Overview about *Candida auris*: what's up 12 years after its first description?

Guillaume Desoubeaux[1], Alix T. Coste[2], Christine Imbert[3], Christophe Hennequin[4, #]

1. Parasitologie – Mycologie – Médecine tropicale, Hôpital Bretonneau, F-37044 CHRU Tours, France
2. Institute of Microbiology, University hospital Lausanne, 1011 Lausanne, Switzerland
3. Laboratoire Ecologie et Biologie des Interactions, Université de Poitiers, UMR CNRS 7267, F-86073 Poitiers, France
4. Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, AP-HP, Hôpital Saint-Antoine, Service de Parasitologie-Mycologie, F-75012 Paris, France

*Corresponding author: christophe.hennequin@sorbonne-universite.fr

Hôpital St-Antoine, laboratoire de Parasitologie - Mycologie

184 Rue du Faubourg Saint-Antoine, 75012 Paris - FRANCE

Tel.: +33(0)1 49 28 30 30 Fax: +33(0)2 47 47 8082

Abstract

Candida auris has been described as an emerging yeast species during the last decade. As many as 25% of its strains may naturally exhibit multi-drug resistance to the currently available antifungal drugs. Probably due to its ability to survive more than two weeks on inert surfaces, several large outbreaks have been reported, primarily due to nosocomial transmissions. In addition, due to a rapid worldwide spreading, *C. auris* is now considered as a major public health threat. This review aims at describing the current knowledge about *C. auris*, with specific focuses on its global epidemiology, virulence features, most reliable diagnostic approaches, and the current and future therapeutic options.

Keywords: *Candida auris*; epidemiology; genetic; diagnosis; resistance

Number of words: 3105

Number of figures: 2

Number of table: 1

Introduction

First described in 2009, *Candida auris* has rapidly been placed in the spotlight, not only of medical journals, but also making the headlines of mass media (1,2) (Figure 1). Indeed, this yeast species causing large hospital outbreaks and characterized by a high level of antifungal resistance has emerged as a major threat for the public health over the last ten years (3,4). *Candida auris* cases have now been reported over all the continents (Figure 2) (5–8). However, the true prevalence of *C. auris* over the world remains partly unknown as the species identification can be challenging, notably in low-income countries. Yet, it is critical that all microbiology laboratories are able to rapidly recognize the species and test the *in vitro* susceptibility for every *C. auris* isolates (9). Indeed, a rapid and reliable detection is of utmost importance to limit the nosocomial transmission. Controlling and preventing the spread of *C. auris* requires the isolation of any colonized/infected individual and the screening of any contact cases. Sampling the medical environment for detecting a source of contamination can complete the investigation. The reinforcement of standard hygiene measures remains also a key-feature to limit outbreaks expansion.

This brief review focuses on the latest scientific data published on *C. auris*, regarding its epidemiology and virulence, the diagnostic approaches, and the preventive and curative strategies.

Epidemiology: history and current trends

The origins of *Candida auris* and its initial ecological niche(s) are still largely unknown to date. The emergence of very different clades in different places of the world in a very short period of time is particularly intriguing. Some have suggested the global warming may have played a role in the selection of this organism (10,11). It is then assumed that spreading may have been ensured

thanks to animals with high body temperature, *e.g.* birds, that would have been responsible for distributing the fungus into urban areas where it could subsequently infect humans (10).

Soon after the species was first described from an isolate collected from the external ear canal of a Japanese patient in 2009 (1), several clusters of cases were reported from India in 2009-11 (*n*=12 patients) and 2010-14 (*n*=90) (12,13). However, it was *a posteriori* shown that *C. auris* had been introduced in some countries, notably France, before the original description of the species (14). Similar conclusions arose from Asia, where retrospective analysis of stored strains have detected the presence of *C. auris* before 2009 in South Korea (15,16). So far, Portugal, Ireland Republic, and Scandinavian countries (except Norway) are the only western European nations having not declared any case (17,18).

It clearly appears that *C. auris* has a noticeable propensity to generate outbreaks. Some of the largest ones are summarized in Table 1. However outbreak spreading is not systematic as shown with a single case of colonization reported in France (Tours) in 2020, in a Lebanese patient who visited Iran and India before arriving in Europe (9). To date, the United States of America has been the country with the highest number of cases declared: 1,157 cases of proven or probable infection notified to the Center for Diseases Control (CDC) and more than 3,043 cases of colonization were reported (https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html). However, it is noteworthy that the incidence of *C. auris* infection in the US is actually greatly heterogeneous depending on the geographic areas: more than 285, 242 and 245 deep-seated infections have been reported in the state of New York, Illinois and California, respectively (19,20), while some neighbor states, such as Vermont, Wisconsin or Oregon, are free of *C. auris* detection to date. A 4-cases cluster has also been reported from Canada (Greater Vancouver area) in 2018 (21). More recently, several South American countries have reported *C. auris* outbreaks for the first time in the context of COVID-19 pandemic (22). Similarly, in India, *C. auris* was responsible for 60%

cases of candidemia in a single COVID-19 ward (23). Considering the length of stay of such infected patients in ICU, the viral infection may represent an indirect predisposing factor for the (re)emergence of *C. auris* (9,22,23).

In the more advanced countries, after the occurrence of large outbreaks, cases became more sporadic and *C. auris* only represent a minority of candidiasis cases, sometimes grouped in small clusters (4,24). In contrast, in some low-income countries such as South Africa, *C. auris* may represent as much as 14% of the causative species for candidemia (25) and has become the fifth most common cause of fungal bloodstream infection in children (26).

Thanks to whole genome sequencing (WGS) population genetic studies revealed that *C. auris* species is split into four major clades (27). Genetic distribution follows the geographic origin of the strains with clade I, so-called the South Asian clade, made of strains of Indo-Pakistani origin, clade II, referred to as the East clade, made of Korean and Japanese strains, clade III is the South African clade, and clade IV referenced as the South American clade composed of Colombian and Venezuelan strains. In the USA, the clade I is largely predominant, except in Illinois and Indiana where clades III and IV are the most prevalent (19), suggesting different timing for the introduction of those strains. In Europe, most *C. auris* isolates belong to the clade I (7), although the strains of the Valencia hospital (Spain) were slightly genotypically-distinct from all those previously reported (24). Noteworthy, a strain of the clade II was also found in Austria (28). In 2019, some Iranian authors suggested the existence of a potential fifth clade, separated from the other clades by >200,000 single-nucleotide polymorphisms (SNP), in a patient who had never traveled outside the country (29).

Virulence: is something different from other *Candida* species?

Virulence of *C. auris* is more and more investigated using a wide variety of models, either *in vitro* (30), *in vivo* - mouse (31,32), or invertebrate nematodes like *Caenorhabditis elegans* (33,34), or the wax moth *Galleria mellonella* (34–36) -, or *ex vivo* – oral (31) and skin models (37). As commonly seen with opportunistic fungal pathogens, results greatly vary according to the model, but some results also support difference in virulence according to the tested strains.

By studying more than 100 *C. auris* isolates, Carvajal *et al.* looking at the mortality at day-5 post infection, in a *G. mellonella* model, were able distinguish between a highly pathogenic population (35.5% of the isolates) and a moderately pathogenic one (36). In a mouse model undergoing cortisone acetate-induced immunosuppression, Abe *et al.* reported that the capability of colonization and dissemination from gastro-intestinal tracts was higher for four strains isolated from pathogenic condition (bloodstream infections) than for two non-invasive strains (isolated from chronic otitis media) (32). The virulence of *C. auris* was also compared to other *Candida* species. Using the *G. mellonella* model, Romera *et al*. concluded on a higher pathogenicity of *C. albicans* clinical strains, when considering the larva death rate as primary outcome (35). However, other authors observed that the pathogenicity pattern of a *C. albicans* reference strain (SC5314) was somewhat comparable to that of 38% of their 107 *C. auris* isolates (36).

Understanding how *C. auris* invade the epithelial layer, while it does not form hyphae, remains a challenge. Indeed, Ben-Ami *et al*. reported considerable virulence of *C. auris* in mice, more than what could be expected for a *Candida* species that produces no – or only rudimentary, after experimental passages through mammalian hosts (38) – hyphae. Depending on isolates from certain clades, the formation of large yeast cell aggregating in infected tissue, a phenomenon also found in *Galleria* larvae infected (39,40) and in a model of neutropenic mice, may play a role in the virulence (41). Actually, the capacity to form aggregates, referred to as the aggregative

phenotype, is a unique pathogenic feature displayed by some isolates of *C. auris* (30). Recent results suggested that the non-aggregative phenotype of *C. auris* isolates may exhibit some level of immune evasion (30). For instance, Hernando-Ortiz *et al.* recently concluded that the pathogenicity of 11 non-aggregative clinical isolates was higher than that of an aggregative strain in a nematode and the wax moth host models. (34). In contrast, Carvajal *et al*. observed no significant difference in *G. mellonella* mortality induced by either aggregative (*n*=35) or non-aggregative *C. auris* strains (*n*=72) (36), which was consistent with some previous findings (35).

