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Candidemia in Immunocompromised Patients: Dental Diagnosis, Treatment, and Nursing Care-An Updated Review.

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Abstract

Background: Candidemia is a major healthcare-associated bloodstream infection associated with substantial morbidity and mortality, particularly among critically ill and immunocompromised patients. Its management remains challenging because of diagnostic delays, increasing antifungal resistance, and differences in the epidemiology of Candida species across geographical regions.

Aim: This review examines the epidemiology, antifungal susceptibility, diagnostic approaches, and current therapeutic strategies for candidemia, with emphasis on emerging resistance patterns and clinical management challenges.

Methods: Relevant literature was reviewed to summarize the distribution of Candida species, regional antifungal resistance profiles, and advances in diagnostic methods. The review also evaluates conventional blood cultures, molecular techniques, next-generation sequencing, T2 Candida, MALDI-TOF, non-culture-based biomarkers, and biosensors. Therapeutic approaches, including antifungal prophylaxis, empirical and targeted treatment, vascular catheter removal, ophthalmological assessment, therapeutic monitoring, and emerging antifungal agents, were also examined.

Results: Non-albicans Candida species are increasingly contributing to candidemia, with substantial geographical variation in antifungal susceptibility. Although blood cultures remain the diagnostic reference standard, their limited sensitivity and delayed results support the use of rapid molecular and biomarker-based techniques. Echinocandins remain the preferred initial treatment for many non-neutropenic patients with candidemia. However, treatment outcomes are influenced by species identification, antifungal susceptibility, infection site, pharmacokinetic and pharmacodynamic factors, and timely source control. New agents, including rezafungin and fosmanogepix, offer potential therapeutic alternatives.

Conclusion: Improved outcomes require early diagnosis, appropriate antifungal selection, source control, and individualized management guided by microbiological findings and patient characteristics.

Keywords: Candidemia; invasive candidiasis; Candida species; antifungal resistance; molecular diagnosis; echinocandins; antifungal therapy.

Introduction

Invasive candidiasis (IC) comprises a range of systemic fungal infections caused by different species of the genus *Candida*. Candidemia is the most frequently recognized clinical presentation and is defined by the detection of *Candida* in at least one blood culture obtained from a peripheral or central venous sample [1]. The principal causative organisms include *Candida albicans*, *Candida glabrata* (currently *Nakaseomyces glabratus*), *Candida parapsilosis*, *Candida krusei* (currently *Pichia kudriavzevii*), *Candida auris* (currently *Candidozyma auris*), and *Candida tropicalis* [2]. Although these species share several biological characteristics, they differ in their epidemiological distribution, virulence, antifungal susceptibility, and clinical outcomes. Most invasive infections originate from the patient's endogenous fungal reservoir. *Candida* species normally colonize anatomical sites such as the oral cavity, gastrointestinal tract, and genital mucosa

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without causing disease. However, disruption of epithelial barriers, alterations in the microbiota, and impairment of host immune defenses can facilitate fungal invasion and hematogenous dissemination. Once organisms enter the bloodstream, they may reach multiple organs, including the kidneys, liver, spleen, heart, eyes, bones, joints, and central nervous system [3]. The clinical manifestations therefore vary according to the extent of dissemination, the affected organs, and the patient's underlying condition.

Several patient groups have an increased risk of invasive candidiasis. These include individuals with hematological or solid malignancies, recipients of hematopoietic stem cell or solid organ transplants, patients receiving immunosuppressive therapy, individuals undergoing major surgery, and patients requiring hemodialysis. Malignant wounds involving tumor infiltration into the skin may also provide conditions that facilitate infection [4]. Additional hospital-related factors include central venous catheters, prolonged hospitalization, broad-spectrum antibiotic exposure, parenteral nutrition, and intensive care admission. Biofilm formation on intravascular devices further complicates treatment because biofilms reduce antifungal susceptibility and may sustain bloodstream infection despite appropriate therapy [5]. Reported mortality rates remain substantial, ranging from approximately 36% to 60% in several regions, making candidemia an important global healthcare problem [5]. The epidemiology of candidemia continues to change because of differences in patient populations, healthcare practices, fungal species distribution, and antifungal exposure. Diagnostic limitations, particularly in resource-constrained hospitals, may delay species identification and appropriate treatment. Emerging organisms, including *Candidozyma vulturna*, also highlight the need for updated surveillance and diagnostic approaches [6]. This review examines the major etiological agents of candidemia, regional antifungal susceptibility patterns, and the clinical implications of emerging resistance. Particular attention is given to accurate fungal identification and the selection of appropriate antifungal therapy.

Main Etiological Agents of Candidemia

The species responsible for candidemia vary across geographical regions and healthcare settings. Reports published during the last five years indicate that cases have been documented worldwide, with a substantial proportion of the available evidence originating from Asia, followed by Europe, the Americas, Africa, and Oceania (Figure 1). Despite these geographical differences, *C. albicans*, *C. parapsilosis*, *C. glabrata* (currently *Nakaseomyces glabratus*), *C. tropicalis*, and *C. krusei* (currently *Pichia kudriavzevii*) remain among the most frequently identified causative organisms (Table S1). *C. albicans* continues to be the predominant species in many epidemiological studies [7–17]. However, its dominance is not consistent across all countries or patient populations. Several reports from Bangladesh, Turkey, South Africa, Taiwan, the United States, Israel, Belgium, Spain, and India have documented a higher frequency of non-*albicans Candida* (NAC) species. In these settings, *C. parapsilosis*, *C. glabrata*, *C. tropicalis*, and *C. guilliermondii* (currently *Meyerozyma guilliermondii*) may exceed *C. albicans* in frequency [18–22]. These findings demonstrate that local epidemiological surveillance is necessary because the species distribution observed in one country cannot necessarily predict the pattern in another.

The distribution of individual species is also influenced by age and underlying clinical conditions. *C. glabrata* is frequently reported in North America and is more commonly associated with adult patients, whereas *C. parapsilosis* has a notable distribution in Latin America, Europe, and Africa [7–9,15,19,23–27]. *C. tropicalis* and *C. glabrata* are also frequently reported in parts of Asia and Oceania. In neonatal populations, *C. parapsilosis* is particularly important because of its association with hospital-acquired infections and outbreaks involving vascular catheters [7,23]. These differences have implications for empirical antifungal selection and infection prevention. In addition to the major species, several uncommon or emerging NAC organisms have been implicated in bloodstream infections. These include *C. palmioleophila*, *C. pelliculosa*, *C. rugosa*, *Clavispora lusitaniae*, *C. kefyr*, *C. norvegensis*, *C. intermedia*, and *C. auris*. Species belonging to the *C. glabrata* and *C. parapsilosis* complexes, including *C. metapsilosis*, *C. orthopsilosis*, and *Nakaseomyces nivariensis*, have also been identified [7–47]. Such infections have been reported in children, critically ill patients, and individuals with severe COVID-19 or other complications. Among emerging pathogens, *C. auris* is particularly important because of its ability to persist in healthcare environments, colonize patients for prolonged periods, form biofilms, and develop resistance to multiple antifungal classes. Its accurate identification may also be difficult with conventional laboratory methods [48]. Failure to identify the causative species can therefore compromise treatment decisions, particularly when resistant organisms are involved [52]. Regional variation reflects differences in host characteristics, healthcare exposure, medical devices, and antifungal use [53,54].

***Candida* spp. Susceptibility to Antifungals**

Antifungal resistance represents a major challenge in the treatment of candidemia. Among the studies reporting susceptibility testing results for bloodstream *Candida* isolates, 69% (46/67) identified resistance to at least one antifungal agent. This finding indicates that reduced susceptibility is not restricted to a single species or drug class. Instead, resistance has been documented against azoles, echinocandins, polyenes, and flucytosine, although its frequency varies according to geographical

location and the causative organism. During the last five years, reports of antifungal resistance in candidemia have originated mainly from Asia, followed by Europe, the Americas, Africa, and Oceania. Within Asia, East Asia contributed the largest number of reports, followed by Western and Southern Asia. Southern Europe accounted for a considerable proportion of European reports, whereas Northern America had more documented reports than Latin America. Only a limited number of studies were identified from Africa and Oceania. These differences should be interpreted cautiously because the number of published reports does not necessarily reflect the actual prevalence of resistance in each region. Fluconazole resistance has been reported worldwide and remains a major concern in the management of invasive candidiasis [11]. Resistance to other azoles, including voriconazole, itraconazole, and posaconazole, has also been identified. The extent of resistance differs between species, with *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, and *C. auris* frequently implicated in reports of reduced azole susceptibility. These findings are clinically relevant because azoles are commonly used for treatment or step-down therapy in selected patients.

Resistance to echinocandins has also emerged in several regions. Although this drug class remains an important option for initial treatment of candidemia, resistant isolates have been reported among *C. auris*, *C. glabrata*, *C. parapsilosis*, and other species. Reduced susceptibility to amphotericin B has likewise been documented, particularly in *C. auris* and selected uncommon NAC organisms. Flucytosine resistance has been reported less frequently, but its occurrence across several species raises concerns about the reliability of combination regimens when susceptibility is not established. The geographical distribution of published resistance reports cannot be interpreted as a direct comparison of regional resistance prevalence. Differences in surveillance capacity, laboratory methods, sample sizes, and publication patterns may influence the available evidence. Nevertheless, the findings demonstrate the importance of species-level identification and standardized antifungal susceptibility testing. These investigations can guide targeted therapy, support antimicrobial stewardship, and reduce exposure to ineffective antifungal agents. They are particularly important in critically ill patients, patients with persistent candidemia, and those infected with organisms associated with multidrug resistance.

Geographical Distribution of Antifungal Resistance

Antifungal resistance among *Candida* isolates causing candidemia varies across geographical regions, reflecting differences in species distribution, antifungal exposure, healthcare practices, and surveillance capacity. Asia accounts for a substantial proportion of published reports, with distinct patterns across its subregions. In South Asia, resistance to major antifungal classes has generally remained below 14%, while resistance to newer azoles has been reported at rates below 5%. Nevertheless, echinocandin and amphotericin B resistance has been identified in several species [17,22,55,56]. East Asia demonstrates wider resistance variation, with azole resistance reaching 42.9%, particularly in *C. tropicalis*. Resistance to echinocandins and amphotericin B has also been documented [12,14,20,43,49,50]. Western Asia has reported voriconazole resistance reaching 50% in *C. tropicalis*, alongside occasional resistance to anidulafungin and amphotericin B [21,45,47,57,58]. In Europe, Southern countries have reported resistance to multiple azoles, particularly among *C. tropicalis*, with rates reaching 32%. Echinocandin resistance has also been identified in *C. auris*, *C. parapsilosis*, *C. glabrata*, and *C. albicans* [9,10,34,35,59–61]. Reports from Western Europe mainly identified resistance in *C. tropicalis*, whereas Eastern European studies reported limited resistance beyond fluconazole [62]. In North America, resistance involving azoles, echinocandins, amphotericin B, and flucytosine has been reported in several species, particularly *C. auris* [18,24,29,31,63,64]. In Latin America, reported resistance to other antifungal classes is more limited, although amphotericin B resistance has been identified in *Clavispora lusitaniae* and *C. parapsilosis* [7,23,28,65]. African reports remain limited but include voriconazole resistance in *C. auris* (31%) and amphotericin B resistance in *C. parapsilosis* (7%) and *C. auris* (15%) [8]. In Oceania, no resistance beyond fluconazole was reported [26,33]. These findings highlight the importance of regional surveillance, accurate species identification, standardized susceptibility testing, and susceptibility-guided treatment. Differences in publication volume prevent reliable comparisons of actual regional resistance prevalence. Strengthening laboratory capacity and antifungal stewardship is essential to detect emerging resistance and improve candidemia management.

