Scientific Research Publishing

Pharmacology & Pharmacy, 2024, 15, 81-112
https://www.scirp.org/journal/pp
ISSN Online: 2157-9431
ISSN Print: 2157-9423

Global Burden of Fungal Infections and Antifungal Resistance from 1961 to 2024: Findings and Future Implications

Steward Mudenda

Department of Pharmacy, School of Health Sciences, University of Zambia, Lusaka, Zambia
Email: steward.mudenda@unza.zm

How to cite this paper: Mudenda, S. (2024) Global Burden of Fungal Infections and Antifungal Resistance from 1961 to 2024: Findings and Future Implications. *Pharmacology & Pharmacy*, **15**, 81-112.
https://doi.org/10.4236/pp.2024.154007

Received: March 19, 2024
Accepted: April 20, 2024
Published: April 23, 2024

Abstract

Background: Antifungal resistance (AFR) is a global public health problem with devastating effects, especially among immunocompromised individuals. Addressing AFR requires a One Health approach including Antifungal Stewardship (AFS). This study aimed to comprehensively review global studies published on fungal infections and AFR and to recommend solutions to address this growing problem. **Materials and Methods:** This was a narrative review that was conducted using published papers on fungal infections, AFR, and AFS between January 1961 and March 2024. The literature was searched using PubMed, Google Scholar, Web of Science, and EMBASE. **Results:** This found that there has been an increase in fungal infections globally, especially among immunocompromised patients. Due to this increase in fungal infections, there has been a proportionate increase in the use of antifungal agents to prevent and treat fungal infections. This increased use of antifungal agents has worsened the problem of AFR contributing to increased morbidity and mortality. Globally, fungal infections have contributed to 150 million infections annually and 1.7 million deaths per year. By the year 2023, over 3.8 million people died from fungal infections. Addressing AFR remains a challenge because the treatment of antifungal-resistant infections is difficult. Finally, the treatment of fungal infections is a global challenge exacerbated by the limited number of antifungal agents to treat invasive fungal infections. **Conclusion:** The results of this study indicated that fungal infections and AFR are prevalent across humans, animals, agriculture, and the environment. Addressing this problem requires the provision of solutions such as improving the awareness of AFR, conducting further research on the discovery of new antifungal agents, and implementing AFS programs. If this global problem is not addressed, the morbidity and mortality associated with AFR will continue to rise in the future.

Keywords

Antifungal Resistance, Antifungal Stewardship, Antimicrobial Resistance, Fungal Infections, Global Burden, Immunocompromised, Mycosis

1. Introduction

Antifungal resistance (AFR) is a global public health issue [1] [2] [3] [4] [5], that has been exacerbated by the exposure of fungi to antifungal agents and as a result of an increased number of immunocompromised patients [1] [2] [6]. This problem has been worsened by the lack of a variety of antifungal arsenals to treat fungal infections [2] [7] [8]. This phenomenon is a subset of antimicrobial resistance (AMR) which occurs when bacteria, viruses, and protozoa resist or adapt to the lethal effects of antimicrobial drugs [9] [10] [11] [12]. The resistance of microorganisms to antimicrobial drugs may cause negative consequences including increased morbidity, mortality, medical costs, and economic breakdown [9] [13] [14] [15]. If these problems are not addressed, global and regional deaths will continue and worsen in the next decades [16] [17] [18].

The WHO developed a fungal priority pathogens list to help develop strategies to address the growing problem of fungal infections and AFR [19]. Consequently, fungal infections have increased in the recent past, especially among immunocompromised patients [20] [21] [22] [23]. Additionally, systemic fungal infections are often diagnosed late thereby increasing the mortality rate of patients [24] [25]. On top of that, the burden of fungal infections increased during the COVID-19 pandemic leading to increased morbidity and mortality [26]-[34]. An approximate number of 150 million people have been infected with fungal infections annually with approximately 1.7 million deaths reported annually due to fungal infections, indicating the need to address this problem [20]. By the year 2023, more than 6.5 million people had suffered from fungal infections annually of which more than about 3.8 million deaths were recorded [35] [36]. Consequently, the use of antifungal agents has proportionately increased to circumvent fungal infections [37] [38] [39]. It is pertinent to note that AFR is a natural phenomenon where fungi are naturally resistant to certain Antifungal agents [40] [41]. However, the overuse and misuse of antifungal agents have contributed to the development of AFR [37] [39] [41] [42] [43]. Antifungal agents are overused or misused in humans [44] [45], animals [46], agriculture [47] [48], and other environmental sectors [49]. This overuse and misuse have contributed to the occurrence of AFR in the One Health ecosystem [50] [51]. On top of that, like other antimicrobial drugs [52] [53] [54] [55], antifungal agents are widely accessed without prescriptions [56]. Therefore, the inappropriate use of antifungals is a huge burden that magnifies AFR [2] [57] [58], this is similar to reports on the inappropriate use of antibiotics [59] [60] [61] [62].

Evidence has shown that some fungi have developed resistance to antifungal agents [63] [64]. The first AFR was reported in 1961 and involved the resistance of dermatophytes to griseofulvin [65]. Some of the mechanisms involved in the resistance of fungi to antifungals include a reduction in the intercellular concentration of the target enzyme, alteration in sterol biosynthesis, overexpression of the antifungal drug target, and alteration in drug target [37]. Examples of fungi that have developed resistance to azoles include *Candida* species and *Aspergillus* species [66] [67] [68] [69] [70]. Resistance to echinocandins has also been reported in other studies [66] [71] [72]. Consequently, many fungi species have developed resistance to many of the current antifungal agents thereby making control and treatment of fungal infections difficult or impossible [66] [73]. In turn, this will continue to raise the morbidity and mortality associated with fungal infections [20] [22] [74].

Strategies to address AFR have been documented and require urgent attention just like those implemented to address AMR [14] [66] [75]. Antifungal stewardship (AFS) programs have been reported to be effective in addressing AFR [76]. AFR involves promoting the rational prescribing of antifungal agents, especially only when they are required [77] [78] [79]. Studies have reported an improvement in the prescribing and consumption of antifungals after the implementation of AFS [80] [81]. Therefore, adequate sensitisation and awareness campaigns concerning AFR may help curb this problem [2] [14] [82].

In this paper, a comprehensive narrative review of the global burden of fungal infections and AFR was provided. This review is critical and provides recommendations on the strategies to employ to combat AFR. Therefore, this narrative review comprehensively reviewed global studies published on fungal infections and AFR and recommended solutions for addressing this growing problem.

2. Materials and Methods

This study adopted a narrative review design to collect data on studies published from January 1961 to March 2024. This study used a narrative review design to comprehensively include all studies published on AFR and AFS globally and regionally. Narrative reviews have been reported to be effective in reporting such global issues. Hence, a similar approach from previous studies was adopted [61] [83] [84] [85] [86] [87]. All literature search was done using PubMed, Google Scholar, Web of Science, and EMBASE. The literature involved using words including "antifungal resistance", "antifungal stewardship", "antifungals", "antifungal agents", "antifungal drugs", "burden", AND "fungal infections". This review included articles that were published between January 1961 to March 2024 on fungal infections, AFR, and AFS. To address the aim of this narrative review, all published studies that focused on the burden of fungal infections and AFR, and strategies to address AFR were included in the study. This provided comprehensive literature that can be built on by other researchers in the future. Additionally, only articles that were published in English were included in this review. This review excluded abstracts and articles not published in English.

3. Results and Discussion

Antifungal resistance (AFR) remains a problem that has been neglected compared to antibacterial and antiviral resistance [58] [73] [76] [88] [89]. This study was conducted to comprehensively provide information on the global and regional studies published on AFR and AFS and provide recommendations to address this problem. The study found that AFR is a growing problem and has been reported globally and regionally across the One Health ecosystem and requires urgent attention. The high resistance of fungi to antifungal agents demonstrates the growing problem of reduced effectiveness of most of these drugs. Addressing AFR requires a One Health approach alongside instigating strategies for the discovery of antifungal agents, implementing AFR, and international collaborations (**Table 1**).

3.1. Global Burden of Fungal Infections and Associated Mortality

Fungal infections are among the common infections reported in the healthcare

Table 1. Burden of fungal infections and AFR and some proposed strategies to address this problem.

Authors and year	Area of research	Findings
WHO, 2022 [19]	Fungal infections	The WHO classified 19 fungi as priority fungal pathogens and these include *Cryptococcus*, *neoformans*, *Candida auris*, *Aspergillus fumigatus*, *Candida albicans*, *Nakaseomyces glabrata* (*Candida glabrata*), *Histoplasma spp.*, Eumycetoma causative agents, Mucorales, *Fusarium* spp., *Candida tropicalis*, *Candida parapsilosis*, *Scedosporium spp.*, *Lomentospora prolificans*, *Coccidioides* spp., *Pichia kudriavzeveii* (*Candida krusei*), *Cryptococcus gattii*, *Talaromyces marneffei*, *Pneumocystis jirovecii*, and *Paracoccidioides* spp
Denning, 2024 [35]	Fungal infections	Globally, over 6.5 million people suffer from invasive fungal infections annually with more than 2.1 million suffering from invasive aspergillosis, 1.8 million suffering from chronic pulmonary aspergillosis, and over 1.5 million found to have invasive candidiasis or *Candida* bloodstream infections. A total of 500,000 people were diagnosed with Pneumocystis pneumonia, 194,000 had Cryptococcal meningitis, and 11.5 were affected with fungal asthma. Notably, other life-threatening fungal infections caused 300,000 infections annually. Fungal infections cause approximately 3.8 million deaths annually, with over 2.5 million deaths directly attributed to fungal infections.
Kanafani and Perfect, 2008 [90]	AFR	AFR is a global public health problem and causes an increase in morbidity and mortality, especially among high-risk populations.
Pfaller, 2012 [91]	AFR	The overuse and misuse of antifungal agents have contributed to AFR, especially through acquired resistance, across the One Health ecology.
Kara *et al.*, 2021 [80]	AFS	Instigation of AFS has been demonstrated to promote rational use of antifungal agents.
Agrawal *et al.*, 2016 [92]	AFS	AFS is essential in addressing AFR and must be implemented in a multidisciplinary approach.
Vitiello *et al.*, 2023 [2]	Antifungal drug discovery	The discovery of new antifungal agents will be critical in addressing the problem of AFR.
Vandeputte, Ferrari, and Coste, 2012 [93]	Antifungal drug discovery	The identification and discovery of new antifungal agents can contribute towards addressing AFR.

system, especially among immunocompromised patients. The growing problem of fungal infections prompted the WHO to develop a fungal priority pathogens list to guide research, development and public health action [19] [94]. As shown in **Table 1**, a total of 19 fungi have been reported to be of public health concern and have been listed under the priority fungal pathogens including *Cryptococcus*, *neoformans*, *Candida auris*, *Aspergillus fumigatus*, *Candida albicans*, *Nakaseomyces glabrata* (*Candida glabrata*), *Histoplasma spp.*, Eumycetoma causative agents, Mucorales, *Fusarium* spp., *Candida tropicalis*, *Candida parapsilosis*, *Scedosporium spp.*, *Lomentospora prolificans*, *Coccidioides* spp., *Pichia kudriavzeveii* (*Candida krusei*), *Cryptococcus gattii*, *Talaromyces marneffei*, *Pneumocystis jirovecii*, and *Paracoccidioides* spp [19] [95]. Global statistics have shown that over 6.5 million people suffer from invasive fungal infections annually [35] [36]. Of the 6.5 million invasive fungal infections, more than 2.1 million had invasive aspergillosis, 1.8 million suffered from chronic pulmonary aspergillosis, and over 1.5 million were found to have invasive candidiasis or *Candida* bloodstream infections [35]. Consequently, a total of 500,000 people were diagnosed with Pneumocystis pneumonia, 194,000 had Cryptococcal meningitis, and 11.5 were affected with fungal asthma [35]. Finally, other life-threatening fungal infections caused 300,000 infections annually [35].

Fungal infections have been reported to cause approximately 3.8 million deaths annually, which included over 2.5 million deaths directly attributed to fungal infections [35] [36]. Of these deaths, 995,000 were due to chronic pulmonary aspergillosis while 214,000 were due to Pneumocystis pneumonia [35]. Additionally, a total of 147,000 deaths resulted from Cryptococcal meningitis while 46,000 were caused by fungal asthma [35]. Furthermore, other life-threatening fungal infections caused a total of 161,000 deaths annually [35].

A study conducted in Africa, specifically in Zimbabwe, reported that 14.9% of Zimbabweans were annually affected with fungal infections [96]. Fungal infections were prevalent in immunocompromised patients including those suffering from HIV/AIDs, tuberculosis, cancer, chronic obstructive pulmonary disease, and asthma [96].

The burden of fungal infections was worsened during the COVID-19 outbreak [97]-[103]. Consequently, this led to an increase in morbidity and mortality in patients who had COVID-19 and fungal infections [104] [105].

3.2. Treatment of Fungal Infections

The treatment of fungal infections has relied heavily on four major classes of systemically acting antifungal agents including azoles, echinocandins, polyenes, and the pyrimidine analogues [41]. Examples of azoles include fluconazole, isavuconazole, itraconazole, voriconazole, and posaconazole whereas examples of polyenes include conventional amphotericin B and its lipid formulations [38]. Additionally, examples of echinocandins include caspofungin, micafungin, and anidulafungin [38]. An example of a pyrimidine analogue is 5-flucytosine [41]. Of these examples of antifungal drugs, the most used first line of treatment for

Candida species include fluconazole and some echinocandins [106]. However, the treatment of fungal infections is affected by the emergence of drug-resistant fungal infections [67] [106] [107].

3.3. Antifungal Resistance as a Global Public Health Problem

Antifungal resistance (AFR) has been reported as a global public health problem and has been recognized as a significant global public health problem, posing serious threats to human health, agriculture, and the environment [74] [108]. Consequently, AFR can lead to treatment failures, prolonged illnesses, and increased mortality rates. Infections caused by resistant fungi are more difficult to treat, resulting in higher morbidity and mortality rates among affected individuals [4]. On top of that, AFR has economic implications for the patient, healthcare system, and countries [109] [110].

