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FOCUS ON

Candida auris

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Key Messages

- The rise and geographic spread of *Candida auris* in recent years is concerning, given the extent of resistance to treatment and disinfectant agents, the high mortality rates of invasive infections, and the ability of this organism to cause prolonged outbreaks in health care settings.
- In Canada, there have been 43 individuals known to test positive for *Candida auris* from 2012 to 2022; 19 of whom were identified in the last 3 years. Around the world, *C. auris* has been reported in at least 50 countries on six continents.
- Commonly reported sites of *C. auris* colonization in adults include the skin (especially the groin and axilla areas), mucosal surfaces of the gastrointestinal tract and genitourinary tract, the respiratory tract (oropharynx, nose), and the ear. In geographic areas where *C. auris* incidence was high, colonization rates of 2.5%–33.9% have been reported. Reports on *C. auris* colonization in children are rare, possibly due to fewer nosocomial outbreaks and subsequently less common screening practice.
- Nearly 10% of *C. auris*-colonized patients develop invasive infections, particularly those with mechanical ventilation and placement of invasive devices in intensive care settings.
- The pooled mortality for patients with *C. auris* infection was estimated at 39% (95% confidence interval [CI]: 32%–78%).
- *C. auris* is often resistant to at least one class of antifungals. Resistance rates vary considerably in different areas and settings, and are mainly due to different clade distributions. Worldwide, resistance rates of *C. auris* were as high as 87%–100% for fluconazole, relatively moderate at 8%–35% for amphotericin B; lower at 0%–8% for echinocandins but resistance to echinocandins has been demonstrated to develop while patients are on treatment (with an echinocandin). Nearly 4% of *C. auris* isolates are resistant to all three classes of antifungal drugs and has been reported in the U.S., South America and India.
- *C. auris* is able to withstand many common hospital disinfectants and to remain viable on surfaces for prolonged period of time.
- Prevention of colonization and surveillance are key measures to prevent the spread of *C. auris* as a vaccine against this highly resistant pathogen is not yet available. Further studies are required to develop rapid and affordable diagnostics, guide improvement of existing therapies and disinfectants, generate new therapeutic agents, and inform the optimal prevention strategies.

Introduction

C. auris is an emerging fungal pathogen capable of causing invasive disease, especially in critically-ill individuals, with mortality rates greater than 40%, which is similar to other antimicrobial-resistant organisms.[1] Since the recognition of this pathogen in Japan in 2009,[2] it has spread around the world, causing prolonged and difficult to control outbreaks in hospitals and long-term care homes.[3-17] These outbreaks have resulted in long-term endemic colonization and infections in the affected facilities,[6-12,15,17] dissemination of this multi-drug resistant organism to other facilities[6,13,14] and regional or country-wide spread within health care facilities.[18-20]

In March 2023, the Centers of Disease Control and Prevention (CDC) in the United States (U.S.) stated that *C. auris* was spreading at an alarming rate in U.S. health care facilities in 2020–2021. Furthermore, the number of isolates resistant to echinocandins, which is the recommended antifungal drug for treatment of *C. auris* infections, has tripled in 2021.[21]

This Focus On summarizes the epidemiology of *C. auris*; the colonization and infections it causes and their severity; the risk factors for acquiring *C. auris* colonization or infection, its mode of transmission and antifungal susceptibility profiles; diagnostics and surveillance for *C. auris*; and control measures to reduce or prevent its spread.

Background

C. auris is the first *Candida* species to be classified as multidrug-resistant.[22]

The epidemiology of *C. auris* infections has changed in many jurisdictions, from sporadic invasive infections when first reported,[23] to outbreaks involving multi-institutions or health care facilities.[19,24] The Public Health Agency of Canada (PHAC) has noted the spread of *C. auris* in hospital and long-term care settings across the globe, including Canada. It has been challenging to estimate the actual global incidence rates of *C. auris* colonization and infection, as this fungus may not be on the surveillance list in many countries, and capacity for laboratory detection may be limited in some jurisdictions.[25,26] However, available data indicate an increasing trend during the last decade due to outbreaks in many countries, which also reported increases in the number of cases during the COVID-19 pandemic.[25]

C. auris has become a global concern, with cases reported in at least 50 countries on six continents.[24,27] *C. auris* is considered by the World Health Organization (WHO) as a critical fungal pathogen on the WHO fungal priority pathogens list,[25] and by CDC as a public health threat that requires urgent and aggressive action,[28] due to the following characteristics:

- Ability to cause invasive infections with high mortality.[25,28]
- High potential for outbreaks in health care settings,[25,28] which are often difficult to control and involve large numbers of cases.[26]
- Ability to colonize the skin without causing infection, allowing spread to others.[28]
- Intrinsic resistance to most available antifungals, with some pan-resistant strains (resistant to all three groups of antifungals).[25,28]
- Unavailability of some recommended antifungals in some countries.[25]
- Difficult to identify using traditional laboratory techniques.[25]

- Thermoresistance and partial resistance to commonly used disinfectants.[25,28]
- Lack of well-established preventive measures.[25]

C. auris can be separated into five clades based on its geographic origin.[27] These clades differ from each other by 40,000 to 400,000 single nucleotide variants (SNVs). Within a clade, isolates are almost identical within regions with less than 70 SNV differences.[29] While these clades were reported to emerge around the same time from different continents, clades I and III have been reported more often and from wider geographical locations.[1] See Table 1 for a summary of the geographical distribution, clinical isolation sites, antifungal resistance profiles and associated outbreaks of each clade.

Table 1. Summary Features of *C. auris* Clades

Features	Clade I (South Asian)	Clade II (East Asian)	Clade III (South African)	Clade IV (South American)	Clade V (Iranian)
Dominant Locations	U.S., Europe, South Asia[30]	Korea, Japan[30]	Europe, Africa[30]	South America[30]	Iran[30]
Clinical Isolation Sites	Ear, blood, other invasive sites[30]	Mainly ear[30]	Ear, urine, blood, other invasive sites[30]	Blood, other invasive sites[30]	Nail, skin, ear[30]
Antifungal Resistance Profile	Resistant to fluconazole, echinocandins, amphotericin B Pan-resistance identified in some strains[30]	Usually susceptible to antifungal drugs[24]	Resistant to fluconazole Cross-resistant to echinocandins, amphotericin B Pan-resistance identified in some strains[30]	Resistant to fluconazole Cross-resistant to echinocandins, amphotericin B Pan-resistance identified in some strains[30] Note: the first isolates in Ontario were all clade IV and all were pan-susceptible	Resistant to fluconazole[31]
Outbreaks	Invasive infections[29,30]	Ear infections and colonization[29]	Invasive infections[29,30]	Invasive infections[29,30]	Skin and ear infections[31]

Methods

The PubMed database and grey literature on "*Candida auris*" was searched up to April 9, 2023 for peer-reviewed and preprint publications in the English language. Reference lists of articles were also scanned. A single reviewer selected relevant articles and extracted data for this report.

Epidemiology of *C. auris*

A 2020 review of 57 studies noted a rapid increase in the global incidence of *C. auris* colonization or infection in 2014, which peaked in 2016 to 1,395 cases, and dropped to 241 cases in 2019. The authors noted uncertainty if the reduction in case count was due to delay in case reporting.[1] Another 2023 review noted that incidence of *C. auris* colonization or infection first rose among adults in 2009 then among children in 2011 in Asia. Following that, reports of nosocomial outbreaks of *C. auris* began to increase across Europe and Africa during 2013–2015, and in North and South America (mostly in intensive care settings) since 2016. Reports of *C. auris* transmission among adults began to surface in 2018.[29]

A 2018 review of 742 isolates from 16 countries noted that before the COVID-19 pandemic, about one-third of the isolates (32.75%) were reported in India, 31.26% in the U.S., and 13.9% in the UK from 2013 to 2017.[3] Screening for *C. auris* is generally lacking in most countries, so these numbers may not reflect the true incidence. Another 2022 review of data published between Dec 2019 and Apr 2022 recorded 65 patients infected with *C. auris* out of 1,942 patients hospitalized with COVID-19 in the U.S., Brazil, Colombia, Spain, Italy, Pakistan, the United Arab Emirates, and India; with a pooled prevalence of 5.70% (95% CI: 2.77%–9.58%).[27] In some jurisdictions (e.g., U.S., Italy), a rise in reported cases of *C. auris* has been noted during the COVID-19 pandemic. Factors contributing to such increase in incidence may include: more testing of *C. auris*, an increase in the number of vulnerable patients requiring intensive care, overloaded health care systems, a shift in focus to COVID-19 precautions while overlooking proper implementation of Contact Precautions and environmental cleaning.[32,33]

A systematic review using data from 38 studies published up to July 21, 2017 noted that individuals colonized or infected with *C. auris* (at least 340 patients) frequently have comorbidities:[3]

- Diabetes: ≥ 52
- Sepsis/blood stream infection (BSI) and multi-organ dysfunction: ≥ 48
- Pulmonary diseases/pneumonia: ≥ 39
- Chronic/acute kidney disease/failure: ≥ 32
- Immunosuppressive conditions: ≥ 29
- Solid tumour/malignancies: ≥ 26
- Cardiovascular/hypertension: ≥ 2
- Chronic otitis media: ≥ 18
- Liver disease: ≥ 7
- Gastrointestinal disease: ≥ 7

The ages of COVID-19 patients with *C. auris* colonization or infection ranged from 1 to 101 years (mean = 65.4 years; n = 58); and the ages of COVID-19 patients with *C. auris* BSI ranged from 1 to 86 years (mean = 65.3 years).[34]

