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Antifungal Stewardship - Principles, Current Practices, Limitations, and Potential Solutions: A Narrative Review

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ABSTRACT

This narrative review explores the critical role of antifungal stewardship (AFS) programs in optimizing antifungal use to improve patient outcomes and combat the rising threat of antifungal resistance. The global incidence of invasive fungal infections (IFIs) is increasing, necessitating urgent and effective AFS strategies. We outline the core principles of AFS, including appropriate antifungal selection, tailored treatment, optimized therapy, timely initiation and de-escalation, minimizing adverse effects, reducing healthcare costs, and preventing resistance emergence. Key components essential for the successful implementation of AFS programs are discussed. Current AFS practices are examined, highlighting significant variability in implementation across healthcare settings due to resource availability, local epidemiology, and provider expertise. Additionally, evidence on the effectiveness of AFS programs across multiple institutions worldwide is reviewed. The limitations hindering widespread AFS adoption, including resource constraints, diagnostic challenges, lack of standardization, and inadequate training, are acknowledged. Potential solutions such as enhanced collaboration, comprehensive education and training programs, and a One Health approach to address health disparities are proposed. AFS plays a central role in optimizing antifungal use, improving patient outcomes, and preserving the effectiveness of these essential therapies for future generations.

KEYWORDS: Antifungal stewardship; Invasive fungal infections; Stewardship components; Challenges

INTRODUCTION

Antifungal stewardship (AFS) is an important component of antimicrobial stewardship (AMS) programs, which focuses specifically on optimizing the usage of antifungal agents and preventing the spread of drug resistant fungal infections.^{1,3} The occurrence of invasive fungal infections (IFIs) are being increasingly reported worldwide^{4,6} together with increasing resistance to antifungal agents.^{7,9} This highlights that there is an urgent need for building and practicing efficient antifungal stewardship strategies. This narrative review summarizes the core principles of antifungal stewardship, elaborating on the key

components and current practices that are being followed, highlighting both successful outcomes and challenges. Also, potential solutions for these challenges and future directions for enhancing antifungal stewardship practices are reviewed.

PRINCIPLES OF ANTIFUNGAL STEWARDSHIP

The basic principles of antifungal stewardship are very much like those of antimicrobial stewardship. It emphasizes using antifungal medications responsibly to

Citation: Rajbongshi J, V M, Durairaj E.Antifungal Stewardship - Principles, Current Practices, Limitations, and Potential Solutions: A Narrative Review. JASPI. 2025;3(1):26-36 improve patient outcomes while preserving their efficacy for future generations. ^{1,3,5} Key principles include:

Appropriate Usage: Choosing the right antifungal agent, dose, route and duration of administration is the first and foremost principle. It should be decided for each patient individually based on their specific presentation and laboratory findings including fungal microscopy, culture and antifungal susceptibility testing results.^{4,5,7} Antifungal resistance emerges mainly due to the inappropriate use, including overuse and baseless empiric therapy without adequate diagnostics.^{2,6,10}

Optimized therapy: Early and rapid initiation of appropriate empirical therapy with antifungal agents in patients with confirmed or highly suspected IFIs is essential for better outcomes⁷ Also, this should be followed by prompt de-escalation of antifungal therapy as soon as the causative agent and its susceptibility profile are identified.^{4,7} Early discontinuation of unnecessary empiric therapy is very essential to minimize the exposure and subsequent development of antifungal resistance.^{6,7}

Minimal Adverse Events: Another important aspect that need to be considered is that most of the antifungal agents can result in serious adverse effects.^{5,10} This warrants careful patient selection and close monitoring during the period of administration especially with parenteral and oral antifungal agents. AFS programs when implemented properly, can minimize these adverse events. This involves judicious drug selection, dose adjustments and appropriate duration of therapy.^{1,3}

Reduced expenditure: Antifungal agents are often expensive^{2,3} and their overuse contributes significantly to increased healthcare expenditure.^{5,10} AFS programs work on reducing the unnecessary expenditure by promoting rational prescription practices and efficient utilization of resources for antifungal therapy.^{11,12}

Preventing Resistance: The increasing incidence and spread of antifungal resistance globally pose a major threat. ^{7,9} AFS programs play a critical role in slowing down this resistance emergence by optimizing the antifungal therapy usage in a judicious manner.^{2,6,10}

COMPONENTS OF ANTIFUNGAL STEWARDSHIP PROGRAMS

The antifungal stewardship programs comprise of multi-component strategies that together bring out

successful outcome.^{1,4,13} The key components of an AFS program are:

Multi-disciplinary Team: A collaborative effort among various healthcare professionals, including handling clinicians, infectious disease (ID) specialists, clinical microbiologists, pharmacists and nursing staff who are involved in the care of patients at risk for IFIs is very essential for the success of an AFS program.^{14,16} This collaborative approach ensures cumulative expertise and coordinated efforts that efficiently addresses appropriate use of antifungal agents.^{12,17}

Diagnostic Stewardship: The appropriate use of antifungal therapy, the key principle of any AFS program, relies mostly on the accurate and timely diagnosis of IFIs.^{4,7} Availability of the essential diagnostic tools, such as fungal microscopy, cultures, serum biomarkers (e.g., β -D-glucan, galactomannan), and advanced imaging techniques, is needed to minimize unnecessary empiric therapy.^{18,20} Diagnostic stewardship also includes good quality control practices, appropriate selection among the available tests and appropriate interpretation of these diagnostic tests, avoiding redundant or unnecessary testing.⁷

Formulary Restriction and Prior Authorization: Similar to AMS programs, some AFS programs have implemented the process of getting prior authorization and formulary restriction for selected antifungal agents, especially the ones which are expensive or those with higher potential for developing resistance.^{2,21} This approach has helped to some extent to control the use and ensured appropriate selection of antifungal agents.⁷