Consequently, the emergence of AFR limits the effectiveness of available antifungal agents [90]. As resistance spreads, the number of effective treatment options decreases, leaving patients with fewer alternatives for managing fungal infections [93]. Evidence has revealed that vulnerable populations, such as those with compromised immune systems (e.g., transplant recipients, HIV/AIDS patients, and cancer patients), are particularly susceptible to fungal infections [96] [111] [112]. AFR disproportionately affects these individuals, leading to increased health disparities [113].

The AFR problem has been magnified by the limited number of new antifungal agents in the manufacturing pipeline compared to antibacterial agents [43] [114]. The challenges in antifungal drug development, coupled with the economic considerations of pharmaceutical companies, contribute to a scarcity of novel antifungal agents [115] [116]. For instance, there are very few antifungal agents used in the treatment of invasive fungal infections compared to antibacterial agents [115]. With this limited number of antifungal agents, the problem of AFR is a huge issue and must be tackled in a One Health approach [40].

Fungal infections are often underdiagnosed, leading to delayed treatment and increased likelihood of resistance development [117]. Lack of awareness among healthcare professionals and the general public about fungal infections and resistance further exacerbates the problem. This challenge has been worsened by the readily availability of antifungal agents [118] [119]. Besides, AFR has been driven by the ease of access to antifungal agents and increased self-medication practices among individuals [120]. AFR is considered a global health security concern [121] [122] [123]. Resistant fungal strains can lead to outbreaks that have the potential to spread rapidly and cause significant public health crises [122] [124].

Concerns about AFR are of public health importance because fungal infections and resistance do not respect national borders [5]. In this case, resistant fungal strains can easily spread across countries and continents, making it a global challenge that requires collaborative efforts to monitor, control, and mitigate [125]. Thereupon, AFR imposes a substantial economic burden on healthcare systems [126]. Prolonged hospital stays, increased healthcare costs, and the need for more expensive treatments contribute to the economic impact of resistant fungal infections [127]. Further, AFR in agriculture contributes to crop losses and decreased food production [47]. This not only affects food security but also has economic implications for farmers and the global food supply chain [109] [128]. Furthermore, the use of antifungal agents in agriculture, as well as their discharge into the environment, can lead to the development of resistance in environmental fungi [47]. This poses risks to ecosystems, wildlife, and the overall environmental balance [129] [130]. This indicates that AFR affects the One Health ecosystem and exemplifies the interconnectedness of human health, animal health, and environmental health [50] [131] [132]. A One Health approach, considering the health of humans, animals, and ecosystems, is essential to comprehensively address the issue [133].

3.4. Examples of Fungi Resistant to Antifungal Agents

Resistance to azoles including fluconazole has increased in recent years due to azoles being overused [134]. A study that was conducted in India revealed that fungi demonstrated a 1.02-fold increase in resistance to voriconazole per year, with Fusarium species having a 1.04-fold increase in resistance to this drug per year [135]. Resistance to azoles has been reported in other studies [107] [108] [133] [136]. Consequently, the resistance of *Aspergillus* species is a public health problem that requires urgent attention due to its impact on poor treatment outcomes [25] [137]. A common resistance mechanism of *Aspergillus fumigatus* is a combination of mutations in the gene *cyp51A* (TR34/L98H) [128]. A high resistance of *Candida auris* to fluconazole was reported during the COVID-19 pandemic in Lebanon [138]. Consequently, Pandrug-resistant Candida auris was reported in the United States indicating that the isolates were resistant to all four classes of antifungal agents [139].

An Indian study reported that fungi had a 1.06-fold increase in resistance to natamycin, a polyene macrolide, per year, with *Fusarium* species having a 1.06-fold increase in resistance to this drug. *Aspergillus* species demonstrated a 1.09-fold increase in resistance while other filamentous fungi exhibited a 1.07-fold increase in resistance to natamycin per annum [135]. Resistance of fungi to other polyene macrolide antifungals including Amphotericin B has also been reported in other studies [39] [140] [141] [142] [143]. A study in the United States also reported high fluconazole-resistant candida species [143]. A study that was conducted in Lebanon among COVID-19 patients demonstrated that all isolates of *Candida auris* were resistant to Amphotericin B [138]. Consequently, this caused an increase in morbidity and mortality among patients suffering from COVID-19 [138].

The resistance of *C. albicans* to echinocandins has been reported and said to be due to spontaneous mutations in two hot spot regions of *the Fks1* gene in the fungi, this is the target protein of echinocandins which serves to reduce the sensitivity of the enzyme to the echinocandins [72] [144]. Similarly, the resistance of *C. glabrata* to echinocandins has been reported to be due to mutations in the drug target genes, *FKS1* and *FSK2* [145]. The resistance of *C. glabrata* to echinocandins is approximately 3% - 5%, indicating a public health concern and a need for urgent action to address this issue [146]. The prevalence of *C. glabrata* to echinocandins can even reach 10% - 15% [144] [147]. Consequently, the development of resistance of *C. glabrata* to echinocandins has continued to rise [148]. Some of the examples of fungi that have developed resistance to antifungal agents are shown in **Table 2**.

Over the years, fungi have developed resistance to antifungal agents thereby causing difficulties in treating fungal infections and consequently increased morbidity and mortality.

3.5. Strategies to Address Antifungal Resistance

AFR poses a significant threat to global health, necessitating comprehensive strategies to mitigate its impact including the establishment of robust surveillance systems for monitoring resistance patterns in both clinical and environmental settings [158]. By collecting and analyzing data on AFR, healthcare professionals and policymakers can make informed decisions and respond promptly to emerging challenges [158]. Further, the WHO developed the fungal priority pathogens list to contribute towards galvanizing fungal infections and AFR by promoting surveillance, public health interventions, and research and development, and innovation [19]. Therefore, there is a need to promote a One Health approach in addressing fungal infections and AFR [57] [159].

Table 2. Emergence of antifungal drug resistance over the years, 1961-2024.

Author, year, citation	Drug-resistant Fungi	Country	Study year
Michaelides *et al.*, 1961 [65]	*Trichophyton tonsurans*	United States	1961
Khan *et al.*, 2007 [156]	*Candida haemulonii*	Kuwait	2007
Satoh *et al.*, 2009 [149]	*Candida auris*	Japan	2009
Khan *et al.*, 2007 [156]	*Candida haemulonii*	Kuwait	2007
Kim *et al.*, 2009 [157]	*Candida haemulonii*	Korea	2009
Pfaller *et al.*, 2011 [152]	*Candida* species	Unites States	2010
Chowdhary *et al.*, 2016 [150]	*Candida auris*	Korea	2011
Beyda *et al.*, 2014 [153]	*Candida glabrata*	United State	2012
Pfaller *et al.*, 2015 [154]	*Candida* and *Aspergillus* species	China	2012
Sarma *et al.*, 2012 [136]	*Candida auris*	India	2012
Chowdhary *et al.*, 2020 [151]	*Candida auris*	India	2020
Magnasco *et al.*, 2021 [104]	*Candida auris*	Italy	2021
Allaw *et al.*, 2021 [138]	*Candida auris*	Lebanon	2021
Xu *et al.*, 2022 [155]	*Candida auris*	China	2022
Jocobs *et al.*, 2022 [139]	*Candida auris*	United States	2022

3.5.1. Antifungal Stewardship Programs, Research and Development, and Improved Diagnostics to Address Antifungal Resistance

Antifungal stewardship (AFS) programs are essential in promoting the rational use of antifungals [78] [92] [160]. The rational use of antifungal agents is paramount in addressing AFR [79]. Therefore, educating and encouraging healthcare workers to adhere to evidence-based guidelines when prescribing antifungals can prevent overuse and misuse, helping to maintain the efficacy of existing medications [161]. On top of that, education and awareness campaigns play a pivotal role in this regard, informing healthcare providers, farmers, and the general public about responsible antifungal use, the risks of resistance, and the importance of compliance with prescribed regimens [2] [14] [82] [162]. AFS programs are critical because they provide training to healthcare workers thereby raising awareness, promoting the rational use of antifungal agents, and reducing the emergence and spread of AFR [161] [163] [164] [165] [166]. The introduction of AFS in hospitals has been reported to reduce the overuse of antifungal agents and improve their rational use while reducing the expenditure associated with their use [77] [167] [168]. Moreover, just like in antibiotic resistance [169]-[177], there is a need to adhere to the antifungal treatment guidelines. Consequently, healthcare facilities must be guided to develop AFS programs to address AFR [79] [81] [178].

There is an urgent need to raise awareness of AFR and predisposing factors. Public health campaigns are essential for engaging individuals in the fight against AFR, as enshrined in the WHO fungal priority pathogens list [19]. By raising awareness about the responsible use of antifungal agents and emphasizing the role of each person in preventing the spread of fungal infections, these campaigns empower communities to actively participate in the collective effort to combat resistance [40].

The WHO fungal priority pathogens list promotes research, development, and innovation in galvanizing AFR [19]. Investing in research and development is crucial to discovering new antifungal agents and developing combination therapies [7] [93] [179] [180] [181]. By diversifying the available treatments and mechanisms of action, the likelihood of resistance can be reduced [182]. Improved diagnostics also play a key role, enabling timely identification of fungal infections and facilitating targeted therapy [183]. The development and deployment of rapid and accurate diagnostic tools, including point-of-care options, PCR, next-generation sequencing, microfluidic chip technology, nanotechnology tools, new-generation biosensors, T 2 Candida, and artificial intelligence models are essential components of a comprehensive strategy to address fungal infections and AFR [21] [183] [184] [185]. Nanotechnology has been reported to be a good source of antifungal agents [186]. Therefore, there is a need to promote the use of nanotechnology to address AMR [187] [188].

3.5.2. Restricting Access to Antifungal Agents without a Prescription

Restricting access to antifungal agents without a prescription is a regulatory measure aimed at promoting responsible use, minimizing overuse, and addressing the growing concern of antifungal resistance [2]. The prescription requirement serves as a reminder to patients about the importance of using antifungal medications responsibly [189]. This includes completing the full course of treatment as prescribed, which is crucial for preventing the development of resistance. Requiring a prescription ensures that individuals consult with healthcare professionals before using antifungal agents. This helps prevent self-diagnosis and self-medication, reducing the risk of inappropriate use and the development of resistance. Additionally, a prescription requirement encourages proper diagnosis of fungal infections by qualified healthcare providers. This is essential for determining the most appropriate antifungal treatment based on the specific type and severity of the infection. Consequently, access restrictions help control the overuse of antifungal agents, which is a significant contributor to the emergence of resistance. Healthcare providers can assess the necessity of antifungal treatment and prescribe it judiciously, avoiding unnecessary exposure to these medications [118].

Restricting access to antifungal agents without a prescription is a proactive measure to address the global challenge of AMR, including AFR [189]. By controlling the distribution of these medications, regulatory authorities can play a role in preserving the effectiveness of existing antifungal agents. Requiring a prescription facilitates healthcare professionals in monitoring patients for potential adverse effects and ensuring appropriate follow-up care. This enhances patient safety and contributes to better overall healthcare outcomes. On top of that, many countries align their healthcare policies with international guidelines that recommend prescription-based access to antimicrobial drugs, including antifungals. Such alignment promotes a unified global effort to address the broader issue of antimicrobial resistance.

However, it is important to balance access restrictions with ensuring timely and appropriate access to antifungal medications for those who genuinely need them. Regulatory authorities should consider the potential impact on public health and work towards striking a balance that prevents misuse while ensuring patients with legitimate needs can obtain timely treatment. Additionally, comprehensive education and awareness campaigns should accompany such regulatory measures to inform the public about the rationale behind the restrictions and promote understanding of responsible medication use.

3.5.3. Restricting the Use of Antifungal Agents in Agriculture

Agricultural practices contribute significantly to the emergence of AFR, and regulatory measures are needed to address this issue [47]. Regulating the use of antifungal agents in agriculture and promoting sustainable farming practices can help minimize environmental exposure to these drugs [47]. Restricting the use of antifungal agents in agriculture is a critical strategy to address the emergence of AFR and safeguard both human and environmental health [47] [132].

It is critical to conduct thorough risk assessments to evaluate the impact of antifungal use in agriculture on human health, animal health, and the environment. There is a need to develop risk management strategies based on these assessments to minimize potential negative effects [47]. Besides, countries need to establish surveillance systems to monitor the prevalence of AFR in agricultural settings. Moreover, regular monitoring can provide insights into the effectiveness of restriction measures and help identify emerging resistance patterns [47].

It is essential to provide education and training programs for farmers on sustainable farming practices and the potential risks associated with the overuse of antifungal agents [47]. This can enhance farmers' understanding of antifungal use and resistance thereby leading to more responsible use of antifungals and helping prevent unnecessary applications [58]. Hence, much must be done to conduct public awareness campaigns to inform consumers about the potential risks associated with excessive use of antifungal agents in agriculture. This can influence consumer choices and create demand for sustainably produced agricultural products. In the agricultural sector, there is a need to encourage and promote alternative agricultural practices that reduce the reliance on antifungal agents [130]. This may include adopting crop rotation, using resistant crop varieties, and implementing integrated pest management strategies [40]. There is also a strong need to enforce regulations to restrict the use of certain antifungal agents in agriculture. This may involve setting limits on dosage, application frequency, or specific application methods. The implementation of regulatory frameworks can help ensure compliance with responsible use guidelines. Besides, there is a need to introduce systems that require farmers to obtain prescriptions or approvals from agricultural experts or authorities before using antifungal agents to ensure that these medicines are used only when necessary and per established guidelines [47].

Countries should invest in research and development to identify and promote alternative methods for controlling fungal infections in crops [43]. This includes developing biopesticides, resistant crop varieties, and sustainable agricultural practices that minimize the need for antifungal treatments. Other than that, it is critical to collaborate with international partners to share best practices, research findings, and regulatory approaches [165]. Global collaborations are essential to address the transboundary nature of AFR in agriculture [165]. Finally, there is a need to provide incentives, subsidies, or support programs for farmers who adopt sustainable and responsible agricultural practices that reduce the need for antifungal treatments.

