CANDIDA AURIS: A GLOBAL THREAT HIDING IN PLAIN SIGHT – DIAGNOSTICS, RESISTANCE, AND CLINICAL FALLOUT

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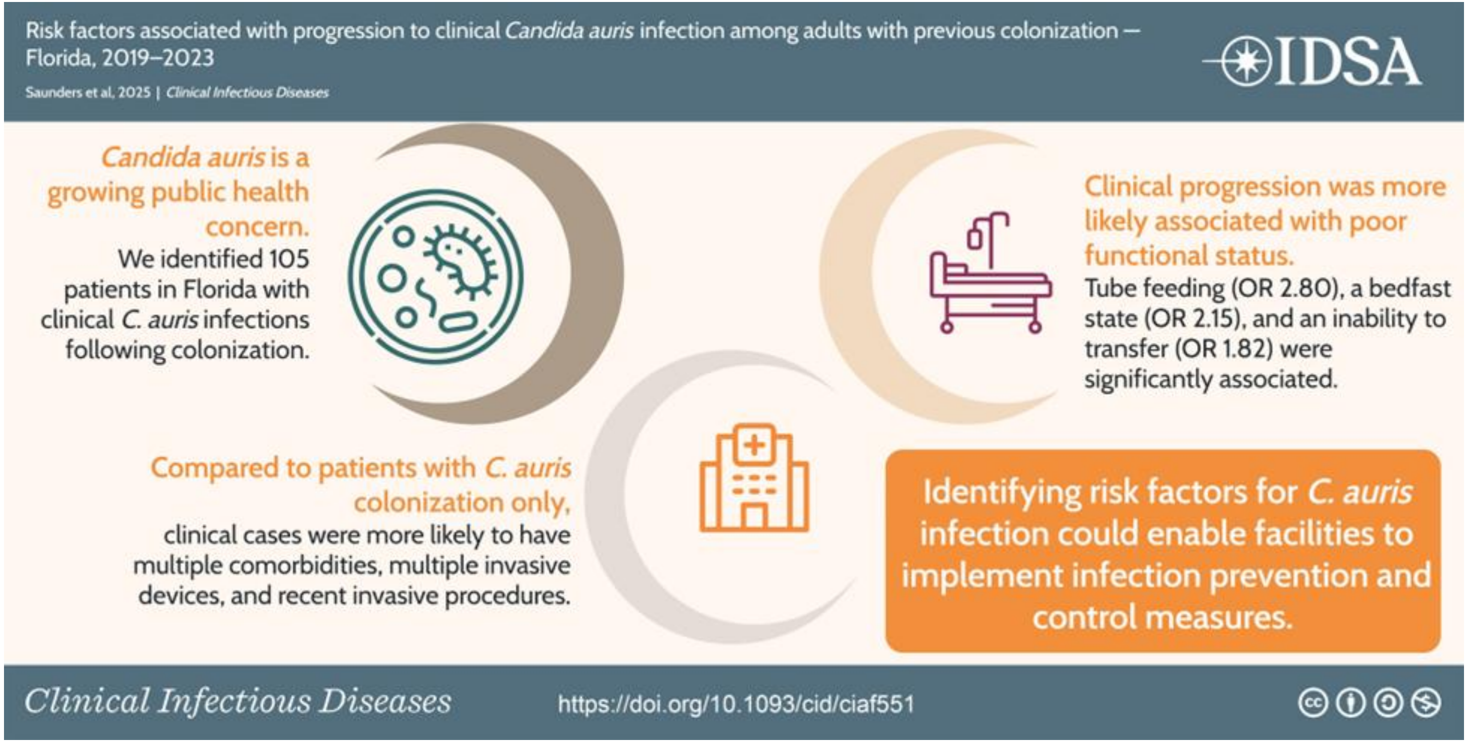
WHY IS EVERYONE SO CONCERNED ABOUT *CANDIDA AURIS?*

THE CLINICAL SYNDROMES OF *C. AURIS*

- Typical presentation includes non-specific symptoms:
  - Fever
  - Rigors
  - Fatigue
  - Body aches
- Common Clinical Syndromes:
  - Bloodstream infection
  - Would and SSI Infections
  - Urinary Tract Infections
  - Ear Infections
  - Respiratory tract Infections
  - Central Nervous System Infections

RISK FACTORS ASSOCIATED WITH *C. AURIS* INFECTION



A PERSPECTIVE ON RISK FROM CANADIAN ACUTE CARE HOSPITALS – CIRCA 2018

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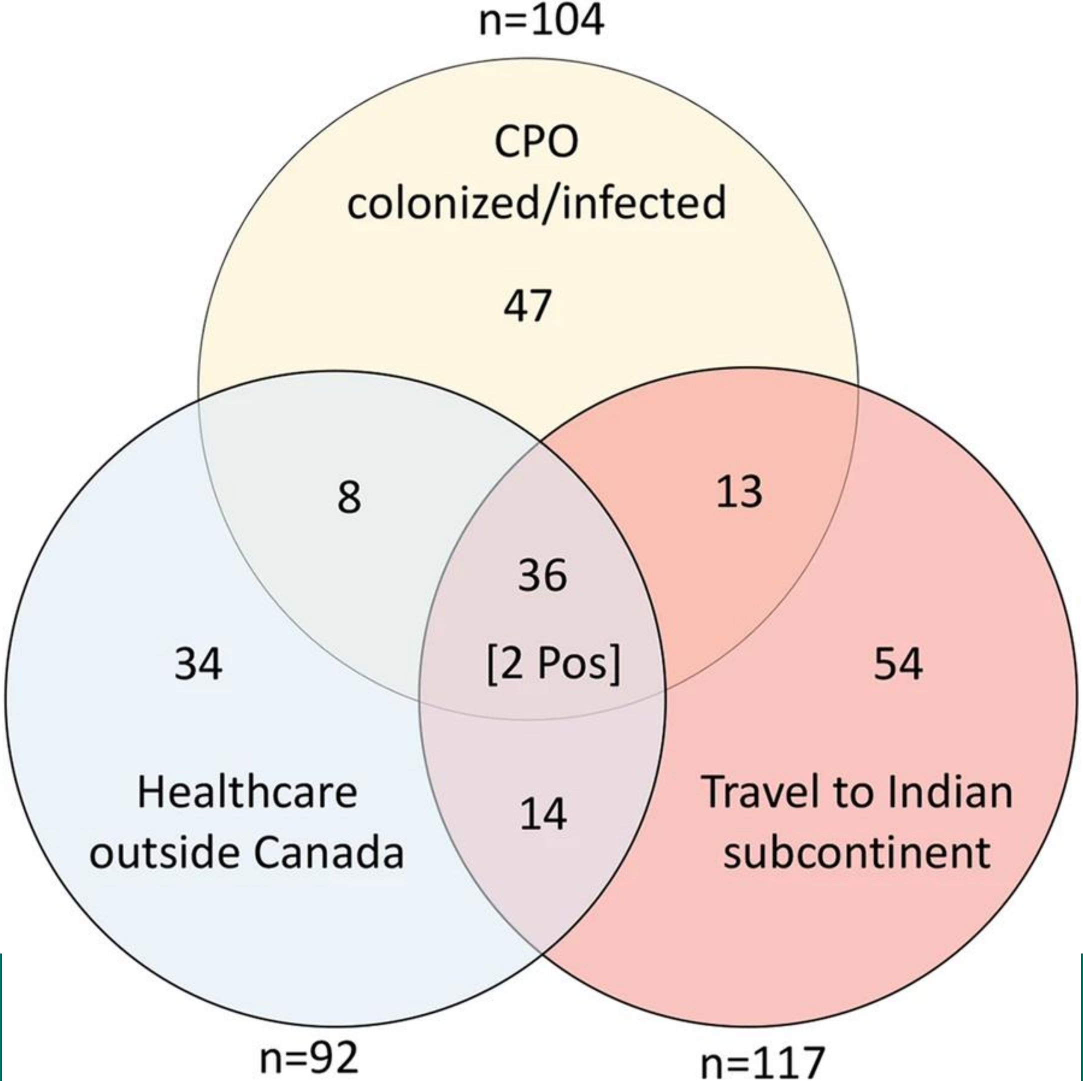


THE CLINICAL CHALLENGE OF *C. AURIS*

- Typically spread in healthcare environments (includes long-term care and long-term acute care settings)
  - Patients with invasive medical devices like ET tubes, G tubes, catheters, or urinary catheters tend to be at increased risk for getting *C. auris* and developing an infection.
- Frequently resistant to azoles and increasing reports of echinocandin resistance
  - AST for all *C. auris* isolates should be performed
- Difficult to eradicate from environment
- Nationally notifiable in all jurisdictions (all states and local health departments)

MULTICENTER STUDY OF *C. AURIS* INFECTIONS

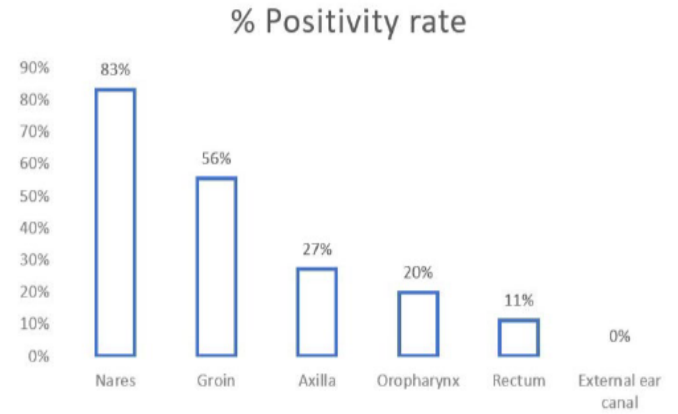
- Retrospective observational multicentre study, 10 centers, 5 countries
- Significant risk factors for *C. auris* infection include the age group of 61–70 years (39%), recent history of ICU admission (63%), diabetes (63%), renal failure (52%), presence of CVC (91%) and previous history of antibiotic treatment (96%). *C. auris* was commonly isolated from blood (76%).
- All-cause crude mortality rate after 30 days was 37%. Antifungal therapy was associated with a reduction in mortality (OR:0.27) and so was source removal (OR:0.74). Contact isolation precautions were followed in 87% patients.

