RAPID RISK ASSESSMENT

Candida auris outbreak in healthcare facilities in northern Italy, 2019-2021

21 February 2022

Main conclusions and options for response

Italy has reported an outbreak of *Candida auris* in the region of Liguria with at least 277 cases. The first *C. auris* case in Liguria was detected in one hospital in July 2019 and cases continued to occur sporadically in the same hospital. In February 2020, *C. auris* was detected in an intensive care unit (ICU) for treatment of patients with severe COVID-19 in the same hospital, with a subsequent increase in case numbers throughout 2020 and 2021. To date, 277 cases have occurred in at least eight healthcare facilities in Liguria, and 11 cases in facilities in the neighbouring region of Emilia-Romagna.

C. auris poses a risk for patients in healthcare facilities across the European Union/European Economic Area (EU/EEA) due to its ability to cause infections in critically ill patients and its resistance to several antifungal agents, which makes infections difficult to treat. Patients hospitalised with severe COVID-19 are at risk of healthcare-associated infections, including candidaemia, and various outbreaks of *C. auris* among COVID-19 patients have been reported worldwide.

Given the high number of cases, the spread of *C. auris* to various healthcare facilities in Liguria and interregional spread to Emilia-Romagna, and the difficulty to contain the outbreak (which has been ongoing for more than two years, with the last cases occurring in October 2021 in Liguria and in December 2021 in Emilia-Romagna), the risk of further spread within Italy is considered to be **HIGH**. As local and national control measures are being implemented, the risk of introduction of *C. auris* into other EU/EEA countries from this specific outbreak in northern Italy remains **LOW** unless hospitalised patients are transferred from this region. However, given the worldwide spread of *C. auris* and related previous detection of sporadic cases and outbreaks in the EU/EEA, it is likely that more undetected cases will eventually enter the EU/EEA from regions with less capacity for *C. auris* surveillance and control, and therefore continued vigilance is needed.

It is therefore of high importance that EU/EEA countries have adequate laboratory capacity and national surveillance in place to detect *C. auris* cases early and immediately implement control measures such as alerts to healthcare staff, screening for carriage, contact tracing and enhanced infection prevention and control measures. Control will be more difficult to achieve once *C. auris* dissemination has reached the level of interfacility and interregional spread. Local control of *C. auris* as soon as possible after introduction to delay the establishment of *C. auris* in a country's healthcare facilities will have a nationwide benefit by reducing future healthcare-associated infections with *C. auris*. For this reason, national and regional public health authorities should follow-up and offer advice and support to healthcare facilities for all detected *C. auris* cases to make sure adequate measures are implemented, including screening to detect underrecognised transmission, where appropriate. Cases of *C. auris* and multidrug-resistant organisms occurring in units for COVID-19 patients should trigger a review of procedures with the aim of ensuring the ability of staff to adhere to standard and contact precautions. Detailed control measures are outlined in the 'Options for control' section of this risk assessment.

Suggested citation: European Centre for Disease Prevention and Control. *Candida auris* outbreak in healthcare in northern Italy, 2019-2021. ECDC: Stockholm; 2022.

