

Ignored fungal infections kill more people annually than HIV and malaria combined

By [Carolina Pohl-Albertyn](#), issued by [University of the Free State](#)

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With the Covid-19 pandemic currently on the forefront of news and public awareness, we have all become more attuned to seeing data regarding numbers of infections and deaths, and as I write this article today, the worldwide cumulative case count of Covid-19 stands at more than 20 million, with more than 700,000 deaths. You may also know that there are other infections causing great concern, such as HIV (690,000 deaths/year), tuberculosis (1.5 million deaths/year), and malaria (405,000 deaths/year). But what would be your reaction if you knew that fungal infections (ranging from skin and mucosal infections, e.g. vaginal or oral thrush, to deadly systemic and organ infections, e.g. candidiasis, cryptococcal meningitis and bronchopulmonary aspergillosis) affect more than one billion people each year, of which more than 150 million cases are severe and life-threatening and cause 1.7 million deaths per year?



Professor Carolina Pohl-Albertyn, NRF SARCHI Research Chair in Pathogenic Yeast

Recently published estimates put the burden of disease due to fungal infection in South Africa at more than 3 million cases per year. These figures are especially shocking given that prior to 1980, fungal infections were not a major health problem.

Reasons for the rise in fungal infections

One of the important reasons for the rising number of fungal infections is the increase in the number of people who are vulnerable to these infections. These include elderly people as well as critically ill and immunocompromised patients. The overall increase in life span due to modern medicine and improvements in living standards are contributing factors. A second reason for the increase in fungal infections is the increased resistance of these fungi to the available antifungal drugs.

Although there are more than 20 different classes of antibiotics (with different action mechanisms) that may be used to treat bacterial infections, antifungals all belong to one of three classes of drugs (azoles, polyenes or echinocandins). The most widely used class is the azoles. These antifungals are the safest and also the only ones that can be taken orally. This has led to the widespread and often long-term use of these drugs to prevent fungal infections in vulnerable patients. In addition, antifungal drugs, which are closely related to those used in medicine, are widely used in agriculture.

All these practices have led to fungi becoming resistant to our limited number of antifungals (similar to the better-known bacterial resistance to antibiotics). Also, fungal species that were previously not generally associated with infection in humans, are becoming more prevalent. Previously, most infections were caused by the yeast *Candida albicans*, but now we see more non-albicans *Candida* species (e.g. *Candida glabrata*, *Candida parapsilosis*, *Candida tropicalis*, *Candida krusei*) causing disease. Many of these species are inherently resistant to some of the current antifungals. This is why the Centers for Disease Control and Prevention (CDC) classified drug-resistant *Candida* yeasts as "serious threats", placing them in the same category as, for instance, methicillin-resistant *Staphylococcus aureus* (MRSA).

Infections cannot be treated

A very worrying development is the recent worldwide rise in infections caused by a new yeast species first described in 2009, *Candida auris*. This yeast causes disease, especially in healthcare facilities, and can be easily transmitted between patients in a hospital. It can survive for long periods on surfaces and is resistant to many routinely used disinfectants. In addition, 90% of *Candida auris* strains are resistant to at least one class of antifungal drugs, and about 30% are resistant to

two or all three classes of antifungal drugs, effectively meaning that infection by these yeasts cannot be treated. This has resulted in the CDC increasing the threat level of this yeast to 'urgent'.

Neglected infections

Although the numbers of fungal infections are steadily increasing, this microbial threat has been largely neglected by healthcare authorities. Although the World Health Organisation has recently included certain fungal infections on its list of neglected diseases, there is still no specific information on their plans to combat fungal infections. In addition, the money made available for research on fungal diseases is much less than for other infectious diseases. For instance, for each person dying from malaria, US\$1,315 is invested in research, and US\$334 for each person dying from tuberculosis, while only US\$31 is invested per death from cryptococcal meningitis.

This background clearly provides motivation for the work of the NRF SARCHI Research Chair in Pathogenic Yeasts. We urgently need to find new treatment options beyond the established antifungals. Research conducted under the SARCHI chair includes avenues such as evaluating compounds as potential novel antifungals; repurposing of existing drugs for other diseases as possible antifungal drugs, as well as finding new drug targets that may be exploited in the development of novel antifungals. In addition, we are studying the basic biology of pathogenic yeasts, including *Candida auris*, in order to understand how they are able to cause disease. We are also interested in understanding how these pathogenic yeasts interact with bacteria that may co-infect a susceptible patient. All these studies make use of cutting-edge technologies, such as CRISPR-Cas9 gene-editing tools, state-of-the-art confocal laser scanning and electron microscopy, and non-mammalian infection models such as nematodes and zebrafish. These projects also ensure the postgraduate training of much-needed experts in the study of pathogenic fungi, who can lead the way in the future to deal with this increasing health threat.

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