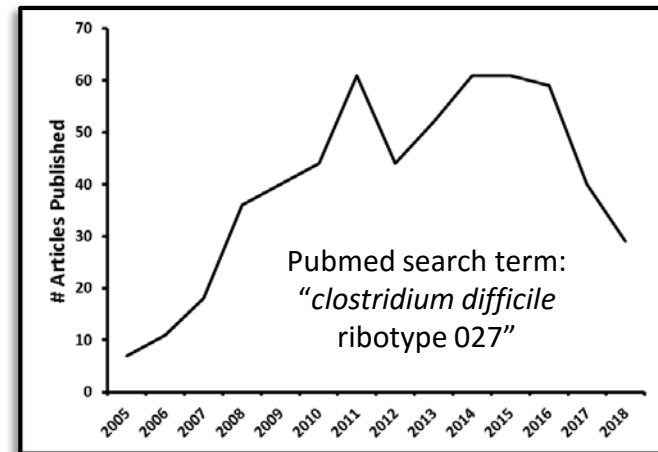
- In 2016, we were consulted on an increased number of CDI cases at a nursing home (n=4). One patients was originally symptomatic with three subsequent cases developing over the next month. This was the first case of CDI occurring at this nursing home ever!
- ALL STOOL SAMPLES WERE POSITIVE FOR RIBOTYPE 027
- Environmental samples also positive to ribotype 027
- Based on these results, the nursing home underwent an institution-wide terminal clean
- We then performed a follow-up environmental sampling study

Proportion of positive environmental samples before and after facility-wide terminal clean with 10% bleach solution



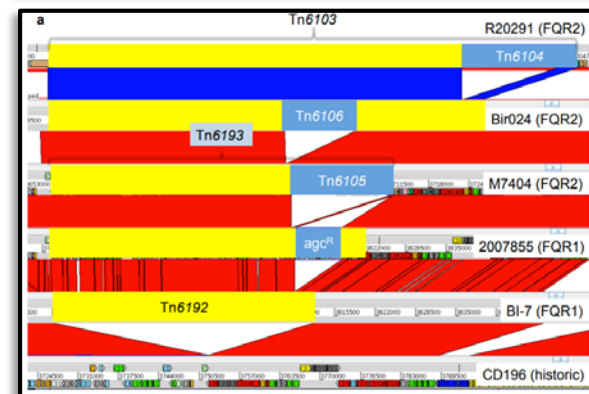
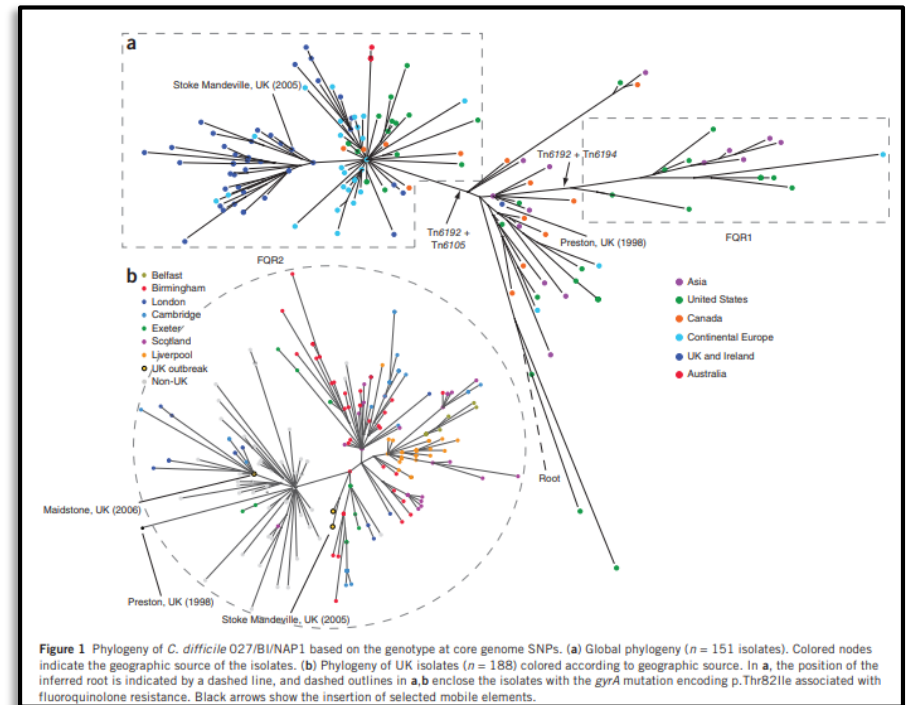
Clostridioides difficile – Focus on ribotype 027

- Global pandemic of CDI began in the early 2000's and was caused by the ribotype 027 strain
- Epidemiological studies in Houston indicates RT027 is still one of the most prominent ribotypes in the hospital/clinic



Ribotype 027: the man, the myth, the PANDEMIC legend

- WGS of 151 worldwide RT027s identified 2 distinct lineages that diverged independently (denoted FQR1 and FQR2)
- Both lineages emerged in North America with high probability
- Both epidemic lineages inherited the same *gyrA* mutation, but different transposable elements (*Tn6192* and *Tn6105*)
- FQR2 strains spread more widely in Europe, therefore, <20 FQR1 strains sampled in this study
- Little is known about the emergence and spread of FQR1



He M, et al. Nature Genetics 2013

Goal: Provide a better understanding of the emergence and dissemination of the ribotype 027 strain in the USA

- Objective 1: WGS US strains and identify SNP differences amongst RT027's
- Objective 2: Determine the gene differences between US and world wide strains
- Objective 3: Conduct phylogeographic analyses



Goal: Provide a better understanding of the emergence and dissemination of the ribotype 027 strain in the USA

- **Objective 1: WGS US strains and identify SNP differences amongst RT027's**
- Objective 2: Determine the gene differences between US and world wide strains
- Objective 3: Conduct phylogeographic analyses



SLIDES embargoed

- The next set of slides are embargoed while they are going through the peer review process for publication

Some amazing data can come out of active surveillance programs

- FQR1 and FQR2 lineages are present in Houston in equal proportions
 - Novel SNPs identified may lend insight into changes in metronidazole responsiveness
- Presence or absence of genes/transposable elements are lineage-specific with some unique strain-specific exceptions
 - FQR1 strains have more antimicrobial resistance than FQR2 strains
- Emergence of RT027 lineages was associated with FDA approval of first fluoroquinolones in early 1980's
 - Texas-wide RT027 lineages originated from Houston

Defending the need for active surveillance

- In a short amount of time, our C diff surveillance efforts have:
 - Been able to inform circulating ribotypes
 - Confirmed CDC reports on emergence of 106 strain
 - Identified the R255 emerging strain
 - Able to confirm successful eradication of the epidemic 027 strain in a LTC facility
 - Enabled global (and state-wide) surveillance of epidemic strains
- Pretty cool, eh!!

CANDIDA AURIS



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

Fungal Diseases

Fungal Diseases	
Types of Fungal Diseases	+
Who Gets Fungal Infections?	+
Outbreaks	+
CDC at Work	
Global Fungal Diseases	+
Antifungal Resistance	
Think Fungus: Fungal Disease Awareness Week	+

[CDC](#)

Candida auris



Candida auris is an emerging fungus that presents a serious global health threat. CDC is concerned about *C. auris* for three main reasons:

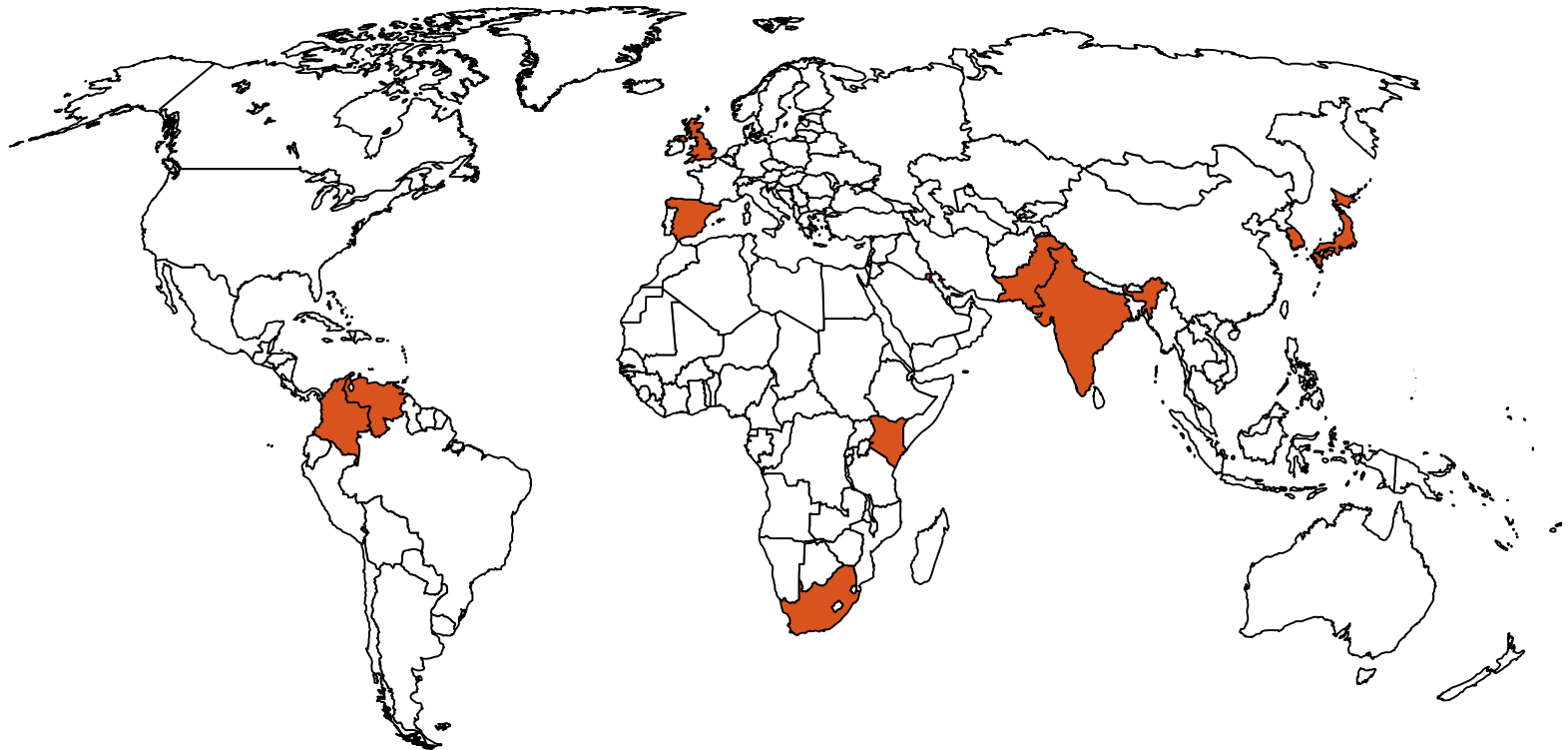
1. It is often multidrug-resistant, meaning that it is resistant to multiple antifungal drugs commonly used to treat *Candida* infections.
2. It is difficult to identify with standard laboratory methods, and it can be misidentified in labs without specific technology. Misidentification may lead to inappropriate management.

***C. auris* first reported in Japan in 2009**

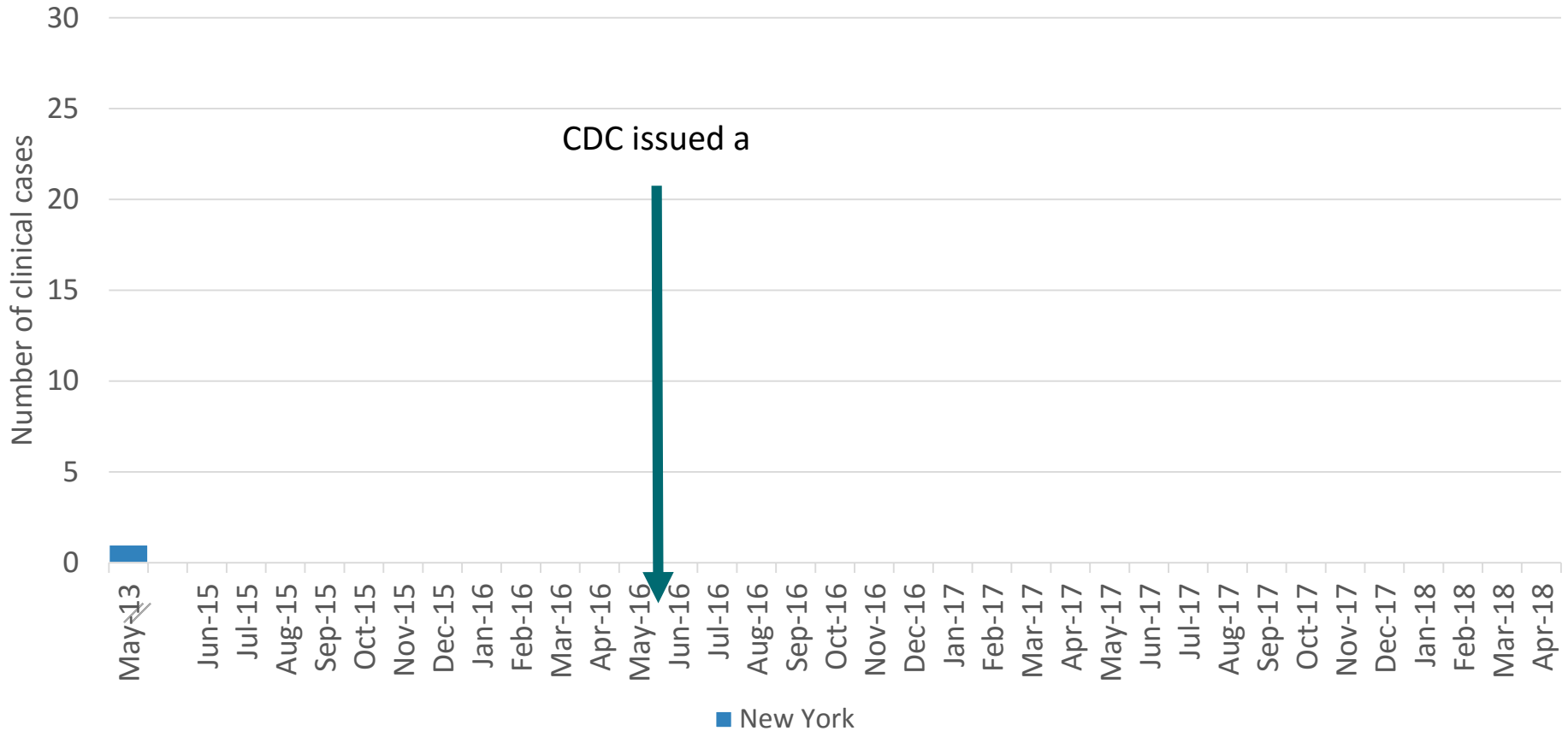


Many of these slides are courtesy of Snigdha Vallabhaneni (CDC/OID/NCEZID)

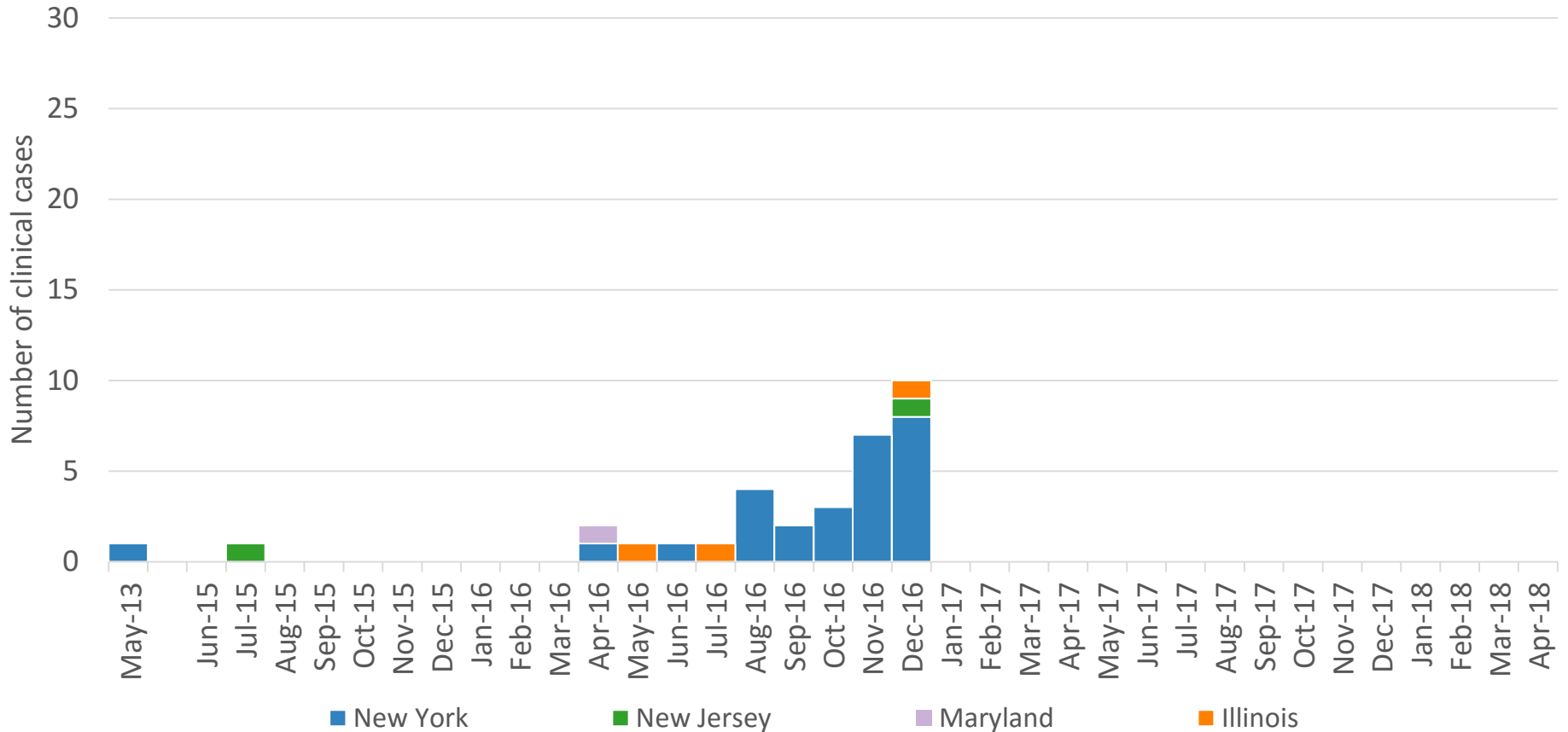
Countries from which *C. auris* cases had been reported by 2016



