Convegno internazionale
GIORNATE INFETTIVOLOGICHE «LUIGI SACCO» 2018

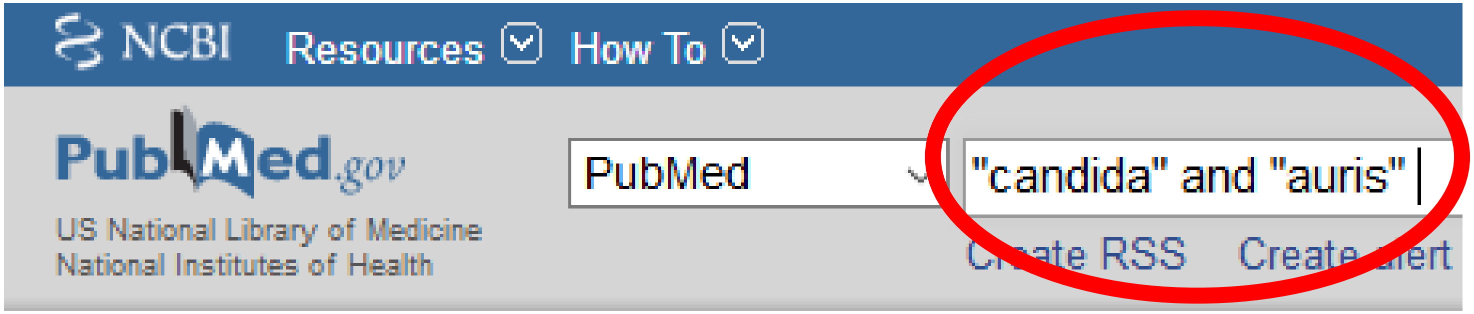
Candida auris:

un nuovo *multidrug-resistant yeast*

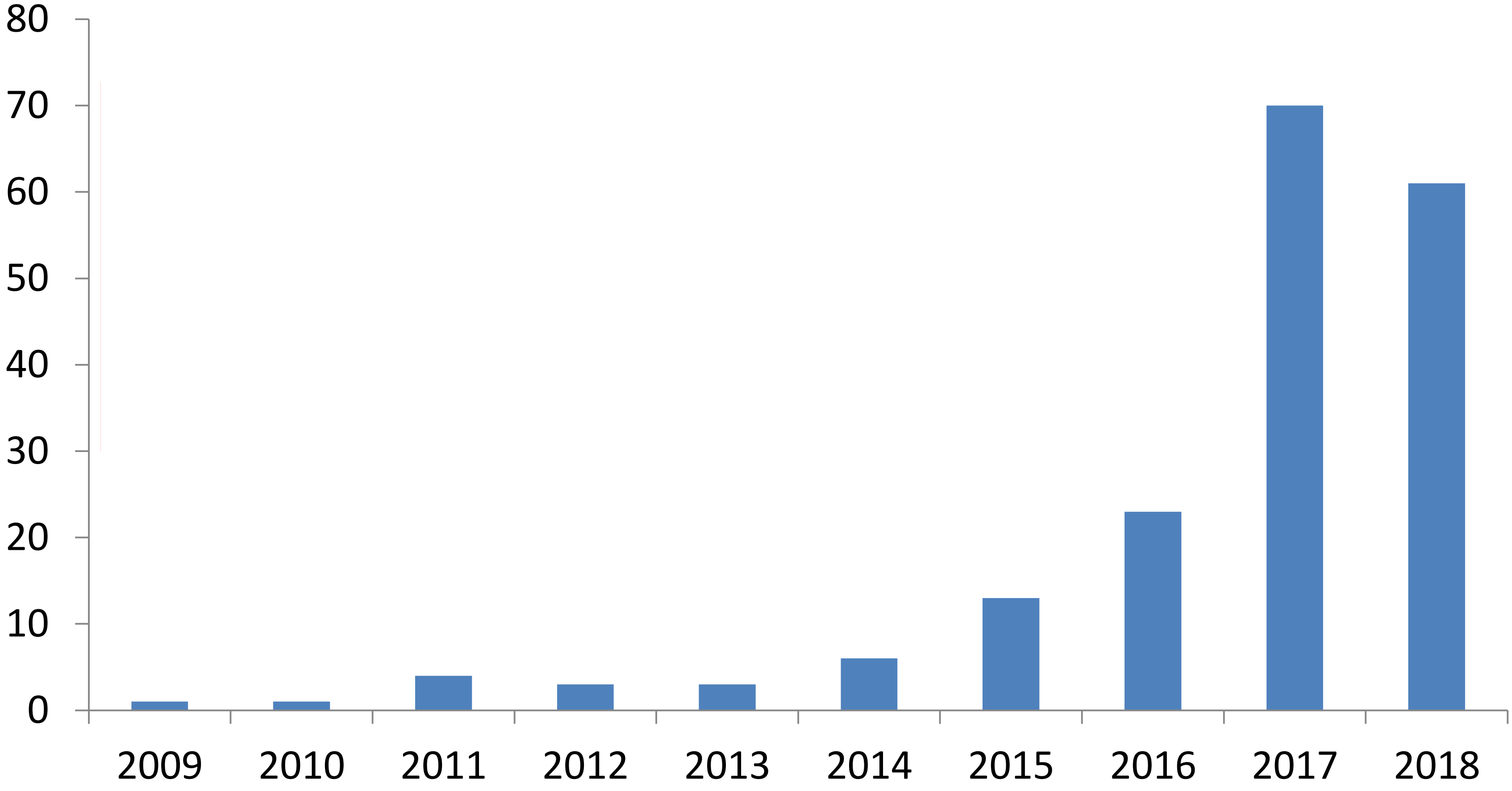
Francesco Barchiesi

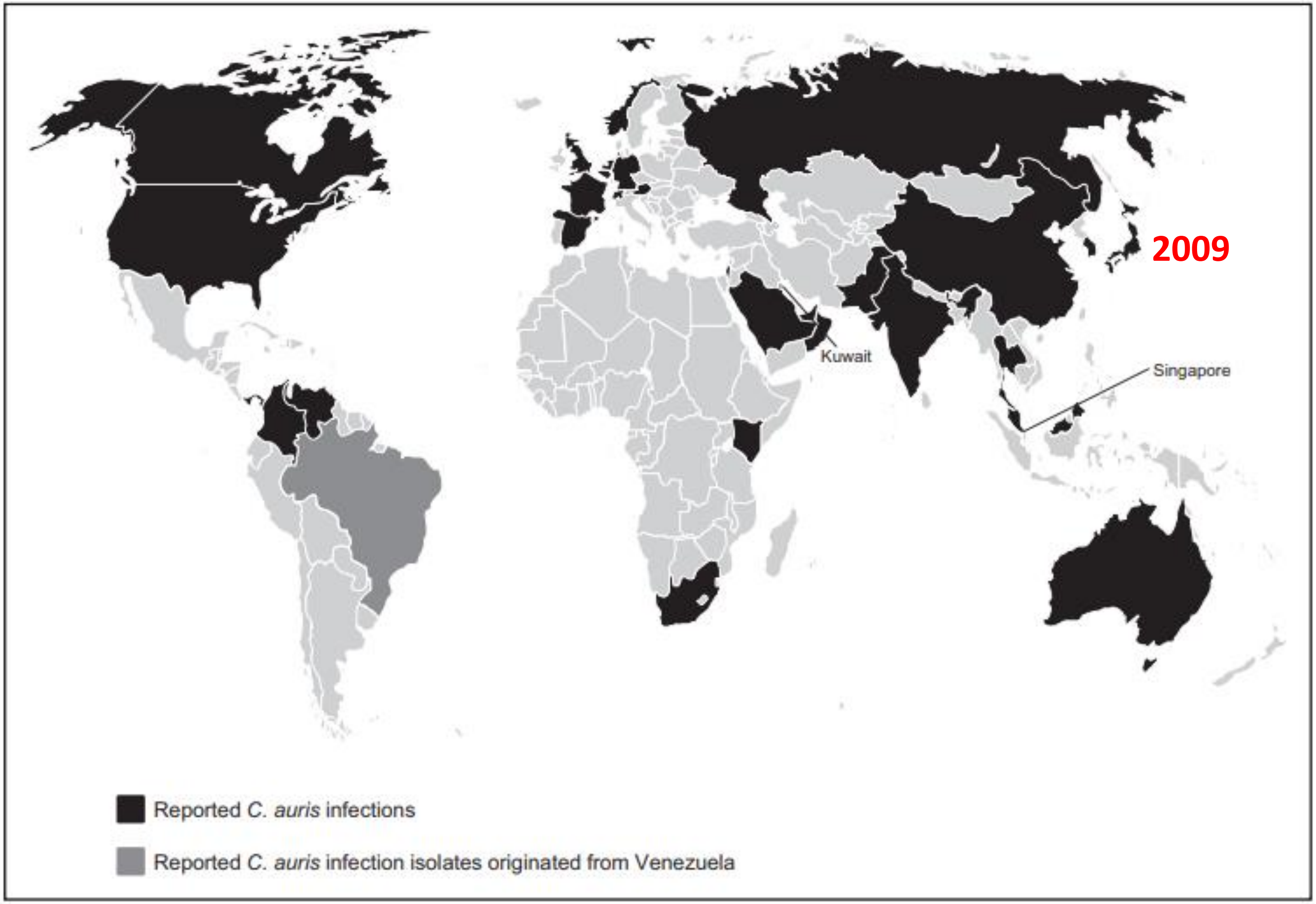
Dipartimento di Scienze Biomediche e Sanità Pubblica
Università Politecnica delle Marche;

