# The Global Burden of Fungal Diseases



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#### **KEYWORDS**

- Global burden Epidemiology Fungal diseases Candida Cryptococcus
- Aspergillus Mold Endemic mycoses

#### **KEY POINTS**

- Fungal pathogens are emerging as an even more important cause of disease as the number of people with severely immunocompromising conditions, such as HIV, cancer, and organ transplantation, who are at higher risk for fungal diseases, increases.
- Candida species are the most important cause of serious invasive fungal infections, but infections caused by Cryptococcus, Pneumocystis, invasive molds, and dimorphic molds also contribute to a substantial burden of disease.
- Systematic surveillance for fungal infections is scarce and is needed to make informed estimates of the global burden of fungal diseases.

#### INTRODUCTION

Assessment of the global burden and epidemiologic trends of fungal diseases is critical to prioritizing prevention strategies, diagnostic modalities, and therapeutic interventions. The global burden of fungal diseases is increasing, given the expanding number of patients at risk for these infections, including people living with human immunodeficiency virus (PLHIV), transplant recipients, patients with cancer, patients receiving immunomodulators (eg, tumor necrosis factor- $\alpha$  inhibitors), premature neonates, and the elderly. Recent increases in travel and changes in climate may also result in changes in geographic distribution of fungi.

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Quantifying the global burden of fungal diseases is challenging. Fungal diseases are often difficult to diagnose because they manifest with nonspecific symptoms and are not routinely suspected. Diagnosis frequently requires invasive tissue specimens, fungi do not always grow in culture, histopathologic identification is challenging, fungal antibody tests may cross-react, and skin testing for latent infection is generally not available. The most comprehensive estimates of any disease come from surveillance (formal systematic case counts within a specified population). In some parts of the world, limited single institution-based, population-based, or sentinel surveillance for some fungal diseases provides helpful information on trends in the burden of that infection. However, the lack of routine surveillance for most fungal diseases greatly limits the availability of data needed to inform burden estimates. In some cases, administrative health care data documenting hospital discharge diagnoses or registries of patients with fungal diseases have been used in lieu of surveillance.1 Although helpful, these assessments do not capture the full burden of disease. Recent attempts to estimate fungal disease burden have been made using far-reaching extrapolations from limited available data on susceptible populations and prevalence of disease.<sup>2</sup> These estimates highlight important data gaps and should be interpreted cautiously.

This article reports on distribution, incidence, and prevalence of selected fungal disease, and points out the gaps in knowledge where such data were not available. The review is organized by pathogen and by global region, highlighting the fungal diseases that contribute the most to global morbidity and mortality.

#### YEASTS Candida

Candida bloodstream infection (candidemia) is the most common form of invasive Candida infection and is associated with substantial morbidity and mortality. The incidence of candidemia in the general population and hospitalized and intensive care unit patients has been reported from multiple countries. These estimates vary widely within regions of the same country and over time.<sup>3</sup> Representative studies are listed in Table 1.<sup>4–14</sup> The reasons for these differences in candidemia incidence are likely multifactorial, including underlying ecology of Candida spp, differences in underlying patient populations, resources available for medical care and training programs, difficulties in implementing hospital infection control programs, and differences in surveillance methodologies.<sup>3</sup> Although a plethora of single-institution studies have been reported, only a few countries have conducted geographically widespread surveillance, and in still fewer countries has this been sustained over time to describe trends in candidemia.<sup>5,12,15</sup> To truly understand the global burden of candidemia, there is a need for within- and between-country collaborations to systematically study candidemia in different settings.

Species distribution of *Candida* infections in various parts of the world are listed in **Box 1.**<sup>5,8,16–19</sup> The differences in species distribution may relate to local ecology of *Candida* spp and is important because variation in antifungal susceptibility patterns by species has implications for treatment success. Furthermore, the predominance of some species, such as *Candida parapsilosis*, signals a need for examination of hospital infection control practices.

Invasive infection caused by antifungal-resistant *Candida* spp is an emerging problem. Fluconazole resistance among *Candida albicans* isolates is estimated between 0% and 5%, with the highest rate reported in South Africa.<sup>20</sup> Fluconazole resistance is a much bigger problem among non-*albicans* spp and ranges between 5% and

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