Table 4. Analysis to determine the risk factors for mortality among C. *auris* cases.

Risk Factor	Group-1 (Expired Patients)	Group-2 (Patients with Other Outcome)	Odds Ratio
Renal failure	67%	40%	3.0
Congestive Heart Failure	46%	17%	4.23
Invasive ventilator	75%	63%	1.74
Haemodialysis	63%	17%	8.33
Total parenteral Nutrition	33%	13%	3.25
Central Venous Catheter	100%	83%	4.60
Candidemia	88%	67%	3.5
Bacterial co-infection	58%	40%	2.1

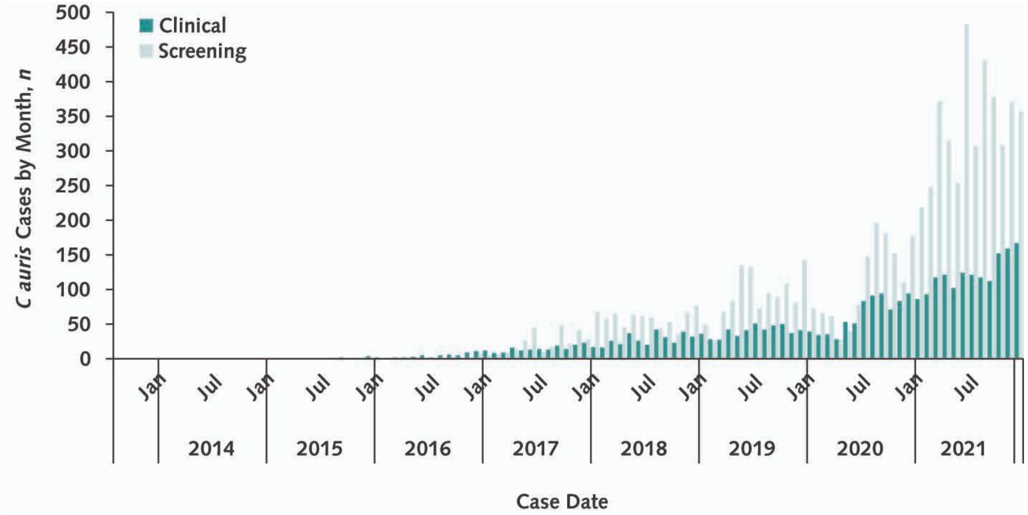
Table 2. Time from admission to positive culture.

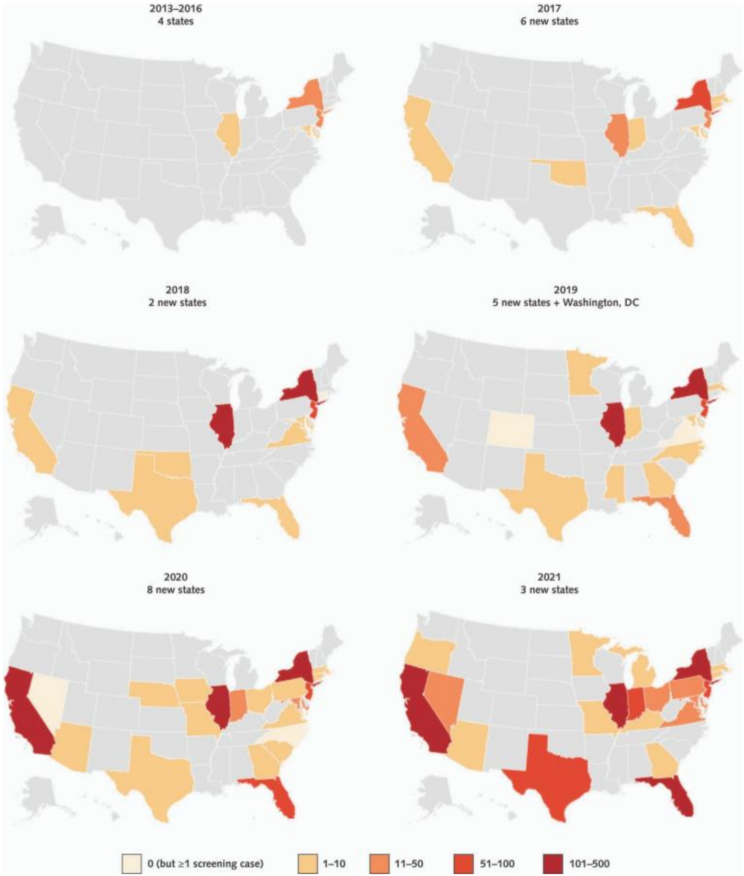
No. of Days	Patient No.	Patient %
≤2 days	5	9%
3–7 days	8	15%
8–14 days	8	15%
15–30 days	17	31%
>1 month	16	30%



Pandya N, et al. J Fungi 2021;7:878

SPREAD OF *C. AURIS*





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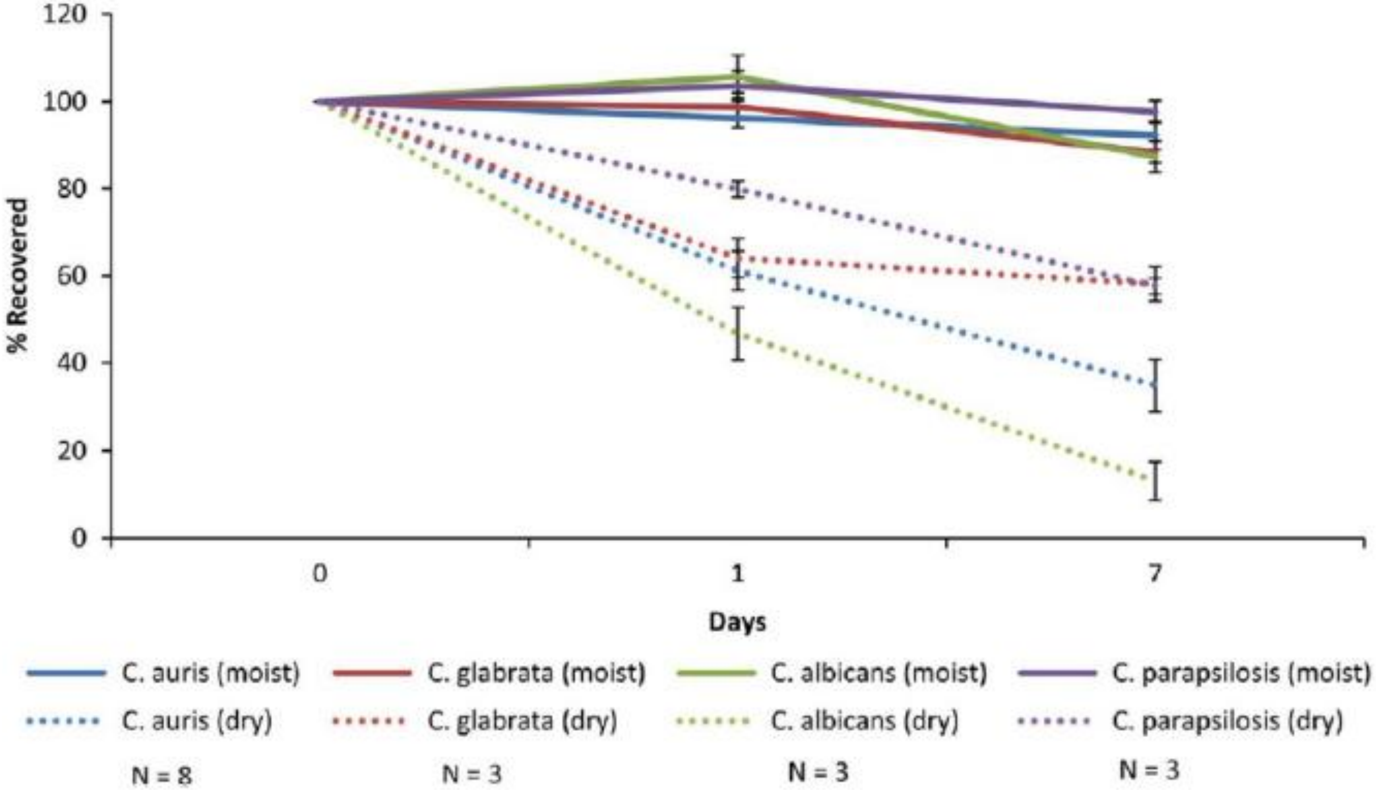
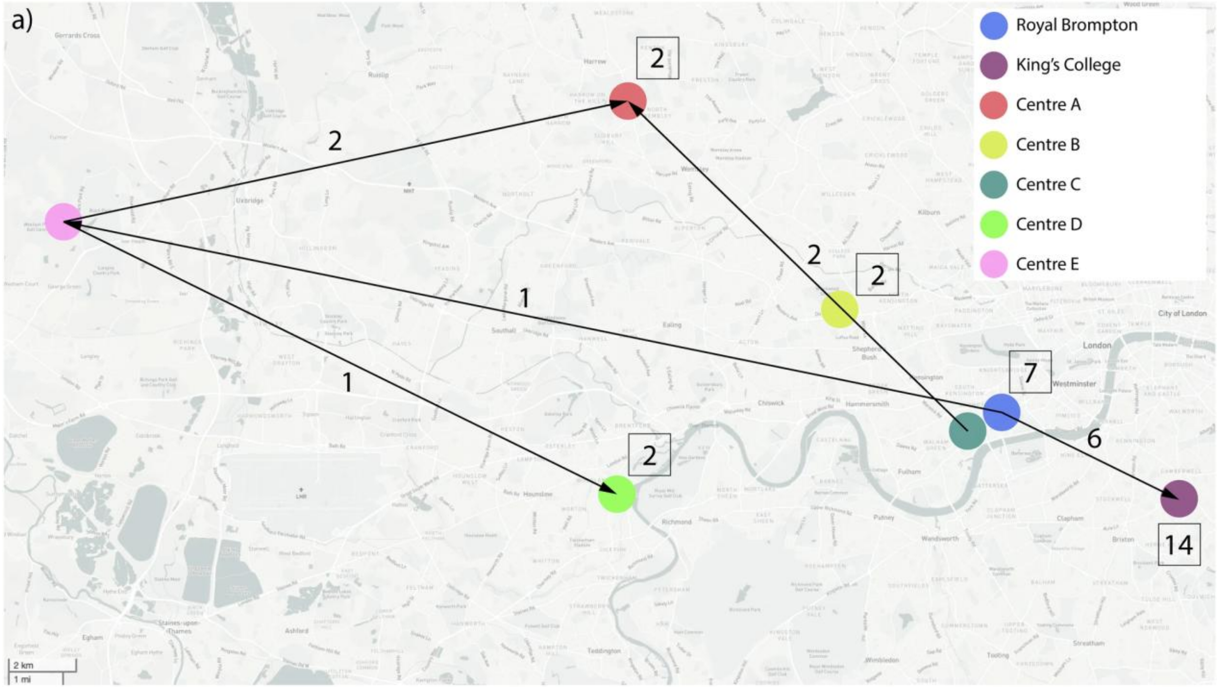
CANDIDA AURIS ENVIRONMENTAL SURVIVAL