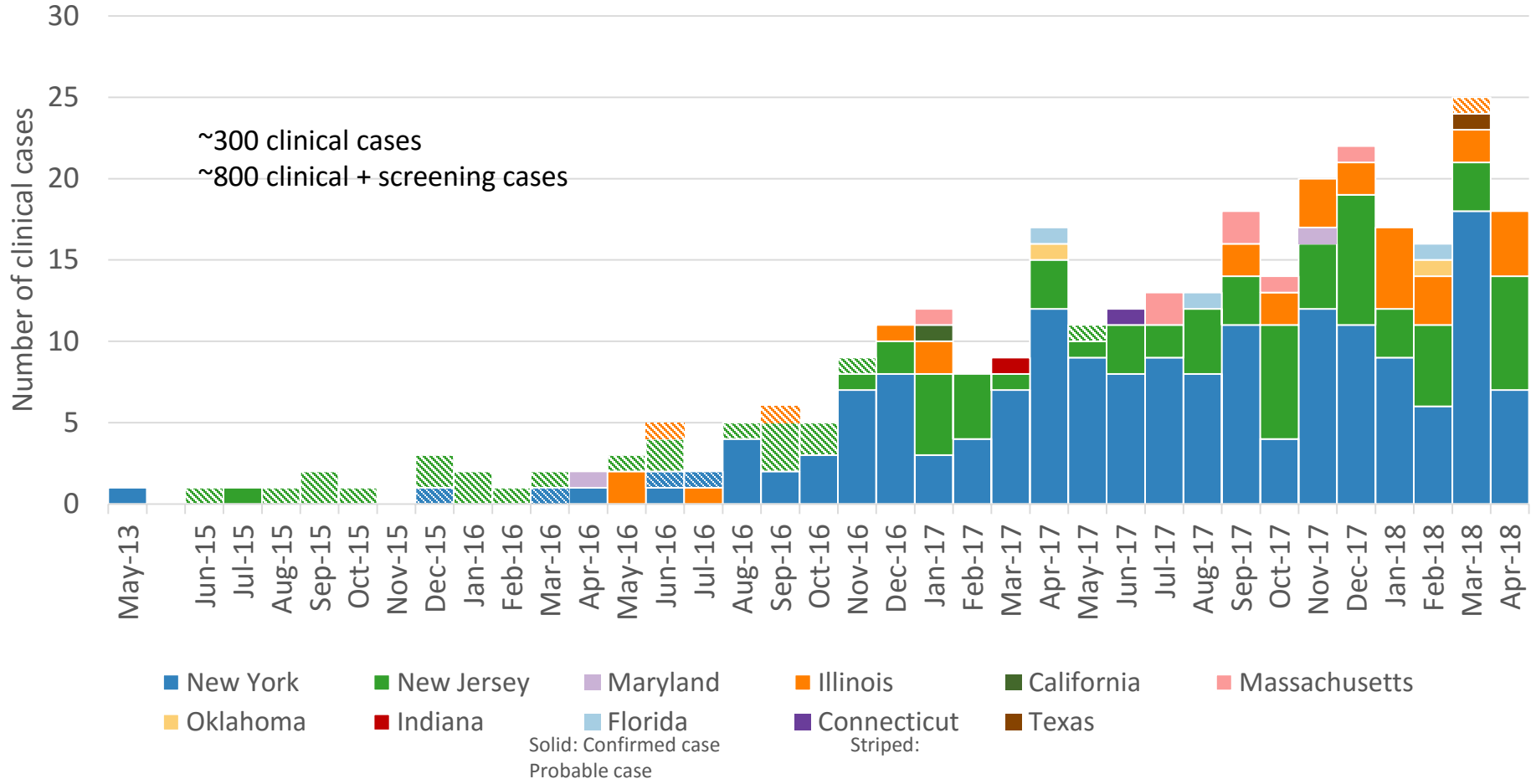
C. auris clinical cases reported by state — United States, June 2016



***C. auris* clinical cases reported by state — United States, 2013–December 2016**

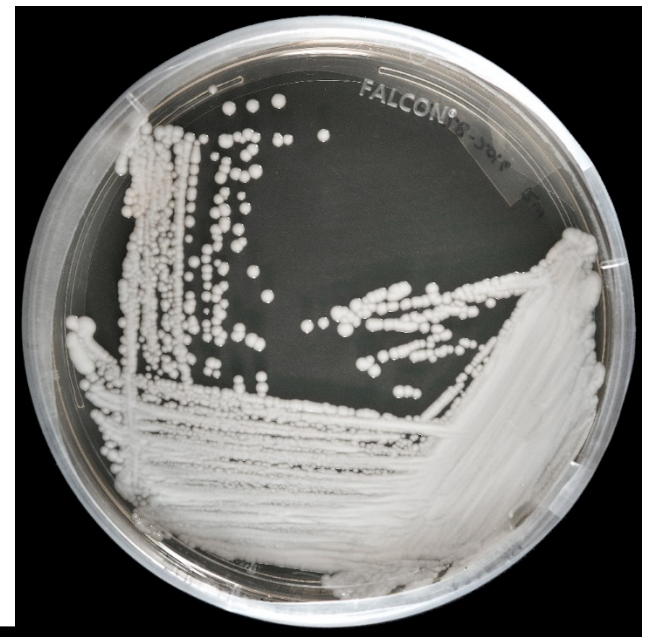


C. auris clinical cases reported by state — United States, 2013–April 2018



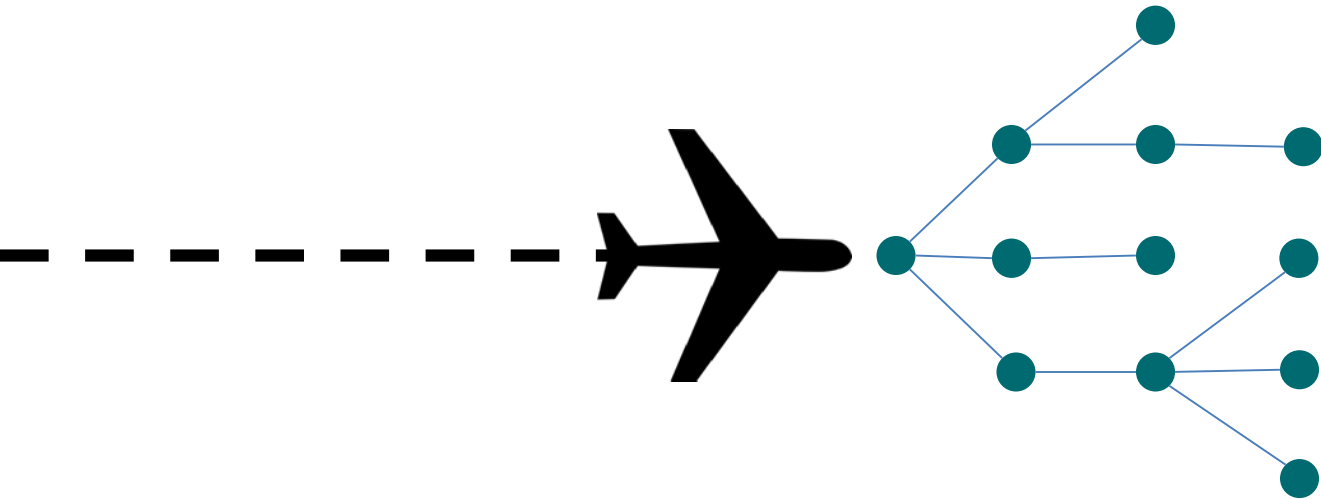
Eleven cases linked to healthcare abroad

- Patients from India, Pakistan, South Africa, and Venezuela
- Identified weeks to two years after hospitalization in that country
- WGS showed isolates were related to those from the countries where patients received healthcare
- Isolates were from all different body sites



Healthcare abroad is risk factor for *C. auris*

- Majority of US cases don't have links to healthcare abroad
- US *C. auris* cases are a result of introductions from abroad followed by local transmission

