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Hot Topic

Control of *Candida auris* in healthcare institutions: Outcome of an International Society for Antimicrobial Chemotherapy expert meeting

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ABSTRACT

Candida auris (*C. auris*) is an emerging fungal pathogen causing invasive infections and outbreaks that have been difficult to control in healthcare facilities worldwide. There is a lack of current evidence for pragmatic infection prevention and control recommendations. The aim of this paper was to review the epidemiology of *C. auris* and identify best practices with a panel of experts, in order to provide guidance and recommendations for infection prevention and control measures based on available scientific evidence, existing guidelines and expert opinion. The Infection Prevention and Control working group of the International Society of Antimicrobial Chemotherapy organised an expert meeting with infection prevention and mycology experts to review recommendations for healthcare workers on infection prevention and control measures for *C. auris* at inpatient healthcare facilities. The most common interventions included: screening, standard precautions, cleaning and disinfection, inpatient transfer, outbreak management, decolonisation, and treatment.

1. Introduction

Candida auris (*C. auris*) is an emerging yeast that has a significant impact on healthcare, as it has been associated with invasive infections (e.g. bloodstream infections) and outbreaks. Furthermore, up to 90% of strains are resistant to fluconazole, and *C. auris* is able to adapt and become resistant to other antifungal agents. Additionally, strains may differ in their antifungal susceptibilities [1].

Since its 'discovery' in 2009, *C. auris* has been reported from every continent in the world [2,3]. However, further examination of strains related to *Candida haemulonii* (*C. haemulonii*) have disclosed a case of bloodstream infection by *C. auris* as early as 1996 [4]. Whilst isolated sporadic cases occur, clusters and outbreaks have become more common and there is a growing concern about the ability of *C. auris* to cause widespread nosocomial outbreaks. *Candida auris* is likely to have been spreading from patient to patient even before 'index' cases of clinical infection were discovered [5]. In general, *C. auris* is often only detected several days or weeks after hospital admission [6–8], providing an opportunity for the fungus to spread extensively in healthcare facilities [9].

Candida auris is able to remain viable for several months on environmental surfaces and equipment, likely due to the formation of 'dry' biofilms [10,11]. Considerable difficulties are presented by *C. auris* in environmental decontamination and patient decolonisation and eradication [12–17]. Carriage of *C. auris* seems to be harder to

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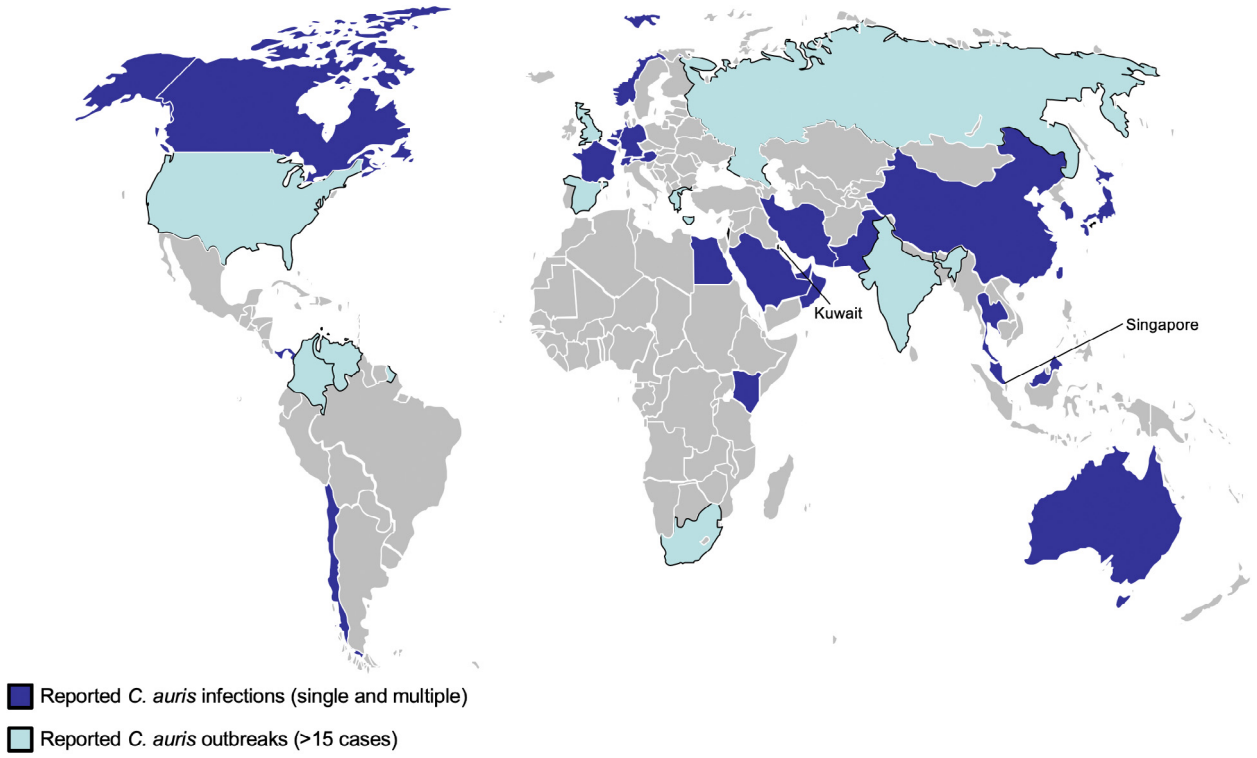