Malattie Infettive, Azienda Ospedaliera – Ospedali Riuniti
Marche Nord, Pesaro



"candida" and "auris"





■ Reported *C. auris* infections

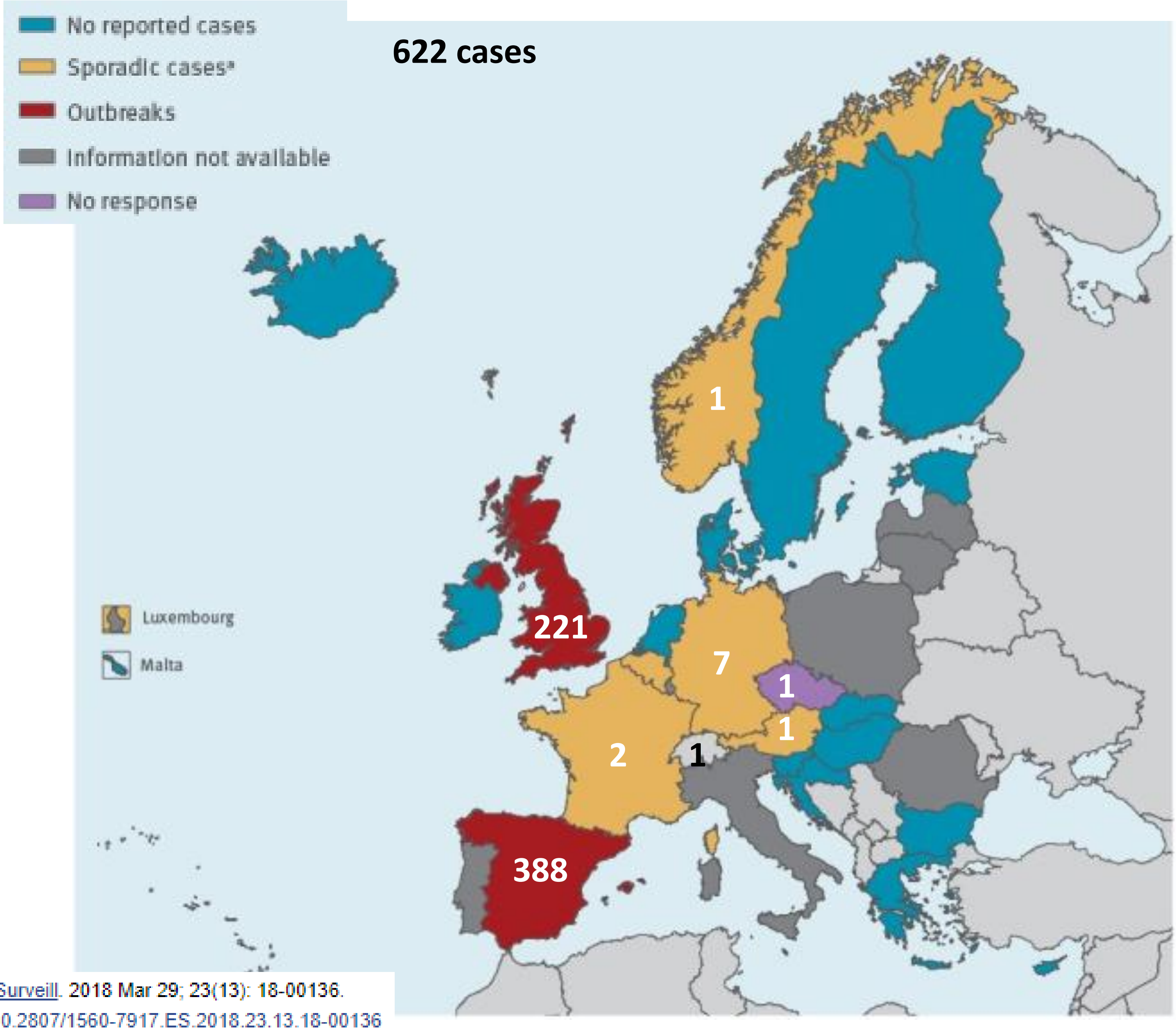
■ Reported *C. auris* infection isolates originated from Venezuela

Candida auris.

Saris K, Meis JF, Voss A.

Curr Opin Infect Dis. 2018 Jun 6.

622 cases



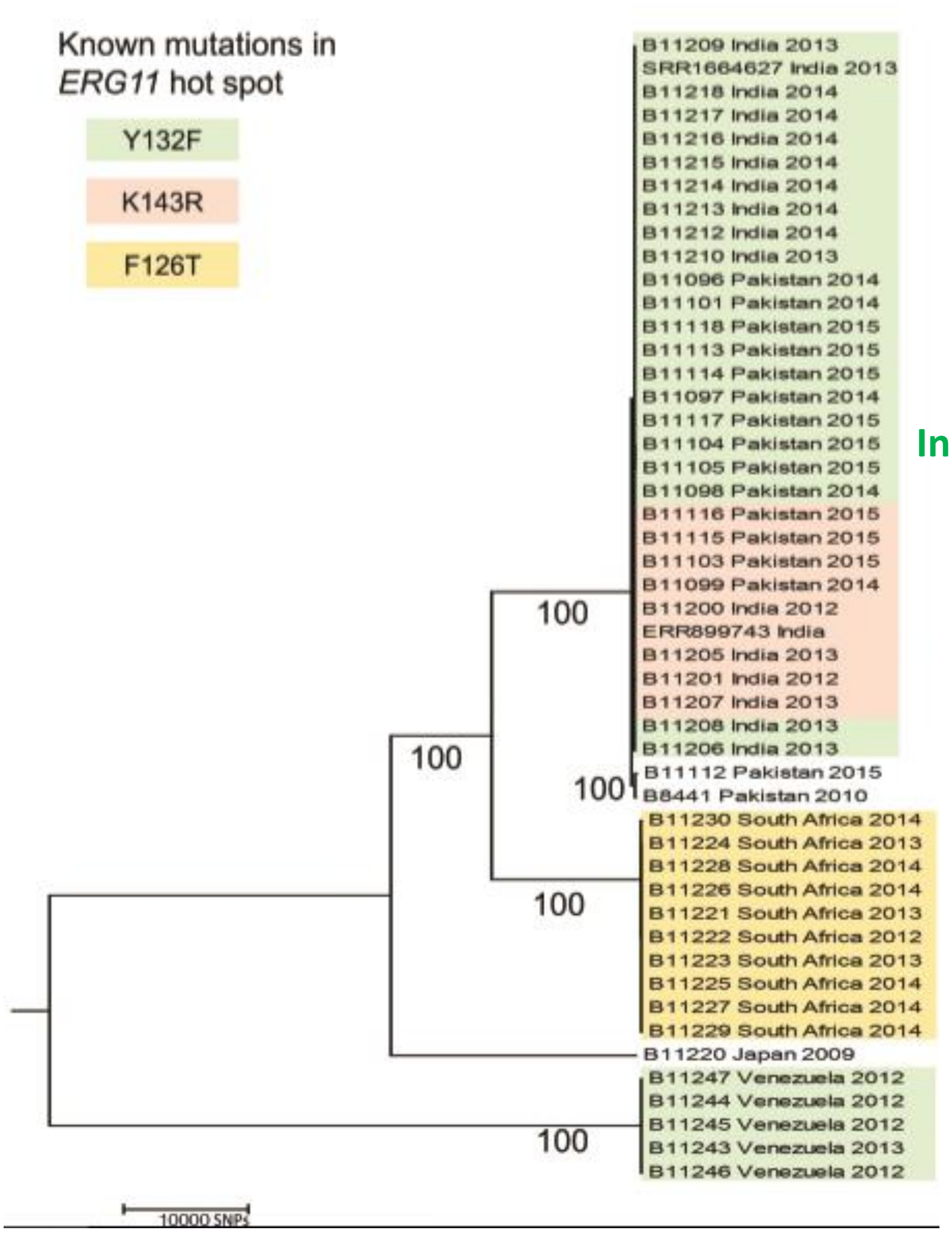
Euro Surveill. 2018 Mar 29; 23(13): 18-00136.
doi: 10.2807/1560-7917.ES.2018.23.13.18-00136

Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses

Shawn R. Lockhart,[1] Kizee A. Etienne,[1] Snigdha Vallabhaneni,[1] Joveria Farooqi,[4] Anuradha Chowdhary,[6] Nelesh P. Govender,[7] Arnaldo Lopes Colombo,[8] Belinda Calvo,[9] Christina A. Cuomo,[2] Christopher A. Desjardins,[2] Elizabeth L. Berkow,[1] Mariana Castanheira,[3] Rindidzani E. Magobo,[7] Kauser Jabeen,[4] Rana J. Asghar,[5] Jacques F. Meis,[10,11] Brendan Jackson,[1] Tom Chiller,[1] and Anastasia P. Litvintseva[1]