By combining these strategies, it is possible to create a more sustainable and responsible approach to antifungal use in agriculture, thereby mitigating the risk of resistance development and promoting environmental and human health.

3.5.4. Heightened Infection Prevention and Control Measures in Healthcare Facilities to Prevent Fungal infections and Address Antifungal Resistance

In healthcare settings, strict infection prevention and control (IPC) measures are imperative to minimize the spread of fungal infections [190]. Some of the IPC includes promoting hygiene practices in both healthcare and community settings [191]. Additionally, regulatory measures, such as enforcing restrictions on the sale and use of antifungal medicines, can further contribute to the overall effort. IPC reduces the use of antibiotics and antifungal agents thereby preventing the emergence and spread of AMR, and specifically AFR [192].

Implementing heightened IPC measures in healthcare facilities is crucial for addressing AFR and preventing the spread of fungal infections [193]. It is important to ensure rigorous adherence to hand hygiene protocols among healthcare workers in clinical settings [191]. On top of that, proper handwashing with soap and water or using alcohol-based hand sanitisers can significantly reduce the transmission of fungal infections within healthcare settings [194]. Alongside this, there is a critical need to establish and promote AFS programs within healthcare facilities [80] [162]. These programs can optimize the use of antifungal medications, ensuring they are prescribed judiciously and by established guidelines [81]. There is also a need to provide ongoing education and training for healthcare workers on IPC measures specific to fungal infections [190]. This includes recognizing signs of fungal infections, proper use of antifungal medications, and adherence to established protocols [190] [191]. Ensure healthcare workers consistently use appropriate personal protective equipment (PPE), including masks, gloves, gowns, and eye protection, when dealing with patients with fungal infections [195]. This is essential for preventing direct contact and airborne transmission. Healthcare facilities should regularly review and update IPC protocols based on the latest scientific evidence and emerging trends in antifungal resistance [195]. Finally, healthcare must be flexible in adapting to new information is crucial for maintaining effective control measures [195].

It is critical to identify and isolate patients with confirmed or suspected fungal infections to prevent the spread of resistant strains. Implementing cohorts, where patients with similar infections are grouped, can further enhance infection control. Implement regular screening and surveillance for fungal infections, particularly in high-risk areas such as intensive care units. Early detection allows for timely intervention and prevents the spread of infections. Therefore, it is critical to educate patients and visitors about the importance of infection prevention measures, including hand hygiene and adherence to facility-specific protocols [196]. Consequently, informed individuals can actively participate in reducing the risk of infection transmission [191].

There is a need to implement stringent cleaning and disinfection protocols for surfaces and equipment in healthcare facilities [197]. However, fungi can persist on surfaces, and thorough cleaning is essential to minimize the risk of transmission. Hence, there is a need to emphasize and monitor aseptic techniques during medical procedures, especially those involving invasive devices or surgical interventions [198] [199]. Strict adherence to sterile procedures minimizes the risk of introducing fungal pathogens. Consequently, it is essential to implement environmental monitoring programs to assess fungal contamination in healthcare settings. This can help identify areas at risk for fungal transmission and guide targeted infection control measures [93].

Finally, countries must foster collaboration and open communication between healthcare teams, infection control specialists, and microbiology laboratories [200] [201] [202]. Timely sharing of information allows for prompt responses to emerging fungal infections and potential resistance issues [200].

By integrating these heightened IPC measures into healthcare practices, facilities can contribute significantly to the containment of fungal infections and the prevention of AFR within healthcare settings.

3.5.5. International Collaborations in Addressing Antifungal Resistance

Addressing AMR, including AFR requires international collaborations [203]. International collaborations play a crucial role in addressing AFR, as fungal infections and the emergence of AFR are global health concerns that transcend national borders [201]. Countries must work together to share information, harmonize guidelines, implement surveillance programs, and collectively develop strategies to preserve the efficacy of existing antifungal agents. Additionally, international collaboration is crucial for addressing global challenges associated with AFR. Countries must share knowledge, expertise, and resources to develop and implement effective strategies on a global scale.

International collaborations must foster global information sharing and collaboration on surveillance data related to AFR [165]. In addition, establishing international databases allows countries to share information, monitor trends, and identify emerging resistance patterns. On top of that, we need to develop and promote harmonized international guidelines and standards for the diagnosis, treatment, and prevention of fungal infections. It is recommended that consistent approaches ensure that best practices are implemented globally, reducing the risk of AFR development. There is also a need to facilitate international research consortia to pool resources, expertise, and data for advancing research on antifungal resistance. Collaborative efforts can accelerate the development of new antifungal agents and improve treatment strategies.

Countries must support capacity-building initiatives in countries with limited resources to enhance their ability to address AFR effectively [92] [204] [205] [206]. This includes training healthcare professionals, improving laboratory capabilities, and strengthening surveillance systems [92]. Moreover, there is a need for coordinated efforts to implement and monitor AFS programs on an international scale. This involves optimizing the use of antifungal medications to minimize overuse and reduce the risk of resistance [92]. There is also a need to establish joint surveillance programs that involve multiple countries working together to monitor AFR, similar to what has been done under AMR [207] [208] [209] [210] [211]. This collaborative approach provides a more comprehensive understanding of the global landscape of resistance and enables coordinated responses. Over and above that, there is an urgent need to advocate for international policies that prioritize the fight against AFR. Collaborative efforts in policy development can lead to unified strategies and commitments to address this global health challenge [40].

We need to facilitate the formation of cross-border research networks that bring together scientists, clinicians, and policymakers to collaborate on specific aspects of AMR, including AFR research [212]. This can include clinical trials, epidemiological studies, and surveillance initiatives. Additionally, there is a need to participate in and support global surveillance networks focused on AMR, including AFR. These networks, often facilitated by international health organizations, enable real-time information exchange and collaboration. Alongside this, there is a need to instigate collaborations on international public awareness campaigns to educate healthcare professionals, policymakers, and the public about the risks of AFR. A unified message can have a broader impact and promote collective action.

There is a need to promote regulatory harmonization to ensure consistent standards for the approval and monitoring of antifungal agents globally [40] [213], similar to reports regarding antibiotics [214] [215] [216]. Streamlining regulatory processes can facilitate timely access to effective treatments and promote responsible use [213]. On the other hand, countries must develop collaborative emergency response plans for fungal outbreaks that may have international implications. This includes sharing resources, and expertise, and coordinating efforts to contain and manage outbreaks effectively [213].

By fostering international collaborations across these various dimensions, the global community can strengthen its collective response to antifungal resistance, enhance surveillance capabilities, and promote effective strategies for prevention, diagnosis, and treatment on a global scale.

This review demonstrated that fungal infections and AFR affect humans, animals, and plants, and have an impact on the environment.

4. Conclusion

Antifungal resistance is a public health problem that already claimed many lives globally. This problem has been worsened by the inappropriate use of antifungal agents across humans, animals, and agriculture to treat or prevent fungal infections. Consequently, fungal infections have increased thereby causing a burden to the communities and the healthcare system. To address this problem, many strategies must be instigated and implemented across the One Health ecosystem. Additionally, AFS must be developed and implemented across all healthcare systems. Furthermore, recognizing AFR as a global public health problem necessitates a coordinated and multisectoral response. Efforts should focus on surveillance, research, education, policy development, and international cooperation to effectively combat the challenges posed by resistant fungal infections worldwide. Finally, there is a need to institute a multifaceted approach encompassing surveillance, education, research, regulatory measures, and international collaboration to effectively address AFR. Thus, by combining these strategies, stakeholders can work towards preserving the efficacy of existing antifungal agents and ensuring the continued success of fungal infection treatment.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] Kontoyiannis, D.P. (2017) Antifungal Resistance: An Emerging Reality and a Global Challenge. *The Journal of Infectious Diseases*, **216**, S431-S435. https://doi.org/10.1093/infdis/jix179

[2] Vitiello, A., Ferrara, F., Boccellino, M., Ponzo, A., Cimmino, C., Comberiati, E., Zovi, A., Clemente, S. and Sabbatucci, M. (2023) Antifungal Drug Resistance: An Emergent Health Threat. *Biomedicines*, **11**, Article 1063. https://doi.org/10.3390/biomedicines11041063

[3] Mudenda, S., Matafwali, S.K., Mukosha, M., Daka, V., Chabalenge, B., Chizimu, J., Yamba, K., Mufwambi, W., Banda, P., Chisha, P., *et al.* (2023) Antifungal Resistance and Stewardship: A Knowledge, Attitudes and Practices Survey among Pharmacy Students at the University of Zambia; Findings and Implications. *JAC-Antimicrobal Resistance*, **5**, dlad141. https://doi.org/10.1093/jacamr/dlad141

[4] Arastehfar, A., Gabaldón, T., Garcia-Rubio, R., Jenks, J.D., Hoenigl, M., Salzer, H.J.F., Ilkit, M., Lass-Flörl, C. and Perlin, D.S. (2020) Drug-Resistant Fungi: An Emerging Challenge Threatening Our Limited Antifungal Armamentarium. *Antibiotics*, **9**, Article 877. https://doi.org/10.3390/antibiotics9120877

[5] Berman, J. and Krysan, D.J. (2020) Drug Resistance and Tolerance in Fungi. *Nature Reviews Microbiology*, **18**, 319-331. https://doi.org/10.1038/s41579-019-0322-2

[6] Ben-Ami, R. and Kontoyiannis, D.P. (2021) Resistance to Antifungal Drugs. *Infectious Disease Clinics of North America*, **35**, 279-311. https://doi.org/10.1016/j.idc.2021.03.003

[7] Nicola, A.M., Albuquerque, P., Paes, H.C., Fernandes, L., Costa, F.F., Kioshima, E.S., Abadio, A.K.R., Bocca, A.L. and Felipe, M.S. (2019) Antifungal Drugs: New Insights in Research & Development. *Pharmacology & Therapeutics*, **195**, 21-38. https://doi.org/10.1016/j.pharmthera.2018.10.008

[8] Osherov, N. and Kontoyiannis, D.P. (2017) The Anti-*Aspergillus* Drug Pipeline: Is the Glass Half Full or Empty? *Medical Mycology*, **55**, 118-124. https://doi.org/10.1093/mmy/myw060

[9] Murray, C.J., Ikuta, K.S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., Han, C., Bisignano, C., Rao, P., Wool, E., *et al.* (2022) Global Burden of Bacterial Antimicrobial Resistance in 2019: A Systematic Analysis. *The Lancet*, **399**, 629-655. https://doi.org/10.1016/S0140-6736(21)02724-0

[10] Prestinaci, F., Pezzotti, P. and Pantosti, A. (2015) Antimicrobial Resistance: A Global Multifaceted Phenomenon. *Pathogens and Global Health*, **109**, 309-318. https://doi.org/10.1179/2047773215Y.0000000030

[11] Tang, K.W.K., Millar, B.C. and Moore, J.E. (2023) Antimicrobial Resistance (AMR). *British Journal of Biomedical Science*, **80**, Article 11387. https://doi.org/10.3389/bjbs.2023.11387

[12] Arip, M., Selvaraja, M., Mogana, R., Tan, L.F., Leong, M.Y., Tan, P.L., Yap, V.L., Chinnapan, S., Tat, N.C., Abdullah, M., *et al.* (2022) Review on Plant-Based Management in Combating Antimicrobial Resistance—Mechanistic Perspective. *Frontiers in Pharmacology*, **13**, Article 879495. https://doi.org/10.3389/fphar.2022.879495

[13] Ikuta, K.S., Swetschinski, L.R., Robles Aguilar, G., Sharara, F., Mestrovic, T., Gray, A.P., Davis Weaver, N., Wool, E.E., Han, C., Gershberg Hayoon, A., *et al.* (2022) Global Mortality Associated with 33 Bacterial Pathogens in 2019: A Systematic Analysis for the Global Burden of Disease Study 2019. *The Lancet*, **400**, 2221-2248. https://doi.org/10.1016/S0140-6736(22)02185-7

[14] Srinivasan, A., Lopez-Ribot, J.L. and Ramasubramanian, A.K. (2014) Overcoming Antifungal Resistance. *Drug Discovery Today: Technologies*, **11**, 65-71. https://doi.org/10.1016/j.ddtec.2014.02.005

[15] Dadgostar, P. (2019) Antimicrobial Resistance: Implications and Costs. *Infection and Drug Resistance*, **12**, 3903-3910. https://doi.org/10.2147/IDR.S234610

[16] Jonas, O.B., Irwin, A., Berthe, F.C.J., Le Gall, F.G. and Marquez, P. (2017) Drug-Resistant Infections: A Threat to Our Economic Future. World Bank Report, 1-132. https://documents1.worldbank.org/curated/en/323311493396993758/pdf/final-report.pdf

[17] O'Neill, J. (2014) Review on Antibiotic Resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations. https://wellcomecollection.org/works/rdpck35v

[18] O'Neill, J. (2016) Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance. https://amr-review.org/sites/default/files/160518_Final paper_with cover.pdf

[19] World Health Organization (2022) WHO Fungal Priority Pathogens List to Guide Research, Development and Public Health Action, Vol. 1, 1-48. https://www.who.int/publications/i/item/9789240060241

[20] Kainz, K., Bauer, M.A., Madeo, F. and Carmona-Gutierrez, D. (2020) Fungal Infections in Humans: The Silent Crisis. *Microbial Cell*, **7**, 143-145. https://doi.org/10.15698/mic2020.06.718

[21] Fang, W., Wu, J., Cheng, M., Zhu, X., Du, M., Chen, C., Liao, W., Zhi, K. and Pan, W. (2023) Diagnosis of Invasive Fungal Infections: Challenges and Recent Developments. *Journal of Biomedical Science*, **30**, Article No. 42. https://doi.org/10.1186/s12929-023-00926-2

