Open Forum Infectious Diseases

REVIEW ARTICLE

Candida auris: A Systematic Review of a Globally Emerging Fungal Pathogen in Africa

Iriagbonse I. Osaigbovo,[1,2] Bassey E. Ekeng,[3] Adeyinka A. Davies,[4] Ejime Ebeigbe,[2] Felix Bongomin,[5,6] Alice Kanyua,[7] Gunturu Revathi,[7] and Rita O. Oladele[8]

[1]Department of Medical Microbiology, School of Medicine, College of Medical Sciences, University of Benin, Benin City, Nigeria, [2]Department of Medical Microbiology, University of Benin Teaching Hospital, Benin City, Nigeria, [3]Department of Medical Microbiology and Parasitology, University of Calabar Teaching Hospital, Calabar, Nigeria, [4]Department of Medical Microbiology and Parasitology, Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria, [5]Department of Medical Microbiology and Immunology, Faculty of Medicine, Gulu University, Gulu, Uganda, [6]Manchester Fungal Infection Group, Division of Evolution, Infection and Genomics, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK, [7]Department of Pathology and Laboratory Medicine, Aga Khan University, Nairobi, Kenya, and [8]Department of Medical Microbiology and Parasitology, Faculty of Basic Medical Sciences, College of Medicine, University of Lagos, Lagos, Nigeria

Candida auris is a World Health Organization critical priority fungal pathogen. We conducted a systematic review to describe its epidemiology in Africa. PubMed and Google scholar databases were searched between January 2009 and September 2023 for clinical studies on *C. auris* cases and/or isolates from Africa. Reviews were excluded. We included 19 studies, involving at least 2529 cases from 6 African countries with the most, 2372 (93.8%), reported from South Africa. Whole-genome sequencing of 127 isolates identified 100 (78.7%) as clade III. Among 527 isolates, 481 (91.3%) were resistant to fluconazole, 108 (20.5%) to amphotericin B, and 9 (1.7%) to micafungin. Ninety of 211 (42.7%) patients with clinical outcomes died. *C. auris* is associated with high mortality and antifungal resistance, yet this critical pathogen remains underreported in Africa. Collaborative surveillance, fungal diagnostics, antifungals, and sustainable infection control practices are urgently needed for containment.

Keywords. Africa; antifungal resistance; *Candida auris*; whole genome sequencing.

Candida auris is an emerging yeast unique for its ability to colonize skin, spread horizontally in healthcare settings, and resist multiple classes of antifungal agents and conventional disinfectants [1]. Its propensity to cause outbreaks of invasive candidiasis associated with high mortality rates has earned it a place in the critical priority group of the World Health Organization's fungal priority pathogen List [2]. The first report of *C. auris* emanated from Japan in 2009 [3]. However, retrospective reviews of *Candida* strain collections date the earliest known strain back to 1996 in South Korea [4]. By 2018, cases of *C. auris* had been reported from all 6 inhabited continents [5].

Although its precise origins remain unclear, the discovery of reservoirs of *C. auris* in remote coastal wetlands suggest a niche in the natural environment that predates its recognition and emergence as a human pathogen in healthcare settings [6]. Global warming is hypothesized to have played a role in the emergence of this thermotolerant yeast, an event postulated to have occurred simultaneously and independently on several continents [6, 7]. This hypothesis is supported by whole-genome sequencing (WGS) analysis of *C. auris* strains, which shows clustering by geographic region [7]. Phylogenetically, *C. auris* strains are classified into 5 distinct populations or clades corresponding to the region of independent emergence: clade I (South Asian), clade II (East Asian), clade III (African), clade IV (South American), and clade V (Middle Eastern/Iranian) [7, 8]. Other than clade V, which has only been found in Iran so far, considerable phylogeographic mixing has occurred because of global travel, with multiple clades circulating in some countries [8, 9]. A possible sixth clade was reported from Singapore and Bangladesh in August 2023 [10].

The laboratory identification of *C. auris* can be challenging. Conventional biochemical methods routinely misidentify the pathogen as *Candida haemulonii*, *Candida famata* (now *Debaryomyces hansenii)*, *Saccharomyces cerevisiae*, or *Rhodotorula glutinis* [11]. Initially, identification of *C. auris* using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-ToF-MS) was also problematic because the novel species was excluded from evaluation databases. Currently, MALDI-ToF-MS with up-to date databases provide accurate identification. VITEK-2 also has an updated database that can identify the yeast, although misidentifications

Received 12 November 2023; editorial decision 18 December 2023; accepted 22 December 2023; published online 27 December 2023

Correspondence: Iriagbonse Iyabo Osaigbovo, MBBS, FMCPath (Medical Microbiology), Department of Medical Microbiology, School of Medicine, College of Medical Sciences, University of Benin, PMB 1154, Benin City, Nigeria. (iyabo.osaigbovo@uniben.edu). Alternate corresponding author: Bassey Ewa Ekeng, MBBCh, Diploma in Mycology (Centre of Excellence, Manchester, UK), FMCPath (Medical Microbiology), Department of Medical Microbiology and Parasitology, University of Calabar Teaching Hospital, Calabar, Nigeria (basseyewaekeng@gmail.com).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad681

with the African clade still occur [12]. As an alternative, *C. auris* can be reliably confirmed by sequencing of the internal transcribed spacer region. Recently, a chromogenic medium has been developed to identify the yeast, although validation studies are rare [13].

In current mycology practice across Africa, most laboratories lack the capacity for definitive *C. auris* identification, rarely identifying yeasts isolated from clinical specimens beyond the performance of a rudimentary germ tube test that differentiates *Candida albicans* from other *Candida* species [14, 15]. To such laboratories, *C. auris* remains phantasmal, perhaps hiding in plain sight under the canopy of "non-*albicans Candida*". The requirements for sophisticated detection systems make the emergence and spread of *C. auris* in healthcare settings particularly bothersome in Africa since transmission in hospitals may remain undetected because of limited facilities for fungal identification and antifungal susceptibility testing [16]. This systematic review summarizes the published literature on *C. auris* in Africa to ascertain its epidemiology.