- 54 patients with *C. auris* infection *(Pakistan, India, South Africa, Venezuela)*
- 2012-2015
- BSIs: 61% *(17% urine, 5% respiratory tract, 17% other)*
- Median age 54 years (7% neonates)
- Predisposing conditions: similar to those usually found in invasive candidiasis *(41% DM, 51% recent surgery, 73% CVC, 41% receiving AT, 24% steroid, 15% ST)*
- Median time after admission: 19 days
- Overall crude mortality 59% *(68% BSIs)*

Clinical Infectious Diseases, 2017;64(2):134–40



India-Pakistan

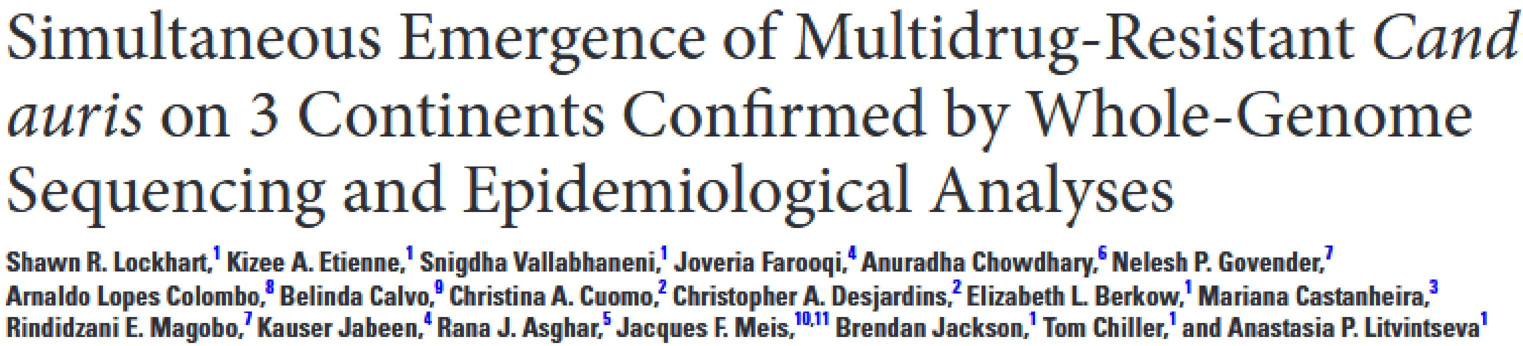
South-Africa

East Asia

Venezuela

4 distinct clades representing each geographical region

Clinical Infectious Diseases, 2017;64(2):134–40



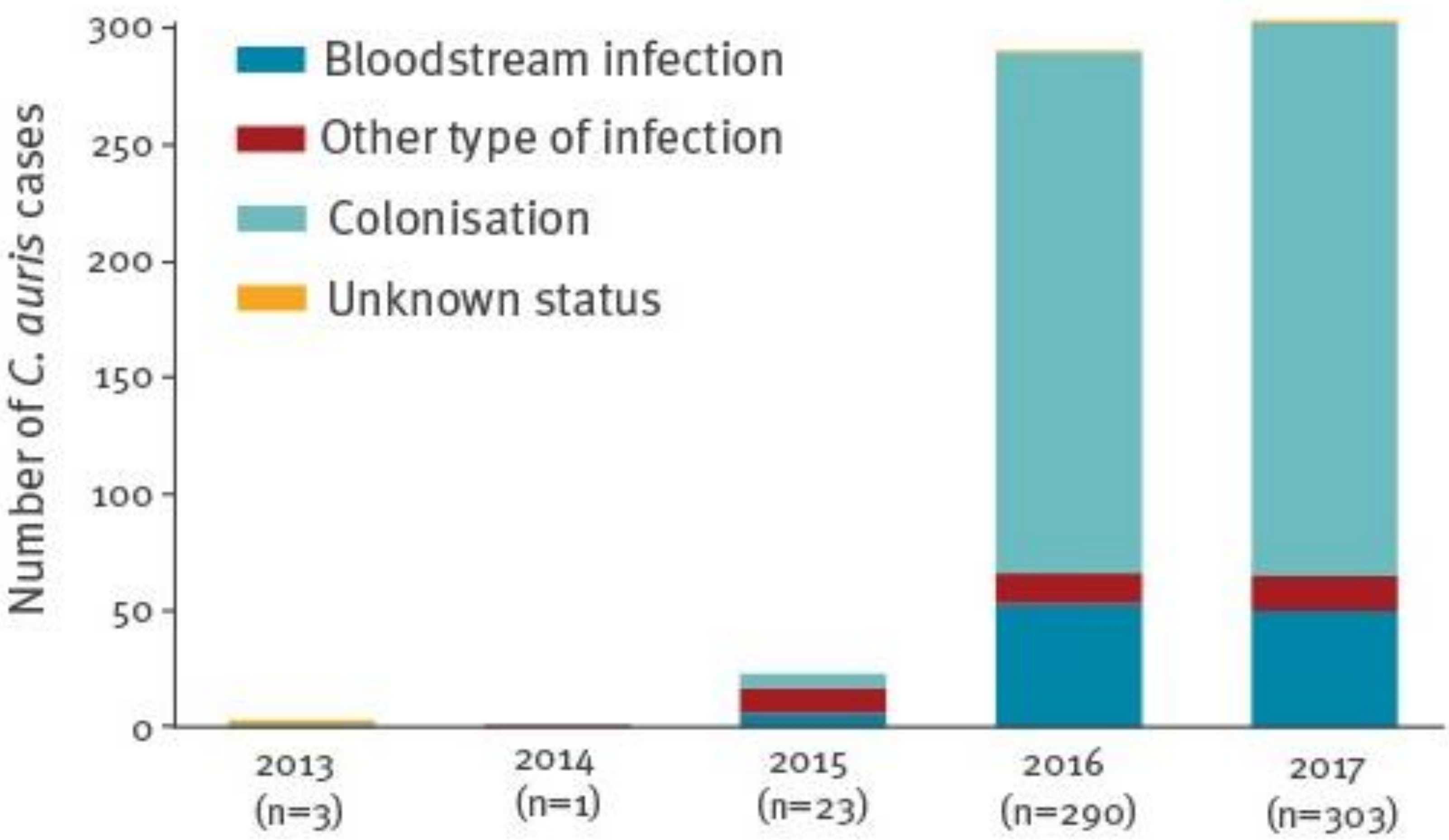
Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses

Shawn R. Lockhart,[1] Kizee A. Etienne,[1] Snigdha Vallabhaneni,[1] Joveria Farooqi,[4] Anuradha Chowdhary,[6] Nelesh P. Govender,[7] Arnaldo Lopes Colombo,[8] Belinda Calvo,[9] Christina A. Cuomo,[2] Christopher A. Desjardins,[2] Elizabeth L. Berkow,[1] Mariana Castanheira,[3] Rindidzani E. Magobo,[7] Kauser Jabeen,[4] Rana J. Asghar,[5] Jacques F. Meis,[10,11] Brendan Jackson,[1] Tom Chiller,[1] and Anastasia P. Litvintseva[1]

Resistant to Fluconazole:	93%
Resistant to Voriconazole:	54%
Resistant to Amphotericin B:	35%
Resistant to Echinocandins:	7%
Resistant to Flucytosine:	6%
Resistant to ≥ 2 Classes (MDR):	41%