Among the 24 COVID-19 patients co-infected with *C. auris* with underlying conditions reported (5 studies), the most prevalent comorbidities were:[27]

- Hypertension = 59.374% (95% CI = 21.505%–91.624%); 15/24 cases
- Diabetes mellitus = 52.898% (95% CI = 20.584%–83.897%); 12/24 cases
- Cardiovascular diseases = 31.392% (95% CI = 16.090%–49.131%); 1/24 cases

Europe

In the European Union, a total of 1,812 *C. auris* cases have been identified between 2013 and 2021.[33] Sporadic cases of *C. auris* have been detected in all European countries, with hospital outbreaks reported in the UK, Denmark, France, Germany, Greece, Italy and Spain.[33] Despite overall advances in laboratory capacities to identify *C. auris*, the capability to identify *C. auris* is not universal. A survey conducted by the European Centre for Disease Prevention and Control (ECDC) in 2018 and 2019 found that only 60% of laboratories were able to identify a strain of *C. auris* correctly. And European quality control trials confirmed that more than 40% of *C. auris* isolates may have been misidentified.[29]

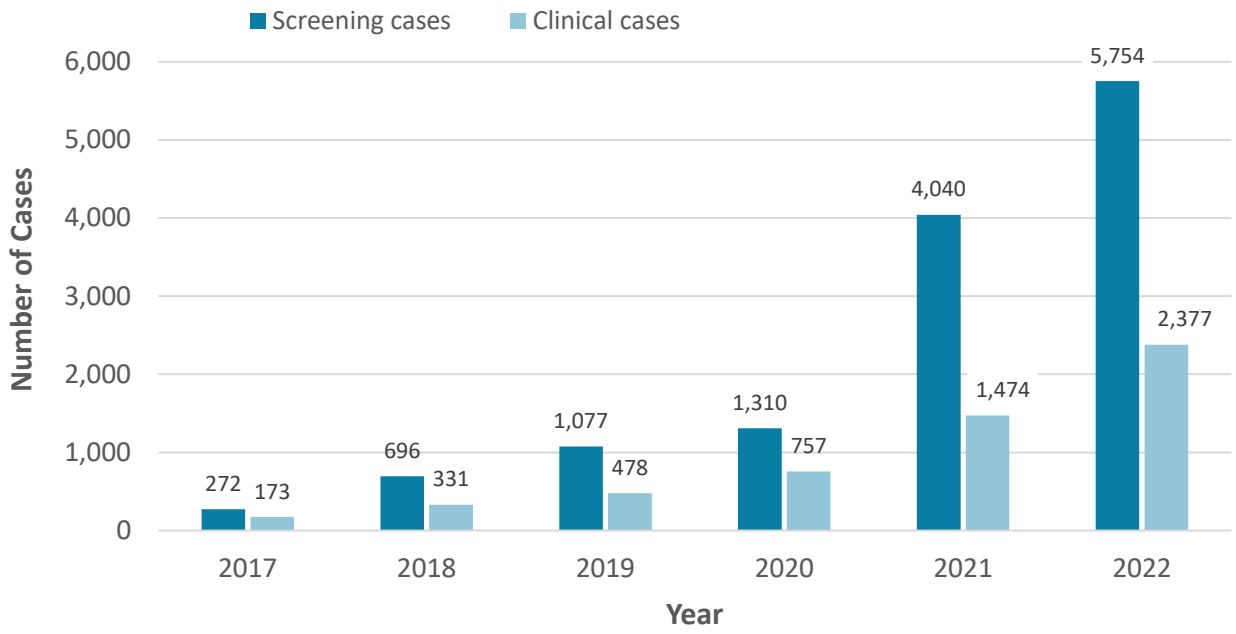
In Spain, 786 cases of *C. auris* have been reported from its first identification in 2016 through to 2019. Incidence dropped from 266 cases in 2017 to 135 cases in 2019; but rose to 260 cases in 2020 to 331 cases in 2021 during the COVID-19 pandemic.[33]

In Italy, an ongoing outbreak with 361 cases involving 17 health care facilities in the Liguria, Piedmont, Emilia-Romagna, and Veneto regions has been reported from July 2019 (when the first *C. auris* case was detected) up to December 2022. 91.8% of the cases were colonizations. The incidence rate of the affected regions ranged from 19.6 per 1,000 residents in Liguria to 0.02 per 1,000 residents in Veneto.[35] Multiple transmission chains starting from different sources may have occurred simultaneously, aggravated by inter-facility transfer of individuals with unrecognized *C. auris* colonization or infection.[35]

United States

C. auris became nationally notifiable in the U.S. in 2018 and its incidence has been increasing since then (see Figure 1).[36] Most cases have been identified in long-term care and high-acuity post-acute care facilities,[28,32] and in recent years, acute care hospitals have reported several large *C. auris* outbreaks.[32] Factors that could have contributed to this rising incidence include enhanced surveillance of colonizations and infections, lapses in infection prevention and control practices in health care facilities (e.g., extended use or reuse of personal protective equipment, inappropriate use of multiple gowns and gloves at a time, insufficient cleaning of shared medical equipment), which may have been aggravated by the strain on the health care system during the COVID-19 pandemic.[21,32]

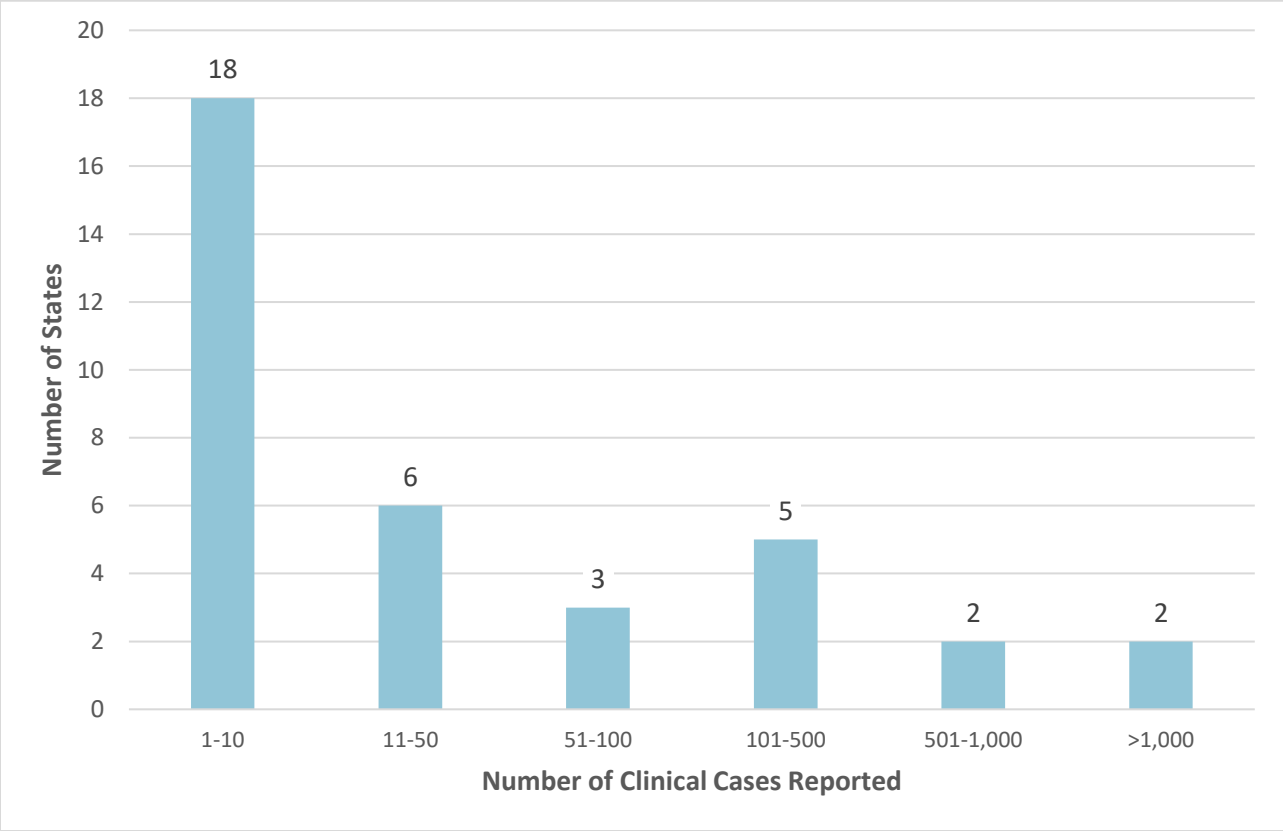
Figure 1. Incidence of *C. auris* Colonization and Infection in the U.S. (2017–2022)



In the U.S., there have been 5,653 clinical cases and 13,163 cases identified through screening (colonizations) reported by 36 states from 2013 to December 31, 2022 (see also Figure 2):[36]

- States reporting > 1,000 clinical cases = 2: New York (1,325) and Illinois (1,044).
- States reporting 501–1,000 clinical cases = 2: California (813) and Florida (683).
- States reporting 101–500 clinical cases = 5: New Jersey (419), Nevada (408), Texas (224), Indiana (177), and Ohio (111).
- States reporting 51–100 clinical cases = 3
- States reporting 11–50 clinical cases = 6
- States reporting 1–10 clinical cases = 18

Figure 2. Number of States Reporting Clinical *C. auris* Cases from 2013 to December 31, 2022