[22] Brown, G.D., Denning, D.W., Gow, N.A.R., Levitz, S.M., Netea, M.G. and White, T.C. (2012) Hidden Killers: Human Fungal Infections. *Science Translational Medicine*, **4**, 165rv13. https://doi.org/10.1126/scitranslmed.3004404

[23] Calandra, T., Roberts, J.A., Antonelli, M., Bassetti, M. and Vincent, J.L. (2016) Diagnosis and Management of Invasive Candidiasis in the ICU: An Updated Approach to an Old Enemy. *Critical Care*, **20**, Article No. 125. https://doi.org/10.1186/s13054-016-1313-6

[24] Reddy, G.K.K., Padmavathi, A.R. and Nancharaiah, Y.V. (2022) Fungal Infections: Pathogenesis, Antifungals and Alternate Treatment Approaches. *Current Research in Microbial Sciences*, **3**, Article 100137. https://doi.org/10.1016/j.crmicr.2022.100137

[25] Verweij, P.E., Chowdhary, A., Melchers, W.J.G. and Meis, J.F. (2016) Azole Resistance in *Aspergillus fumigatus*: Can We Retain the Clinical Use of Mold-Active An-

tifungal Azoles? *Clinical Infectious Diseases*, **62**, 362-368. https://doi.org/10.1093/cid/civ885

[26] Koehler, P., Bassetti, M., Chakrabarti, A., Chen, S.C.A., Colombo, A.L., Hoenigl, M., Klimko, N., Lass-Flörl, C., Oladele, R.O., Vinh, D.C., *et al.* (2021) Defining and Managing COVID-19-Associated Pulmonary Aspergillosis: The 2020 ECMM/ISHAM Consensus Criteria for Research and Clinical Guidance. *The Lancet Infectious Diseases*, **21**, e149-e162. https://doi.org/10.1016/S1473-3099(20)30847-1

[27] van Arkel, A.L.E., Rijpstra, T.A., Belderbos, H.N.A., van Wijngaarden, P., Verweij, P.E. and Bentvelsen, R.G. (2020) COVID-19-Associated Pulmonary Aspergillosis. *American Journal of Respiratory and Critical Care Medicine*, **202**, 132-135. https://doi.org/10.1164/rccm.202004-1038LE

[28] Negm, E.M., Mohamed, M.S., Rabie, R.A., Fouad, W.S., Beniamen, A., Mosallem, A., Tawfik, A.E. and Salama, H.M. (2023) Fungal Infection Profile in Critically Ill COVID-19 Patients: A Prospective Study at a Large Teaching Hospital in a Middle-Income Country. *BMC Infectious Diseases*, **23**, Article No. 246. https://doi.org/10.1186/s12879-023-08226-8

[29] Hoenigl, M., Seidel, D., Sprute, R., Cunha, C., Oliverio, M., Goldman, G.H., Ibrahim, A.S. and Carvalho, A. (2022) COVID-19-Associated Fungal Infections. *Nature Microbiology*, **7**, 1127-1140. https://doi.org/10.1038/s41564-022-01172-2

[30] Dubey, R., Sen, K.K., Mohanty, S.S., Panda, S., Goyal, M. and Menon, S.M. (2022) The Rising Burden of Invasive Fungal Infections in COVID-19, Can Structured CT Thorax Change the Game. *Egyptian Journal of Radiology and Nuclear Medicine*, **53**, Article No. 18. https://doi.org/10.1186/s43055-022-00694-3

[31] Arastehfar, A., Shaban, T., Zarrinfar, H., Roudbary, M., Ghazanfari, M., Hedayati, M.T., Sedaghat, A., Ilkit, M., Najafzadeh, M.J. and Perlin, D.S. (2021) Candidemia among Iranian Patients with Severe COVID-19 Admitted to ICUs. *Journal of Fungi*, **7**, Article 280. https://doi.org/10.3390/jof7040280

[32] Villanueva-Lozano, H., Treviño-Rangel, R. de J., González, G.M., Ramírez-Elizondo, M.T., Lara-Medrano, R., Aleman-Bocanegra, M.C., Guajardo-Lara, C.E., Gaona-Chávez, N., Castilleja-Leal, F., Torre-Amione, G., *et al.* (2021) Outbreak of *Candida auris* Infection in a COVID-19 Hospital in Mexico. *Clinical Microbiology and Infection*, **27**, 813-816. https://doi.org/10.1016/j.cmi.2020.12.030

[33] Cataldo, M.A., Tetaj, N., Selleri, M., Marchioni, L., Capone, A., Caraffa, E., Di Caro, A. and Petrosillo, N. (2020) Incidence of Bacterial and Fungal Bloodstream Infections in COVID-19 Patients in Intensive Care: An Alarming "Collateral Effect". *Journal of Global Antimicrobial Resistance*, **23**, 290-291. https://doi.org/10.1016/j.jgar.2020.10.004

[34] Ramadan, H.K.A., Mahmoud, M.A., Zakaria, M., Aburahma; Elkhawaga, A.A., El-Mokhtar, M.A., Sayed, I.M., Hosni, A., Hassany, S.M. and Medhat, M.A. (2020) Predictors of Severity and Co-Infection Resistance Profile in COVID-19 Patients: First Report from Upper Egypt. *Infection and Drug Resistance*, **13**, 3409-3422. https://doi.org/10.2147/IDR.S272605

[35] Denning, D. (2024) Global Incidence and Mortality of Severe Fungal Disease. *The Lancet Infectious Diseases*. https://doi.org/10.1016/S1473-3099(23)00692-8

[36] Dall, C. (2024) Global Mortality from Fungal Diseases Has Nearly Doubled. https://www.cidrap.umn.edu/antimicrobial-stewardship/global-mortality-fungal-diseases-has-nearly-doubled

[37] Ghannoum, M.A. and Rice, L.B. (1999) Antifungal Agents: Mode of Action, Mechanisms of Resistance, and Correlation of These Mechanisms with Bacterial Resis-

tance. *Clinical Microbiology Reviews*, **12**, 501-517. https://doi.org/10.1128/CMR.12.4.501

[38] Nami, S., Aghebati-Maleki, A., Morovati, H. and Aghebati-Maleki, L. (2019) Current Antifungal Drugs and Immunotherapeutic Approaches as Promising Strategies to Treatment of Fungal Diseases. *Biomedicine & Pharmacotherapy*, **110**, 857-868. https://doi.org/10.1016/j.biopha.2018.12.009

[39] Hossain, C.M., Ryan, L.K., Gera, M., Choudhuri, S., Lyle, N., Ali, K.A. and Diamond, G. (2022) Antifungals and Drug Resistance. *Encyclopedia*, **2**, 1722-1737. https://doi.org/10.3390/encyclopedia2040118

[40] Fisher, M.C., Alastruey-Izquierdo, A., Berman, J., Bicanic, T., Bignell, E.M., Bowyer, P., Bromley, M., Brüggemann, R., Garber, G., Cornely, O.A., *et al.* (2022) Tackling the Emerging Threat of Antifungal Resistance to Human Health. *Nature Reviews Microbiology*, **20**, 557-571. https://doi.org/10.1038/s41579-022-00720-1

[41] Robbins, N., Caplan, T. and Cowen, L.E. (2017) Molecular Evolution of Antifungal Drug Resistance. *The Annual Review of Microbiology*, **71**, 753-775. https://doi.org/10.1146/annurev-micro-030117-020345

[42] Pathadka, S., Yan, V.K.C., Neoh, C.F., Al-Badriyeh, D., Kong, D.C.M., Slavin, M.A., Cowling, B.J., Hung, I.F.N., Wong, I.C.K. and Chan, E.W. (2022) Global Consumption Trend of Antifungal Agents in Humans from 2008 to 2018: Data from 65 Middle- and High-Income Countries. *Drugs*, **82**, 1193-1205. https://doi.org/10.1007/s40265-022-01751-x

[43] Osset-Trénor, P., Pascual-Ahuir, A. and Proft, M. (2023) Fungal Drug Response and Antimicrobial Resistance. *Journal of Fungi*, **9**, Article 565. https://doi.org/10.3390/jof9050565

[44] Dhasarathan, P., AlSalhi, M.S., Devanesan, S., Subbiah, J., Ranjitsingh, A.J.A., Binsalah, M. and Alfuraydi, A.A. (2021) Drug Resistance in *Candida albicans* Isolates and Related Changes in the Structural Domain of Mdr1 Protein. *Journal of Infection and Public Health*, **14**, 1848-1853. https://doi.org/10.1016/j.jiph.2021.11.002

[45] Papadimitriou-Olivgeris, M., Andrianaki, A.M., Marangos, M., Sipsas, N., Apostolidi, E.A., Maltezos, E., Panagopoulos, P., Karapiperis, D., Arvaniti, K., Perdikouri, E.I., *et al.* (2020) Hospital-Wide Antifungal Prescription in Greek Hospitals: A Multicenter Repeated Point-Prevalence Study. *European Journal of Clinical Microbiology & Infectious Diseases*, **39**, 243-248. https://doi.org/10.1007/s10096-019-03713-w

[46] Russo, T.P. and Santaniello, A. (2023) Tackling Antibiotic and Antifungal Resistance in Domestic Animals, Synanthropic Species, and Wildlife: A Global Health Imperative. *Antibiotics*, **12**, Article 1632. https://doi.org/10.3390/antibiotics12111632

[47] Brauer, V.S., Rezende, C.P., Pessoni, A.M., De Paula, R.G., Rangappa, K.S., Nayaka, S.C., Gupta, V.K. and Almeida, F. (2019) Antifungal Agents in Agriculture: Friends and Foes of Public Health. *Biomolecules*, **9**, Article 521. https://doi.org/10.3390/biom9100521

[48] Miller, S.A., Ferreira, J.P. and Lejeune, J.T. (2022) Antimicrobial Use and Resistance in Plant Agriculture: A One Health Perspective. *Agriculture*, **12**, Article 289. https://doi.org/10.3390/agriculture12020289

[49] Monapathi, M.E., Oguegbulu, J.C., Adogo, L., Klink, M., Okoli, B., Mtunzi, F. and Modise, J.S. (2021) Pharmaceutical Pollution: Azole Antifungal Drugs and Resistance of Opportunistic Pathogenic Yeasts in Wastewater and Environmental Water. *Applied and Environmental Soil Science*, **2021**, Article ID: 9985398.

https://doi.org/10.1155/2021/9985398

[50] Fisher, M.C., Hawkins, N.J., Sanglard, D. and Gurr, S.J. (2018) Worldwide Emergence of Resistance to Antifungal Drugs Challenges Human Health and Food Security. *Science*, **360**, 739-742. https://doi.org/10.1126/science.aap7999

[51] Osorio-Lombana, J.P., Cuervo-Maldonado, S.I., López-Mora, M.J. and Gómez-Rincón, J.C. (2019) Prescripción Inapropiada de Antifúngicos y La Necesidad de Programas Para Su Uso Racional. *Revista Chilena de Infectología*, **36**, 403-413. https://doi.org/10.4067/S0716-10182019000400403

[52] Mudenda, S., Daka, V., Matafwali, S.K., Kanaan, M.H.G., Abdullah, S.S., Mohamed, S., Mufwambi, W., Kasanga, M., Mulenga, B., Chabalenge, B., *et al.* (2023) Prevalence of Self-Medication and Associated Factors among Healthcare Students during the COVID-19 Pandemic: A Cross-Sectional Study at the University of Zambia. *Open Journal of Social Sciences*, **11**, 340-363. https://doi.org/10.4236/jss.2023.1110021

[53] Mudenda, S., Mukela, M., Matafwali, S., Banda, M., Mutati, R.K., Muungo, L.T., Daka, V., Saad, S.A.M., Bumbangi, F.N. and Chabalenge, B. (2022) Knowledge, Attitudes, and Practices towards Antibiotic Use and Antimicrobial Resistance among Pharmacy Students at the University of Zambia: Implications for Antimicrobial Stewardship Programmes. *Scholars Academic Journal of Pharmacy*, **11**, 117-124. https://doi.org/10.36347/sajp.2022.v11i08.002

[54] Ngoma, M.T., Sitali, D., Mudenda, S., Mukuma, M., Bumbangi, F.N., Bunuma, E., Skjerve, E. and Muma, J.B. (2024) Community Antibiotic Consumption and Associated Factors in Lusaka District of Zambia: Findings and Implications for Antimicrobial Resistance and Stewardship. *JAC-Antimicrobal Resistance*, **6**, dlae034. https://doi.org/10.1093/jacamr/dlae034

[55] Kalungia, A.C., Burger, J., Godman, B., de Oliveira Costa, J. and Simuwelu, C. (2016) Non-Prescription Sale and Dispensing of Antibiotics in Community Pharmacies in Zambia. *Expert Review of Anti-Infective Therapy*, **14**, 1215-1223. https://doi.org/10.1080/14787210.2016.1227702

[56] Morgan, D.J., Okeke, I.N., Laxminarayan, R., Perencevich, E.N. and Weisenberg, S. (2011) Non-Prescription Antimicrobial Use Worldwide: A Systematic Review. *The Lancet Infectious Diseases*, **11**, 692-701. https://doi.org/10.1016/S1473-3099(11)70054-8

[57] Langfeldt, A., Gold, J.A.W. and Chiller, T. (2022) Emerging Fungal Infections: From the Fields to the Clinic, Resistant *Aspergillus fumigatus* and Dermatophyte Species: A One Health Perspective on an Urgent Public Health Problem. *Current Clinical Microbiology Reports*, **9**, 46-51. https://doi.org/10.1007/s40588-022-00181-3

[58] Hassoun, N., Kassem, I.I., Hamze, M., El Tom, J., Papon, N. and Osman, M. (2023) Antifungal Use and Resistance in a Lower-Middle-Income Country: The Case of Lebanon. *Antibiotics*, **12**, Article 1063. https://doi.org/10.3390/antibiotics12091413