Piedrahita C, et al. ICHE 2017;38:1107-1109

TRANSMISSION ACROSS HOSPITALS – UK STUDY



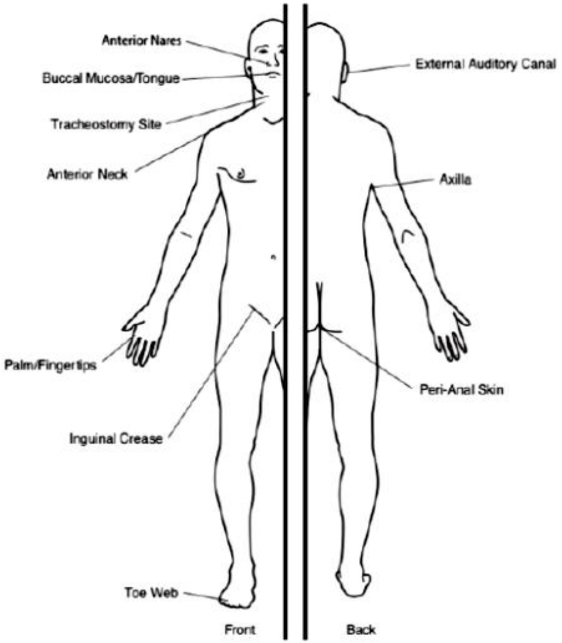
CANDIDA AURIS SCREENING APPROACHES

WHO TO SCREEN?

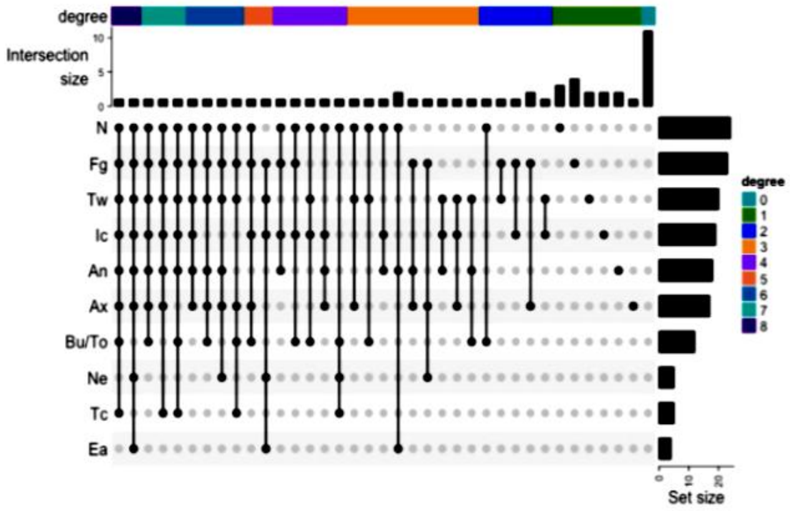
- Those with an epidemiologic link to a patient or resident who is infected or colonized with *C. auris*.
- Patients with risk factors for acquiring *C. auris:*
  - Mechanical ventilation
  - Indwelling medical devices
  - Receipt of complex or high acuity medical care
  - Frequent or long healthcare stays, especially at high-risk facilities
- Colonization or infection with other multidrug-resistant organis
- Patients with current or previous healthcare encounters at facilities including:
  - Facilities with currently suspected or confirmed *C. auris* transmission
  - High acuity post-acute care facilities including long-term acute care hospitals [LTACHs] and ventilator-capable skilled nursing facilities [vSNFs]
  - Facilities located outside the United States or in a part of the country with a high burden of *C. auris*

https://www.cdc.gov/fungal/candida-auris/c-auris-screening.html

WHAT BODY SITE TO SCREEN



Extended Data Fig. 1 | Map of sample sites.
We surveyed 10 body sites per subject, including the anterior nares (N), tracheostomy site (Tc), anterior neck (Ne), palms/fingertips (Fg), buccal mucosa/tongue (Bu/To), inguinal crease (Ic), axilla (Ax), toe web (Tw), external auditory canal (Ea), and peri-anal skin (An).



Extended Data Fig. 2 | Patterns of body site colonization visualized with UpSetR.
Colors map to degree, a measure of the number of co-colonized sizes. A total of 36 distinct co-colonization patterns were observed, each arranged from the left to the right as a function of decreasing degree. The intersection size is the number of subjects whose body-site colonization matches the points connecting sites for each of the 36 unique co-colonization patterns. For example, the nares (N) and fingertips/palm (Fg) are more frequently mono-colonized than any of the other sites while the buccal mucosa/tongue (Bu/To), neck (Ne), tracheostomy site (Tc), and external auditory canal (Ea) are never mono-colonized. Most patients have a distinct pattern of co-colonization with the most frequent pattern being singular colonization of the nares (N) or fingertips/palm (Fg). The set size corresponds to the frequency of colonization for each site for the first time point.

Proctor DM, et al. Nat Med 2021:27:1401-1409

MORE ON BODY SITES FOR SCREENING

TABLE 1

Candida auris screening activity by hospital and body site tested, England, 2017–2018 (n = 998)

Hospital ICU	Start month	End month	Total days screened	Admissions screened	Nose		Throat		Axilla		Groin		Perineum		Rectum		Urine	
			n	n	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Hospital A	May 2017	July 2017	55	154	142	92	142	92	146	95	141	92	137	89	137	89	124	81
Hospital B	June 2017	Mar 2018	284	97	90	93	0	0	90	93	80	82	80	82	80	82	46	47
Hospital C	July 2017	Sep 2017	65	76	58	76	54	71	25	33	10	13	18	24	58	76	46	61
Hospital D	July 2017	Sep 2017	64	169	133	79	133	79	135	80	28	17	134	79	129	76	112	66
Hospital E	Aug 2017	Apr 2018	267	98	76	78	0	0	76	78	72	73	72	73	72	73	55	56
Hospital F	Oct 2017	Jan 2018	92	168	143	85	0	0	143	85	135	80	135	80	135	80	116	69
Hospital G	Dec 2017	Mar 2018	81	191	180	94	177	93	177	93	172	90	169	88	0	0	163	85
Hospital H	Jan 2018	Feb 2018	23	45	28	62	28	62	27	60	0	0	28	62	27	60	22	49
Total	**NA**	**NA**	**NA**	**998**	**850**	**85**	**534**	**54**	**819**	**82**	**638**	**64**	**773**	**77**	**638**	**64**	**684**	**69**

ICU: intensive care unit; NA: not applicable.