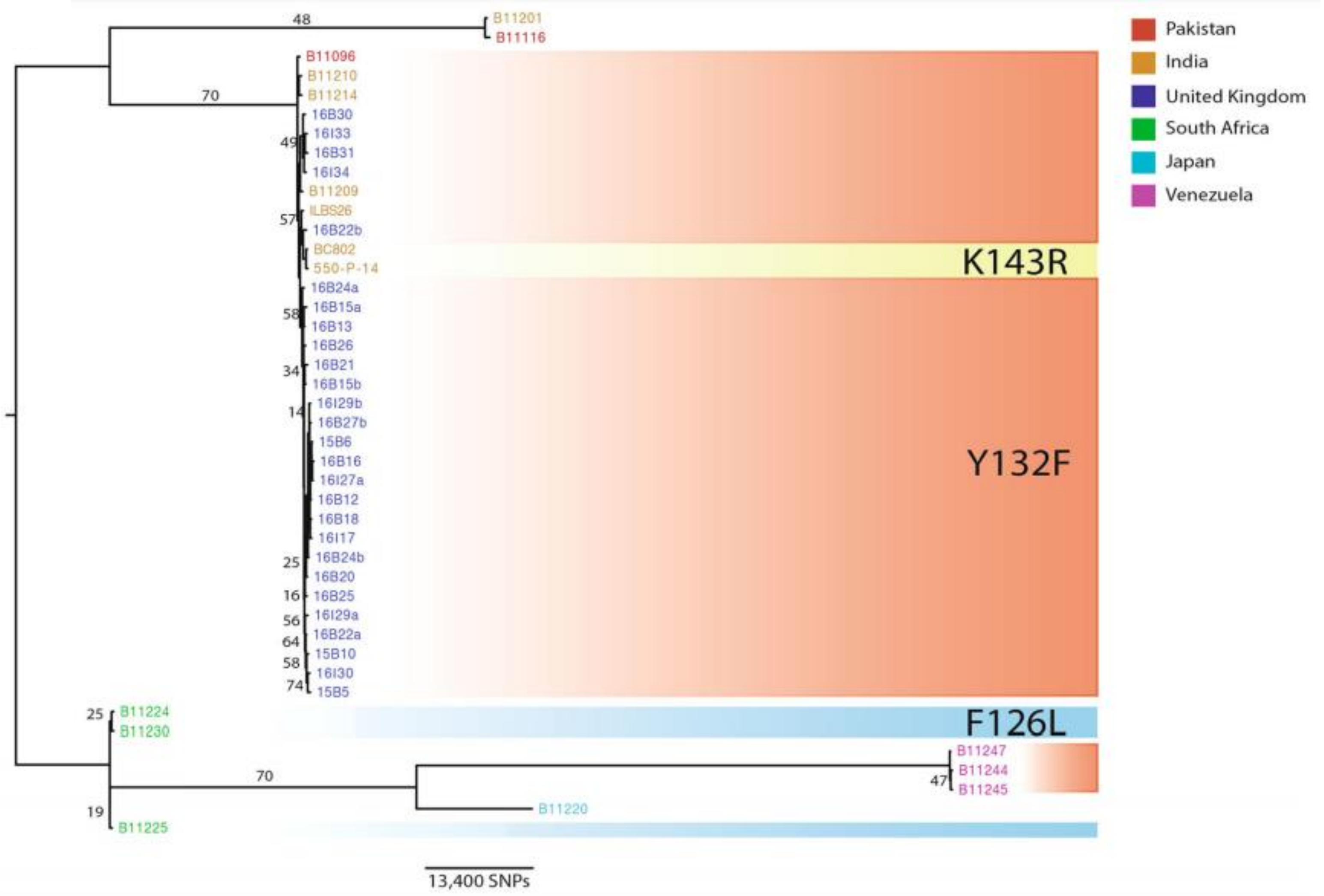
Clinical Infectious Diseases, 2017;64(2):134–40

Candida auris: epidemiological situation, laboratory capacity and preparedness in European Union and European Economic Area countries, 2013 to 2017



Euro Surveill. 2018 Mar 29; 23(13): 18-00136.
doi: 10.2807/1560-7917.ES.2018.23.13.18-00136

Genomic epidemiology of the UK outbreak of the emerging human fungal pathogen *Candida auris*



Rhodes et al. *Emerging Microbes & Infections* (2018)7:43

Candida auris candidaemia in Indian ICUs: analysis of risk factors

- 1400 cases of candidemia in 27 ICUs across India (2011-2012)

- 74 pts (5.4%) infected with *C. auris*

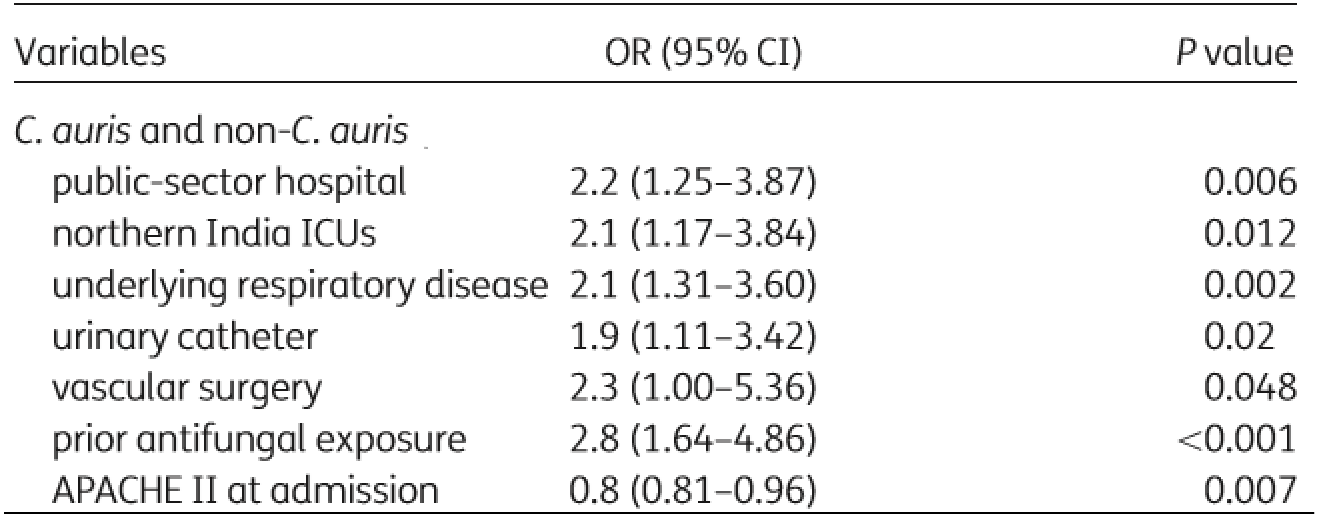
- 30-d-crude-mortality: 42%
  - *C. albicans* 37%
  - *C. tropicalis* 35%
  - *C. parapsilosis* 32%
  - *C. krusei* 24%
  - *C. glabrata* 43%

- Antifungal resistance:
  - Fluconazole 58%
  - Voriconazole 3%
  - Itraconazole 4%
  - Amphotericin B 14%
  - Caspofungin 10%
  - MDR 16%

J Antimicrob Chemother. 2017 Jun 1;72(6):1794-1801.

Candida auris candidaemia in Indian ICUs: analysis of risk factors

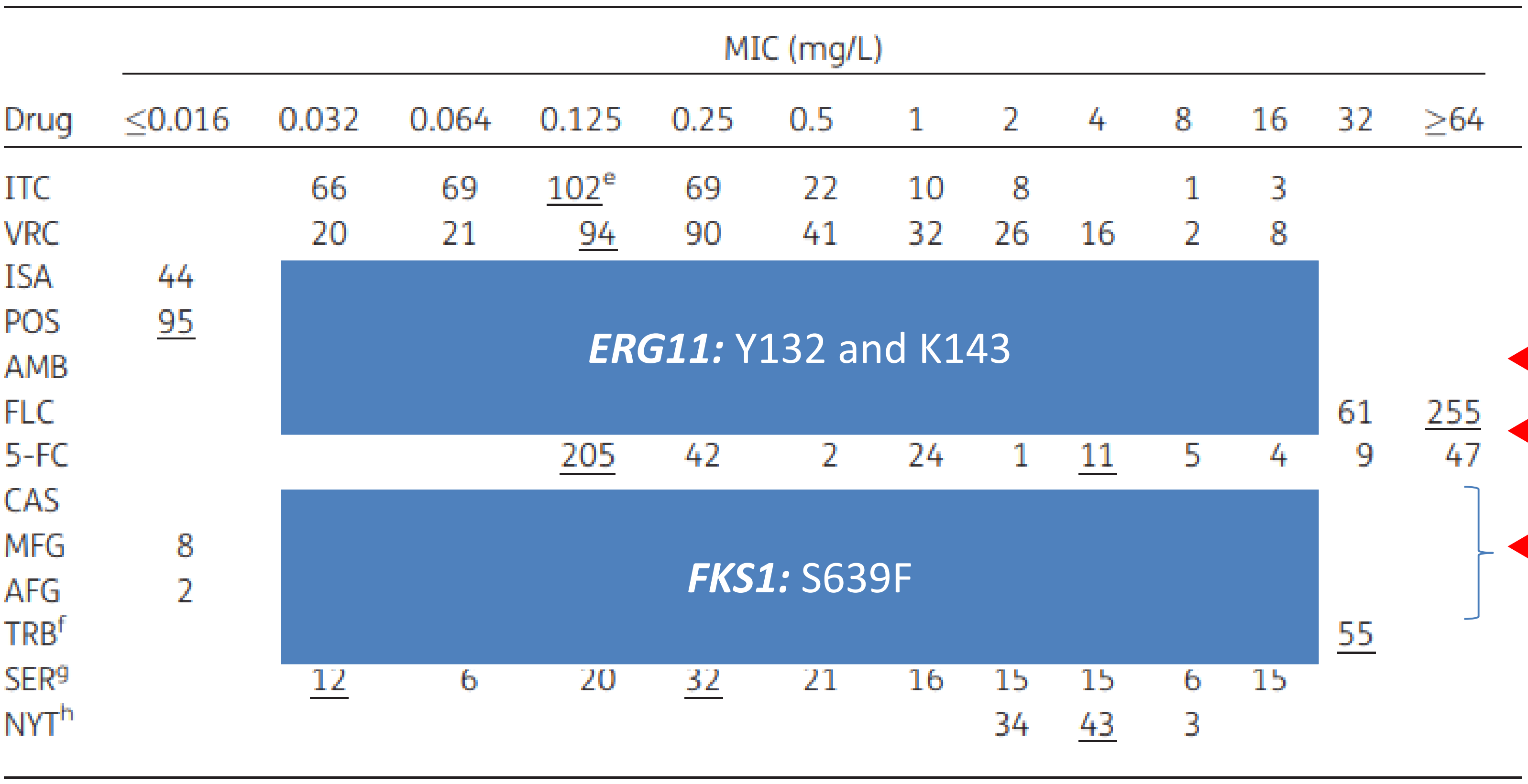
Multivariate analysis of *C. auris* and non-*auris* candidaemia cases



Variables	OR (95% CI)	*P* value
C. auris and non-*C. auris*		
public-sector hospital	2.2 (1.25–3.87)	0.006
northern India ICUs	2.1 (1.17–3.84)	0.012
underlying respiratory disease	2.1 (1.31–3.60)	0.002
urinary catheter	1.9 (1.11–3.42)	0.02
vascular surgery	2.3 (1.00–5.36)	0.048
prior antifungal exposure	2.8 (1.64–4.86)	<0.001
APACHE II at admission	0.8 (0.81–0.96)	0.007

J Antimicrob Chemother. 2017 Jun 1;72(6):1794-1801.