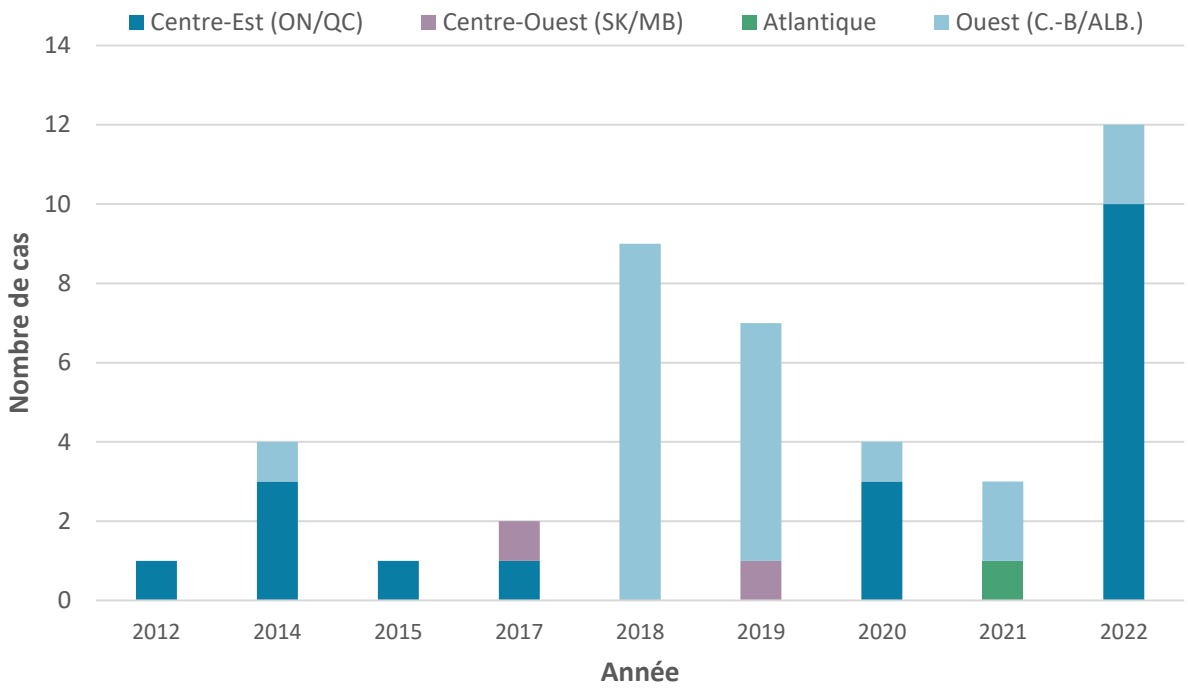


Canada

Prospective surveillance for *C. auris* has been conducted by the Canadian Nosocomial Infection Surveillance Program (CNISP) in collaboration with 88 sentinel hospitals across Canada since 2019.[37] In addition, all 10 provincial public health laboratories voluntarily report all cases of *C. auris* to PHAC that they are aware of and send isolates to the National Microbiology Laboratory (NML) for whole genome sequencing (WGS) analysis.

From 2012 to 2022, there have been 43 individuals known to test positive for *C. auris* in Canada; 19 (44.2%) of whom were identified in the last 3 years (see also Figure 3). [38]

Figure 3. Number of *C. auris* Cases in Canada, 2012-2022 (n=43)



Source: National Microbiology Laboratory, Public Health Agency of Canada[38]
Notes: 21 of the 43 cases of *C. auris* were identified in Western Canada (British Columbia/Alberta), 2 cases in the Central West (Saskatchewan/Manitoba), 19 cases in Central East (Ontario/Quebec), and 1 case in the Atlantic region (New Brunswick, Newfoundland, Nova Scotia, or Prince Edward Island). Of the 43 cases, four reported no travel, eight had recently received healthcare abroad (in India, the USA, South Africa and Hong Kong) and one had recently migrated to Canada. There is no travel data for the remaining cases. WGS was able to confirm transmission between 2 individuals in the same health care facility in 2022.

A summary by De Luca et al. (2021) describes the distribution across four genomic clades of 24 cases of *C. Auris* colonization or infection discovered in Canada from 2012 to 2019. [39] Twelve cases were found to be in Clade I, 3 cases in Clade II, 4 cases in Clade III and 5 cases in Clade IV. [39]

A prospective point prevalence study was conducted from September 4 to November 6, 2018 in 23 acute care hospitals from six provinces (British Columbia, Alberta, Saskatchewan, Ontario, Quebec, and New Brunswick), as well as inpatients and outpatients from 25 hospitals in south-central Ontario who were colonized or infected with a carbapenemase-producing organism (CPO). A low prevalence of *C. auris* was found with 2 out of 448 at-risk patients screening positive [0.4% (95% CI: 0.1%–1.5%)].[40] Both isolates were identified at the same health care facility; both belonged to clade I but differed by 70 SNVs, suggesting separate introductions into the facility. Both had recent exposure to health care in India.[40] The prevalence of *C. auris* in patients who had recently received health care services in the Indian subcontinent and were colonized or infected with a CPO was 5.7% (2/35; 95% CI: 0.7%–19.2%), compared to 0% among those without these two risk factors, P = 0.005.[40] Findings from the study support the hypothesis that the greatest risk of *C. auris* in Canada comes from the import and further spread of existing clades from endemic areas. However, the authors noted that residents in long-term care homes were not included in this study, although this population has been identified as an at-risk group in the U.S.[40]

ONTARIO

C. auris is not a reportable disease in Ontario. Front line laboratories are encouraged to submit all *C. auris* (or isolates in question) to Public Health Ontario's (PHO) laboratory for confirmation of identification and antifungal susceptibility testing, as well as for forwarding to the NML for national surveillance and WGS analysis. The following are data collected by PHO from 2014 to April 5, 2023:[41]

From 2014 to 2021:

- 7 individuals were known to test positive for *C. auris*:
    - 5 individuals had *C. auris* infections between 2014 and 2020; sources of clinical specimen included bloodstream, peritoneal fluid, and wound.
    - 2 individuals were identified as being colonized with *C. auris* via surveillance screening in 2019 and 2020. One of these individual was persistently positive and later developed an invasive *C. auris* infection.
- 5 isolates belonged to clade IV and were pan-susceptible; WGS analysis showed that these isolates were genetically related.
- All 7 isolates were susceptible to echinocandin. Isolates from 2 individuals were multidrug resistant (to amphotericin B and fluconazole). These isolates belonged to clade I. Both individuals were reported to have had hospitalization overseas (India and Saudi Arabia).

From 2022 to 2023:

- 8 individuals were known to test positive for *C. auris*:
    - 4 individuals had infections (urine, blood).
    - 4 individuals were colonized and tested positive for *C. auris* via surveillance screening.
    - 4 isolates belonged to clade I; 3 isolates belonged to clade III; results for the 8th isolate are unavailable at this time.
- 5 individuals were linked to hospitalization abroad (the U.S., South Africa, or India).
- 2 individuals were linked epidemiologically and by WGS analysis (with 8 SNV differences). The Index patient was not known to have had hospitalization abroad and was identified as a clinical case in-hospital; the secondary case was identified via contact screening.
- 5 isolates were resistant to fluconazole; 3 isolates were resistant to fluconazole and amphotericin B based on CDC interpretations. All isolates were susceptible to echinocandin.

The data above may not include all cases of *C. auris* in Ontario, as many health care facilities do not have screening programs for detection of *C. auris* colonization.

- In the 2-year period of 2020 to 2021, 11/61 (18.0%) of hospitals in Ontario reported having a screening policy for colonization with *C. auris*, compared to 16/74 (21.6%) in 2019.[42,43] Reported reasons for not having a screening policy of *C. auris* include:[42]
    - Not having any cases in the facility: 17/61 (27.9%)
    - Risk level in the facility's geographic area not warranting a screening program: 13/61 (21.3%)
    - Implementation of screening program was delayed by the COVID-19 pandemic: 11/61 (18.0%)
- In the 2020–2021 period, 16/47 (34.0%) laboratories reported screening for *C. auris* from clinical isolates, compared to 24/49 (49.0%) in 2019. Reasons for not screening for *C. auris* from clinical isolates were not reported by the authors.[42,43]

C. auris Colonization and Infection

Colonization by *C. auris*

In adults, commonly reported sites of colonization include the skin (especially the groin and axilla areas), mucosal surfaces of the gastrointestinal tract and genitourinary tract, the respiratory tract (oropharynx, nose), and the ear.[29] In addition, colonization of the tips of central venous catheters has been reported.[26] In geographic areas where *C. auris* incidence was high, colonization rates of 2.5%–33.9% have been reported.[35,44]

- 188/2,062 (9.1%) individuals tested positive for *C. auris* via admission screening conducted in 5 high-risk units in 3 nursing homes and 1 hospital in New York City from November 2017 to November 2019. Colonization rates varied by facility:[44]
    - Nursing home A: 20.7% (67/323) residents
    - Nursing home B: 22.0% (42/191) residents
    - Hospital ventilator/pulmonary unit: 5.7% (16/282) patients
    - Hospital ICU: 3.7% (45/1,208) patients
    - Hospital cardiac care unit: 2.5% (18/722) patients
- 116/342 (33.9%) asymptomatic individuals tested positive for *C. auris* in a retrospective survey of *C. auris* in the Liguria and surrounding regions in Italy in October 2021.[35] The survey was requested by the Ministry of Health after an outbreak with 277 cases of *C. auris* infection or colonization between November 2020 and October 2021 was reported.