MCW/Froedtert Hospital Surveillance Program

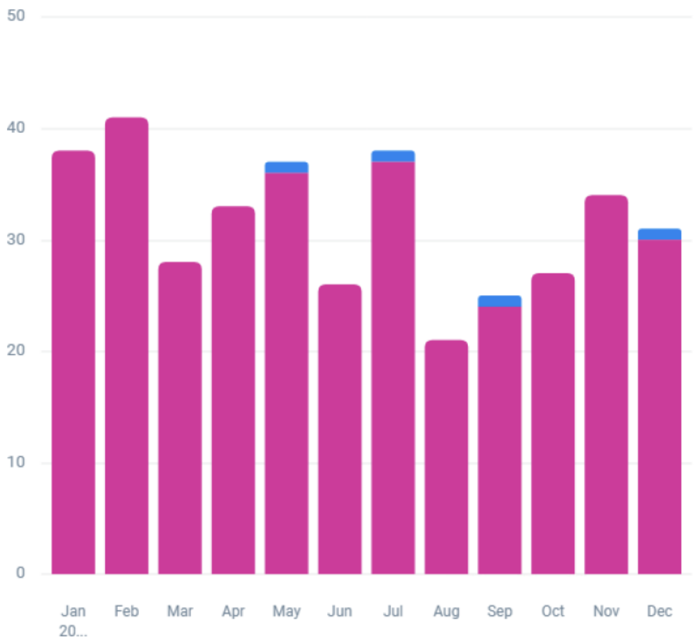
Froedtert Hospital surveillance program

Implemented ~2018
    Screen skin swab

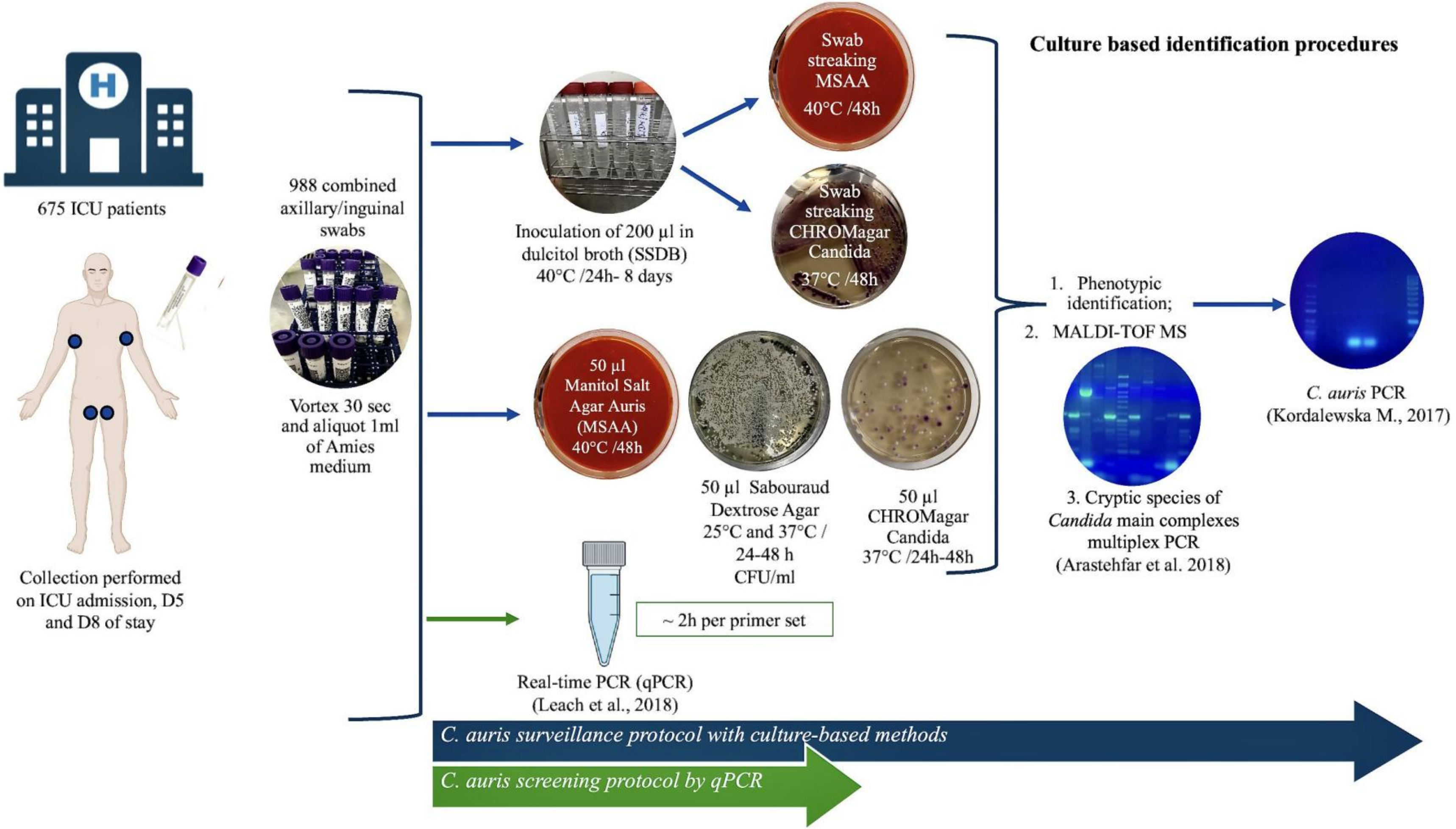
All patients admitted with surgical airway (overlap with CRAB)
Point-prevalence for hospital onset *C. auris*

Testing performed at state laboratory
    Considering need for in house testing

~30-40 cultures performed per month (significant variability)
    2024: 4 detections



SCREENING APPROACHES



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C. auris Screening Methods - Molecular

Molecular
1 FDA cleared assay (DiaSorin Simplexa *C. auris* Direct, 2024)
LDTs, ASRs also in use

Rapid, high sensitivity (>90%)/specificity (>97%)

Expensive (relatively)

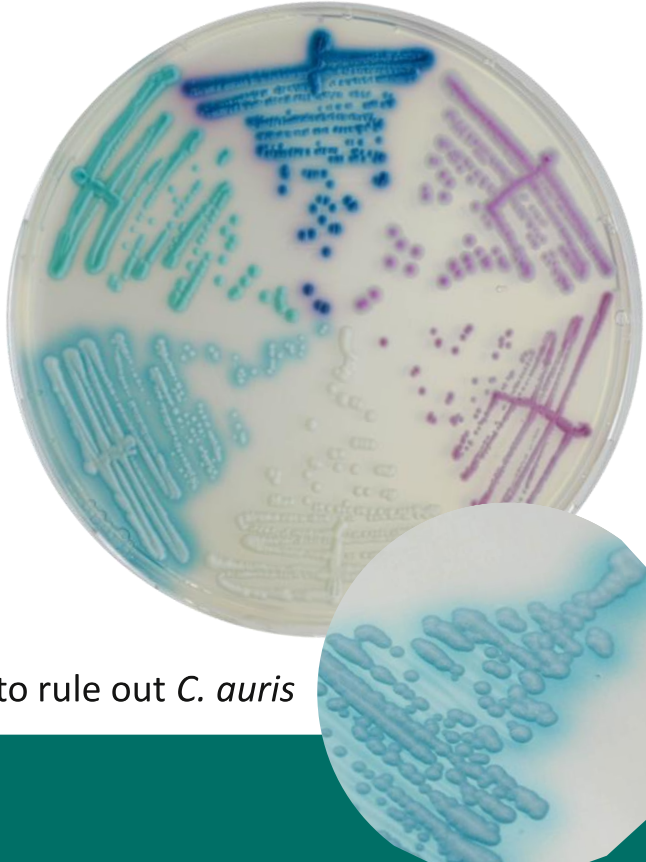
C. auris Screening Methods

Culture

No well-established conventional agar based approach

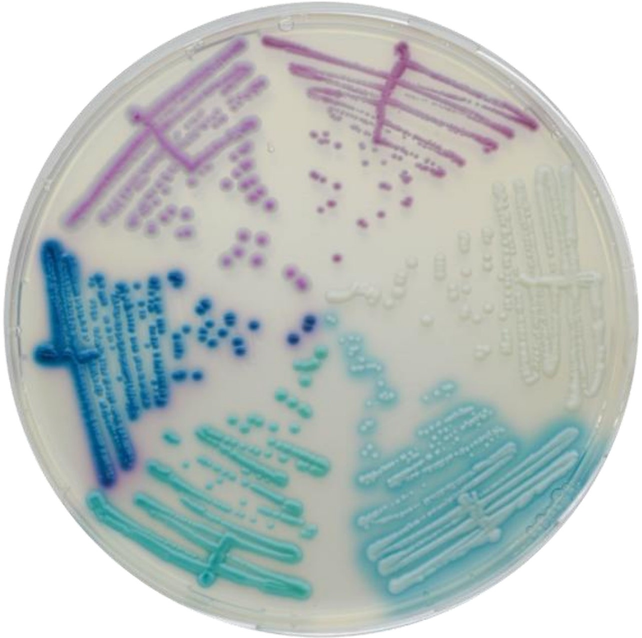
Chromogenic agar

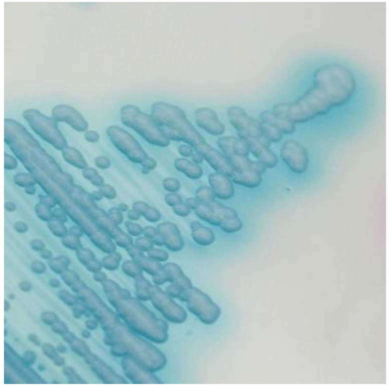
- Not all chromogenic agars support *C. auris* growth / ID
- **CHROMagar *Candida* PLUS**
  - Incubate 24-48h
  - *C. auris* light blue with blue halo; confirm by MALDI



* In areas of high risk, consider IDing ALL yeasts from routine cultures to rule out *C. auris*

CHROMagar *CANDIDA* PLUS





- *C. auris* – Light blue with blue halo
- *C. albicans* – Green-blue
- *C. tropicalis* – Metallic blue with pink halo
- *C. krusei* – Pink
- *C. glabrata* – Mauve
- Must be differentiated from CHROMagar *Candida* which does not include *C. auris*
- Recommended incubation of 24-48 h at 37^{o}C
- Confirmation of ID by MALDI or reference lab should be considered

PERFORMANCE

Table 4. Sensitivity, specificity, PPV, and PNV of CC-Plus for the most common isolated *Candida* species, compared with CC.