Recent data also showed the ability of *C. auris* to adhere and to form biofilm. Highlighting the importance of the model, Vila et al showed that *C. auris* avidly adhere to an *ex-vivo* oral tissue (tongue epithelium), but failed *in vivo* to colonize the oral cavity (31). Through *in vitro* tests, Vila *et al.* observed that *C. auris* formed less biofilm than *C. albicans*, despite some substantial variability for the former (31). Using scanning electron microscopy, they also demonstrated the formation in 72 hours of biofilm within catheter lumens implanted subcutaneously in mouse, *C. auris* and *C. albicans* producing comparable levels of biofilm. The influence of the environmental conditions was also highlighted by Horton *et al*. who compared biofilm produced by *C. auris* and *C. albicans* strains in a synthetic sweat medium mimicking axillary skin conditions and in RPMI culture medium (37). Interestingly, *C. auris* produced a significantly denser biofilm than *C. albicans* in the mimicked skin medium, whereas the almost contrary was observed in RPMI medium (32,33). Using an immunosuppressed mouse model, Abe *et al.* found that invasive strains of *C. auris* form more biofilm than non-invasive ones (32). They correlated this difference to the higher capability of the formers to colonize the gastrointestinal tract (32). Hernando-Ortiz *et al*. also suggested that the biofilm formation could be related to the aggregative phenotype, as the strains exhibiting this trait produced more biofilm than the non-aggregative ones (34), a result

147 inconsistent with others previously published (42). Recent analyses suggested that, irrespective of
148 the ability to produce biofilm, the transcriptome of aggregative cells was significantly different
149 from that of non-aggregative ones during the biofilm formation (30). Of note, these data have to be
150 interpreted with caution, because of the low number of strains that were studied and the great
151 variability of their capacity to form biofilm independently of their aggregative/non aggregative
152 phenotype.

153 Despite a dramatic increase in our knowledge in the biology of *C. auris*, altogether, these results
154 highlight how parceled is our understanding of the pathogenicity that is obviously a multifactorial
155 phenomenon. Further studies comparing large groups of strains belonging to the different clades in
156 different models are thus warranted.

157

158 **Diagnosis: steps to reach a reliable identification**

159 Identification of *C. auris* is crucial to initiate adequate treatment and contain hospital outbreaks.
160 As a member of the *Candida/Clavispora* clade, *C. auris* does not have different requirements for
161 growth from other *Candida* species (43). Colonies can be easily obtained after 24 hours incubation
162 at 30-35°C on conventional media, such as Sabouraud dextrose agar or malt extract agar. Of note,
163 *C. auris* is tolerant to temperature up to 42°C (9), which is not the case of many other *Candida*
164 species. On the conventional CHROMagar Candida® chromogenic media (Becton-Dickinson,
165 Rungis, France), *C. auris* colonies appear white, pink, or purple (9). On the CAN2® plates
166 (bioMérieux, Capronne, France), colonies are initially whitish, and then display a light reddish-
167 pink color, very close to that of *Candida kefyr* or *Candida tropicalis* (9). Two specific chromogenic
168 media, so called CHROMagar Candida Plus® (Becton-Dickinson, Rungis, France) and HiCrome
169 *C. auris* MDR® selective agar (HiMedia, Mumbai, India), have been recently set-up to isolate and

presumptively identify *C. auris* with an almost 100% sensitivity and specificity rates after 36-48 h of incubation (44–46). *C. auris* can also grow in blood culture vial, in aerobic flasks or using Fungal IC/F® bottles (Becton-Dickinson, Rungis, France) (personal data). At direct examination, the yeasts appear ovoid and budding without pseudo-hyphae.

When using auxanogram, *C. auris* can be recognized through its capability of assimilation of N-acetylglucosamine, succinic acid and gluconic acid. However, the species is not referenced in most of the databases of former handbooks, thus leading to false negative results or misidentifications (47), notably with strains of the *Candida haemulonii* clade (13).

Nowadays, definitive identification of *C. auris* species can be achieved by the mean of mass spectrometry MALDI-TOF combined with an up-to-date spectra database. This is the case for the Bruker Biotyper® (Palaiseau, France) and the bioMérieux Vitek® systems (Capronne, France), as well as the independent user-made MSI® library (Paris, France).

Several molecular tools have also been developed for the identification and/or detection of *C. auris*. Once colonies are isolated onto agar plates, they can be confidently identified by sequencing either the D1/D2 region of the large subunit (LSU) or the internal transcribed spacer (ITS) of the ribosomal DNA. Interestingly, combining the analysis of these tow loci allows the assignation of strains to one of the four major clades without recourse to WGS approaches (48). Otherwise, a few molecular protocols have been proposed to detect *C. auris* directly from swabs (49,50), allowing thus rapid screening of asymptomatic patients. Recently, two commercial kits have been evaluated with noticeable differences in terms of sensitivity and specificity (51).

Therapeutic options: multi-resistance and current limits

Almost all *C. auris* strains exhibit *in vitro* resistance to fluconazole, with strains from certain clades also showing elevated minimum inhibitory concentrations (MICs) to the other azole antifungal agents higher than those of other *Candida* species, especially *C. albicans* and even *C. glabrata* (52) (53). Some resistance profiles were found to be clade-dependant (54): for example, fluconazole and voriconazole exhibited significantly higher MICs against isolates of the South African lineage than against isolates of the Southern Asian lineage. In addition, lesser susceptibility to amphotericin B and to echinocandins has been reported in some isolates, and rapid emergence of multidrug resistance (defined by resistance against at least two antifungal classes) has been documented to occur during antifungal treatment. Clinical breakpoints were recently proposed for echinocandins with values set at 2, 4, and 4 µg/mL, for caspofungin, anidulafungin, and micafungin, respectively, at 2 for amphotericin B and at 32 for fluconazole (no data are available for other azole drugs) (55). Using these values, Chowdary *et al*. showed that 90% of 350 Indian strains were resistant to fluconazole, 8% to amphotericin B, and 2% to echinocandins, with 25% of the strains exhibiting a multidrug profile (56). These data were used to propose therapeutic recommendations, suggesting an echinocandin as first line therapy in the case of proven or probable diagnosis of *C. auris* invasive infection (57).

The investigation of molecular mechanisms underlying the phenotype of azole resistance in *C. auris* first allowed the demonstration of homologues of genes involved directly or not in the ergosterol biosynthesis pathway in *C. albicans*. A limited number of non-synonymous point mutations (F126, Y132, K143 and F444 (3)) were found the *ERG11* homologue that correlates with an increase in azoles MICs (56,58). Moreover, two homologues of the *C. albicans TAC1* gene, so called *TAC1a* and *TAC1b*, have also been described. In *C. albicans*, Tac1 is a transcription factor regulating the ABC transporters Cdr1 and Cdr2, two efflux pumps, which overexpression due to

Commenté [CA1]: Ici il y a un probleme avec les ref....

Commenté [CH2]: Manque la ref 54 non ?

Commenté [CH3]: je ne comprends pas ce que fait cette ref ici ?

Mis en forme : Couleur de police : Texte 1

Mis en forme : Couleur de police : Texte 1

Tac1 gain of function mutation is responsible for azoles resistance. However, only *TAC1b* displayed a (moderate) role in azole susceptibility of *C. auris* (59–61): Li *et al.* and Ryback *et al.* specified the role of two gain-of-function mutations in *TAC1b*, at position S611P and A640V, respectively (59,61). Thus, some authors clearly pointed out the importance of the Cdr1 protein in the azole resistance of *C. auris* (61,62), whereas others evidenced a Cdr1-independent pathway of action for Tac1b, which remains to be elucidated (59–61). Mrr1 is another transcription factor that regulates the expression of the Major facilitator transporter Mdr1 which overexpression due to Mrr1 gain of function mutation is responsible for fluconazole resistance. ~~However, up-to-now, no clear role of the~~Recent data suggest a role of *C. auris* homologue of *MRR1*, ~~has been demonstrated~~in azole susceptibility. Indeed, deletion of *MRR1a* in clade III strains (60), and N647T mutation (Dr F. Lamoth, personal communication) were shown to be responsible for azoles decrease susceptibility. Regarding the resistance to echinocandins, the role of the S639F mutation in *FKS1* hot-spot 1 has been highlighted (56). Some strains were shown to exhibit an eagle effect in presence of high concentration of caspofungin *in vitro*, but with no apparent impact on the *in vivo* efficacy at human dosage in a murine model of infection (63).

Commenté [DIH4]: Je pense que tu peux écrire une phrase à ce sujet, Alix. Le temps que l'article soit revu et publié, peut-être que le tien sera accepté avant (sinon, on mettra unpublished data)

A very recent *in vitro* study demonstrated by WGS the high potential of *C. auris* to rapidly adapt to drug pressure whatever the antifungal drug (64). The elevation of MIC resulted from acquisition of different point mutations in genes already known to be associated with antifungal resistance (64,65), but also by duplicating part of the genome carrying those genes to further increase MIC, as previously shown in *C. albicans* (66,67). This was further supported by karyotyping experiments described by Bravo Ruiz *et al.* (68) who showed how extreme the genomic plasticity of *C. auris* is when the yeast is confronted to a large range of stresses. It is thus crucial to explore in the near future innovative therapeutic options. New triazoles or tetrazoles (VT-1598) appeared to be

efficient on azole-resistant *C. auris* strains (69). The new echinocandin, referred as rezafungin, was also found to be as or more active than other echinocandin drugs both *in vitro* (70–72) and in mouse models (73,74). More interestingly, new antifungals currently under development, such as ibrexafungrep, the first drug of the triterpenoid class, and the fosmanogepix could be available soon. The latter, first member of a new therapeutic class targetting the Gwt1 protein (involved in GPI anchor biosynthesis pathway), exhibits interesting results, including on strains that are multi-resistant to current treatments (69,75).