Reports on colonization in children are rare, possibly due to fewer nosocomial outbreaks and subsequently less common screening practice.[29] An incidence of colonization in the eyes, ears and axilla in a neonate born to a colonized mother has been described.[29] However, no colonizations were identified in a 2019 prevalence survey in a pediatric long-term transitional care hospital in Chicago, U.S. despite a high prevalence of *C. auris* among adult patients in health care facilities of similar acuity in the region.[45]

Continuous carriage for more than a year after initial isolation of *C. auris* has been documented.[46] This poses a risk for both transmission to others and invasive infections.[26] Duration of *C. auris* carriage was explored in a survey of a cohort of New York City residents who had a history of positive *C. auris* culture identified during clinical or screening activities in health care settings and discharged to a community setting during October 2017–February 2019. Those who have had at least 2 assessments for *C. auris* colonization after initial *C. auris* identification were screened approximately every 3 months for *C. auris* colonization, which included swabs of groin, axilla, and body sites yielding *C. auris* previously:[46]

- At 0–6 months after initial *C. auris* identification, 8/24 (33%) eligible patients were reported as serially negative. Serially negative is defined as having 2 consecutive negative *C. auris* rt-PCR tests and negative fungal culture on all screening specimens.
- At 7–12 months, 15/29 (52%) of eligible patients were reported as serially negative.
- At 13–18 months, 4/10 (40%) of eligible patients were reported as serially negative.
- At 19+ months, 1/3 (33%) of eligible patients was reported as serially negative.
- Median time from initial *C. auris* identification to being serially negative at assessment was 8.6 months (interquartile range = 5.7–10.8 months).
- There were no clinical characteristics that were significantly different between serially negative and positive patients.

Infections by *C. auris*

Nearly 10% of *C. auris*-colonized patients develop invasive infections, particularly those with mechanical ventilation and placement of invasive devices in intensive care unit (ICU) settings.[24]

C. auris infections have been reported to predominantly affect male and critically ill patients in ICUs.[47] The spectrum of *C. auris* infection ranges widely from superficial skin infection to invasive disease.[29]

Non-invasive infections associated with *C. auris* include:[22,47] respiratory tract infections, urinary tract infections, otitis externa, wound infections, and skin abscesses (often related to catheters).

Invasive infections associated with *C. auris* include: BSI, pericarditis; myocarditis, meningitis, and osteomyelitis, and rarely with spondylodiscitis. In particular, BSI with *C. auris* can be fatal.[22,47] In immunocompromised individuals, *C. auris* can cause vulvovaginitis, pleuritis, intra-abdominal infections, pericarditis, ventriculitis, surgical wound infections, and osteomyelitis; and has been implicated in panophthalmitis and otomastoiditis in that population.[47]

A review of pediatric *C. auris* infections includes 22 reports published before November 30, 2022 identified 256 patients, aged 1 day to 14 years. Neonates and children born prematurely comprised 33% (70/214) of cases with available data. BSI was the most common type of invasive infections (94%; 194/206 patients). Duration of BSI was available for 7 patients, and ranged from 7–11 days. Where data were available, having a central venous catheter (70%; 94/135) was the most common underlying condition for *C. auris* BSI, followed by total parenteral nutrition (62%; 82/135), exposure to broad-spectrum antibiotics (40%; 54/135), history of a surgical procedure (22%; 29/135), having congenital or acquired immune deficiency (23%; 31/135). Other infections included meningitis, endocarditis, intravascular infection, peritonitis, urinary tract infection, and skin abscess.[29] Most of these pediatric cases were associated with nosocomial outbreaks in South America (45%; 114/246) and South Asia (26%; 67/256). Only one case was identified during the COVID-19 pandemic. The authors noted that incidence may be underreported due to variable surveillance and reporting policies in different jurisdictions.[29]

Before the COVID-19 pandemic, the pooled rate of *C. auris* BSI was estimated at 32% (95% CI: 21%–42%) among patients with *C. auris* infections, with high heterogeneity observed between studies. Clades I and IV had a higher percentage of BSI (53% and 60%, respectively) compared to clades II and III (3% and 10%, respectively).[1]

Severity of Disease

C. auris is thermotolerant because it grows optimally at 37°C, but it can remain viable at 42°C. This gives *C. auris* the ability to cause invasive infections and tolerate fever.[23] *C. auris* has been shown to be less virulent than *C. albicans* in murine and *Galleria mellonella* infection models, but significantly more virulent than *C. glabrata* and *C. haemulonni* in murine models.[33,47] However, pathogenicity and virulence seem to differ by the strain.[3] Also, despite its lower virulence compared to *C. albicans*, the spread of *C. auris* is concerning as there are fewer treatment options due to its resistance to antifungal drugs.

Compared to BSI by other *Candida* species, those by *C. auris* were associated with longer median length of stay in hospital or ICU; ranging from 46–68 days for adult patients and 70–140 days for pediatric patients.[25]

In a 2020 review, the pooled mortality of *C. auris* infection was estimated at 39% (95% CI: 32%–78%; range = 0%–78%).[1] Mortality of patients in Asia (44%; 95% CI: 38%–51%) was significantly higher than that of patients in Europe (20%; 95% CI: 4%–37%; $P < 0.001$).[1] However, the crude mortality of patients with *C. auris* BSI (45%; 95% CI: 39%–51%) was significantly higher than that of patients without BSI (21%; 95% CI: 8%–33%; $P = 0.002$).[1] No association was found between mortality and resistance to fluconazole or amphotericin B in two reviews conducted in 2020 and 2023; and the 2020 review found no association with clade or publication year either.[1,33]

However, the authors noted that most studies reported crude mortality rather than attributable mortality, and significant heterogeneity was observed between studies.[1] A high mortality rate of 83% in COVID-19 patients with *C. auris* BSI was reported from Mexico.[30]

The reported rates of mortality for pediatric *C. auris* infections are about 40% (range from 0%–80%). However, not all the mortality reported was attributable to *C. auris* infection.[29]

Overall mortality appeared higher in pediatric patients with BSI by *C. auris* (~40%) than by *C. albicans* or non-albicans species (12–20%).[29] The relation between age and disease severity in children is not clear:

- A nationwide Indian study of BSI in children in intensive care settings reported higher mortality with *C. auris* only among non-neonates, whereas among neonates, mortality was similar for *C. auris* (33%), *C. parapsilosis* (40%) and *C. albicans* (40%).[29]

- A retrospective review of *C. auris* cases in 2 hospitals in Colombia reported higher in-hospital mortality rate in neonates (57%; 4/7) than in infants (50%; 8/16), in children aged 1–5 years (17%; 1/6), and in children > 5 years of age (20%; 1/5).[48]

The mortality rate of COVID-19 patients with *C. auris* co-infection was estimated at 67.9% (95% CI: 46.1%–86.1%) (4 studies, 1,942 patients),[27] and 64.7% (22/34 BSI patients) among COVID-19 patients with *C. auris* BSI.[34] In a retrospective survey of *C. auris* in the Liguria and surrounding regions in Italy in October 2021, in-hospital mortality was estimated at 40.3% (145/360). For patients with data on age, the median ages of patients who died with or by *C. auris* were 59.5 years (Emilia-Romagna region, n = 6), 63 years (Piedmont region, n = 20), and 70.6 years (Liguria region, n = 28); (range 0–87 years).[35] The following were found to be risk factors associated with death in patients with COVID-19 and *C. auris* BSI compared to patients with COVID-19 patients colonized with *C. auris:*[34]

- Diabetes mellitus: 9/12 vs. 2/11
- Central venous catheter: 18/27 vs. 3/19
- ICU stay: 22/33 vs. 6/27
- Broad spectrum antibiotics: 22/34 vs. 5/26
- Mechanical ventilation: 18/24 vs. 5/22
- Steroid therapy: 20/27 vs. 5/24
- Urinary catheter: 13/19 vs. 3/17
- Previous antifungal therapy: 4/7 vs. 0/12

In a 2022 Italian study on *C. auris* invasive infections in critically-ill patients, the 30-day mortality after the onset of *C. auris* BSI was 26% (7/27).[49] In contrast, in the UK outbreak, no fatality could be directly attributed to *C. auris*.[33] One should note that attributable mortality is difficult to determine as invasive *Candida* infections often occur in severely ill patients with multiple comorbidities.[26]

Risk Factors for Acquisition

Risk factors for *C. auris* colonization were explored in a survey involving admission screening for *C. auris* in five high-risk units in three nursing homes and one hospital in New York City from November 2017 to November 2019.[44]

- Risk factors for *C. auris* colonization among patients admitted to the hospital were:
    - Presence of a drain: 11.3% vs. 2.2% (P = 0.0006)
    - Intubation/having a tracheostomy: 19.7% vs. 8.7% (P = 0.0034)
    - Presence of a central venous catheter: 16.3% vs. 6.3% (P = 0.0096)
    - Receipt of oral or IV antifungal: 8.7% vs. 2.0% (P = 0.0142)
- Risk factor for *C. auris* colonization among individuals admitted to the nursing homes was having a drain: 65.3% vs. 52.4% (P = 0.0476)
- There was no significant difference in age between those who tested positve and those who tested negative in both nursing homes and the hospital.