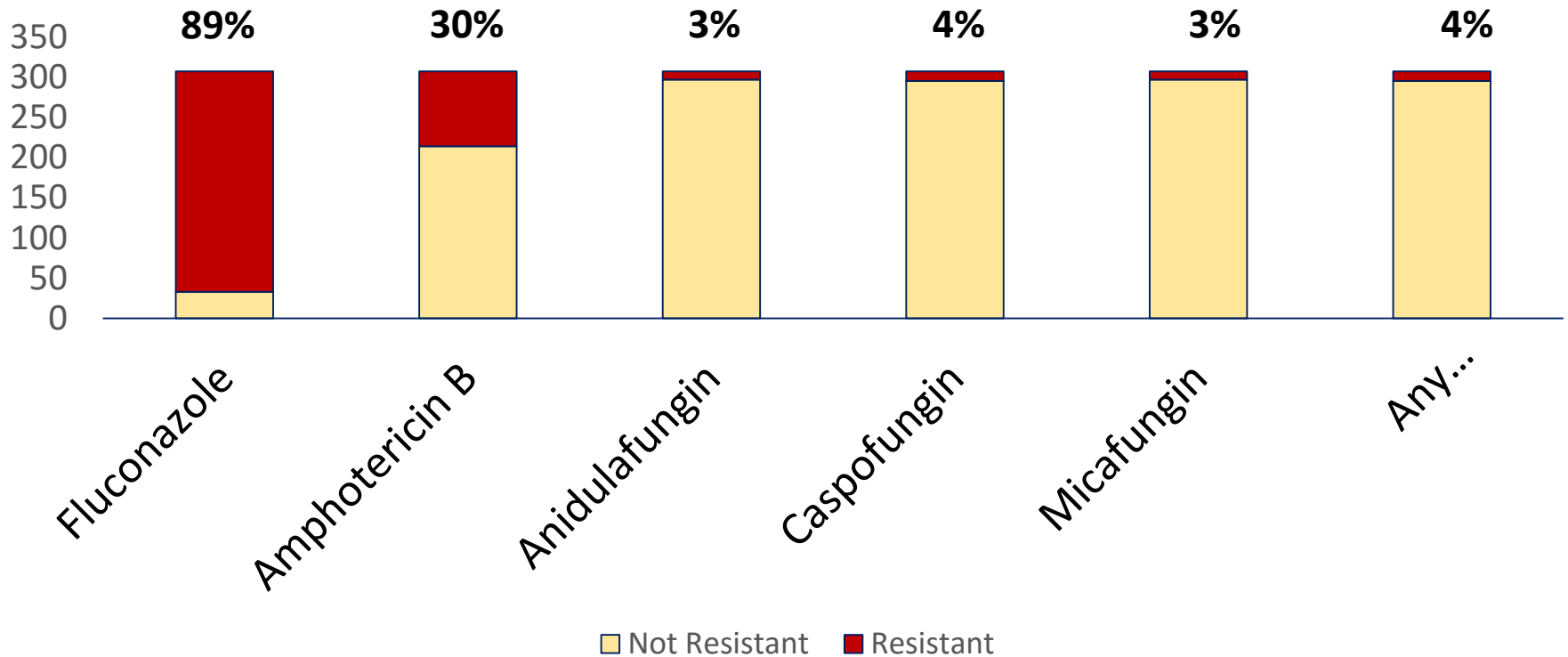


Why is *Candida auris* a public health threat?

- Highly drug-resistant yeast
- Causes invasive infections associated with high mortality
- Spreads easily in healthcare settings



Antifungal Resistance, *C. auris* isolates United States, 2013-2018



Causes invasive infections

- 40-50% of clinical cases are bloodstream infections
- 40% in-hospital mortality in BSI cases

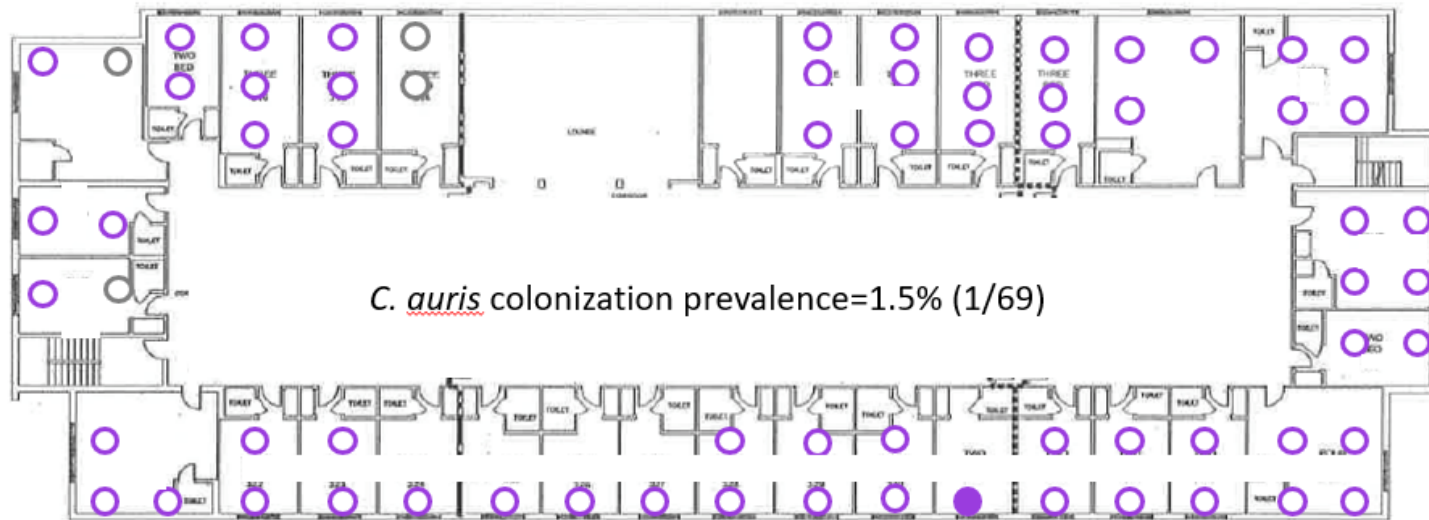


Risk factors for *C. auris*

- Multiple healthcare stays (LTCFs)
- Tracheostomy/Ventilator
- PEG tubes
- Central venous catheters
- On antibiotics and antifungals
- Being colonized with another MDRO is a risk factor for *C. auris* colonization
- Receipt of healthcare abroad

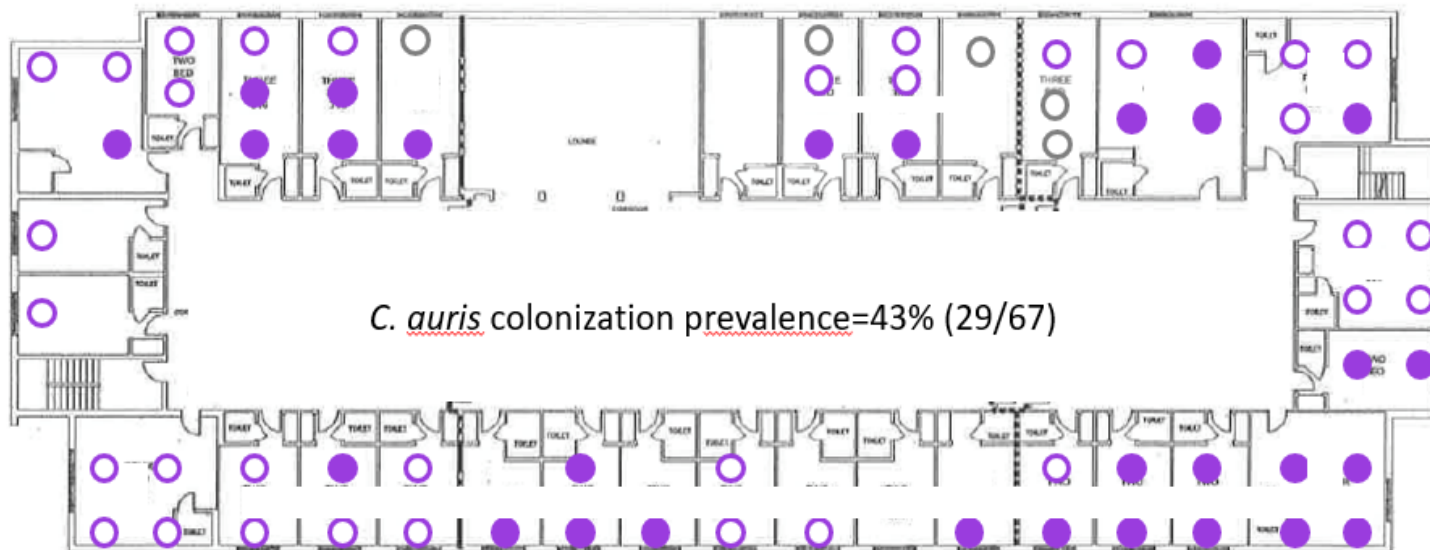


vSNF A Ventilator/Trach Floor March 2017 *C. auris* PPS Results



- *C. auris* positive
- Screened negative for *C. auris*
- Not tested for *C. auris* (refused or not in room)