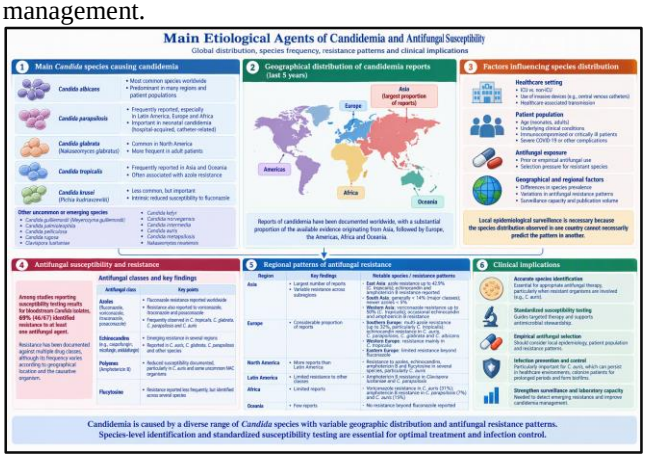


Figure-1: Etiology and Geographical Distribution of Candidemia.

Mechanisms of Antifungal Resistance

Antifungal agents used for the prevention and treatment of candidemia include azoles, echinocandins, polyenes, and flucytosine. These drugs target distinct fungal structures and metabolic pathways. Azoles inhibit ergosterol biosynthesis by targeting lanosterol 14α-demethylase, whereas echinocandins inhibit cell wall synthesis through their action on β-(1,3)-D-glucan synthase. Polyenes, including amphotericin B, bind to membrane ergosterol and disrupt membrane integrity. Flucytosine interferes with fungal nucleic acid synthesis. Despite their therapeutic effectiveness, *Candida* species have developed several resistance mechanisms that reduce antifungal susceptibility and contribute to treatment failure. Azole resistance primarily involves increased drug efflux and alterations in ergosterol biosynthesis. Overexpression of ATP-binding cassette transporters encoded by *CDR* genes and major facilitator transporters encoded by *MDR* genes reduces intracellular drug concentrations. Mutations or overexpression of *ERG11* can alter the structure or expression of lanosterol 14α-demethylase, reducing azole binding. Mutations in *ERG3* may also modify sterol production. Additional mechanisms include sterol uptake through transporters such as Aus1p and Pdr11p in *C. glabrata*, as well as genomic changes, including aneuploidy and loss of heterozygosity, which can increase resistance [66,67].

Polyenes resistance is associated with changes in membrane sterol composition. Mutations affecting *ERG11* and *ERG3* may reduce ergosterol levels and promote the accumulation of alternative sterols, decreasing amphotericin B binding. Changes in cell wall composition may also restrict drug penetration. For example, increased glucan content has been associated with amphotericin B resistance in *C. tropicalis* [68,69]. Echinocandin resistance mainly results from point mutations in *FKS1* and *FKS2*, which encode subunits of β-(1,3)-D-glucan synthase. These mutations modify the drug-binding region and reduce antifungal activity. Substitutions involving serine 645 in *FKS1* have been reported in *C. albicans*, *C. glabrata*, and *C. krusei* [67]. Flucytosine resistance involves mutations in *FCY1* and *FCY2*, which encode enzymes responsible for drug activation and uptake. Their inactivation reduces intracellular drug activity [70]. Understanding these mechanisms supports the development of rapid diagnostic and susceptibility-testing methods, enabling species-specific treatment and improved outcomes in patients with candidemia.

Risk Factors for Candidemia

Candidemia is a multifactorial infection associated with host-related vulnerabilities and healthcare exposures. These factors contribute to impaired immune defense, disruption of the normal microbiota, and increased opportunities for fungal invasion. Host-related risk factors include immunosuppression caused by corticosteroids, chemotherapy, transplantation medications, and neutropenia associated with malignancy or other conditions [71,72]. Defects in cellular immunity, particularly impaired Th1 and Th17 responses, reduce the ability to control *Candida* colonization and infection. Mutations affecting *STAT1* and *RORC* can impair IL-17 production and mucosal defense [73–75]. HIV infection further increases susceptibility through CD4+ T-cell depletion, disruption of mucosal immunity, and microbial translocation [76]. Alterations in intestinal microbiota also contribute. Reduced abundance of *Clostridia* decreases short-chain fatty acid production and disrupts intestinal physiological hypoxia, creating conditions that favor *Candida* colonization [77–79]. Transplant recipients face additional risks because immunosuppressive therapy, antibiotic exposure, prolonged catheterization, and repeated surgical procedures frequently occur together [81,82]. Age and chronic diseases also influence susceptibility. Children with malignancies, congenital immune defects, or prolonged central venous catheter use are particularly vulnerable. Candidemia incidence may be high among pediatric patients with acute lymphoblastic leukemia [83,84]. In adults, diabetes, dyslipidemia, and age-related immune dysfunction increase susceptibility, while previous hospitalization and antimicrobial exposure may complicate treatment [85–88]. Healthcare-related factors are particularly important in intensive care units. Hospitalization promotes progressive *Candida* colonization, with reported cutaneous colonization increasing from 27.3% at admission to 52.7% by day eight [89]. Broad-spectrum antibiotics disrupt bacterial microbiota and facilitate fungal overgrowth. Exposure to these agents, particularly carbapenems, has been associated with increased candidemia risk [90–92]. Central venous catheters provide surfaces for fungal adhesion and biofilm formation. Prolonged catheterization, multiple lumens, and biofilm development increase bloodstream infection risk [93,94]. Total parenteral nutrition may further support fungal growth through its lipid components [91]. Abdominal surgery, intestinal perforation, anastomotic leakage, and necrotizing pancreatitis can facilitate bloodstream invasion from gastrointestinal colonization [97]. Collectively, these factors highlight the importance of antimicrobial stewardship, catheter management, and early identification of high-risk patients.

Diagnosis of Candidemia

The diagnosis of candidemia remains challenging because conventional methods have limited sensitivity and may delay the initiation of appropriate antifungal therapy. Rapid and reliable

diagnostic approaches are therefore essential to improve clinical outcomes, reduce unnecessary antifungal exposure, and support timely treatment decisions.

Blood Cultures and Histopathology

Blood culture remains the reference standard for diagnosing candidemia, as recommended by the European Society for Clinical Microbiology and Infectious Diseases and the Infectious Diseases Society of America [98]. However, its sensitivity is limited, with *Candida* species detected in approximately 21–71% of patients with invasive candidiasis. Increasing blood sample volume and collection frequency may improve detection, but results generally require 72–96 hours, potentially delaying treatment [99]. In neonates, blood cultures may have particularly low diagnostic yield. Thrombocytopenia and elevated C-reactive protein have therefore been investigated as supportive indicators, although procalcitonin has not demonstrated sufficient discriminatory capacity to distinguish candidemia from bacteremia [99–101]. Histopathological examination can support fungal detection through special staining techniques. Periodic acid–Schiff and Gomori–Grocott methenamine silver stains identify fungal cell-wall components, while calcofluor white enhances visualization under fluorescence microscopy [102]. A modified calcofluor-based assay demonstrated 90% sensitivity and an 82% negative predictive value, with results available within approximately 10 minutes. These findings suggest potential value as a rapid screening method, although conventional culture remains necessary for confirmation [102]. The time to blood culture positivity also varies according to species and antifungal susceptibility. Differences have been reported between *C. albicans*, *C. tropicalis*, *C. glabrata*, and other yeasts [103]. A multicenter Australian study involving 527 candidemia episodes found differences in both positivity time and 30-day mortality across species. *C. tropicalis* showed a relatively short positivity time of 27 hours but substantial mortality, whereas *C. parapsilosis* required approximately 48 hours and was associated with lower mortality. These findings indicate that culture kinetics may provide prognostic information, although patient characteristics and disease severity also influence outcomes [104].

Molecular-Based Diagnostic Techniques

Polymerase chain reaction (PCR) assays detect fungal DNA directly from blood or other clinical specimens without requiring prior culture. Commercial platforms include species-specific quantitative and real-time PCR assays for *C. auris*, as well as multiplex PCR systems capable of identifying common species such as *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. tropicalis* [105,106]. However, low fungal concentrations may reduce sensitivity, and several assays require further multicenter clinical validation. Random amplified polymorphic DNA PCR (RAPD-PCR) and microsatellite analysis can also distinguish *Candida* genotypes. These methods support epidemiological investigations, identification of related isolates, and recognition of potential hospital transmission. Their relatively low cost and short processing time make them useful alternatives for laboratories with limited resources [105,107]. Next-generation sequencing and whole-genome sequencing provide more detailed genetic characterization. These techniques can identify closely related isolates, investigate hospital outbreaks, and detect mutations associated with antifungal resistance. Their application to multidrug-resistant *C. parapsilosis* has supported the investigation of echinocandin resistance associated with alterations in *FKS1* [108]. Nevertheless, sequencing requires specialized equipment, technical expertise, and additional processing time.

T2 Candida and Other Rapid Identification Methods

The T2 Candida assay is a non-culture-based molecular platform that detects five major *Candida* species directly from blood. It can detect fungal concentrations as low as 1 CFU/mL and provide results in less than five hours [109]. Clinical studies have demonstrated variable sensitivity and specificity, with reported sensitivity ranging from 65% to 100% and specificity from 90% to 100%. Its ability to detect infection in patients receiving antifungal therapy is an important advantage [110]. However, performance differs across clinical populations. A prospective study of patients with probable intra-abdominal candidiasis reported 46% sensitivity and 97% specificity, indicating that a negative result does not exclude infection in every high-risk patient [111]. Another investigation reported sensitivity of 63.6% in proven candidemia and 73% when proven and probable cases were combined [112]. Although T2 Candida offers rapid detection, its limited species coverage and variable sensitivity remain important limitations. The MoiM assay represents another molecular approach for identifying *Candida* species from positive blood cultures. In a study involving 39 candidemia cases and 40 negative controls, it demonstrated 97.1% positive percentage concordance and 100% negative percentage concordance compared with the reference identification method [113]. Matrix-assisted laser desorption–ionization time-of-flight mass spectrometry (MALDI-TOF MS) identifies fungal species by comparing their protein spectra with established databases. It can provide identification within approximately 15 minutes after obtaining suitable material and has been used to identify several clinically important species, including *C. auris* and *C. krusei* [16,99,114,115]. Its integration into blood-culture workflows can shorten identification time and support earlier selection of targeted antifungal

therapy. However, equipment costs may restrict its availability in resource-limited laboratories [116,117].

Non-Culture-Based Methods and Biosensors

Non-culture-based biomarkers provide additional diagnostic information. Serum 1,3-β-D-glucan (BDG), a component of the fungal cell wall, is included in the mycological criteria for invasive fungal infections. Although reported sensitivity and specificity can reach 92% and 81%, respectively, false-positive results may occur following administration of albumin, intravenous immunoglobulin, or certain antimicrobials [118,119]. Anti-mannan IgM and IgG assays have also been investigated, with IgM generally demonstrating better diagnostic performance. Combining both antibody tests may increase sensitivity but can reduce specificity [98]. Other biomarkers, including presepsin, C-reactive protein, and procalcitonin, have been evaluated in diagnostic panels. Combining presepsin with BDG may improve diagnostic assessment, while presepsin levels may also provide information about mortality risk and treatment response [119]. A separate investigation found that combining BDG with Candida-specific PCR increased sensitivity to 91% while maintaining 100% specificity, supporting the value of complementary diagnostic methods [121]. Biosensors offer another emerging approach for detecting *Candida* through measurable biological signals. Available platforms include optical and electrochemical sensors, lateral-flow assays, loop-mediated isothermal amplification, immunosensors, and microfluidic systems. These technologies have been investigated for detecting several *Candida* species in blood, urine, cultures, and other clinical specimens. Their potential advantages include rapid processing, low sample requirements, and reduced dependence on conventional laboratory infrastructure. However, sensitivity, specificity, reproducibility, and clinical validation remain essential considerations before routine implementation [107,122]. Overall, no single diagnostic method provides optimal performance in every clinical setting. Combining blood cultures with molecular assays, fungal biomarkers, and rapid identification platforms may improve diagnostic accuracy and facilitate earlier targeted treatment. The selection of diagnostic strategies should consider patient risk, local laboratory capacity, species distribution, and the need for antifungal susceptibility testing.