Prevention: which prophylactic means in healthcare facilities?

While modes of acquisition remain uncertain, the ability to form biofilms and to acquire antifungal resistance points out the need to rapidly implement appropriate prevention measures to limit the spread of *C. auris* in healthcare facilities. In a recent study carried out in a Chicago hospital, 31 colonized residents were found to have high *C. auris* burden on their skin, estimated at 1.22×10^5 cells/swabbing by culture. This was positively correlated with contamination of their surrounding environment with the demonstration of *C. auris* on all handrails of beds, on doorknobs and windowsills (76). Therefore, every patient suspected to host *C. auris* either because of a history of contact-case or a recent stay in an endemic country should be systematically screened. Serial sampling sessions have to be repeated weekly until hospital discharge (77). All cases of *C. auris* colonization or infection should be clearly identified and notified to a multi-disciplinary staff specialized in hygiene issues and nosocomial infection (4,78). Deployment of subsequent containment measures should expectedly lead to a gradual decline in the incidence of positive cases and prevent further emergence of cluster. Thus, strict isolation of concerned subjects, similar to that set up for patients harboring multi-drug resistant bacteria, is highly recommended.

It is considered that *C. auris* can be transmitted either by direct or indirect contact (79). For instance contaminated reusable skin/surface temperature probes have been clearly demonstrated the source of infection in an English hospital outbreak (80). It is thus crucial to recall healthcare givers the importance to thoroughly wash their hands when moving from one patient to another. Gloves, lab-coat must also be changed, and all and medical instruments, like stethoscopes, ultrasound devices, or thermometers, carefully cleaned. For cleaning inert material, quaternary ammonium disinfectants should be avoided because they have been shown to be ineffective against *C. auris* (81). In contrast, sodium hypochlorite, peracetic acid, and hydrogen peroxide have been experimentally proven to reduce the fungal load as measured by CFU counting by 5.0 to 6.0 Log_{10} (81,82). Disposable wipes soaked with sodium hypochlorite must be preferred for cleaning surfaces. Recent reports suggested chlorhexidine- or iodine-povidone-based products to be greatly efficient to reducing the fungal burden on the skin (83–85). Those skin antiseptics should be used for cleaning localized wound or to reduce the cutaneous burden before surgery for example. National guidelines regarding prevention ~~meseasures~~measures and the optimal care of patients infected or colonized with *C. auris* have been recently published (78,86).

Beside the human impact, controlling *C. auris* in healthcare facilities leads to a huge overcost~~s~~. In a tertiary care center in London, the cost for implementing specific measures were assessed at £1 million (1.332 M€, 1.176 M$), followed by £58,000/month during the subsequent year (87).

Conclusion

In less than 15 years, *C. auris* became of major fungal pathogen, both because of its capability to generate large outbreaks and the possible therapeutic dead-end it represents. Critical advances in

the knowledge of this species have been obtained, but mycologists have to keep staying vigilant for reliably diagnosing the cases during possible advent of outbreaks in their healthcare facilities.

Ethics

Not applicable

Disclosure of conflicts of interest

AC, CI and CH are editors-in-chief of the *Journal of Medical Mycology*; GD serves as a recurrent associate editor.

Funding

Neither grant nor industrial funding was required for this study.

References

1. 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 Jan;53(1):41–4.

2. A Mysterious Infection, Spanning the Globe in a Climate of Secrecy - The New York Times [Internet]. [cited 2021 Aug 9]. Available from: https://www.nytimes.com/2019/04/06/health/drug-resistant-candida-auris.html

3. Lockhart SR, Etienne KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender NP, et al. Simultaneous emergence of multidrug-Resistant *Candida auris* on 3 continents confirmed by whole-genomesequencing and epidemiological analyses. Clin Infect Dis. 2017 Jan 15;64(2):134–40.

4. Schelenz S, Hagen F, Rhodes JL, Abdolrasouli A, Chowdhary A, Hall A, et al. First hospital outbreak of the globally emerging *Candida auris* in a European hospital. Antimicrob Resist Infect Control. 2016;5:35.

5. Umamaheshwari S, Neelambike SM, Shankarnarayan SA, Kumarswamy KS, Gopal S, Prakash H, et al. Clinical profile, antifungal susceptibility, and molecular characterization of *Candida auris* isolated from patients in a South Indian surgical ICU. J Med Mycol. 2021 Dec 1;31(4):101176.

6. Rodriguez JY, Le Pape P, Lopez O, Esquea K, Labiosa AL, Alvarez-Moreno C. *Candida auris*: a latent threat to critically ill patients with COVID-19. Clin Infect Dis. 2020 Oct 18;ciaa1595.

7. Rhodes J, Fisher MC. Global epidemiology of emerging *Candida auris*. Curr Opin Microbiol. 2019 Dec;52:84–9.

8. Du H, Bing J, Hu T, Ennis CL, Nobile CJ, Huang G. *Candida auris*: epidemiology, biology, antifungal resistance, and virulence. PLOS Pathog. 2020 Oct 22;16(10):e1008921.

9. Desoubeaux G, Bailly É, Guillaume C, De Kyvon M-A, Tellier A-C, Morange V, et al. *Candida auris* in contemporary mycology labs: a few practical tricks to identify it reliably according to one recent French experience. J Mycol Medicale. 2018 Jun;28(2):407–10.

10. van Rhijn N, Bromley M. The consequences of our changing environment on life threatening and debilitating fungal diseases in humans. J Fungi Basel Switz. 2021 May 7;7(5):367.

11. Casadevall A, Kontoyiannis DP, Robert V. Environmental *Candida auris* and the global warming emergence hypothesis. mBio. 2021 Mar 16;12(2):e00360-21.

12. Chowdhary A, Sharma C, Duggal S, Agarwal K, Prakash A, Singh PK, et al. New clonal strain of *Candida auris*, Delhi, India. Emerg Infect Dis. 2013 Oct;19(10):1670–3.

13. Kathuria S, Singh PK, Sharma C, Prakash A, Masih A, Kumar A, et al. Multidrug-resistant *Candida auris* misidentified as *Candida haemulonii*: characterization by Matrix-assisted laser desorption ionization-time of flight mass spectrometry and DNA sequencing and its antifungal susceptibility profile variability by Vitek 2, CLSI broth microdilution, and Etest method. J Clin Microbiol. 2015 Jun;53(6):1823–30.

14. Desnos-Ollivier M, Fekkar A, Bretagne S. Earliest case of *Candida auris* infection imported in 2007 in Europe from India prior to the 2009 description in Japan. J Med Mycol. 2021 Apr 8;31(3):101139.

15. Kim M-N, Shin JH, Sung H, Lee K, Kim E-C, Ryoo N, et al. *Candida haemulonii* and closely related species at 5 university hospitals in Korea: identification, antifungal susceptibility, and clinical features. Clin Infect Dis Off Publ Infect Dis Soc Am. 2009 Mar 15;48(6):e57-61.

16. Shin JH, Kim M-N, Jang SJ, Ju MY, Kim SH, Shin MG, et al. Detection of amphotericin B resistance in *Candida haemulonii* and closely related species by use of the Etest, Vitek-2 yeast susceptibility system, and CLSI and EUCAST broth microdilution methods. J Clin Microbiol. 2012 Jun;50(6):1852–5.

17. Chen J, Tian S, Han X, Chu Y, Wang Q, Zhou B, et al. Is the superbug fungus really so scary? A systematic review and meta-analysis of global epidemiology and mortality of *Candida auris*. BMC Infect Dis. 2020 Dec;20(1):1–10.

18. Plachouras D, Lötsch F, Kohlenberg A, Monnet DL, Group the C auris survey collaborative. *Candida auris*: epidemiological situation, laboratory capacity and preparedness in the European Union and European Economic Area*, January 2018 to May 2019. Eurosurveillance. 2020 Mar 26;25(12):2000240.

19. Chow NA, Gade L, Tsay SV, Forsberg K, Greenko JA, Southwick KL, et al. Multiple introductions and subsequent transmission of multidrug-resistant *Candida auris* in the USA: a molecular epidemiological survey. Lancet Infect Dis. 2018 Dec;18(12):1377–84.

20. Adams E, Quinn M, Tsay S, Poirot E, Chaturvedi S, Southwick K, et al. *Candida auris* in healthcare facilities, New York, USA, 2013-2017. Emerg Infect Dis. 2018 Oct;24(10):1816–24.

21. Eckbo EJ, Wong T, Bharat A, Cameron-Lane M, Hoang L, Dawar M, et al. First reported outbreak of the emerging pathogen *Candida auris* in Canada. Am J Infect Control. 2021 Jun;49(6):804–7.

22. de Jong AW, Francisco EC, de Almeida JN, Brandão IB, Pereira FM, Dias PHP, et al. Nanopore genome sequencing and variant analysis of the susceptible *Candida auris* strain L1537/2020, Salvador, Brazil. Mycopathologia. 2021 Dec;186(6):883–7.