	Sensitivity (%)	**Specificity (%)**	**PPV (%)**	**PNV (%)**
C. albicans	99.3	100	100	99.8
C. glabrata	98.8	100	100	99.8
C. tropicalis	100	100	100	100
C. parapsilosis	100	100	100	100
C. krusei	100	100	100	100
C. auris	100	100	100	100
Total	99.5	100	100	99.1

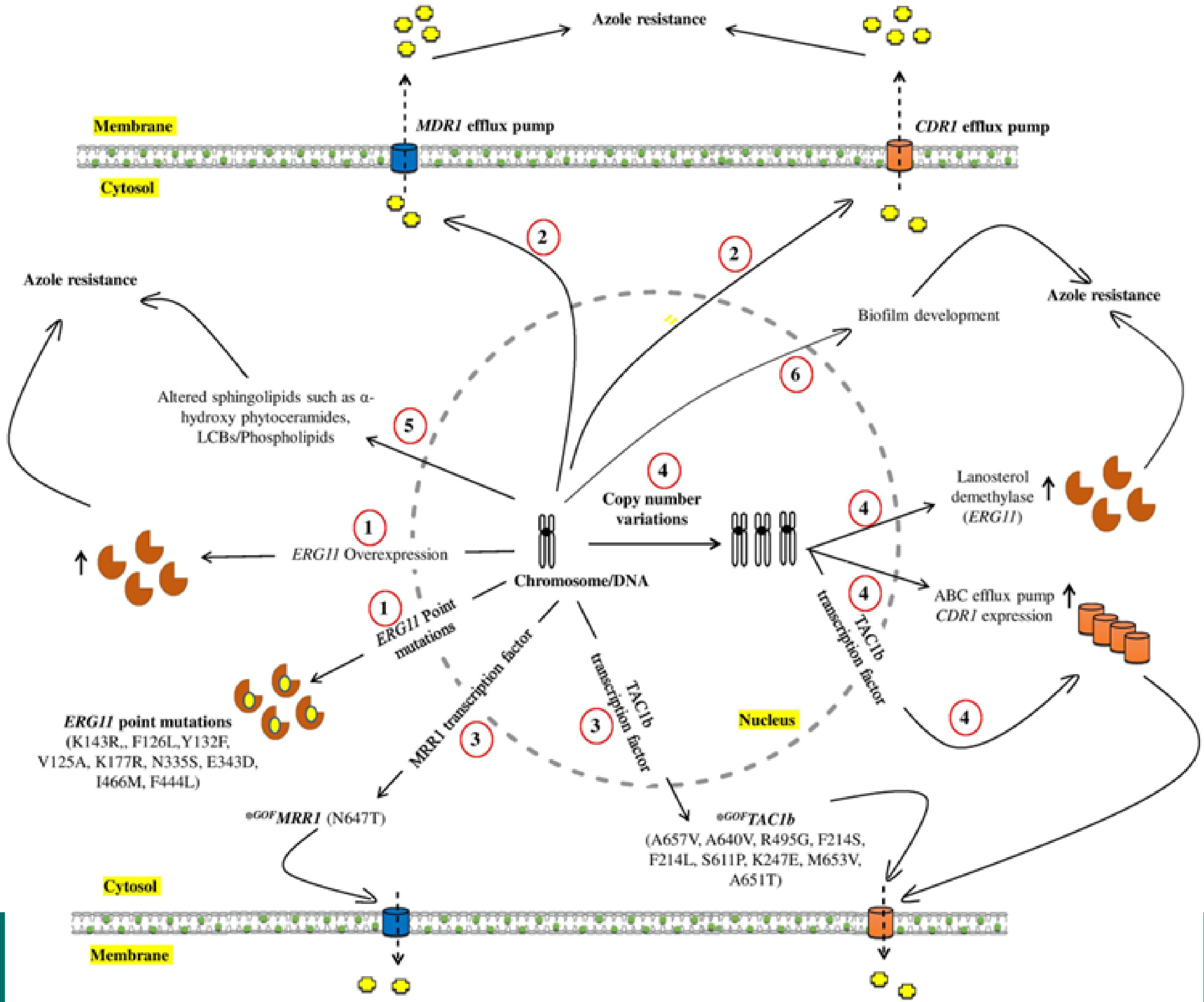
- 3 center study from Spain
- Included patient surveillance specimens and environmental specimens
- Study enriched as they selected previous positive and negative specimens

PMID 35330283

RESISTANCE AND APPROACHES FOR AST TESTING IN *CANDIDA AURIS*

MULTIPLE MECHANISMS OF RESISTANCE TO AZOLES

- Point Mutations (1)
- Overexpression of targets (ergosterol) (1 and 4)
- Efflux Pumps (2 and 3)
- Target Alteration (5)
- Biofilm formation (6)



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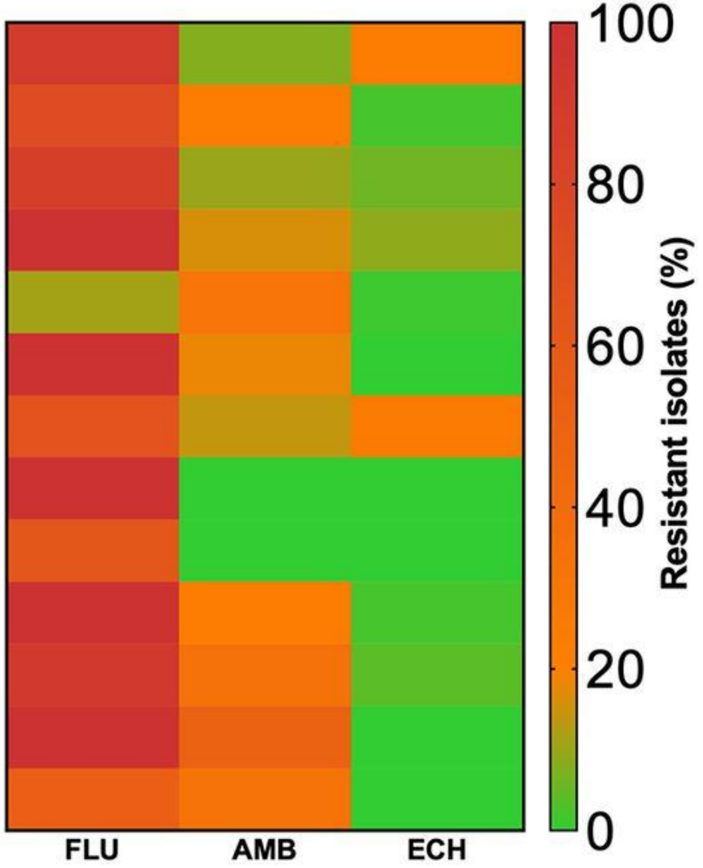
GLOBAL HEATMAP OF RESISTANCE RATES - 2019

Reference	Country (no. of isolates)	Method
(8)	India (350)	CLSI
(39)	United Kingdom[a] (119-128)	CLSI
(72)	India[*] (123)	CLSI
(11)	India (90)	CLSI
(14)	Colombia (87)	CLSI, Etest for AMB
(13)	United Kingdom[#] (73-79)	SYO
(32)	India (74)	CLSI
(10)	Spain (73)	EUCAST
(2)	Korea[#] (61)	CLSI
(9)	Kuwait (56)	Etest
(4)	Multiple[b] (54)	CLSI
(12)	Venezuela (18)	CLSI
(1)	Korea (15)	CLSI, Etest for AMB