Fig. 1. World map highlighting reported *C. auris* infections including single and multiple case reports, and outbreaks (published and unpublished).

eradicate than other fungal species and bacteria [18,19]. Healthcare facilities have tried a range of approaches to decolonise patients without success [18,19]. In addition, not all environmental disinfectants are effective in eradicating *C. auris* [10]. Currently, The Centers for Disease Control and Prevention and Public Health England have issued recommendations for managing patients with *C. auris* [20,21]. Both recommendations advocate standard precautions used for multidrug-resistant organisms and *Clostridium difficile* [20,21]. However, existing guidelines for effective infection prevention and control (IPC) measures, diagnostics, patient decolonisation and treatment become quickly outdated as knowledge is accumulating [22]. Thus, the Infection Prevention and Control working group of the International Society for Antimicrobial Chemotherapy identified the prevention and control of *C. auris* as a current priority for the global infection control agenda. The goal was to provide an update on best practices in containing the spread of *C. auris* in healthcare facilities based upon the most current information.

2. Epidemiology

Currently, *C. auris* infections have been reported in more than 35 countries [23–40] from every continent in the world, excluding Antarctica [22]. Single cases or small series of cases are still the most frequently reported. However, outbreaks or clusters of cases ($n > 15$), have been reported from the UK, Spain, USA, India, Russia, Venezuela, Colombia, South Korea, Kuwait, Israel, Kenya, Pakistan and South Africa [3,12,23,24,40–45]. In some hospitals, *C. auris* has become the second most common cause of bloodstream infections by yeasts after *Candida tropicalis* [46]. Whole-genome sequencing of *C. auris* has shown four major populations (clades) in which isolates cluster by geography, and all worldwide infections to date have been found clustering in these four clades (Fig. 1) [47–51]. Recently, a fifth clade has been found with > 200 000 SNPs difference from the next closest clade [47]. Most cases reported in non-endemic areas have acquired the pathogen during travel or through contact with the local healthcare system (e.g. South Asia) [7,52,53].

Screening for *C. auris* is not yet routine practice in most countries because *C. auris* is deemed endemic, due to a lack of adequate detection methods, or a lack of perceived importance of the problem. At present, patients admitted to intensive care from endemic countries and transfers from hospitals known to have *C. auris* cases should be seen as a (minimum) risk group and, therefore, be screened. However, any screening policy may change when *C. auris* becomes more widespread. Consequently, Fig. 1 is likely to be an underestimate of the real number of cases.

3. Optimal diagnostics

It is crucial to correctly identify and report *C. auris*, in order to provide optimal patient care, treatment and initiate appropriate IPC measures. All isolates should be susceptibility tested, from whatever body site, because of varying levels of resistance. *Candida auris* is a budding yeast that forms white, pink, or purple colonies on CHROMagar and can be difficult to distinguish from *C. glabrata*. It does not form germ tubes and rarely produces short pseudo hyphae. Some strains form aggregates of cells and others do not. In contrast with most other *Candida* spp., it grows well at higher temperatures (40–42 °C) and can tolerate salt concentrations in the culture medium of up to 10%. This can be exploited to prepare selective media, including SDA-A enriched with 10% salt during screening [14,54]. At present, chromogenic yeast agar is not yet validated for screening directly from swabs. First attempts to identify *C. auris* using PCR directly from swabs seem to have produced frequent 'false positive' – positive in PCR, negative in culture swabs – results (personal communicate Schelenz). The first report of three cases of nosocomial fungaemia due to *C. auris* in South Korea [55] showed that this yeast is commonly misidentified as *C. haemulonii* and *Rhodotorula glutinis* using traditional phenotypic methods.