23. Chowdhary A, Tarai B, Singh A, Sharma A. Multidrug-resistant *Candida auris* infections in critically ill coronavirus sisease patients, India, April-July 2020. Emerg Infect Dis. 2020 Nov;26(11):2694–6.

24. Ruiz-Gaitán A, Moret AM, Tasias-Pitarch M, Aleixandre-López AI, Martínez-Morel H, Calabuig E, et al. An outbreak due to *Candida auris* with prolonged colonisation and candidaemia in a tertiary care European hospital. Mycoses. 2018 Jul;61(7):498–505.

25. van Schalkwyk E, Mpembe RS, Thomas J, Shuping L, Ismail H, Lowman W, et al. Epidemiologic shift in candidemia driven by *Candida auris*, South Africa, 2016-2017. Emerg Infect Dis. 2019 Sep;25(9):1698–707.

26. Shuping L, Mpembe R, Mhlanga M, Naicker SD, Maphanga TG, Tsotetsi E, et al. Epidemiology of culture-confirmed candidemia among hospitalized children in South Africa, 2012-2017. Pediatr Infect Dis J. 2021 Aug 1;40(8):730–7.

27. Muñoz JF, Gade L, Chow NA, Loparev VN, Juieng P, Berkow EL, et al. Genomic insights into multidrug-resistance, mating and virulence in Candida auris and related emerging species. Nat Commun. 2018 Dec 17;9(1):5346.

28. Pekard-Amenitsch S, Schriebl A, Posawetz W, Willinger B, Kölli B, Buzina W. Isolation of *Candida auris* from ear of otherwise healthy patient, Austria, 2018. Emerg Infect Dis. 2018 Aug;24(8):1596–7.

29. Chow NA, de Groot T, Badali H, Abastabar M, Chiller TM, Meis JF. Potential fifth clade of *Candida auris*, Iran, 2018. Emerg Infect Dis. 2019 Sep;25(9):1780–1.

30. Brown JL, Delaney C, Short B, Butcher MC, McKloud E, Williams C, et al. *Candida auris* phenotypic heterogeneity determines pathogenicity *in vitro*. mSphere. 2020 Jun 24;5(3):e00371-20.

31. Vila T, Montelongo-Jauregui D, Ahmed H, Puthran T, Sultan AS, Jabra-Rizk MA. Comparative evaluations of the pathogenesis of *Candida auris* phenotypes and *Candida albicans* using clinically relevant murine models of infections. mSphere. 2020 Aug 5;5(4):e00760-20.

32. Abe M, Katano H, Nagi M, Higashi Y, Sato Y, Kikuchi K, et al. Potency of gastrointestinal colonization and virulence of *Candida auris* in a murine endogenous candidiasis. PloS One. 2020;15(12):e0243223.

33. Lima SL, Rossato L, Salles de Azevedo Melo A. Evaluation of the potential virulence of *Candida haemulonii* species complex and *Candida auris* isolates in *Caenorhabditis elegans* as an *in vivo* model and correlation to their biofilm production capacity. Microb Pathog. 2020 Nov;148:104461.

34. Hernando-Ortiz A, Mateo E, Perez-Rodriguez A, de Groot PWJ, Quindós G, Eraso E. Virulence of *Candida auris* from different clinical origins in *Caenorhabditis elegans* and *Galleria mellonella* host models. Virulence. 2021 Dec;12(1):1063–75.

35. Romera D, Aguilera-Correa J-J, García-Coca M, Mahillo-Fernández I, Viñuela-Sandoval L, García-Rodríguez J, et al. The *Galleria mellonella* infection model as a system to investigate the virulence of *Candida auris* strains. Pathog Dis. 2020 Nov 23;78(9):ftaa067.

36. Carvajal SK, Alvarado M, Rodríguez YM, Parra-Giraldo CM, Varón C, Morales-López SE, et al. Pathogenicity assessment of Colombian strains of *Candida auris* in the *Galleria mellonella* invertebrate model. J Fungi Basel Switz. 2021 May 21;7(6):401.

37. Horton MV, Johnson CJ, Kernien JF, Patel TD, Lam BC, Cheong JZA, et al. *Candida auris* forms high-burden biofilms in skin niche conditions and on porcine skin. mSphere. 2020 Jan 22;5(1):e00910-19.

38. Yue H, Bing J, Zheng Q, Zhang Y, Hu T, Du H, et al. Filamentation in *Candida auris*, an emerging fungal pathogen of humans: passage through the mammalian body induces a heritable phenotypic switch. Emerg Microbes Infect. 2018 Nov 28;7(1):188.

39. Borman AM, Szekely A, Johnson EM. Comparative pathogenicity of United Kingdom isolates of the emerging pathogen *Candida auris* and other key pathogenic *Candida* species. mSphere. 2016 Aug;1(4):e00189-16.

40. Garcia-Bustos V, Ruiz-Saurí A, Ruiz-Gaitán A, Sigona-Giangreco IA, Cabañero-Navalon MD, Sabalza-Baztán O, et al. Characterization of the differential pathogenicity of *Candida auris* in a *Galleria mellonella* infection model. Microbiol Spectr. 2021 Sep 3;9(1):e0001321.

41. Forgács L, Borman AM, Prépost E, Tóth Z, Kardos G, Kovács R, et al. Comparison of *in vivo* pathogenicity of four *Candida auris* clades in a neutropenic bloodstream infection murine model. Emerg Microbes Infect. 2020 Dec;9(1):1160–9.

42. Sherry L, Ramage G, Kean R, Borman A, Johnson EM, Richardson MD, et al. Biofilm-forming capability of highly virulent, multidrug-resistant *Candida auris*. Emerg Infect Dis. 2017 Feb;23(2):328–31.

43. Du H, Bing J, Hu T, Ennis CL, Nobile CJ, Huang G. Candida auris: Epidemiology, biology, antifungal resistance, and virulence. PLOS Pathog. 2020 Oct 22;16(10):e1008921.

44. Mulet Bayona JV, Salvador García C, Tormo Palop N, Gimeno Cardona C. Evaluation of a novel chromogenic medium for Candida spp. identification and comparison with CHROMagar™ Candida for the detection of Candida auris in surveillance samples. Diagn Microbiol Infect Dis. 2020 Dec 1;98(4):115168.

45. Borman AM, Fraser M, Johnson EM. CHROMagarTM Candida Plus: a novel chromogenic agar that permits the rapid identification of *Candida auris*. Med Mycol. 2021 Mar 4;59(3):253–8.

46. de Jong AW, Dieleman C, Carbia M, Mohd Tap R, Hagen F. Performance of two novel chromogenic media for the identification of multidrug-resistant *Candida auris* compared with other commercially available formulations. J Clin Microbiol. 2021 Mar 19;59(4):e03220-20.

47. Parra-Giraldo CM, Valderrama SL, Cortes-Fraile G, Garzón JR, Ariza BE, Morio F, et al. First report of sporadic cases of *Candida auris* in Colombia. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2018 Apr;69:63–7.

48. Borman AM, Szekely A, Johnson EM. Isolates of the emerging pathogen *Candida auris* present in the UK have several geographic origins. Med Mycol. 2017 Jul 1;55(5):563–7.

49. Leach L, Zhu Y, Chaturvedi S. Development and Validation of a Real-Time PCR Assay for Rapid Detection of Candida auris from Surveillance Samples. J Clin Microbiol. 2018 Feb;56(2):e01223-17.

50. Sexton DJ, Kordalewska M, Bentz ML, Welsh RM, Perlin DS, Litvintseva AP. Direct Detection of Emergent Fungal Pathogen Candida auris in Clinical Skin Swabs by SYBR Green-Based Quantitative PCR Assay. J Clin Microbiol. 2018 Dec;56(12):e01337-18.

51. Sattler J, Noster J, Brunke A, Plum G, Wiegel P, Kurzai O, et al. Comparison of Two Commercially Available qPCR Kits for the Detection of Candida auris. J Fungi. 2021 Feb;7(2):154.

52. Chowdhary A, Sharma C, Meis JF. *Candida auris*: a rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. PLoS Pathog. 2017 May;13(5):e1006290.

53. Antifungal Susceptibility Testing and Interpretation | *Candida auris* | Fungal Diseases | CDC [Internet]. 2020 [cited 2021 Jul 21]. Available from: https://www.cdc.gov/fungal/candida-auris/c-auris-antifungal.html

54. Szekely A, Borman AM, Johnson EM. *Candida auris* isolates of the Southern Asian and South African lineages exhibit different phenotypic and antifungal susceptibility profiles *in vitro*. J Clin Microbiol. 2019 May;57(5):e02055-18.

55. Spivak ES, Hanson KE. *Candida auris*: an emerging fungal pathogen. J Clin Microbiol. 2018 Jan 24;56(2):e01588-17.

56. Chowdhary A, Prakash A, Sharma C, Kordalewska M, Kumar A, Sarma S, 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 Apr 1;73(4):891–9.