A multicentre study of antifungal susceptibility patterns among 350 *Candida auris* isolates (2009–17) in India: role of the *ERG11* and *FKS1* genes in azole and echinocandin resistance



	MIC (mg/L)											
Drug	≤0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	≥64
ITC		66	69	102^{e}	69	22	10	8		1	3		
VRC		20	21	94	90	41	32	26	16	2	8		
ISA	44												
POS	95												
AMB													
FLC												61	255
5-FC				205	42	2	24	1	11	5	4	9	47
CAS													
MFG	8												
AFG	2												
TRB^{f}												55	
SER^{g}		12	6	20	32	21	16	15	15	6	15		
NYT^{h}								34	43	3			

ERG11: Y132 and K143

FKS1: S639F

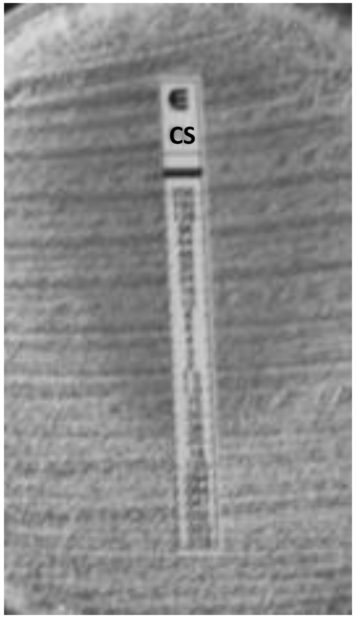
8%

90%

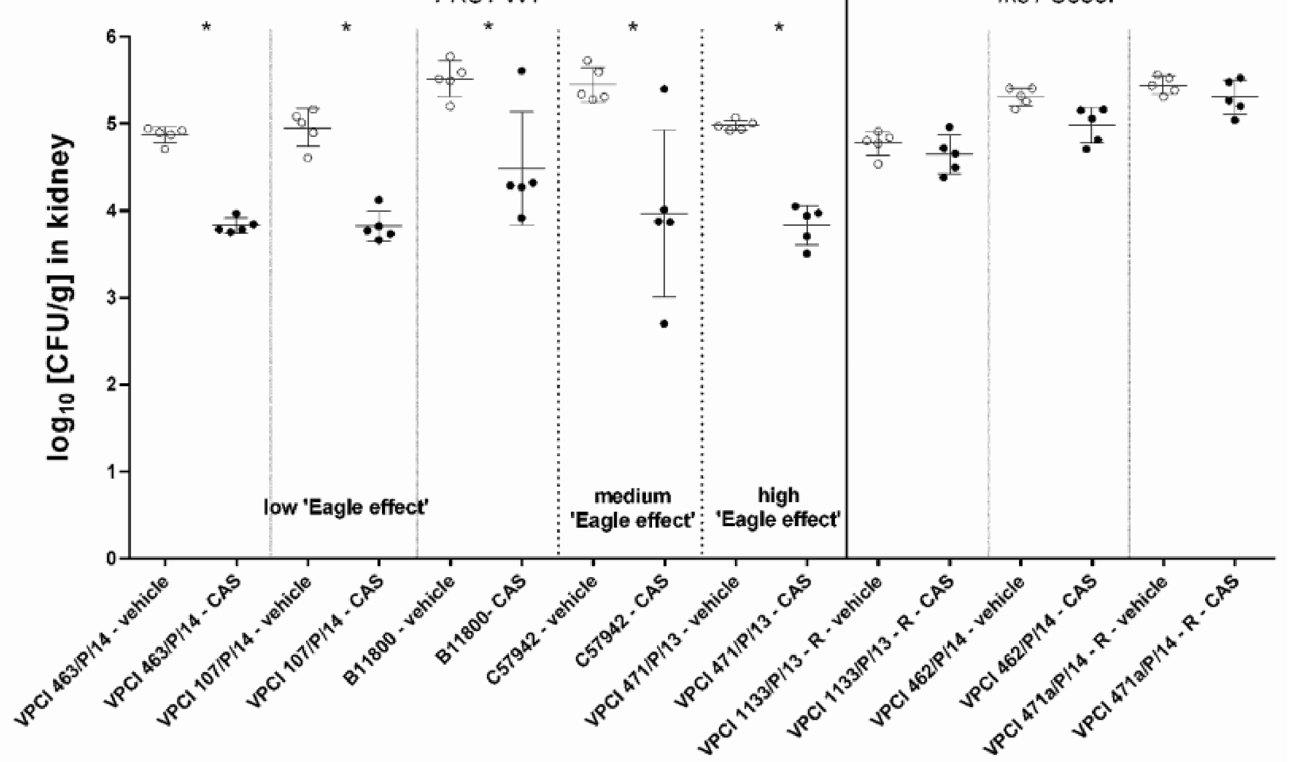
2%

J Antimicrob Chemother. 2018 Apr 1;73(4):891-899. doi: 10.1093/jac/dkx480.