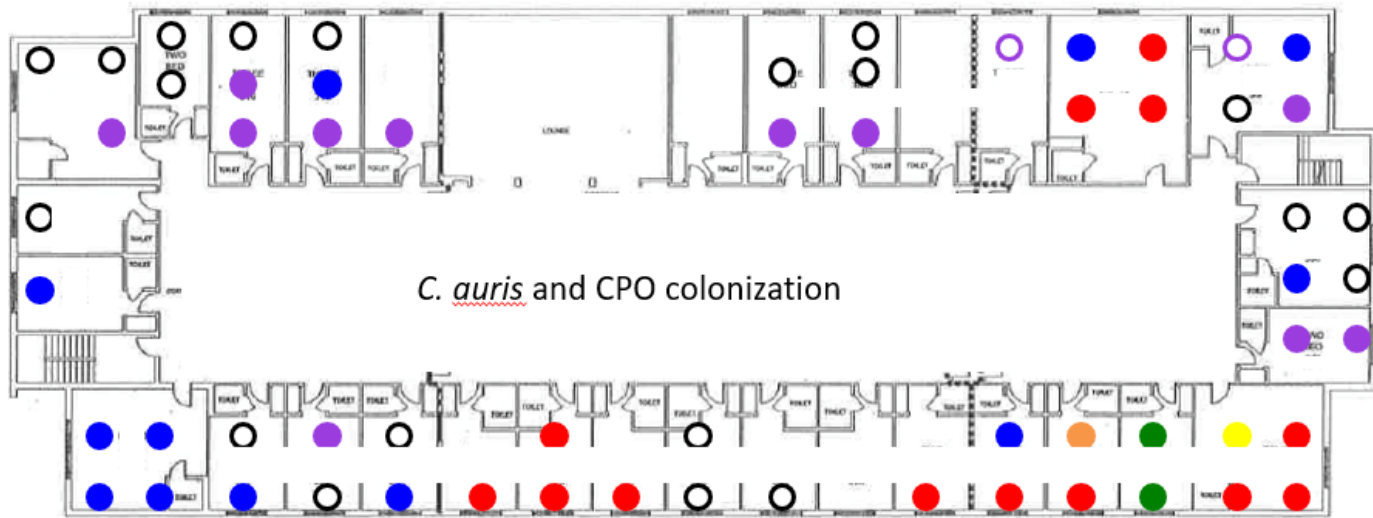
vSNF A Ventilator/Trach Floor January 2018 *C. auris* PPS Results



- *C. auris* positive
- Screened negative for *C. auris*
- Not tested for *C. auris* (refused or not in room)

Slide courtesy of Chicago Department of Public Health.

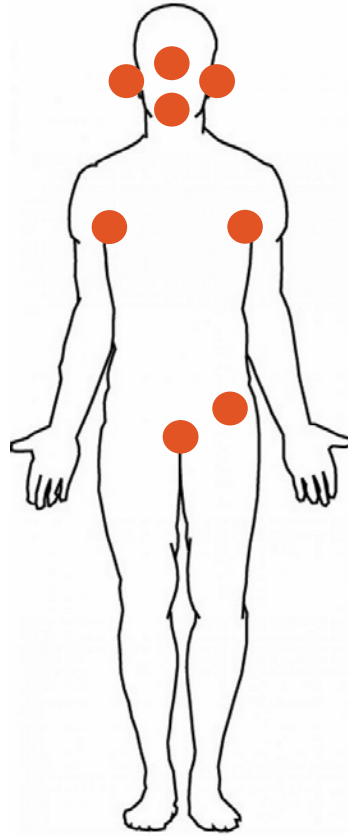
vSNF A Ventilator/Trach Floor January 2018 CPO and *C. auris* PPS Results



- *C. auris*
- *C. auris* and KPC
- KPC or CRE with unknown mechanism of resistance
- *C. auris*, KPC, and NDM
- *C. auris*, VIM-CRPA, and KPC
- *C. auris* and KPC-CRPA
- Screened negative for *C. auris*, but not tested for CRE
- Screened negative for CRE and *C. auris*

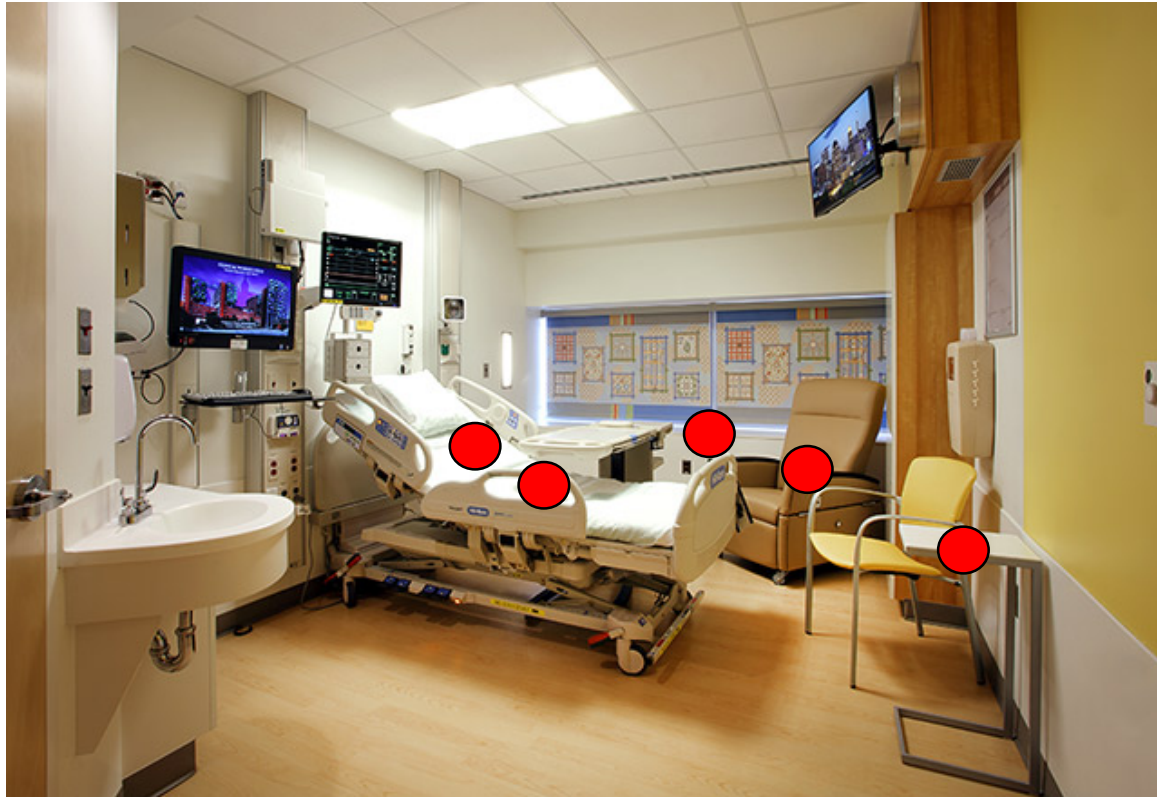
Slide courtesy of Chicago Department of Public Health.

Patients are colonized for the long term



In NY, of ~300 patients being followed with *C. auris*, only 16 have “cleared” colonization

C. auris in the Hospital Environment



Other places where *C. auris* has been cultured from:



Temperature probe



Challenges with identification

C. auris can be **misidentified** as:

- *Candida haemulonii*
- *Candida famata*
- *Candida sake*
- *Candida catenulata*
- *Candida guilliermondii*
- *Candida lusitanae*
- *Rhodotorula glutinis*,
- *Candida* spp. after a validated method of *Candida* identification attempted.

For the clinical lab experts

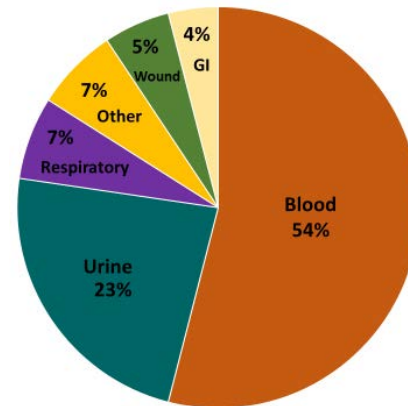
Identification Method	Organism <i>C. auris</i> can be misidentified as
Vitek 2 YST	<i>Candida haemulonii</i> <i>Candida duobushaemulonii</i>
API 20C	<i>Rhodotorula glutinis</i> (characteristic red color not present) <i>Candida sake</i>
BD Phoenix yeast identification system	<i>Candida haemulonii</i> <i>Candida catenulata</i>
MicroScan	<i>Candida famata</i> <i>Candida guilliermondii</i> * <i>Candida lusitaniae</i> * <i>Candida parapsilosis</i> *
RapID Yeast Plus	<i>Candida parapsilosis</i> *

Continuing challenges with identification

- Half of clinical cases in the U.S. have been from non-bloodstream isolates (e.g., urine, bile, wounds)
- Species from non-sterile isolates often not identified



Initial culture site of *C. auris* clinical cases (n = 150)



Controlling the spread of *C. auris*



DETECT



TREAT



INFECTION CONTROL

Challenges

- Detection/Identification
- Lack of decolonization/ source control strategies
- Environmental disinfection

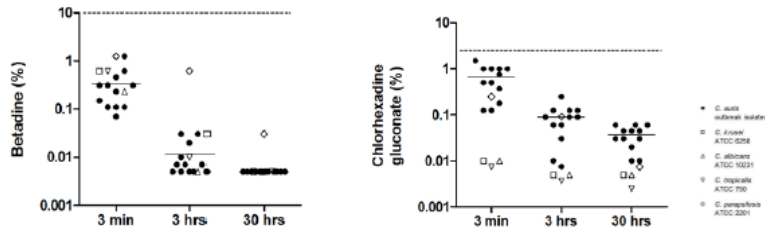
Decolonization/source control

- Chlorhexidine?
- Antifungals?
- Remove pressure of antibiotics and antifungals?