These widely used routine identification methods for yeasts are based on phenotypic assimilation/fermentation tests using sets of carbon and nitrogen compounds. Up to 2017, most commercial identification systems – such as VITEK (BioMérieux, Marcy l'Etoile, France), API-20C AUX (BioMérieux), Phoenix (BD-Diagnostics, Sparks, MD), MicroScan (Beckman Coulter, Pasadena, CA) and RapID Yeast Plus (Innovative Diagnostic Systems, Norcross, Ga) [56–59] – have been misnaming *C. auris* as *C. haemulonii*, *Rhodotorula* glutinis, *Candida sake*, *Candida catenulate*, *Candida famata*, *Candida guilliermondii*, *Candida lusitaniae*, and *Candida parapsilosis*. An investigation of 102 clinical isolates previously identified as *C. haemulonii* or *Candida famata* with the VITEK system showed that 88.2%% of the isolates were in fact *C. auris*, when confirmed by internal transcribed spacer sequencing [60]. Several studies have since reported that, in routine microbiology laboratories, *C. auris* remains a problematic and difficult-to-identify pathogen because commercial biochemical identification systems have lacked this yeast in their databases. However, the updated VITEK 2 (BioMérieux), MALDI Biotyper (Bruker-Daltonics, Bremen, Germany) and VITEK MS (BioMérieux) with software version 8.01 [61] detect *C. auris*, although misidentification of strains from certain clades are still possible. Supplemental MALDI-TOF databases that include *C. auris* strains from all the phylogenetic clades may overcome these identification challenges [62]. Sequencing of the D1/D2 domain of the large ribosomal subunit of the 26S rRNA gene and the internal transcribed spacer regions of the nuclear rRNA gene operon can differentiate with confidence among species of the *C. haemulonii* species complex, of which *C. auris* is a member.

4. Patient screening upon admission

From experience of the Royal Brompton hospital (UK), the screening sites most frequently culturing positive for *C. auris* are the axilla and groin (unpublished data Schelenz et al.), which was confirmed in the New York outbreak investigation [54]. However, in the outbreak of La Fe University hospital (Spain), rectum and urine were the sites mostly colonised by *C. auris* (unpublished data Pemán et al.). Other sites for screening, even if less sensitive to colonisation are: nose, mouth, external ear canals, urine catheter, and wounds [21]. If a patient has open wounds and/or intravascular catheters, they should be included for screening in addition to the swabbing sites. However, it is important to only swab open wounds if they are not sealed by a wound dressing. Opening a sealed wound can cause a risk for patients to become colonised with *C. auris* if they are carriers. The axilla is often not a typical screening site for multidrug-resistant organisms (MDRO) and, therefore, a screening strategy for the axilla may be difficult to implement.

Risk groups admitted to hospital are patients previously admitted into intensive care units in endemic countries and transfers from hospitals known to have *C. auris*. Hospitals that have *C. auris* should liaise with the receiving hospital's infection control teams and ensure that appropriate information is passed on. If institutions have an existing surveillance screening protocol in place for patients at high-risk for colonisation with MDRO, it might be more valuable to add *C. auris* to the existing testing panel in the lab, rather than to re-implement additional swabbing sites.

5. Infection prevention and control

Healthcare-associated infections caused by *C. auris* have been reported [12,40,63,64]. In future, the risk of invasive infections caused by *C. auris* may increase as the number of co-morbidities in today's patients increase every year.

For healthcare facilities to be prepared for a first case of *C. auris,* it is important to have a screening protocol and adequate IPC procedures in place. Any detection of *C. auris* should be immediately reported to the infection control department, leading to timely implementation of strict IPC measures. Patients who are colonised or infected with *C. auris* should be isolated until discharge and flagged for at least 1 year after the first negative screening culture. When patients are transferred within an institution or to other healthcare facilities, it is vital to ensure that their *C. auris* status is handed over. Patient contact screening of direct contacts should be initiated on detection of a 'first' case, including those being discharged from the healthcare facility; this may involve tracking back throughout the patient's admission if internal transfers have taken place. Every patient should be screened in the axilla and groin, including any other relevant sites (e.g. nose, urine, rectum, throat, wounds and catheter exit sites).

The required IPC measures to be implemented for *C. auris* cases are summarised (Table 1). Hospital administration should ensure availability and support for all IPC measures, while ICDs should audit the correct use and application of the measures.