METHODS

Design and Search Strategy

A systematic literature search was conducted between January 2009 and September 2023 using PubMed and Google Scholar following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The study protocol was unregistered.

The search terms were "*Candida auris* OR *C. auris*" AND "Africa", followed by individual countries in Africa. The literature search was independently conducted by 2 researchers (B. E. E. and A. A. D.). All inconsistencies were resolved before agreeing on the publications included. References in all relevant articles were reviewed for additional publications regarding the topic that may not have been captured in the searched databases.

Study Selection, Inclusion and Exclusion Criteria

We included case reports and series and observational studies involving patients or isolates of *C. auris* reported in African countries. We excluded cases of *C. auris* detected outside Africa irrespective of African descent, reviews, editorials, letters, and other articles lacking information on the epidemiology, diagnosis, or resistance patterns of actual *C. auris* cases and/or isolates from African countries.

Screening and Data Extraction

Two reviewers independently screened the search using titles and abstracts first, and then full texts of eligible articles were retrieved and relevant data extracted unto a standardized data collection tool designed using Microsoft Excel. Key data extracted include location of study, type of study, sex, age, underlying risks, specimen types, diagnostic tools, clade distribution, resistance profile, and clinical outcomes (dead or alive).

Antifungal Resistance Data Interpretation

For antifungal resistance profiles, only isolates whose susceptibilities were conducted using broth microdilution (BMD) or E-test were included. Tentative breakpoints proposed by the Centers for Disease Control and Prevention (CDC) were used for interpretation of the minimum inhibitory concentrations (MIC) as follows: resistance to fluconazole ≥32 μg/mL, amphotericin B ≥2 μg/mL, flucytosine ≥128 μg/mL, anidulafungin ≥4 μg/mL, caspofungin ≥2 μg/mL, and micafungin ≥4 μg/mL [17]. For all azoles other than fluconazole, MICs ≥2 μg/mL were defined as non-susceptible (ie, high and potentially resistant). Isolates resistant to 2 antifungal drug classes were designated multidrug resistant, whereas those resistant to 3 drug classes were regarded as pan-drug resistant. Studies that did not specify the MICs of isolates were excluded from the computation of resistance rates.

Data Synthesis

Data were entered into a Microsoft Excel sheet and analyzed. Categorical variables were described using frequency counts and proportions.

Patient Consent Statement

No ethical approval or patient consent was required for this study because the underlying data were retrieved from publicly available sources.

RESULTS

We identified 19 articles published between 2014 and 2023 that reported cases and isolates of *C. auris* in African countries. The selected documents and information retrieved from each are shown in Supplementary Table 1.

The bibliography on *C. auris* in South Africa is extensive compared with the rest of the continent and is driven mostly by surveillance work by the National Institute of Communicable Diseases (NICD). The NICD team authored 10 articles [18–27], each addressing aspects of *C. auris* epidemiology in South Africa (Supplementary Table 1); there was 1 independent report of the epidemiology of *C. auris* in a tertiary hospital and a multicenter phase 2 clinical trial involving patients with *C. auris* candidemia [28, 29]. Because of overlapping timeframes of some of these articles and to avoid duplicating cases, only aspects of the epidemiology of *C. auris* in South Africa were synthesized with the rest of the continent.

Geography

C. auris infection has been reported from 6 countries in all 4 African subregions (Figure 1). Specifically, the yeast has been reported in South Africa (Southern Africa), Kenya (East

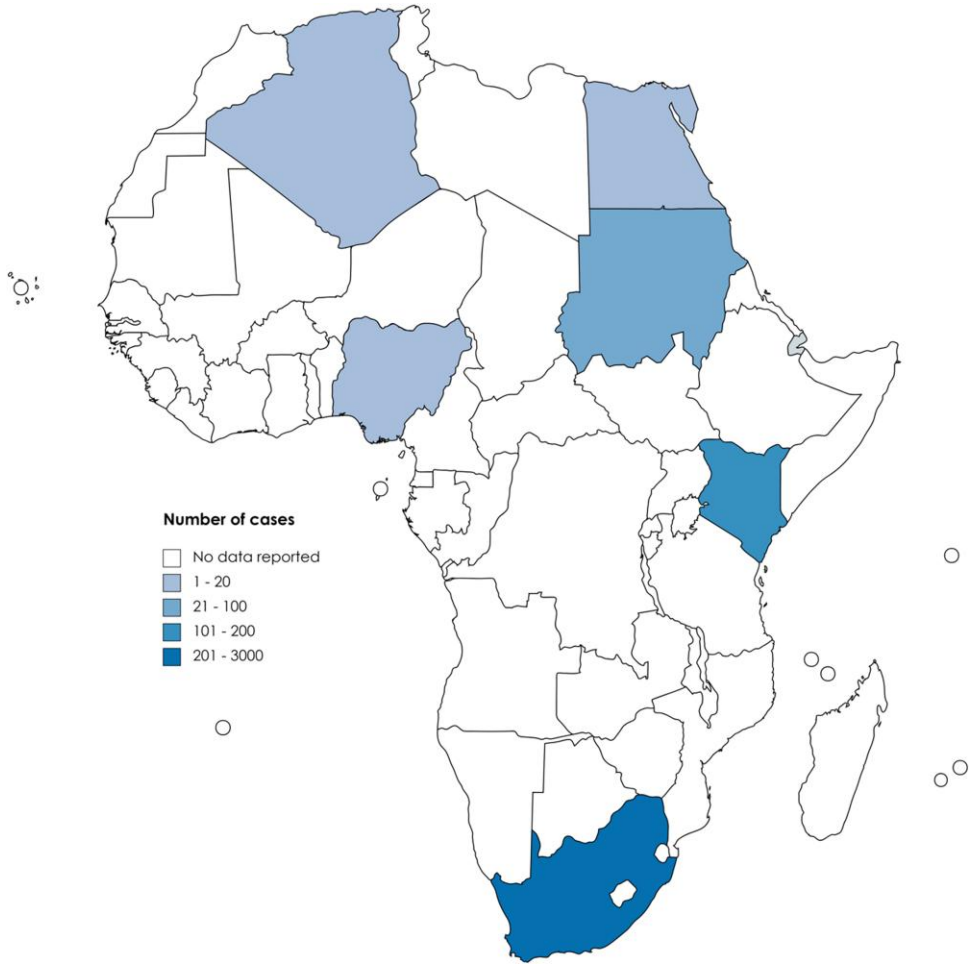

Figure 1. Map of Africa showing countries where *Candida auris* has been detected and estimated case counts. (created using http://mapchart.net/africa.html)

Africa), Nigeria (West Africa), Sudan, Egypt, and Algeria (North Africa).