Understanding echinocandin resistance in the emerging pathogen *Candida auris*



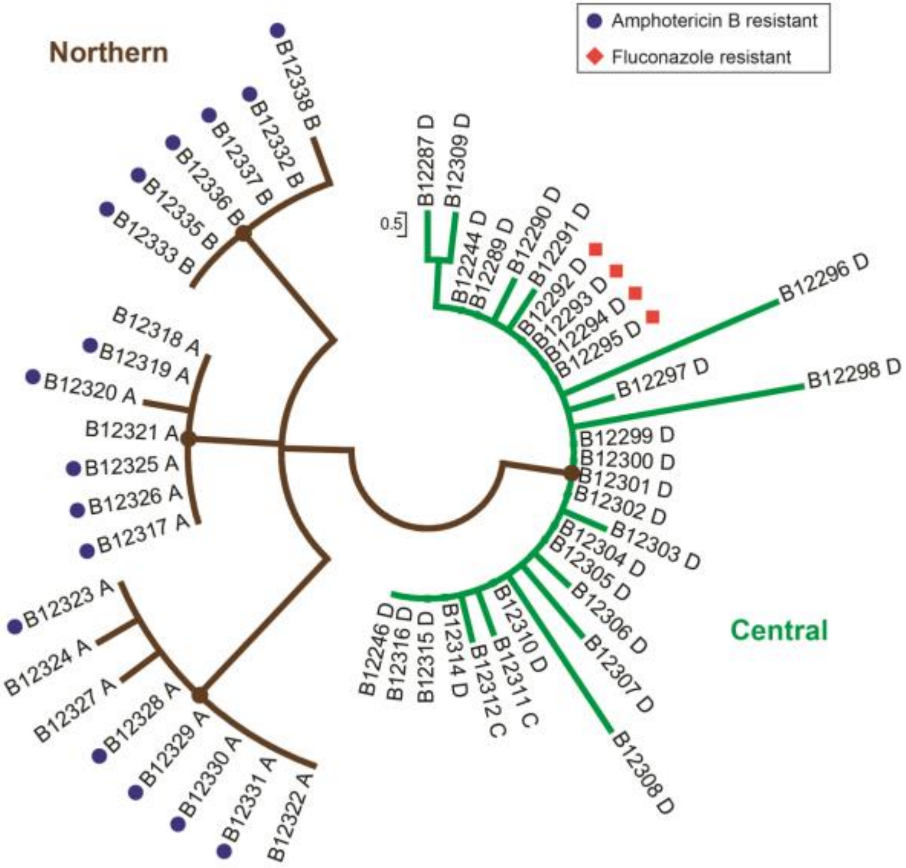
Kidney burdens at 24 h post-infection



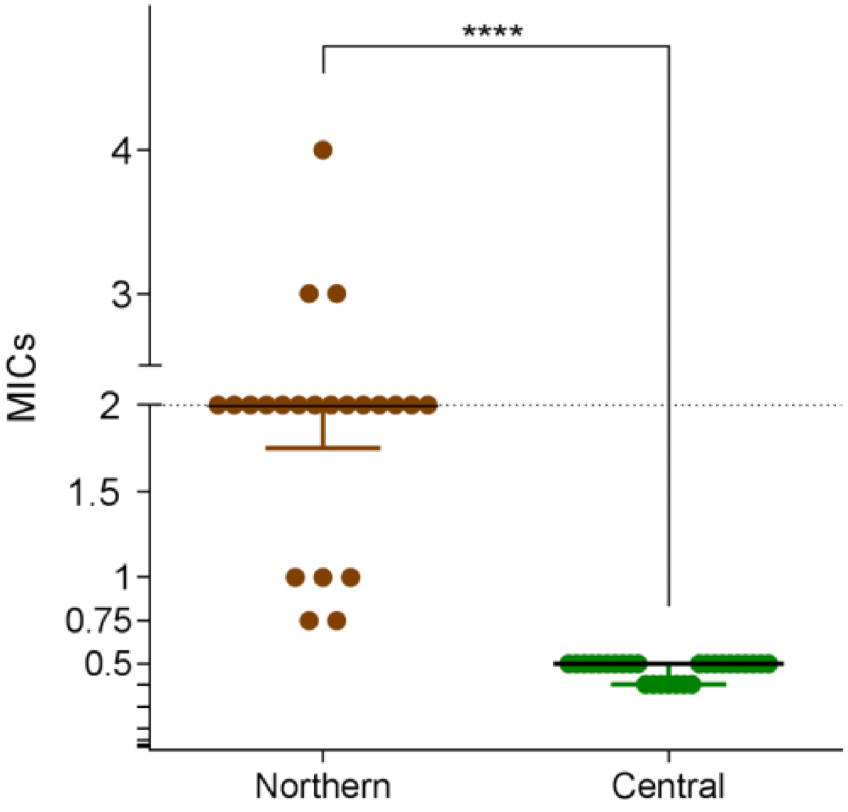
AAC Accepted Manuscript Posted Online 9 April 2018
Antimicrob. Agents Chemother. doi:10.1128/AAC.00238-18

Clin Infect Dis. 2018 May 16. doi: 10.1093/cid/ciy411. [Epub ahead of print]

Molecular epidemiology of Candida auris in Colombia reveals a highly-related, country-wide colonization with regional patterns in Amphotericin B resistance.



AmB MICs for isolates recovered from Hospitals A-D



How to explain this apparent emergence of *C. auris*?

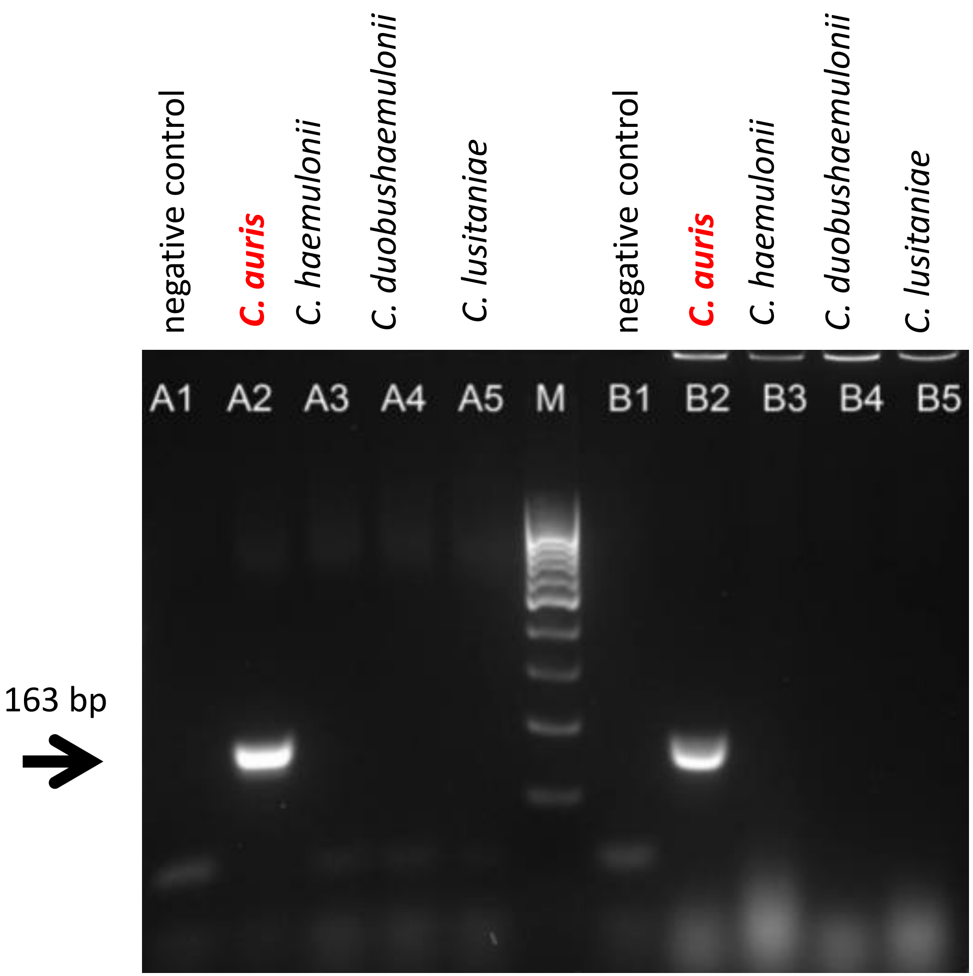
Clancy J.C. and Nguyen M.H., Clin. Infec. Dis. 2017, 64:141-143

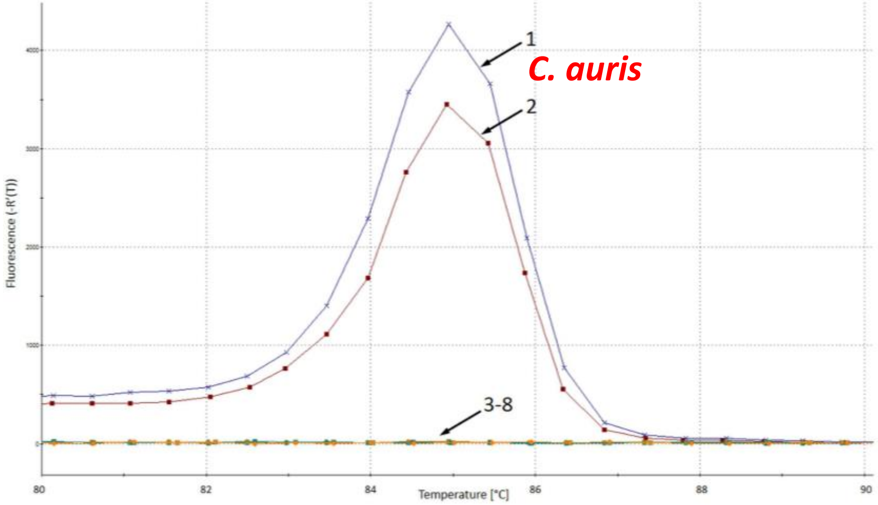
Laboratory testing and misidentification of *C. auris*

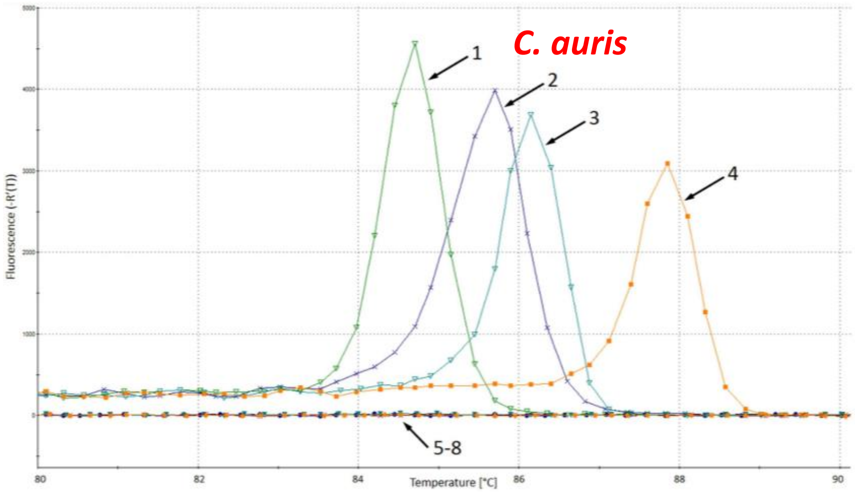
Diagnostic system	Comments
API-20C	May misidentify *C. auris* as *Rhodotorula glutinis, C. sake, Saccharomyces cerevisiae*
Vitek-2	May misidentify *C. auris* as *C. haemulonii*, *C. famata*
MALDI-TOF	Will identify *C. auris* if appropriate sequences are in the database. The Bruker Biotyper library has 3 isolates from Japan and South Korea in its database. If sequencing are not in the database (FDA database), isolates will be identified as yeast that gives no score
DNA sequencing	Sequencing of the internal transcribed spacer (ITS) and D1-D2 domain of the large subunit rRNA gene has been performed most commonly

Mizusawa M et al., J. Clin. Microbiol., 2017, 55:638-640
Kathuria S et al., J. Clin. Microbiol., 2015, 53:1823-1830

Rapid and accurate molecular identification of the emerging multidrug resistant pathogen *Candida auris*

