Introduction to the updated Australasian consensus guidelines for the management of invasive fungal disease and use of antifungal agents in the haematology/oncology setting, 2021

Introduction

This is the first of nine chapters in the 2021 Australasian Consensus Guidelines for the management of invasive fungal disease (IFD) and use of antifungal agents in the haematology/oncology setting. Seven years on from the publication of the 2014 consensus guidelines, the chapters that follow serve as a timely update, and we encourage clinicians to read this iteration of the guidelines in conjunction with previous editions. In this chapter, we introduce the rationale for these guidelines, outline any pertinent contextual change since the preceding edition, and explain our approach to guideline development, review and feedback.

Rationale and clinical imperative

Purpose

IFD continues to be a major cause of mortality for patients with haematological and solid organ malignancy. Rapid advances in the fields of haematology and oncology, including the advent of biological agents, along with the broadening of clinical indications for intensive treatment by age and comorbidities, continually push the limits of cancer therapeutics and related outcomes. Within this context, the haematology/oncology setting presents a growing population at risk of IFD. Clinicians

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must be on high alert for potential IFDs and remain up to date with current best practice, so as to effectively prevent, diagnose and treat these infections in often complex patients with multiple comorbidities.

As such, these guidelines aim to provide clinicians with a robust, evidence-based framework for:

- Planning and implementing quality processes and surveillance strategies to monitor and prevent IFD;
- Optimising antifungal therapies, including understanding potential antifungal drug-drug interactions, toxicities and therapeutic drug monitoring (TDM);
- Stratifying patients at risk of IFD and prescribing appropriate antifungal prophylaxis;
- Managing aspergillosis, candidiasis, cryptococcosis, mucormycosis and other rarer mould infections (e.g. scedosporiosis); and
- Imparting important information to patients to help them better manage exposure risks outside the hospital environment, understand the type of prophylaxis or treatment they are receiving, and appreciate the importance of medication adherence and TDM.

Target population

The target population of these guidelines remains patients in the haematology/oncology setting, given that this patient population is disproportionately affected by IFD and are the largest consumers of antifungal agents, both in terms of

prophylaxis and treatment within hospitals. Data specific to other immunocompromised host settings, such as critically ill patients in intensive care units (e.g. candidiasis), patients post-solid organ transplantation, and patients with HIV (e.g. cryptococcosis), are included only where relevant.

Intended audience

The intended audience for these guidelines are clinicians caring for patients with underlying haematological or solid organ malignancy, including but not limited to infectious diseases physicians, haematologists, oncologists, pharmacists, general physicians, nurses, nurse practitioners and trainees practising in Australia and New Zealand. As such, some background knowledge is assumed. We recognise that some care providers may apply these guidelines to other settings and patient populations, in which case we advise clinicians to also consult relevant local guidelines and/or guidelines targeted to that specific population.

History and changing scope

This special issue of the *Internal Medicine Journal* (IMJ) represents the fourth edition of the antifungal guidelines. Originally published in 2004 as a stand-alone paper,[1] the guidelines were updated and expanded upon in 2008 to a set of six separate articles,[2-7] then further updated and expanded in 2014 to a set of eight articles, including an accompanying survey.[8-15]

In 2021, we continue to prioritise real-world challenges and locally-applicable management approaches. Thus, diagnostic tests and therapeutic options are discussed

predominantly for clinical settings in Australia and New Zealand. In providing updated recommendations, we primarily focus on new developments in the diagnosis, treatment and prophylaxis of clinically-important moulds and yeasts, while also emphasising contemporary infection prevention strategies. New antifungal drugs, and new formulations of established antifungal agents that have become licensed since the 2014 guidelines, are discussed where relevant.

Expanded scope

The 2014 guidelines featured two, individual chapters dedicated to the treatment of mould and yeast infections.[8, 11] In 2021, both these topic areas have been expanded upon, leading to four separate articles. This includes stand-alone chapters on the treatment of invasive aspergillosis and invasive candidiasis, in recognition of their increasing importance, plus new gains in knowledge. The *Aspergillus* chapter focuses on diagnostics and antifungal drug resistance, while also updating our position on the use of antifungal agents for which data were either absent or sparse in 2014. The *Candida* chapter now includes coverage of *Candida auris,* an emergent multi-resistant yeast with important infection prevention repercussions. A second 'filamentous fungi' chapter expands on management strategies for mucormycosis, lomentosporiosis, scedosporiosis and other moulds, while a second 'yeast' chapter focuses on cryptococcosis together with a large repertoire of increasingly important rare yeast infections.