Treatment of Candidemia

Candidemia remains associated with substantial mortality, ranging from 27% to 52.7%. Outcomes are influenced by host characteristics, infecting *Candida* species, disease severity, comorbidities, and the timing of appropriate antifungal therapy. Neutropenia, corticosteroid exposure, renal replacement therapy, chronic liver disease, malignancy, high APACHE II scores, and failure to remove infected vascular catheters are among the major predictors of poor outcomes [125–130]. Adherence to international recommendations, assessed using tools such as the EQUAL Candida Score, has been associated with improved survival, although mortality remains high even with guideline-based management [131].

Antifungal Treatment and Prophylaxis

Therapeutic management includes prophylactic, preemptive, empirical, and targeted treatment. Prophylaxis is considered for patients with established clinical and epidemiological risk factors. Preemptive therapy is initiated when microbiological evidence suggests fungal infection before definitive confirmation. Empirical treatment is based on clinical manifestations and risk factors, whereas targeted therapy follows microbiological identification and susceptibility testing [123]. Early initiation of appropriate antifungal treatment is particularly important because treatment delays contribute to adverse outcomes [127]. Treatment failure may also occur despite in vitro susceptibility because of biofilm formation, fungal tolerance, phenotypic variation, and adaptive stress responses [48,69,133]. Prophylactic fluconazole has demonstrated benefits in extremely low-birth-weight neonates. In infants weighing less than 1000 g, six weeks of prophylaxis significantly reduced invasive candidiasis, with an absolute risk reduction of 20%. A meta-analysis of eight clinical trials also demonstrated reductions in fungal colonization and invasive infection, although no significant mortality benefit was observed [138,139]. However, increasing infections caused by non-*albicans Candida* species, particularly *C. parapsilosis*, highlight the need to consider local epidemiology when selecting prophylactic regimens [8,140]. For patients with hematological malignancies and prolonged neutropenia, posaconazole prophylaxis has demonstrated superiority over fluconazole or itraconazole. In a randomized trial involving patients receiving chemotherapy for acute myeloid leukemia or myelodysplastic syndrome, posaconazole reduced confirmed or probable fungal infections from 8% to 2% and decreased 100-day mortality from 21% to 14% [142]. Nevertheless, breakthrough infections may occur, particularly with *Nakaseomyces glabratus* and *C. parapsilosis*, depending on the prophylactic agent used [143–145]. Fluconazole prophylaxis may also be considered in selected patients following abdominal surgery, particularly those with recurrent gastrointestinal perforation or anastomotic leakage [146]. Transplant recipients with additional risk factors, including repeated surgery, hemodialysis, substantial transfusion requirements, and *Candida* colonization, may require prophylaxis for 2–4 weeks [147]. However, evidence from liver and pancreatic transplant populations remains inconsistent [148,149].

Treatment of Established Infection

Echinocandins are recommended as first-line treatment for severely ill, non-neutropenic patients with candidemia without deep-seated infection. Their advantages include broad activity against many *Candida* species, favorable safety, limited drug interactions, and effective microbiological clearance [123,124,146,152,153]. A meta-analysis involving 1,915 patients associated echinocandin treatment with lower mortality than other antifungal classes (27% versus 36%, $p < 0.0001$) [154]. However, treatment selection should consider species identification, susceptibility results, infection site, and previous antifungal exposure. Intra-abdominal candidiasis presents additional therapeutic challenges, particularly following abdominal surgery. Echinocandins may achieve lower concentrations in peritoneal fluid than in serum, potentially reducing their effectiveness against organisms with higher minimum inhibitory concentrations. Dose optimization and consideration of alternative agents, including amphotericin B formulations, may therefore be necessary in selected patients [156,157]. Antifungal exposure should also be considered in relation to body weight and pharmacokinetic parameters. Micafungin clearance increases with body weight, potentially reducing drug exposure in patients with obesity. Individualized dosing based on body surface area has been associated with shorter time to therapeutic success [158,161]. Obesity may also prolong microbiological clearance in patients receiving standard-dose anidulafungin [162]. Therapeutic drug monitoring is supported for selected agents, including posaconazole, voriconazole, and flucytosine, to optimize efficacy and limit toxicity [146,158].

Emerging Antifungal Agents

Rezafungin is a long-acting echinocandin that inhibits β-(1,3)-D-glucan synthesis. Clinical trials have demonstrated non-inferiority to caspofungin, with a weekly dosing regimen and an acceptable safety profile [163,164]. Its prolonged exposure and potential activity against resistant species may offer advantages in selected patients. Fosmanogepix, a prodrug of manogepix, represents another promising agent. It inhibits the fungal enzyme Gwt1 and has demonstrated activity against several yeasts, including *C. auris*. A phase II study reported an 80% treatment success rate and 85% 30-day survival among patients with candidemia [18]. Further clinical evaluation and regulatory approval are needed before routine use.

Complementary Management and Follow-Up

Antifungal therapy should be combined with appropriate source control. Removal of infected vascular catheters is recommended as early as possible, preferably within 48–72 hours when clinically feasible [123,146]. Although studies report variable effects of early removal after adjustment for disease severity, retaining infected vascular access may contribute to persistent infection and recurrence [166,167]. When removal is not possible, antifungal selection should consider biofilm activity, with echinocandins and liposomal amphotericin B among the options investigated [169]. Ophthalmological examination is recommended by several international guidelines to identify ocular complications, although recommendations differ regarding routine screening in asymptomatic patients [123,170–172]. Consultation with infectious disease and clinical microbiology specialists also improves adherence to treatment recommendations and has been associated with lower 30- and 90-day mortality [131,177–180]. Overall, successful candidemia management requires early antifungal treatment, species identification, susceptibility-guided drug selection, appropriate source control, and individualized dosing. Integrating these measures with local epidemiological data and specialist assessment is essential to improve survival and reduce treatment failure.

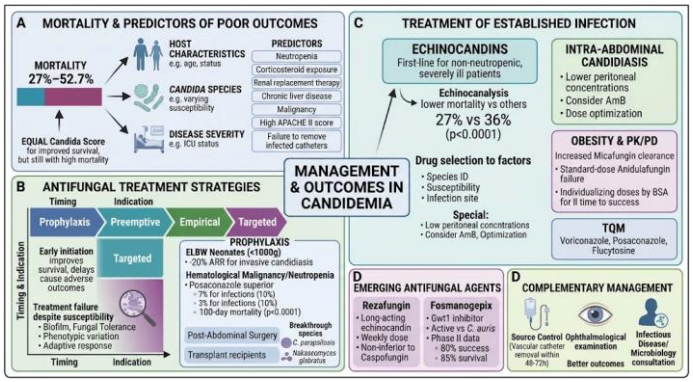


Figure-2: Treatment and Management of Candidemia.

Conclusion:

Candidemia remains a major clinical challenge because of its high mortality, evolving epidemiology, and increasing antifungal resistance. The growing contribution of non-albicans Candida species highlights the importance of accurate species identification and continuous regional surveillance. Although blood cultures remain the diagnostic reference standard, their limited sensitivity and delayed results emphasize the need for rapid molecular assays, biomarkers, and emerging diagnostic technologies. Echinocandins remain the preferred initial treatment for many non-neutropenic patients, while therapeutic decisions should account for antifungal susceptibility, infection site, disease severity, and pharmacokinetic and pharmacodynamic characteristics. Prophylaxis in selected high-risk populations, timely vascular catheter removal, ophthalmological assessment, and specialist consultation also contribute to appropriate management. Rezafungin and fosmanogepix represent promising developments, although further evidence is needed to establish their roles in routine practice. Ultimately, reducing candidemia-associated mortality requires an integrated approach combining

early diagnosis, individualized antifungal therapy, effective source control, and adherence to evidence-based recommendations.

References:

1. Mora Carpio, A.L.; Climaco, A. Candidemia. In *StatPearls*; StatPearls Publishing: Treasure Island, FL, USA, 2025.
2. Lass-Flörl, C.; Kanj, S.S.; Govender, N.P.; Thompson, G.R.; Ostrosky-Zeichner, L.; Govrins, M.A. Invasive candidiasis. *Nat. Rev. Dis. Prim.* **2024**, *10*, 20.
3. McCarty, T.P.; White, C.M.; Pappas, P.G. Candidemia and Invasive Candidiasis. *Infect. Dis. Clin. N. Am.* **2021**, *35*, 389–413.
4. Uraguchi, K.; Makino, T.; Kariya, S.; Noda, Y.; Marunaka, H.; Doi, A.; Kozakura, K.; Takao, S.; Ando, M. Candidemia in patients with head and neck cancer: Mortality and a novel risk factor. *Support. Care Cancer* **2022**, *30*, 5921–5930.
5. Atiencia-Carrera, M.B.; Cabezas-Mera, F.S.; Tejera, E.; Machado, A. Prevalence of biofilms in *Candida* spp. bloodstream infections: A meta-analysis. *PLoS ONE* **2022**, *17*, e0263522.
6. Harchand, R.; Spruijtenburg, B.; Meijer, E.F.J.; de Groot, T.; Rudramurthy, S.M.; Meis, J.F. *Candida vulturna*, the Next Fungal Menace? A Narrative Review. *Mycoses* **2025**, *68*, e70070.
7. Pérez-Camacho, P.M.; Vargas-Moran, C.; Torres-Canchala, L.; Ariza-Insignares, C.; Sandoval-Calle, L.M.; Gómez-Hernández, I.E.; Solís-Núñez, P.; Cedeño-Castaño, J.V.; Aguilar-González, A.M.; Patiño-Niño, J.A. Epidemiological characteristics of pediatric patients with invasive candidiasis in an intensive care unit in southwestern Colombia. *Biomedica* **2025**, *45*, 151–164.
8. Cook, A.; Ferreras-Antolin, L.; Adhisivam, B.; Ballot, D.; Berkley, J.A.; Bernaschi, P.; Carvalheriro, C.G.; Chaikittisuk, N.; Chen, Y.; Chibabhai, V. Neonatal invasive candidiasis in low- and middle-income countries: Data from the NeoOBS study. *Med. Mycol.* **2023**, *61*, myad010.
9. Brescini, L.; Mazzanti, S.; Orsetti, E.; Morroni, G.; Masucci, A.; Pocognoli, A.; Barchiesi, F. Species distribution and antifungal susceptibilities of bloodstream *Candida* isolates: A nine-years single center survey. *J. Chemother.* **2020**, *32*, 244–250.
10. Posteraro, B.; De Carolis, E.; Criscuolo, M.; Ballanti, S.; De Angelis, G.; Del Principe, M.I.; Delia, M.; Fracchiolla, N.; Marchesi, F.; Nadali, G. Candidaemia in haematological malignancy patients from a SEIFEM study: Epidemiological patterns according to antifungal prophylaxis. *Mycoses* **2020**, *63*, 900–910.
11. Egger, M.; Salmanton-García, J.; Barac, A.; Gangneux, J.P.; Guegan, H.; Arsic-Arsenijevic, V.; Matos, T.; Tomazin, R.; Klimko, N.; Bassetti, M.; et al. ECMM Candida III Study Group Predictors for Prolonged Hospital Stay Solely to Complete Intravenous Antifungal Treatment in Patients with Candidemia: Results from the ECMM *Candida* III multinational European observational cohort study. *Mycopathologia* **2023**, *188*, 983–994.
12. Liu, T.; Sun, S.; Zhu, X.; Wu, H.; Sun, Z.; Peng, S. Epidemiology, clinical characteristics, and outcome in candidemia: A retrospective five-year analysis from two tertiary general hospitals. *BMC Infect. Dis.* **2025**, *25*, 512.
13. Zhang, W.; Song, X.; Wu, H.; Zheng, R. Epidemiology, species distribution, and predictive factors for mortality of candidemia in adult surgical patients. *BMC Infect. Dis.* **2020**, *20*, 506.
14. Kajihara, T.; Yahara, K.; Nagi, M.; Kitamura, N.; Hirabayashi, A.; Hosaka, Y.; Abe, M.; Miyazaki, Y.; Sugai, M. Distribution, trends, and antifungal susceptibility of *Candida* species causing candidemia in Japan, 2010–2019: A retrospective observational study based on national surveillance data. *Med. Mycol.* **2022**, *60*, myac071.
15. Doğan, Ö.; Yeşilkaya, A.; Menekşe, Ş.; Güler, Ö.; Karakoç, Ç.; Çınar, G.; Kapmaz, M.; Aydin, M.; Keske, S.; Sahin, S.; et al. Effect of initial antifungal therapy on mortality among patients with bloodstream infections with different *Candida* species and resistance to antifungal agents: A multicentre observational study by the Turkish Fungal Infections Study Group. *Int. J. Antimicrob. Agents* **2020**, *56*, 105992.
16. Arastehfar, A.; Yazdanpanah, S.; Bakhtiari, M.; Fang, W.; Pan, W.; Mahmoudi, S.; Pakshir, K.; Daneshina, F.; Boekhout, T.; Ilkit, M.; et al. Epidemiology of candidemia in Shiraz, southern Iran: A prospective multicenter study (2016–2018). *Med. Mycol.* **2021**, *59*, 422–430.
17. Szekely, J.; Rakchang, W.; Rattanaphan, P.; Kositpantawong, N. Fluconazole and echinocandin resistance of *Candida* species in invasive candidiasis at a university hospital during pre-COVID-19 and the COVID-19 outbreak. *Epidemiol. Infect.* **2023**, *151*, e146.
18. Pappas, P.G.; Vazquez, J.A.; Oren, I.; Rahav, G.; Aoun, M.; Bulpa, P.; Ben-Ami, R.; Ferrer, R.; Mccarty, T.; Thompson, G.R.; et al. Clinical safety and efficacy of novel antifungal, fosmanogepix, for the treatment of candidaemia: Results from a Phase 2 trial. *J. Antimicrob. Chemother.* **2023**, *78*, 2471–2480.
19. Shuping, L.; Mpembe, R.; Mhlanga, M.; Naicker, S.D.; Maphanga, T.G.; Tsotetsi, E.; Wadula, J.; Velaphi, S.; Nakwa, F.; Chibabhai, V. Epidemiology of culture-confirmed candidemia among hospitalized children in South Africa, 2012–2017. *Pediatr. Infect. Dis. J.* **2021**, *40*, 730–737.

20. Huang, Y.S.; Wang, F.D.; Chen, Y.C.; Huang, Y.T.; Hsieh, M.H.; Hii, I.M.; Lee, Y.L.; Ho, M.W.; Liu, C.E.; Chen, Y.H.; et al. High rates of misidentification of uncommon *Candida* species causing bloodstream infections using conventional phenotypic methods. *J. Formos. Med. Assoc.* **2021**, *120*, 1179–1187.
21. Mirza, A.; Senol, E.; Kalkanci, A. Epidemiology and risk factors of candidemia among hospitalized patients in a Turkish tertiary care hospital. *Clin. Lab.* **2022**, *68*.
22. Sathi, F.A.; Alam, M.M.; Haque, N.; Khan, M.J.A.; Mamun, A.A.; Hossain, T.; Chowdhury, C.S.; Islam, M.N.; Ferdaus, S.J.; Sultana, M. An alarming rise of candidemia caused by non-*albicans Candida* species in intensive care unit in Mymensingh, Bangladesh. *Mymensingh Med.* **2024**, *33*, 671–676.
23. Corzo-Leon, D.E.; Peacock, M.; Rodriguez-Zulueta, P.; Salazar-Tamayo, G.J.; MacCallum, D.M. General hospital outbreak of invasive candidiasis due to azole-resistant *Candida parapsilosis* associated with an Erg11 Y132F mutation. *Med. Mycol.* **2021**, *59*, 664–671.
24. Kerai, A.; Doshi, S.; Laleker, A.; Majumdar, A. Fungal foe and mechanical hearts: A retrospective case series on *Candida auris* bloodstream infection with left ventricular assist devices. *Open Forum Infect. Dis.* **2024**, *11*, ofae286.
25. Cabanilla, M.G.; Villalobos, N. A successful daptomycin and micafungin dosing strategy in veno-venous ECMO and continuous renal replacement. *J. Clin. Pharm. Ther.* **2022**, *47*, 251–253.
26. Bartolo, C.; Hall, V.; Friedman, N.D.; Lanyon, C.; Fuller, A.; Morrissey, C.O.; Athan, E. Bittersweet: Infective complications of drug-induced glycosuria in patients with diabetes mellitus on SGLT2-inhibitors: Two case reports. *BMC Infect. Dis.* **2021**, *21*, 284.
27. Rahimli, L.; Salmanton-García, J.; Kasper, P.; Simon, M.; Cornely, O.A.; Stemler, J. Necrotizing pancreatitis with invasive candidiasis and candidemia due to *Candida albicans* and pan-echinocandin-resistant *Candidaglabrata*. *Med. Mycol. Case Rep.* **2024**, *43*, 100636.
28. Rodríguez de la Garza, P.; Cruz-de la Cruz, C.; Bejarano, J.I.C.; Romo, A.E.L.; Delgado, J.V.; Ramos, B.A.; Martínez Neira, M.N.; Siller Rodríguez, D.; Sánchez Rodríguez, H.M.; Rangel Selvera, O.A. A multicentric outbreak of *Candida auris* in Mexico: 2020 to 2023. *Am. J. Infect. Control* **2024**, *52*, 1384–1389.
29. Vazquez, J.A.; Pappas, P.G.; Boffard, K.; Paruk, F.; Bien, P.A.; Tawadrous, M.; Ople, E.; Wedel, P.; Oborska, I.; Hodges, M.R. Clinical Efficacy and safety of a novel antifungal, fosmanogepix, in patients with candidemia caused by *Candida auris:* Results from a phase 2 trial. *Antimicrob. Agents Chemother.* **2023**, *67*, e0141922.
30. Randazza, O.; Erickson, K.; Denmeade, T.; Luther, V.; Palavecino, E.; Beardsley, J. Treatment of *Candida nivariensis* blood stream infection with oral isavuconazole. *Cureus* **2022**, *14*, e32137.
31. Griffith, E.M.; Marsalisi, C.; Verdecia, J.; Buchanan, S.R.; Goulart, M.A. Recurrent fungemia due to *Candida auris*. *Cureus* **2024**, *16*, e62478.
32. Lingas, E.; Lucio Paredes, M.D.M.; Jahan, M.; Bathina, P.; Dahdouh, M. A Case of *Candida auris* candidemia in an immunocompetent traumatic brain injury patient post ventriculoperitoneal shunt and peripherally inserted central catheter line. *Cureus* **2020**, *12*, e8850.
33. Xie, O.; Streitberg, R.; Hughes, C.; Stuart, R.; Graham, M. *Candida duobushaemulonii* sepsis and *Candida auris* co-isolation following hospitalisation in Vietnam. *Pathology* **2020**, *52*, 590–591.
34. Katsiari, M.; Nikolaou, C.; Palla, E.; Theodoridou, K.; Tsakris, A.; Vrioni, G. Impact of *Candida auris* on critically ill patients: A three-year observational study in a Greek intensive care unit. *Pathogens* **2025**, *14*, 328.
35. Rimoldi, S.G.; Nodari, R.; Rizzo, A.; Tamoni, A.; Longobardi, C.; Pagani, C.; Grosso, S.; Salari., F.; Galimberti, L.; Olivieri, P. First imported case of *Candida auris* infection in Milan, Italy: Genomic characterisation. *Infection* **2024**, *52*, 1633–1638.
36. Stolfa, S.; Caggiano, G.; Ronga, L.; Dalfino, L.; Centrone, F.; Sallustio, A.; Sacco, D.; Mosca, A.; Stufano, M.; Saracino, A.; et al. First case of *Candida auris* Sepsis in Southern Italy: Antifungal susceptibility and genomic characterisation of a difficult-to-treat emerging yeast. *Microorganisms* **2024**, *12*, 1962.
37. Reque, J.; Arlandis, R.; Panizo, N.; Pascual, M.J.; Perez-Alba, A. *Candida auris* invasive infection after kidney transplantation. *Case Rep. Nephrol.* **2022**, *2022*, 6007607.
38. Apsemidou, A.; Füller, M.A.; Idelevich, E.A.; Kurzai, O.; Tragiannidis, A.; Groll, A.H. *Candida lusitaniae* breakthrough fungemia in an immuno-compromised adolescent: Case report and review of the literature. *J. Fungi* **2020**, *6*, 380.
39. Mnichowska-Polanowska, M.; Adamowicz, M.; Wojciechowska-Koszko, I.; Kisiel, A.; Wojciuk, B.; Jarosz, K.; Dolegowska, B. Molecular investigation of the fatal bloodstream *Candida orthopsilosis* infection case following gastrectomy. *Int. J. Mol. Sci.* **2023**, *24*, 6541.