[59] Mudenda, S., Chilimboyi, R., Matafwali, S.K., Daka, V., Lindizyani Mfune, R., Arielle, L., Kemgne, M., Bumbangi, F.N., Hangoma, J., Chabalenge, B., *et al.* (2024) Hospital Prescribing Patterns of Antibiotics in Zambia Using the WHO Prescribing Indicators Post-COVID-19 Pandemic: Findings and Implications. *JAC-Antimicrobal Resistance*, **6**, dlae023. https://doi.org/10.1093/jacamr/dlae023

[60] Mudenda, S., Chomba, M., Chabalenge, B., Hikaambo, C.N., Banda, M., Daka, V., Zulu, A., Mukesela, A., Kasonde, M., Lukonde, P., *et al.* (2022) Antibiotic Prescribing Patterns in Adult Patients According to the WHO AWaRe Classification: A Multi-Facility Cross-Sectional Study in Primary Healthcare Hospitals in Lusaka,

Zambia. *Pharmacology & Pharmacy*, **13**, 379-392.
https://doi.org/10.4236/pp.2022.1310029

[61] Sono, T.M., Yeika, E., Cook, A., Kalungia, A., Opanga, S.A., Acolatse, J.E.E., Sefah, I.A., Jelić, A.G., Campbell, S., Lorenzetti, G., *et al.* (2023) Current Rates of Purchasing of Antibiotics without a Prescription across Sub-Saharan Africa; Rationale and Potential Programmes to Reduce Inappropriate Dispensing and Resistance. *Expert Review of Anti-Infective Therapy*, **21**, 1025-1055.
https://doi.org/10.1080/14787210.2023.2259106

[62] Yamba, K., Mudenda, S., Mpabalwani, E., Mainda, G., Mukuma, M., Samutela, M.T., Lukwesa, C., Chizimu, J., Kaluba, C.K., Mutalange, M., *et al.* (2024) Antibiotic Prescribing Patterns and Carriage of Antibiotic-Resistant Escherichia Coli and Enterococcus Species in Healthy Individuals from Selected Communities in Lusaka and Ndola Districts, Zambia. *JAC-Antimicrobal Resistance*, **6**, dlae027.
https://doi.org/10.1093/jacamr/dlae027

[63] Lamb, D., Kelly, D., Manning, N. and Kelly, S. (2006) Reduced Intracellular Accumulation of Azole Antifungal Results in Resistance in *Candida albicans* Isolate NCPF 3363. *FEMS Microbiology Letters*, **147**, 189-193.
https://doi.org/10.1111/j.1574-6968.1997.tb10240.x

[64] Cowen, L.E., Sanglard, D., Howard, S.J., Rogers, P.D. and Perlin, D.S. (2015) Mechanisms of Antifungal Drug Resistance. *Cold Spring Harbor Perspectives in Medicine*, **5**, a019752. https://doi.org/10.1101/cshperspect.a019752

[65] Michaelides, P., Rosenthal, S.A., Sulzberger, M.B. and Witten, V.H. (1961) *Trichophyton tonsurans* Infection Resistant to Griseofulvin: A Case Demonstrating Clinical and *in Vitro* Resistance. *Archives of Dermatology*, **83**, 988-990.
https://doi.org/10.1001/archderm.1961.01580120100025

[66] Wiederhold, N.P. (2017) Antifungal Resistance: Current Trends and Future Strategies to Combat. *Infection and Drug Resistance*, **10**, 249-259.
https://doi.org/10.2147/IDR.S124918

[67] Arendrup, M.C. (2014) Update on Antifungal Resistance in Aspergillus and Candida. *Clinical Microbiology and Infection*, **20**, 42-48.
https://doi.org/10.1111/1469-0691.12513

[68] Mayr, A. and Lass-Flörl, C. (2011) Epidemiology and Antifungal Resistance in Invasive Aspergillosis According to Primary Disease—Review of the Literature. *European Journal of Medical Research*, **16**, 153-157.
https://doi.org/10.1186/2047-783X-16-4-153

[69] Sugui, J.A., Peterson, S.W., Figat, A., Hansen, B., Samson, R.A., Mellado, E., Cuenca-Estrella, M. and Kwon-Chung, K.J. (2014) Genetic Relatedness versus Biological Compatibility between *Aspergillus fumigatus* and Related Species. *Journal of Clinical Microbiology*, **52**, 3707-3721. https://doi.org/10.1128/JCM.01704-14

[70] Daneshnia, F., de Almeida Júnior, J.N., Ilkit, M., Lombardi, L., Perry, A.M., Gao, M., Nobile, C.J., Egger, M., Perlin, D.S., Zhai, B., *et al.* (2023) Worldwide Emergence of Fluconazole-Resistant *Candida parapsilosis*: Current Framework and Future Research Roadmap. *The Lancet Microbe*, **4**, e470-e480.
https://doi.org/10.1016/S2666-5247(23)00067-8

[71] Park, S., Kelly, R., Kahn, J.N., Robles, J., Hsu, M.J., Register, E., Li, W., Vyas, V., Fan, H., Abruzzo, G., *et al.* (2005) Specific Substitutions in the Echinocandin Target Fks1p Account for Reduced Susceptibility of Rare Laboratory and Clinical Candida Sp. Isolates. *Antimicrobial Agents and Chemotherapy*, **49**, 3264-3273.
https://doi.org/10.1128/AAC.49.8.3264-3273.2005

[72] Walker, L.A., Gow, N.A.R. and Munro, C.A. (2010) Fungal Echinocandin Resistance. *Fungal Genetics and Biology*, **47**, 117-126. https://doi.org/10.1016/j.fgb.2009.09.003

[73] Denning, D.W. (2022) Antifungal Drug Resistance: An Update. *European Journal of Hospital Pharmacy*, **29**, 109-112. https://doi.org/10.1136/ejhpharm-2020-002604

[74] Bongomin, F., Gago, S., Oladele, R.O. and Denning, D.W. (2017) Global and Multi-National Prevalence of Fungal Diseases—Estimate Precision. *Journal of Fungi*, **3**, Article 57. https://doi.org/10.3390/jof3040057

[75] Peghin, M., Vena, A., Graziano, E., Giacobbe, D.R., Tascini, C. and Bassetti, M. (2022) Improving Management and Antimicrobial Stewardship for Bacterial and Fungal Infections in Hospitalized Patients with COVID-19. *Therapeutic Advances in Infectious Disease*, **9**. https://doi.org/10.1177/20499361221095732

[76] Mudenda, S., Chabalenge, B., Kasanga, M., Mufwambi, W., Mfune, R.L., Daka, V. and Matafwali, S.K. (2023) Antifungal Resistance and Stewardship: A Call to Action in Zambia. *PAMJ*, **45**, Article 152. https://doi.org/10.11604/pamj.2023.45.152.41232

[77] Micallef, C., Aliyu, S.H., Santos, R., Brown, N.M., Rosembert, D. and Enoch, D.A. (2014) Introduction of an Antifungal Stewardship Programme Targeting High-Cost Antifungals at a Tertiary Hospital in Cambridge, England. *Journal of Antimicrobial Chemotherapy*, **70**, 1908-1911. https://doi.org/10.1093/jac/dkv040

[78] Hamdy, R.F., Zaoutis, T.E. and Seo, S.K. (2017) Antifungal Stewardship Considerations for Adults and Pediatrics. *Virulence*, **8**, 658-672. https://doi.org/10.1080/21505594.2016.1226721

[79] Ray, A., Das, A. and Panda, S. (2023) Antifungal Stewardship: What We Need to Know. *Indian Journal of Dermatology*, *Venereology and Leprology*, **89**, 5-11. https://doi.org/10.25259/IJDVL_91_2022

[80] Kara, E., Metan, G., Bayraktar-Ekincioglu, A., Gulmez, D., Arikan-Akdagli, S., Demirkazik, F., Akova, M., Unal, S. and Uzun, O. (2021) Implementation of Pharmacist-Driven Antifungal Stewardship Program in a Tertiary Care Hospital. *Antimicrobial Agents and Chemotherapy*, **65**, e00629-21. https://doi.org/10.1128/AAC.00629-21

[81] Valerio, M., Muñoz, P., Rodríguez, C.G., Caliz, B., Padilla, B., Fernández-Cruz, A., Sánchez-Somolinos, M., Gijón, P., Peral, J., Gayoso, J., *et al.* (2015) Antifungal Stewardship in a Tertiary-Care Institution: A Bedside Intervention. *Clinical Microbiology and Infection*, **21**, 492.e1-492.e9. https://doi.org/10.1016/j.cmi.2015.01.013

[82] Firacative, C. (2020) Invasive Fungal Disease in Humans: Are We Aware of the Real Impact? *Memórias do Instituto Oswaldo Cruz*, **115**, e200430. https://doi.org/10.1590/0074-02760200430

[83] Mudenda, S., Chabalenge, B., Daka, V., Mfune, R.L., Salachi, K.I., Mohamed, S., Mufwambi, W., Kasanga, M., Matafwali, S.K., Mudenda, S., *et al.* (2023) Global Strategies to Combat Antimicrobial Resistance: A One Health Perspective. *Pharmacology & Pharmacy*, **14**, 271-328. https://doi.org/10.4236/pp.2023.148020

[84] Haque, M., McKimm, J., Sartelli, M., Dhingra, S., Labricciosa, F.M., Islam, S., Jahan, D., Nusrat, T., Chowdhury, T.S., Coccolini, F., *et al.* (2020) Strategies to Prevent Healthcare-Associated Infections: A Narrative Overview. *Risk Management and Healthcare Policy*, **13**, 1765-1780. https://doi.org/10.2147/RMHP.S269315

[85] Probst, V., Islamovic, F. and Mirza, A. (2021) Antimicrobial Stewardship Program in Pediatric Medicine. *Pediatric Investigation*, **5**, 229-238. https://doi.org/10.1002/ped4.12292

[86] Machowska, A. and Lundborg, C.S. (2019) Drivers of Irrational Use of Antibiotics

in Europe. *International Journal of Environmental Research and Public Health*, **16**, Article 27. https://doi.org/10.3390/ijerph16010027

[87] Selvarajan, R., Obize, C., Sibanda, T., Abia, A.L.K. and Long, H. (2023) Evolution and Emergence of Antibiotic Resistance in Given Ecosystems: Possible Strategies for Addressing the Challenge of Antibiotic Resistance. *Antibiotics*, **12**, Article 28. https://doi.org/10.3390/antibiotics12010028

[88] (2017) Stop Neglecting Fungi. *Nature Microbiology*, **2**, Article No. 17120. https://www.nature.com/articles/nmicrobiol2017120

[89] Klepser, M.E., Ernst, E.J. and Pfaller, M.A. (1997) Update on Antifungal Resistance. *Trends in Microbiology*, **5**, 372-375. https://doi.org/10.1016/S0966-842X(97)01108-6

[90] Kanafani, Z.A. and Perfect, J.R. (2008) Resistance to Antifungal Agents: Mechanisms and Clinical Impact. *Clinical Infectious Diseases*, **46**, 120-128. https://doi.org/10.1086/524071

[91] Pfaller, M.A. (2012) Antifungal Drug Resistance: Mechanisms, Epidemiology, and Consequences for Treatment. *The American Journal of Medicine*, **125**, S3-S13. https://doi.org/10.1016/j.amjmed.2011.11.001

[92] Agrawal, S., Barnes, R., Brüggemann, R.J., Rautemaa-Richardson, R. and Warris, A. (2016) The Role of the Multidisciplinary Team in Antifungal Stewardship. *Journal of Antimicrobial Chemotherapy*, **71**, ii37-ii42. https://doi.org/10.1093/jac/dkw395

[93] Vandeputte, P., Ferrari, S. and Coste, A.T. (2012) Antifungal Resistance and New Strategies to Control Fungal Infections. *International Journal of Microbiology*, **2012**, Article ID: 713687. https://doi.org/10.1155/2012/713687

[94] Burki, T. (2023) WHO Publish Fungal Priority Pathogens List. *The Lancet Microbe*, **4**, E74. https://doi.org/10.1016/S2666-5247(23)00003-4

[95] Paneri, M., Sevta, P., Paneri, M. and Sevta, P. (2023) Overview of Antimicrobial Resistance: An Emerging Silent Pandemic. *Global Journal of Medical Pharmaceutical and Biomedical Update*, **18**, 11. https://doi.org/10.25259/GJMPBU_153_2022

[96] Pfavayi, L.T., Denning, D.W., Baker, S., Sibanda, E.N. and Mutapi, F. (2021) Determining the Burden of Fungal Infections in Zimbabwe. *Scientific Reports*, **11**, Article No. 13240. https://doi.org/10.1038/s41598-021-92605-1

[97] Prestel, C., Anderson, E., Forsberg, K., Lyman, M., de Perio, M.A., Kuhar, D., Edwards, K., Rivera, M., Shugart, A., Walters, M., *et al.* (2021) *Candida auris* Outbreak in a COVID-19 Specialty Care Unit—Florida, July-August 2020. *Morbidity and Mortality Weekly Reports*, **70**, 56-57. https://doi.org/10.15585/mmwr.mm7002e3

[98] Meijer, E.F.J., Dofferhoff, A.S.M., Hoiting, O. and Meis, J.F. (2021) COVID-19-Associated Pulmonary Aspergillosis: A Prospective Single-Center Dual Case Series. *Mycoses*, **64**, 457-464. https://doi.org/10.1111/myc.13254

[99] Rawson, T.M., Moore, L.S.P., Zhu, N., Ranganathan, N., Skolimowska, K., Gilchrist, M., Satta, G., Cooke, G. and Holmes, A. (2020) Bacterial and Fungal Coinfection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing. *Clinical Infectious Diseases*, **71**, 2459-2468. https://doi.org/10.1093/cid/ciaa530

[100] Nucci, M., Barreiros, G., Guimarães, L.F., Deriquehem, V.A.S., Castiñeiras, A.C. and Nouér, S.A. (2021) Increased Incidence of Candidemia in a Tertiary Care Hospital with the COVID-19 Pandemic. *Mycoses*, **64**, 152-156. https://doi.org/10.1111/myc.13225