An entirely new chapter entitled 'Consensus guidelines for improving patients' understanding of IFD and related risk prevention in the haematology/oncology setting, 2021' has also been included. This chapter collates important patient information that

we felt was lacking in the literature. As such, it aims to provide clinicians with a repository of highly practical information and advice they can share with patients to raise their awareness of potential drug interactions, and to help them understand how they can minimise their exposure to fungal infection in day-to-day settings outside the hospital environment (e.g. home, work, travel).

Finally, the paediatric focus remains high in the 2021 guidelines with dedicated paediatric-specific sections in each chapter as appropriate.

Notable omissions in the 2021 guidelines

We deliberately sought to reduce background text on organism description and epidemiology; interested readers may turn to the numerous published reviews and book chapters on these aspects, referred to in each chapter. We also give special mention to *Mycology Online*, a helpful website on identification of fungi and management of human and animal fungal infections.[16]

There has been little development in the treatment of *Pneumocystis jirovecii* infections since the previous guidelines and thus we have opted not to provide updated recommendations here. Instead, we refer readers to the relevant 2014 chapter[12] and other recent guidelines[17] for formal guidance.

The current guidelines also do not include a stand-alone chapter dedicated to diagnostic strategies. Rather, we now discuss diagnosis in context within the relevant mould and yeast chapters. In addition, we do not discuss emerging *Aspergillus* species

outside of the section Fumigati or non-pathogenic *Cryptococcus* species. We also do not address geographically unique, endemic fungi not commonly encountered in Australasia, such as *Talaromyces* and *Histoplasma* species.

Wider context

Changes in fungal nomenclature

These guidelines have been written within the context of the 'One Health' concept, the accompanying reclassification of fungi[18] and updated research definitions for IFD, as proposed in recent years by the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium (EORTC/MSGERC).[19]

Fungal nomenclature has undergone significant change in the last decade due to a confluence of factors. First, the rise in molecular technology has allowed for identification of fungi regardless of their morphological characteristics. Second, the long-standing teleomorph (sexual) – anamorph (asexual) dual nomenclature and the primacy of the teleomorph-typified name no longer apply. As such, fungal nomenclature now seeks to unify any one species into a single name (i.e. the 'one fungus, one name' concept).[20]

Previously familiar species names may have been completely reclassified to reflect their molecular evolutionary relationships. Although these guidelines focus on clinical management, clinicians do need to be aware of relevant nomenclature changes so they can reconcile the names of any fungi discussed with mentions in previous literature,

i.e. names may differ, yet refer to the same organism. For example, *Lomentospora prolificans* (previously *Scedosporium prolificans*) was determined to be phylogenetically separate from other *Scedosporium* species;[21] this name change has been widely accepted in clinical practice and in the literature. In contrast, names such as *Pichia kudriavzeveii* (previously *Candida krusei)*, *Clavispora lusitaniae* (previously *Candida lusitaniae)* and *Meyerozyma guilliermondii* (previously *Candida guilliermondii)*, [18] are still relatively underutilised in clinical medicine. Further the reclassification of the *Cryptococcus neoformans–Cryptococcus gattii* complex into seven new species (two derived from *C. neoformans* and five from *C. gattii*)[22] remains controversial (see accompanying chapter on cryptococcosis by Chang *et al*. 2021). Throughout these guidelines, we refer to the currently accepted and valid species name used in clinical practice for the organism and only mention newly proposed or older names as appropriate.

Notably, laboratories in Australia and New Zealand co-report both old and new names, supported by an external quality assurance module provided by the Royal College of Pathologists of Australasia (RCPA).[23] For ease and familiarity, we continue to discuss the three previous *Candida* species mentioned above (and others) within the *Candida* chapter, despite their recent reclassification. Note also that when discussing *Aspergillus fumigatus*, we imply the broader *A. fumigatus* species complex, which is known to encompass >50 phylogenetically distinct species, of which *A. fumigatus sensu stricto* is the more (if not most) commonly, encountered species. Similarly, when discussing cryptococcosis, we imply the broad complex of *C. neoformans–C gattii*.