Prospective Audit and Feedback: The antifungal prescription practices need to regularly reviewed and feedback should be provided to the prescribing clinicians. This is a crucial component of AFS.^{7,21,22} This process when done iteratively can help in identifying areas with scope of improvement and also promotes good adherence to established protocols and guidelines.¹⁴

Therapeutic Drug Monitoring (TDM): Though it is not possible with every case, TDM, wherever applicable, can help in optimizing the antifungal dosing and it can ensure therapeutic drug levels are achieved at target site. This reduces the treatment failure rates and development of antifungal resistance.^{4,5,23} This can be particularly relevant for those antifungal agents with narrow therapeutic indices.⁴

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Guidelines and Educational Programs: Developing and disseminating clear and concise institutional guidelines for the diagnosis and treatment of IFIs are essential. This guides appropriate antifungal use at multiple levels.^{4,6,7} Regularly conducted educational initiatives for the healthcare providers improve the awareness and promote adherence to AFS principles.^{1,2,24}

Surveillance and Data Collection: Routine surveillance activity to monitor the incidence of IFIs, antifungal utilization rates and emerging resistance patterns is important. This helps in monitoring and assessing the effectiveness of ongoing AFS programs and in recognizing emerging trends.^{4,17,25} This data enables adjustments in the program and makes it sustainable.¹⁷

CURRENT PRACTICES IN ANTIFUNGAL STEWARDSHIP

The current practices followed for implementation of AFS programs varies considerably across different healthcare settings. These are influenced by factors such as available resources, local epidemiology and the expertise of healthcare provider team ^{7,21,22} The practices followed by most institutions identified from published studies are highlighted below:

Hospital-Based Programs: Many hospitals do not have dedicated AFS programs. They have incorporated certain components of AFS activities into their existing AMS programs. ^{14,22,26} The main components that are incorporated includes prospective audit and feedback, formulary restrictions, and educational initiatives. ^{7,11,21} However, the way AFS programs are implemented varies significantly between these institutions and they lack comprehensive standard guidelines. ^{7,22,27}

Regional and National Initiatives: Several countries and regions have initiated national or regional AFS programs to standardize the AFS practices and to promote collaboration among different healthcare institutions.^{28,29} These often involve the development of national guidelines and surveillance systems. Also, regular educational programs are organized and monitored by national bodies.²⁵

Focus on Specific Patient Populations: There are few AFS programs that specifically focus on certain high-risk patient populations. Specific AFS programs have been implemented in patient population with hematological malignancies or those undergoing organ transplantation.^{13,30,31} These programs often involve targeted strategies for prophylaxis and close surveillance of antifungal use.^{13,30}

Impact of the COVID-19 Pandemic: The healthcare systems were affected globally following COVID-19 pandemic which affected AMS programs including antifungal prescribing practices.³² Some studies reported increased antifungal use during the pandemic, potentially due to increased rates of IFIs or broader use of empirical antifungal therapy.^{14,32} This highlights the need for adaptable AFS strategies that can respond to evolving clinical needs.

Pharmacist Involvement: Pharmacists play a vital role in many AFS programs, providing expertise in antifungal pharmacokinetics and pharmacodynamics, medication reconciliation, and optimizing therapy. Their involvement often leads to improved adherence to guidelines and reduced antifungal consumption.^{15,33}

EFFECTIVENESS OF CURRENT ANTIFUNGAL STEWARDSHIP PROGRAMS

Most studies analyzing the ongoing antifungal stewardship programs have shown that significant reduction of antifungal use can be achieved through education, standard guidelines and collaborative consultations. These programs frequently resulted in improved adherence to standard guidelines guiding appropriate antifungal drug selection, dosing and duration. Substantial cost savings have been observed without compromising patient outcomes. A summary of multiple studies conducted in different settings and countries assessing the impact of antifungal stewardship program is provided in Table 1.

LIMITATIONS OF CURRENT PRACTICES

Several limitations hinder the widespread adoption and effectiveness of current AFS practices. These limitations stem from various factors including resource constraints, diagnostic challenges, and a lack of standardization across different healthcare settings.

Resource Constraints: Many healthcare facilities, particularly in low- and middle-income countries (LMICs), face significant resource limitations that impede the implementation of comprehensive AFS programs.^{18,52} These limitations include a lack of funding, insufficient staffing levels (especially trained mycologists and infectious disease specialists), and limited access to advanced diagnostic technologies.^{28,29} The absence of dedicated antifungal stewardship teams further hampers effective implementation.²⁷ The high cost of antifungal agents themselves also presents a particularly in resource-constrained barrier, environments, creating a financial burden that can limit access to essential medications.^{2,3}

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Table 1: Summary of studies on effectiveness of Antifungal stewardship programs with their key findings and conclusion.