[101] Falcone, M., Tiseo, G., Giordano, C., Leonildi, A., Menichini, M., Vecchione, A., Pistello, M., Guarracino, F., Ghiadoni, L., Forfori, F., *et al.* (2020) Predictors of

Hospital-Acquired Bacterial and Fungal Superinfections in COVID-19: A Prospective Observational Study. *Journal of Antimicrobial Chemotherapy*, **76**, 1078-1084. https://doi.org/10.1093/jac/dkaa530

[102] Mastrangelo, A., Germinario, B.N., Ferrante, M., Frangi, C., Li Voti, R., Muccini, C. and Ripa, M. (2021) Candidemia in Coronavirus Disease 2019 (COVID-19) Patients: Incidence and Characteristics in a Prospective Cohort Compared with Historical Non-COVID-19 Controls. *Clinical Infectious Diseases*, **73**, E2838-E2839. https://doi.org/10.1093/cid/ciaa1594

[103] Lai, C.C. and Yu, W.L. (2021) COVID-19 Associated with Pulmonary Aspergillosis: A Literature Review. *Journal of Microbiology, Immunology and Infection*, **54**, 46-53. https://doi.org/10.1016/j.jmii.2020.09.004

[104] Magnasco, L., Mikulska, M., Giacobbe, D.R., Taramasso, L., Vena, A., Dentone, C., Dettori, S., Tutino, S., Labate, L., *et al.* (2021) Spread of Carbapenem-Resistant Gram-Negatives and *Candida auris* during the Covid-19 Pandemic in Critically Ill Patients: One Step Back in Antimicrobial Stewardship? *Microorganisms*, **9**, Article 95. https://doi.org/10.3390/microorganisms9010095

[105] Rodriguez, J.Y., Le Pape, P., Lopez, O., Esquea, K., Labiosa, A.L. and Alvarez-Moreno, C. (2021) *Candida auris*: A Latent Threat to Critically Ill Patients with Coronavirus Disease 2019. *Clinical Infectious Diseases*, **73**, e2836-e2837. https://doi.org/10.1093/cid/ciaa1595

[106] Arendrup, M.C. and Patterson, T.F. (2017) Multidrug-Resistant Candida: Epidemiology, Molecular Mechanisms, and Treatment. *The Journal of Infectious Diseases*, **216**, S445-S451. https://doi.org/10.1093/infdis/jix131

[107] Pristov, K.E. and Ghannoum, M.A. (2019) Resistance of Candida to Azoles and Echinocandins Worldwide. *Clinical Microbiology and Infection*, **25**, 792-798. https://doi.org/10.1016/j.cmi.2019.03.028

[108] Perea, S. and Patterson, T.F. (2002) Antifungal Resistance in Pathogenic Fungi. *Clinical Infectious Diseases*, **35**, 1073-1080. https://doi.org/10.1086/344058

[109] Benedict, K., Whitham, H.K. and Jackson, B.R. (2022) Economic Burden of Fungal Diseases in the United States. *Open Forum Infectious Diseases*, **9**, ofac097. https://doi.org/10.1093/ofid/ofac097

[110] Warshaw, E.M. (2006) Evaluating Costs for Onychomycosis Treatments: A Practitioner's Perspective. *Journal of the American Podiatric Medical Association*, **96**, 38-52. https://doi.org/10.7547/0960038

[111] Mei-Sheng Riley, M. (2021) Invasive Fungal Infections among Immunocompromised Patients in Critical Care Settings: Infection Prevention Risk Mitigation. *Critical Care Nursing Clinics of North America*, **33**, 395-405. https://doi.org/10.1016/j.cnc.2021.07.002

[112] Low, C.Y. and Rotstein, C. (2011) Emerging Fungal Infections in Immunocompromised Patients. *F*1000 *Medicine Reports*, **3**, 14. https://doi.org/10.3410/M3-14

[113] Xia, J., Wang, Z., Li, T., Lu, F., Sheng, D. and Huang, W. (2022) Immunosuppressed Patients with Clinically Diagnosed Invasive Fungal Infections: The Fungal Species Distribution, Antifungal Sensitivity and Associated Risk Factors in a Tertiary Hospital of Anhui Province. *Infection and Drug Resistance*, **15**, 321-333. https://doi.org/10.2147/IDR.S351260

[114] Robertson, E., Abera, C., Wood, K., Deressa, K., Mesfin, S. and Scantlebury, C. (2023) Striving towards Access to Essential Medicines for Human and Animal Health; a Situational Analysis of Access to and Use of Antifungal Medications for Histoplasmosis in Ethiopia. *PLOS ONE*, **18**, e0278964.

https://doi.org/10.1371/journal.pone.0278964

[115] Roemer, T. and Krysan, D.J. (2014) Antifungal Drug Development: Challenges, Unmet Clinical Needs, and New Approaches. *Cold Spring Harbor Perspectives in Medicine*, **4**, a019703. https://doi.org/10.1101/cshperspect.a019703

[116] Ahmad, A., Molepo, J. and Patel, M. (2016) Challenges in the Development of Antifungal Agents against Candida: Scope of Phytochemical Research. *Current Pharmaceutical Design*, **22**, 4135-4150. https://doi.org/10.2174/1381612822666160607072748

[117] Rodrigues, M.L. and Nosanchuk, J.D. (2023) Recognition of Fungal Priority Pathogens: What Next? *PLOS Neglected Tropical Diseases*, **17**, e0011136. https://doi.org/10.1371/journal.pntd.0011136

[118] Hudson, M.M.T. (2001) Antifungal Resistance and Over-the-Counter Availability in the UK: A Current Perspective. *Journal of Antimicrobial Chemotherapy*, **48**, 345-350. https://doi.org/10.1093/jac/48.3.345

[119] Kneale, M., Bartholomew, J.S., Davies, E. and Denning, D.W. (2016) Global Access to Antifungal Therapy and Its Variable Cost. *Journal of Antimicrobial Chemotherapy*, **71**, 3599-3606. https://doi.org/10.1093/jac/dkw325

[120] Khairy, W.A., Nasser, H.A., Sarhan, M.D., El Shamy, A.A. and Galal, Y.S. (2021) Prevalence and Predictors of Self-Medication with Antifungal Drugs and Herbal Products among University Students: A Cross-Sectional Study from Egypt. *Risk Management and Healthcare Policy*, **14**, 2191-2200. https://doi.org/10.2147/RMHP.S308400

[121] Revie, N.M., Iyer, K.R., Robbins, N. and Cowen, L.E. (2018) Antifungal Drug Resistance: Evolution, Mechanisms and Impact. *Current Opinion in Microbiology*, **45**, 70-76. https://doi.org/10.1016/j.mib.2018.02.005

[122] Zhao, Y., Ye, L., Zhao, F., Zhang, L., Lu, Z., Chu, T., Wang, S., Liu, Z., Sun, Y., Chen, M., *et al.* (2023) *Cryptococcus neoformans,* a Global Threat to Human Health. *Infectious Diseases of Poverty*, **12**, Article No. 20. https://doi.org/10.1186/s40249-023-01073-4

[123] Xu, J. (2022) Assessing Global Fungal Threats to Humans. *mLife*, **1**, 223-240. https://doi.org/10.1002/mlf2.12036

[124] Rhodes, J. (2019) Rapid Worldwide Emergence of Pathogenic Fungi. *Cell Host & Microbe*, **26**, 12-14. https://doi.org/10.1016/j.chom.2019.06.009

[125] Lima, R., Ribeiro, F.C., Colombo, A.L. and de Almeida, J.N. (2022) The Emerging Threat Antifungal-Resistant *Candida tropicalis* in Humans, Animals, and Environment. *Frontiers in Fungal Biology*, **3**, Article 957021. https://doi.org/10.3389/ffunb.2022.957021

[126] Drgona, L., Khachatryan, A., Stephens, J., Charbonneau, C., Kantecki, M., Haider, S. and Barnes, R. (2014) Clinical and Economic Burden of Invasive Fungal Diseases in Europe: Focus on Pre-Emptive and Empirical Treatment of Aspergillus and Candida Species. *European Journal of Clinical Microbiology & Infectious Diseases*, **33**, 7-21. https://doi.org/10.1007/s10096-013-1944-3

[127] Slobbe, L., Polinder, S., Doorduijn, J.K., Lugtenburg, P.J., El Barzouhi, A., Steyerberg, E.W. and Rijnders, B.J.A. (2008) Outcome and Medical Costs of Patients with Invasive Aspergillosis and Acute Myelogenous Leukemia-Myelodysplastic Syndrome Treated with Intensive Chemotherapy: An Observational Study. *Clinical Infectious Diseases*, **47**, 1507-1512. https://doi.org/10.1086/591531

[128] Berger, S., Chazli, Y. El Babu, A.F. and Coste, A.T. (2017) Azole Resistance in *As-*

pergillus fumigatus: A Consequence of Antifungal Use in Agriculture? *Frontiers in Microbiology*, **8**, Article 1024. https://doi.org/10.3389/fmicb.2017.01024

[129] Stevenson, E.M., Gaze, W.H., Gow, N.A.R., Hart, A., Schmidt, W., Usher, J., Warris, A., Wilkinson, H. and Murray, A.K. (2022) Antifungal Exposure and Resistance Development: Defining Minimal Selective Antifungal Concentrations and Testing Methodologies. *Frontiers in Fungal Biology*, **3**, Article 918717. https://doi.org/10.3389/ffunb.2022.918717

[130] Burks, C., Darby, A., Londoño, L.G., Momany, M. and Brewer, M.T. (2021) Azole-Resistant *Aspergillus fumigatus* in the Environment: Identifying Key Reservoirs and Hotspots of Antifungal Resistance. *PLOS Pathogens*, **17**, e1009711. https://doi.org/10.1371/journal.ppat.1009711

[131] Picot, S., Beugnet, F., Leboucher, G. and Bienvenu, A.L. (2022) Drug Resistant Parasites and Fungi from a One-Health Perspective: A Global Concern That Needs Transdisciplinary Stewardship Programs. *One Health*, **14**, Article 100368. https://doi.org/10.1016/j.onehlt.2021.100368

[132] Verweij, P.E., Arendrup, M.C., Alastruey-Izquierdo, A., Gold, J.A.W., Lockhart, S.R., Chiller, T. and White, P.L. (2022) Dual Use of Antifungals in Medicine and Agriculture: How Do We Help Prevent Resistance Developing in Human Pathogens? *Drug Resistance Updates*, **65**, Article 100885. https://doi.org/10.1016/j.drup.2022.100885

[133] Verweij, P.E., Lucas, J.A., Arendrup, M.C., Bowyer, P., Brinkmann, A.J.F., Denning, D.W., Dyer, P.S., Fisher, M.C., Geenen, P.L., Gisi, U., *et al.* (2020) The One Health Problem of Azole Resistance in *Aspergillus fumigatus*: Current Insights and Future Research Agenda. *Fungal Biology Reviews*, **34**, 202-214. https://doi.org/10.1016/j.fbr.2020.10.003

[134] Sahu, S., Panda, A., Dash, S., Ramani, Y.R. and Behera, J. (2023) Changing Pattern of Antifungal Drug Resistance in a Tertiary Health-Care Facility—A Cross-Sectional Study. *Current Medical Issues*, **21**, 208-213. https://doi.org/10.4103/cmi.cmi_63_23

[135] Prajna, N.V., Lalitha, P., Krishnan, T., Rajaraman, R., Radnakrishnan, N., Srinivasan, M., Devi, L., Das, M., Liu, Z., Zegans, M.E., *et al.* (2022) Patterns of Antifungal Resistance in Adult Patients with Fungal Keratitis in South India: A Post Hoc Analysis of 3 Randomized Clinical Trials. *JAMA Ophthalmology*, **140**, 179-184. https://doi.org/10.1001/jamaophthalmol.2021.5765

[136] Sarma, S., Kumar, N., Sharma, S., Govil, D., Ali, T., Mehta, Y. and Rattan, A. (2013) Candidemia Caused by Amphotericin B and Fluconazole Resistant *Candida auris*. *Indian Journal of Medical Microbiology*, **31**, 90-91. https://doi.org/10.4103/0255-0857.108746

[137] Achilonu, C.C., Davies, A., Kanu, O.O., Noel, C.B. and Oladele, R. (2023) Recent Advances and Future Perspectives in Mitigating Invasive Antifungal-Resistant Pathogen *Aspergillus fumigatus* in Africa. *Current Treatment Options in Infectious Diseases*, **16**, 14-33. https://doi.org/10.1007/s40506-023-00269-4

[138] Allaw, F., Zahreddine, N.K., Ibrahim, A., Tannous, J., Taleb, H., Bizri, A.R., Dbaibo, G. and Kanj, S.S. (2021) First *Candida auris* Outbreak during a Covid-19 Pandemic in a Tertiary-Care Center in Lebanon. *Pathogens*, **10**, Article 157. https://doi.org/10.3390/pathogens10020157

[139] Jacobs, S.E., Jacobs, J.L., Dennis, E.K., Taimur, S., Rana, M., Patel, D., Gitman, M., Patel, G., Schaefer, S., Iyer, K., *et al.* (2022) *Candida auris* Pan-Drug-Resistant to Four Classes of Antifungal Agents. *Antimicrobial Agents and Chemotherapy*, **66**, e0005322. https://doi.org/10.1128/aac.00053-22

[140] Purkait, B., Kumar, A., Nandi, N., Sardar, A.H., Das, S., Kumar, S., Pandey, K., Ravidas, V., Kumar, M., De, T., *et al.* (2012) Mechanism of Amphotericin B Resistance in Clinical Isolates of *Leishmania donovani*. *Antimicrobial Agents and Chemotherapy*, **56**, 1031-1041. https://doi.org/10.1128/AAC.00030-11

[141] Mano, C., Kongkaew, A., Tippawangkosol, P., Somboon, P., Roytrakul, S., Pescher, P., Späth, G.F., Uthaipibull, C., Tantiworawit, A., Siriyasatien, P., *et al.* (2023) Amphotericin B Resistance Correlates with Increased Fitness *in Vitro* and *in Vivo* in Leishmania (Mundinia) Martiniquensis. *Frontiers in Microbiology*, **14**, Article 1156061. https://doi.org/10.3389/fmicb.2023.1156061