In vitro data on chlorhexidine looks good

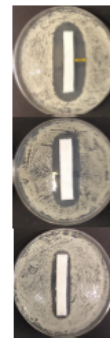
Chlorhexidine activity

- C. auris* was effectively inhibited by chlorhexidine (Hibiscrub, Ecolab, UK) *in vitro* at concentrations below 2 and 4% for skin decolonization.
- Iodinated povidone (Videne, UK) demonstrated an even greater activity much below the average 10% concentration used as antiseptic.



Skin antiseptic chlorhexidine wash cloth

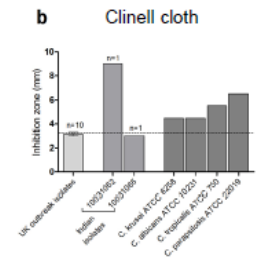
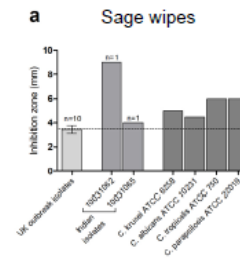
All UK outbreak chlorhexidine wipes (Sage, Geneva, Switzerland) and wash cloth (Clinell, Gama healthcare, Watford, UK) after 18-48 hours incubation at $30 \pm 2^\circ\text{C}$.



Increased inhibition zone
C. auris 10031062 (India)

Average inhibition zone
C. albicans ATCC 10231

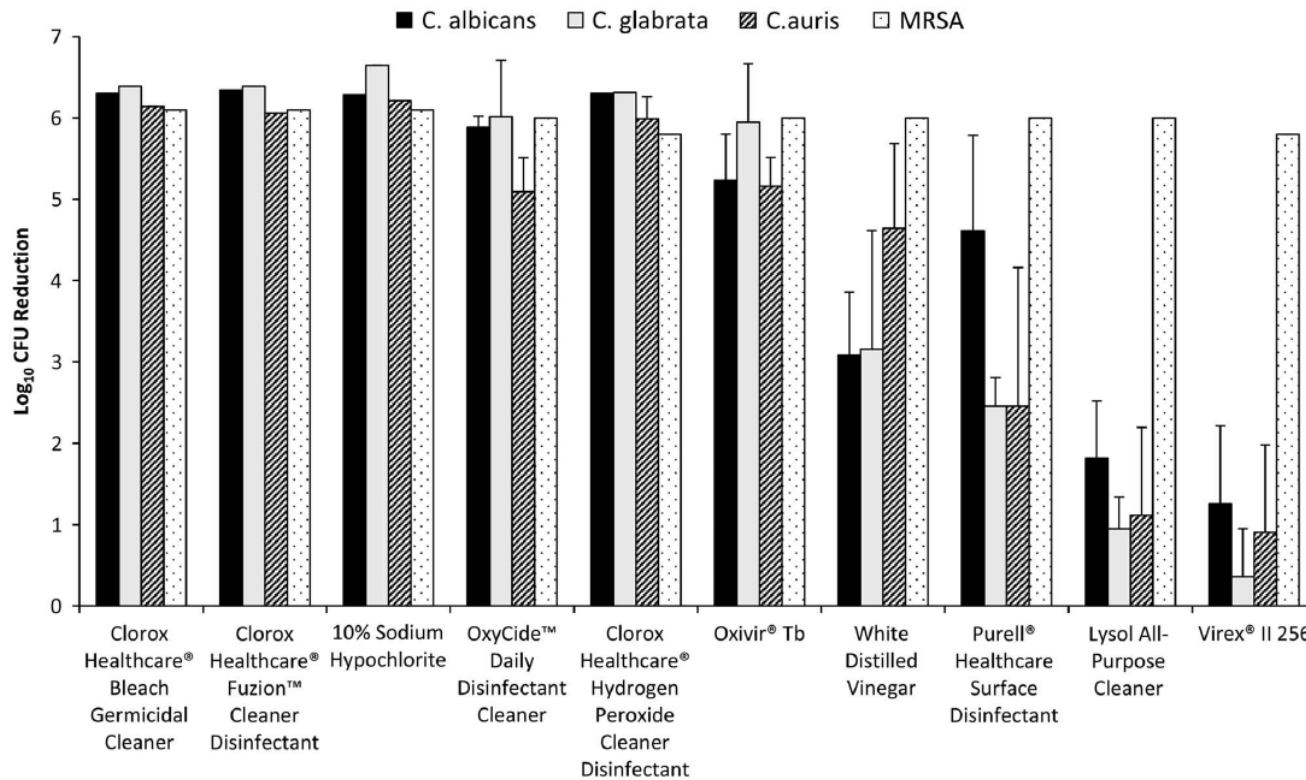
Reduced inhibition zone
UK outbreak



But...

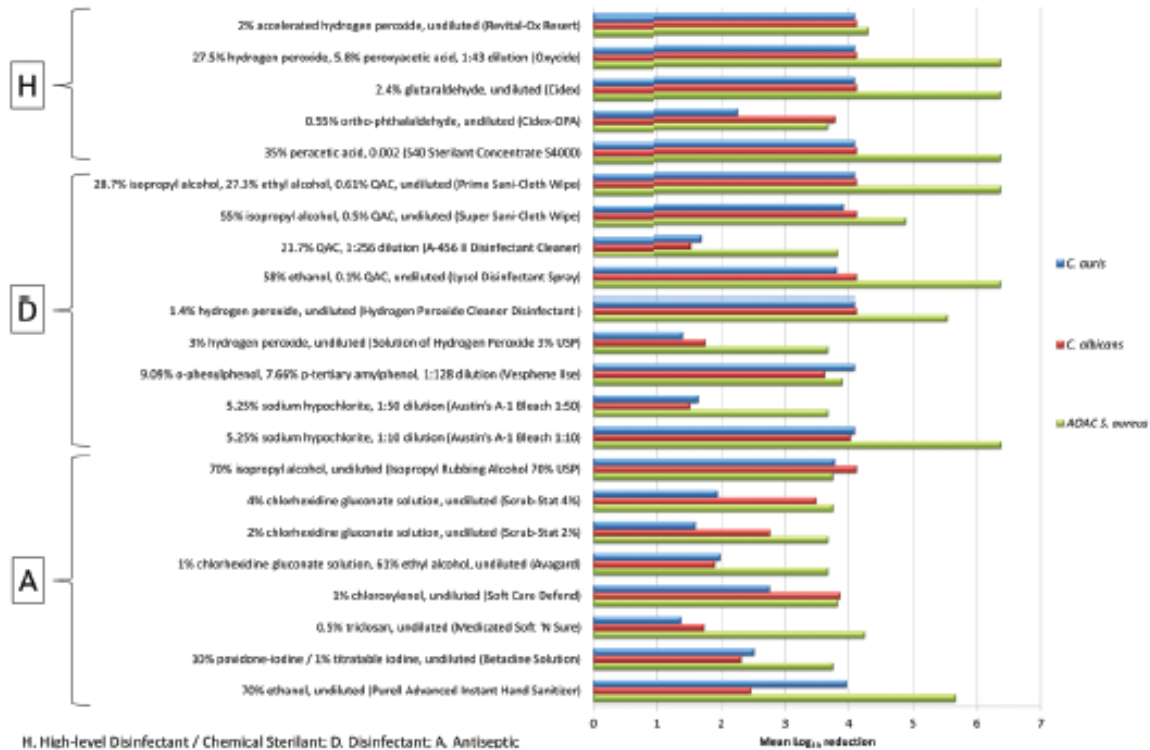
- In vivo studies on reduction in burden of colonization have not been done
- Facilities where *C. auris* outbreaks have occurred have not seen improvements in incidence of colonization even when using CHG bathing