57. Treatment and management of infections and colonization | *Candida auris* | Fungal Diseases | CDC [Internet]. 2021 [cited 2021 Aug 12]. Available from: https://www.cdc.gov/fungal/candida-auris/c-auris-treatment.html

58. Healey KR, Kordalewska M, Jiménez Ortigosa C, Singh A, Berrío I, Chowdhary A, et al. Limited *ERG11* Mutations Identified in Isolates of Candida auris Directly Contribute to Reduced Azole Susceptibility. Antimicrob Agents Chemother [Internet]. 2018 Oct [cited 2021 Jul 14];62(10). Available from: https://journals.asm.org/doi/10.1128/AAC.01427-18

59. Li J, Coste AT, Liechti M, Bachmann D, Sanglard D, Lamoth F. Novel *ERG11* and *TAC1b* Mutations Associated with Azole Resistance in Candida auris. Antimicrob Agents Chemother [Internet]. 2021

Apr 19 [cited 2021 Jul 14];65(5). Available from: https://journals.asm.org/doi/10.1128/AAC.02663-20

60. Mayr E-M, Ramírez-Zavala B, Krüger I, Morschhäuser J. A zinc cluster transcription factor contributes to the intrinsic fluconazole resistance of *Candida auris*. Mitchell AP, editor. mSphere [Internet]. 2020 Apr 29 [cited 2021 Jul 14];5(2). Available from: https://journals.asm.org/doi/10.1128/mSphere.00279-20

61. Rybak JM, Muñoz JF, Barker KS, Parker JE, Esquivel BD, Berkow EL, et al. Mutations in *TAC1B* : a novel genetic determinant of clinical fluconazole resistance in *Candida auris*. Berman J, editor. mBio [Internet]. 2020 Jun 30 [cited 2021 Jul 14];11(3). Available from: https://journals.asm.org/doi/10.1128/mBio.00365-20

62. Kim SH, Iyer KR, Pardeshi L, Muñoz JF, Robbins N, Cuomo CA, et al. Genetic analysis of *Candida auris* implicates Hsp90 in morphogenesis and azole tolerance and Cdr1 in azole resistance. Kronstad JW, editor. mBio [Internet]. 2019 Feb 26 [cited 2021 Jul 15];10(1). Available from: https://journals.asm.org/doi/10.1128/mBio.02529-18

63. Kordalewska M, Lee A, Park S, Berrio I, Chowdhary A, Zhao Y, et al. Understanding echinocandin resistance in the emerging pathogen *Candida auris*. Antimicrob Agents Chemother [Internet]. 2018 Jun [cited 2021 Jul 14];62(6). Available from: https://journals.asm.org/doi/10.1128/AAC.00238-18

64. Carolus H, Pierson S, Muñoz JF, Subotić A, Cruz RB, Cuomo CA, et al. Genome-wide analysis of experimentally evolved *Candida auris* reveals multiple novel mechanisms of multidrug resistance. Chowdhary A, editor. mBio [Internet]. 2021 Apr 27 [cited 2021 Jul 14];12(2). Available from: https://journals.asm.org/doi/10.1128/mBio.03333-20

65. Bing J, Hu T, Zheng Q, Muñoz JF, Cuomo CA, Huang G. Experimental evolution identifies adaptive aneuploidy as a mechanism of fluconazole resistance in *Candida auris*. Antimicrob Agents Chemother [Internet]. 2020 Dec 16 [cited 2021 Jul 15];65(1). Available from: https://journals.asm.org/doi/10.1128/AAC.01466-20

66. Coste A, Selmecki A, Forche A, Diogo D, Bougnoux M-E, d'Enfert C, et al. Genotypic evolution of azole resistance mechanisms in sequential *Candida albicans* isolates. Eukaryot Cell. 2007 Oct;6(10):1889–904.

67. Coste AT, Karababa M, Ischer F, Bille J, Sanglard D. TAC1, transcriptional activator of CDR genes, is a new transcription factor involved in the regulation of *Candida albicans* ABC transporters CDR1 and CDR2. Eukaryot Cell. 2004 Dec;3(6):1639–52.

68. Bravo Ruiz G, Ross ZK, Holmes E, Schelenz S, Gow NAR, Lorenz A. Rapid and extensive karyotype diversification in haploid clinical *Candida auris* isolates. Curr Genet. 2019 Oct;65(5):1217–28.

69. Seiler GT, Ostrosky-Zeichner L. Investigational Agents for the Treatment of Resistant Yeasts and Molds. Curr Fungal Infect Rep [Internet]. 2021 May 28 [cited 2021 Jul 22]; Available from: https://link.springer.com/10.1007/s12281-021-00419-5

70. Helleberg M, Jørgensen KM, Hare RK, Datcu R, Chowdhary A, Arendrup MC. Rezafungin *in vitro* activity against contemporary nordic clinical *Candida* isolates and *Candida auris* determined by the EUCAST reference method. Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02438-19.

71. Tóth Z, Forgács L, Locke JB, Kardos G, Nagy F, Kovács R, et al. *In vitro* activity of rezafungin against common and rare *Candida species* and *Saccharomyces cerevisiae*. J Antimicrob Chemother. 2019 Dec 1;74(12):3505–10.

72. Kovács R, Tóth Z, Locke JB, Forgács L, Kardos G, Nagy F, et al. Comparison of *in vitro* killing activity of rezafungin, anidulafungin, caspofungin, and micafungin against four *Candida auris* clades in RPMI-1640 in the absence and presence of human serum. Microorganisms. 2021 Apr 16;9(4):863.

73. Lepak AJ, Zhao M, Andes DR. Pharmacodynamic evaluation of rezafungin (CD101) against *Candida auris* in the neutropenic mouse invasive candidiasis model. Antimicrob Agents Chemother. 2018 Nov;62(11):e01572-18.

74. Hager CL, Larkin EL, Long LA, Ghannoum MA. Evaluation of the efficacy of rezafungin, a novel echinocandin, in the treatment of disseminated *Candida auris* infection using an immunocompromised mouse model. J Antimicrob Chemother. 2018 Aug 1;73(8):2085–8.

75. Giacobbe DR, Magnasco L, Sepulcri C, Mikulska M, Koehler P, Cornely OA, et al. Recent advances and future perspectives in the pharmacological treatment of Candida auris infections. Expert Rev Clin Pharmacol. 2021 Jun 26;0(0):1–16.

76. Sexton DJ, Bentz ML, Welsh RM, Derado G, Furin W, Rose LJ, et al. Positive correlation between *Candida auris* skin-colonization burden and environmental contamination at a ventilator-capable skilled nursing facility in Chicago. Clin Infect Dis Off Publ Infect Dis Soc Am. 2021 May 12;ciab327.

77. Sharp A, Muller-Pebody B, Charlett A, Patel B, Gorton R, Lambourne J, et al. Screening for *Candida auris* in patients admitted to eight intensive care units in England, 2017 to 2018. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2021 Feb;26(8).

78. Government of United Kingdom. *Candida auris*: laboratory investigation, management and infection prevention and control [Internet]. [cited 2017 Dec 28]. Available from: https://www.gov.uk/government/publications/candida-auris-laboratory-investigation-management-and-infection-prevention-and-control

79. Welsh RM, Bentz ML, Shams A, Houston H, Lyons A, Rose LJ, et al. Survival, persistence, and isolation of the emerging multidrug-resistant pathogenic yeast *Candida auris* on a plastic health care surface. J Clin Microbiol. 2017 Oct;55(10):2996–3005.

80. Eyre DW, Sheppard AE, Madder H, Moir I, Moroney R, Quan TP, et al. A *Candida auris* outbreak and its control in an intensive care setting. N Engl J Med. 2018 Oct 4;379(14):1322–31.

81. Cadnum JL, Shaikh AA, Piedrahita CT, Sankar T, Jencson AL, Larkin EL, et al. Effectiveness of disinfectants against *Candida auris* and other *Candida* species. Infect Control Hosp Epidemiol. 2017 Oct;38(10):1240–3.

82. Zatorska B, Moser D, Diab-Elschahawi M, Ebner J, Lusignani LS, Presterl E. The effectiveness of surface disinfectants and a micellic H2O2 based water disinfectant on *Candida auris*. J Med Mycol. 2021 Dec 1;31(4):101178.

83. Moore G, Schelenz S, Borman AM, Johnson EM, Brown CS. Yeasticidal activity of chemical disinfectants and antiseptics against *Candida auris*. J Hosp Infect. 2017 Dec;97(4):371–5.

84. Abdolrasouli A, Armstrong-James D, Ryan L, Schelenz S. *In vitro* efficacy of disinfectants utilised for skin decolonisation and environmental decontamination during a hospital outbreak with *Candida auris*. Mycoses. 2017 Nov;60(11):758–63.

85. Chesnay A, Bailly É, Desoubeaux G. Demonstration of the yeasticidal efficacy of povidone-iodine-based commercial antiseptic solutions against *Candida auris*. J Mycol Medicale. 2021 Jul 2;31(4):101173.

86. HCSP. Mesures de prise en charge de patient infecté ou colonisé par Candida auris [Internet]. Rapport de l'HCSP. Paris: Haut Conseil de la Santé Publique; 2019 Jun [cited 2021 May 20]. Available from: https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=730

87. Taori SK, Khonyongwa K, Hayden I, Athukorala GDA, Letters A, Fife A, et al. *Candida auris* outbreak: mortality, interventions and cost of sustaining control. J Infect. 2019 Dec;79(6):601–11.