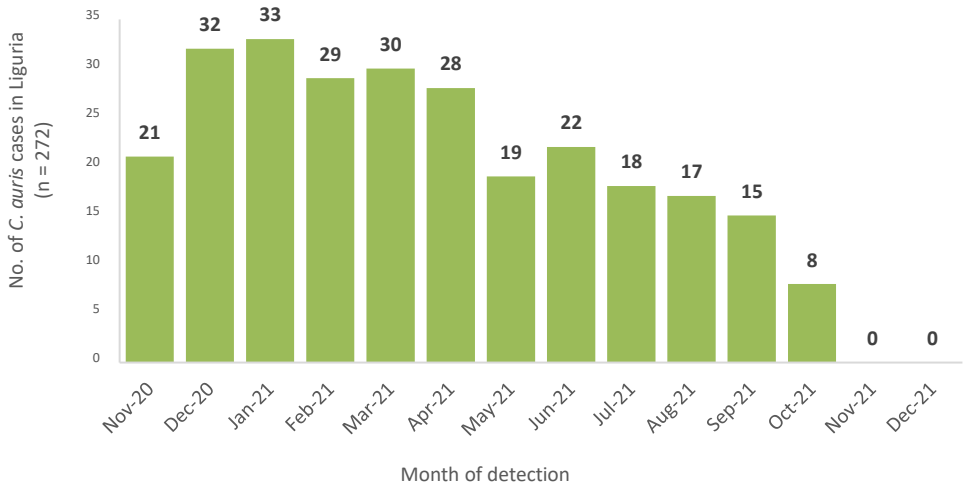
Event background

Italy reported a healthcare-associated outbreak of *C. auris* occurring in the region of Liguria with at least 277 cases in eight healthcare facilities. The first *C. auris* case was detected in one hospital (hospital A) in July 2019 [1] and, since then, subsequent cases have been sporadically reported in the same hospital. In February 2020, *C. auris* was detected in an intensive care unit (ICU) dedicated to the treatment of patients with severe COVID-19 in hospital A [2]. A subsequent increase in case numbers was observed throughout 2020 and 2021. Whole genome sequencing of *C. auris* isolates from 10 of the early cases from hospital A in 2019 and 2020 showed that the isolates belonged to the Southern Asian clade (clade I) and that all isolates except one were part of the same cluster originating from the index case [2]. Phylogenetic molecular clock analysis suggested a recent introduction into hospital A (around May 2019) and suggested that most transmissions occurred in the affected COVID-19 ICU [2]. Several cases of this outbreak were published in the scientific literature [1-5] and others were formally notified at the national level (including one *C. auris* case in January 2020, a cluster of five cases in February 2021, two cases in September 2021, 17 cases in October 2021 and one case in December 2021).

In June 2020, the Ministry of Health, in coordination with the National Institute of Health (ISS), published a Circular Letter including a case definition; recommendations for identification of *C. auris* isolates and management of cases, infection prevention and control measures, surveillance and notification; and information for cases and healthcare staff. In March 2021, another Circular Letter followed, with an update of *C. auris* epidemiology and a reminder regarding adequate laboratory identification and antifungal susceptibility testing, as well as prompt notification of cases.

In October 2021, following notification of a cluster of 15 hospitalised cases, the Ministry of Health asked for a retrospective investigation of confirmed *C. auris* cases in public and private healthcare facilities in the entire Liguria region. On 25 November 2021, the region reported the detection of 277 *C. auris* cases since November 2020 (Figure 1). Most cases (n = 210) had occurred in hospital A, while the remaining 67 cases were distributed throughout seven other healthcare facilities in Liguria. In four of these healthcare facilities, there were documented transfers of patients with *C. auris* from hospital A. An example of such a patient transfer, published in the scientific literature, is the transfer of an extremely low birth weight preterm neonate colonised with *C. auris* from hospital A to a hospital with paediatric specialisation within a few hours after vaginal delivery following complicated preterm labour. The mother of this neonate was admitted to an ICU in hospital A with severe COVID-19 necessitating mechanical ventilation. Upon admission to the paediatric facility, the neonate had positive cultures for *C. auris* from the axilla, eyes and ears [5]. Among the healthcare facilities that reported *C. auris* cases were two long-term care facilities (LTCFs), one in Liguria and one in the Emilia-Romagna region.

Figure 1. Epidemiological curve of *C. auris* cases in Liguria, northern Italy, from November 2020 to December 2021 (n = 272*)



** Source: Italian Ministry of Health. Only cases with known date of diagnosis are included.*

Control measures taken at the national level after receipt of the report from the Liguria region included the publication of a short update on the national and global epidemiological situation with a reminder on best practices for the management of *C. auris* cases and the need for national notification, as well as a request to neighbouring regions for detailed reports on *C. auris* cases in the same period. In response, the region of Emilia-Romagna notified 11 cases of *C. auris* with the first case recorded in December 2020. No replies from Lombardy, Piedmont or Tuscany had been received at the time of this assessment. One case of a *C. auris* bloodstream infection had been detected in Rome as of November 2019 [6].

Disease background

Epidemiology

Invasive candidiasis is the most common fungal disease in hospitalised patients [7]. In the document, 'ECDC point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011–2012', *Candida* spp. was the fifth most common pathogen associated with bloodstream infections, isolated in 7.4% of all documented cases [8]. While *C. albicans* remains the predominant cause of invasive candidiasis, there has been a shift towards an increasing proportion of non-*albicans Candida* spp. such as *C. glabrata* in recent years [7,9]. Although non-*albicans Candida* spp. have emerged in healthcare settings worldwide, presumably related to the use of prophylactic antifungal drugs in high-risk populations [10,11], *C. auris* seems to be unique in its propensity to be transmitted between patients, contaminate the hospital environment, and cause outbreaks in healthcare settings. Several hospital outbreaks have been reported and several molecular studies confirming intra- or interhospital transmission of *C. auris* have been published [12-14].

C. auris is a newly emerging yeast that was first described in 2009 after isolation from the ear canal of a Japanese patient [15], and has subsequently been associated with invasive infections and outbreaks in healthcare settings. At present, the earliest known *C. auris* case was retrospectively identified in South Korea and dated back to 1996 [16]. However, reanalysis of a large international surveillance collection including 20 788 invasive *Candida* isolates from 1997 to 2016 (SENTRY study) detected only six *C. auris* isolates, with the earliest of these isolates dating from 2009 [17]. These findings suggest that increasing detection of *C. auris* in healthcare settings is caused mainly by a recent emergence and not only by improved fungal diagnostics. Five genetically distant clades of *C. auris* have been discovered: the South Asian clade detected in India and Pakistan (clade I), the East Asian clade detected in Japan (clade II), the South African clade detected in South Africa (clade III), the South American clade detected in Venezuela (clade IV), and a recently detected clade in Iran (clade V) [18]. None of these five clades includes isolates identified prior to 1996 [18].