Environmental disinfection



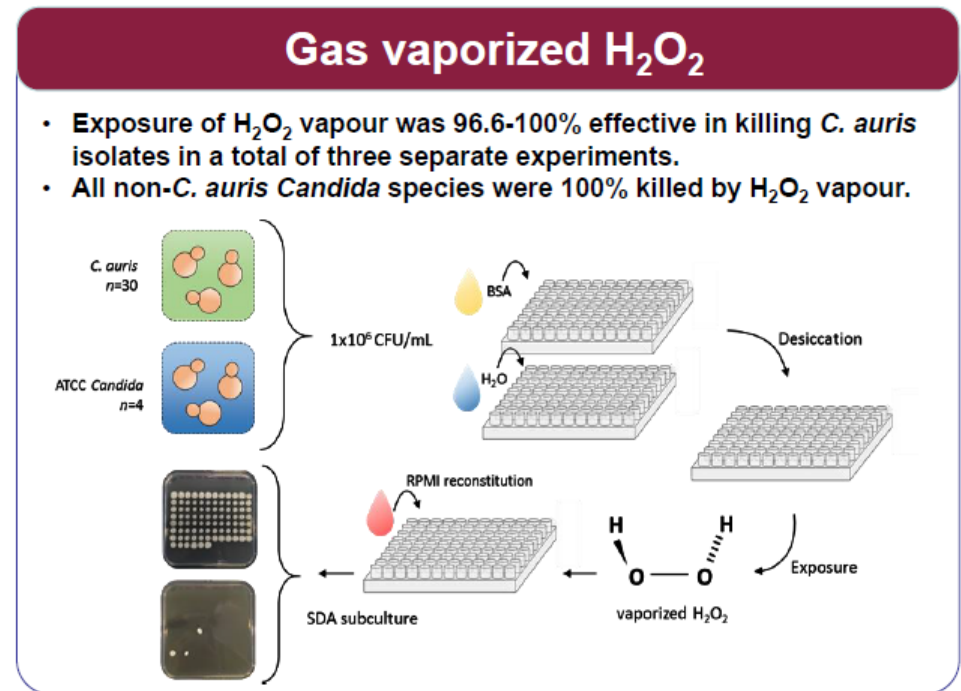
Environmental disinfection

Figure 1. Germicidal Activity against *C. auris*, *C. albicans*, and *S. aureus*



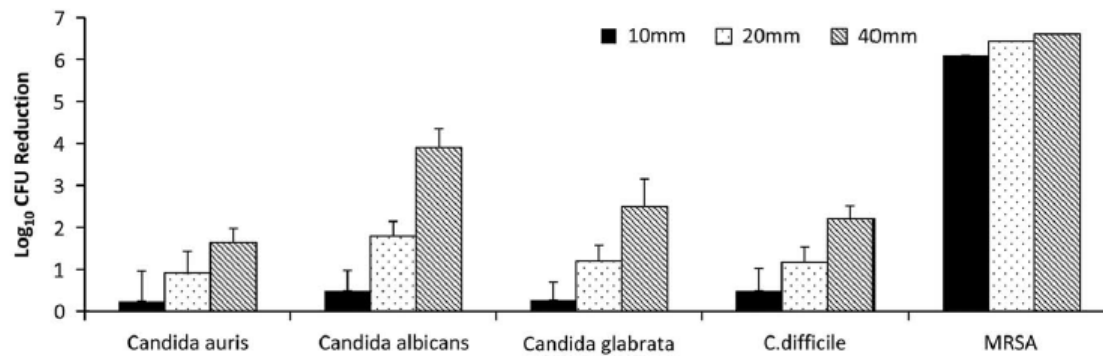
Environmental disinfection – Hydrogen Peroxide

- In vitro studies promising
- Need real world assessments



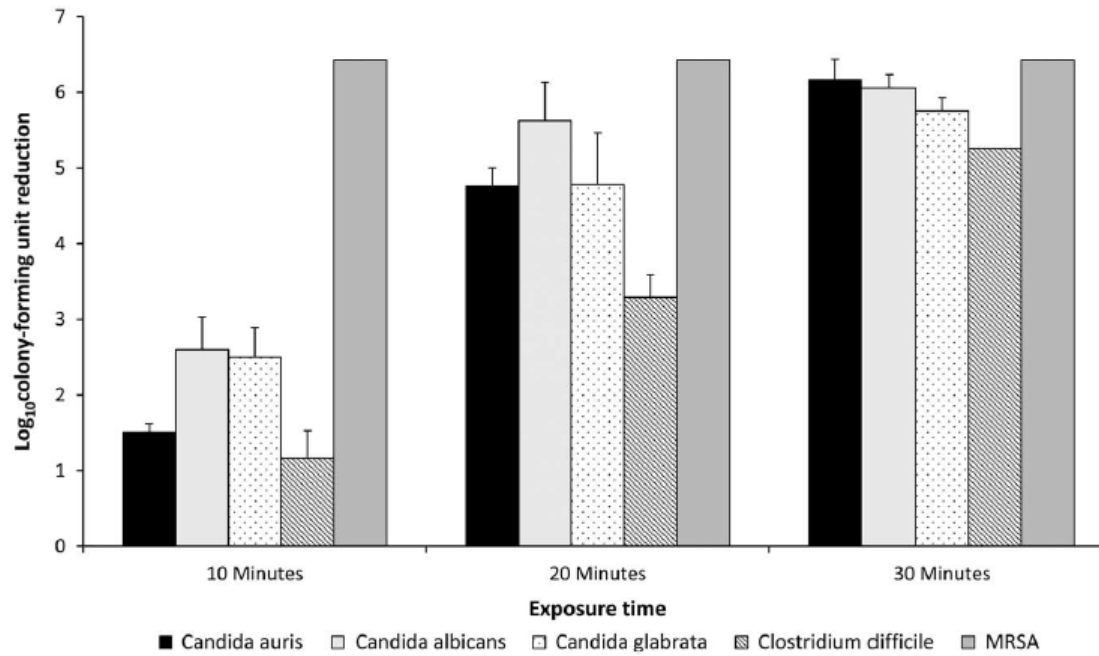
Schelenz, Federation of Infection Societies Poster, 2017

Environmental disinfection—UV Light



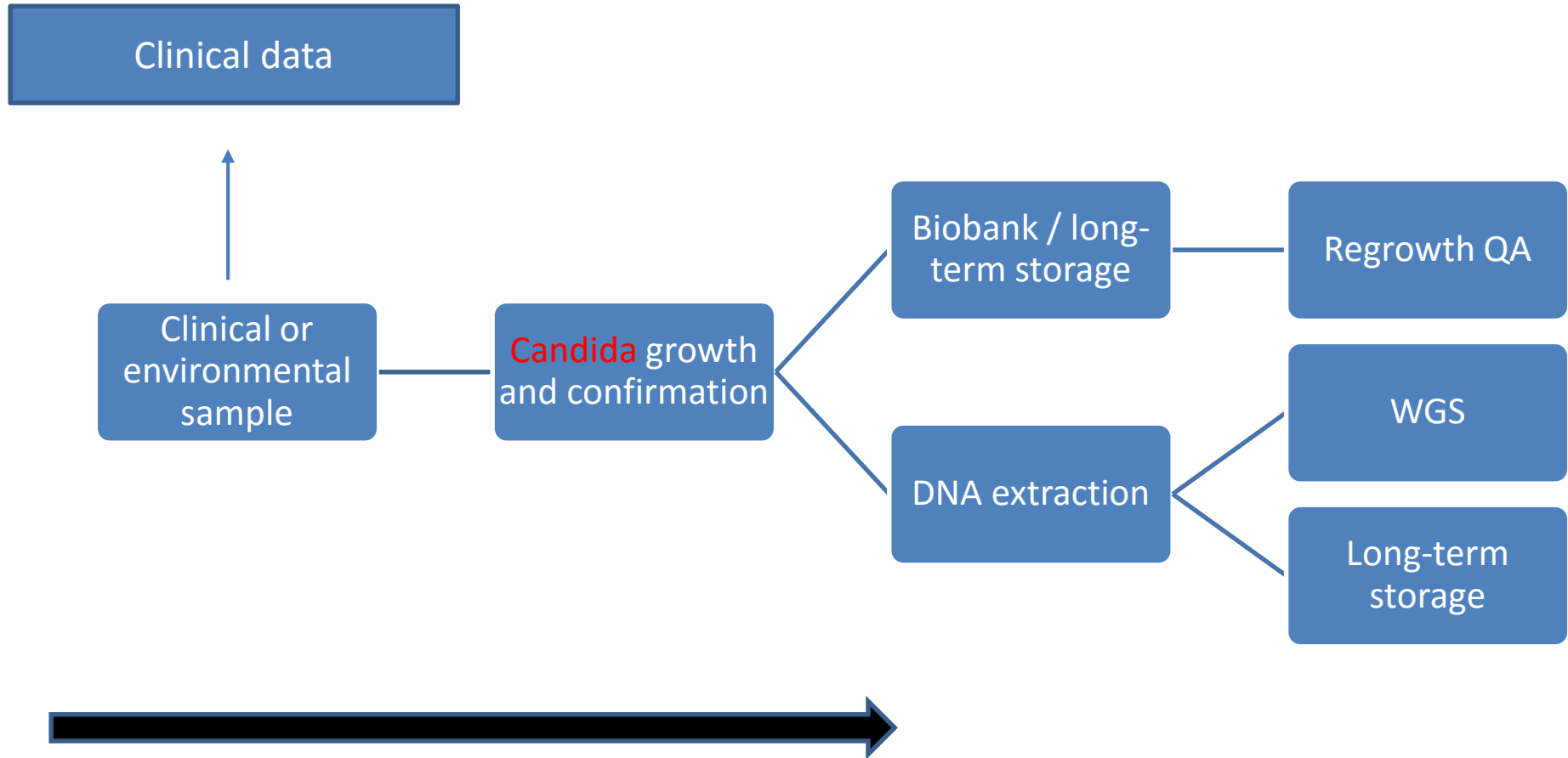
Cadnum et al 2017

Environmental disinfection—UV Light



Cadnum et al 2017

Components of an active surveillance system: C. auris



Candida auris surveillance

- Details
 - 1-2 year evaluation of *Candida* bloodstream isolates from 2 health systems
 - WGS for clonal relatedness and identification of *C. auris* (if it is present in Houston)
 - Outreach to the Houston medical community for evaluation of *Candida* outbreaks or difficult to identify isolates

Future: XDRO registry

Facilities work together to protect patients.