88. Arensman K, Miller JL, Chiang A, Mai N, Levato J, LaChance E, et al. Clinical outcomes of patients treated for *Candida auris* infections in a multisite health system, Illinois, USA. Emerg Infect Dis. 2020 May;26(5):876–80.

89. Adam RD, Revathi G, Okinda N, Fontaine M, Shah J, Kagotho E, et al. Analysis of *Candida auris* fungemia at a single facility in Kenya. Int J Infect Dis. 2019 Aug 1;85:182–7.

90. Chakrabarti A, Sood P, Rudramurthy SM, Chen S, Kaur H, Capoor M, et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive Care Med. 2015 Feb 1;41(2):285–95.

91. Rudramurthy SM, Chakrabarti A, Paul RA, Sood P, Kaur H, Capoor MR, et al. *Candida auris* candidaemia in Indian ICUs: analysis of risk factors. J Antimicrob Chemother. 2017 Jun 1;72(6):1794–801.

92. Chowdhary A, Anil Kumar V, Sharma C, Prakash A, Agarwal K, Babu R, et al. Multidrug-resistant endemic clonal strain of *Candida auris* in India. Eur J Clin Microbiol Infect Dis. 2014 Jun 1;33(6):919–26.

93. Calvo B, Melo ASA, Perozo-Mena A, Hernandez M, Francisco EC, Hagen F, et al. First report of *Candida auris* in America: clinical and microbiological aspects of 18 episodes of candidemia. J Infect. 2016 Oct 1;73(4):369–74.

94. Magobo RE, Corcoran C, Seetharam S, Govender NP. Candida auris–Associated Candidemia, South Africa. Emerg Infect Dis. 2014 Jul;20(7):1250–2.

95. Govender NP, Magobo RE, Mpembe R, Mhlanga M, Matlapeng P, Corcoran C, et al. *Candida auris* in South Africa, 2012-2016. Emerg Infect Dis. 2018 Nov;24(11):2036–40.

96. Chatterjee S, Alampalli SV, Nageshan RK, Chettiar ST, Joshi S, Tatu US. Draft genome of a commonly misdiagnosed multidrug resistant pathogen *Candida auris*. BMC Genomics. 2015 Sep 7;16(1):686.

97. Ostrowsky B, Greenko J, Adams E, Quinn M, O'Brien B, Chaturvedi V, et al. *Candida auris* isolates resistant to three classes of antifungal medications - New York, 2019. MMWR Morb Mortal Wkly Rep. 2020 Jan 10;69(1):6–9.

98. Zhu Y, O'Brien B, Leach L, Clarke A, Bates M, Adams E, et al. Laboratory analysis of an outbreak of *Candida auris* in New York from 2016 to 2018: impact and lessons learned. J Clin Microbiol. 2020 Mar 25;58(4):e01503-19.

99. Ben-Ami R, Berman J, Novikov A, Bash E, Shachor-Meyouhas Y, Zakin S, et al. Multidrug-resistant *Candida haemulonii* and *C. auris*, Tel Aviv, Israel. Emerg Infect Dis. 2017 Feb;23(1).

100. Khan Z, Ahmad S, Al-Sweih N, Joseph L, Alfouzan W, Asadzadeh M. Increasing prevalence, molecular characterization and antifungal drug susceptibility of serial *Candida auris* isolates in Kuwait. PLOS ONE. 2018 Apr 9;13(4):e0195743.

101. Berrio I, Caceres DH, Coronell R W, Salcedo S, Mora L, Marin A, et al. Bloodstream infections with *Candida auris* among children in Colombia: clinical characteristics and outcomes of 34 cases. J Pediatr Infect Dis Soc. 2021 Feb 1;10(2):151–4.

102. Sayeed MA, Farooqi J, Jabeen K, Awan S, Mahmood SF. Clinical spectrum and factors impacting outcome of Candida auris: a single center study from Pakistan. BMC Infect Dis. 2019 May 6;19(1):384.

103. Sayeed MA, Farooqi J, Jabeen K, Mahmood SF. Comparison of risk factors and outcomes of *Candida auris* candidemia with non*Candida auris* candidemia: a retrospective study from Pakistan. Med Mycol. 2020 Aug 1;58(6):721–9.

104. Ahmad S, Khan Z, Al-Sweih N, Alfouzan W, Joseph L. *Candida auris* in various hospitals across Kuwait and their susceptibility and molecular basis of resistance to antifungal drugs. Mycoses. 2020 Jan;63(1):104–12.

105. Caceres DH, Rivera SM, Armstrong PA, Escandon P, Chow NA, Ovalle MV, et al. Case-case comparison of *Candida auris versus* other *Candida* species bloodstream infections: results of an outbreak investigation in Colombia. Mycopathologia. 2020 Oct;185(5):917–23.

106. Farooqi JQ, Soomro AS, Baig MA, Sajjad SF, Hamid K, Jabeen K, et al. Outbreak investigation of *Candida auris* at a tertiary care hospital in Karachi, Pakistan. J Infect Prev. 2020 Sep;21(5):189–95.

107. Escandón P, Cáceres DH, Espinosa-Bode A, Rivera S, Armstrong P, Vallabhaneni S, et al. Notes from the field: surveillance for *Candida auris* - Colombia, September 2016-May 2017. MMWR Morb Mortal Wkly Rep. 2018 Apr 20;67(15):459–60.

108. Escandón P, Chow NA, Caceres DH, Gade L, Berkow EL, Armstrong P, et al. Molecular epidemiology of *Candida auris* in Colombia reveals a highly related, countrywide colonization with regional patterns in amphotericin B resistance. Clin Infect Dis Off Publ Infect Dis Soc Am. 2019 Jan 1;68(1):15–21.

109. Ruiz-Gaitán A, Martínez H, Moret AM, Calabuig E, Tasias M, Alastruey-Izquierdo A, et al. Detection and treatment of *Candida auris* in an outbreak situation: risk factors for developing colonization and candidemia by this new species in critically ill patients. Expert Rev Anti Infect Ther. 2019 Apr;17(4):295–305.

110. Ruiz Gaitán AC, Moret A, López Hontangas JL, Molina JM, Aleixandre López AI, Cabezas AH, et al. Nosocomial fungemia by *Candida auris*: first four reported cases in continental Europe. Rev Iberoam Micol. 2017 Mar;34(1):23–7.

111. Garcia-Bustos V, Salavert M, Ruiz-Gaitán AC, Cabañero-Navalon MD, Sigona-Giangreco IA, Pemán J. A clinical predictive model of candidaemia by *Candida auris* in previously colonized critically ill patients. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2020 Nov;26(11):1507–13.

112. Shastri PS, Shankarnarayan SA, Oberoi J, Rudramurthy SM, Wattal C, Chakrabarti A. *Candida auris* candidaemia in an intensive care unit - prospective observational study to evaluate epidemiology, risk factors, and outcome. J Crit Care. 2020 Jun;57:42–8.

113. Vallabhaneni S, Kallen A, Tsay S, Chow N, Welsh R, Kerins J, 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. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2017 Jan;17(1):296–9.

114. Belkin A, Gazit Z, Keller N, Ben-Ami R, Wieder-Finesod A, Novikov A, et al. *Candida auris* infection leading to nosocomial transmission, Israel, 2017. Emerg Infect Dis. 2018 Apr;24(4):801–4.

115. Tian S, Bing J, Chu Y, Chen J, Cheng S, Wang Q, et al. Genomic epidemiology of *Candida auris* in a general hospital in Shenyang, China: a three-year surveillance study. Emerg Microbes Infect. 2021 Dec;10(1):1088–96.

116. Pacilli M, Kerins JL, Clegg WJ, Walblay KA, Adil H, Kemble SK, et al. Regional emergence of *Candida auris* in Chicago and lessons learned from intensive follow-up at 1 ventilator-capable skilled nursing facility. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020 Dec 31;71(11):e718–25.

117. Mohsin J, Hagen F, Al-Balushi ZAM, de Hoog GS, Chowdhary A, Meis JF, et al. The first cases of *Candida auris* candidaemia in Oman. Mycoses. 2017 Sep;60(9):569–75.

118. Al-Siyabi T, Al Busaidi I, Balkhair A, Al-Muharrmi Z, Al-Salti M, Al'Adawi B. First report of *Candida auris* in Oman: clinical and microbiological description of five candidemia cases. J Infect. 2017 Oct;75(4):373–6.

119. Park JY, Bradley N, Brooks S, Burney S, Wassner C. Management of patients with *Candida auris* fungemia at Community Hospital, Brooklyn, New York, USA, 2016–2018. Emerg Infect Dis. 2019 Mar;25(3):601–2.

120. Morales-López SE, Parra-Giraldo CM, Ceballos-Garzón A, Martínez HP, Rodríguez GJ, Álvarez-Moreno CA, et al. Invasive infections with multidrug-resistant yeast *Candida auris*, Colombia. Emerg Infect Dis. 2017 Jan;23(1):162–4.

121. Theodoropoulos NM, Bolstorff B, Bozorgzadeh A, Brandeburg C, Cumming M, Daly JS, et al. *Candida auris* outbreak involving liver transplant recipients in a surgical intensive care unit. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2020 Dec;20(12):3673–9.