To date, *C. auris* cases have been reported from more than 40 countries on six continents [19]. According to the last ECDC survey for the EU/EEA and the United Kingdom (UK)[1], nine countries had detected *C. auris* cases, including Austria (n = 1), France (n = 1), Germany (n = 3), Greece (n = 1), the Netherlands (n = 2), Norway (n = 1), Poland (n = 1), Spain (n = 291) and the UK (n = 48) between 1 January 2018 and 31 May 2019. Two countries had detected outbreaks, involving two hospitals in Spain and six hospitals in the UK, between January 2013 and May 2019 [20]. The number of cases per outbreak ranged from 39 to 382 cases, according to national reporting [21]. The first case in Italy was published in late 2019 [1]. Finland reported the first *C. auris* case in the country in 2021 [22].

Disease spectrum

C. auris infection reports include intra-abdominal, wound and ear infections, but most of the published cases have been bloodstream infections [12,15,16,23]. *C. auris* has also been isolated from urine [24], the respiratory tract, bile, bone and a jejunal biopsy [25], though detection from these sites may represent carriage rather than infection. Central venous catheter tips have been reported to be colonised with *C. auris*, which can lead to the development of device-associated infections [26]. Carriage of *C. auris* poses a risk for both transmission to others and invasive infections. Prolonged carriage after initial detection has been reported [27]. Identified risk factors for *C. auris* infection include administration of antibacterial and antifungal agents, vascular and abdominal surgery, the presence of invasive medical devices (such as central venous catheters, post-operative drains and urinary catheters), immunosuppression, chronic renal disease, haemodialysis, diabetes mellitus and prolonged ICU admission [28].

Antifungal resistance

Based on the use of various tentative breakpoints for susceptibility testing of outbreak-related isolates, most of the *C. auris* isolates described worldwide have been reported as resistant to fluconazole, and multidrug-resistant isolates with varying levels of resistance to other azoles, amphotericin B, and echinocandins have been reported [29-32]. Clusters of pandrug-resistant and echinocandin-resistant *C. auris* in healthcare facilities have also been described in the United States (US) [33].

[1] Please note that the UK was still a Member State of the EU at the time of this survey. This explains the inclusion of UK data in this report.

Laboratory identification, molecular typing and antimicrobial susceptibility testing

In the context of the emergence of *C. auris* and the increase of antifungal-resistant *Candida* infections, isolates of *Candida* non-*albicans* from invasive infections should be identified to the species level. It is difficult to identify *C. auris* to species level with traditional laboratory methods [34]. Today, various options for species identification are available, including specific chromogenic isolation medium agar plates and matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) mass spectrometry [35]. MALDI-TOF can reliably differentiate *C. auris* from other *Candida* spp. [36,37]. Molecular identification of *C. auris* can be performed by sequencing various DNA loci within specific domains of ribosomal genes (18S rDNA, 28S rDNA or internal transcribed spacers ITS1, ITS2), by conventional or real-time polymerase chain reaction (PCR) and loop-mediated isothermal amplification (LAMP) [14,38]. Molecular typing of *C. auris* can be performed using a variety of methods. Sequencing of rDNA loci (D1/D2 or ITS regions) can be used to differentiate between the major phylogeographic clades of this species. Further delineation of local hospital outbreaks requires higher resolution methods, including typing by amplified fragment length polymorphism (AFLP) and whole genome sequencing analysis [38].

Minimum inhibitory concentration (MIC) clinical breakpoints for *C. auris* have not yet been established. Tentative breakpoints have been suggested by the US Centers for Disease Control and Prevention (CDC), based on expert opinion and breakpoints already established for other closely related *Candida* spp., and are now widely used [39]. A comparison of the EUCAST and CLSI broth microdilution methods showed very similar MIC values and estimated epidemiological cut-off values for a range of antifungal agents against a collection of *C. auris* isolates from India, confirming uniform resistance to fluconazole [30].

Active *C. auris* surveillance, including performing cultures among contact patients, is an important part of outbreak control. In the UK outbreak in 2015 and 2016, contact patients were screened at multiple sites (nose, axilla, groin, throat, rectum/faeces, vascular line and drain exit sites), as well as from clinical samples (urine, wound, drain fluid and respiratory specimens) [12,38]. In the US, close contacts of patients were screened for colonisation using composite axilla and groin swabs [31]. Adding nasal swabs to surveillance cultures has also resulted in the detection of additional *C. auris* carriers, with nine (25%) of 36 carriers detected by nasal culture alone in another investigation in the US [40].

