



HAL
open science

The Nairobi Declaration 2023: A Commitment to Address Deadly Yet Neglected Fungal Diseases in Africa

Iriagbonse I Osaigbovo, Nelesh Govender, A Jordan, Felix Bongomin, David B Meya, Alice Kanyua, Olga M Mashedi, David Koffi, Angela Loyse, Aude Sturny-Leclère, et al.

► To cite this version:

Iriagbonse I Osaigbovo, Nelesh Govender, A Jordan, Felix Bongomin, David B Meya, et al.. The Nairobi Declaration 2023: A Commitment to Address Deadly Yet Neglected Fungal Diseases in Africa. *Medical Mycology*, 2024, *Medical Mycology*, 62 (1), pp.myad141. 10.1093/mmy/myad141 . hal-04384887

HAL Id: hal-04384887

<https://hal.science/hal-04384887v1>

Submitted on 10 Jan 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 **THE NAIROBI DECLARATION 2023: A COMMITMENT TO ADDRESS DEADLY YET NEGLECTED**

2 **FUNGAL DISEASES IN AFRICA**

3

4 Iriagbonse I. Osaigbovo^{1*}, Nelesh P. Govender², Alexander M. Jordan³, Felix Bongomin⁴,
5 David B. Meya⁵, Alice Kanyua⁶, Olga M. Mashedi⁷, David Koffi⁸, Angela Loyse⁹, Aude Sturny-
6 Leclère¹⁰, Jean-Pierre Gangneux¹¹, David W. Denning¹², Tom Chiller³, Oliver Cornely¹³, Rita
7 O. Oladele¹⁴

8

- 9 1. Department of Medical Microbiology, School of Medicine, College of Medical
10 Sciences, University of Benin, Benin City, Nigeria
- 11 2. National Institute for Communicable Diseases, a Division of the National Health
12 Laboratory Service, School of Pathology, University of the Witwatersrand,
13 Johannesburg, South Africa
- 14 3. Mycotic Diseases Branch, Division of Foodborne, Waterborne, and Environmental
15 Diseases, Centers for Disease Control and Prevention, Atlanta, United States of
16 America
- 17 4. Department of Medical Microbiology and Immunology, Faculty of Medicine, Gulu
18 University, Gulu, Uganda
- 19 5. Infectious Diseases Institute, Makerere University, Kampala, Uganda
- 20 6. Department of Pathology and Laboratory Medicine, Aga Khan University, Nairobi,
21 Kenya
- 22 7. Kenya Medical Research Institute, Nairobi, Kenya
- 23 8. Institut Pasteur de Côte d'Ivoire, Abidjan, Cote d'Ivoire.

- 24 9. Division of Infection and Immunity Research Institute, St George's University of
25 London, London, United Kingdom
- 26 10. Institut Pasteur, Université Paris Cité, National Reference Center for Invasive
27 Mycoses and Antifungals, Translational Mycology research group, Mycology
28 Department, F-75015 Paris, France.
- 29 11. CHU de Rennes, University of Rennes, INSERM, Irset (Institut de recherche en santé,
30 environnement et travail) - UMR_S 1085, Rennes, France
- 31 12. Manchester Fungal Infection Group, Division of Evolution, Infection and Genomics,
32 Faculty of Biology, Medicine and Health, University of Manchester, Manchester
33 Academic Health Sciences Centre, Manchester, United Kingdom
- 34 13. Department of Internal Medicine, European Diamond Excellence Center of Medical
35 Mycology, University Hospital Cologne, Cologne, Germany
- 36 14. Department of Medical Microbiology and Parasitology, Faculty of Basic Medical
37 Sciences, College of Medicine, University of Lagos, Lagos, Nigeria.