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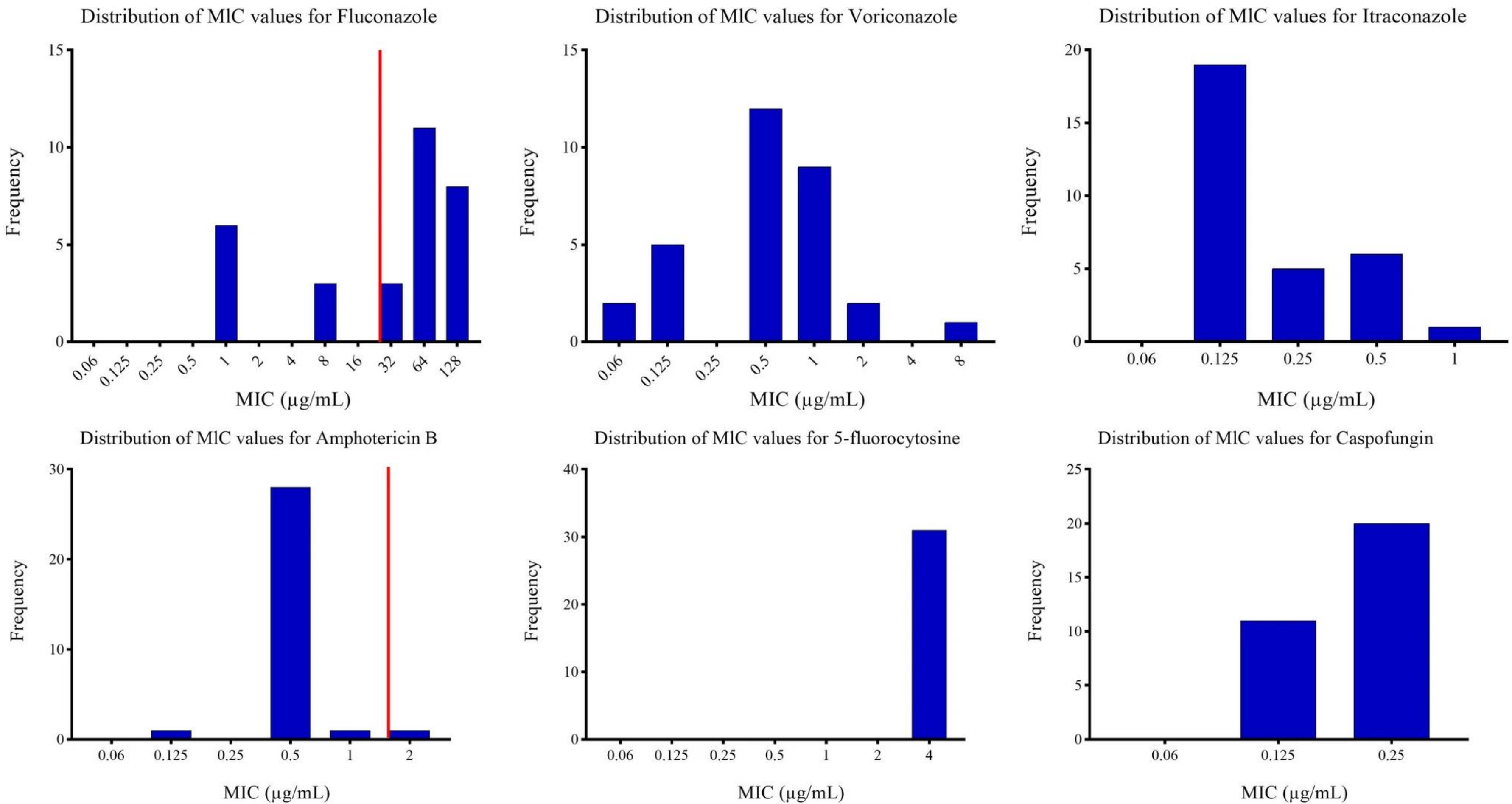
THE PROBLEM OF RESISTANCE IN *C. AURIS*



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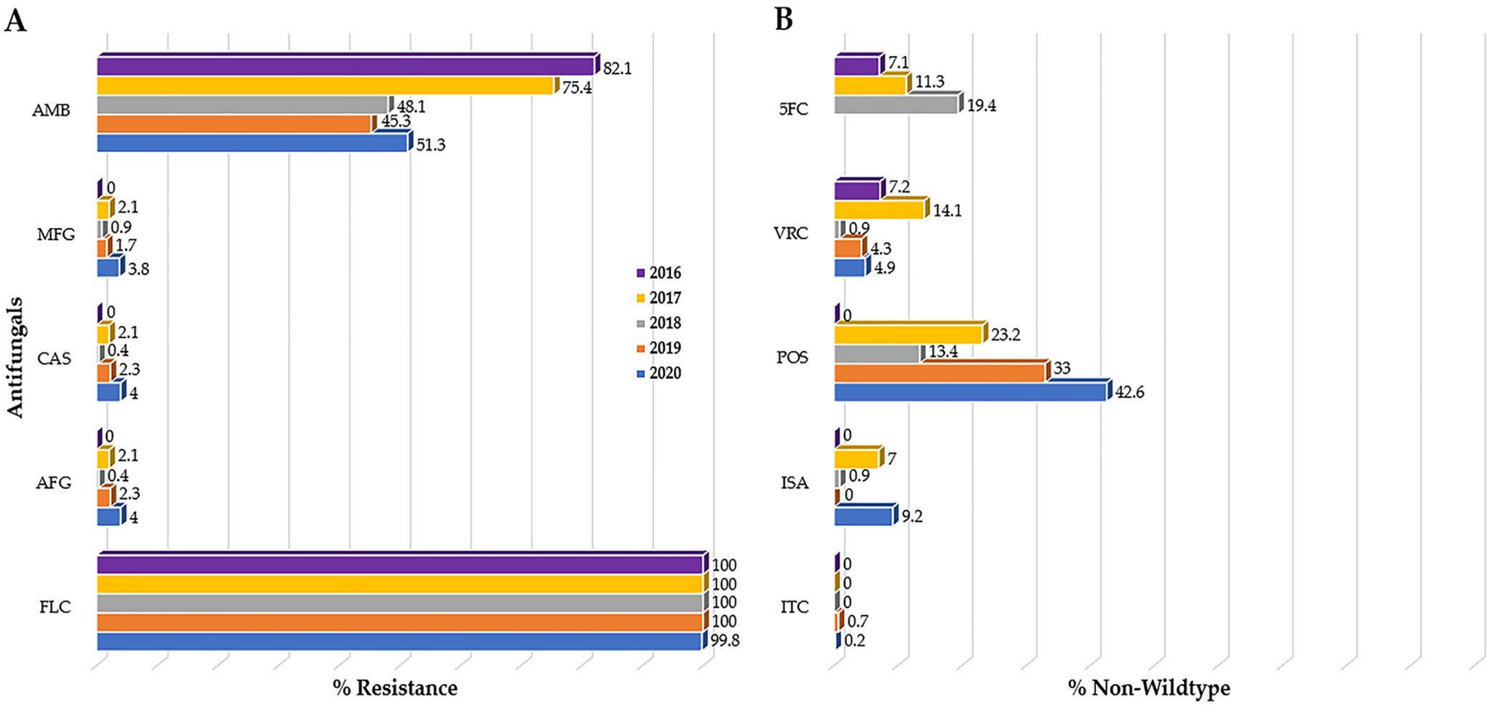
RESISTANCE IN NEW YORK AND NEW JERSEY

- Greater than ½ of US cases of *Candida auris* originate in NY or NJ
- >99% of NY-NJ cases were fluconazole resistant and >50% were AMPB resistant



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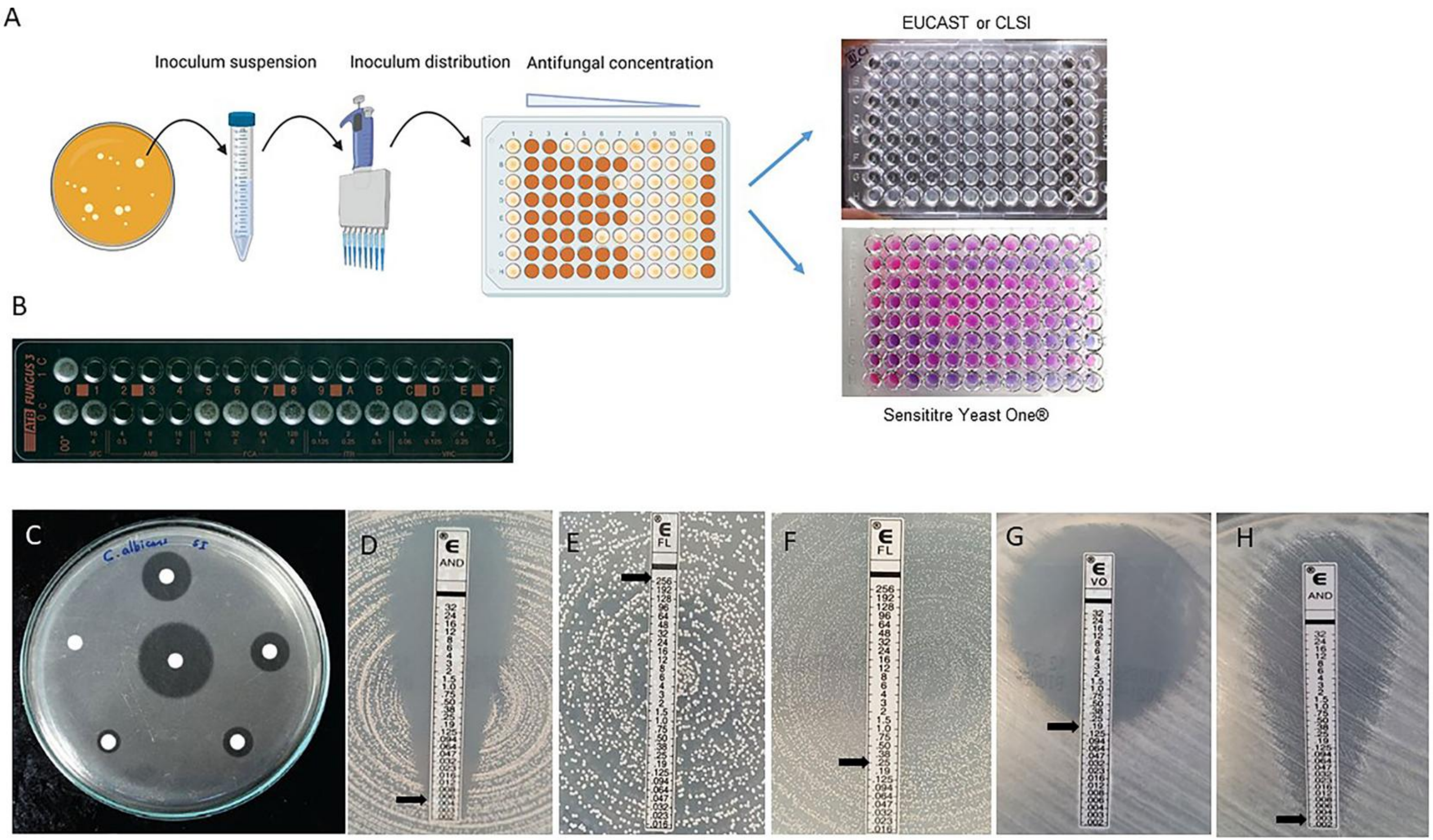
SUSCEPTIBILITY TESTING METHODS FOR *C. AURIS*