Study – Author, Year Country & Setting	Primary Objectives	Key Findings	Limitations	Conclusion
López-Medrano et al., 2013 ³⁴ Spain, University Hospital	Evaluate a non-compulsory antifungal stewardship program's impact on antifungal use and cost.	Reviewed 662 antifungal prescriptions; 29% received change recommendations; reduced intravenous antifungal use and cost by 11.8% without affecting care quality.	Non-randomized study; lack of control group; single-center data.	Antifungal stewardship programs can reduce costs without compromising patient outcomes.
Reed et al., 2014 ³⁵ USA, Ohio State University Wexner Medical Center	Assess impact of antimicrobial stewardship on time to antifungal therapy, mortality, and cost.	Time to effective therapy reduced from 13.5 to 1.3 hours; increased proportion of patients receiving timely treatment; no significant mortality reduction.	Single-center study; selection bias possible; external validity limited.	Antimicrobial stewardship can improve candidemia management and standardize care but may not reduce mortality.
Menichetti et al., 2018 ³⁶ Italy, University Hospital Pisa	Evaluate the impact of infectious diseases consultation (IDC) on candidemia management.	IDC showed lower 30-day mortality (20% vs. 37%); increased echinocandin use and antifungal cost.	Retrospective study; selection bias possible.	Infectious diseases consultation improves candidemia survival but increases antifungal costs.
Apisarnthanarak et al., 2010 ³⁷ Thailand, Thammasat University Hospital	Assess effects of education and stewardship on antifungal use and resistance.	59% reduction in antifungal prescriptions; 71% to 24% decrease in inappropriate use; reduced fluconazole-resistant Candida infections.	Non-randomized study; absence of routine fungal susceptibility testing.	Antifungal stewardship with education effectively reduces inappropriate antifungal use and resistance.
Alfandari et al., 2014 ³⁸ France, Lille Regional Teaching Hospital	Examine antifungal stewardship's role in hematology patients.	Standardized antifungal prescribing guidelines improved practice; integrated stewardship into hematology care. 40% decrease in antifungal consumption observed.	Lack of controlled trial data; findings limited to hematology patients.	Antifungal stewardship improves prescribing practices and cost control in hematology patients.
Lisa Nwankwo et al., 2018 ³⁹ UK, Tertiary Respiratory Hospital	Assess the impact of an antifungal stewardship program on antifungal expenditure and therapeutic drug monitoring	Significant reduction in antifungal expenditure (44.8% reduction, saving ~\$1 million annually), increased therapeutic levels of posaconazole, reduced defined daily dose (DDD)/100 bed days	No control group, potential confounders in cost reduction	Antifungal stewardship can effectively reduce expenditure and improve antifungal use in respiratory disease patients.
Minoru Murakami et al., 2018 ⁴⁰ Japan, Tertiary Hospital	Evaluate the impact of a non-ID physician antimicrobial stewardship team on candidemia outcomes	Improved adherence to IDSA guidelines: appropriate empirical therapy (100% vs. 60%), appropriate duration (84.7% vs. 43.3%), catheter removal (94.4% vs. 70.8%), ophthalmological exams (93.5% vs. 63.3%)	No significant reduction in 30-day mortality, single-center study	Non-ID physician-led antimicrobial stewardship improved adherence to guidelines but did not significantly impact mortality.
Daniel Hare et al., 2020 ⁴¹ Ireland, Critical Care Unit	Assess the impact of a biomarker-based antifungal stewardship program using (1-3)-β-D-glucan (BDG)	63% compliance with care pathway, reduced empirical antifungal therapy duration (median 5.5 days), no increase in mortality or subsequent invasive candidiasis	No observed reduction in antifungal consumption (anidulafungin use unchanged), once-weekly BDG testing was a limitation	BDG-based diagnostics can optimize antifungal use in critical care but may not significantly reduce overall antifungal consumption.

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Carlos Mejia-Chew et al., 2019 ⁴² USA, Tertiary Hospital	Assess impact of ID consultation on mortality in Candida bloodstream infections	ID consultation associated with lower 90-day mortality (40.8% vs. 45.9%), longer antifungal treatment duration (18 vs. 14 days), increased central line removal (75.6% vs. 58.8%), and higher ophthalmologic exams (53.1% vs. 17.5%)	Retrospective study, possible unmeasured confounders	ID consultation should be standard practice for Candida bloodstream infections to improve outcomes.
Yasmine Nivoix et al., 2012 ⁴³ France, Tertiary Hospital	Evaluate adherence to antifungal prescribing guidelines	40% of antifungal prescriptions were inappropriate, inappropriate dosing observed in 21% of cases, better adherence associated with improved survival (81% vs. 68%)	Retrospective study, limited to one hospital	High proportion of inappropriate antifungal use highlights need for better adherence to guidelines
Antworth et al., 2013 ⁴⁴ USA, University Teaching Hospital	To assess the impact of an antifungal care bundle on antifungal use and clinical outcomes	The antifungal care bundle was associated with improved management of candidemia, but no significant reduction in mortality was observed. Care bundle implementation significantly improved selection of appropriate antifungal therapy (100% vs 86.5%), and compliance with an appropriate duration of therapy (97.6% vs 67.7%). Also, fewer excess total days of therapy beyond the recommended duration observed compared to control group.	Lack of randomized control group, small sample size	Implementation of a standardized care bundle improved antifungal management but requires further studies to confirm mortality benefits
Anthony J Guarascio et al., 2012 ⁴⁵ USA, University of Tennessee Health Science Center	To assess the utility of an antifungal bundle protocol in limiting excessive use of echinocandins in the intensive-care inpatient setting	A significant reduction in median days of caspofungin therapy (4 days vs. 2 days) was found in the bundle group.	small sample size and non-parallel design.	Use of an antifungal bundle approach appears to facilitate a reduction in caspofungin use in the ICU without adversely affecting patient outcomes.
Benoist et al., 2019 ⁴⁶ France, University Hospital	To compare clinical outcomes of candidaemia before and after implementing an antifungal stewardship program	Increased consults with infectious disease specialists, improved adherence to echinocandin use, and a decrease in 3-month mortality (though not statistically significant)	Small sample size, presence of other risk factors affecting mortality	The antifungal stewardship program improved clinical practices but did not significantly impact overall mortality
Lachenmayr et al., 2019 ⁴⁷ Germany, Haematology/Oncology Department, University Hospital LMU Munich	To assess the effect of antifungal stewardship on quality of antifungal prescriptions	Improved prescription accuracy, reduced drug-drug interactions, increased appropriate drug selection	Short study period, need for more physician engagement in indication review	Stewardship interventions were effective in optimizing antifungal use, but infectious disease specialists should be involved for best results
Swoboda et al., 2009 ⁴⁸ Germany, Surgical ICU	To assess the effect of antifungal guidelines on antifungal use and costs	Guidelines led to a significant reduction in antifungal use and a 50% cost reduction	Limited to one hospital setting, potential variability in adherence	Standardized antifungal guidelines significantly reduced costs and improved stewardship efforts
Matthaios Papadimitriou-Olivgeris et al., 2019 ⁴⁹ Greece, Multicenter hospital study	Evaluate antifungal prescriptions in Greek hospitals	Antifungal prescriptions were deemed inappropriate in 25% of cases; echinocandins were the most used in ICUs	Limited to point-prevalence data, no long-term trends analyzed	Highlights the need for a nationwide antifungal stewardship program