Impact of *C. auris* infection on human health

Healthcare-associated *C. auris* infections

Healthcare-associated *C. auris* bloodstream infections have affected patients with severe underlying diseases or immunosuppression, such as patients with diabetes mellitus, chronic kidney disease, HIV infection, solid tumours and haematological malignancies [14,24] and, as described previously, patients with severe COVID-19. Neonates, most of them premature, have also been affected [41]. However, in the ongoing outbreaks, invasive *C. auris* infections have also been reported in patients without any underlying severe disease. Patients who developed a *C. auris* infection had frequently been exposed to medical procedures and invasive devices such as mechanical ventilation, central venous and urinary catheters, surgery, treatment with broad-spectrum antibiotics, and admission to ICUs [10,14,42]. Treatment with systemic antifungals prior to *C. auris* infection has also been reported for several patients [29].

Limited treatment options

Fluconazole and the echinocandins are the antifungal agents most used for the treatment of *Candida* bloodstream infection (candidaemia). Both are better tolerated than amphotericin B, which is less often prescribed due to the risk of toxicity. Fluconazole cannot be used for treatment of *C. auris* infection, as nearly all isolates are resistant to fluconazole. Resistance to other antifungals seems to be more variable; however, isolates with resistance to all three major classes of antifungals (azoles, echinocandins, and amphotericin B) have been described [43]. This is a concern, as it seriously limits available treatment options for patients with invasive *C. auris* infections. In light of the antifungal resistance patterns identified to date, empirical treatment with an echinocandin drug is recommended until availability of susceptibility testing results [44]. As development of echinocandin resistance during treatment has been described [45], patients with *C. auris* bloodstream infections should be monitored for clinical improvement and follow-up cultures should be taken. Treatment of *C. auris* identified from sites such as the respiratory tract, urine or skin is not recommended in the absence of signs of clinical disease [44].

Mortality

Invasive candidiasis has a mortality rate of up to 30-40%, even in patients receiving antifungal treatment [7,46]. There is currently limited information on the case-fatality rate specifically for invasive *C. auris* infections due to the small number of patients included in published case series or outbreak descriptions. A study published in 2013 reported case-fatality rates of 33% for all patients with *C. auris* bloodstream infections and of 57% for the subgroup of patients admitted to ICUs, but these rates might be attributable to the severity of underlying diseases in these patients [14]. Findings from an outbreak in the US showed that, among patients with blood isolates of

C. auris, the 30-day mortality rate was 39% and the 90-day mortality rate was 58% [40]. In the UK outbreak, no fatality could be directly attributed to *C. auris* infection [12,38]. The mortality rate of *C. auris* bloodstream infections in neonates has been reported to be as high as 57%, but with decreasing rates in older children [47]. However, as invasive *Candida* infections often occur in severely ill patients with multiple comorbidities, attributable mortality is difficult to determine [38,48].

Potential for spread of *C. auris*

Outbreaks and spread in healthcare settings

Based on molecular typing, transmission of *C. auris* between separate wards that did not share healthcare personnel was reported from a hospital in India [14]. Interfacility transmission of *C. auris* was also reported in the same study [14] and has occurred in four outbreaks in the EU/EEA [21]. The majority of *C. auris* infections reported in the literature were acquired in healthcare settings. The capacity for intra- and interhospital spread, combined with multidrug resistance, suggests that *C. auris* has the typical characteristics of a healthcare-associated pathogen and spread in healthcare settings can be expected.

C. auris outbreaks have been difficult to control, with cases in affected hospitals being detected over periods longer than a year [12,13]. The described outbreak in northern Italy has been ongoing for more than two years. Widespread environmental contamination of surfaces and equipment surrounding patients carrying *C. auris* has been reported [12,24]. The *C. auris* burden on the skin of carriers in other hospital settings has been shown to be associated with the extent of contamination of the surrounding healthcare environment [49]. More specifically, *C. auris* survives on moist or dry surfaces for up to seven days and on plastic devices for up to 14 days [50,51]. During outbreak investigations in the US, environmental samples from glucometers, mobile ultrasounds, temperature probes, pulse oximeters, stethoscopes, and blood-pressure cuffs were found contaminated with *C. auris* [52]. In an outbreak in the UK, *C. auris* was likely spread via shared thermometer probes [53].

Carriers also represent an important reservoir of *C. auris.* Continuous carriage for more than a year after initial isolation of *C. auris* has been documented. However, a study in the US found that a substantial proportion of carriers did not remain positive for *C. auris* in follow-up cultures after discharge to the community setting [54]. Decolonisation has been attempted in outbreak settings [12,55]; however, there is currently insufficient evidence regarding decolonisation regimens and their effectiveness to eradicate *C. auris* carriage.