Sociodemographic Characteristics and Risk Factors

For South Africa, demographic data were derived from 2 nationwide surveillance reports [18, 19], a retrospective study from a tertiary hospital [28], and another academic hospital with a persistent neonatal unit outbreak [20]. The total number of cases reported from surveillance was 2373. Median age of cases in South Africa ranged from 1.4 years in the hospital that experienced an outbreak (2016–2020) to 60 years in the 2012–2016 surveillance period (Table 1). Males exceeded females in all the studies, although data on sex were missing for some cases (Table 1).

Table 2 summarizes the sociodemographic characteristics and underlying risks for 156 cases reported from countries besides South Africa [30–36]. There were more males, 88 (56.4%), than females, 68 (43.6%), giving a male-to-female ratio of 1.3:1. The most frequently documented risk factor was the use of broad-spectrum antibiotics in 120/156 (76.9%), followed by admission into intensive care units in 112/156 (71.8%) persons. Travel history was implicated in 1 case each from Egypt (travel to Saudi Arabia) and Nigeria (travel to United Arab Emirates) and 7 cases from Kenya (countries of travel were not listed, but patients received healthcare outside of Kenya).

Isolation and Identification of *C. auris*

In South Africa, *C. auris* was isolated from various specimens obtained from both normally sterile sites as well as probable colonization sites (Table 1). Outside South Africa, specimens were less diverse, with blood as the near-universal source 149/156 (95.5%), except in Algeria, where *C. auris* was isolated from bronchial aspirates 4/7 (57.1%), urine 1/7 (14.3%), wound 1/7 (14.3%), and peritoneal fluid 1/7 (14.3%) (Table 2).

Most isolates from outside South Africa (Egypt, Nigeria, Kenya) were identified using VITEK 2 (version 8.1) [30–34]. Polymerase chain reaction alone was used in Sudan, whereas in Algeria, MALDI-ToF-MS and polymerase chain reaction were used [29, 35]. In South Africa, some hospitals and diagnostic laboratories used VITEK-2 to identify *C. auris*, followed

Table 1. Sociodemographic and Underlying Risk Factors in *Candida auris* Cases in South Africa

Variable	Surveillance (2012–2016)	Surveillance (2016–2017)	Non-outbreak Hospital (2015–2018)	Outbreak Hospital (2016–2020)
Number of cases	1579	794	45	287
Median age (interquartile range), y	60 (46–72)	54 (34–67)	32 (26–46) y	1.4 (22 d to 21 y)
Sex	n = 1579	n = 794	n = 45	n = 287
Male	957 (60.6)	284 (35.8)	32 (71.1)	155 (54.0)
Female	583 (36.9)	179 (22.5)	13 (28.9)	121 (42.2)
Unspecified	39 (2.5)	331 (41.7)	0 (0.0)	11 (3.8)
Underlying risk factor	n = 1579	n = 794	n = 45	n = 287
ICU admission	NS	110 (13.9)	36 (80.0)	NS
Mechanical Ventilation	NS	44 (5.5)	37 (82.2)	NS
Hemodialysis	NS	0 (0.0)	18 (40.0)	NS
Central venous catheter	NS	69 (8.7)	42 (93.3)	NS
Surgery	NS	0 (0.0)	35 (77.8)	NS
Diabetes mellitus	NS	0 (0.0)	4 (8.9)	NS
Hypertension	NS	0 (0.0)	0 (0.0))	NS
Malignancy	NS	0 (0.0)	2 (4.4)	NS
Broad-spectrum antibiotics	NS	77 (9.7)	42 (93.3)	NS
Prior systemic antifungal use	NS	30 (3.8)	0 (0.0)	NS
HIV	NS	11 (1.4)	9 (20.0)	NS
Province	n = 1465	n = 794	n = 45	n = 287
Gauteng	1336 (91.1)	680 (60.4)	45 (100.0)	287 (100.0)
Other	129 (8.8)	114 (39.6)	0 (0.0)	0 (0.0)
Health sector	n = 1549	n = 794	n = 45	n = 287
Private	1435 (92.6)	695 (87.5)	0 (0.0)	0 (0.0)
Public	114 (7.4)	99 (12.5)	45 (100.0)	287 (100.0)
Specimen source				
Blood	344 (21.8)	NS	26 (57.8)	161 (56.1)
CVC tip	288 (18.2)	NS	15 (33.3)	24 (8.4)
Urine	622 (39.4)	NS	9 (20.0)	11 (3.8)
Tissue	49 (3.1)	NS	3 (6.7)	6 (2.1)
Respiratory specimens	173 (11.0)	NS	0 (0.0)	8 (2.8)
Wound/skin/superficial swab	45 (2.8)	NS	3 (6.7)	34 (11.8)
Other fluid from sterile site	58 (3.7)	NS	1 (2.2)	3 (1.0)
Mortality	NS	46/102 (45.1)	18/45 (40.0)	NS

Abbreviations: CVC, central venous catheter; ICU, intensive care unit; NS, not specified.

by confirmation with MALDI-ToF-MS (including isolates identified as *C. haemulonii*) at the NICD [18, 19]. Sequencing of the D1/D2 internal transcribed spacer region was used to confirm identity of isolates that had MALDI-TOF-MS scores of <2.00 or a low-discrimination identification [19].