40. Tsai, Y.T.; Lu, P.L.; Tang, H.J.; Huang, C.H.; Hung, W.C.; Tseng, Y.T.; Lee, K.-M.; Lin, S.-Y. The first invasive *Candida auris* infection in Taiwan. *Emer. Microbes Infect.* **2022**, *11*, 1867–1875.
41. Ohashi, Y.; Matono, T.; Suzuki, S.; Yoshino, S.; Alshahni, M.M.; Komori, A.; Makimura, K. The first case of clade I *Candida auris* candidemia in a patient with COVID-19 in Japan. *J. Infect. Chemother.* **2023**, *29*, 713–717.
42. Murata, S.; Mimura, K.; Kawamura, T.; Saito, H.; Ohno, H.; Tsujii, E.; Shinohara, T.; Miyazaki, Y.; Ohki, T. Bloodstream infection caused by *Wickerhamiella pararugosa* in a patient with intestinal obstruction: A case report. *J. Infect. Chemother Off. J. Jpn. Soc. Chemother.* **2024**, *30*, 942–945.
43. Xu, Z.; Zhang, L.; Han, R.; Ding, C.; Shou, H.; Duan, X.; Zhang, S. A candidemia case caused by a novel drug-resistant *Candida auris* with the Y132F mutation in Erg11 in Mainland China. *Infect. Drug Resist.* **2023**, *16*, 3065–3072.
44. Aboutalebian, S.; Nikmanesh, B.; Mohammadpour, M.; Charsizadeh, A.; Mirhend, H. *Candida palmioleophila* candidemia and bacterial co-infection in a 3-month-old infant with biliary atresia. *Front. Cell Infect. Microbiol.* **2023**, *13*, 1277607.
45. Awada, B.; Alam, W.; Chalfoun, M.; Araj, G.; Bizri, A.R. COVID-19 and *Candida duobushaemulonii* superinfection: A case report. *J. Mycol. Med.* **2021**, *31*, 101168.
46. Alashqar, M.B.; Alabdan, L.; Khan, M.; Almakadma, A.H.; Almustanyir, S. A case report of a *Candida auris* infection in Saudi Arabia. *Cureus* **2021**, *13*, e15240.
47. Mirhendi, H.; Charsizadeh, A.; Aboutalebian, S.; Mohammadpour, M.; Nikmanesh, B.; de Groot, T.; Meis, J.F.; Badali, H. South Asian (Clade I) *Candida auris* meningitis in a paediatric patient in Iran with a review of the literature. *Mycoses* **2022**, *65*, 134–139.
48. Mallick, D.C.; Kaushik, N.; Goyal, L.; Mallick, L.; Singh, P. A Comprehensive Review of Candidemia and Invasive Candidiasis in Adults: Focus on the Emerging Multidrug-Resistant Fungus *Candida auris*. *Diseases* **2025**, *13*, 93. [
49. Li, Y.; Gu, C.; Yang, Y.; Ding, Y.; Ye, C.; Tang, M.; Liu, J.; Zeng, Z. Epidemiology, antifungal susceptibility, risk factors, and mortality of persistent candidemia in adult patients in China: A 6-year multicenter retrospective study. *BMC Infect. Dis.* **2023**, *23*, 369.
50. Zeng, Z.; Ding, Y.; Tian, G.; Yang, K.; Deng, J.; Li, G.; Liu, J. A seven-year surveillance study of the epidemiology, antifungal susceptibility, risk factors and mortality of candidaemia among paediatric and adult inpatients in a tertiary teaching hospital in China. *Antimicrob. Resist. Infect. Control* **2020**, *9*, 133.
51. Zeeshan, M.; Memon, S.; Malick, A.; Naqvi, S.F.; Farooqi, J.; Ghanchi, N.K.; Jabeen, K. Fluconazole-resistant *Candida parapsilosis* complex candidemia and analysis of mutations in the ERG11 gene from Pakistan. *Mycoses* **2024**, *67*, e13677.
52. Salmanton-García, J.; Cornely, O.A.; Stemler, J.; Barać, A.; Steinmann, J.; Siváková, A.; Akalin, E.H.; Arikan-Akdagli, S.; Loughlin, L.; Toscano, C.; et al. Attributable mortality of candidemia—Results from the ECMM Candida III multinational European Observational Cohort Study. *J. Infect.* **2024**, *89*, 106229.
53. Khan, Z.; Ahmad, S.; Al-Sweih, N.; Mokaddas, E.; Al-Banwan, K.; Alfouzan, W.; Al-Obaid, I.; Al-Obaid, K.; Asadzadeh, M.; Jeragh, A.; et al. Changing trends in epidemiology and antifungal susceptibility patterns of six bloodstream *Candida* species isolates over a 12-year period in Kuwait. *PLoS ONE* **2019**, *14*, e0216250.
54. Guinea, J. Global trends in the distribution of *Candida* species causing candidemia. *Clin. Microbiol. Infect.* **2014**, *20* (Suppl. 6), 5–10.
55. Lamba, M.; Sharma, D.; Sharma, R.; Vyas, A.; Mamoria, V. To study the profile of *Candida* isolates and antifungal susceptibility pattern of neonatal sepsis in a tertiary care hospital of North India. *J. Matern. Fetal Neonatal Med.* **2021**, *34*, 2655–2659.
56. Subba, S.H.; Sharma, T.D.; Dopthapa, Y.P.; Bhutia, U.G.N.; Sharma, R. *Candida glabrata* meningitis in a patient with newly diagnosed acquired immunodeficiency syndrome from Sikkim, India. *Curr. Med. Mycol.* **2024**, *10*, e2024.345242.1542.
57. Najafzadeh, M.J.; Shaban, T.; Zarrinfar, H.; Sedaghat, A.; Hosseinikargar, N.; Berenji, F.; Jalali, M.; Lackner, M.; James, J.E.; Iikit, M. COVID-19 associated candidemia: From a shift in fungal epidemiology to a rise in azole drug resistance. *Med. Mycol.* **2024**, *62*, myae031.
58. Arastehfar, A.; Hilmioğlu-Polat, S.; Daneshnia, F.; Hafez, A.; Salehi, M.; Polat, F.; Yasar, M.; Arslan, N.; Hosbul, T.; Unal, N.; et al. Recent increase in the prevalence of fluconazole-non-susceptible *Candida tropicalis* blood isolates in Turkey: Clinical implication of azole-non-susceptible and fluconazole tolerant phenotypes and genotyping. *Front. Microbiol.* **2020**, *11*, 587278.
59. Ponta, G.; Morena, V.; Strano, M.; Molteni, C.; Pontiggia, S.; Cavalli, E.M.; Grancini, A.; Mauri, C.; Castagna, A.; Galanti, A.; et al. Safety of rezafungin as a long-term treatment option in two patients with complicated fungal infections: Two cases from Lecco Hospital (Italy). *Antimicrob. Agents Chemother.* **2024**, *68*, e0075024.
60. Trovato, L.; Bongiorno, D.; Calvo, M.; Migliorisi, G.; Boraccino, A.; Musso, N.;

Oliveri, S.; Stefani, S.; Scalia, G. Resistance to echinocandins complicates a case of *Candida albicans* bloodstream infection: A case report. *J. Fungi* **2021**, *7*, 405.
61. Teixeira da Silva, F.; Cardoso, F.S.; Esteves, A.; Carvalho, J.; Maia, R. Relapsing *Candida parapsilosis* endocarditis with septic embolization: A case report. *Cureus* **2021**, *13*, e13159.
62. Arastehfar, A.; Daneshnia, F.; Hafez, A.; Khodavaisy, S.; Najafzadeh, M.J.; Charsizadeh, A.; Zarrinfar, H.; Salehi, M.; Shahrabadi, Z.Z.; Sasani, E. Antifungal susceptibility, genotyping, resistance mechanism, and clinical profile of *Candida tropicalis* blood isolates. *Med. Mycol.* **2020**, *58*, 766–773.
63. Alghamdi, A.; Oravec, T.; Nishi, C.; Eckbo, E.; Marcon, K.; Wright, A.; Mah, A.; White, J.; Nevill, T.; Belga, S. Severe hypercalcemia as a result of disseminated *Candida krusei* infection. *Int. J. Infect. Dis.* **2024**, *140*, 110–112.
64. Prabhudas-Strycker, K.K.; Butt, S.; Reddy, M.T. *Candida tropicalis* endocarditis successfully treated with AngioVac and micafungin followed by long-term isavuconazole suppression. *IDCases* **2020**, *21*, e00889.
65. Paucar-Miranda, C.J.; Sandoval-Ahumada, R.E.; López-Martínez, R.L.; Terrel-Gutierrez, L.; Zurita-Macalapu, S.; Urcia-Ausejo, F.; Flores-León, D.; Gavilan-Chávez, R.; Quispe-Pardo, Z.; Yagui-Moscoso, M. Primer reporte de *Candida auris* en Perú. *An. Fac. Med.* **2021**, *82*, 56–61.
66. Li, Y.; Hind, C.; Furner-Pardoe, J.; Sutton, J.M.; Rahman, K.M. Understanding the mechanisms of resistance to azole antifungals in *Candida* species. *JAC-Antimicrob. Resist.* **2025**, *7*, dlaf106.
67. Pristov, K.E.; Ghannoum, M.A. Resistance of *Candida* to azoles and echinocandins worldwide. *Clin. Microbiol. Infect.* **2019**, *25*, 792–798.
68. Carolus, H.; Pierson, S.; Lagrou, K.; Van Dijck, P. Anfotericin B and other polyenes: Discovery, clinical use, mode of action and drug rsistence. *J. Fungi* **2020**, *6*, 321.
69. Berman, J.; Krysan, D.J. Drug resistance and tolerance in fungi. *Nat. Rev. Microbiol.* **2020**, *18*, 539.
70. Czajka, K.M.; Venkataraman, K.; Brabant-Kirwan, D.; Santi, S.A.; Verschoor, C.; Appanna, V.D.; Singh, R.; Saunders, D.P.; Tharmalingam, S. Molecular Mechanisms Associated with Antifungal Resistance in Pathogenic *Candida* Species. *Cells* **2023**, *12*, 2655.
71. Wurster, S.; Albert, N.D.; Kontoyiannis, D.P. *Candida auris* Bloodstream Infection Induces Upregulation of the PD-1/PD-L1 Immune Checkpoint Pathway in an Immunocompetent Mouse Model. *mSphere* **2022**, *7*, e00817–e00821.
72. Pathakumari, B.; Liu, W.; Wang, Q.; Kong, X.; Liang, G.; Chokkakula, S.; Pathakamuri, V.; Nunna, V. Comparative Evaluation of Candida Species-Specific T-Cell Immune Response in Human Peripheral Blood Mononuclear Cells. *Biomedicines* **2024**, *12*, 1487.
73. Carey, B.; Lambourne, J.; Porter, S.; Hodgson, T. Chronic mucocutaneous candidiasis due to gain-of-function mutation in STAT1. *Oral Dis.* **2019**, *25*, 684–692.
74. Okada, S.; Markle, J.G.; Deenick, E.K.; Mele, F.; Averbuch, D.; Lagos, M. Impairment of immunity to Candida and Mycobacterium in humans with bi allelic RORC mutations. *Science* **2015**, *349*, 606–613.
75. Smeekens, S.P.; Plantinga, T.S.; van de Veerdonk, F.L.; Heinhuis, B.; Hoischen, A.; Joosten, L.A. *STAT1* hyperphosphorylation and defective IL12R/IL23R signaling underlie defective immunity in autosomal dominant chronic mucocutaneous candidiasis. *PLoS ONE* **2011**, *6*, e29248.
76. Zaongo, S.D.; Jing, O.; Stéphane, I.; Xin, Z.; Vijay, H.; Hongjuan, C.; Routy, J.-P.; Chen, Y. *Candida albicans* can foster gut dysbiosis and systemic inflammation during HIV infection. *Gut Microbes* **2023**, *15*, 2167171.
77. Savage, H.P.; Bays, D.J.; Tiffany, C.R.; Gonzalez, M.A.F.; Bejarano, E.J.; Carvalho, T.P.; Luo, Z.; Masson, H.L.P.; Nguyen, H.; Santos, R.L.; et al. Epithelial hypoxia maintains colonization resistance against *Candida albicans*. *Cell Host Microbe* **2024**, *32*, 1103–1113.e1106.
78. Guinan, J.; Wang, S.; Hazbun, T.R.; Yadav, H.; Thangamani, S. Antibiotic-induced decreases in the levels of microbial-derived short-chain fatty acids correlate with increased gastrointestinal colonization of *Candida albicans*. *Sci. Rep.* **2019**, *9*, 8872.
79. Huang, D.; Li, H.; Lin, Y.; Lin, J.; Li, C.; Kuang, Y.; Zhou, W.; Huang, B.; Wang, P. Antibiotic-induced depletion of *Clostridium* species increases the risk of secondary fungal infections in preterm infants. *Front. Cell. Infect. Microbiol.* **2022**, *12*, 981823.
80. Bromuro, C.; Posteraro, B.; Murri, R.; Fantoni, M.; Tumbarello, M.; Sanguinetti, M.; Dattilo, R.; Cauda, R.; Cassone, A.; Torosantucci, A. Identification of two anti *Candida* antibodies associated with the survival of patients with candidemia. *mBio* **2024**, *15*, e02769-23.
81. Sari, N.; Yanik Yalçin, T.; Erol, Ç.; Kurt Azap, Ö.; Arslan, H.; Karakaya, E.; Sezgin, A.; Haberal, M. Evaluation of Candidemia in Solid-Organ Transplant Recipients. *Exp. Clin. Transplant.* **2024**, *22*, 160–166.