Invasive *Candida* infection is a serious nosocomial infection that especially affects critically ill and immunocompromised patients, such as cancer or bone marrow and organ transplant patients.[25] Neonates, most of them premature, have also been affected.[26] Other risk factors cited in a WHO 2022 report include renal impairment, hospital stay longer than 10–15 days, use of mechanical ventilation, central venous catheterization, total parenteral nutrition and sepsis. Previous use of antifungal medicines, especially triazoles, is also associated with increased risk for *C. auris*.[25] However, a 2022 meta-analysis found no significant differences in underlying comorbidities and iatrogenic risk factors among COVID-19 patients with colonization/non-invasive of *C. auris* compared to those with *C. auris* BSI.[34] Another 2022 meta-analysis also did not find any significant relationship between *C. auris* infection (odds ratio = 2.635; 95% CI = 0.278–25.003; 2 studies, 24 cases) and having central venous catheters or being on mechanical ventilation (odds ratio = 0.510; 95% CI = 0.176–1.476; 3 studies, 24 cases) in COVID-19 patients.[27] A 2023 review of pediatric patients with *Candida* infections noted that the risk factors for invasive infection were similar between infections caused by *C. auris* and by other *Candida* species. Also, the review did not find definitive evidence for prior colonization by *C. auris* as a risk factor for *C. auris* BSI.[29]

In vitro data suggest a possible risk associated with prolonged use of vancomycin in the onset of *C. auris* infections. When vancomycin at 15g/mL was present in the culture medium, biofilm formation of reference strain *C. auris* was increased by 22% in total biomass (P < 0.0001) and by 14% in viable biomass (P < 0.0001) on polystyrene surface, and by 28% in viable biomass (P < 0.05) on silicone surface—a material commonly used in indwelling devices. The effectiveness of caspofungin (2.5–50 μg/mL) in eradicating *C. auris* biofilm was also found to be significantly reduced in the presence of vancomycin, suggesting a more robust biofilm developed in the presence of the antibiotic. In addition, *C. auris* was found to be able to colonize a residual *Staphylococcus aureus* biofilm in the presence of vancomycin. Furthermore, results from a *Galleria mellonella* infection model suggest that vancomycin may promote *C. auris* growth and/or virulence, as the mortality of the larvae 24 hours post infection of *C. auris* was greatly increased in the presence of vancomycin.[50] The authors cautioned that further studies using clinical strains of *C. auris* are needed to enlighten the significance of these results.

Mode of Transmission

Outbreak investigations show that *C. auris* can be transmitted via inanimate objects or hands contaminated by this organism. *C. auris* can be isolated on the skin of colonized patients for several months,[33] and it can be shed from the skin at a rate of approximately 10^6 cells per hour.[3] Outbreak investigation and surveillance studies also report widespread environmental contamination of surfaces and equipment (e.g., glucometers, mobile ultrasounds, temperature probes, pulse oximeters, stethoscopes, and blood-pressure cuffs) surrounding patients colonized or infected with *C. auris*.[11,15] In addition, *C. auris* can survive on inanimate surfaces for at least 14 days, and on contaminated bedding for up to 7 days.[33] Yadav et al. took environmental samples of all rooms with colonized patients at the day of hospitalisation and weekly afterwards until discharge:[51]

- Out of 148 samples, 15 (10%) cultured *C. auris*:
    - Floor: 4/15 (26.6%)
    - Bed railing: 3/15 (20%)
    - Bedside trollies: 2/15 (13.3%)
    - Bed sheet: 1/15
    - IV pole: 1/15
    - Oxygen mask: 1/15
    - Air conditioner air wings: 1/15
    - Pillow: 1/15
    - Mobile phone: 1/15
- The environmental samples became positive on average of 8.5 days (range = 7–14 days) after patient's colonization was detected.

Zhu *et al*. conducted an investigation of an ongoing *C. auris* outbreak in New York State from August 2016 through 2018, and isolated *C. auris* from 3.0% (109/3,672) of the environmental samples. The extent of contamination ranged from <50 colony forming units (CFU) to >10^5 CFU per surface; the median *C. auris* CFU was approximately 3-fold higher ($P < 0.001$) on nonporous (i.e., plastic and metal devices) than porous (i.e., linen and carpet) surfaces. However, many more nonporous samples were analyzed than porous samples.[52]

In an outbreak in a neurosciences ICU in the UK, the incidence of new cases was reduced only after removal of the reusable skin-surface axillary temperature probes, which was found to be a risk factor for *C. auris* colonization or infection: OR = 6.8 (95% CI: 2.96–15.63; $P < 0.001$).[15]

Alanio *et al.* speculated that transmission of clade I *C. auris* between two patients in a burn ICU in France could have occurred via shared medical equipment or health care worker hands before *C. auris* colonization on the index case was recognized. Environmental cleaning of the unit was carried out with a disinfectant effective against *C. auris*, and all environmental samples tested negative for *C. auris* by culture. Also, no other ward-mates tested positive, making it unlikely that the transmission was due to environmental persistence of *C. auris*.[53] The index patient was not screened for *C. auris* on admission

but was put on Contact Precautions in a single room equipped with dedicated air treatment and a decontamination room given her transfer from the United Arab Emirates. A skin swab tested positive for *C. auris* 9 days after admission. Weekly screening of 32 ward-mates by axillary and groin swabs for 3 weeks all tested negative.[53] About 30 days after the last of 3 weekly negative screening, another patient tested positive at 61 days after the first positive test of the index patient, or 41 days after the last day the index patient was present in the ward. Whole genome sequencing showed the isolate from the second patient was genetically related to the 3 isolates from the index patient (with ≤ 12 SNVs) but distant from other clade I isolates from cases in France and reference strains, suggesting the second patient was infected with the strain from the index patient.[53]

In a hospital outbreak investigation in the UK, the authors reported that transmission may occur after a minimum contact period of 4 hours with a person carrying *C. auris* or an environment contaminated by *C. auris*. However, the investigation did not identify any single point of transmission.[8]

A low-birth-weight (800g) neonate tested positive for *C. auris* within a few hours after birth by vaginal delivery; the mother was colonized with *C. auris*. However, the authors could not determine if the neonate acquired *C. auris* via vertical transmission or from the ICU environment. The infant did not show any signs or symptoms of infection but died on her third day of life due to complications from prematurity.[54]

Some scientists have hypothesized that wild ancestors of *C. auris* may have existed in marine ecosystems and later acquired virulence factors that enabled it to colonize and infect humans. Population genomic analyses have estimated that the most recent ancestor of *C. auris* may date back to the last 360 years.[55] Meanwhile, *C. auris* has been isolated from a salt marsh and a sandy beach in the Andaman Islands of the Indian Ocean, and in estuaries in Colombia. One of the strains in the Andaman Islands was more susceptible to antifungals but less thermotolerant, and it differs significantly from clinical isolates.[56] Further research is needed to inform any transmission risk of *C. auris* from the marine environment.

C. auris with cross-resistance to medical and agricultural azoles has also been isolated from the surface of apples in storage and previously treated with fungicidal agents.[24,30] However, *C. auris* was not detected in freshly picked apples.[56] Further studies are needed to determine if the agricultural use of fungicidal agents may have contributed to the development of antifungal resistance in *C. auris*, or was the contamination a result of human handling.[24,30] The association between azole resistance in other fungal species than *C. auris* and the usage of fungicides in the environment has also been reported.[56] However, this review did not identify any report of *C. auris* transmission via food consumption.

In silico screening of the internal transcribed spacer region of *C. auris* in publicly available metabarcoding and metagenomic datasets has traces of *C. auris* in the environment (e.g., air dust from Kuwait, activated sludge from South Korea, peanut fields of Florida) and in some animals (e.g., from the ear canal of a Spanish dog with otitis externa, in the skin of two species of newt [*Lissotriton vulgaris* and *Triturus cristatus]*) in the UK. However, it is uncertain whether *C. auris* colonizes or causes infections in animals, and no animal cultured-based isolations of *C. auris* have been described to date. [56]

Antifungal Susceptibility

Currently, there are no formal clinical breakpoints for any antifungal drugs used to treat *C. auris* infections. The interpretations of *C. auris* antifungal resistance are provided by the CDC and are provisional, as they are based on breakpoints established for closely-related *Candida* species and on expert opinion.[57]

Unlike other *Candida*, *C. auris* is often resistant to at least one class of antifungals and in many cases more than one class. Worldwide, resistance rates of *C. auris* to fluconazole were as high as 87%–100%, while susceptibility to other azoles was variable. *C. auris* isolates showed relatively moderate resistance rates of 8%–35% to amphotericin B, and a lower resistance of 0%–8% to echinocandins.[25] Nearly 4% isolates are pan-resistant,[24] which has been reported in the U.S., South America and India.[39] Resistance rates in different countries and different health care settings vary considerably and are mainly due to different clade distributions in different settings.[24]

- In the U.S., nearly 90% of *C. auris* isolates were resistant to fluconazole; 30% to amphotericin B; and approximately 5% to echinocandins. However, in the New York-New Jersey area where 55% of all U.S. isolates occur, 99.8% of the isolates were fluconazole-resistant, and 50% isolates were amphotericin B-resistant.[24]
- In India, 90–95% of *C. auris* isolates were resistant to fluconazole; 7–37% to amphotericin B; and < 2% to echinocandins.[24]
- In South Africa, 90% of *C. auris* isolates were resistant to fluconazole; 5.5% to amphotericin B; and 0.25% to echinocandins.[24]

A meta-analysis using data published between 2016 and 2019 estimated the resistant rates of *C. auris* to antifungals at:[1]

- Fluconazole: 91% (95% CI: 88%–95%; 18 studies)
- Amphotericin B: 12% (95% CI: 7%–17%; 15 studies)

In addition, two systematic reviews of the resistance rates of *C. auris* to antifungals from data published before the COVID-19 pandemic reported the following:[1,58]

- Voriconazole: 38.11% (141)[58]
- Caspofungin: 8.05% (21 isolates)[58] to 12.1% (101/838 isolates; 100 of the resistant isolates were from India, with a resistance rate of 23.6%)[1]
- Isoconazole: 9.24% (11)[58]
- Flucytosine: 8.03% (22)[58]
- Itraconazole: 7.24% (11)[58]
- Posaconazole: 6.33% (10)[58]
- Anidulafungin: 1.1% (9/840 isolates)[1] to 5.25% (17 isolates)[58]
- Micafungin: 0.8% (8/927 isolates)[1] to 5.02% (13 isolates)[58]