Other contemporary guidelines in practice

We recognise that many other antifungal guidelines are currently available to clinicians, and may be read in conjunction with these guidelines. A list of available guidelines by organism can be found on the International Society of Human and Animal Mycology (ISHAM) website.[24] In terms of recently published guidelines, we particularly refer readers to two existing aspergillosis guidelines by Ullmann *et al*. 2018 and Patterson *et al*. 2016,[25, 26] and to a candidiasis guideline by Pappas *et al.* 2016.[27] The American Society of Transplantation also recently published a guideline for the management and prevention of aspergillosis in haemopoietic stem cell transplantation recipients.[28]

The European Confederation of Medical Mycology (ECMM) have launched a 'One World – One Guideline' initiative involving clinicians, microbiologists and medical professionals from across the globe to tackle the diagnosis and treatment of IFD.[29] To date, guidelines have been developed for the management of mucormycosis;[30] uncommon or rare mould infections;[31] and rare yeast infections (Chen *et al*., in press). A guideline for cryptococcosis is also in progress.

While guidelines vary by evidence and recommendation grading systems, they also require contextualisation to the intended target audience, local epidemiology, available resources and health systems. Within this context, Australian and New Zealand clinicians still require their own locally relevant, contemporaneous guidelines to guide best clinical practice in local settings.

Changes in IFD definitions

The EORTC/MSGERC consensus definitions for IFD were updated in 2019.[19] Notable changes include additional criteria to classify infection as 'probable' disease and a diminution of the 'possible' IFD category. In the probable IFD category, host factors have been expanded to include inherited severe immunodeficiency and low CD4 T-cell counts, while radiological features have been expanded to include wedge-shaped and segmental or lobar consolidation and a reverse halo sign. Importantly, *Aspergillus* PCR is now included as a mycological criterion for diagnosis. Further, galactomannan measurement thresholds for various body fluids and sampling strategies have also been revised.[19] Attempts have been made to address the definitions of pneumocystosis, cryptococcosis, endemic mycoses and IFD in paediatric populations. A separate initiative on IFD in ICU populations[32] and COVID-19 associated pulmonary aspergillosis (CAPA) are in progress.[33] While these research definitions are useful in harmonising research categorisations, physician discretion and judgement must continue to apply in clinical practice.

Process for guideline development

Steering Committee

The 2021 Australasian Antifungal Guidelines Steering Committee (SC) was again led by Professor Monica Slavin and included four infectious diseases (ID) physicians, one adult ID physician/medical microbiologist, one paediatric ID physician/medical microbiologist, one clinical pharmacologist, and one pharmacist. These clinicians were drawn from our previous guideline steering committees with the addition of two new members (see Appendix 1). All SC members are clinician researchers, active in the field of clinical

mycology. Each SC member was responsible for leading and overseeing the development of at least one of the nine guideline chapters.

Chapter writing groups

Writing group members were drawn from the cohort of clinicians who had contributed to earlier versions of the guidelines, as well as from clinicians who responded to a national call in late 2019 for expressions of interest via The Australasian Society for Infectious Diseases (ASID), The Australian and New Zealand Mycology Interest Group (ANZMIG), and local infectious diseases, haematology, oncology and pharmacy departments.

All relevant areas of practice were represented by writing group members. Contributing authors included ID physicians (adult and paediatric), haematologists (adult), hospital pharmacists, microbiologists, scientists, infection prevention consultants and consumers. A concerted effort was also made to include early career clinicians and to promote gender balance.

While many writing group members had broad and overlapping interests, each member was allocated to a single chapter. This enabled more clinicians to provide input into the guidelines, and promoted a more inclusive writing experience. Members were assigned to chapters based on their expertise and self-reported personal interest. We also ensured that the chapter writing groups were multidisciplinary, with the requisite representatives from haematology/oncology, paediatrics and pharmacy included in each group. A total of 64 individual clinician-writers contributed in 2021

compared to 40 (with multiple authorships) in 2014, and we recognise the significant, combined effort of those involved (see Appendix 1 for complete author list).

Structure of guidelines

In order to serve as a useful update to the previous guidelines, we structured each chapter by identifying a set of clinically-important questions. This framework allowed the writing groups to focus on new and important developments, emphasising key recommendations for contemporary prophylaxis, diagnosis and treatment. The questions proposed by each writing group were reviewed and endorsed by the SC.