82. Marinelli, T.; Pennington, K.M.; Hamandi, B.; Donahoe, L.; Rotstein, C.; Martinu, T.; Husain, S. Epidemiology of candidemia in lung transplant recipients and risk factors for candidemia in the early posttransplant period in the absence of universal antifungal prophylaxis. *Transpl. Infect. Dis.* **2022**, *24*, e13812.
83. Puel, A. Human inborn errors of immunity underlying superficial or invasive candidiasis. *Hum. Genet.* **2020**, *139*, 1011–1022.
84. Silvester, E.J.; Watanabe, M.M.Y.; Pittet, L.F.; Boast, A.; Bryant, P.A.; Haeusler, G.M.; Daley, A.J.; Curtis, N.; Gwee, A. Candidemia in Children: A 16-year Longitudinal Epidemiologic Study. *Pediatr. Infect. Dis. J.* **2021**, *40*, 537–543.
85. Keighley, C.L.; Pope, A.; Marriott, D.J.E.; Chapman, B.; Bak, N.; Daveson, K. Risk factors for candidaemia: A prospective multi-centre case-control study. *Mycoses* **2021**, *64*, 257–263.
86. Rodrigues, C.F.; Rodrigues, M.E.; Henriques, M. *Candida* sp. Infections in Patients with Diabetes Mellitus. *J. Clin. Med.* **2019**, *8*, 76
87. Quiros-Roldan, E.; Sottini, A.; Natali, P.G.; Imberti, L. The Impact of Immune System Aging on Infectious Diseases. *Microorganisms* **2024**, *12*, 775.
88. Hesstvedt, L.; Gaustad, P.; Müller, F.; Torp Andersen, C.; Brunborg, C.; Mylvaganam, H.; leiva, R.A.; Berdal, J.E.; Ranheim, T.E.; Johnsen, B.O.; et al. The impact of age on risk assessment, therapeutic practice and outcome in candidemia. *Infect. Dis.* **2019**, *51*, 425–434.
89. Nascimento, T.; Inácio, J.; Guerreiro, D.; Patrício, P.; Proença, L.; Toscano, C.; Diaz, P.; Barroso, H. Insights into *Candida* Colonization in Intensive Care Unit Patients: A Prospective Multicenter Study. *J. Fungi* **2024**, *10*, 378.
90. Bassetti, M.; Vena, A.; Giacobbe, D.R.; Trucchi, C.; Ansaldi, F.; Antonelli, M.; Adamkova, V.; Alicino, C.; Almyroudi, M.-P.; Atchade, E.; et al. Risk Factors for Intra-Abdominal Candidiasis in Intensive Care Units: Results from EUCANDICU Study. *Infect. Dis. Ther.* **2022**, *11*, 827–840.
91. Thomas-Rüddel, D.O.; Schlattmann, P.; Pletz, M.; Kurzai, O.; Bloos, F. Risk Factors for Invasive *Candida* Infection in Critically Ill Patients: A Systematic Review and Meta-analysis. *Chest* **2022**, *161*, 345–355.
92. Dougherty, J.; Turner, N.A.; Yarrington, M.E.; Shaefer Spires, S.; Rebekah, W.M.; Alexander, B.D.; Park, L.P.; Johnson, M.D. Cumulative Antibiotic Exposure and Risk for Candidemia. *Open Forum Infect. Dis.* **2022**, *9*, ofac492.099.
93. Jung, P.; Mischo, C.E.; Gunaratnam, G.; Spengler, C.; Becker, S.L.; Hube, B.; Jacobs, K.; Bischoff, M. *Candida albicans* adhesion to central venous catheters: Impact of blood plasma-driven germ tube formation and pathogen-derived adhesins. *Virulence* **2020**, *11*, 1453–1465.
94. Huang, L.; Li, S.; Jiang, R.; Lei, S.; Wu, J.; Huang, L.; Zhu, M. Glucocorticoid use and parenteral nutrition are risk factors for catheter-related Candida bloodstream infection: A retrospective study. *Asian Biomed. (Res. Rev. News)* **2024**, *18*, 109–115.
95. Malinovská, Z.; Čonková, E.; Váczi, P. Biofilm Formation in Medically Important *Candida* Species. *J. Fungi* **2023**, *9*, 955.
96. Gulati, M.; Nobile, C.J. *Candida albicans* biofilms: Development, regulation, and molecular mechanisms. *Microbes Infect.* **2016**, *18*, 310–321.
97. Oliva, A.; Venditti, M. Candidiasis invasiva en cirugía. In *Infecciones en Cirugía. Actualizaciones en Cirugía*; Bartoli, S., Cortese, F., Sartelli, M., Sganga, G., Eds.; Springer: Cham, Switzerland, 2025.
98. Meng, Y.; Kang, M.; Li, D.; Wang, T.; Kuang, Z.; Ma, Y. Performance of a new *Candida* anti-mannan IgM and IgG assays in the diagnosis of candidemia. *Rev. Inst. Med. Trop. Sao Paulo* **2020**, *62*, e25.
99. Barantsevich, N.; Barantsevich, E. Diagnosis and Treatment of Invasive Candidiasis. *Antibiotics* **2022**, *11*, 718.
100. Montagna, M.T.; Coretti, C.; Rella, A.; Barbuti, G.; Manca, F.; Montagna, O.; Laforgia, N.; Caggiano, G. The role of procalcitonin in neonatal intensive care unit patients with candidemia. *Folia Microbiol.* **2013**, *58*, 27–31.
101. Cortegiani, A.; Misseri, G.; Ippolito, M.; Bassetti, M.; Giarratano, A.; Martin-Loeches, I.; Einav, S. Procalcitonin levels in candidemia versus bacteremia: A systematic review. *Crit. Care* **2019**, *23*, 190.
102. Chen, B.; Li, W.; Pang, Y.; Zhang, N.; Bian, S.; Liu, C.; Yang, Z.; Jiang, Y.; Li, R.; Xie, Y.; et al. Rapid detection of fungi from blood samples of patients with candidemia using modified calcofluor white stain. *J. Microbiol. Methods* **2021**, *184*, 106202.
103. Kaur, H.; Kanaujia, R.; Singh, S.; Kajal, K.; Jayashree, M.; Peter, N.J.; Verma, S.; Gupta, M.; Ray, P.; Ghosh, A.; et al. Clinical utility of time to positivity of blood cultures in cases of fungaemia: A prospective study. *Indian. J. Med. Microbiol.* **2023**, *43*, 85–89
104. Keighley, C.; Pope, A.L.; Marriott, D.; Chen, S.C.; Slavin, M.A.; Australia and New Zealand Mycoses Interest Group. Time-to-positivity in bloodstream infection for Candida species as a prognostic marker for mortality. *Med. Mycol.* **2023**, *61*, myad028.
105. Bonfim-Mendonça, P.d.S.; Fiorini, A.; Shinobu-Mesquita, C.S.; Baeza, L.C.; Fernandez, M.A.; Svidzinski, T.I. Molecular typing of *Candida*

albicans isolates from hospitalized patients. *Rev. Inst. Med. Trop.* **2013**, *55*, 385–391.
106. Camp, I.; Spettel, K.; Willinger, B. Molecular Methods for the Diagnosis of Invasive Candidiasis. *J. Fungi* **2020**, *6*, 101.
107. Mesini, A.; Mikulska, M.; Giacobbe, D.R.; Del Puente, F.; Gandolfo, N.; Codda, G.; Orsi, A.; Tassinari, F.; Beltramini, S.; Marchese, A.; et al. Changing epidemiology of candidaemia: Increase in fluconazole-resistant *Candida parapsilosis*. *Mycoses* **2020**, *63*, 361–368.
108. Daneshnia, F.; Hilmioğlu-Polat, S.; Ilkit, M.; Fuentes, D.; Lombardi, L.; Binder, U.; Scheler, J.; Hagen, F.; Mansour, M.K.; Butler, G.; et al. Whole-genome sequencing confirms a persistent candidaemia clonal outbreak due to multidrug-resistant Candida parapsilosis. *J. Antimicrob. Chemother.* **2023**, *78*, 1488–1494.
109. Monday, L.M.; Parraga Acosta, T.; Alangaden, G. T2Candida for the Diagnosis and Management of Invasive *Candida* Infections. *J. Fungi* **2021**, *7*, 178.
110. Park, K.; Huh, J.W.; Choi, S.H.; Sung, H.; Kim, M.N. Clinical evaluation of the T2Candida assay for the rapid diagnosis of candidemia. *Diagn. Microbiol. Infect. Dis.* **2024**, *110*, 116406.
111. Krifors, A.; Ullberg, M.; Castegren, M.; Petersson, J.; Sparrelid, E.; Hammarström, H.; Sjolin, J.; Ozenci, V.; Blennow, O. T2Candida Assay in the Diagnosis of Intraabdominal Candidiasis: A Prospective Multicenter Study. *J. Fungi* **2022**, *8*, 86.
112. Camp, I.; Füszl, A.; Selitsch, B.; Kröckel, I.; Kovac, K.; Wahrmann, M.; Steinlechner, B.; Weber, J.; Schellongowski, P.; Zauner, C.; et al. Is the T2MR Candida Panel a suitable alternative to the SeptiFast for the rapid diagnosis of candidemia in routine clinical practice? *Clin. Microbiol. Infect.* **2024**, *30*, 816–821.
113. Park, B.; Oh, E.H.; Won, E.J.; Kang, J.; Jin, D.; Yoo, C.; Park, J.; Sung, H.; Kim, M.-N. Detection of clinically relevant *Candida* species from positive blood cultures using a novel sample-to-answer molecular assay. *Sci. Rep.* **2025**, *15*, 5417.
114. Balaji, L.; Manoharan, H.; Prabhakaran, N.; Manivannan, N. Time-to-Positivity for *Candida* in Bloodstream Infections: Prognostic Implications for Mortality. *Cureus* **2024**, *16*, e66364.
115. Aziz, H.S.A.; Ismail, D.K.; Mohammed, N.S.A.; Elgendy, M.O.; Bassiouny, D.M. Distribution and antifungal susceptibility profiles of Candida species isolated from candidemia patients admitted to Egyptian tertiary hospitals: A cross-sectional study. *BMC Infect. Dis.* **2024**, *24*, 1177.
116. de Souza, Â.C.; Pereira, D.C.; Barth, P.O.; Roesch, E.W.; Lutz, L.; Aquino, V.R.; Goldani, L.Z. Rapid identification, fluconazole and micafungin susceptibility testing of *Candida* species from blood culture by a short incubation method. *Diagn. Microbiol. Infect. Dis.* **2024**, *109*, 116271.
117. Meawed, T.E.; AlNakeera, A.M.; Attia, O.; Hassan, N.A.M.; Anis, R.H. *Candida auris* central line-associated blood stream infection in critically ill patients: The worst end of a bad scenario. *Int. Microbiol.* **2025**, *28*, 377–383.
118. Peter Donnelly, J.; Chen, S.C.; Kauffman, C.A.; Steinbach, W.J.; Baddley, J.W.; Verweij, P.E.; Clancy, C.J.; Wingard, J.R.; Lockhart, S.R.; Groll, A.H.; et al. Revision and Update of the Consensus Definitions of Invasive Fungal Disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. *Clin. Infect. Dis.* **2020**, *71*, 1367–1376.
119. Dobiáš, R.; Káňová, M.; Petejová, N.; Pisti, Š.K.; Bocek, R.; Krejčí, E.; Struzkoca, H.; Cachová, M.; Tomasková, H.; Hamal, P.; et al. Combined Use of Presepsin and (1, 3)-β-D-glucan as Biomarkers for Diagnosing *Candida* Sepsis and Monitoring the Effectiveness of Treatment in Critically Ill Patients. *J. Fungi* **2022**, *8*, 308.
120. Zacharioudakis, I.M.; Zervou, F.N.; Marsh, K.; Siegfried, J.; Yang, J.; Decano, A.; Dubrovskaya, Y.; Mazo, D.; Aguero-Rosenfeld, M. Utility of incorporation of beta-D-glucan and T2Candida testing for diagnosis and treatment of candidemia. *Diagn. Microbiol. Infect. Dis.* **2024**, *108*, 116107.
121. Kinet-Poleur, A.; Deckers, C.; Saad Albichr, I.; Bogaerts, P.; Honoré, P.M.; Bulpa, P.; Ausselet, N.; Foret, F.; Kidd, F.; Huang, T.-D.; et al. Evaluation of Serum Biomarkers for Improved Diagnosis of Candidemia. *J. Fungi* **2025**, *11*, 224.
122. Lorenzo-Villegas, D.L.; Gohil, N.V.; Lamo, P.; Gurajala, S.; Bagiu, I.C.; Vulcanescu, D.D.; Horhat, F.G.; Sorop, V.B.; Diaconu, M.; Sorop, M.I.; et al. Innovative Biosensing Approaches for Swift Identification of *Candida* Species, Intrusive Pathogenic Organisms. *Life* **2023**, *13*, 2099.
123. Martin-Loeches, I.; Antonelli, M.; Cuenca-Estrella, M.; Dimopoulos, G.; Einav, S.; De Waele, J.J.; Garnacho-Montero, J.; Kanj, S.S.; Machado, F.R.; Montravers, P.; et al. ESICM/ESCMID task force on practical management of invasive candidiasis in critically ill patients. *Intensive Care Med.* **2019**, *45*, 789–805.
124. Pappas, P.G.; Kauffman, C.A.; Andes, D.R.; Clancy, C.J.; Marr, K.A.; Ostrosky-Zeichner, L.; Reboli, A.C.; Schuster, M.G.; Vazquez, J.A.; Walsh, T.J.; et al. Clinical Practice Guideline for