5.1. Standard precautions

Hand hygiene is key to prevent transmission of any microorganism, including *C. auris.* While caring for patients in isolation, special attention should be given to adequate compliance with hand hygiene. Hand hygiene should be performed at the point of care using an alcohol-based hand rub conforming to European Standard EN 1500, which has also been found to be effective in eliminating *C. auris* from hands [65]. While alcohol-based hand rub is the preferable choice, water and soap should be used when hands are visibly soiled, and a dedicated sink needs to be in place to wash hands.

5.2. Patient environment

Patients colonised or infected with *C. auris* need to be placed in 'contact precautions' in a single room, ideally with negative pressure, and preferably with an ante-room and en-suite bathroom/toilet. If the latter is not available, patients should use a dedicated washroom or a waterless washing product, as well as a dedicated commode. The use of an isolation room with anteroom might be preferable, not because airborne spread is assumed, but because compliance with isolation measures might possibly be higher, as the double doors function as a reminder. A flagging system indicating the isolation needs to be visible at the entry of the patient's room and instructions for healthcare workers (HCWs) and visitors need to be available [54]. All biomedical products and equipment should be used as disposables, or if re-usable should be left in the patient's room until discharge and thorough disinfection. Sharing biomedical products and equipment to other wards poses a risk of additional transmission. For mattresses and pillows, HCWs should ensure that they are 100% sealed before using them for a *C. auris* patient and its integrity should be assessed upon discharge if they are to be used for another patient [12].

5.3. Personal protective precautions

It has become evident that the use of a long-sleeved gown and gloves are sufficient to enter the room of patients found positive for *C. auris*. Taking into consideration that people often (unconsciously) touch their face, a surgical mask could be considered to prevent colonisation of healthcare staff, since one HCW was found to be transiently positive in the nose in a previous outbreak [12].

5.4. Environmental cleaning

Enhanced daily and terminal disinfection has been shown to be crucial to control the spread of *C. auris* within healthcare facilities.

Table 1
An overview of infection prevention and control measures for *Candida auris* single cases and outbreaks.

Infection prevention and control measures overview for *Candida auris*			
	Single case		*Outbreak*
	Minimum standard	Best practice	Single room and cohort
Patient room			
Room	Single room	Single isolation room with ante room, private, en-suite bathroom	Single room or cohort
Ventilation	Neutral	Negative	Neutral
Toilet/commode	Commode Validated machine	Single-use commode Single-use bedpan	Single-use commode Single-use bedpan
Washroom	Dedicated washroom	Washing without water	Washing without water/dedicated wash
Bedding	Check pillow and mattresses (when linen is removed) for damage	Check pillow and mattresses (when linen is removed) for damage	Single-use pillows or check pillows and mattresses (when linen is removed) for damage
Personal protective equipment			
Gown	Cuffed long sleeves (water repellent) + apron if needed	Cuffed long sleeves (grade 3)[1]	Cuffed long sleeves per patient in cohort
Gloves	Yes	Yes	Gloves per patient in cohort
Hand hygiene	Alcohol based*	Alcohol based*	Alcohol based*
Shoe covers	Discouraged	Discouraged	Discouraged
Cleaning			
Cleaning material	Single-use cloths	Disposable microfibre cloths	Single-use (microfibre) cloths
Cleaning frequency	Twice daily	Twice daily	Three times a day

* The product needs to meet the EN1500 testing standard[2].
[1] Bartels VT, ed. *Handbook of Medical Textiles*. Sawston, United Kingdom, Cambridge, Woodhead publishers; 2011. [2] Europena Standard. Chemical disinfectants and antiseptics. Hygienic handrub. Test method and requirements. Brussels: European Committee for standardization; 1997.

In addition, the frequency of cleaning and disinfection should be at least twice daily and of at least all high-touch surfaces. Terminal cleaning and disinfection of the rooms after patient discharge needs to be performed with great diligence. To date, multiples studies have found sodium hypochlorite, with concentrations of 1000 ppm or higher, to be effective in eradicating *C. auris* [64,66]. However, high-strength sodium hypochlorite agents, especially the 5000-ppm concentration, can be highly toxic for staff and are reserved for terminal cleaning. In a study by Ledwoch et al. it was observed that a number of commercially available products, including sodium hypochlorite products, were not effective against dry biofilm containing *C. auris* [10]. Other disinfectants and methods that have been shown to be effective are: peracetic acid, hydrogen peroxide < 1%, and vaporised hydrogen peroxide [11,67,68]. When selecting a product, users should bear in mind the toxicity of a product and select one that is safer to use near a patient. Other products, such as one containing ethyl alcohol 29.4% and phenols may be effective against *C. auris*, but evidence to date on their efficacy is low. However, 70 g/% alcohol kills *C. auris* and may be suitable for small surfaces (e.g. spills). Not all quaternary ammonium disinfectants, such as Lysol all and Virex II 256, have been found to be effective against *C. auris* and their effectiveness may depend on the specific formulation [10,68,69].