[142] Silva, L.N., Oliveira, S.S.C., Magalhães, L.B., Andrade Neto, V. V., Torres-Santos, E.C., Carvalho, M.D.C., Pereira, M.D., Branquinha, M.H. and Santos, A.L.S. (2020) Unmasking the Amphotericin B Resistance Mechanisms in *Candida haemulonii* Species Complex. *ACS Infectious Diseases*, **6**, 1273-1282. https://doi.org/10.1021/acsinfecdis.0c00117

[143] Messer, S.A., Diekema, D.J., Boyken, L., Tendolkar, S., Hollis, R.J. and Pfaller, M.A. (2006) Activities of Micafungin against 315 Invasive Clinical Isolates of Fluconazole-Resistant Candida Spp. *Journal of Clinical Microbiology*, **44**, 324-326. https://doi.org/10.1128/JCM.44.2.324-326.2006

[144] Alexander, B.D., Johnson, M.D., Pfeiffer, C.D., Jiménez-Ortigosa, C., Catania, J., Booker, R., Castanheira, M., Messer, S.A., Perlin, D.S. and Pfaller, M.A. (2013) Increasing Echinocandin Resistance in *Candida glabrata*: Clinical Failure Correlates with Presence of FKS Mutations and Elevated Minimum Inhibitory Concentrations. *Clinical Infectious Diseases*, **56**, 1724-1732. https://doi.org/10.1093/cid/cit136

[145] Healey, K.R. and Perlin, D.S. (2018) Fungal Resistance to Echinocandins and the MDR Phenomenon in *Candida glabrata*. *Journal of Fungi*, **4**, Article 105. https://doi.org/10.3390/jof4030105

[146] Perlin, D.S. (2015) Mechanisms of Echinocandin Antifungal Drug Resistance. *Annals of the New York Academy of Sciences*, **1354**, 1-11. https://doi.org/10.1111/nyas.12831

[147] Farmakiotis, D., Tarrand, J.J. and Kontoyiannis, D.P. (2014) Drug-Resistant *Candida glabrata* Infection in Cancer Patients. *Emerging Infectious Diseases*, **20**, 1833-1840. https://doi.org/10.3201/eid2011.140685

[148] Thompson, G.R., Wiederhold, N.P., Vallor, A.C., Villareal, N.C., Lewis, J.S. and Patterson, T.F. (2008) Development of Caspofungin Resistance Following Prolonged Therapy for Invasive Candidiasis Secondary to *Candida glabrata* Infection. *Antimicrobial Agents and Chemotherapy*, **52**, 3783-3785. https://doi.org/10.1128/AAC.00473-08

[149] Satoh, K., Makimura, K., Hasumi, Y., Nishiyama, Y., Uchida, K. and Yamaguchi, H. (2009) *Candida auris* Sp. Nov., a Novel Ascomycetous Yeast Isolated from the External Ear Canal of an Inpatient in a Japanese Hospital. *Microbiology and Immunology*, **53**, 41-44. https://doi.org/10.1111/j.1348-0421.2008.00083.x

[150] Chowdhary, A., Voss, A. and Meis, J.F. (2016) Multidrug-Resistant *Candida auris*: 'New Kid on the Block' in Hospital-Associated Infections? *Journal of Hospital Infection*, **94**, 209-212. https://doi.org/10.1016/j.jhin.2016.08.004

[151] Chowdhary, A., Tarai, B., Singh, A. and Sharma, A. (2020) Multidrug-Resistant *Candida auris* Infections in Critically Ill Coronavirus Disease Patients, India, April-July 2020. *Emerging Infectious Diseases*, **26**, 2694-2696. https://doi.org/10.3201/eid2611.203504

[152] Pfaller, M.A., Messer, S.A., Moet, G.J., Jones, R.N. and Castanheira, M. (2011) Can-

dida Bloodstream Infections: Comparison of Species Distribution and Resistance to Echinocandin and Azole Antifungal Agents in Intensive Care Unit (ICU) and Non-ICU Settings in the SENTRY Antimicrobial Surveillance Program (2008-2009). *International Journal of Antimicrobial Agents*, **38**, 65-69. https://doi.org/10.1016/j.ijantimicag.2011.02.016

[153] Beyda, N.D., John, J., Kilic, A., Alam, M.J., Lasco, T.M. and Garey, K.W. (2014) FKS Mutant *Candida glabrata*: Risk Factors and Outcomes in Patients with Candidemia. *Clinical Infectious Diseases*, **59**, 819-825. https://doi.org/10.1093/cid/ciu407

[154] Pfaller, M.A., Castanheira, M., Messer, S.A. and Jones, R.N. (2015) *In Vitro* Antifungal Susceptibilities of Isolates of Candida Spp. and Aspergillus Spp. from China to Nine Systemically Active Antifungal Agents: Data from the SENTRY Antifungal Surveillance Program, 2010 through 2012. *Mycoses*, **58**, 209-214. https://doi.org/10.1111/myc.12299

[155] Xu, Z., Zhang, L., Han, R., Ding, C., Shou, H., Duan, X. and Zhang, S. (2023) A Candidemia Case Caused by a Novel Drug-Resistant *Candida auris* with the Y132f Mutation in Ergii in Mainland China. *Infection and Drug Resistance*, **16**, 3065-3072. https://doi.org/10.2147/IDR.S409708

[156] Khan, Z.U., Al-Sweih, N.A., Ahmad, S., Al-Kazemi, N., Khan, S., Joseph, L. and Chandy, R. (2007) Outbreak of Fungemia among Neonates Caused by *Candida haemulonii* Resistant to Amphotericin B, Itraconazole, and Fluconazole. *Journal of Clinical Microbiology*, **45**, 2025-2027. https://doi.org/10.1128/JCM.00222-07

[157] Kim, M.N., Shin, J.H., Sung, H., Lee, K., Kim, E.C., Ryoo, N., Lee, J.S., Jung, S.L., Park, K.H., Kee, S.J., *et al.* (2009) *Candida haemulonii* and Closely Related Species at 5 University Hospitals in Korea: Identification, Antifungal Susceptibility, and Clinical Features. *Clinical Infectious Diseases*, **48**, e57-61. https://doi.org/10.1086/597108

[158] Galia, L., Pezzani, M.D., Compri, M., Callegari, A., Rajendran, N.B., Carrara, E. and Tacconelli, E. (2022) Surveillance of Antifungal Resistance in Candidemia Fails to Inform Antifungal Stewardship in European Countries. *Journal of Fungi*, **8**, Article 249. https://doi.org/10.3390/jof8030249

[159] Woods, M., McAlister, J.A. and Geddes-McAlister, J. (2023) A One Health Approach to Overcoming Fungal Disease and Antifungal Resistance. *WIREs Mechanisms of Disease*, **15**, e1610. https://doi.org/10.1002/wsbm.1610

[160] Urbancic, K.F., Thursky, K., Kong, D.C.M., Johnson, P.D.R. and Slavin, M.A. (2018) Antifungal Stewardship: Developments in the Field. *Current Opinion in Infectious Diseases*, **31**, 490-498. https://doi.org/10.1097/QCO.0000000000000497

[161] Nivoix, Y., Launoy, A., Lutun, P., Moulin, J.C., Phai Pang, K.A., Fornecker, L.M., Wolf, M., Levěque, D., Letscher-Bru, V., Beretz, L., *et al.* (2012) Adherence to Recommendations for the Use of Antifungal Agents in a Tertiary Care Hospital. *Journal of Antimicrobial Chemotherapy*, **67**, 2506-2513. https://doi.org/10.1093/jac/dks256

[162] Albahar, F., Alhamad, H., Abu Assab, M., Abu-Farha, R., Alawi, L. and Khaleel, S. (2024) The Impact of Antifungal Stewardship on Clinical and Performance Measures: A Global Systematic Review. *Tropical Medicine and Infectious Disease*, **9**, Article 8. https://doi.org/10.3390/tropicalmed9010008

[163] Samura, M., Hirose, N., Kurata, T., Ishii, J., Nagumo, F., Takada, K., Koshioka, S., Uchida, M., Yamamoto, S., Inoue, J., *et al.* (2020) Support for Fungal Infection Treatment Mediated by Pharmacist-Led Antifungal Stewardship Activities. *Journal of Infection and Chemotherapy*, **26**, 272-279.

https://doi.org/10.1016/j.jiac.2019.09.016

[164] Cook, P.P. and Gooch, M. (2015) Long-Term Effects of an Antimicrobial Stewardship Programme at a Tertiary-Care Teaching Hospital. *International Journal of Antimicrobial Agents*, **45**, 262-267. https://doi.org/10.1016/j.ijantimicag.2014.11.006

[165] Alegria, W. and Patel, P.K. (2021) The Current State of Antifungal Stewardship in Immunocompromised Populations. *Journal of Fungi*, **7**, Article 352. https://doi.org/10.3390/jof7050352

[166] Valerio, M., Muñoz, P., Rodríguez-González, C., Sanjurjo, M., Guinea, J. and Bouza, E. (2015) Training Should Be the First Step toward an Antifungal Stewardship Program. *Enfermedades Infecciosas y Microbiología Clínica*, **33**, 221-227. https://doi.org/10.1016/j.eimc.2014.04.016

[167] Mondain, V., Lieutier, F., Hasseine, L., Gari-Toussaint, M., Poiree, M., Lions, C. and Pulcini, C. (2013) A 6-Year Antifungal Stewardship Programme in a Teaching Hospital. *Infection*, **41**, 621-628. https://doi.org/10.1007/s15010-013-0431-1

[168] Talento, A.F., Qualie, M., Cottom, L., Backx, M. and White, P.L. (2021) Lessons from an Educational Invasive Fungal Disease Conference on Hospital Antifungal Stewardship Practices across the UK and Ireland. *Journal of Fungi*, **7**, Article 801. https://doi.org/10.3390/jof7100801

[169] Mudenda, S., Daka, V. and Matafwali, S.K. (2023) World Health Organization AWaRe Framework for Antibiotic Stewardship: Where Are We Now and Where Do We Need to Go? An Expert Viewpoint. *Antimicrobial Stewardship & Healthcare Epidemiology*, **3**, e84. https://doi.org/10.1017/ash.2023.164

[170] World Health Organization (2023) AWaRe Classification of Antibiotics for Evaluation and Monitoring of Use. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.04

[171] Graham, K., Sinyangwe, C., Nicholas, S., King, R., Mukupa, S., Källander, K., Counihan, H., Montague, M., Tibenderana, J. and Hamade, P. (2016) Rational Use of Antibiotics by Community Health Workers and Caregivers for Children with Suspected Pneumonia in Zambia: A Cross-Sectional Mixed Methods Study. *BMC Public Health*, **16**, Article No. 897. https://doi.org/10.1186/s12889-016-3541-8

[172] Hagen, T.L., Hertz, M.A., Uhrin, G.B., Dalager-Pedersen, M., Schønheyder, H.C. and Nielsen, H. (2017) Adherence to Local Antimicrobial Guidelines for Initial Treatment of Community-Acquired Infections. *Danish Medical Journal*, **64**, A5381.

[173] Mekonnen Eticha, E. and Gemechu, W.D. (2021) Adherence to Guidelines for Assessment and Empiric Antibiotics Recommendations for Community-Acquired Pneumonia at Ambo University Referral Hospital: Prospective Observational Study. *Patient Preference and Adherence*, **15**, 467-473. https://doi.org/10.2147/PPA.S295118

[174] Tell, D., Engström, S. and Mölstad, S. (2015) Adherence to Guidelines on Antibiotic Treatment for Respiratory Tract Infections in Various Categories of Physicians: A Retrospective Cross-Sectional Study of Data from Electronic Patient Records. *BMJ Open*, **5**, e008096. https://doi.org/10.1136/bmjopen-2015-008096

[175] Boltena, M.T., Woldie, M., Siraneh, Y., Steck, V., El-Khatib, Z. and Morankar, S. (2023) Adherence to Evidence-Based Implementation of Antimicrobial Treatment Guidelines among Prescribers in Sub-Saharan Africa: A Systematic Review and Meta-Analysis. *Journal of Pharmaceutical Policy and Practice*, **16**, Article 137. https://doi.org/10.1186/s40545-023-00634-0

[176] Wiedenmayer, K., Ombaka, E., Kabudi, B., Canavan, R., Rajkumar, S., Chilunda, F., Sungi, S. and Stoermer, M. (2021) Adherence to Standard Treatment Guidelines

among Prescribers in Primary Healthcare Facilities in the Dodoma Region of Tanzania. *BMC Health Services Research*, **21**, Article No. 272. https://doi.org/10.1186/s12913-021-06257-y

[177] Metz, J., Oehler, P., Burggraf, M., Burdach, S., Behrends, U. and Rieber, N. (2019) Improvement of Guideline Adherence after the Implementation of an Antibiotic Stewardship Program in a Secondary Care Pediatric Hospital. *Frontiers in Pediatrics*, **7**, Article 478. https://doi.org/10.3389/fped.2019.00478

[178] Barlam, T.F., Cosgrove, S.E., Abbo, L.M., Macdougall, C., Schuetz, A.N., Septimus, E.J., Srinivasan, A., Dellit, T.H., Falck-Ytter, Y.T., Fishman, N.O., *et al.* (2016) Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clinical Infectious Diseases*, **62**, e51-e77. https://doi.org/10.1093/cid/ciw118

[179] Rabaan, A.A., Sulaiman, T., Al-Ahmed, S.H., Buhaliqah, Z.A., Buhaliqah, A.A., AlYuosof, B., Alfaresi, M., Al Fares, M.A., Alwarthan, S., Alkathlan, M.S., *et al.* (2023) Potential Strategies to Control the Risk of Antifungal Resistance in Humans: A Comprehensive Review. *Antibiotics*, **12**, Article 608. https://doi.org/10.3390/antibiotics12030608