C. auris outbreaks in intensive care unit and acute hospital settings caring for COVID-19 patients

Americas

In December 2020, the first patient with *C. auris* carriage was identified in a COVID-19 ICU in Brazil [56]. An outbreak investigation was performed and all patients, as well as their close contacts hospitalised in the COVID-19 ICU and healthcare workers, were sampled for *C. auris.* Samples were also collected from inanimate surfaces. Among the 47 patients with collected samples, eight (17%) were found positive for *C. auris* from the axilla, five (10.6%) from the groin, three (6.4%) from the nostrils and two (4.3%) from the ears. Among samples collected from inanimate surfaces, digital thermometers had the highest rate of positive cultures (n = 8/47; 17%). Among the three patients who developed bloodstream infections with *C. auris* and died, one death was considered attributable to candidaemia [56].

A *C. auris* outbreak reported in Mexico started with a non-COVID-19 patient at the end of May 2020, while the hospital was undergoing transition to become a facility exclusive for COVID-19 patients. Three months later, an outbreak of *C. auris* occurred in three ICUs in this hospital, affecting 12 patients. Whole genome sequencing showed a close relationship between the outbreak isolates and the isolate from the non-COVID-19 patient. Five (83.3%) of the six patients with candidaemia died [57].

In July 2020, in an acute care hospital in Florida, four COVID-19 patients experienced bloodstream infections (n = 3) or urinary tract infection (n = 1) caused by *C. auris* [58]. In response, 67 patients admitted to the COVID-19 unit were screened, of which 35 (52%) patients were found positive for *C. auris*. Six (17%) colonised patients later had clinical cultures positive for *C. auris*. Eight (40%) patients with *C. auris* died within 30 days of screening; however, the contribution of *C. auris* to death is unknown. Investigators observed that a combination of factors – such as the multiple gown and glove layers worn by healthcare staff in the COVID-19-unit (which extended the use of the underlayer of personal protective equipment (PPE)), lapses in cleaning and disinfection of shared medical equipment, and lapses in adherence to hand hygiene – likely contributed to widespread *C. auris* transmission in the COVID-19 unit [58].

Additional *C. auris* cases and outbreaks mainly affecting COVID-19 patients occurred in Colombia, Guatemala, Panama and Peru [59]. Four of these countries (Brazil, Guatemala, Mexico and Peru) did not report any *C. auris* cases prior to 2020. The increase in healthcare-associated *C. auris* outbreaks in the Americas and the association with the COVID 19 pandemic prompted the Pan American Health Organization (PAHO) to publish an epidemiological alert '*Candida auris* outbreaks in healthcare services in the context of the COVID-19 pandemic' [59].

Asia

In India, candidaemia occurred in 15 (2.5%) of 596 COVID-19 patients admitted to an ICU between April and July 2020 [60]. *C. auris* was isolated from blood cultures in 10 of these patients. These 10 patients were elderly, had been hospitalised in the ICU for prolonged periods and had underlying chronic medical conditions. Six (60%) of the 10 patients with candidaemia died. Death was considered to be mainly related to the underlying health conditions; however, four patients had persistent candidaemia, which likely contributed to their deaths [60]. Four cases of *C. auris* candidaemia in COVID-19 patients were also reported from Pakistan [61].

Middle East

An outbreak involving 14 patients with *C. auris* carriage or infection admitted to four separate critical care units occurred in a tertiary care facility in Beirut between October and December 2020 [62]. The first case was detected in the neurological ICU. Seven patients had an underlying malignancy, seven had COVID-19 pneumonia prior to detection of *C. auris*, and all but one patient received mechanical ventilation [62]. Six patients received antifungal treatment, while the remaining eight cases were considered to be carriers. Five (35%) of 14 patients died [62]. Co-infection with COVID-19 and *C. auris* was also identified in the United Arab Emirates and Turkey [63,64].

EU/EEA

A *C. auris* outbreak in a Spanish tertiary care hospital, which had started in 2017 and seemed under control, worsened during the COVID-19 pandemic (from June 2020 onwards), resulting in *C. auris* becoming the most frequent *Candida* spp. isolated from blood cultures from candidaemia cases at that hospital. Between April 2019 and February 2021, 56 cases of *C. auris* candidaemia were detected [65]. The authors mention the overoccupancy of the ICU, the high workload of healthcare workers and low compliance with infection control measures as potential causes for the worsening of the outbreak [65].

In the outbreak in northern Italy described in this risk assessment, *C. auris* transmission was amplified after introduction of *C. auris* in an ICU dedicated to COVID-19 patients. A study carried out in hospital A between February and May 2020 found a high rate of acquisition of multidrug-resistant organisms, including not only *C. auris,* but also carbapenem-resistant *Pseudomonas aeruginosa* and carbapenem-resistant *Klebsiella pneumoniae*, in COVID-19 patients admitted to ICUs [3]. As possible reasons for this high rate, the authors pointed at the enhanced vulnerability of COVID-19 patients, who require a higher level of care and longer hospital stays than non-COVID-19 patients; the frequent use of broad-spectrum antibiotics in these patients; and suboptimal infection prevention and control measures, such as the use of open spaces to allow easier management of a high number patients, the focus on respiratory PPE with less attention to standard and contact precautions, the reluctance of staff to change PPE frequently to avoid personal contamination during undressing, as well as PPE shortages, in some cases [3].