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PERFORMANCE OF CLSI MICROBROTH DILUTION VERSUS MTS

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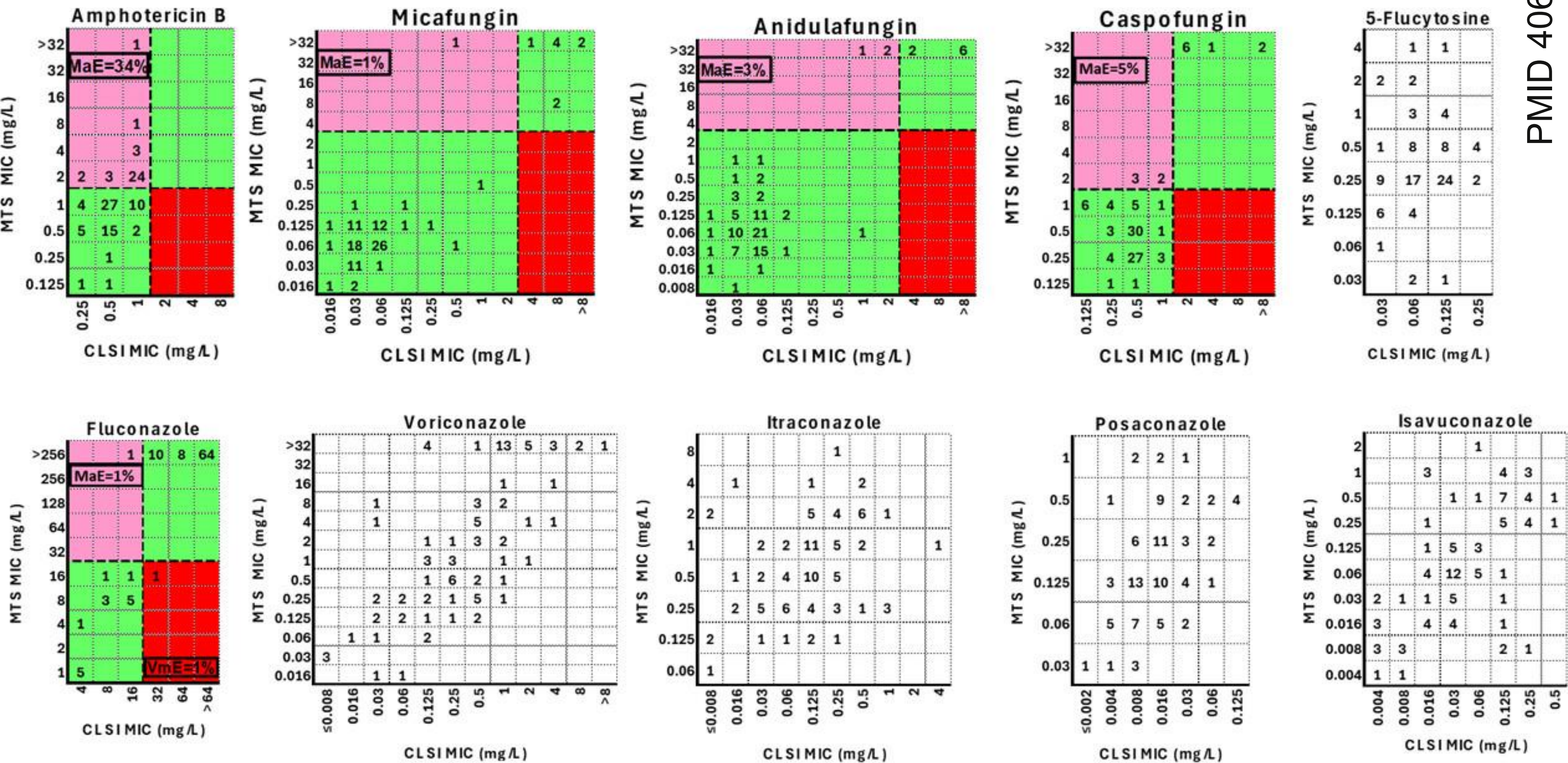

PERFORMANCE OF CLSI MICROBROTH DILUTION VERSUS MTS

Antifungal agent	Clade (No of isolates)	Modal (range) MIC (mg/L)[a] CLSI	Modal (range) MIC (mg/L)[a] MTS	Median (range) difference CLSI-MTS[b]	% agreement ±1	% agreement ±2	CDC BP (mg/L) R ≥	% CA (MaE, VmE) based on CDC BP
Amphotericin B	All (100)	0.5 (0.25–1)	1 (0.125–>32)	1 (−2 to 6)	85%	96%	2	66% (34%, 0%)
	I (47)	1 (0.25–1)	2 (0.25–>32)	1 (−1 to 6)	83%	91%	2	32% (68%, 0%)
	II (3)	0.25 (0.25–0.5)	0.125 (0.125–0.5)	−1 (−2 to 1)	67%	100%	2	100% (0%, 0%)
	III (23)	0.5 (0.25–0.5)	0.5 (0.5–1)	1 (0 to 2)	83%	100%	2	100% (0%, 0%)
	IV (22)	0.5 (0.5–1)	1 (0.5–2)	1 (−1 to 2)	95%	100%	2	96% (4%, 0%)
	V (5)	0.5 (0.5–1)	0.5 (0.5–2)	0 (−1 to 2)	80%	100%	2	80% (20%, 0%)
Micafungin	All (100)	0.03 (0.016–>8)	0.06 (0.016–>32)	1 (−3 to 7)	77%	91%	4	99% (1%, 0%)
	I (47)	0.03 (0.016–>8)	0.125 (0.016–>32)	1 (−3 to 7)	55%	81%	4	98% (2%, 0%)
	II (3)	0.03 (0.03–0.03)	0.03 (0.016–0.03)	0 (−1 to 0)	100%	100%	4	100% (0%, 0%)
	III (23)	0.03 (0.03–0.06)	0.06 (0.03–0.125)	0 (−1 to 2)	96%	100%	4	100% (0%, 0%)
	IV (22)	0.06 (0.03–0.06)	0.06 (0.06–0.125)	0 (0 to 1)	100%	100%	4	100% (0%, 0%)
	V (5)	0.03 (0.03–0.06)	0.06 (0.016–0.125)	0 (−1 to 2)	80%	100%	4	100% (0%, 0%)
Voriconazole	All (100)	0.5/1 (≤0.008–>8)	>32 (0.016–>32)	2 (−2 to 9)	31%	52%	NA	ND
	I (47)	0.5 (≤0.008–>8)	0.25 (0.03–>32)	2 (−2 to 9)	40%	70%	NA	ND
	II (3)	0.125 (≤0.008–0.125)	ND[c] (0.03–2)	3 (2 to 4)	0%	33%	NA	ND
	III (23)	1 (0.03–8)	>32 (0.5–>32)	6 (−1 to 9)	9%	13%	NA	ND
	IV (22)	1/2/4 (0.03–4)	>32 (0.06–32)	2 (−1 to 6)	41%	55%	NA	ND
	V (5)	0.125 (0.03–0.125)	0.016 (0.016–>32)	2 (−2 to 9)	20%	60%	NA	ND
Isavuconazole	All (100)	0.03 (0.004–0.5)	0.06 (0.004–2)	1 (−5 to 6)	58%	82%	NA	ND
	I (47)	0.125 (0.004–0.5)	0.016 (0.004–2)	1 (−4 to 6)	57%	79%	NA	ND
	II (3)	ND[c] (0.004–0.25)	ND[c] (0.004–1)	1 (0 to 2)	67%	100%	NA	ND
	III (23)	0.03 (0.0160.06)	0.06 (0.03–0.5)	1 (0 to 3)	61%	91%	NA	ND
	IV (22)	0.125 (0.03–0.5)	0.5 (0.06–1)	1 (0 to 3)	59%	86%	NA	ND
	V (5)	0.016 (0.004–0.25)	0.008/1 (0.008–1)	1 (−5 to 6)	40%	40%	NA	ND