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March 2025/Volume 3/Issue1

Lourdes Eguiguren et al., 2020 ²¹ USA, Pediatric hospitals	Assess antifungal stewardship practices in pediatric antimicrobial stewardship programs	93% of ASPs conducted antifungal stewardship activities; preauthorization was required in 76% of cases	Variability in stewardship strategies across hospitals, potential reporting bias	Standardized antifungal stewardship strategies are needed
Natalia Mendoza-Palomar et al., 2021 ⁵⁰ Spain, Tertiary pediatric hospital	Describe antifungal use and appropriateness in a pediatric hospital	89% of antifungal prescriptions were appropriate; non-optimal prescriptions mostly related to lack of indication	Single-center study, may not be generalizable	Pediatric antifungal stewardship improves prescription appropriateness but needs targeted interventions
C. Micallef et al., 2015 ⁵¹ UK, Tertiary hospital	Evaluate impact of antifungal stewardship on cost and prescribing patterns	Stewardship program led to significant cost savings (~\$180,000) and improved prescribing	Observational study, no control group for comparison	Antifungal stewardship can improve patient management and reduce healthcare costs

The cost-effectiveness of AFS programs needs careful evaluation, balancing the potential savings from reduced drug consumption and improved outcomes against the investment required for program establishment and maintenance.^{11,53} A statewide study, even in a developed country, revealed that only a minority of hospitals had institutional guidelines for candidemia treatment, reflecting a significant gap in practice.²²

Diagnostic Challenges: Accurate and timely diagnosis of invasive fungal infections (IFIs) is crucial for guiding appropriate antifungal therapy.⁵ However, diagnosing IFIs can be challenging, often involving delays in obtaining results from traditional culture-based methods.^{2,12} This often leads to the prolonged use of empiric therapy, increasing the risk of adverse effects and potentially driving antifungal resistance.² Also, affordable rapid diagnostic tests, are not readily available in many regions, especially in LMICs, which further magnifies this problem.^{18,52} For example, in a study, obtaining specimens from lungs through bronchoscopy was found to be a key barrier to rational prescribing practices. This highlights the need for improved access to better diagnostic facilities.¹⁷ The study by Mylonakis et al. highlighted the potential benefits of rapid diagnostic tests, such as the T2 magnetic resonance (T2MR) assay, which significantly reduced the time to diagnosis of Candida species. However, the high cost of such technologies can be a major barrier to their widespread utility.^{54,55} The use of nonculture-based tests, such as serum (1,3)- β -D-glucan and galactomannan tests, may enhance AFS, but refinement of target populations and clinical pathways is necessary for their optimal utilization.³ A study on diagnostics-driven AFS highlighted the effectiveness of various diagnostic approaches, including serum (1,3)-β-D-glucan tests and MALDI-TOF MS, in reducing time to species identification and targeted therapy.⁵⁶

Lack of Standardization and Guidelines: There is significant variability in AFS practices across different healthcare settings.^{7,21} The lack of standardized guidelines and protocols makes it difficult to compare the effectiveness of different AFS interventions and to establish best practices.^{28,29} While some institutions have developed internal guidelines, their content and implementation vary widely.⁷ The absence of national or international consensus on core AFS metrics further complicates the evaluation of program effectiveness.⁴ A study in England revealed that only a small percentage of NHS Trusts had dedicated AFS programs,²⁷ indicating a lack of widespread adoption of formal AFS strategies even in developed countries. Many hospitals included antifungal strategies within their broader antimicrobial stewardship programs, but this integration may not be sufficient to address the unique challenges of antifungal management.27 The lack of standardized measures across studies evaluating AFS outcomes complicates comparisons and assessments of effectiveness.57

Inadequate Training and Education: Many healthcare professionals lack adequate training and education on the principles and practices of AFS.¹ This knowledge gap hinders the effective implementation of AFS programs and contributes to suboptimal antifungal prescribing practices.^{2,58} A survey among pharmacy students revealed good knowledge and attitudes towards AFS but suboptimal practices, highlighting the need for educational interventions to bridge the gap between knowledge and practice.⁵⁸ The study by Valerio et al. highlighted significant knowledge gaps among European prescribing physicians regarding invasive fungal infections and their management, underscoring the need for tailored training programs to enhance knowledge and improve antifungal stewardship practices.¹⁰ A study revealed that only 37% of pediatric ASPs felt confident in making antifungal



March 2025/Volume 3/Issue1

recommendations,²¹ indicating a need for enhanced training programs focused on antifungal management.