All writing groups then performed a literature review using PubMed, Medline and contemporary conference abstracts to identify relevant publications, censored to June 2020. The COVID-19 pandemic caused significant delays to this body of work. As such, important practice-changing papers published after this censor date were included as appropriate.

Within reason, we sought to optimise harmonisation between the different chapters, striving for internal consistency and concise content, while avoiding duplication or contradictions.

Grading of evidence and recommendations

These guidelines utilise the Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[34, 35] approach to assess and classify the supporting body of evidence. We followed the GRADE adaptation used by the ECCM global guidelines (with

the exception of indexing the source of Level II evidence by superscripts) throughout our chapters (see Table 1).[30, 31] We moved away from the Australian National Health and Medical Research Centre (NHRMC) grading systems[24, 36] used in our previous editions and readers should be aware of this difference when referring to prior guidelines, as this impacts the gradings assigned to recommendations and level of evidence. For example, under the NHMRC grading system, Level I evidence mandates for a systematic review, while Level I evidence using GRADE accepts evidence from at least one properly designed clinical trial.

Table 1 Definitions for strength of recommendation and quality of evidence, as applied in these guidelines

	Grade/level	Definition
Strength of recommendation	**Grade A**	The guideline group **strongly** supports a recommendation for use
	Grade B	The guideline group **moderately** supports a recommendation for use
	Grade C	The guideline group **marginally** supports a recommendation for use
	Grade D	The guideline group supports a recommendation **against** use
Quality of evidence	**Level I**	Evidence from at least one properly designed randomised, controlled trial
	Level II	Evidence from at least one well-designed clinical trial, without randomisation; from cohort or case-controlled analytic studies (preferably from >1 centre); from multiple time series; or from dramatic results of uncontrolled experiments
	Level III	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies, or reports of expert committees

Oversight by the SC

From July 2020, near-final drafts of each chapter were systematically reviewed by the SC and suggested revisions provided to each writing group. Multiple iterations were reviewed, and points of contention were raised and debated rigorously by the SC and writing group representatives. All revisions were reviewed by the SC, with careful attention paid to finalising the grades assigned to recommendations. As mentioned previously, each chapter seeks to address a set of clinically-important questions. Within this structure, major recommendations are summarised at the start of each question covered, with other recommendations then **bolded** within the text as part of a more detailed discussion. More than 40 hours of formal meetings were held between the SC members, notwithstanding the time spent writing, editing and reviewing the chapters individually.

Review by professional bodies

Prior to journal submission and publication, all nine draft chapters were made available to the ASID, the Australasian Leukaemia and Lymphoma Group (ALLG), the Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG), the Medical Oncology Group of Australia (MOGA) and the Haematology Society of Australia and New Zealand (HSANZ), for distribution to their member networks for feedback and commentary.

The ASID has a network of over 1000 members, including infectious diseases physicians and trainees in Australia and New Zealand, as well as specialist pharmacists, infection prevention nurses, clinical microbiologists, veterinarians, public health

physicians and medical scientists. The ALLG has a national network of more than 700 haematologists, stem cell transplant physicians, research nurses, study co-ordinators and supportive care experts. The ANZCHOG membership is primarily drawn from eleven dedicated children's oncology centres in Australia and New Zealand with members from both regional and shared-care facilities. The MOGA is the national professional organisation for medical oncologists in Australia while the HSANZ is comprised of haematologists in laboratory and clinical practice, those in training, and nurses involved in haematology practice.

Following this wider review process, the feedback received was collated and incorporated into the guidelines, as appropriate. Key recommendations from the draft guidelines were also presented at ASID educational webinars and feedback invited.

Highlights of the 2021 guidelines

The current guidelines remain focused on the Australian and New Zealand setting and their strength is in their local applicability. Table 2 summarises the focus of each Chapter while Table 3 aims to aid navigation of these guidelines by identifying where key recommendations can be found.