38

39 *Correspondence

40 Iriagbonse I. Osaigbovo

41 Highest Qualification: FMCPATH (Medical Microbiology)

42 Address: Department of Medical Microbiology, School of Medicine, College of Medical
43 Sciences, University of Benin, Benin City, Nigeria

44 Email: iyabo.osaigbovo@uniben.edu

45 Phone number: +234-803-577-8626

46

47

48 **Abstract**

49 On May 30th and 31st, 2023, delegates representing various African subregions, together
50 with global representatives from the International Society of Human and Animal Mycology
51 (ISHAM), European Confederation of Medical Mycology (ECMM,) United States Centre for
52 Disease Control and Prevention (CDC) and Global Action for Fungal Infections (GAFFI),
53 convened in Nairobi, Kenya under the aegis of the Pan African Mycology Working Group, a
54 working group of ISHAM. The meeting objectives were, amongst others, to deliberate on a
55 continental response to the World Health Organization Fungal Priority Pathogen List and
56 facilitate interaction between global and regional leaders. Country delegates and
57 international speakers addressed Africa's fungal disease burden; capacity for diagnosis and
58 management; ongoing surveillance; knowledge gaps and trends in invasive fungal diseases
59 such as *Candida auris*, mucormycosis, aspergillosis and Acquired Immune Deficiency
60 Syndrome (AIDS)-related mycoses; and current laboratory practice. During the technical
61 sessions, expert panels deliberated on establishing and financing of national/regional
62 surveillance networks for mycoses; establishing and sustaining African-led collaborations;
63 expanding on existing laboratory and point of care diagnostic capacity as well as planning a
64 mycology reference laboratory service and network in Africa. The meeting also highlighted
65 successful African-led collaborations, capacity building and clinical trial initiatives. The
66 meeting conclusions informed the resolutions of the Nairobi Declaration calling for
67 improved awareness; strong collaborations between clinical and laboratory teams across
68 Africa; improved fungal disease surveillance within the continent; access to antifungals and
69 diagnostics; and leveraging qualified human resources for mycology present within and
70 outside Africa to facilitate trainings, collaborations and exchanges.

72

73

74 **Key words:** Africa, *Aspergillus*, *Candida*, Laboratory, Antifungal

75

76 **Lay summary**

77 This review presents the current state of the art in medical mycology in Africa discussed at

78 the first scientific meeting of the Pan African Mycology Working Group, an affiliate of the

79 International Society for Human and Animal Mycology (ISHAM) held in Nairobi, Kenya on

80 May 30th and 31st, 2023.

81

82

83

84

85

86

87

88

89

90

91

92

93

94

95

96

97

98 **Introduction**

99 The Pan African Mycology Working Group (PAMWG) is a network of medical mycology
100 experts set up under the auspices of the International Society for Human and Animal
101 Mycology (ISHAM) during an international conference hosted by the Medical Mycology
102 Society of Nigeria in Lagos in 2018.¹ The group provides a platform for leaders in the field of
103 medical mycology from multiple African countries to initiate epidemiological studies,
104 develop regional guidelines, and educational programs to increase the capacity of African
105 health care personnel (HCP) to quickly detect and treat serious fungal infections. Amongst
106 other activities, the organisation of local meetings in collaboration with ISHAM is pivotal to
107 the realisation of the group's objectives. Due to the coronavirus 2019 (COVID-19) pandemic,
108 initial plans to organise an inaugural meeting were deferred to 2023. The release of a Fungal
109 Priority Pathogens list (FPPL) by the World Health Organization (WHO) in October 2022,²
110 besides communicating a global commitment to tackling the under-recognised and
111 underfunded burden of invasive fungal diseases (IFDs), also sounded a call to action which
112 stimulated the leadership of the PAMWG to re-ignite plans for the 1st PAMWG meeting.
113 The meeting was a two-day conference convened in Nairobi, Kenya from May 30th to 31st,
114 2023 with opportunity for virtual participation. Delegates from Cameroon, Egypt, Ghana,
115 Ivory Coast, Kenya, Morocco, Nigeria, Senegal, Sudan, South Africa, Tanzania and Uganda,
116 converged for what was unanimously perceived as an epoch-defining moment for medical
117 mycology in the continent. Also present were delegates from the International Society for
118 Human and Animal Mycology (ISHAM), European Confederation of Medical Mycology

119 (ECMM), United States Centers for Disease Control and Prevention (CDC) and Global Action
120 for Fungal Infections (GAFFI).