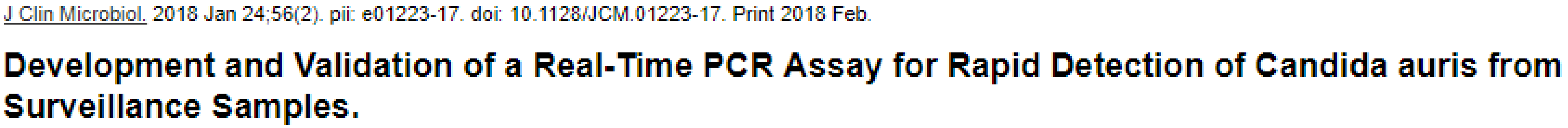






Sensitivity 100%
Specificity 100%

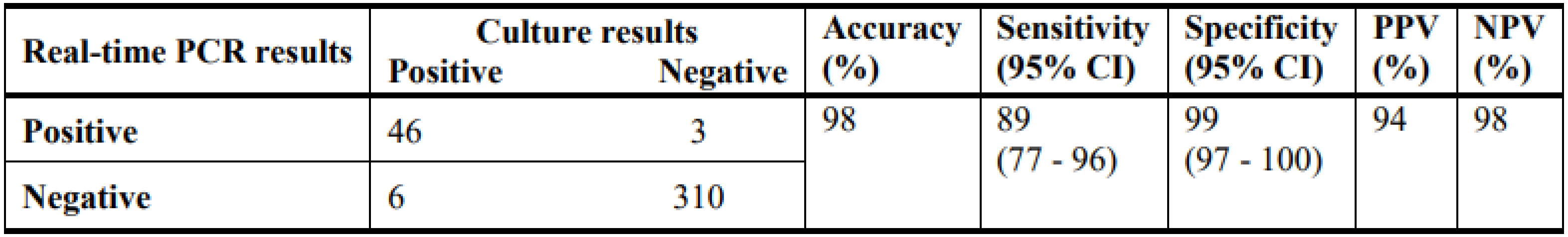
Kordalewska M et al., *J Clin Microbiol. 2017 May 24. pii: JCM.00630-17. doi: 10.1128/JCM.00630-17.*



J Clin Microbiol. 2018 Jan 24;56(2). pii: e01223-17. doi: 10.1128/JCM.01223-17. Print 2018 Feb.

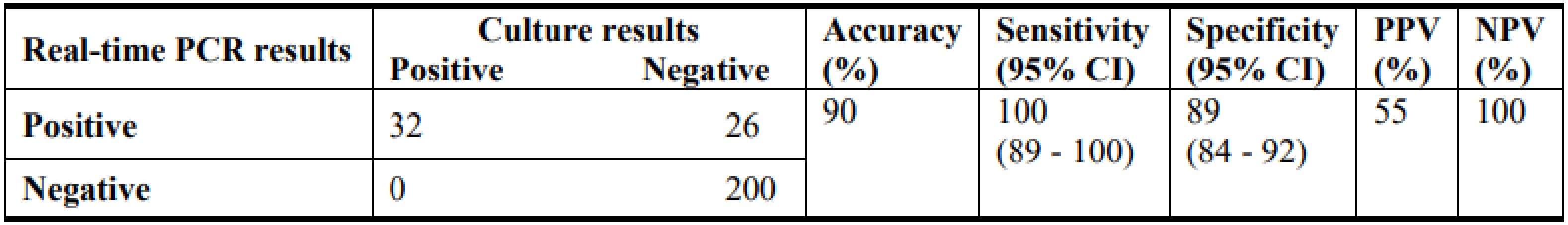
Development and Validation of a Real-Time PCR Assay for Rapid Detection of Candida auris from Surveillance Samples.

Swab surveillance samples

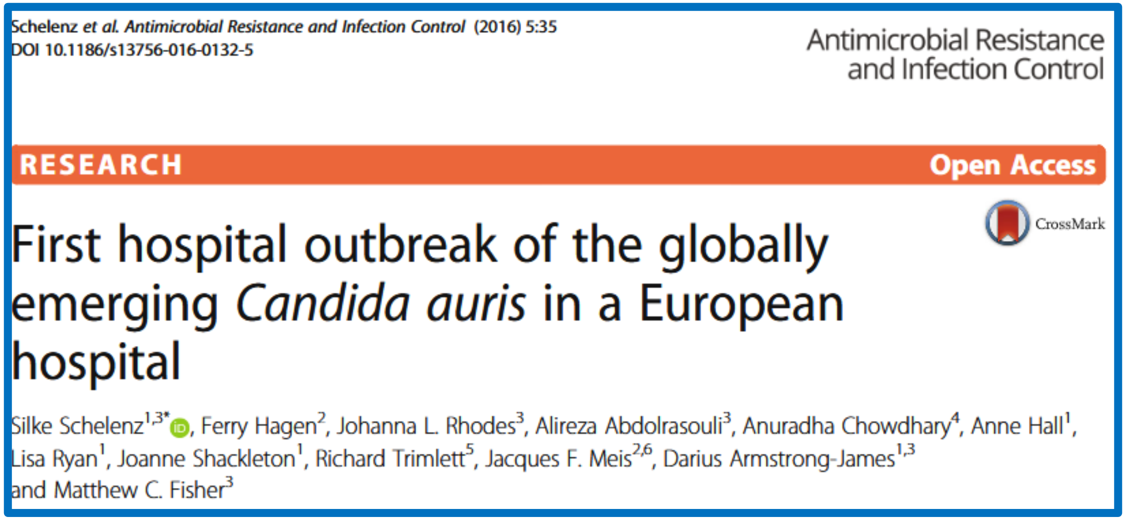


Real-time PCR results	Culture results		Accuracy (%)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (%)	NPV (%)
	Positive	Negative					
Positive	46	3	98	89 (77 - 96)	99 (97 - 100)	94	98
Negative	6	310					

Sponge surveillance samples



Real-time PCR results	Culture results		Accuracy (%)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (%)	NPV (%)
	Positive	Negative					
Positive	32	26	90	100 (89 - 100)	89 (84 - 92)	55	100
Negative	0	200					



Schelenz *et al. Antimicrobial Resistance and Infection Control* (2016) 5:35
DOI 10.1186/s13756-016-0132-5

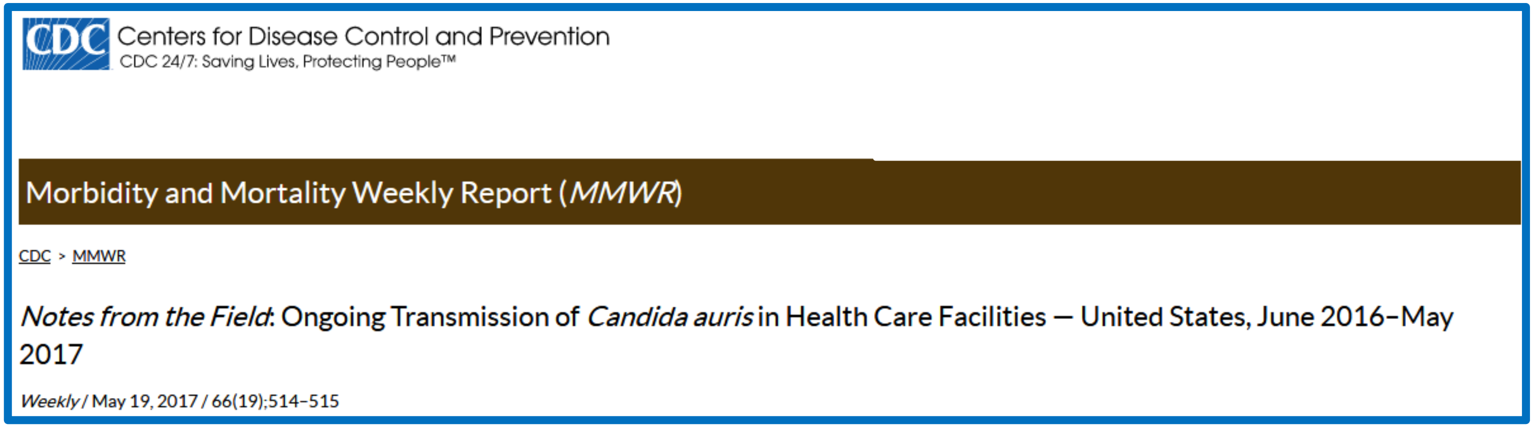
Antimicrobial Resistance
and Infection Control

RESEARCH **Open Access**

First hospital outbreak of the globally emerging *Candida auris* in a European hospital

Silke Schelenz[1,3*], Ferry Hagen[2], Johanna L. Rhodes[3], Alireza Abdolrasouli[3], Anuradha Chowdhary[4], Anne Hall[1], Lisa Ryan[1], Joanne Shackleton[1], Richard Trimlett[5], Jacques F. Meis[2,6], Darius Armstrong-James[1,3] and Matthew C. Fisher[3]

Investigation of the First Seven Reported Cases of *Candida auris*, a Globally Emerging Invasive, Multidrug-Resistant Fungus—United States, May 2013–August 2016



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

Morbidity and Mortality Weekly Report (*MMWR*)