122. Abdalhamid B, Almaghrabi R, Althawadi S, Omrani A. First report of *Candida auris* infections from Saudi Arabia. J Infect Public Health. 2018 Aug;11(4):598–9.

123. Almaghrabi RS, Albalawi R, Mutabagani M, Atienza E, Aljumaah S, Gade L, et al. Molecular characterisation and clinical outcomes of *Candida auris* infection: single-centre experience in Saudi Arabia. Mycoses. 2020;63(5):452–60.

124. Sathyapalan DT, Antony R, Nampoothiri V, Kumar A, Shashindran N, James J, et al. Evaluating the measures taken to contain a *Candida auris* outbreak in a tertiary care hospital in South India: an outbreak investigational study. BMC Infect Dis. 2021 May 6;21(1):425.

125. Barantsevich NE, Orlova OE, Shlyakhto EV, Johnson EM, Woodford N, Lass-Floerl C, et al. Emergence of *Candida auris* in Russia. J Hosp Infect. 2019 Aug;102(4):445–8.

126. Barantsevich NE, Vetokhina AV, Ayushinova NI, Orlova OE, Barantsevich EP. *Candida auris* bloodstream infections in Russia. Antibiot Basel Switz. 2020 Aug 30;9(9):E557.

127. Bajpai V, Govindaswamy A, Sagar S, Kumar S, Garg P, Xess I, et al. Multidrug-resistant *Candida auris* fungemia in critical care units: experience from a tertiary care hospital in India. Microb Drug Resist Larchmt N. 2020 Feb;26(2):145–9.

128. Mulet Bayona JV, Salvador García C, Tormo Palop N, Gimeno Cardona C. Evaluation of a novel chromogenic medium for *Candida* spp. identification and comparison with CHROMagar™ Candida for the detection of *Candida auris* in surveillance samples. Diagn Microbiol Infect Dis. 2020 Dec 1;98(4):115168.

129. García CS, Palop NT, Bayona JVM, García MM, Rodríguez DN, Álvarez MB, et al. *Candida auris*: report of an outbreak. Enfermedades Infecc Microbiol Clin Engl Ed. 2020 Jan;38 Suppl 1:39–44.

130. Alobaid K, Ahmad S, Asadzadeh M, Mokaddas E, Al-Sweih N, Albenwan K, et al. Epidemiology of xandidemia in Kuwait: a nationwide, population-based study. J Fungi Basel Switz. 2021 Aug 20;7(8):673.

131. Alfouzan W, Ahmad S, Dhar R, Asadzadeh M, Almerdasi N, Abdo NM, et al. Molecular epidemiology of *Candida auris* outbreak in a major secondary-care hospital in Kuwait. J Fungi Basel Switz. 2020 Nov 21;6(4):E307.

132. Alshamrani MM, El-Saed A, Mohammed A, Alghoribi MF, Al Johani SM, Cabanalan H, et al. Management of *Candida auris* outbreak in a tertiary-care setting in Saudi Arabia. Infect Control Hosp Epidemiol. 2021 Feb;42(2):149–55.

133. Salah H, Sundararaju S, Dalil L, Salameh S, Al-Wali W, Tang P, et al. Genomic epidemiology of <i>Candida auris<i> in Qatar reveals hospital transmission dynamics and a south Asian origin. J Fungi Basel Switz. 2021 Mar 23;7(3):240.

134. Lane CR, Seemann T, Worth LJ, Easton M, Pitchers W, Wong J, et al. Incursions of *Candida auris* into Australia, 2018. Emerg Infect Dis. 2020 Jun;26(6):1326–8.

135. O'Connor C, Bicanic T, Dave J, Evans TJ, Moxey P, Adamu U, et al. *Candida auris* outbreak on a vascular ward – the unexpected arrival of an anticipated pathogen. J Hosp Infect. 2019 Sep 1;103(1):106–8.

136. Di Pilato V, Codda G, Ball L, Giacobbe DR, Willison E, Mikulska M, et al. Molecular epidemiological investigation of a nosocomial cluster of *C. auris*: evidence of recent emergence in Italy and ease of transmission during the COVID-19 pandemic. J Fungi Basel Switz. 2021 Feb 15;7(2):140.

137. Price TK, Mirasol R, Ward KW, Dayo AJ, Hilt EE, Chandrasekaran S, et al. Genomic characterizations of clade III lineage of *Candida auris*, California, USA. Emerg Infect Dis. 2021 Apr;27(4):1223–7.

138. Alvarado-Socarras JL, Vargas-Soler JA, Franco-Paredes C, Villegas-Lamus KC, Rojas-Torres JP, Rodriguez-Morales AJ. A cluster of neonatal infections caused by *Candida auris* at a large referral center in Colombia. J Pediatr Infect Dis Soc. 2021 May 28;10(5):549–55.

139. Tse H, Tsang AKL, Chu Y-W, Tsang DNC. Draft genome sequences of 19 clinical isolates of *Candida auris* from Hong Kong. Microbiol Resour Announc. 2021 Jan 7;10(1):e00308-20.

140. Patterson CA, Wyncoll D, Patel A, Ceesay Y, Newsholme W, Chand M, et al. Cloth lanyards as a source of intermittent transmission of *Candida auris* on an ICU. Crit Care Med. 2021 Apr 1;49(4):697–701.

141. Moin S, Farooqi J, Rattani S, Nasir N, Zaka S, Jabeen K. *C. auris* and non-*C. auris* candidemia in hospitalized adult and pediatric COVID-19 patients; single center data from Pakistan. Med Mycol. 2021 Dec 1;59(12):1238–42.

142. Prestel C, Anderson E, Forsberg K, Lyman M, de Perio MA, Kuhar D, et al. *Candida auris* outbreak in a COVID-19 specialty care unit — Florida, July–August 2020. Morb Mortal Wkly Rep. 2021 Jan 15;70(2):56–7.

143. Hanson BM, Dinh AQ, Tran TT, Arenas S, Pronty D, Gershengorn HB, et al. *Candida auris* invasive infections during a COVID-19 case surge. Antimicrob Agents Chemother. 65(10):e01146-21.

144. Allaw F, Kara Zahreddine N, Ibrahim A, Tannous J, Taleb H, Bizri AR, et al. First w*Candida auris* outbreak during a COVID-19 pandemic in a tertiary-care center in Lebanon. Pathog Basel Switz. 2021 Feb 3;10(2):157.

145. Nobrega de Almeida J, Brandão IB, Francisco EC, de Almeida SLR, de Oliveira Dias P, Pereira FM, et al. Axillary digital thermometers uplifted a multidrug-susceptible *Candida auris* outbreak among COVID-19 patients in Brazil. Mycoses. 2021 Sep;64(9):1062–72.

146. Bacchani D, Rajni E, Garg VK, Sharma R, Mamoria VP. Prevalence, epidemiology and clinical outcome of *Candida auris* infections: experience from a tertiary care hospital in Jaipur. Trop Doct. 2021 Oct;51(4):508–13.

147. Lyman M, Forsberg K, Reuben J, Dang T, Free R, Seagle EE, et al. Notes from the field: transmission of pan-resistant and echinocandin-resistant *Candida auris* in health care facilities — Texas and the district of Columbia, January–April 2021. Morb Mortal Wkly Rep. 2021 Jul 23;70(29):1022–3.

Figure legends

Figure 1: Number of publications *per* year retrieved about "*Candida auris*" in the PubMed database as of August 10th 2021 (including original articles and reviews).

Figure 2: Countries from which *Candida auris* cases have been reported, as of February 15, 2021

https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html#historical.

732 **Table 1 : Listing of the major outbreaks of *Candida auris* cases reported so far.** Were only considered the available articles written

733 in English and those that mentioned original description of ≥2 clustered cases.

Reference	**Country (city)**	**Period**	**Number of cases of colonization or infection (Nb of centers)**	**Genotypic analysis (clade)**
Arensman *et al.* 2020 (88)	USA (Chicago, IL)	Jan. 2008 – April 2019	28 (8 centers)	NA
Chowdhari *et al.* 2013 (12)	India (Dehli)	2009-2011	12 (2 centers)	AFLP: 1 clone (I)
Kathuria *et al.* 2015 (13)	India (Dehli)	2010-2014	90 (5 centers)	NA
Adam *et al.* 2019 (89)	Kenya (Nairobi)	Sept. 2010 – Dec. 2016	77* (1 center)	PFGE: 1 clone
Chakrabarti *et al.* 2020 (90)	India (multiple sites)	April 2011 – Sept. 2012	22 (27 centers)	NA
Chakrabarti *et al.* 2015 (90)	India (multiple places)	April 2011 – Sept. 2012	48* (27 centers)	NA
Rudramurthy *et al.* 2017 (91)	India (multiple places)	April 2011 – Sept. 2012	74 (19 centers)	AFLP: 88% with similar profiles (I)
Chowdhary *et al.* 2014 (92)	India (Kochi)	Nov. 2011 - June 2013	7 (1 center)	AFLP: 1 clone (I)
Sarma *et al.* 2013	India (Gurgaon)	2011	2 (1 center)	NA
Calvo *et al.* 2016 (93)	Venezuela (Maracaibo)	March 2012 - July 2013	18 (1 center)	AFLP: 1 clone (IV)