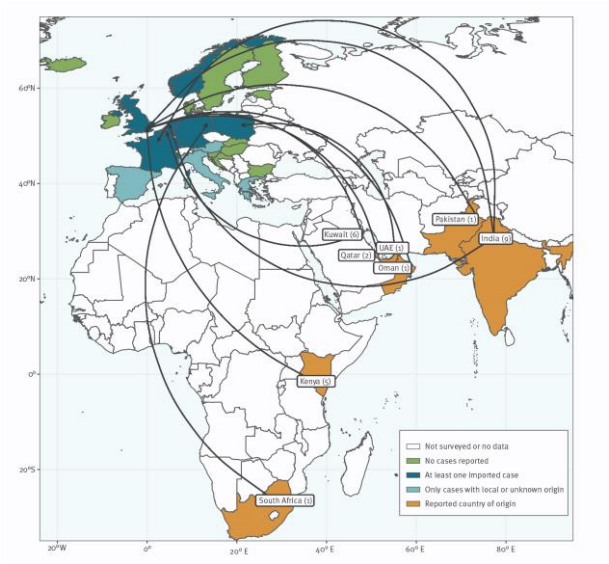
As described previously, various *C. auris* outbreaks in COVID-19 patients have also been reported from other countries [56-58,60,62]. The main reason for the co-occurrence of COVID-19 and *C. auris* is likely that the COVID-19 pandemic has created favourable conditions for transmission of *C. auris* and other multidrug-resistant organisms in these settings. An increase in the number of vulnerable patients who require a high intensity of care, combined with the concurrent shortage and overload of healthcare staff, may have resulted in an inability to maintain a sufficient level of standard and contact precautions. Divergence from standard infection prevention and control monitoring procedures and possibly the need to recruit staff from outside areas unfamiliar with established infection prevention and control routines may also have contributed to transmission of *C. auris*. A recent report from France also showed that COVID-19 patients more frequently acquired multidrug-resistant organisms and developed healthcare-associated infections (including but not limited to ventilator-associated pneumonia) than patients without COVID-19 [66].

Cross-border transmission

Due to lack of surveillance and limited capacity for laboratory detection, the worldwide prevalence of *C. auris* is likely to be underestimated. Nevertheless, C*. auris* isolates, cases and outbreaks have now been reported from six continents: Africa, Asia, Europe, Oceania (Australia), North America and South America [19]. A recent study showed that isolates of *C. auris* from the UK had several diverse geographical origins, suggesting multiple introductions into the country and multiple introductions of different clades in the same hospital [67]. Likewise, whole genome sequencing analysis of all clinical *C. auris* isolates reported to the US CDC from hospitals across the US revealed clonal dissemination of closely related isolates that grouped either with the South Asian clade (New York and New Jersey) or with the South American clade (Illinois) [31].

Although *C. auris* is not included in EU/EEA routine surveillance, ECDC has conducted two surveys to collect information on *C. auris* cases in EU/EEA countries. The last survey collected data up to May 2019. While at this time most cases of *C. auris* in Europe were part of previous outbreaks in two countries (Spain and the UK), sporadic cases with a reported origin outside of the EU/EEA were reported from an increasing number of countries (Figure 2) [20]. Large outbreaks within Europe could potentially increase the number of cross-border transfers of *C. auris*, with potential subsequent onward transmission and establishment of *C. auris* in the country. One example of such an intra-European transfer was the import of *C. auris* to Switzerland by a tourist that had been hospitalised in Spain (where previous *C. auris* outbreaks occurred) [68]. The tourist had developed community-acquired pneumonia while on vacation in north-eastern Spain and required hospital admission and mechanical ventilation. *C. auris* carriage at multiple sites was detected after transfer to Geneva [68].

Figure 2. Geographical distribution and reported origin of *C. auris* infection and carriage, EU/EEA, January 2013–May 2019 (n = 26)*



Source: Plachouras, et al. [20]
** Information on cases for 2020 and 2021 were not available.*

ECDC risk assessment for the EU/EEA

Risk assessment questions

What is the probability for and the impact of further spread of *C. auris* in healthcare facilities in Italy and in other EU/EEA countries as a result of the recent outbreak in Italy?