CDC > MMWR

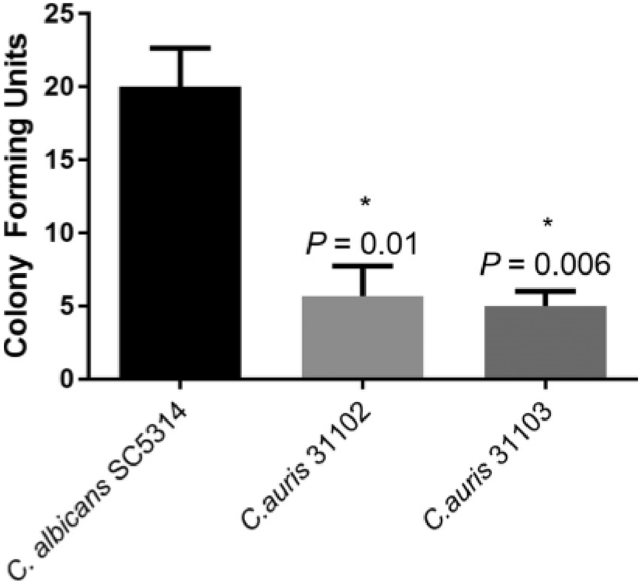
Notes from the Field: Ongoing Transmission of *Candida auris* in Health Care Facilities — United States, June 2016–May 2017

Weekly / May 19, 2017 / 66(19);514–515

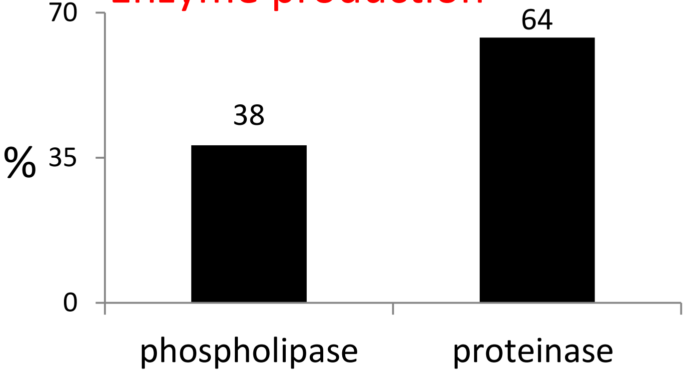
- **Positive environmental cultures**
- **Long environmental resilience**
- **Envirom. acquisition ≥ 4 h**
- **Long time colonization**
- **HCW as source (rare)**

Does genetic predisposition make *C. auris* virulent?

Adherence

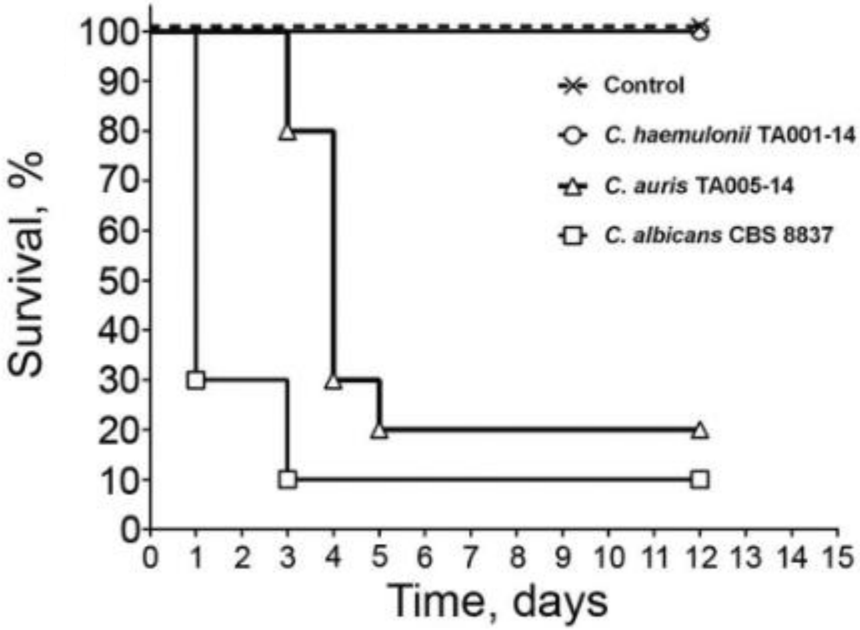


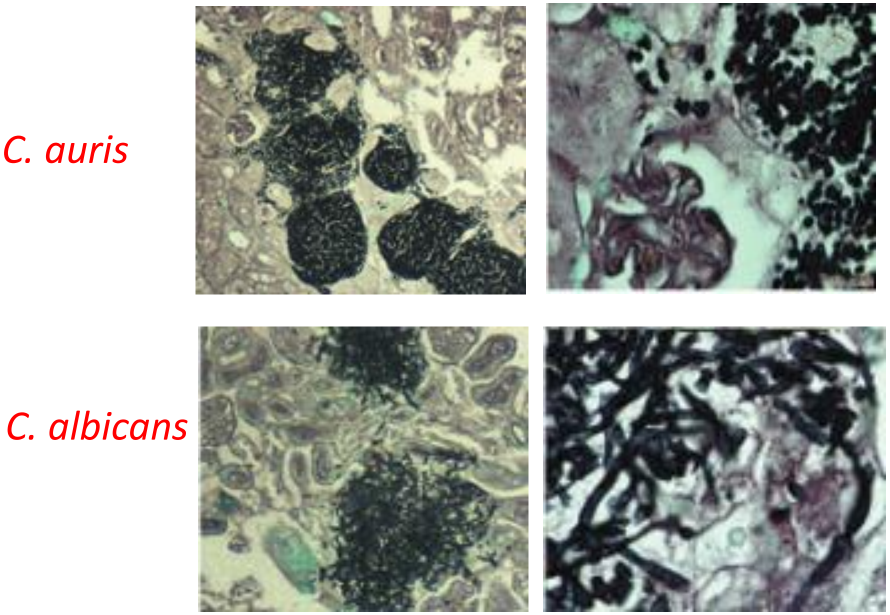
Enzyme production

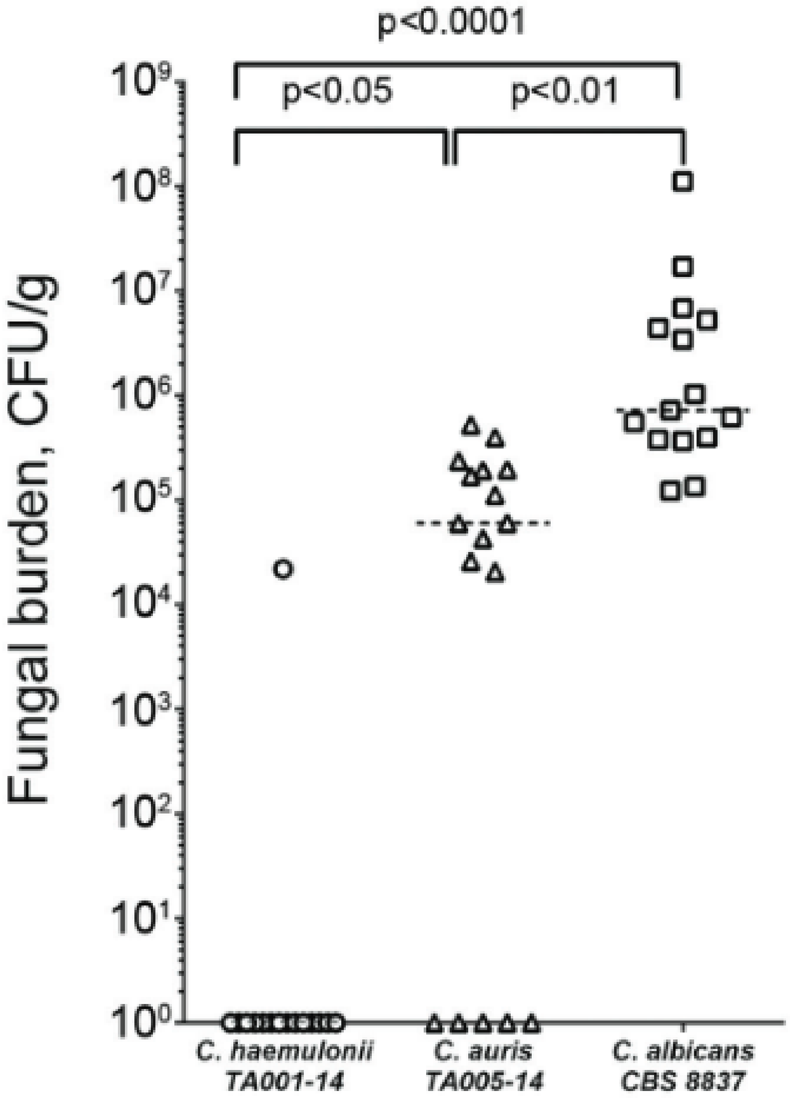


Larkin E et al., Antimicrob Agents Chemother, May 2017, 61 e02396-16
Sherry L et al., Emerging Infectious Diseases, February , 2017

Does genetic predisposition make *C. auris* virulent?







Ben-Ami R et al., Emerging Infectious Diseases, February , 2017

Conclusions

- In a span of only 9 years *C. auris* has become widespread across several countries
- *C. auris* causes a broad range of healthcare associated invasive and non-invasive infections
- Crude mortality of *C. auris* BSIs is somewhat higher than that reported for other *Candida* species

Conclusions

- *C. auris* is «always» misidentified in the routine microbiology laboratory
- Antifungal resistance in *C. auris* is not uncommon and includes MDR isolates
- The lack of awareness of this new *Candida* spp. might result in transmission and outbreaks remaining unnoticed

Grazie
per
l’attenzione