Table 2 2021 guidelines – chapter highlights

Chapter	Topic	Authors	Highlights
1	Introduction	Chang *et al*.	Provides an overview of the entire guidelines, including grading of recommendations and levels of evidence
2	Antifungal stewardship, surveillance and infection prevention	Khanina *et al.*	Reviews AFS interventions and metrics, as well as fungal infection surveillance and prevention strategies, including the use of artificial intelligence for automated surveillance
3	Optimising antifungal drug delivery and monitoring	Chau *et al.*	Focuses on optimising drug delivery and therapeutic drug monitoring to avoid toxicity and improve outcomes in patients
4	Antifungal prophylaxis	Teh *et al*.	Focuses on the haematological malignancy and HSCT settings, for which prophylaxis is most pertinent; discusses emerging new hosts at risk and the expanding spectrum of new agents used in malignant haematological settings; provides a particularly strong emphasis on evolving literature in the paediatric setting

5	Diagnosis and management of *Candida* infections	Keighley *et al*.	Discusses the increasing rates of invasive candidiasis and candidaemia, including the emerging threat of *Candida auris*; also provides paediatric management and dosing recommendations
6	Diagnosis and management of cryptococcosis and rare yeast infections	Chang *et al*.	Focuses on guiding principles in the management of cryptococcosis including cryptococcal meningitis, pulmonary cryptococcosis, cryptococcal antigenemia and C-IRIS; sheds light on emerging rare yeast infections, including *Geotrichum, Trichosporon, Malassezia* and *Rhodotorula*, and discusses key laboratory features and management principles
7	Diagnosis and management of invasive aspergillosis	Douglas *et al*.	Discusses diagnostic and management features of IA in various contexts, as still the most important IFD in the haematology/oncology setting; highlights of this chapter include a summary of of non-culture based tests for IA and management flowcharts for primary, breakthrough and refractory IA

8	Diagnosis and management of non-*Aspergillus* moulds	Bupha-Intr *et al.*	Discusses diagnosis and treatment of the non-*Aspergillus* moulds, with an emphasis on mucormycosis, scedosporiosis, lomentosporiosis and fusariosis; also discusses the importance of a multidisciplinary approach and adjunctive therapies, and describes the new anti-mould drugs in development
9	Key patient information for healthcare workers caring for patients with or at risk of IFD	Fernando *et al.*	This chapter is a new and important addition to these guidelines, and provides advice designed to assist clinicians in their efforts to convey key information to patients about IFD, antifungal treatment and risk prevention strategies. By doing so, we aim to improve health literary and help clinicians to engage patients in productive conversations and partnerships. The material found here may also aid the development of locally-relevant patient information sheets.

AFS, antifungal stewardship; C-IRIS, cryptococcosis-associated immune reconstitution inflammatory syndrome; EORTC/MSGERC, The European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium; HSCT, haemopoietic stem cell transplantation; IA, invasive aspergillosis; IFD, invasive fungal disease

Table 3 Quick guide to finding key prophylaxis and treatment recommendations

Topic	**Chapter**	**Table**
Adult recommendations		
Antifungal prophylaxis	Teh *et al.* 2021	4
Treatment of invasive pulmonary aspergillosis	Douglas *et al.* 2021	5
Treatment of *Candida* spp.	Keighley *et al.* 2021	7
Treatment of *Cryptococcus* spp. (cryptococcal meningitis)	Chang *et al.* 2021	1
Treatment of non-*Candida*, non-cryptococcus rare yeasts	Chang *et al.* 2021	5
Treatment of Mucorales	Bupha-Intr *et al.* 2021	3
Treatment of *Scedosporium, Lomentospora prolificans* and *Fusarium*	Bupha-Intr *et al.* 2021	3
Paediatric recommendations		
Antifungal prophylaxis	Teh *et al.* 2021	6, 7
Treatment of *Aspergillus* spp.	Douglas *et al.* 2021	6
Treatment of *Candida* spp.	Keighley *et al.* 2021	6, 7
Summary of toxicity and adverse effects of currently available systemic antifungal agents	Chau *et al.* 2021	5

Implementability of guidelines

Ensuring the feasibility and implementability of any recommendations provided were key objectives of the SC and were carefully considered by each chapter writing group. We used the GuideLine Implementability Appraisal (GLIA)[37, 38] tool, which emphasises key intrinsic factors such as executability (what to do), decidability (under what conditions), validity (strength of recommendation and evidence), and flexibility (allowability for interpretation and alternatives). The SC were also cognisant of local operational challenges and strived to minimise any potential adverse impact that recommendations could have on workflow. As such, the SC made an effort to avoid proposing any unconventional behaviours, unless clearly warranted.