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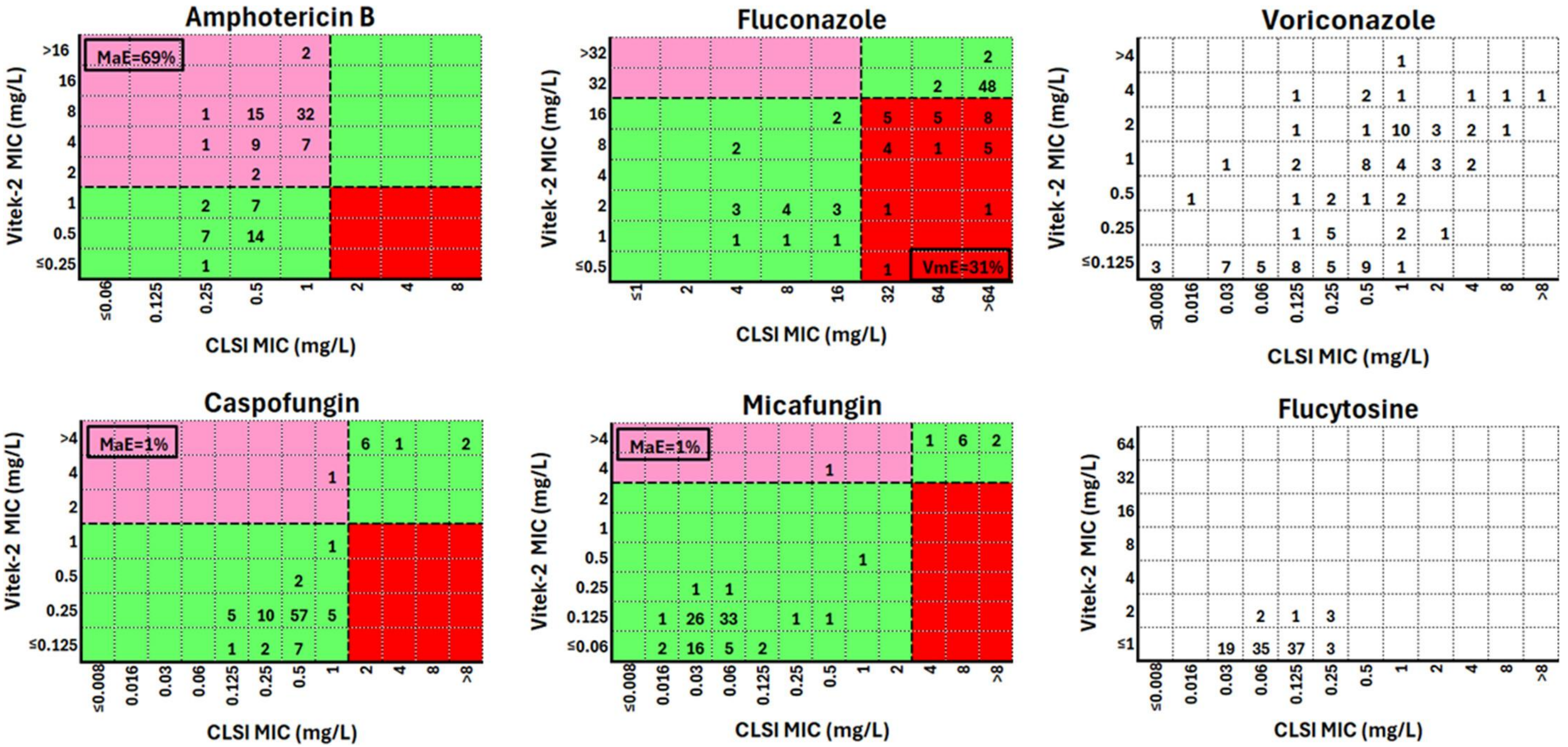
PERFORMANCE OF CLSI MICROBROTH DILUTION VERSUS VITEK 2



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CLSI VS EUCAST VS YEASTONE

Table 3. Quantitative agreement among MIC results via CLSI, EUCAST and SYO methods

	EUCAST versus CLSI				EUCAST versus SYO				CLSI versus SYO			
	Agreement within 2-fold dilutions			EA %	Agreement within 2-fold dilutions			EA%	Agreement within 2-fold dilutions			EA%
Drug	0	±1	±2		0	±1	±2		0	±1	±2	
AMB	8	12	2	100	9	10	3	100	7	13	2	100
AFG	4	15	3	100	3	10	8	95	9	7	6	100
CAS	—	—	—	—	—	—	—	—	3	7	7	77
FLC	10	8	4	100	1	12	8	95	4	12	4	91
5-FC	9	11	2	100	2	6	6	64	3	6	3	55
ISA	—	—	—	—	—	—	—	—	—	—	—	—
ITC	3	16	2	95	5	13	3	95	9	10	2	95
MFG	5	15	2	100	11	10	1	100	12	6	3	95
POS	3	13	4	91	7	10	3	91	7	12	1	91
VRC	11	8	1	91	7	11	2	91	9	9	3	95
IBF	8	6	4	82	—	—	—	—	—	—	—	—
MGPX	13	7	1	95	—	—	—	—	—	—	—	—
RZF	5	9	6	91	—	—	—	—	—	—	—	—
Overall				95				91				89

PMID 40110552

INTERPRET AMPHOTERICIN B WITH CARE

Table 1
Overview of amphotericin B MICs against 40 *Candidia auris* isolates obtained by EUCAST and CLSI reference methods, and by Etest and MTS gradient strips

Test method	MIC (mg/L)										% "R"	GM-MIC	Total
	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16			
Reference methods													
EUCAST ISO-1					15	25[a]					0%	0.77	40
EUCAST ISO-2				1	15	24[a]					0%	0.74	40
EUCAST serial					14	26[a]					0%	0.78	40
CLSI medium #1					7	22[a]	11				28%	1.07	40
CLSI medium #2					1	36[a]	3				8%	1.04	40
Etest													
One swab inoc, consecutive testing	1	5[b]	5[b]	3	7	9[a]	8	1		1	25%	0.51	40
One swab inoc, batched testing				11[b]	4	13[a]	12				30%	0.78	40
Two swab inoc 24 h person R1					3	6	17[a]	1			45%	0.82	40
Two swab inoc 24 h person R2				9[b]	6	4	15[a]	6			53%	1.37	40
Two swab inoc 24 h person R3			1	11[b]	3	2	14[a]	9			58%	1.05	40
Two swab inoc 48 h person R1				1	13[b]	2	15[a]	9			60%	1.74	40
Two swab inoc 48 h person R2					13[b]	2	6	18[a]	1		63%	1.07	40
Two swab inoc 48 h person R3					11[b]	4	5	18[a]	2		63%	1.87	40
MTS													
MTS		2	10[b]	0	1	10	14[b]	2			41%	0.69	39

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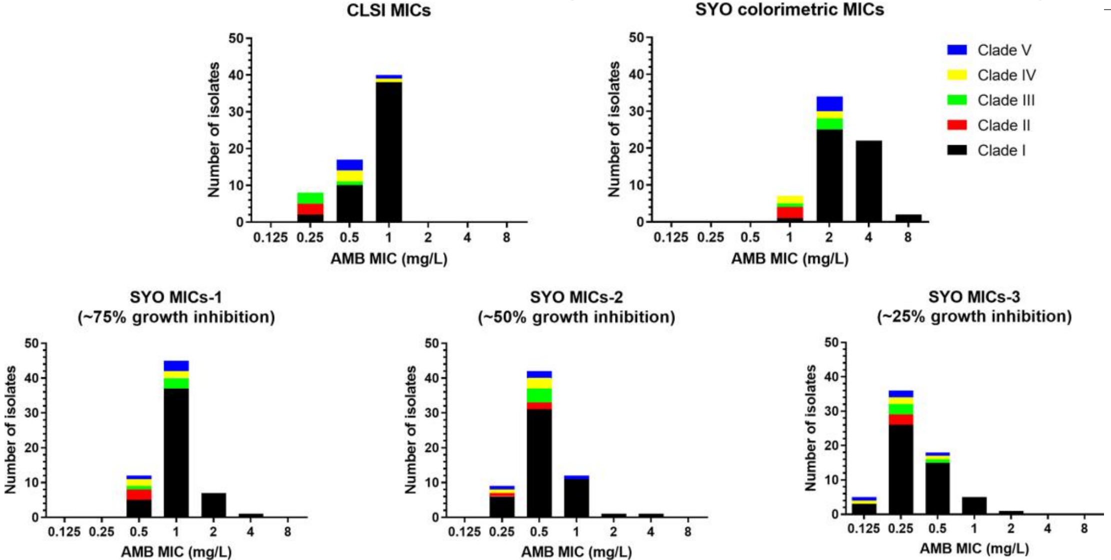

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SUMMARY

- Screening is not limited to MRSA and CRE, may be a role for screening for organisms like CRAB and *C. auris*
- The incidence of *C. auris* is increasing exponentially along with resistance to common antifungals
- Screening for *C. auris* using chromogenic media may offer an economical and rapid option for clinical laboratories to offer a locally performed test
- Rapid AST testing of *C. auris* isolates causing clinically significant infections is essential
- Overall, excellent agreement between commercial and reference methods for *C. auris* AST methods