Common Approach *(Not enough)*

- Patients can be transferred back and forth from facilities for treatment without all the communication and necessary infection control actions in place.

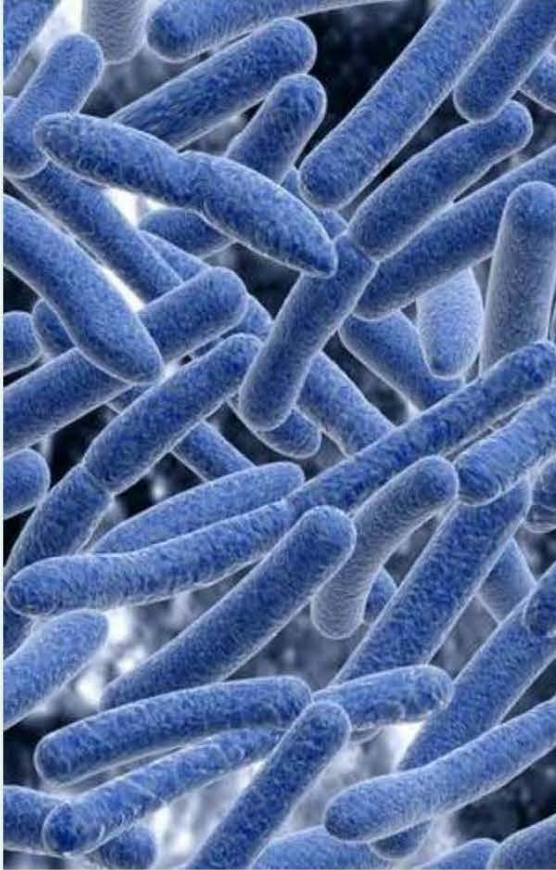
Independent Efforts *(Still not enough)*

- Some facilities work independently to enhance infection control but are not often alerted to antibiotic-resistant or *C. difficile* germs coming from other facilities or outbreaks in the area.
- Lack of shared information from other facilities means that necessary infection control actions are not always taken and germs are spread to other patients.

Coordinated Approach *(Needed)*

- Public health departments track and **alert** health care facilities to antibiotic-resistant or *C. difficile* germs coming from other facilities and outbreaks in the area.
- Facilities and public health authorities share information and implement shared infection control actions to stop spread of germs from facility to facility.





The XDRO registry is a product of collaboration between IDPH, Medical Research Analytics and Informatics Alliance (MRAIA), and the Chicago CDC Prevention Epicenter.

Carbapenem-resistant Enterobacteriaceae (CRE) are extensively drug resistant organisms (XDROs) that have few treatment options and high mortality rates. CRE are increasingly detected among patients in Illinois, including in acute and long term care healthcare facilities.

In response to the CRE public health threat, the Illinois Department of Public Health (IDPH) has guided development of an infection control tool called the XDRO registry. The purpose of the XDRO registry is two-fold:

1. **Improve CRE surveillance:** The first CRE-positive culture per patient stay must be reported to the XDRO registry.
2. **Improve inter-facility communication:** Healthcare facilities can query the XDRO registry to see whether a patient has been previously reported as CRE-positive.

[For access to the XDRO registry, click here](#)

UPDATES

As of April 2017, IDPH is entering carbapenemase-producing *Pseudomonas aeruginosa* cases into the XDRO registry. Link: [[CDC Pseudomonas aeruginosa in Healthcare Settings](#)]

As of January 2017, IDPH is entering *Candida auris* cases into the XDRO registry. Links: [[CDC C. auris Questions and Answers](#)][[CDC Interim Recommendations](#)]

IL CRE Detect and Protect Campaign. [More...](#)

CRE are reportable to IDPH via the XDRO registry. Links: [[IDPH letter to facilities, September 2013](#)][[Reporting rule](#)]

Electronic Public Health Registry of Extensively Drug-Resistant Organisms, Illinois, USA

William E. Trick, Michael Y. Lin, Robynn Cheng-Leidig, Mary Driscoll, Angela S. Tang,
Wei Gao, Erica Runningdeer, M. Allison Arwady, Robert A. Weinstein

XDRO registry
ROBYNN LEIDIG

Illinois Department Of Public Health [change facility](#)

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XDRO Report

XDRO culture information

* **Organism name (genus/species)**
Please Select Organism:

* **Specimen source**
Please Select Specimen:

* **XDRO criteria** (select all that apply)
[Reporting rule](#)

Molecular test (e.g. PCR) specific for carbapenemase

Phenotypic test (e.g. Modified Hodge) specific for carbapenemase production

For E. coli and Klebsiella spp. only: Resistant to ALL 3rd gen cephalosporins tested and non-susceptible (intermediate or resistant) to one carbapenem. Ignore ertapenem.

* **Date (culture acquisition)**
 / /

* **Mechanism of resistance**
Please Select Mechanism:
(molecular test required)

Facility information

* **Facility name**

* **Patient MRN**

* **Date of admission/Encounter Date**
 / /

Culture obtained as outpatient

Patient demographics

* **First name**

Middle name(if applicable)

* **Last name**

* **Gender**
 Male Female

* **Date of birth(mm/dd/yyyy)**
 / /

Social Security Number(last4)

Race
Please Select One:

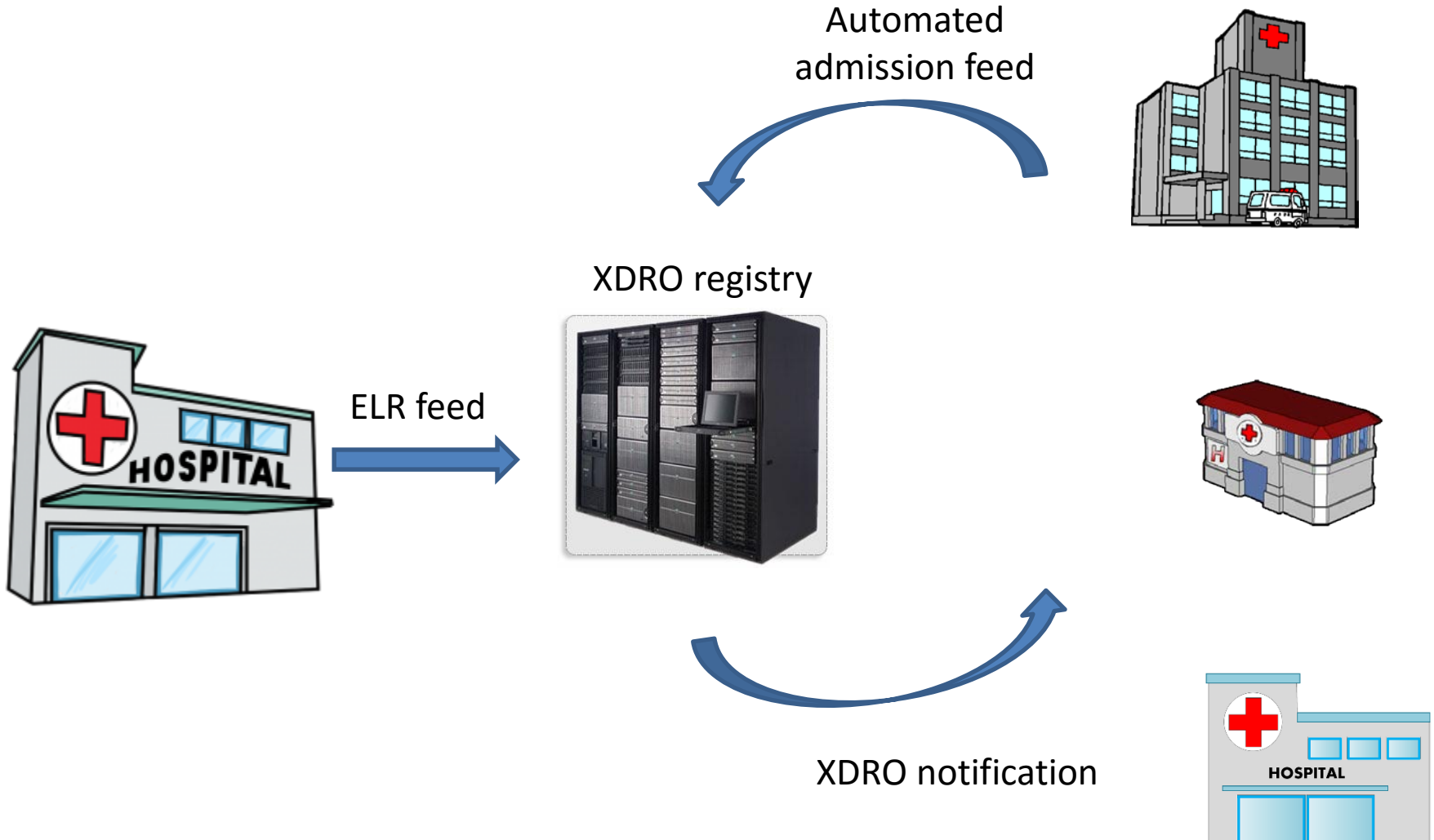
Ethnicity
 Hispanic or Latino
 Not Hispanic or Latino

* **Street address**

* **City** * **County**

* **State** * **Zip code**

XDRO registry: Texas style!



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