Risk assessment

Information on the outbreak in northern Italy is limited at this stage. Detailed case-based information, antifungal susceptibility testing results of *C. auris* isolates, and information on disease severity, treatment and clinical outcomes are not available for most of the cases. In addition, information from adjacent regions was not yet available at the time of this risk assessment. However, given the high number of cases, the spread of *C. auris* to at least eight healthcare facilities in Liguria, interregional spread to Emilia-Romagna, and the difficulty to contain the outbreak despite more than two years of enhanced control measures, the probability of further spread of *C. auris* in Italy is considered to be **HIGH**. Even though case numbers seem to be declining, the outbreak cannot be considered over at the time of this risk assessment. Given the long-time carriage of *C. auris* by patients and the known persistence of *C. auris* in the hospital environment, at least a six-month interval without new cases would be needed to determine the end of an outbreak. In addition, current case numbers should be interpreted with caution due to potential reporting delays. The impact of the outbreak of *C. auris* in Italy is considered to be **MODERATE**, as long as control measures are instituted and treatment options – even if few – still remain available. The overall risk of further spread of *C. auris* in Italy is considered to be **HIGH**.

For other EU/EEA countries, the probability of introduction of *C. auris* specifically from this outbreak in Italy remains **VERY LOW**, as local and national control measures are being implemented. Together with an assumed **MODERATE** impact, the overall risk is **LOW** unless hospitalised patients are transferred from this region.

However, given the worldwide spread of *C. auris* and related previous detections of sporadic cases and outbreaks in the EU/EEA, it is likely that more undetected cases will eventually enter the EU/EEA from regions with less capacity for surveillance and control, and therefore continued vigilance is needed. It is therefore of high importance that EU/EEA countries have adequate national surveillance and laboratory capacity in place to detect *C. auris* cases early and implement control measures immediately, as control will be more difficult to achieve once *C. auris* dissemination has reached the level of interfacility and interregional spread. Local control of *C. auris* as soon as possible after introduction to delay establishment of *C. auris* in a country's healthcare facilities will have a nationwide benefit by reducing the risk of future healthcare-associated infections with *C. auris*. Rapid risk assessments regarding *C. auris* in healthcare settings in Europe have been published by ECDC in 2016 and 2018 [69,70].

Options for response

Infection prevention and control measures

Good standard infection prevention and control, including environmental cleaning, adequate cleaning and reprocessing of medical devices, adequate capacity of microbiological laboratories, and sufficient capacity of healthcare facilities for patient isolation, are the basis for the prevention of transmission of any pathogen in healthcare settings.

Preventing transmission from patients known to carry *C. auris*

When identifying a *C. auris* case, early, robust action is recommended to prevent further spread, as outbreaks can be prolonged, costly and may pose significant risk to compromised patients. Prompt notification of *C. auris* to the clinical team and the infection prevention and control team is essential to implement infection prevention and control measures in a timely manner and to ensure monitoring for development of infections in patients found to be colonised. The detection of even a single case of *C. auris* should trigger an investigation, including a detailed case review and screening of close contact patients for *C. auris* carriage. More extensive contact tracing can be considered based on a case-by-case risk assessment (e.g. taking into account the type of patient population and ward, the extent of *C. auris* colonisation, the number of contacts of the affected patient and the extent of use of shared equipment).

Infection control options for implementation in hospitals include enhanced control measures such as contact precautions, single room isolation or patient cohorting, and dedicated nursing staff for patients who are colonised or infected with *C. auris.* As there are currently no established protocols for decolonisation and determining when it is safe to end isolation, these precautions need to be applied until the patient is discharged from the hospital and upon potential readmission. Screening of close contacts of identified cases for *C. auris* carriage with axilla and groin swabs is an important component of the response to *C. auris*. Other sites (urine, wounds, catheter exit sites, throat, etc.) can be sampled, if clinically relevant or indicated.

It is critical to emphasise regular cleaning of surfaces and equipment (including after discharge of patients who carry or are infected with *C. auris*), terminal cleaning, and disinfection of rooms with chlorine-based disinfectants (at a concentration of 1 000 ppm), hydrogen-peroxide or other disinfectants with documented fungicidal activity. Quaternary ammonium compound disinfectants should be avoided. Single-use equipment and dedicated equipment for each *C. auris* patient or cohort is preferable where possible, as equipment shared between patients has been found to be contaminated with *C. auris* in outbreak situations. Cleaning and disinfection of reusable equipment (e.g. monitoring devices, thermometers, pulse oximeters, blood pressure measuring instruments) according to manufacturer's instructions should be ensured. Environmental sampling or screening of healthcare workers is not routinely recommended.

Additional control options for outbreaks

Raising awareness and providing education to all healthcare groups is essential for outbreak management. Prompt initiation of an epidemiological investigation, complemented by cross-sectional screening of patients for *C. auris* carriage, is useful to establish the source of the outbreak and thus prevent further cases. Potentially effective enhanced measures to control *C. auris* outbreaks include regular active surveillance cultures for *C. auris* carriage of all patients in affected wards, cohorting of *C. auris*-positive patients with dedicated nursing staff in separate areas, as well as rigorous environmental cleaning and disinfection. Education and practice audits to improve compliance of healthcare workers with hand hygiene, contact precautions and supervision of appropriate implementation of environmental cleaning are important supportive interventions. In particular, *C. auris* cases occurring in COVID-19 units should trigger a review of changes in procedures during the pandemic that may have had a negative impact on the staff's ability to maintain standard precautions. Support from hospital senior management is needed to provide adequate resources for the implementation of appropriate infection control measures.