Magobo *et al*. 2014 (94)	Republic of South Africa (Johannesburg)	Oct. 2012 – Oct. 2013	4 (1 center)	NA
Govender *et al.* (95)	Republic of South Africa (multiple places)	Oct. 2012 – Nov. 2016	1692 (≥94 centers) including 1087 cases in 20 centers	NA
Chatterjee *et al.* 2015 (96)	India (Bengaluru)	2012-14	34* (1 center)	PFGE: 1 clone
Adams *et al.* 2018 (20), Ostrowsky *et al.* 2020 (97) and Zhu *et al.* 2020 (98)	USA (New York, NY)	May 2013 - April 2017	112 (19 centers)	WGS: 2 clones (I)
Chow *et al.* 2018 (19)	USA (multiple places)	May 2013 – Aug. 2017	133 (not specified)	WGS (mostly I)
Parra-Giraldo *et al*. 2015 (47)	Colombia (Bogotá)	Nov. 2013 – Feb. 2015	3 (1 center)	MALDI-TOF: 2 clones
Borman *et al*. 2016 (39)	United Kingdom (multiple places)	2013	12* (6 centers)	NA
Lockhart *et al.* 2017 (3)	Pakistan (not specified)	2014-2015	18 (2 centers)	WGS: 1 clone (I)
Ben-Ami *et al.* 2017 (99)	Israel (Tel Aviv)	May 2014 - April 2015	6 (2 centers)	NA
Khan *et al.* 2018 (100)	Kuweit (not specified)	May 2014 – Sept. 2017	56 (not specified)	PCR fingerprinting 1 clone (6 strains only)
Berrio *et al.* 2020 (101)	Colombia (Barranquilla and Cartagena)	July 2014 – Oct.	34 (2 centers)	Not specified: 2 clones
Sayeed *et al.* 2019 and 2020 (102,103)	Pakistan (Karachi)	Sept. 2014 – March 2017	92 (1 center)	WGS: 1 clone (I)

Ahmad *et al.* 2020 (104)	Kuwait (multiple places)	2014-2018	126 (8 centers)	ITS sequencing (I)
Caceres *et al.* 2020 (105)	Colombia (multiple places)	Jan. 2015 – Sept. 2016	40 (4 centers)	NA
Eyre *et al.* 2019 (80)	United Kingdom (Oxford)	Feb. 2015 - August 2017	60 (1 center)	WGS (mostly III)
Farooqi *et al.* 2020 (106)	Pakistan (Karachi)	April 2015 – Jan. 2016	30 (1 center)	NA
Escandón *et al.* 2018 (107,108)	Colombia (multiple places)	Feb. 2015 - July 2016	45* (6 centers)	NA
		Sept. 2016 - May 2017	78* (24 centers)	NA
Schelenz *et al.* 2016 (4)	United Kingdom (London)	April 2015 - July 2016	50 (1 center)	AFLP: 1 clone
Ruiz-Gaitán *et al.* 2017-19 (24,109–111)	Spain (Valencia)	April 2016 - January 2017	140 (1 center)	AFLP: 1 clone (I)
Shastri *et al.* 2020 (112)	India (Dehli)	April 2016 – Sept. 2017	42 (1 center)	AFLP and ITS/28S rDNA sequencing: 1 clone (I)
Vallabhaneni *et al*. 2017 (113)	USA (multiple places)	May 2016 – Aug. 2016	7 (6 centers)	NA
Belkin *et al.* 2018 (114)	Israel (Tel Hashomer)	July 2016 – Jan. 2017	2 (1 center)	WGS (III)
Taori *et al*. 2019 (87)	United Kingdom (London)	July 2016 – Feb. 2017	34 (1 center)	WGS (I)
Tian *et al.* 2021 (115)	China (Shenyang)	April 2016 – March 2018	93* (1 center)	WGS (III)

Pacilli *et al.* 2020 (116)	USA (Chicago, IL)	Aug. 2016 – Dec. 2018	490 (4 centers)	NA
Mohsin *et al.* 2017 (117)	Oman (Muscat)	Aug. 2016 – Jan. 2017	2 (1 center)	AFLP: 2 clones
Al-Siyabi *et al.* 2017 (118)	Oman (Muscat)	Dec. 2016 – Feb. 2017	5 (1 center)	NA
Park *et al.* 2019 (119)	USA (New York, NY)	2016-2018	9 (1 center)	NA
Morales-López *et al.* 2017 (120)	Colombia (multiple places)	Feb. 2017 – July 2017	17 (6 centers)	NA
Theodoropoulos *et al.* 2020 (121)	USA (Worcester, MA)	May 2017 – Oct. 2017	5 (1 center)	WGS: 1 clone (I)
Abdalhamid *et al.* 2018 (122) and Almaghrabi *et al*. 2020 (123)	Kingdom of Saudi Arabia (Dammam and Riyadh)	June 2017 – Oct. 2018	10 (2 center)	WGS: 2 clones (I)
Sathyapalan *et al*. 2021 (124)	India (Kochi)	Sept. 2017 - 2019	15 (1 center)	NA
Barantsevith *et al.* 2019 (125,126)	Russian federation (Moskow and Siberian region)	Oct. 2017 – Dec. 2017	49 (1 center) and 38 (2 centers)	ITS and D1/D2 sequencing (I)
Bajpai *et al.* 2020 (127)	India (Dehli)	NA	5 (1 center)	NA
Mulet Bayona *et al.* 2020 (128,129)	Spain (Valencia)	Nov. 2017 – May 2020	334 (1 center)	Not specified (III)
Alobaid *et al.* 2021 (130)	Kuweit (multiple places)	Jan. 2018 – Dec. 2018	33 (12 centers)	NA

Alfouzan *et al.* 2020 (131)	Kuweit (Farwaniya)	Jan. 2018 - June 2019	71 (1 center)	ITS sequencing and microsatellite typing (I)
Alshamrani *et al*. 2020 (132)	Kingdom of Saudi Arabia (Riyadh)	March 2018 – June 2019	23 (1 center)	NA
Salah *et al.* 2021 (133)	Qatar (Doha)	April 2018 – Nov. 2020	40 (2 centers)	WGS: 2 clones (I)
Eckbo *et al*. (21)	Canada (Vancouver, BC)	Spring 2018	4 (1 center)	WGS: 1 clone (I)
Lane *et al.* 2020 (134)	Australia (Melbourne)	July 2018 – Dec. 2018	4 (1 center)	Not specified (I)
Sexton *et al.* 2021 (76)	USA (Chicago)	December 2018	31 (1 center)	NA
O'Connor *et al.* 2019 (135)	United Kingdom (London)	Dec. 2018 – Jan. 2019	4 (1 center)	NA
Umamaheshwari *et al.* 2021 (5)	India (Karnataka)	Dec. 2018– March 2019	8 (1 center)	ITS and 26S sequencing (I)
Di Pilato *et al.* (136)	Italy (Genoa)	July 2019 – May 2020	10 (1 center)	WGS: 1 clone for 9 isolates (I)
Price *et al.* 2021 (137)	USA (Los Angeles, CA)	Sept. 2019– Sept. 2020	6 (2 centers)	WGS: 3 clones (mostly III)
Alvarado-Socarras *et al.* 2021 (138)	Colombia (Bucaramanga)	NA	8 (1 center)	NA

Tse *et al.* 2021 (139)	Hong Kong	2019	15 (1 center)	WGS: 1 clone (I)
Patterson et al. 2020 (140)	United Kingdom (London)	April 2020 – Sept. 2020	7 (2 centers)	MALDI-TOF (I)
Moin *et al.* 2021 (141)	Pakistan (Karachi)	April 2020 – Dec. 2020	6 (1 center)	NA
Chowdhary *et al.* 2020 (23)	India (Dehli)	April–July 2020	10 (1 center)	NA
Piatti G *et al.* 2021	Italy (Genoa)	June 2020 – Jan. 2021	77 (1 center)	NA
Prestel *et al.* 2021 (142)	USA (FL)	July 2020 – Aug. 2020	6 (1 center)	NA
Hanson *et al.* 2021 (143)	USA (Miami, FL)	Summer 2020	15 (1 center)	WGS: 1 clone (III)
Allaw et al. 2021 (144)	Lebanon (Beirut)	Oct. 2020 – Dec. 2020	14 (1 center)	NA
Nobrega de Almedia *et al.* 2021 (145)	Brazil (Savaldor de Bahia)	December 2020	7 (1 center)	Microsatellite typing (I)
Bacchani et al. 2021 (146)	India (Jaipur)	NA	24 (1 center)	NA
Lyman *et al.* 2021 (147)	USA (TX and Washington, DC)	Jan. 2021 – April 2021	22 (not specified)	NA

734 Abbreviations: *number of isolates (not specified whether each one corresponded to a distinct patient); AFLP amplified fragment length
735 polymorphism; BC British Columbia; CA California; DC district of Columbia; Dec. December; Feb. February; FL Florida; IL Illinois;
736 Jan. January; MA Massachusetts; MALDI-TOF matrix-associated LASER desorption ionization – time of flight; NA not available; Oct.
737 October; PFGE pulsed-filed gel electrophoresis; Sept. September; Nov. November; NY New York; TX Texas; USA United States of
738 America; WGS whole genome sequencing