the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin. Infect. Dis.* **2015**, *62*, e1–e50.
125. Aydin, S.; Derin, O.; Sahin, M.; Dinleyici, R.; Yilmaz, M.; Ceylan, B.; Tosun, A.I.; Ozturk, R.; Mert, A. Epidemiology of Nosocomial Candidemia, Mortality, and Antifungal Resistance: 7-Year Experience in Turkey. *Jpn. J. Infect. Dis.* **2022**, *75*, 597–603.
126. Horn, D.L.; Neofytos, D.; Anaissie, E.J.; Fishman, J.A.; Steinbach, W.J.; Olyaei, A.J.; Marr, K.A.; Pfaller, M.A.; Chang, C.-H.; Webster, K.M. Epidemiology and outcomes of candidemia in 2019 patients: Data from the prospective antifungal therapy alliance registry. *Clin. Infect. Dis.* **2009**, *48*, 1695–1703.
127. Fang, X.; Su, C.; Luo, Y.; Pan, K.; Lin, J.; Song, Y.; Huang, Y.; Hu, X.; Shen, Z. Risk factors associated with short-term mortality in patients with candidemia and the predictive value of serum cytokine level. *Cytokine* **2025**, *185*, 156803.
128. Liu, F.; Shao, X.; Dong, Z.; Tang, K.; Zhong, L.; Xu, W.; Chen, Z.; Zheng, C.; Zhang, K.; Cai, J.; et al. Clinical characteristics and prognostic risk factors of candidemia in non-neutropenic patients: A retrospective cohort study. *Eur. J. Clin. Microbiol. Infect. Dis.* **2023**, *42*, 1389–1394.
129. Suh, J.W.; Kim, M.J.; Kim, J.H. Risk factors of septic shock development and thirty-day mortality with a predictive model in adult candidemia patients in intensive care units. *Infect. Dis.* **2021**, *53*, 908–919.
130. Kutlu, M.; Sayın-Kutlu, S.; Alp-Çavuş, S.; Öztürk, Ş.B.; Taşbakan, M.; Özhak, B.; Kaya, O.; Kutsoylu, O.E.; Senol-Akar, S.; Turhan, O.; et al. Mortality-associated factors of candidemia: A multi-center prospective cohort in Turkey. *Eur. J. Clin. Microbiol. Infect. Dis.* **2022**, *41*, 597–607.
131. Hoenigl, M.; Salmanton-García, J.; Egger, M.; Gangneux, J.P.; Bicanic, T.; Arikan-Akdagli, S.; Alastruey-Izquierdo, A.; Klimko, N.; Barac, A.; Ozenci, V.; et al. Guideline adherence and survival of patients with candidaemia in Europe: Results from the ECMM Candida III multinational European observational cohort study. *Lancet Infect. Dis.* **2023**, *23*, 751–761.
132. Sahoo, B.; Goyal, R.; Dutta, S.; Joshi, P.; Sanyal, K. *Candida albicans*: Insights into the Biology and Experimental Innovations of a Commonly Isolated Human Fungal Pathogen. *ACS Infect. Dis.* **2025**, *11*, 1780–1815.
133. Murphy, S.E.; Bicanic, T. Drug Resistance and Novel Therapeutic Approaches in Invasive Candidiasis. *Front. Cell. Infect. Microbiol.* **2021**, *11*, 759408.
134. Kollef, M.; Micek, S.; Hampton, N.; Doherty, J.A.; Kumar, A. Septic shock attributed to *Candida* infection: Importance of empiric therapy and source control. *Clin. Infect. Dis.* **2012**, *54*, 1739–1746.
135. Rouzé, A.; Loridant, S.; Poissy, J.; Dervaux, B.; Sendid, B.; Cornu, M.; Nseir, S.; Study Group S-TAFE. Biomarker-based strategy for early discontinuation of empirical antifungal treatment in critically ill patients: A randomized controlled trial. *Intensive Care Med.* **2017**, *43*, 1668–1677.
136. Paiva, J.A.; Charles, P.E. Biomarker-guided antifungal therapy in patients with suspected invasive candidiasis: Ready for prime time? *Intensive Care Med.* **2017**, *43*, 1889–1891.
137. Healy, C.M.; Baker, C.J.; Zaccaria, E.; Campbell, J.R. Impact of fluconazole prophylaxis on incidence and outcome of invasive candidiasis in a neonatal intensive care unit. *J. Pediatr.* **2005**, *147*, 166–171.
138. Kaufman, D.; Boyle, R.; Hazen, K.C.; Patrie, J.T.; Robinson, M.; Grossman, L.B. Twice weekly fluconazole prophylaxis for prevention of invasive *Candida* infection in high-risk infants of <1000 grams birth weight. *J. Pediatr.* **2005**, *147*, 172–179.
139. Cokro, F.; Yolanda, L.; Caroline, S.; Studi Farmasi, P.; Kedokteran dan Ilmu Kesehatan, F. Fluconazole Effectiveness in Preventing Invasive Fungal Infection in Very Low Birth Weight Infants: Systematic Review and Meta-analysis (Efektivitas Flukonazol dalam Mencegah Infeksi Jamur Invasif pada Bayi dengan Berat Lahir Sangat Rendah: Tinjauan Sistematis dan Meta-analisis). *J. Ilmu Kefarmasian Indonesia.* **2022**, *20*, 14–22.
140. Lona-Reyes, J.C.; Gómez-Ruiz, L.M.; Cordero-Zamora, A.; Cortés-González, S.I.; Quiles-Corona, M.; Pérez-Ramírez, R.O.; Pinto-Macedo, H. Incidence and factors associated with invasive candidiasis in a neonatal intensive care unit in Mexico. *An. Pediatr. (Engl. Ed.)* **2022**, *97*, 79–86.
141. Estagnasié, C.; Mohr, C.; Kamus, L.; Zunic, P.; Chirpaz, E.; Moiton, M.P.; Lagrange-Xelot, M. Invasive fungal infections in patients with haematological malignancies at the University Hospital of Reunion Island (2018–2022): An observational study. *Med. Mycol.* **2024**, *62*, myae102.
142. Cornely, O.A.; Maertens, J.; Winston, D.J.; Perfect, J.; Ullmann, A.J.; Walsh, T.J.; Helfgott, D.; Holowiecki, J.; Stockelberg, D.; Goh, Y.-T.; et al. Posaconazole vs. Fluconazole or Itraconazole Prophylaxis in Patients with Neutropenia. *N. Engl. J. Med.* **2007**, *356*, 348-59.
143. Boutin, C.A.; Durocher, F.; Beauchemin, S.; Ziegler, D.; Chakra, C.N.A.; Dufresne, S.F. Breakthrough Invasive Fungal Infections in Patients With High-Risk Hematological Disorders Receiving Voriconazole and