Innovative automated decontamination technologies, such as ultraviolet-C (UV-C) disinfection, can be used to ensure optimal terminal cleaning of surfaces, but are – as HPV – an additional safety and not a replacement of routine cleaning methods [67,70]. Both methods (UV-C and HPV) require vigorous cleaning before being effective against microorganisms. If UV-C is used, the duration of exposure for efficacy is longer than that for vegetative bacteria and a cycle time effective for spores such as *C. difficile* should be selected.

Cleaning and disinfection of reusable equipment is particularly important, especially as these items may be decontaminated at departmental level by clinical staff. As mentioned above, where possible, dedicated equipment should be used. If dedicated equipment is not an option, equipment and devices must be thoroughly disinfected after every use, in line with the manufacturer's instructions and considering the material's compatibility. The surfaces of reusable items should be periodically examined to check for surface integrity and the continued ability to be able to effectively decontaminate [51]. Materials that cannot be disinfected should not be used or discarded after use. Where possible, single-use equipment is preferred to limit possible spread via inadequately disinfected equipment. Equipment that is cleaned at local level by clinical staff should be audited to ensure that it is effective, and organisations may wish to consider whether formal training for clinical staff in decontamination has been or should be provided.

5.5. Patient clothing

The role of patient clothing in the transmission of *C. auris* is unclear. In the experience of the hospitals dealing with outbreaks, patients are asked to use hospital garments or clothes that have been washed at high temperatures. The expert group was not able to give a recommendation on this topic. In view of the fact that *C. auris* has been found to survive on linen, it may be prudent to change bedding and patient attire daily if decolonisation or skin suppression is being attempted.

5.6. Movement of the colonised or suspected patient in the hospital for procedures of investigations

Transfer of colonised or suspected patients for *C. auris* should be performed with great care. The treatment of patients should always come first, but if transfer can be prevented by the use of mobile equipment, this should be considered. When patients need to go to radiology, for example, they should ideally be placed at the end of the schedule to allow time for terminal decontamination of the area.

5.7. Readmission of a previous C. auris-positive patient

If known, previous *C. auris*-positive patients should be placed in contact isolation and screened on three consecutive days. Contact precautions may be stopped if all three screens are negative. Weekly screening is recommended, as *C. auris* may resurface after antibiotic therapy or other interventions such as chemother-

apy. This needs to be seen as a minimum measure. Obviously, local guidelines on MDRO that are stricter (e.g. the Dutch MDRO-guidelines) need to be regarded.

5.8. Outpatient management (i.e. after discharge from hospital)

In the USA it has been shown that family members and healthcare providers can become colonised. However, it is to be pointed out that this is of minimal risk to the 'healthy' HCW or family member. There are no guidelines yet for management of *C. auris*-colonised patients. However, it is prudent that sharing items should be kept to a minimum, in line with the principles for other fungal infections, in particular: towels, clothing, cosmetic items, creams, ointments, etc. should not be shared, even in the absence of studies demonstrating any effectiveness.

5.9. Awareness of healthcare workers

Compliance with and adequacy of using IPC measures is essential to prevent transmission of *C. auris* within the healthcare facility. To increase awareness of the IPC measures for HCWs and housekeeping staff, on-site training and auditing is critical to contain *C. auris*. Training should focus on standard precautions, personal protective equipment, environmental cleaning and other IPC measures applied to control *C. auris*. In addition, compliance and correct execution regarding the use of IPC measures should be monitored, and direct feedback to HCWs should be given ('teaching/learning' audits).

5.10. Outbreak management

The index or any unexpected case colonised or infected with *C. auris* should be isolated in a single/isolation room, and direct contacts (patients within the same room) should be placed in cohort isolation, with contact precautions and no new patients should be admitted to the affected room. Maintaining cohorts of 'proven colonised', 'possibly colonised' and 'no risk' patients is important under all circumstances, even if that would lead to lowered bed capacities, reduction of admitted patients or cancellation of operating procedures. As *C. auris* has been cultured from the hands of HCWs, where possible HCWs should be assigned to one of the cohorts, instead of working throughout the whole unit [71]. If the outbreak is large, creation of a separate unit for all proven colonised patients might be advisable. Single-use equipment or dedicated equipment should be used. A root cause analysis by Schelenz et al. found that patients who had contact with a positive case or contaminated environment were likely to have contracted *C. auris* within just 4 hours of contact [12].