Two reviews of the antifungal resistance status in the *C. auris* co-infected COVID-19 patients (based on CDC-tentative MIC breakpoints) found:[27,34]

- Fluconazole: 80.5% (33/41 isolates)[34] to 94.1% resistant (48/51 isolates) [27]
- Voriconazole: 36.4% resistant (4/11 isolates) [27]
- Amphotericin B: 15.7% resistant (5/51 isolates)[27] to 46.3% (19/41 isolates)[34]
- Flucytosine: 32.4% (11/34 isolates)[27] to 43.8% (7/41 isolates)[34]
- Multi-azole: 13.95% (6/43 isolates)[27]
- Caspofungin: 0% (0/5 isolates)[27] to 12.8% (5/41 isolate)[34]
- Micafungin: 0% (0/1 isolate)[27] to 3.7% (1/27 isolates)[34]
- Echinocandins: 0% (0/10 isolates)[27]
- Resistant to 2 classes of antifungals: 70% (7/10 isolates)[27] to 81.8% (18/22 isolates)[34]
- Resistant to 3 classes of antifungals: 18.2% (4/22 isolates)[34]
    - Amphotericin B, azole and 5-flucytosine: 3 (13.6%)[34]
    - Echinocandins, azole and 5-flucytosine: 1 (4.6%)[34]

Data from CDC's Antimicrobial Resistance Laboratory Network (AR Lab Network) show the following resistance profiles of *C. auris* in the U.S.:[32]

- Azole: resistance increased 7% from 78.2% (787/1,006 isolates) in 2019 to 85.7% (1,109/1,294 isolates) in 2020. Between 2018 and 2020, regional resistance ranged between 10.9% (17/156 isolates; predominately clade IV) in Midwest to 99.5% in Northeast (1,046/1,051 isolates; predominately clade I) and West (553/556 isolates; predominately clade III).[32]
- Amphotericin B: resistance increased 1.5% from 24.1% (242/1,006 isolates) in 2019 to 25.6% (331/1,294 isolates) in 2020. Between 2018 and 2020, regional resistance ranged between 1.4% in Midwest (2/156 isolates; predominately clade IV) to 85.2% (115/135 isolates; predominately clades I and III) in Mid-Atlantic.[32]
- Echinocandins: overall resistance remained the same from 1.4% (14/1,006 isolates) in 2019 to 1.2% (15/1,294 isolates) in 2020. Between 2018 and 2020, regional resistance ranged between 0.0% in Midwest (predominately clade IV), Mountain (predominately clades I and III) and Southeast (predominately clade III) to 3.0% (4/135 isolates) in Mid-Atlantic.[32]
  An increase in resistance to echinocandins was observed in 2021, with 19 patients testing positive for *C. auris* with echinocandins resistance, compared to 3 patients in 2020 and 6 patients before 2020. Investigation suggested that these patients developed resistance during echinocandin treatment and had no epidemiologic links to other resistant cases.[59] Even this subtle increase is concerning because echinocandins are the first-line therapy for invasive *Candida* infections and most *C. auris* infections.[32]

- Pan-resistant: in 2021, 7 patients tested positive for *C. auris* with pan-resistance, compared to 6 patients in 2020 and 4 patients before 2020. Epidemiologic investigation of cases identified 2 independent outbreaks (in Texas and District of Columbia) of echinocandin-resistant and/or pan-resistant *C. auris* among patients with shared health care exposures and no previous use of echinocandins, suggesting the first U.S. health care transmission of echinocandin-resistant *C. auris*.[32]

In Canada, no pan-resistant *C. auris* (resistant to all three classes of antifungal drugs) have been reported. From 2012 to 2022, about one-third (32.56%) of the isolates collected were resistant to fluconazole, and one-third (34.88%) were multidrug-resistant (resistant to two of the three classes of antifungal drugs):[38]

- Clade I: 1/22 (4.5%) was susceptible; 6/22 (27.3%) were resistant to fluconazole; 15/22 (68.2%) were multidrug-resistant fluconazole and amphotericin B
- Clade II: all 7 isolates were susceptible
- Clade III: 1/9 (11.1%) isolates was susceptible; 8/9 (88.9%) were resistant to fluconazole
- Clade IV: all 5 isolates were pan-susceptible

The genetic basis for *C. auris* is different for each drug class and mechanism of action. The genetic basis for azole resistance and echinocandin resistance is clear, but it is less clear for amphotericin B. A number of studies have described the molecular mechanisms in *C. auris* that result in antifungal resistance and clinical failures of azoles and echinocandins:[29]

- Resistance to azoles was shown to be mediated by mutations in ERG11 (F126L, Y132F and K143R) and in CDR1 (V704L) Even though the ERG11 mutations contribute to fluconazole resistance, none alone are sufficient ot confer clinical resistance and cannot explain the significantly elevated MICs among clinical isolates of *C. auris*.
- Resistance to echinocandins, by mutations in FKS1 (S639P, S639F, S639Y, F635C, S635P and S635T).
- Analysis of pan-resistant *C. auris* strains suggested a fitness cost in some strains.

There are reports of resistance to antifungals developing after prolonged exposure:

- In New York, three patients with multiple comorbidities and no known recent domestic or foreign travel were found to have pan-resistant *C. auris* (all clade I) that developed after receipt of antifungal medications, including echinocandins. The pan-resistant samples were taken from blood, urine, and rectal swab from 2 to 22 months after the first isolation of *C. auris* in these patients. The time from isolation of pan-resistant *C. auris* to patient's death ranged from 2 weeks to 10 months.[59]
- In New Jersey, pan-resistance in *C. auris* was detected in a 29-year-old multi-visceral transplantation patient in 2020 after prolonged prophylactic caspofungin treatment. The first isolate collected on day 4 of hospitalization was susceptible to all antifungals except for fluconazole. The 19th isolate taken from the patient on day 72 of hospitalization showed resistance to echinocandin and flucytosine. The authors believe resistance mutations could have arisen from the prolonged exposure to antifungals and refractory peritonitis. Single nucleotide

polymorphism phylogenetic analysis of the isolates suggests in-hospital or inpatient evolution of *C. auris* isolates, rather than introduction from elsewhere.[60]

- Clades I and IV isolates have been shown by genomic analyses and in vitro/in vivo studies to develop resistance to fluconazole rather easily which is not lost even after drug removal.[24]

The level of resistance to antifungals also varies by the clade.

- Clade I has also been associated with increased resistance to antifungals, including echinocandin, compared to the other clades of *C. auris*.[29]
- Clade III has been shown to demonstrate high azole resistance, but lower polyene and echinocandin resistance.[22]
- A fluconazole-resistant *C. auris* belonging to clade V and isolated from fungal otitis externa has also been described.[24]

To overcome the knowledge gap, WHO recommends that in vitro and in vivo synergies between antifungal medicines should be evaluated to optimize treatment regimens against *C. auris*.[25] For recommendations for treatment and management of *C. auris* colonization and infections, see CDC's Treatment and Management of *C. auris* Infections and Colonizations.[61]

Identification and Diagnosis of *C. auris* Infections

Culture-Based Methods

Culture-based methods may take days to obtain the results and may lack sensitivity as in general nearly 50% of cases of invasive candida infections are culture-negative.[24] The gold standard for *C. auris* identification is based on DNA sequence analysis (combination of D1/D2 and ITS sequencing).[30] Other high resolution methods (e.g., amplified fragment length polymorphism [AFLP] and WGS) can further delineate local clusters to inform source of transmission, and molecular sequencing of ribosomal DNA loci further enables clade differentiation.[29] These methods may only be available at reference laboratories.

Most commercial Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) systems, with up-to-date databases, provide confident species-level identification of *C. auris*.[22,30] Recently, new formulations of chromogenic media have been developed to aid in the identification of *C. auris*, including CHROMagar™ Candida Plus, and HiCrome™ *C. auris* MDR selective agar.[22] These media allow for selection and identification of *C. auris* after an incubation time of 36 to 48 hours.[30]

In clinical microbiology laboratories that still rely on commercial biochemical-based tests for yeast identificaion, *C. auris* may be undetected, with up to 90% of isolates possibly misidentified as other *Candida* species, *Rhodotorula glutinis*, or *Saccharomyces cerevisiae,* as these identification systems lack up-to-date and comprehensive databases for yeast identification.[30,33] Examples of these tests include analytical profile index strips, VITEK® 2, BD Phoenix™ yeast identification, MicroScan, and API® 20 C AUX.[22,33]

Direct-From-Specimen Methods

Diagnostic tests that do not rely on culture—e.g., mannan and anti-mannan IgG tests, (1,3)-β-D-glucan (BDG) (non-specific for *Candida* infections), and polymerase chain reaction (PCR)-based assays—have been introduced as adjuncts to cultures.[47] A variety of commercial and laboratory-developed specific, molecular assays designed for the detection of *C. auris* directly from specimens have the potential for high throughput processing of surveillance samples in outbreak investigations.[52,62] In addition, real-time PCR for identification of mutations in *C. auris* ERG11 and FKS1 genes have been developed for rapid detection of antifungal resistance directly from clinical specimens.[29]

See also PHO's *Candida auris Reference Identification and Susceptibility Testing* for more information on *C. auris* confirmation and antifungal susceptibility testing.