FUTURE DIRECTIONS IN ANTIFUNGAL STEWARDSHIP

Several areas require further attention to advance AFS practices:

Development of New Antifungal Agents: The emergence of antifungal resistance necessitates the development of new antifungal agents with novel mechanisms of action. This will require substantial investment in research and development, focusing on compounds that overcome existing resistance mechanisms. Careful consideration is needed regarding the appropriate targeting and use of new antifungals to ensure effective stewardship. The responsible and appropriate use of such novel antifungal agents should be guided by effective surveillance and stewardship mechanisms.59

Improved Diagnostics: Traditional diagnostic methods are time consuming lack in sensitivity or specificity. The diagnostic tests that can identify fungal agents rapidly and accurately should be developed and validated. The results from such tests should guide appropriate antifungal therapy and unnecessary use should be minimized. Research into development of novel diagnostic techniques, including molecular diagnostics and imaging, is essential.^{19,56}

Personalized Antifungal Stewardship: As personalized management strategies play a key role in healthcare, similar personalized approaches should be built into AFS strategies. Tailored antifungal therapy based on individual patient characteristics and risk factors should be adopted. However, this needs better understanding of the factors that influence antifungal susceptibility. Also, there is a need for developing reasonably good predictive biomarkers to identify patients at high risk of IFIs. Evolving technologies, including microbiome analysis and artificial intelligence learning. can help in developing 1 machine individualized risk-factor-based patient profiles and personalized antifungal stewardship based on such profiles. Such personalized approach based on the screening-based and diagnostic-driven strategy could help in reducing consumption of antifungal agents and improving patient outcomes. ¹³

Standardized Metrics and Outcome Measures: Effectiveness of any stewardship program relies heavily on measurement of its performance. It is important to have standardized metrics and outcome measures for AFS programs. This is essential for benchmarking the performance and evaluating the effectiveness of different interventional strategies. All the stakeholders should collaborate to develop and establish consensus definitions that should be valid globally.^{4,60}

Improved Surveillance and Data Collection: The surveillance systems targeting IFI incidence, antifungal utilization and resistance patterns should be strengthened. This is essential for monitoring the effectiveness of AFS programs and identifying emerging trends. Standardized data collection methods should be developed and established, and these should be linked to national or international surveillance networks. Data obtained from these systems should be analyzed regularly. Epidemiological modeling and machine learning can be used to identify risk factors for IFI at an early stage and also to predict the emergence of antifungal resistance. 57,60

Integration of AFS into Electronic Health Records (EHRs): The integration of AFS guidelines and decision-making tools into EHRs will enhance surveillance and the proper implementation of AFS practices. This will facilitate obtaining and analyzing real-time feedback that will promote adherence to best practices.²

Enhanced Collaboration and Knowledge Sharing: Advancements in AFS practices can be achieved only strong collaboration between healthcare by professionals, researchers, and policymakers. Exchange of information, best practices and resources can be facilitated by establishing national or international AFS networks.²⁵ Knowledge-sharing initiatives, such as the Gilead Antifungal Information Network (GAIN), helps in inter-disciplinary sharing of information that supports better patient management and preserves antifungal agents.⁶¹ The sharing of up-to-date information on antifungal resistance patterns, diagnostic techniques, and treatment guidelines helps in optimizing antifungal use.²⁵

Enhanced Education and Training: Comprehensive and regular training programs are essential for healthcare providers. These improve knowledge and promote better adherence to AFS principles.^{1,2,24} This includes incorporating antifungal stewardship strategies into medical curriculum and providing continuous medical education avenues for practicing clinicians.^{24,58}

One Health Approach: It is an established fact that antifungal resistance is driven by both clinical and agricultural uses of antifungals. Hence, a One Health approach is the need of the hour to address this global challenge. Integration of human and animal health, as well as environmental considerations, into AFS strategies is of paramount importance.⁸

Addressing Health Disparities: Though AFS programs are in place in many regions, the equitability is questionable. Addressing health disparities by enabling equitable access to quality antifungal care for all populations is crucial. The factors such as socioeconomic status, geographic location, and access to healthcare resources need to be addressed. Strategies to improve access to antifungal care in LMICs include adequate training for healthcare workers, strengthening diagnostic and therapeutic infrastructure while keeping the affordability in mind. Targeted interventions are needed to address specific disparities within different populations.⁵²

Governmental efforts and policy decisions: A study assessing the current coverage and implementation of policies related to antimicrobial stewardship practices in a global context highlighted varying levels of government commitment. Substantial disagreement and significant gaps were found in the current policy and implementation efforts in various countries especially LMICs. Though many countries are coming with National Action Plans, they need to improve their diagnostic capacities, improve national monitoring systems. Specific policies targeting appropriate use of antifungal agents and coordinating multiple sectors should be part of the action plan framework.⁶²

CONCLUSIONS

Antifungal stewardship is essential for optimizing antifungal use, improving patient outcomes in serious fungal infections, and preventing antifungal resistance. While significant progress has been made in implementing AFS programs globally, several challenges persist. A multidisciplinary approach incorporating advanced diagnostics. standardized metrics, comprehensive guidelines, and robust education is crucial to maximizing the impact of AFS. Future research should focus on developing novel antifungal agents, enhancing diagnostic capabilities, and addressing gaps in AFS implementation to ensure long-term treatment effectiveness. Continued collaboration among healthcare providers, researchers, and policymakers is vital to combating antifungal

resistance and preserving the efficacy of existing antifungal therapies.