[180] McCarty, T.P. and Pappas, P.G. (2021) Antifungal Pipeline. *Frontiers in Cellular and Infection Microbiology*, **11**, Article 732223. https://doi.org/10.3389/fcimb.2021.732223

[181] Castelli, M.V., Butassi, E., Monteiro, M.C., Svetaz, L.A., Vicente, F. and Zacchino, S.A. (2014) Novel Antifungal Agents: A Patent Review (2011-Present). *Expert Opinion on Therapeutic Patents*, **24**, 323-338. https://doi.org/10.1517/13543776.2014.876993

[182] Fuentefria, A.M., Pippi, B., Dalla Lana, D.F., Donato, K.K. and de Andrade, S.F. (2018) Antifungals Discovery: An Insight into New Strategies to Combat Antifungal Resistance. *Letters in Applied Microbiology*, **66**, 2-13. https://doi.org/10.1111/lam.12820

[183] Durdu, M. and Ilkit, M. (2023) Strategies to Improve the Diagnosis and Clinical Treatment of Dermatophyte Infections. *Expert Review of Anti-Infective Therapy*, **21**, 29-40. https://doi.org/10.1080/14787210.2023.2144232

[184] Smith, D.J., Gold, J.A.W., Benedict, K., Wu, K., Lyman, M., Jordan, A., Medina, N., Lockhart, S.R., Sexton, D.J., Chow, N.A., *et al.* (2023) Public Health Research Priorities for Fungal Diseases: A Multidisciplinary Approach to Save Lives. *Journal of Fungi*, **9**, Article 820. https://doi.org/10.3390/jof9080820

[185] Sanguinetti, M., Posteraro, B., Beigelman-Aubry, C., Lamoth, F., Dunet, V., Slavin, M. and Richardson, M.D. (2019) Diagnosis and Treatment of Invasive Fungal Infections: Looking Ahead. *Journal of Antimicrobial Chemotherapy*, **74**, II27-II37. https://doi.org/10.1093/jac/dkz041

[186] Scorzoni, L., de Paula e Silva, A.C.A., Marcos, C.M., Assato, P.A., de Melo, W.C.M.A., de Oliveira, H.C., Costa-Orlandi, C.B., Mendes-Giannini, M.J.S. and Fusco-Almeida, A.M. (2017) Antifungal Therapy: New Advances in the Understanding and Treatment of Mycosis. *Frontiers in Microbiology*, **8**, Article 36. https://doi.org/10.3389/fmicb.2017.00036

[187] Skosana, P.P., Mudenda, S., Demana, P.H. and Witika, B.A. (2023) Exploring Nanotechnology as a Strategy to Circumvent Antimicrobial Resistance in Bone and Joint Infections. *ACS Omega*, **8**, 15865-15882. https://doi.org/10.1021/acsomega.3c01225

[188] Mali, R. and Patil, J. (2023) Nanoparticles: A Novel Antifungal Drug Delivery Sys-

tem. *Antibiotics*, **14**, Article 61. https://doi.org/10.3390/IOCN2023-14513

[189] Al-Jedai, A.H., Almogbel, Y., Eljaaly, K., Alqahtani, N.M., Almudaiheem, H.Y., Awad, N., Alissa, D.A., Assiri, A. and Alaama, T. (2022) Restriction on Antimicrobial Dispensing without Prescription on a National Level: Impact on the Overall Antimicrobial Utilization in the Community Pharmacies in Saudi Arabia. *PLOS ONE*, **17**, e0271188. https://doi.org/10.1371/journal.pone.0271188

[190] Rawson, T.M., Antcliffe, D.B., Wilson, R.C., Abdolrasouli, A. and Moore, L.S.P. (2023) Management of Bacterial and Fungal Infections in the ICU: Diagnosis, Treatment, and Prevention Recommendations. *Infection and Drug Resistance*, **16**, 2709-2726. https://doi.org/10.2147/IDR.S390946

[191] Storr, J., Twyman, A., Zingg, W., Damani, N., Kilpatrick, C., Reilly, J., Price, L., Egger, M., Grayson, M.L., Kelley, E., *et al.* (2017) Core Components for Effective Infection Prevention and Control Programmes: New WHO Evidence-Based Recommendations. *Antimicrobial Resistance & Infection Control*, **6**, Article No. 6. https://doi.org/10.1186/s13756-016-0149-9

[192] Moore, D.P., Chetty, T., Pillay, A., Karsas, M., Cloete, J., Balakrishna, Y., Reddy, T., Archary, M., van Kwawegen, A., Thomas, R., *et al.* (2024) Antibiotic and Antifungal Use in Paediatric Departments at Three Academic Hospitals in South Africa. *IJID Regions*, **10**, 151-158. https://doi.org/10.1016/j.ijregi.2023.12.004

[193] Nagel, J.L., Kaye, K.S., LaPlante, K.L. and Pogue, J.M. (2016) Antimicrobial Stewardship for the Infection Control Practitioner. *Infectious Disease Clinics of North America*, **30**, 771-784. https://doi.org/10.1016/j.idc.2016.04.012

[194] Zhou, S., Nagel, J.L., Kaye, K.S., LaPlante, K.L., Albin, O.R. and Pogue, J.M. (2021) Antimicrobial Stewardship and the Infection Control Practitioner: A Natural Alliance. *Infectious Disease Clinics of North America*, **35**, 771-787. https://doi.org/10.1016/j.idc.2021.04.011

[195] Senbato, F.R., Wolde, D., Belina, M., Kotiso, K.S., Medhin, G., Amogne, W. and Eguale, T. (2024) Compliance with Infection Prevention and Control Standard Precautions and Factors Associated with Noncompliance among Healthcare Workers Working in Public Hospitals in Addis Ababa, Ethiopia. *Antimicrobial Resistance & Infection Control*, **13**, Article No. 32. https://doi.org/10.1186/s13756-024-01381-w

[196] Abalkhail, A. and Alslamah, T. (2022) Institutional Factors Associated with Infection Prevention and Control Practices Globally during the Infectious Pandemics in Resource-Limited Settings. *Vaccines*, **10**, Article 1811. https://doi.org/10.3390/vaccines10111811

[197] Das, A., Garg, R., Kumar, E.S., Singh, D., Ojha, B., Kharchandy, H.L., Pathak, B.K., Srikrishnan, P., Singh, R., Joshua, I., *et al.* (2022) Implementation of Infection Prevention and Control Practices in an Upcoming COVID-19 Hospital in India: An Opportunity Not Missed. *PLOS ONE*, **17**, e0268071. https://doi.org/10.1371/journal.pone.0268071

[198] Mustafa, Z.U., Majeed, H.K., Latif, S., Salman, M., Hayat, K., Mallhi, T.H., Khan, Y.H., Khan, A.H., Abubakar, U., Sultana, K., *et al.* (2023) Adherence to Infection Prevention and Control Measures among Health-Care Workers Serving in COVID-19 Treatment Centers in Punjab, Pakistan. *Disaster Medicine and Public Health Preparedness*, **17**, e298. https://doi.org/10.1017/dmp.2022.252

[199] Ling, M.L., Ching, P., Cheng, J., Lang, L., Liberali, S., Poon, P., Shin, Y. and Sim, C. (2023) APSIC Dental Infection Prevention and Control (IPC) Guidelines. *Antimicrobial Resistance & Infection Control*, **12**, Article No. 53. https://doi.org/10.1186/s13756-023-01252-w

[200] Gahamanyi, N., Umuhoza, T., Saeed, S.I., Mayigane, L.N. and Hakizimana, J.N. (2023) A Review of the Important Weapons against Antimicrobial Resistance in Sub-Saharan Africa. *Applied Biosciences*, **2**, 136-156. https://doi.org/10.3390/applbiosci2020011

[201] Ben-Ami, R., Halaburda, K., Klyasova, G., Metan, G., Torosian, T. and Akova, M. (2013) A Multidisciplinary Team Approach to the Management of Patients with: Suspected or Diagnosed Invasive Fungal Disease. *Journal of Antimicrobial Chemotherapy*, **68**, iii25-iii33. https://doi.org/10.1093/jac/dkt390

[202] Janssen, N.A.F., Brüggemann, R.J.M., Reijers, M.H., Henriet, S.S.V., Ten Oever, J., de Mast, Q., Berk, Y., de Kort, E.A., Kullberg, B.J., Netea, M.G., *et al.* (2020) A Multidisciplinary Approach to Fungal Infections: One-Year Experiences of a Center of Expertise in Mycology. *Journal of Fungi*, **6**, Article 274. https://doi.org/10.3390/jof6040274

[203] Ashiru-Oredope, D., Langford, B.J., Bonaconsa, C., Nampoothiri, V., Charani, E. and Goff, D.A. (2023) Global Collaborations in Antimicrobial Stewardship: All Hands on Deck. *Antimicrobial Stewardship & Healthcare Epidemiology*, **3**, e66. https://doi.org/10.1017/ash.2023.122

[204] Ashiru-Oredope, D., Nabiryo, M., Zengeni, L., Kamere, N., Makotose, A., Olaoye, O., Townsend, W., Waddingham, B., Matuluko, A., Nambatya, W., *et al.* (2023) Tackling Antimicrobial Resistance: Developing and Implementing Antimicrobial Stewardship Interventions in Four African Commonwealth Countries through a Health Partnership Model. *Journal of Public Health in Africa*, **14**, 2335.

[205] Lakoh, S., Bawoh, M., Lewis, H., Jalloh, I., Thomas, C., Barlatt, S., Jalloh, A., Deen, G.F., Russell, J.B.W., Kabba, M.S., *et al.* (2023) Establishing an Antimicrobial Stewardship Program in Sierra Leone: A Report of the Experience of a Low-Income Country in West Africa. *Antibiotics*, **12**, Article 424. https://doi.org/10.3390/antibiotics12030424

[206] Veepanattu, P., Singh, S., Mendelson, M., Nampoothiri, V., Edathadatil, F., Surendran, S., Bonaconsa, C., Mbamalu, O., Ahuja, S., Birgand, G., *et al.* (2020) Building Resilient and Responsive Research Collaborations to Tackle Antimicrobial Resistance—Lessons Learnt from India, South Africa, and UK. *International Journal of Infectious Diseases*, **100**, 278-282. https://doi.org/10.1016/j.ijid.2020.08.057

[207] Moyo, P., Moyo, E., Mangoya, D., Mhango, M., Mashe, T., Imran, M. and Dzinamarira, T. (2023) Prevention of Antimicrobial Resistance in Sub-Saharan Africa: What Has Worked? What Still Needs to Be Done? Journal of Infection and Public Health, **16**, 632-639. https://doi.org/10.1016/j.jiph.2023.02.020

[208] Musa, K., Okoliegbe, I., Abdalaziz, T., Aboushady, A.T., Stelling, J. and Gould, I.M. (2023) Laboratory Surveillance, Quality Management, and Its Role in Addressing Antimicrobial Resistance in Africa: A Narrative Review. *Antibiotics*, **12**, Article 1313. https://doi.org/10.3390/antibiotics12081313

[209] Iwu, C.D. and Patrick, S.M. (2021) An Insight into the Implementation of the Global Action Plan on Antimicrobial Resistance in the WHO African Region: A Roadmap for Action. *International Journal of Antimicrobial Agents*, **58**, Article 106411. https://doi.org/10.1016/j.ijantimicag.2021.106411

[210] Mader, R., Muñoz Madero, C., Aasmäe, B., Bourély, C., Broens, E.M., Busani, L., Callens, B., Collineau, L., Crespo-Robledo, P., Damborg, P., *et al.* (2022) Review and Analysis of National Monitoring Systems for Antimicrobial Resistance in Animal Bacterial Pathogens in Europe: A Basis for the Development of the European Antimicrobial Resistance Surveillance Network in Veterinary Medicine (EARS-Vet). *Frontiers in Microbiology*, **13**, Article 807.

https://doi.org/10.3389/fmicb.2022.838490

[211] Arieti, F., Göpel, S., Sibani, M., Carrara, E., Pezzani, M.D., Murri, R., Mutters, N.T., Lòpez-Cerero, L., Voss, A., Cauda, R., *et al.* (2020) White Paper: Bridging the Gap between Surveillance Data and Antimicrobial Stewardship in the Outpatient Sector—Practical Guidance from the JPIAMR ARCH and COMBACTE-MAGNET EPI-Net Networks. *Journal of Antimicrobial Chemotherapy*, **75**, II42-II51. https://doi.org/10.1093/jac/dkaa428

[212] He, S., Shrestha, P., Henry, A.D. and Legido-Quigley, H. (2023) Leveraging Collaborative Research Networks against Antimicrobial Resistance in Asia. *Frontiers in Public Health*, **11**, Article 1191036. https://doi.org/10.3389/fpubh.2023.1191036

[213] World Health Organization (2024) Regulation and Prequalification. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/regulatory-convergence-networks/harmonization?page=10

[214] Kållberg, C., Mathiesen, L., Gopinathan, U. and Salvesen Blix, H. (2023) The Role of Drug Regulatory Authorities and Health Technology Assessment Agencies in Shaping Incentives for Antibiotic R&D: A Qualitative Study. *Journal of Pharmaceutical Policy and Practice*, **16**, Article 53. https://doi.org/10.1186/s40545-023-00556-x

[215] Kirchhelle, C., Atkinson, P., Broom, A., Chuengsatiansup, K., Ferreira, J.P., Fortané, N., Frost, I., Gradmann, C., Hinchliffe, S., Hoffman, S.J., *et al.* (2020) Setting the Standard: Multidisciplinary Hallmarks for Structural, Equitable and Tracked Antibiotic Policy. *BMJ Global Health*, **5**, e003091. https://doi.org/10.1136/bmjgh-2020-003091

[216] Muteeb, G., Rehman, M.T., Shahwan, M. and Aatif, M. (2023) Origin of Antibiotics and Antibiotic Resistance, and Their Impacts on Drug Development: A Narrative Review. *Pharmaceuticals*, **16**, Article 1615. https://doi.org/10.3390/ph16111615