Posaconazole Prophylaxis: A Systematic Review. *Clin. Infect. Dis.* **2024**, *79*, 151–160.
144. Rausch, C.R.; DiPippo, A.J.; Jiang, Y.; DiNardo, C.D.; Kadia, T.; Maiti, A.; Montalban-Bravo, G.; Ravandi, F. Kontoyiannis, D.P. Comparison of Mold Active Triazoles as Primary Antifungal Prophylaxis in Patients with Newly Diagnosed Acute Myeloid Leukemia in the Era of Molecularly Targeted Therapies. *Clin. Infect. Dis.* **2022**, *75*, 1503–1510.
145. Calle-Miguel, L.; Garrido-Colino, C.; Santiago-García, B.; Moreno Santos, M.P.; Gonzalo Pascual, H.; Ponce Salas, B.; Beléndez Bieler, C.; Navarro Gómez, M.; Guinea Ortega, J.; Rincón-López, E.M. Changes in the epidemiology of invasive fungal disease in a Pediatric Hematology and Oncology Unit: The relevance of breakthrough infections. *BMC Infect. Dis.* **2023**, *23*, 348.
146. Cornely, O.A.; Sprute, R.; Bassetti, M.; Chen, S.C.A.; Groll, A.H.; Kurzai, O.; Lass-Florl, C.; Ostrosky-Zeichner, L.; Rautemaa-Richardson, R.; Revathia, G.; et al. Global guideline for the diagnosis and management of candidiasis: An initiative of the ECMM in cooperation with ISHAM and ASM. *Lancet Infect. Dis.* **2025**, *25*, e280–e293.
147. Aslam, S.; Rotstein, C. *Candida* infections in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin. Transpl.* **2019**, *33*, e13623.
148. Carugati, M.; Arif, S.; Yarrington, M.E.; King, L.Y.; Harris, M.; Evans, K.; Barbas, A.S.; Sudan, D.L.; Perfect, J.R.; Miller, R.A.; et al. Limitations of antifungal prophylaxis in preventing invasive Candida surgical site infections after liver transplant surgery. *Antimicrob. Agents Chemother.* **2024**, *68*, e0127923.
149. López-Medrano, F.; de la Espada, M.M.; Asín, M.A.P.; Fernández-Ruiz, M.; Herrero-Martínez, J.M.; Alonso-Carrillo, J.; San Juan, R.; Rodríguez-Goncer, I.; Andrés, A.; González, E.; et al. Fluconazole versus micafungin for initial antifungal prophylaxis against Candida in pancreas transplant recipients: A comparative study of two consecutive periods. *Mycoses* **2022**, *65*, 517–525.
150. Bloos, F.; Held, J.; Kluge, S.; Simon, P.; Kogelmann, K.; de Heer, G.; Kuhn, S.-O.; Jarczak, D.; Motsch, J.; Hempel, G.; et al. (1 → 3)-β-d-Glucan-guided antifungal therapy in adults with sepsis: The CandiSep randomized clinical trial. *Intensive Care Med.* **2022**, *48*, 865–875.
151. Erb, T.; Mihai, S.; Strauß, R.; Herbst, L.; Castellanos, I.; Diesch, K.; Cipa, F.; Bihlmaier, K.; Lang, A.-K.; Ganslmayer, M.; et al. β-(1→3)-D-glucan- and mannan-guided early termination of antifungal therapy in ICU patients: A randomized controlled study. *Antimicrob. Agents Chemother.* **2023**, *67*, e0072523.
152. Tissot, F.; Agrawal, S.; Pagano, L.; Petrikkos, G.; Groll, A.H.; Skiada, A.; Lass-Florl, C.; Calandra, T.; Viscoli, C.; Herbrecht, R. ECIL-6 guidelines for the treatment of invasive candidiasis, aspergillosis and mucormycosis in leukemia and hematopoietic stem cell transplant patients. *Haematologica* **2017**, *102*, 433–444.
153. Keighley, C.; Cooley, L.; Morris, A.J.; Ritchie, D.; Clark, J.E.; Boan, P.; Worth, L.J.; Australasian Antifungal Guidelines Steering Committee. Consensus guidelines for the diagnosis and management of invasive candidiasis in haematology, oncology and intensive care settings, 2021. *Intern. Med. J.* **2021**, *51*, 89–117.
154. Andes, D.R.; Safdar, N.; Baddley, J.W.; Playford, G.; Reboli, A.C.; Rex, J.H.; Sobel, J.D.; Pappas, P.G.; Kullberg, B.J.; Mycoses Study Group. Impact of treatment strategy on outcomes in patients with candidemia and other forms of invasive candidiasis: A patient-level quantitative review of randomized trials. *Clin. Infect. Dis.* **2012**, *54*, 1110–1122.
155. Wolfgruber, S.; Sedik, S.; Klingspor, L.; Tortorano, A.; Gow, N.A.R.; Lagrou, K.; Gangneux, J.-P.; Maertens, J.; Meis, J.F.; Lass-Florl, C.; et al. Insights from Three Pan-European Multicentre Studies on Invasive Candida Infections and Outlook to ECMM Candida IV. *Mycopathologia* **2024**, *189*, 70.
156. Maseda, E.; Martín-Loeches, I.; Zaragoza, R.; Pemán, J.; Fortún, J.; Grau, S.; Aguilar, G.; Varela, M.; Borges, M.; Giménez, M.-J.; et al. Critical appraisal beyond clinical guidelines for intraabdominal candidiasis. *Crit. Care* **2023**, *27*, 382.
157. Pais, M.M.; Zaragoza, R.; Martín-Loeches, I.; Gómez-Bertomeu, F.F.; Rodríguez, A. Management of Intra-Abdominal Candidiasis in Intensive Care Setting: A Narrative Review. *J. Fungi* **2025**, *11*, 362.
158. Kim, H.Y.; Baldelli, S.; Märtson, A.G.; Stocker, S.; Alffenaar, J.W.; Cattaneo, D.; Marriott, D.J. Therapeutic Drug Monitoring of the Echinocandin Antifungal Agents: Is There a Role in Clinical Practice? A Position Statement of the Anti-Infective Drugs Committee of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology. *Ther. Drug Monit.* **2022**, *44*, 198–214.
159. Beyda, N.D.; John, J.; Kilic, A.; Alam, M.J.; Lasco, T.M.; Garey, K.W. FKS mutant *Candida glabrata*: Risk factors and outcomes in patients

with candidemia. *Clin. Infect. Dis.* **2014**, *59*, 819–825.
160. Hoenigl, M.; Arastehfar, A.; Arendrup, M.C.; Brüggemann, R.; Carvalho, A.; Chiller, T.; Chen, S.; Egger, M.; Feys, S.; Ganneux, J.-P.; et al. Novel antifungals and treatment approaches to tackle resistance and improve outcomes of invasive fungal disease. *Clin. Microbiol. Rev.* **2024**, *37*, e0007423.
161. Nagamizu, M.; Hotta, Y.; Noda, M.; Nakamura, D.; Hori, M.; Otsuka, Y.; Takemoto, R.; Horita, Y.; Wakita, E.; Morishita, N.; et al. Association of doses based on body constitutional parameters with the efficacy of micafungin in candidemia. *J. Infect. Chemother.* **2025**, *31*, 102654.
162. Alsowaida, Y.S.; Sulaiman, K.A.; Mahrous, A.J.; Alharbi, A.; Bifari, N.; Alshahrani, W.A.; Almangour, T.A.; Damfu, N.; Banamah, A.; Abu Raya, R.R.; et al. Evaluation of clinical outcomes of anidulafungin for the treatment of candidemia in hospitalized critically ill patients with obesity: A multicenter, retrospective cohort study. *Int. J. Infect. Dis.* **2024**, *148*, 107234.
163. Thompson, G.R.; Soriano, A.; Skoutelis, A.; Vazquez, J.A.; Honore, P.M.; Horcajada, J.P.; Spapen, H.; Bassetti, M.; Ostrosky-Zeichner, L.; Das, A.F.; et al. Rezafungin Versus Caspofungin in a Phase 2, Randomized, Double-blind Study for the Treatment of Candidemia and Invasive Candidiasis: The STRIVE Trial. *Clin. Infect. Dis.* **2021**, *73*, E3647–E3655.
164. Thompson, G.R.; Soriano, A.; Cornely, O.A.; Kullberg, B.J.; Kollef, M.; Vazquez, J.; Honore, P.M.; Bassetti, M.; Pullman, J.; Chayakulkeeree, M.; et al. Rezafungin versus caspofungin for treatment of candidaemia and invasive candidiasis (ReSTORE): A multicentre, double-blind, double-dummy, randomised phase 3 trial. *Lancet* **2023**, *401*, 49–59.
165. Soriano, A.; Locke, J.B.; Cornely, O.A.; Roilides, E.; Ramos-Martinez, A.; Honoré, P.M.; Castanheira, M.; Carvalhaes, C.G.; Nseir, S.; Bassetti, M.; et al. Clinical and mycological outcomes of candidaemia and/or invasive candidiasis by *Candida* spp. and antifungal susceptibility: Pooled analyses of two randomized trials of rezafungin versus caspofungin. *Clin. Microbiol. Infect.* **2025**, *31*, 250–257.
166. Nucci, M.; Anaissie, E.; Betts, R.F.; Dupont, B.F.; Wu, C.; Buell, D.N.; Kovanda, L.; Lortholary, O. Early removal of central venous catheter in patients with candidemia does not improve outcome: Analysis of 842 patients from 2 randomized clinical trials. *Clin. Infect. Dis.* **2010**, *51*, 295–303.
167. Nucci, M.; Braga, P.R.; Nouér, S.A.; Anaissie, E. Time of catheter removal in candidemia and mortality. *Braz. J. Infect. Dis.* **2018**, *22*, 455–461.
168. Lee, Y.M.; Ryu, B.H.; Hong, S.I.; Cho, O.H.; Hong, K.W.; Bae, I.G.; Kwack, W.G.; Kim, Y.J.; Chung, E.K.; Kim, D.Y.; et al. Clinical impact of early reinsertion of a central venous catheter after catheter removal in patients with catheter-related bloodstream infections. *Infect. Control. Hosp. Epidemiol.* **2021**, *42*, 162–168.
169. Zuo, X.S.; Liu, Y.; Cai, X.; Zhan, L.; Hu, K. Association of different Candida species with catheter-related candidemia, and the potential antifungal treatments against their adhesion properties and biofilm-forming capabilities. *J. Clin. Lab. Anal.* **2021**, *35*, e23738.
170. Breazzano, M.P.; Bond, J.B.; Bearelly, S.; Kim, D.H.; Donahue, S.P.; Lum, F.; Olsen, T.W.; American Academy of Ophthalmology. American Academy of Ophthalmology Recommendations on Screening for Endogenous *Candida* Endophthalmitis. *Ophthalmology* **2022**, *129*, 73–76.
171. Breazzano, M.P.; Day, H.R.; Bloch, K.C.; Tanaka, S.; Cherney, E.F.; Sternberg, P.; Donahue, S.P.; Bond 3rd, J.B. Utility of Ophthalmologic Screening for Patients with Candida Bloodstream Infections: A Systematic Review. *JAMA Ophthalmol.* **2019**, *137*, 698–710.
172. Phongkhun, K.; Pothikamjorn, T.; Srisurapanont, K.; Manothummetha, K.; Sanguankeo, A.; Thongkam, A.; Chuleerarux, N.; Leksuwankun, S.; Meejun, T.; Thanakitcharu, J.; et al. Prevalence of Ocular Candidiasis and Candida Endophthalmitis in Patients with Candidemia: A Systematic Review and Meta-Analysis. *Clin. Infect. Dis.* **2023**, *76*, 1738–1749.
173. Lehman, A.; Tessier, K.M.; Sattarova, V.; Montezuma, S.R.; Kline, S.; Erayil, S.E. Do Patients With Candidemia Need an Ophthalmologic Examination? *Open Forum Infect. Dis.* **2024**, *11*, ofae663.
174. Shin, S.U.; Yu, Y.H.; Kim, S.S.; Oh, T.H.; Kim, S.E.; Kim, U.J.; Kang, S.-J.; Jang, H.-C.; Park, K.-H.; Jung, S.I. Clinical characteristics and risk factors for complications of candidaemia in adults: Focus on endophthalmitis, endocarditis, and osteoarticular infections. *Int. J. Infect. Dis.* **2020**, *93*, 126–132.
175. Soriano, A.; Honore, P.M.; Puerta-Alcalde, P.; Garcia-Vidal, C.; Pagotto, A.; Gonçalves-Bradley, D.C.; Verweij, P.E. Invasive candidiasis: Current clinical challenges and unmet needs in adult populations. *J. Antimicrob. Chemother.* **2023**, *78*, 1569–1585.
176. Permpalung, N.; Sedik, S.; Pappas, P.G.; Hoenigl, M.; Ostrosky-Zeichner, L. Diagnosis and Management of *Candida* Endophthalmitis and Chorioretinitis. *Clin. Microbiol. Infect.* 2025; *in press*.

177. Turner, R.B.; Valcarlos, E.; Won, R.; Chang, E.; Schwartz, J. Impact of infectious diseases consultation on clinical outcomes of patients with *Staphylococcus aureus* bacteremia in a community health system. *Antimicrob. Agents Chemother.* **2016**, *60*, 5682–5687.
178. Kobayashi, T.; Marra, A.R.; Schweizer, M.L.; Eyck, P.T.; Wu, C.; Alzunitan, M.; Salinas, J.L.; Siegel, M.; Farmakiotis, D.; Auwaerter, P.G.; et al. Impact of infectious disease consultation in patients with candidemia: A retrospective study, systematic literature review, and meta-analysis. *Open Forum Infect. Dis.* **2020**, *7*, ofaa270.
179. Lee, R.A.; Vo, D.T.; Zurko, J.C.; Griffin, R.L.; Rodriguez, J.M.; Camins, B.C. Infectious diseases consultation is associated with decreased mortality in enterococcal bloodstream infections. *Open Forum Infect. Dis.* **2020**, *7*, ofaa064.

Schmitt, S.; McQuillen, D.P.; Nahass, R.; Martinelli, L.; Rubin, M.; Schwebke, K.; Petrak, R.; Ritter, J.T.; Chansolme, D.; Slama, T.; et al. Infectious diseases specialty intervention is associated with decreased mortality and lower healthcare costs. *Clin. Infect. Dis.* **2014**, *58*, 22–28.