Clade Distribution

To describe the clade distribution of *C. auris* strains in Africa, we included sequencing data from Algeria, Egypt, Nigeria, and South Africa. In South Africa, a nationally representative sample of *C. auris* isolates subjected to WGS included 92 randomly selected clinical isolates from national candidemia surveillance (2009–2018), 10 isolates recovered from environmental sampling conducted in outbreak and nonoutbreak intensive care units, and 11 isolates obtained from axillae and groins of admitted babies during a point-prevalence survey conducted in a public hospital reporting an outbreak of *C. auris* candidemia [21]. Another study reporting 188 isolates subjected to WGS was excluded because the study was conducted in a single hospital with a persistent outbreak and was not nationally representative [20]. Moreover, including these isolates would have amounted to duplication of data because some of the isolates are captured in the surveillance analysis. Table 3 shows the distribution among clades of *C. auris* isolates from the various countries, whereas Supplementary Figure 1 shows the overall clade distribution in Africa. Most sequenced isolates, 115 (90.6%), were from South Africa. Overall, the most common clade is clade III, 100 (78.7%), followed by clade I, 18 (14.2%), clade IV, 8 (6.3%), and clade II, 1 (0.8%).

Resistance Profiles

Antifungal susceptibility was reported for isolates from Algeria [29], Egypt [30], Nigeria [34], and Kenya [31, 32], with surveillance isolates from South Africa and isolates from a phase 2 clinical trial in South Africa [22, 23, 29]. In 1 Kenyan study, susceptibilities for 77 isolates of *C. auris* were obtained from

Table 2. Sociodemographic Characteristics and Underlying Risk Factors for *Candida auris* in Countries Outside of South Africa

Variable	Algeria (n = 7)	Egypt (n = 1)	Kenya (n = 118)	Nigeria (n = 4)	Sudan (n = 26)	Total (N = 156)
Median age (interquartile range), y	55 (51–69.5)	53	55 (43–65); 58 (20)	63.5 (54–70.5)	NS	…
Sex						
Male	5 (71.4)	1 (100.0)	65 (55.1)	2 (50.0)	15 (57.7)	88 (56.4)
Female	2 (28.6)	0 (0.0)	53 (44.9)	2 (50.0)	11 (42.3)	68 (43.6)
Underlying risk factors						
ICU admission	7 (100.0)	1 (100.0)	93 (78.8)	2 (50.0)	NA	112 (71.8)
Surgery	5 (71.4)	0 (0.0)	0 (0.0)	2 (50.0)	NA	7 (4.5)
Mechanical ventilation	…	…	17 (14.4)	…	NA	17 (10.9)
Hemodialysis	…	…	…	2 (50.0)	NA	…
Central venous catheter	…	…	96 (81.4)	…	NA	65 (41.7)
Total parenteral nutrition	…	…	29 (24.6)	1 (25.0)	NA	…
Diabetes mellitus	3 (42.9)	1 (100.0)	25 (21.2)	2 (50.0)	NA	23 (14.7)
Hypertension	1 (14.3)	0 (0.0)	29 (24.6)	1 (25.0)	NA	19 (12.2)
Malignancy	…	…	16 (13.6)	1 (25.0)	NA	8 (5.1)
HIV	0 (0.0)	0 (0.0)	4 (3.4)	0 (0.0)	NA	4 (2.6)
Broad spectrum antibiotics	7 (100.0)	…	109 (92.4)	4 (100.0)	NA	120 (76.9)
Travel	0 (0.0)	1 (100.0)	7 (5.9)	1 (25.0)	NA	12 (7.7)
Others[a]	…	3	…	2 (50.0)	NA	5 (3.2)
Specimen sources						
Blood	0 (0.0)	1 (100.0)	118 (100.0)	4 (100.0)	26 (100.0)	149 (95.5)
Urine	1 (14.3)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	2 (1.3)
Sterile site fluids[b]	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Respiratory tract[c]	4 (57.1)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	5 (3.2)
Swabs	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
Mortality	NS	1 (100.0)	40/105 (38.1)	3 (75.0)	NS	44/109 (40.4)

Abbreviations: ICU, intensive care unit; NA, not applicable; NS, not specified.

[a]Others include heart disease (2), diabetes insipidus (1), COVID-19 (1), systemic lupus erythematosus (1), urinary catheterization (4).

[b]Sterile site fluids include peritoneal fluid.

[c]Respiratory specimens include bronchial aspirate and sputum.

Table 3. Clade Distribution for 127 *Candida auris* Isolates From Different African Countries

Clade	Algeria (N = 7)	Egypt (N = 1)	Nigeria (N = 4)	South Africa (N = 115)	Total (N = 127)
I	1 (14.3)	1 (100.0)	2 (50.0)	14 (12.2)	18 (14.2)
II	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
III	2 (28.6)	0 (0.0)	0 (0.0)	98 (85.2)	100 (78.7)
IV	3 (42.9)	0 (0.0)	2 (50.0)	3 (2.6)	8 (6.3)
Total	7	1	4	115	127

VITEK 2 with BMD performed for a subset of 21 [31]. We included only the isolates tested using BMD in our analysis. The MIC ranges were 1 μg/mL to 256 μg/mL for fluconazole, 0.125 μg/mL to 16 μg/mL for amphotericin B, 0.008 μg/mL to 32 μg/mL for voriconazole, 0.008 μg/mL to 16 μg/mL for caspofungin, 0.008 μg/mL to 2 μg/mL for anidulafungin, 0.008 μg/mL to 4 μg/mL for micafungin, 0.015 μg/mL to 64 μg/mL for flucytosine, and <0.008 μg/mL to 0.06 μg/mL for manogepix. Most isolates, 481 (91.3%), were resistant to fluconazole and 108 (20.5%) were resistant to amphotericin B. Among amphotericin B–susceptible isolates, 342/419 (81.6%) had high MICs of 1 mg/L (Table 4). Twenty-seven (5.1%) isolates were multidrug resistant, whereas 2 (0.4%) were pan-drug resistant (Table 4).

Two studies also assessed susceptibility of *C. auris* isolates from South Africa to manogepix, an inhibitor of glycosylphosphatidylinositol biosynthesis and the active moiety of the pro-drug fosmanogepix [24, 29]. Manogepix exhibited potent activity against all isolates; it was 3- to 6-fold more potent than itraconazole, posaconazole, voriconazole, and fluconazole, 4-fold more potent than micafungin and anidulafungin, and 9-fold more potent than amphotericin B [24].