To confirm negative patients, three consecutive *C. auris* screenings should be negative. In the absence of published data, it seems sensible to space out the three screening times (e.g. days 3-5-7, instead of performing them on days 1-2-3 or even all in one day). When de-isolated, it is recommended to weekly screen the negative contact patients until discharge [12]. Healthcare workers have been identified as carriers in the nose and groin [12,71]. During an ongoing outbreak, screening of healthcare staff (nose, groin, axilla) could be considered, as well as unannounced cultures from hands as an educational measure [54].

Daily cleaning and disinfection should be increased to three times daily of at least all high-touch surfaces with a product effective against *C. auris* [12]. Terminal cleaning and disinfection should be monitored with quality indicators that go beyond visual inspection, such as ATP or fluorescent markers, to ensure the quality of terminal cleaning and disinfection. If available, UV-C or HPV should be used after terminal cleaning and disinfection as an additional assurance that the room has been adequately decontaminated and is safe for the next bed occupant.

No recommendations can be given about the effect of decolonising patients (e.g. with chlorhexidine wipes or similar products). In theory, this may lead to a lower burden of yeast on the patient's skin and, thus, a lower risk of transmission. This approach has been adopted in outbreaks; however, non-conflicted data are missing to draw that conclusion for *C. auris*.

Mandatory national reporting of outbreaks in institutions should be considered, as well as mandatory reporting of infections with *C. auris*. In countries that do not have laws accounting for this, mandatory sharing of outbreak status data with regional healthcare providers is advisable.

6. Decolonisation or suppression of *Candida auris*

At the present time, there is limited evidence on the use of topical agents for the control of skin colonisation. In one major UK outbreak, 2% chlorhexidine washcloths or 4% chlorhexidine solution were used to control skin shedding as part of a number of interventions [12]. However, despite daily chlorhexidine bathing, patients described in the UK continued to be colonised with *C. auris* [12]. Chlorhexidine solutions may dry the skin in such a way that they may lead to prolonged colonisation with *C. auris*. Some patients, however, remain persistently colonised, possibly due to recolonisation from bedding, as *Candida* spp. have been found to survive on polyester textiles for up to 8 days [72]. Other outbreaks have also used this approach [64].

More recent studies have examined the effect of skin disinfectants on biofilms, demonstrating that chlorhexidine is effective against *C. auris* planktonic and sessile communities and that this can be advocated for topical control *of C. auris* at standard concentrations used for skin and wound cleansing and disinfection (0.05–4.0%) [16]. Other studies have also demonstrated the efficacy of chlorhexidine at 0.125–1.5%, although the effect may have been confounded by the addition of alcohol [73]. Work undertaken on octenidine dihydrochloride on (more susceptible) planktonic forms of *C. auris* has demonstrated efficacy; however, this may not translate to the clinical environment [74].

7. Treatment

While not a complete review, the current study chose to include a summary of treatment. *Candida auris* is resistant to fluconazole (> 90% R), which is commonly used in the treatment of invasive yeast infections, including candidaemia [75]. The treatment choice for *C. auris* infection depends on the antifungal susceptibility testing results, as echinocandin and amphotericin B resistance varies by region. Caspofungin, micafungin or anidulafungin are the first empirical choice, with liposomal amphotericin B (3 mg/kg) as the usual alternative. In 4% of cases, *C. auris* candidaemia is potentially untreatable, due to resistance to all presently licenced antifungals, although few data are available on flucytosine. Voriconazole may be a suitable oral choice if the isolate is susceptible. As for all patients with candidaemia, vascular catheters should be changed and the line tips cultured.

8. Conclusion

Candida auris is a next step in the evolution of multidrug-resistant pathogens, extending from bacterial resistance to this new fungal multi-resistant pathogen. Learning and sharing of information on mode of transmission, survival on surfaces, and prevalence in patients and communities will help to decrease the threat of *C. auris*.

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Competing Interests

None.

Ethical Approval

Not required.

Authors' contributions

NK, MK, AC, DD, JP, KS, SS, ET, AW, JM and AV drafted the manuscript. All authors read and approved the final manuscript.

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