Prevention of interhospital transmission, including cross-border transmission

Screening for *C. auris* carriage upon admission and pre-emptive isolation of patients who are transferred from or have recently been admitted to healthcare facilities locally or abroad that are aware that they have detected *C. auris* cases should be considered. In addition, healthcare facilities with *C. auris* cases need to notify receiving healthcare facilities and clinicians in the case of transfer of patients with *C. auris* carriage or infection. Moreover, gathering reliable epidemiological data through notification of *C. auris* cases and outbreaks to public health authorities and exchange of information through electronic early warning platforms, such as the European Surveillance Portal for Infectious Diseases (EpiPulse) and the Early Warning and Response System (EWRS), will enable informed and coordinated risk management actions by public health authorities across the EU/EEA. ECDC intends to publish another update to the survey on *C. auris* cases in the EU/EEA.

Improvement of preparedness in EU/EEA countries

EU/EEA countries should continue to alert clinicians and microbiologists in their healthcare facilities and associated clinical microbiology laboratories to raise awareness about this emerging fungal pathogen with epidemic potential, with the aim of adapting laboratory testing practice at primary and reference levels and establishing specific control measures in a timely manner. National guidelines for laboratory testing and control measures for *C. auris* will enable the implementation of appropriate measures in healthcare facilities. Sharing experiences of outbreaks and implementation of control measures can be facilitated by ECDC.

Laboratory capacity for detection and antifungal susceptibility testing of *C. auris*

As not all laboratories serving healthcare facilities have the capacity for *C. auris* identification or susceptibility testing for the whole panel of antifungal agents, a national mycology reference laboratory could assist clinical laboratories with *C. auris* identification, antifungal susceptibility testing, molecular typing and epidemiological investigations. The reference laboratory may also issue guidance for local laboratories on how to proceed with difficult-to-identify *Candida* spp. isolates, as well as isolates suspected as being *C. auris*, and provide instructions for referring samples for further testing and for reporting results. However, clinical laboratory capacity for initial identification and antifungal susceptibility testing of *Candida* spp. should be established and improved throughout the country, especially in laboratories serving facilities with high-risk populations.

Case finding and improved surveillance for *C. auris* infections

EU/EEA countries may consider laboratory-based alerting or notification of cases of *C. auris* carriage and infection, as well as prospective data collection at the national level, even if cases and outbreaks have not occurred in the country. Surveillance systems for healthcare-associated infections should consider updating their definitions to include *C. auris* in the list of reportable pathogens associated with healthcare-associated infections. National and regional public health authorities should follow up and offer advice and support to healthcare facilities for all detected *C. auris* cases to make sure appropriate measures are instituted early enough to delay establishment of *C. auris* in the country.

Antimicrobial stewardship

Although there is no evidence for a specific beneficial effect of antimicrobial stewardship on the emergence and spread of *C. auris*, it is likely that an environment with a high use of broad-spectrum antibacterial and antifungal agents will favour the emergence of multidrug-resistant yeasts, such as *C. auris*. Therefore, the implementation of antimicrobial stewardship is likely to mitigate the risk of *C. auris* emergence and spread, in addition to being an essential component of strategies to reduce antimicrobial resistance in general. The need for antifungal prophylaxis should be reviewed in terms of risk-benefit analysis in settings with evidence of *C. auris* transmission.

Consulted experts

ECDC experts (in alphabetic order): Agoritsa Baka, Jessica Beser, Olivier Briet, Anke Kohlenberg, Anna Machowska, Dominique Monnet, Aikaterini Mougkou, Diamantis Plachouras, Paul Riley, Ettore Severi.

External experts: Francesco Maraglino, Ministry of Health, Italy; Michela Sabbatucci, Ministry of Health, Italy; Camilla Sticchi, Regional Health Agency, Liguria, Italy; Elena Vecchi, Regional Public Health Service, Emilia-Romagna, Italy; Maria Luisa Moro, Regional Health Agency, Emilia-Romagna, Italy; Silvio Brusaferro, Italian National Institute of Health; Ana Alastruey-Izquierdo, Mycology Reference Laboratory, Instituto de Salud Carlos III, Spain; Colin Brown, UK Health Security Agency; Claire Neill, UK Health Security Agency.

All experts have submitted declarations of interest, and a review of these did not reveal any conflict of interest.

Disclaimer

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This report was written with the coordination and assistance of an Internal Response Team at the European Centre for Disease Prevention and Control. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

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