Table 5 shows the resistance profile by clade of 104 isolates with clade identity provided by WGS including all isolates from Egypt (1), Nigeria (4), and Algeria (7), and 92 isolates (13 clade 1, 77 clade III, and 2 clade IV) from a single South African study [23]. Clade 1 showed the most resistance, with all 17 (100%) isolates demonstrating resistance to fluconazole and 13 (81.3) being resistant to amphotericin B. Clade II showed no resistance to any drug; however, there was just 1 isolate.

Antifungal Treatment

Five studies including one clinical trial, a single-center retrospective study, a surveillance report and 2 case report/series reported data on antifungal treatment. To avoid duplicates, we

Table 4. Resistance Rates of *Candida auris* Isolates in African Countries

	Resistance (%)					
Antifungal Agent	Algeria (N = 7)	Egypt (N = 1)	Kenya (N = 21)	Nigeria (N = 4)	South Africa (N = 494)	Total (N = 527)
Fluconazole	5 (71.4)	1 (100.0)	21 (100.0)	2 (50.0)	452 (91.5)	481 (91.3)
Voriconazole	5 (71.4)	NT	7 (33.3)	0 (0.0)	71 (14.4)	83 (15.7)
Amphotericin B	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	107 (21.7)	108 (20.5)
Micafungin	0 (0.0)	0 (0.0)	NT	0 (0.0)	9 (1.8)	9 (1.7)
Anidulafungin	0 (0.0)	0 (0.0)	NT	0 (0.0)	1 (0.2)	1 (0.2)
Flucytosine	NT	NT	NT	NT	0 (0.0)	0 (0.0)
High amphotericin B (MIC = 1 µg/mL)	0 (0.0)	1 (100.0)	21 (100.0)	1 (25.0)	319 (64.6)	342 (64.9)
MDR/PDR	MDR –1; 1 FLZ + AMP B	…	…	…	MDR-7 FLZ + MICA; 19 FLZ + AMB PDR-2	MDR-27 (5.1%) PDR- 2 (0.4%)

Abbreviations: FLZ, fluconazole; MICA, micafungin; MDR, multidrug resistance; NT, not tested; PDR, pan-drug resistance; VCZ, voriconazole.

excluded the single-center retrospective study because it overlapped with the 2016–2017 surveillance period. In total, antifungal treatment for 95 patients is presented (Supplementary Table 2) [23, 28, 29, 30, 35]. Of these, 51 (53.7%) received amphotericin B, 18 (18.9%) received fluconazole, 24 (25.3%) received micafungin, 15 (15.8%) received anidulafungin, 2 (2.1%) received caspofungin, 2 (2.1%) received voriconazole, and all 9 (9.5%) patients in the clinical trial received fosmanogepix. Several patients received multiple antifungal agents (11 [11.6%] received amphotericin B and micafungin; 8 [8.4%] received amphotericin B and anidulafungin; 7 [7.4%] received amphotericin B and fluconazole, whereas 2 [2.1%] received amphotericin B, anidulafungin, and fluconazole).

Clinical Outcome of Patients With *C. auris* Infection/Colonization

In South Africa, mortality ranged from 40% in a single center to 45.1% in a nationwide surveillance sample (2016–2017) (Table 1) [19, 28]. In the single-center study, mortality was 39.3% in patients who received antifungal treatment compared with 46.7% in those who were not treated. Outside South Africa, outcomes for 109 patients were provided. Of these, 44 died, giving a mortality rate of 40.4%. Mortality ranged from 38.1% in Kenya to 100% in Egypt (where there was a single case).

Pediatric *C. auris* Infection

In a South African study that analyzed surveillance data for 2996 cases of candidemia in children from multiple sites between 2012 and 2017, there were 47 cases of *C. auris* candidemia in 7 (14.9%) neonates, 10 (21.3%) infants, 24 (51.1%) children aged 2 to 12 years, and 6 (12.8%) adolescents aged 13 to 17 years [25]. The earliest case of *C. auris* candidemia in a child was recorded in 2016. Another South African study described point prevalence surveys conducted as measures to contain an outbreak in a neonatal ward: 63/195 (32%) neonates were colonized with *C. auris* and were subjected to isolation/cohorting [26].

Outside South Africa, pediatric cases of *C. auris* infection appear rare (1 patient in Kenya was categorized as <20 years and another in Sudan was categorized as <30 years; actual ages were not stated) [33, 36].

DISCUSSION

This review highlights the presence of *C. auris* in all subregions of Africa, with more than 2500 cases documented in literature to date. Only 6 countries account for this documented evidence, with close to 89% lacking published data on the emerging pathogen. Given the absence of routine surveillance and lack of sophisticated mass spectrometric and molecular diagnostics in most African countries [16], *C. auris* is likely more widespread than represented in this review. Unsurprisingly, the majority of cases have been reported from South Africa, which has an established national surveillance infrastructure for antimicrobial drug-resistant pathogens and other infectious diseases [18].

C. auris is endemic in some South African hospitals, especially in the private health sector. Most cases are reported from Gauteng, the most densely populated province, and the economic and travel hub of the country [18, 19]. The earliest cases of infection in South Africa were reported in 2014 [27]. A retrospective review of surveillance isolates, however, identified a case of *C. auris* bloodstream infection (initially misidentified as *C. haemulonii*) from 2009 at an academic hospital in Johannesburg. By 2016, *C. auris* was reported in more than 100 acute care hospitals, including several outbreaks, and had become the third most common cause of candidemia in South Africa. In Kenya, *C. auris,* which was first seen in 2011, accounts for 29% to 38% of candidemia cases as deduced from 2 single-center studies in Nairobi, and has caused hospital outbreaks [32, 33]. Recent importations to the United States and Australia by those who had received healthcare in Kenya further affirm the endemicity of *C. auris* in some Kenyan

Table 5. Resistance Rates of Different Clades of *Candida auris* in Africa

Clade	FLZ	VCZ	AMP B	MICA	FLZ + AMP B	FLZ + AMP B + MICA
I (n = 17)	17 (100)	1 (5.8)	13 (76.5)	0 (0.0)	12 (70.5)	0 (0.0)
II (n = 1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
III (n = 79)	71 (89.9)	2 (2.5)	10 (12.7)	2 (2.5)	7 (8.9)	2 (2.5)
IV (n = 7)	3 (42.9)	2 (28.6)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)
I–IV (n = 104)	91 (87.5)	5 (4.8)	23 (22.1)	2 (1.9)	20 (19.2)	2 (1.9)