Metrics from the *IMJ* website support the ongoing utility of the 2014 guidelines. The number of full text downloads since publication is now approaching 63 000, with the majority of downloads coming from Australia (15 256) and the United States (14 149), followed by China (3809), the United Kingdom (2626) and Canada (2107) (figures correct as of 3 June 2021). We expect to be able to assess the acceptability and impact of the 2021 guidelines via similar metrics and future end-user surveys. We can also monitor appropriateness of antifungal use via the Hospital National Antimicrobial Prescribing Survey (NAPS).[39] The recent publication of recommended metrics for monitoring antifungal stewardship and appropriate antifungal use in hospitals, along with IFD rates from late 2021 onwards, will also support the future evaluation of these guidelines.[40]

The 2014 guidelines were linked to the Therapeutic Guidelines of Australia, which are used across Australian hospitals to guide prescribing and aid auditing of prescription

practices. We expect Therapeutic Guidelines to also adopt the 2021 recommendations, enabling broader dissemination via the print and electronic formats of 'Therapeutic Guidelines: Antibiotic'.

Research gaps

Large research gaps in the intersection of mycology in haematology/oncology remain. This is, in part, due to the heterogeneity of the haematology/oncology patient population, including a broad spectrum of malignant and non-malignant conditions, differences in host immunogenetics, and the diversity of cancer therapeutic options now available, to which access is not equitable. The urgency of diagnosing, preventing and treating IFD in this already-sick population imposes significant challenges to large-scale, multicentre, prospective controlled studies. Recent studies are at best non-inferiority trials, with many using historical controls and an open-label design.

New antifungal agents are urgently required. Partnerships between researchers, pharmaceutical companies and regulators will be critical for translating any research gains into clinical practice. Another major gap in knowledge is knowing when to stop antifungal prophylaxis and treatment. Test-for-cure biomarkers and randomised studies in therapy cessation, be it prophylaxis or treatment, are needed. Studies on immunomodulators and cellular therapies in IFD are also lacking. A large long-term visionary investment on IFD diagnostics and therapeutics, commensurate with the enormous advances seen in cancer therapeutics, is required.

Future directions

These guidelines, which are currently limited to a print format, will be subject to ongoing review. We expect to reissue updates to these guidelines as the need arises, via meetings and online addendums. The next large-scale update will likely follow a large suite of impactful clinical studies of novel antifungal agents expected in the next five years. As such, an online real-time updated summary of IFD recommendations may soon be necessary.

Conclusion

The current guidelines for managing IFD and antifungal use were developed by employing rigorous and independent processes, and were subject to broad end-user review prior to publication. These guidelines have been endorsed by the ASID, ALLG, ANZCHOG, MOGA and HSANZ. The GRADE system was used to assess the evidence upon which all recommendations are based and an internal appraisal to align with GLIA implementability principles was performed. We welcome feedback, critique and suggestions to aid further improvements and increased engagement in future guideline efforts. We also look forward to further research and implementation studies, including locally-derived, investigator-driven trials to strengthen and inform future versions of these guidelines.

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Conflicts of interest

Please see accompanying chapters for individual authors' conflicts of interest.

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Introduction to the updated Australian and New Zealand consensus guidelines for the management of invasive fungal disease and use of antifungal agents in the haematology/oncology setting, 2021

Short title

Antifungal consensus guidelines 2021

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Conflicts of interest

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Abstract

This article introduces the fourth update of the *Australian and New Zealand consensus guidelines for the management of invasive fungal disease and use of antifungal agents in the haematology/oncology setting.* These guidelines are comprised of nine articles as presented in this special issue of the *Internal Medicine Journal*. This introductory chapter outlines the rationale for the current update and the steps taken to ensure implementability in local settings. Given that seven years have passed since the previous iteration of these guidelines, pertinent contextual changes that impacted guideline content and recommendations are discussed, including the evolution of invasive fungal disease (IFD)

definitions. We also outline our approach to guideline development, evidence grading, review and feedback. Highlights of the 2021 update are presented, including expanded scope to provide more detailed coverage of common and emerging fungi such as *Aspergillus* and *Candida* species, and a greater focus on the principles of antifungal stewardship. We also introduce an entirely new chapter dedicated to helping healthcare workers convey important concepts related to IFD, infection prevention and antifungal therapy, to patients.

Keywords

antifungal therapy, invasive fungal disease, treatment guidelines, antifungal prophylaxis, haematological malignancy, *Aspergillus*