Surveillance of *C. auris* Colonization

C. auris predominantly colonizes the skin and has rarely been isolated from the oral and gastrointestinal tracts of healthy individuals who have not been hospitalized.[47] In an admission screening survey for *C. auris* in three nursing homes and one hospital in New York City from November 2017 to November 2019, where 188/2,062 (9.1%) isolates tested positive for *C. auris*, the axilla/groin area and nares were the most often sites yielding positive test results:[44]

- 49.5% (93/188) of persons who screened positive tested positive by axilla/groin swabs only
- 17.0% (32/188) of persons who screened positive tested positive by nares swab only
- 32.4% (61/188) of persons who screened positive tested positive by both axilla/groin and nares swabs

In an investigation of an ongoing *C. auris* outbreak in New York State from August 2016 through 2018, one composite swab of nares/axilla/groin was used for screening colonization. Based on the findings, the investigation found that axilla/groin is the preferred site of *C. auris* colonization compared to nares; however, when nares were colonized, the burden of *C. auris* was relatively higher than that in the axilla/groin:[52]

- 80% (178/222) axilla/groin samples vs. 125/215 (58%) nares samples tested positive for *C. auris*.
- When the extent of *C. auris* colonization in positive axilla/groin and nare sites were analyzed randomly, nares harboured 2 logs ($P < 0.0001$) higher *C. auris* than the axilla/groin.
- When 74 of axilla/groin and nares specimens (from the same patient) were analyzed in parallel, nares harboured *C. auris* 2 logs higher than the axilla/groin.

Control Measures

C. auris has emerged as a cause of nosocomial outbreaks in health care facilities.[25] Given the challenges in correctly and rapidly identifying *C. auris*, implementation of infection prevention and control practices may be delayed, allowing transmission of *C. auris* to other individuals sharing space and/or common facilities and equipment.[24] Outbreaks of *C. auris* infections lasting longer than a year have been reported.[26] In New York State, a *C. auris* outbreak (dominated by clade I) that started in August 2016 is still ongoing despite extensive efforts. As of November 22, 2019, 192 health care facilities had been involved in this outbreak, including 70 hospitals, 118 nursing homes, 2 hospices, 1 long-term acute care hospital, and 1 Veterans Administration hospital.[52] As a vaccine against this highly resistant pathogen is not available, prevention of colonization and surveillance are key measures to prevent the spread of *C. auris* in health care settings and in the community at large.[32,33] The optimal prevention strategies, however, require further study.[25]

- See also PHAC's *Candida auris* Interim Recommendations for Infection Prevention and Control[63] and *PHO's Interim Guide for Infection Prevention and Control of* Candida auris.[64]

Antimicrobial Stewardship

Currently available evidence is insufficient to inform a specific beneficial effect of antimicrobial stewardship on the emergence and spread of *C. auris*. However, evidence is emerging that prolonged exposure to broad-spectrum antibacterial and antifungal agents may favour the selection of multidrug-resistance in *C. auris*.[26,33] It is therefore likely that implementing an antimicrobial (including antifungal) stewardship program may mitigate the risk of *C. auris* spread. In addition, individuals receiving antifungal therapy for *C. auris* should be closely monitored for clinical improvement, and repeat susceptibility testing should be conducted to adapt the treatment as needed.[53] Furthermore, it is prudent to review the need for antifungal prophylaxis with a risk-benefit analysis in settings with evidence of *C. auris* transmission.[26]

Decolonization

Decolonization has been attempted as one of the measures to control a *C. auris* outbreak in two hospital outbreaks of *C. auris*.

- Partial success was reported by a hospital in the UK. Under that protocol, skin was washed with disposable wipes soaked in 2% chlorhexidine gluconate or 4% chlorheidine solution; mouth was rinsed with 0.2% chlorhexidine (or using chlorhexidine 1% dental gel for patients on ventilator support); and oral nystatin when colonization was detected in the oropharyngeal tract. A nurse who tested positive for *C. auris* only in a nasal swab was successfully decolonized after following the decolonization protocol for 5 days and repeat samples all tested negative. On the other hand, patients continue to be colonized or re-colonized with *C. auris* despite daily application of the decolonization protocol.[8] This was despite other outbreak control measures, including isolation and Contact Precautions during the entire hospital stay for all patients who tested positive for *C. auris*; screening all contact patients in sites including nose, axilla, groin, throat, rectum or feces, vascular line exit sites, and clinical samples; isolation of direct contact patients until three consecutive negative screens; environmental cleaning three times a day using 1,000 ppm of a chlorine-based disinfectant; terminal cleaning of rooms on discharge using a chlorine-based detergent at 10,000 ppm; used equipment were disinfected with hydrogen peroxide vapour after cleaning. However, the authors did not report how many patients remained colonized, and how long it took for decolonized patients to become re-colonized.

- An outbreak in a tertiary care academic hospital in South India involving 15 patients over two waves spanned a period of two years. During the 2nd wave, patient decolonization with twice daily body baths with chlorhexidine was performed plus the use of octenidine wipes and mouth washes. Together with other outbreak control measures (see below), a gradual decline in incidence was observed and no further case cluster was identified, and the total survival rate for the two waves was 93%.[65]

Case and Outbreak Management

Reports on successful cessation of *C. auris* transmission are rare. Existing recommendations are, therefore, based both on learnings from reported *C. auris* outbreaks and strategies that have proven effective in controlling other pathogens that result in nosocomial outbreaks, can be transmitted from person-to-person, on medical equipment and via environmental contamination, and that can cause both colonization and clinical infection.[64]

Recommendations by public health organizations (e.g., CDC, Public Health England [PHE], Provincial Infectious Diseases Advisory Committee [PIDAC]) for health care facility preparedness and control of *C. auris* tend to focus on the following:[29,64]

- Pre-identification:
    - Confirm ability to detect *C. auris* at the facility,[29] or ensure protocol is available for forwarding specimens for definitive identification.[64]
    - Confirm ability to care for patients with *C. auris* colonization or infection.[64]
    - Assess local risk and develop a screening policy.[29]
- During identification:
    - Accurate species-level identification of *Candida* species.[29]
    - Susceptibility testing of *C. auris*.[29]
    - Reporting of test results to clinical and IPAC staff.[29]
    - Increasing awareness,[29] such as through regular staff “huddles”, dissemination of evidence-based messaging, emphasizing the importance of this infection without inducing fear or panic, providing training on relevant precautions.[66]
    - Targeted screening,[29] aimed at individuals at highest risk for colonization or infection.[64]
- Post-identification:
    - Contact Precautions, placement in single room with dedicated toileting facilities;[64] cohorting of close contacts;[29] environmental disinfection[29] (cleaning and disinfection at least once a day with disinfectant effective against *C. auris*; terminal cleaning on discharge or transfer).[64]
    - Forward contact tracing (screening close contacts for 4 weeks).[29]

- Backward contact tracing (review of *Candida* spp. isolates in the ward in the 4 weeks prior to diagnosis in the index patient, for possible unrecognized transmission).[29] Every identified case requires immediate investigation to determine probable source and to assess risk of transmission within the facility.[64]

- Report to IPAC at the facility and public health department.[29]

Detection of *C. auris* should prompt an epidemiological investigation and screening of close-contact patients for *C. auris* carriage.[64] Suggested screening sites by PIDAC are the nares plus combined bilateral axillary and groin swab. Other sites considered for sampling are: wound, urine, line exit site; CDC suggests also a throat swab and a rectum swab. In addition, strict adherence to central and peripheral catheter care bundles, urinary catheter care bundle, and proper care of the tracheostomy site are measures considered useful for preventing invasive infections by *C. auris*.[24] In community settings, local authorities are advised to exclude the attendance of children with *C. auris* wound infections from daycare until drainage from wounds, or skin and soft tissue infections are contained.[29]

Lessons learned from an extended *C. auris* outbreak in Italy that involved 361 cases from July 2019 to December 2022 highlight the importance of the following practices: prompt outbreak investigation, availability of dedicated staff and isolation rooms, correct microbiological identification, effective treatment, trained health personnel, rigorous application of infection prevention and control measures including hand hygiene and research for innovative disinfection procedures, accurate patient screening and retrospective surveillance, precise information of cases and their family as well as between healthcare facilities in case of patient transfer. Prompt reporting of cases to the competent health authorities may facilitate local and national alert and shared diagnostic protocols, with the aim of limiting further spread nationally and beyond.[35]

A 2-wave hospital outbreak of *C. auris* in South India (see above) highlighted the ease of incidence rebound when efforts in maintaining infection prevention and control practices were not sustained. During the 1st wave of outbreak, containment efforts focused on cohorting of patients who tested positive for *C. auris*, as well as educating primary clinical care team on the importance of *C. auris* infections, its risks and management. Surveillance activities continued to detect cases albeit at lower number for the following five months before a 2nd wave was encountered.[65] During the 2nd wave, patient decolonization was performed; thorough three-times daily and terminal cleaning of patient areas with 1:10 dilution of sodium hypochlorite solution was reinforced; disinfecting of shared equipment prior to being used in another patient; 1:1 nursing and patient education were implemented; and treatment was optimized. A gradual decline in incidence was observed and no further case cluster was identified, and the total survival rate for the two waves was 93%.[65]

Surveillance

Currently in Canada, *C. auris* is reportable in British Columbia and Alberta but it is not reportable in Ontario.[67-69] Consistent and timely gathering at the national and international levels of epidemiological data of *C. auris* colonization and infection will help inform the annual incidence rates, distribution and trends, and help coordinate public health risk management activities.[25,29,33]

At the facility level, even though a high incidence of *C. auris* colonization has not been observed in Canadian hospitals, the rapidly rising trends in other countries suggest that Canadian hospitals should consider active screening of high-risk individuals and their contacts, in order to detect any cases promptly and limit the spread of *C. auris*.[40]