Abbreviations: AMP B, amphotericin B; FLZ, fluconazole; MICA, micafungin; VCZ, voriconazole.

hospitals [37, 38]. *C. auris* is also probably endemic in at least 1 center in Sudan, where 26 candidemia episodes were detected within the space of 4 months [36]. In Algeria, 7 cases of *C. auris* were detected in a single facility over the course of 2 years, with evidence of nosocomial transmission among some of the patients [30]. In Egypt and Nigeria, *C. auris* appears sporadic. However, the yeast may be more widespread in these countries than suggested by literature. For example, although the fungus was first reported in Nigeria in 2021, the US CDC had previously flagged a Nigerian child receiving medical care in New York in 2020 [35].

The demographic profile and underlying risk factors for *C. auris* infection in Africa are consistent with epidemiology described elsewhere [7]. More males were affected, possibly related to a higher prevalence of underlying chronic diseases such as diabetes mellitus and hypertension in males. The median age of cases ranged from 54 years in South Africa to 63.5 years in Nigeria [19, 36], implying a predilection for older persons. These sex and age predilections are similar to the findings from a study describing *C. auris*–associated hospitalizations in the United States, where 54% of cases were male and the median age was 68 years [39]. In South Africa, a significant number of children were also reported, whereas most, if not all, cases reported from other African countries, were adults. This may reflect suboptimal pediatric blood culturing practices in the other countries. Alternatively, it may be a result of selection pressure induced by high volume of antifungals used in pediatric populations in South Africa. In keeping with reports from other continents, broad-spectrum antibiotic use, followed closely by intensive care unit admission, was the most commonly reported underlying risk for *C. auris* infection [40].

Close to 8 of 10 strains isolated from African patients belong to clade III, the designated African clade. Of note, this cladistic distribution is largely driven by South Africa, where the bulk of sequenced isolates emanated. The earliest known isolate of *C. auris* in South Africa, which was detected retrospectively, belonged to clade IV, suggesting introduction from South America [22]. It was detected in a single tertiary hospital that continues to account for most clade IV isolates reported in South Africa, possibly because of clonal expansion within the facility [20]. Interestingly, no isolate from Egypt and Nigeria belonged to clade III, suggesting recent introductions possibly by cross-border travel of persons with prior exposure in healthcare settings abroad. Indeed, travel history was documented in the only patient reported from Egypt (who had recently travelled to Saudi Arabia) and 1 other patient reported from Nigeria (who had a history of travel to Dubai in the United Arab Emirates) [31, 35]. Algeria, despite a small case series of 7, showed the most phylogenetic diversity with each of clades I to IV (including the first clade II strain to be reported from Africa) represented [30]. Although the reviewed articles did not provide information about the cladistic profile in Kenya and Sudan, Chow and colleagues had earlier reported cocirculation of clades I and III in Kenya [9].

As previously described [9], there were clade-associated variations in antifungal resistance, with clade I isolates exhibiting higher levels of resistance and clade II exhibiting susceptibility to all antifungals. In alignment with global trends [40], 9 of 10 *C. auris* isolates in Africa are resistant to fluconazole. This is particularly worrisome because fluconazole is the least expensive and most accessible systemic antifungal agent in Africa [14, 16]. We also found that one-fifth of isolates were resistant to amphotericin B, and even among susceptible isolates, the majority had high MICs. The 20% resistance rate to amphotericin B is less than 43% described in the United States [41]. Echinocandin resistance was rare but appreciable, ranging from 0.8% resistance for anidulafungin to 1.7% for micafungin. This is much lower than the 7% rate reported globally [40]. We did not report resistance rates for caspofungin because although the US CDC recommendations present tentative clinical breakpoints for caspofungin, studies have demonstrated wide intra- and interlaboratory variations in MICs that make them unreliable for clinical decision-making [41, 42]. Instead, MIC testing of *Candida* species using either anidulafungin or micafungin, which is more reliable, is preferred as a surrogate for caspofungin in performing clinical in vitro testing of echinocandins [42]. Because of the near-universal resistance to azoles and reduced susceptibility to polyenes, experts recommend echinocandins as first-line treatment in *C. auris* infection [5]. However, this class of drugs is not readily available in most African countries and, where it is available, costs are prohibitive [14, 16]. The occurrence of pan-drug resistance involving azoles, polyenes, and echinocandins, although limited to 2 isolates, is alarming in the face of limited treatment options. In a

phase 2 clinical trial, the new drug, fosmanogepix, which is an inhibitor of glycosylphosphatidylinositol biosynthesis, was safe, well-tolerated, and efficacious in participants with *C. auris* candidemia in South Africa [29]. This drug would be useful for treatment of pan-drug–resistant cases.

Resistance to commonly used antifungal agents is 1 of several contributory factors to the high rates of mortality seen in *C. auris*–infected patients. Patients with *C. auris* also often have multiple comorbidities, which make it difficult to ascertain attributable mortality. Although outcomes were not specified for many of the cases, the crude mortality rate of 42.7% falls within the range of 30% to 60% reported from other studies worldwide but was twice as high as the rate of 20% reported in Europe [7]. Though higher than overall crude mortality rate of 34% reported in the United States, it was lower than estimated crude mortality of 47% for bloodstream infections reported in the same country [39].

African health systems face numerous challenges that can impede containing the spread of *C. auris*, including weak disease surveillance systems, limited diagnostic and antifungal susceptibility testing capabilities, inaccessibility of effective antifungal treatments, and poor infection prevention and control practices [16, 43]. To effectively address *C. auris*, 4 key areas of improvement are essential. First, there is a need to update yeast identification practices and improve workflows in laboratories to accurately identify *C. auris*. Strengthening surveillance, particularly for fungal pathogens, is the second crucial step, employing a hub-and-spoke model involving regional reference laboratories. Third, access to antifungal drugs, particularly echinocandins, must be expanded, along with implementing antifungal stewardship to combat resistance. Last, improving infection prevention and control practices, including hand hygiene and cleaning, is vital, especially given the challenges of compliance in many African healthcare settings [44]. Political will and leadership at local, national, and continental levels are essential to tackle the *C. auris* threat. The efforts of organizations such as the US CDC and the NICD in South Africa serve as examples for national public health institutes in the region to emulate [45].