CONFLICTS OF INTEREST STATEMENT

The authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTION

JR: Led the literature search and initial draft writing **ED:** Contributed significantly to refining the content, structure, and critical review

MV: Provided overall supervision

JR, MV, and ED: Collectively conceptualized the review All authors: Read and approved the final submitted version

REFERENCES

- 1. Johnson MD, Lewis RE, Dodds Ashley ES, et al. Core Recommendations for Antifungal Stewardship: A Statement of the Mycoses Study Group Education and Research Consortium. The Journal of Infectious Diseases. 2020;222(Supplement_3):S175-S198. doi:10.1093/infdis/jiaa394
- Science M, Timberlake K. Antifungal stewardship: A budding branch of antimicrobial stewardship. Pediatric Blood & Cancer. 2020;67(4):e28145. doi:10.1002/pbc.28145
- Ananda-Rajah MR, Slavin MA, Thursky KT. The case for antifungal stewardship: Current Opinion in Infectious Diseases. 2012;25(1):107-115. doi:10.1097/QCO.0b013e32834e0680
- Urbancic KF, Thursky K, Kong DCM, Johnson PDR, Slavin MA. Antifungal stewardship: developments in the field. Current Opinion in Infectious Diseases. 2018;31(6):490-498. doi:10.1097/QCO.00000000000497
- 5. Gupta AK, Mann A, Polla Ravi S, Wang T. Navigating fungal infections and antifungal stewardship: drug resistance, susceptibility testing, therapeutic drug monitoring and future directions. Ital J Dermatol Venereol. 2024;159(2). doi:10.23736/S2784-8671.23.07694-6
- Hamdy RF, Zaoutis TE, Seo SK. Antifungal stewardship considerations for adults and pediatrics. Virulence. 2017;8(6):658-672. doi:10.1080/21505594.2016.1226721
- 7. Eschenauer GA. Antifungal stewardship: Still catching up? Commentary on "Variability in antifungal stewardship strategies among Society for Healthcare Epidemiology of America (SHEA)

Research Network facilities." Infect Control Hosp Epidemiol. 2020;41(5):590-591. doi:10.1017/ice.2020.85

- Williams CC, Gregory JB, Usher J. Understanding 8. clinical and environmental drivers the of antifungal resistance in the One Health context. Microbiology. 2024;170(10). doi:10.1099/mic.0.001512
- 9. Arastehfar A, Gabaldón T, Garcia-Rubio R, et al. Drug-Resistant Fungi: An Emerging Challenge Threatening Our Limited Antifungal Armamentarium. Antibiotics. 2020;9(12):877. doi:10.3390/antibiotics9120877
- 10. Muñoz P, Valerio M, Vena A, Bouza E. Antifungal stewardship in daily practice and health economic 2015:58(S2):14-25. implications. Mycoses. doi:10.1111/myc.12329
- 11. Whitney L, Al-Ghusein H, Glass S, et al. Effectiveness of an antifungal stewardship programme at a London teaching hospital 2010-16. Journal of Antimicrobial Chemotherapy. 2018;74(1):234-241.

doi:https://doi.org/10.1093/jac/dky389

- 12. Soni S, Hettle D, Hutchings S, et al. Promoting antifungal stewardship through an antifungal multidisciplinary team in a paediatric and adult tertiary centre in the UK. JAC-Antimicrobial Resistance. 2024;6(4):dlae119. doi:10.1093/jacamr/dlae119
- 13. Taynton T, Allsup D, Barlow G. How can we optimize antifungal use and stewardship in the treatment of acute leukemia? Expert Review of Hematology. 2024;17(9):581-593. doi:10.1080/17474086.2024.2383401
- 14. Yamada K, Kakeya H. Status and Challenge of Antifungal Stewardship at the Osaka Metropolitan University Hospital. Medical Mycology Journal. 2024;65(2):33-38. doi:10.3314/mmj.24.003
- 15. Kara E, Metan G, Bayraktar-Ekincioglu A, et al. Implementation of Pharmacist-Driven Antifungal Stewardship Program in a Tertiary Care Hospital. Antimicrob Agents Chemother. 2021;65(9):e00629-21. doi:10.1128/AAC.00629-21
- 16. Agrawal S, Barnes R, Brüggemann RJ, Rautemaa-Richardson R, Warris A. The role of the multidisciplinary team in antifungal stewardship. J Antimicrob Chemother. 2016;71(suppl 2):ii37-ii42. doi:10.1093/JAC/DKW395
- 17. Ananda-Rajah MR, Fitchett S, Ayton D, et al. Ushering in Antifungal Stewardship: Perspectives of the Hematology Multidisciplinary Team Navigating Competing Demands, Constraints, and

Uncertainty. Open Forum Infectious Diseases. 2020;7(6). doi:10.1093/ofid/ofaa168

- 18. Chakrabarti A, Patel AK, Soman R, Todi S. Overcoming clinical challenges in the management of invasive fungal infections in low- and middle-income countries (LMIC). Expert Review of Anti-infective Therapy. 2023;21(10):1057-1070. doi:10.1080/14787210.2023.2257895
- 19. Gonzalez-Lara MF, Ostrosky-Zeichner L. Update on the Diagnosis of Candidemia and Invasive Candidiasis. Curr Fungal Infect Rep. 2019;13(4):301-307. doi:10.1007/s12281-019-00367-1
- 20. Rautemaa-Richardson R, Rautemaa V, Al-Wathiqi F, et al. Impact of a diagnostics-driven antifungal stewardship programme in a UK tertiary referral teaching hospital. Journal of Antimicrobial Chemotherapy. 2018;73(12):3488-3495. doi:10.1093/jac/dky360
- 21. Eguiguren L, Newland JG, Kronman MP, et al. The current state of antifungal stewardship among pediatric antimicrobial stewardship programs. Control Infect Hosp Epidemiol. 2020;41(11):1279-1284. doi:10.1017/ice.2020.306
- 22. Bromberg R, Leung V, Maloney M, Paranandi A, Banach D. A Statewide Assessment of Antifungal Stewardship Activities in Acute-Care Hospitals in Connecticut. Infect Control Hosp Epidemiol. 2020;41(S1):s105-s105. doi:10.1017/ice.2020.609
- 23. Nwankwo L, Periselneris J, Cheong J, et al. A Prospective Real-World Study of the Impact of an Antifungal Stewardship Program in a Tertiary Respiratory-Medicine Setting. Antimicrob Agents Chemother. 2018;62(10):e00402-18. doi:10.1128/AAC.00402-18
- 24. Keller SC, Nassery N, Melia MT. The case for development antimicrobial curriculum in stewardship interventions. ASHE. 2022;2(1).doi:10.1017/ash.2021.251
- 25. Khanina A, Tio SY, Ananda-Rajah MR, et al. Consensus guidelines for antifungal stewardship, surveillance and infection prevention, 2021. Internal Medicine Journal. 2021;51(S7):18-36. doi:10.1111/imj.15586
- 26. Goff Z, Abbotsford J, Yeoh DK, et al. The Impact of Tertiary Pediatric a Multifaceted Hospital's Antimicrobial Stewardship Service. Pediatric Infectious Disease Journal. 2022;41(12):959-966. doi:10.1097/INF.000000000003704
- 27. Micallef C, Ashiru-Oredope D, Hansraj S, et al. An investigation of antifungal stewardship programmes in England. Journal of Medical 2017;66(11):1581-1589. Microbiology. doi:https://doi.org/10.1099/jmm.0.000612