The scope of screening should be based on local risk assessment. In a pilot study in England where no previous cases of *C. auris* were known, no cases of colonization were detected among 998 patients admitted to ICU. Admission screening for *C. auris* in ICUs may target high-risk individuals where local incidence of *C. auris* colonization or infection is low.[29,53] On the other hand, patients with a history of travel or health care from geographic areas with a high burden of *C. auris* should be tested for *C. auris* immediately upon admission and infection prevention and control measures for *C. auris* should be implemented while awaiting test results.[53] Rowlands *et al*. reported on an admission screening program at five high-risk units in three health care facilities in New York (see above), and noted that reducing the period of leave from ≥30 to ≥7 days increased the number of re-admitted individuals testing positive for *C. auris*. The authors recommended, therefore, that patients who had been outside the facility for less than a month be included in re-admission screening, if feasible.[44]

In addition to admission and re-admission, screening for *C. auris* is also advised in units where a new case of *C. auris* has been identified, or when new cases continue to be detected.[29] In the transmission event described by Alanio *et al*. above, where transmission was not detected until >1 month post-exposure, the authors suggested that the duration of post-exposure screening of contacts (forward contact tracing) at risk of acquiring *C. auris* be increased to beyond 30 days.[53] However, further studies are needed to inform the optimal duration and frequency of screening. Also, whether screening should be done only by real time-PCR or culture depends on the prevalence, the laboratory that supports the facility, the turnaround time and costs that real time-PCR at each facility.[53] Alanio *et al*., also proposed verification of environmental cleaning by swabbing rooms previously occupied by individuals with *C. auris*, and admission of another individual not take place until all environmental test results come back negative for *C. auris*.[53]

Environmental Cleaning

Most strains of *C. auris* have the ability to form biofilms,[47] and clade III has been shown to have a higher propensity to form aggregates that further develop into biofilm.[22] Phenotypical analysis of *C. auris* isolates differentiates the strains into aggregative and non-aggregative ones. Aggregative strains can withstand physical disruption (e.g., vortexing) or chemical disruption (e.g., detergent treatment) *in vitro*, giving *C. auris* the potential to survive in the environment of health care facilities. [47] *C. auris* has been shown to survive on inanimate fomite surfaces for up to 4 weeks despite surface decontamination by differing disinfectants,[70] or remain viable for several months on inanimate surfaces.[23] Compared to other *Candida* spp. (e.g., *C. albicans* and *C. parapsilosis)*, *C. auris* can persist in a viable form on dried or moist surfaces for several weeks longer.[3] Watkins *et al.* reported that when *C. auris* grown in biofilms was tested against 13 commonly used hospital disinfectants, 50% of the products failed to inactivate the cells, 58% did not prevent transfer of *C. auris*, and 75% of the disinfectants could not prevent biofilm regrowth.[22]

In view of the ability of *C. auris* to withstand many common hospital disinfectants and its ability to remain viable on surfaces for prolonged period of time, environmental objects and medical equipment can become a source of *C. auris* spread in health care settings, and these should be thoroughly disinfected after every use as per the manufacturer's instructions for use and their compatibility with the disinfectant.[24] Guidance for environmental cleaning in health care settings have been published by PIDAC, CDC, ECDC, PHE, Queensland Health, and the Pan American Health Organization/World Health Organization (PAHO/WHO).[5,64,71-74] The use of chlorine-based disinfectants for daily and/or terminal disinfection are supported by PIDAC, ECDC, PHE, Queensland Health, and PAHO/WHO;[5,64,72-74] whereas the use of hydrogen peroxide is also supported by PIDAC and ECDC.[5,64] In addition, CDC recommends using disinfectants that are registered with the Environmental Protective Agency as effective against *C. auris* or *Clostridioides difficile* spores, ECDC recommends using disinfectants with certified antifungal

activities, and Queensland Health recommends using peracetic acid (2,000 ppm) or disinfectants effective against *C. difficile* spores for daily and terminal cleaning.[5,71,73] The use of ultraviolet light or hydrogen peroxide vapour has been suggested by some jurisdictions (PHE, ECDC).[5,72] While there is some evidence that these no-touch disinfection methods can reduce levels of environmental contamination with *C. auris*, further studies are required to inform their efficacy in reducing transmission.[64] Meanwhile, the use of quaternary ammonium compounds and chlorhexidine are not recommended due to their suboptimal or lack of efficacy against *C. auris*.[64,73]

The following are some commonly used disinfectants effective against *C. auris*. See also Table 2.

- Chlorine-based products, such as sodium hypochlorite (≥ 1000 parts per million, ppm), are effective against planktonic cells and, at pH of 13.13, against *C. auris* biofilms. Sodium dichloroisocyanurate at 4,000 ppm is also effective against planktonic cells of *C. auris*. However, sodium hypochlorite is irritating to some people and corrosive for medical/dental devices at concentrations of 6,000 ppm or above.[24]

- Peracetic acid at 2,000 ppm is effective against planktonic cells of *C. auris*. Products containing peracetic acid (3,500 ppm, pH 8.82) and chlorine (1,000 ppm, pH 13.13) are most effective in reducing viable *C. auris* counts and delaying the recolonization of biofilms on fomite surfaces.[24,70]

- Chlorhexidine gluconate (2%) in 70% isopropanol and povidone-iodine (10%) are effective against planktonic cells of *C. auris*.[24]

- Hydrogen peroxide (> 1%) or vaporized hydrogen peroxide, ozone, and UV-C light are also effective against *C. auris*. The UV-C light also prevents biofilm formation.[24]

Table 2. Summary of Disinfectant Efficacy Against *C. auris*[70]

Disinfecting Agent	Concentration	Contact Time	Outcome
Ethanol (Purell Advanced instant hand sanitizer)	70%	1 min	4 log reduction in CFU
Chlorhexidine gluconate (Scrub-Stat)	2%–4%	Not reported	3.8 log reduction in CFU
Hydrogen peroxide enhanced formulation (Revital-Ox Resert)	2%	1 min	≥ 4 log reduction in CFU
Hydrogen peroxide (Clorox Healthcare H_2O_2 cleaner disinfectant)	1.4%	1 min	≥ 5 log reduction in CFU
Ozonated water	2.5 ppm	Flushing sinks for 30 s every 4h	Undetectable levels within 2 days
Ozone	300 mg/m^3	40 min	3.6 log reduction in CFU
Peracetic acid	2,000 ppm	5–10 min	100% eradication in cellulose substrates
Peracetic acid wipes	3,500 ppm	10 sec under 500 g pressure	Killed > 7 log of dry biofilms
Peracetic acid (S40 sterilant concentrate)	0.07%	1 min	4.1 log reduction in CFU
Sodium hypochlorite	1,000 ppm	5 min	Significant killing of adherent cells; significant regrowth
Sodium hypochlorite	1,000 ppm	10 min	Significant killing of adherent cells
Sodium hypochlorite	≥ 1,000 ppm	4 min	≥ 6 log reduction in CFU
Sodium hypochlorite	10,000 ppm	5 min	Significant killing of adherent cells
Sodium hypochlorite	≥ 4,000 ppm	1 min	≥ 3 log reduction in CFU
Sodium hypochlorite	610–670 ppm	1 min	≥ 4.1 log reduction in CFU
Sodium dichloroisocyanurate on microfibre cloth	1,000 ppm	10 sec under 500 g pressure	Killed > 7 log of dry biofilms

Disinfecting Agent	Concentration	Contact Time	Outcome
Sodium dichloroisocyanurate	≥ 1,000 ppm	4 min	≥ 6 log reduction in CFU
Sodium dichloroisocyanurate	≥ 4,000 ppm	1 min	≥ 3 log reduction in CFU
UV-C	254 nm	≥ 30 min at 5 ft	> 6 log reduction in CFU
UV-C	254 nm	≥ 30 min at 2 m	> 5 log reduction in CFU
UV-C	254±2 nm	15–30 min at 1 m	Inhibited *C. auris* up to 72h post-treatment
UV-C	200–280 nm	5 min at 1 m	99.4% reduction in CFU
UV-C (pulsated)	200–280 nm	5 min at 2 m	90.2% reduction in CFU
UV-C (pulsated)	200–280 nm	10 min at 2 m	99.6% reduction in CFU

Note: ft = feet; g = gram; h = hour(s); m = metre(s); min = minute(s); nm = nanometre(s); ppm = parts per million; s = seconds

Limitations and strengths

The actual prevalence of *C. auris* may be higher than what has been reported due to lack of surveillance in most facilities and jurisdictions, limitations in laboratory identification systems, and publication bias.[1] The quality of data for mortality rates and risk factors for acquiring *C. auris* is also suboptimal due to possible confounding variables and incomplete data. Furthermore, the findings by different authors may differ due to different case definitions and variable geographical distribution of *C. auris* clades.

Conclusion

The rise and geographic spread of *C. auris* in recent years is concerning, given the extent of resistance to treatment and disinfectant agents, the high mortality rates of invasive infections, and the ability of this organism to cause prolonged outbreaks in health care settings. Public health and infection prevention and control measures require early detection of cases and surveillance to mitigate transmission. In addition, capacity at medical laboratories need to be expanded for accurate and timely identification of *C. auris*, cluster analysis, and antifungal susceptibility testing to facilitate screening and optimize care of persons infected by *C. auris*. Research is urgently needed to develop rapid and affordable diagnostics, guide improvement of existing therapies and disinfectants, generate new therapeutic agents, and identify effective preventive and control practices. Experience from *C. auris* outbreak management as well as the exponential rise in incidence in some countries during the pandemic also highlight the importance of strict adherence to evidence-informed infection prevention and control policies and procedures to limit the spread of *C. auris*.

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