The major limitation of this review is the heterogeneity of reporting used in the different studies. For example, some studies reported age as a categorical variable using varying interval limits, which hampered analysis. There was the possibility of duplicating cases if single-center studies in South Africa were merged with multicenter surveillance data. Surveillance data also had some missing details. Addressing these limitations prevented a complete epidemiological synthesis. Nevertheless, we have provided a comprehensive view of the epidemiology of *C. auris* in Africa.

CONCLUSION

C. auris, with its concerningly high mortality and antifungal resistance rates, is endemic in at least 2 African countries, with sporadic cases described in others. Diagnostic limitations may be contributing to underdetection and underreporting, thereby masking its true burden and geographical spread. To uncover and curb this menace, improvements in surveillance, diagnosis, antifungal susceptibility testing, treatment, and infection control as well as context-specific guidelines for the African setting are urgently needed. Political will and public health leadership are necessary to take these bold, proactive steps.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. F. B. is a Harvard University, Boston University, Northwestern University, and University of New Mexico (HBNU) consortium NIH Fogarty Global Health Research Fellow, and his work is supported by the Fogarty International Center of the National Institutes of Health under Award Number D43 TW010543. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author contributions. I. I. O. and B. E. E. contributed to conceptualization. I. I. O., B. E. E., and A .A. D. contributed to the methodology. B. E. E. and A. A. D. collected the data. B. E. E., A. A. D., and I .I. O. performed the data analysis and data visualization. I. I. O. and E. E. drafted the manuscript, which was edited by all authors. All authors have read and agreed with the submitted version of the manuscript. I. I. O. takes responsibility for the integrity of the work as a whole.

Data Availability Statement. Data used for this study are available on reasonable request.

Financial support. No funds were received for this study.

Potential conflicts of interest. All authors: No reported conflicts,

References

1. Forsberg K, Woodworth K, Walters M, et al. *Candida auris*: the recent emergence of a multidrug-resistant fungal pathogen. Med Mycol **2019**; 57:1–12.
2. World Health Organization. WHO fungal priority pathogens list to guide research, development and public health action. **2022**. Available at: https://www.who.int/publications/i/item/9789240060241. Accessed 10 October 2023.
3. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol **2009**; 53: 41–4.
4. Lee WG, Shin JH, Uh Y, et al. First three reported cases of nosocomial fungemia caused by *Candida auris*. J Clin Microbiol **2011**; 49:3139–42.
5. Govender NP, Avenant T, Brink A, et al. Federation of Infectious Diseases Societies of Southern Africa guideline: recommendations for the detection, management and prevention of healthcare-associated *Candida auris* colonisation and disease in South Africa. S Afr J Infect Dis **2019**; 34:163.
6. Arora P, Singh P, Wang Y, et al. Environmental isolation of *Candida auris* from the coastal wetlands of Andaman Islands, India. mBio **2021**; 12:e03181-20.
7. Lockhart SR, Etienne KA, Vallabhaneni S, et al. Simultaneous emergence of multidrug-resistant *Candida auris* on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis **2017**; 64:134–40.
8. Spruijtenburg B, Badali H, Abastabar M, et al. Confirmation of fifth *Candida auris* clade by whole genome sequencing. Emerg Microbes Infect **2022**; 11:2405–11.
9. Chow NA, Muñoz JF, Gade L, et al. Tracing the evolutionary history and global expansion of *Candida auris* using population genomic analyses. mBio **2020**; 11: e03364-19.
10. Suphavilai C, Ko KK, Lin KM, et al. Discovery of the sixth *Candida auris* clade in Singapore. medRxiv. 023.08.01.23293435 [Preprint]. 2023. Available at:

https://www.medrxiv.org/content/10.1101/2023.08.01.23293435v1.full-text#ref-14. Accessed October 30, 2023
11. Vallabhaneni S, Kallen A, Tsay S, et al. Investigation of the first seven reported cases of *Candida auris*, a globally emerging invasive, multidrug-resistant fungus - United States, May 2013-August 2016. MMWR Morb Mortal Wkly Rep **2016**; 65: 1234–7.
12. Ambaraghassi G, Dufresne PJ, Dufresne SF, et al. Identification of *Candida auris* by use of the updated Vitek 2 yeast identification system, version 8.01: a multilaboratory evaluation study. J Clin Microbiol **2019**; 57:e00884-19.
13. Marathe A, Zhu Y, Chaturvedi V, Chaturvedi S. Utility of CHROMagar™ Candida plus for presumptive identification of *Candida auris* from surveillance samples. Mycopathologia **2022**; 187(5–6):527–34.
14. Driemeyer C, Falci DR, Oladele RO, et al. The current state of clinical mycology in Africa: a European Confederation of Medical Mycology and International Society for Human and Animal Mycology survey. Lancet Microbe **2022**; 3:e464–70.
15. Osaigbovo II, Oladele RO, Orefuwa E, Akanbi OA, Ihekweazu C. Laboratory diagnostic capacity for fungal infections in Nigerian tertiary hospitals: a gap analysis survey. West Afr J Med **2021**; 38:1065–71.
16. Bongomin F, Ekeng BE, Kwizera R, et al. Fungal diseases in Africa: closing the gaps in diagnosis and treatment through implementation research and advocacy. J Med Mycol **2023**; 33:101438.
17. Centers for Disease Control and Prevention. Antifungal susceptibility testing and interpretation. Candida auris. **2020**. Available at: https://www.cdc.gov/fungal/candida-auris/c-auris-antifungal.html. Accessed 30 October 2023.
18. Govender NP, Magobo RE, Mpembe R, et al. *Candida auris* in South Africa, 2012–2016. Emerg Infect Dis **2018**; 24:2036–40.
19. van Schalkwyk E, Mpembe RS, Thomas J, et al. Epidemiologic shift in candidemia driven by *Candida auris*, South Africa, 2016–2017. Emerg Infect Dis **2019**; 25: 1698–707.
20. Kekana D, Naicker SD, Shuping L, et al. *Candida auris* clinical isolates associated with outbreak in neonatal unit of tertiary academic hospital, South Africa. Emerg Infect Dis **2023**; 29:2044–53.
21. Naicker SD, Maphanga TG, Chow NA, et al. Clade distribution of *Candida auris* in South Africa using whole genome sequencing of clinical and environmental isolates. Emerg Microbes Infect **2021**; 10:1300–8.
22. Magobo R, Mhlanga M, Corcoran C, Govender NP. Multilocus sequence typing of azole-resistant *Candida auris* strains, South Africa. S Afr J Infect Dis **2020**; 35:116.
23. Maphanga TG, Naicker SD, Kwenda S, et al. In vitro antifungal resistance of *Candida auris* isolates from bloodstream infections, South Africa. Antimicrob Agents Chemother **2021**; 65:e0051721.
24. Maphanga TG, Mpembe RS, Naicker SD, Govender NP; for GERMS-SA. In vitro antifungal activity of Manogepix and other antifungal agents against South African *Candida auris* isolates from bloodstream infections. Microbiol Spectr **2022**; 10:e0171721.
25. Shuping L, Mpembe R, Mhlanga M, et al. Epidemiology of culture-confirmed candidemia among hospitalized children in South Africa, 2012–2017. Pediatr Infect Dis J **2021**; 40:730–7.
26. Shuping L, Maphanga TG, Naicker SD, et al. High prevalence of *Candida auris* colonization during protracted neonatal unit outbreak, South Africa. Emerg Infect Dis **2023**; 29:1913–6.
27. Magobo RE, Corcoran C, Seetharam S, Govender NP. *Candida auris*–associated candidemia, South Africa. Emerg Infect Dis **2014**; 20:1250.
28. Parak A, Stacey SL, Chibabhai V. Clinical and laboratory features of patients with *Candida auris* cultures, compared to other Candida, at a South African hospital. J Infect Dev Ctries **2022**; 16:213–21.
29. Vazquez JA, Pappas PG, Boffard K, et al. Clinical efficacy and safety of a novel antifungal, Fosmanogepix, in patients with candidemia caused by *Candida auris*: results from a phase 2 trial. Antimicrob Agents Chemother **2023**; 67:e0141922.
30. Zerrouki H, Ibrahim A, Rebiahi SA, et al. Emergence of *Candida auris* in intensive care units in Algeria. Mycoses **2022**; 65:753–9.
31. El-Kholy M, Shawky S, Fayed A, Meis J. *Candida auris* bloodstream infection in Egypt. In: Gangneux JP, Lortholary O, Cornely OA, Pagano L, eds. 9th Trends in medical mycology held on 11–14 October 2019. 9th ed. Vol 5. Nice, France: Organized under the Auspices of EORTC-IDG and ECMM: J Fungi (Basel), **2019**:310–1.
32. Adam RD, Revathi G, Okinda N, et al. Analysis of *Candida auris* fungemia at a single facility in Kenya. Int J Infect Dis **2019**; 85:182–7.
33. Solomon D, Nyerere A, Kanyua A, Ngugi C. Prevalence, species distribution and antifungal susceptibility profile of Candida species isolated from bloodstream of critical care unit patients in a tertiary care hospital in Kenya. Open J Med Microbiol **2021**; 11:32–46.
34. Ombajo L, Correia M, Kanyua A, et al. Characteristics of *Candida auris* patients at a tertiary-care hospital, 2017–2019, Nairobi, Kenya. Infect Control Hosp Epidemiol **2020**; 41(S1):S162–3.
35. Oladele R, Uwanibe JN, Olawoye IB, Ettu AO, Meis JF, Happi CT. Emergence and genomic characterization of multidrug resistant *Candida auris* in Nigeria, West Africa. J Fungi (Basel) **2022**; 8:787.
36. Badri MA, Sherfi SA. First detection of emergent fungal pathogen *Candida auris* in Khartoum state, Sudan. Am J Biomed Sci Res **2019**; 6:4–7.
37. Heath CH, Dyer JR, Pang S, Coombs GW, Gardam DJ. *Candida auris* sternal osteomyelitis in a man from Kenya visiting Australia, 2015. Emerg Infect Dis **2019**; 25:192–4.
38. Brooks RB, Walters M, Forsberg K, Vaeth E, Woodworth K, Vallabhaneni S. *Candida auris* in a U.S. patient with carbapenemase-producing organisms and recent hospitalization in Kenya. MMWR Morb Mortal Wkly Rep **2019**; 68:664–6.
39. Benedict K, Forsberg K, Gold JAW, Baggs J, Lyman M. *Candida auris*–associated hospitalizations, United States, 2017–2022. Emerg Infect Dis **2023**; 29:1485–7.
40. Lockhart SR. *Candida auris* and multidrug resistance: defining the new normal. Fungal Genet Biol **2019**; 131:103243.
41. Espinel-Ingroff A, Arendrup MC, Pfaller MA, et al. Interlaboratory variability of caspofungin MICs for Candida spp. using CLSI and EUCAST methods: should the clinical laboratory be testing this agent? Antimicrob Agents Chemother **2013**; 57:5836–42.
42. Pfaller MA, Diekema DJ, Jones RN, Castanheira M. Use of anidulafungin as a surrogate marker to predict susceptibility and resistance to caspofungin among 4,290 clinical isolates of Candida by using CLSI methods and interpretive criteria. J Clin Microbiol **2014**; 52:3223–9.
43. Chowdhary A, Prakash A, Sharma C, et al. 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. J Antimicrob Chemother **2018**; 73:891–9.
44. Storr J, Twyman A, Zingg W, et al. Core components for effective infection prevention and control programmes: new WHO evidence-based recommendations. Antimicrob Resist Infect Control **2017**; 6:6.
45. Clancy CJ, Nguyen MH. Emergence of *Candida auris*: an international call to arms. Clin Infect Dis **2017**; 64:141–3.