- Schelenz S, Agrawal S, Brady A, et al. Antifungal stewardship in the UK: where are we now? JAC-Antimicrobial Resistance. 2024;7(1):dlae209. doi:10.1093/jacamr/dlae209
- 29. AFS Working Group, Ye F, Cai S, et al. Consensus for antifungal stewardship in China (2024 edition).
 J Thorac Dis. 2024;16(6):4016-4029. doi:10.21037/jtd-24-13
- 30. O'Keeffe JC, Singh N, Slavin MA. Approach to diagnostic evaluation and prevention of invasive fungal disease in patients prior to allogeneic hematopoietic stem cell transplant. Transplant Infectious Dis. 2023;25(S1). doi:10.1111/tid.14197
- 31. Miller RA. Preventing Pulmonary Aspergillosis: Can We Breathe Easy? Transplantation. 2020;104(12):2473-2474. doi:10.1007/JPD00000000002122

doi:10.1097/TP.000000000003188

- 32. Jabbar R, Shang Z, Shah A. P79 Analysis of antifungal use from 2015 – 2021 in a tertiary care cardiopulmonary hospital: the impact of the COVID-19 pandemic on antifungal prescribing practices. In: 'Contagion' – The Impact of COVID-19. BMJ Publishing Group Ltd and British Thoracic Society; 2022:A123.2-A124. doi:10.1136/thorax-2022-BTSabstracts.215
- 33. Akbar Z, Aamir M, Saleem Z. Optimizing antifungal therapy: a systematic review of pharmacist interventions, stewardship approaches, and outcomes. Front Med. 2024;11:1489109. doi:10.3389/fmed.2024.1489109
- 34. López-Medrano F, Juan RS, Lizasoain M, et al. A non-compulsory stewardship programme for the management of antifungals in a university-affiliated hospital. Clin Microbiol Infect. 2013;19(1):56-61.

doi: 10.1111 / j.1469 - 0691.2012.03891.x

- 35. Reed EE. Improving the management of candidemia through antimicrobial stewardship interventions.
- 36. Menichetti F, Bertolino G, Sozio E, et al. Impact of infectious diseases consultation as a part of an antifungal stewardship programme on candidemia outcome in an Italian tertiary-care, University hospital. Journal of Chemotherapy. 2018;30(5):304-309.
 doi:10.1020/1120000X.2012.1507096

doi:10.1080/1120009X.2018.1507086

37. Apisarnthanarak A, Yatrasert A, Mundy LM, Thammasat University Antimicrobial Stewardship Team. Impact of Education and an Antifungal Stewardship Program for Candidiasis at a Thai Tertiary Care Center. Infect Control Hosp Epidemiol. 2010;31(7):722-727. doi:10.1086/653616 Alfandari S, Berthon C, Coiteux V. Antifungal stewardship: Implementation in a French teaching hospital. Médecine et Maladies Infectieuses. 2014;44(4):154-158.
 dai:10.1016/j.ms.dm.cl.2014.01.012

doi:10.1016/j.medmal.2014.01.012

- 39. Nwankwo L, Periselneris J, Cheong J, et al. A Prospective Real-World Study of the Impact of an Antifungal Stewardship Program in a Tertiary Respiratory-Medicine Setting. Antimicrob Agents Chemother. 2018;62(10):e00402-18. doi:10.1128/AAC.00402-18
- 40. Murakami M, Komatsu H, Sugiyama M, et al. Antimicrobial stewardship without infectious disease physician for patients with candidemia: A before and after study. J of Gen and Family Med. 2018;19(3):82-89. doi:10.1002/jgf2.159
- 41. Hare D, Coates C, Kelly M, et al. Antifungal stewardship in critical care: Implementing a diagnostics-driven care pathway in the management of invasive candidiasis. Infection Prevention in Practice. 2020;2(2):100047. doi:10.1016/j.infpip.2020.100047
- 42. Mejia-Chew C, O'Halloran JA, Olsen MA, et al. Effect of infectious disease consultation on mortality and treatment of patients with candida bloodstream infections: a retrospective, cohort study. The Lancet Infectious Diseases. 2019;19(12):1336-1344. doi:10.1016/01472.2000(10)20405.0

 ${\rm doi:} 10.1016 / S1473 \hbox{--} 3099 (19) 30405 \hbox{--} 0$

- 43. Nivoix Y, Launoy A, Lutun P, et al. Adherence to recommendations for the use of antifungal agents in a tertiary care hospital. Journal of Antimicrobial Chemotherapy. 2012;67(10):2506-2513. doi:10.1093/jac/dks256
- 44. Antworth A, Collins CD, Kunapuli A, et al. Impact of an A ntimicrobial S tewardship P rogram C omprehensive C are B undle on M anagement of C andidemia. Pharmacotherapy. 2013;33(2):137-143. doi:10.1002/phar.1186
- 45. Guarascio AJ, Slain D, McKnight R, et al. A matched-control evaluation of an antifungal bundle in the intensive care unit at a university teaching hospital. Int J Clin Pharm. 2013;35(1):145-148. doi:10.1007/s11096-012-9712-5
- 46. Benoist H, Rodier S, De La Blanchardiere A, Bonhomme J, Thibon P, Saint-Lorant G. 4CPS-080 Appropriate use of antifungals: impact of an antifungal stewardship programme on the clinical outcome of candidaemia in a university hospital. In: Section 4: Clinical Pharmacy Services. British Medical Journal Publishing Group; 2019:A105.2-A105.

doi:10.1136/ejhpharm-2019-eahpconf.229

- Lachenmayr SJ, Strobach D, Berking S, Horns H, Berger K, Ostermann H. Improving quality of antifungal use through antifungal stewardship interventions. Infection. 2019;47(4):603-610. doi:10.1007/s15010-019-01288-4
- 48. Swoboda S, Lichtenstern C, Ober MC, et al. Implementation of Practice Guidelines for Antifungal Therapy in a Surgical Intensive Care Unit and Its Impact on Use and Costs. Chemotherapy. 2009;55(6):418-424. doi:10.1159/000264672
- 49. Papadimitriou-Olivgeris M, Andrianaki AM, Marangos M, et al. Hospital-wide antifungal prescription in Greek hospitals: a multicenter repeated point-prevalence study. Eur J Clin Microbiol Infect Dis. 2020;39(2):243-248. doi:10.1007/s10096-019-03713-w
- 50. Mendoza-Palomar N, Garcia-Palop B, Melendo S, et al. Antifungal stewardship in a tertiary care paediatric hospital: the PROAFUNGI study. BMC Infect Dis. 2021;21(1):100. doi:10.1186/s12879-021-05774-9
- 51. Micallef C, Aliyu SH, Santos R, Brown NM, Rosembert D, Enoch DA. Introduction of an antifungal stewardship programme targeting high-cost antifungals at a tertiary hospital in Cambridge, England. Journal of Antimicrobial Chemotherapy. 2015;70(6):1908-1911. doi:10.1093/jac/dkv040
- 52. Riera F, Cortes Luna J, Rabagliatti R, et al. Antifungal stewardship: the Latin American experience. ASHE. 2023;3(1):e217. doi:10.1017/ash.2023.471
- 53. Muñoz P, Bouza E. The current treatment landscape: the need for antifungal stewardship programmes. J Antimicrob Chemother. 2016;71(suppl 2):ii5-ii12. doi:10.1093/jac/dkw391
- 54. Bauer KA, Goff DA. When Diagnostic Technology Is Ahead of the Hospital Budget: What Is Antimicrobial Stewardship to Do? Clin Infect Dis. 2015;61(3):486-487. doi:10.1093/cid/civ355
- Mylonakis E, Clancy CJ, Ostrosky-Zeichner L, et al. T2 Magnetic Resonance Assay for the Rapid Diagnosis of Candidemia in Whole Blood: A Clinical Trial. Clinical Infectious Diseases. 2015;60(6):892-899. doi:10.1093/cid/ciu959
- 56. Chakrabarti A, Mohamed N, Capparella MR, et al. The Role of Diagnostics-Driven Antifungal Stewardship in the Management of Invasive Fungal Infections: A Systematic Literature Review. Open Forum Infectious Diseases. 2022;9(7):ofac234. doi:10.1093/ofid/ofac234

- 57. Hart E, Nguyen M, Allen M, Clark CM, Jacobs DM. A systematic review of the impact of antifungal stewardship interventions in the United States. Ann Clin Microbiol Antimicrob. 2019;18(1). doi:https://doi.org/10.1186/s12941-019-0323-z
- 58. Mudenda S, Matafwali SK, Mukosha M, et al. Antifungal resistance and stewardship: a knowledge, attitudes and practices survey among pharmacy students at the University of Zambia; findings and implications. JAC-Antimicrobial Resistance. 2023;5(6). doi:10.1093/jacamr/dlad141
- 59. Neoh CF, Jeong W, Kong DC, Slavin MA. The antifungal pipeline for invasive fungal diseases: what does the future hold? Expert Review of Anti-infective Therapy. 2023;21(6):577-594. doi:10.1080/14787210.2023.2203383
- 60. Albahar F, Alhamad H, Abu Assab M, Abu-Farha R, Alawi L, Khaleel S. The Impact of Antifungal Stewardship on Clinical and Performance Measures: A Global Systematic Review. TropicalMed. 2023;9(1):8. doi:10.3390/tropicalmed9010008
- 61. Talento AF, Qualie M, Cottom L, Backx M, White PL. Lessons from an Educational Invasive Fungal Disease Conference on Hospital Antifungal Stewardship Practices across the UK and Ireland. JoF. 2021;7(10):801. doi:10.3390/jof7100801
- 62. Zay Ya K, Lambiris MJ, Levine GA, Tediosi F, Fink G. Coverage of policies to improve antimicrobial stewardship in human medicine in low and middle income countries: results from the Global Survey of Experts on Antimicrobial Resistance. BMC Public Health. 2024;24(1):2297. doi:10.1186/s12889-024-19542-2