121 The specific objectives of this conference were

- 122 1. To raise awareness of serious fungal diseases and start the discussion on a
123 continental response to the recently published WHO FPPL which focuses on
124 strengthening laboratory capacity and surveillance; sustainable investments in
125 research, development and innovation and public health interventions
- 126 2. To facilitate interaction and synergy among global and regional leaders to develop
127 educational programs for capacity building to aid in the diagnosis and management
128 of fungal infections in Africa.
- 129 3. To address knowledge gaps about fungal diseases in Africa
- 130 4. To improve access to antifungal agents and diagnostic tests for the major fungal
131 diseases in the different African countries
- 132 5. To address the challenges regarding diagnosis and management of fungal diseases
133 through technical sessions, proffer solutions, set up collaborations and develop a
134 consensus document on the meeting resolutions.

135 This report summarises recent developments concerning epidemiology, diagnosis and
136 management of invasive fungal diseases in Africa as well as the persisting gaps, challenges
137 and future prospects as posited by expert delegates at the first PAMWG conference.

138 **Burden of serious fungal diseases in Africa, capacity for diagnosis and treatment**

139 While there is a growing burden of life-threatening fungal diseases globally, low- and
140 middle-income countries are disproportionately affected because of late presentations,
141 misdiagnoses occasioned by limited diagnostic tools and low index of suspicion; sub-optimal
142 therapy arising from poor antifungal access and affordability as well as low capacity for

143 therapeutic drug monitoring. Prolonged hospitalisations and exorbitant costs due to lack of
144 health insurance complicate matters, often resulting in poor outcomes. In contrast with high
145 income countries where advanced and novel treatments place patients at risk of invasive
146 fungal diseases, the major drivers in Africa are poverty, tuberculosis and human
147 immunodeficiency virus (HIV). Additional contributing factors include chronic obstructive
148 pulmonary disease, asthma, diabetes mellitus, the increasing use of intensive care,
149 haemato-oncological conditions and COVID-19.³ The true burden of IFDs in Africa remains
150 unknown because surveillance data are limited, and clinical studies are few. Nevertheless,
151 there have been efforts by GAFFI to generate credible burden estimates in at least 18
152 African countries and South Africa boasts of robust surveillance data for some fungal
153 diseases. Secondary data sources include modelling studies and systematic reviews.⁴
154 Cryptococcosis, which is the most common and most studied mycosis in Africa, is estimated
155 to affect over 152,000 adults with advanced HIV disease annually and contribute to 19% of
156 AIDs-related deaths.⁵ Diagnosis has been made simpler with the use of a highly-accurate
157 point of care test which is available in many countries and treatment guidelines for HIV-
158 associated cryptococcosis exist. However, management challenges persist since flucytosine
159 and liposomal amphotericin B, cornerstone antifungals, remain expensive and not widely
160 available. More extensive gaps exist in the knowledge of epidemiology, diagnosis and
161 treatment for other mycoses. Recommendations made to bridge these gaps are listed in
162 Table 1.

163 Laboratory diagnostic capacity and access to antifungal treatment are pivotal to the
164 effective management of IFDs. Assessing the regional status of these crucial variables is
165 necessary to guide health professionals, patients, and policy makers.⁶ ECMM/ISHAM have
166 conducted recent surveys providing information on diagnostic and therapeutic capacity for

167 the management of IFDs in Europe, Asia/Pacific and African regions.⁶⁻⁸ These surveys were
168 web-based and included 388 institutions from 45 countries in Europe; 235 institutions from
169 40 countries in Asia/Pacific; but only 40 institutions from 21 countries translating to a
170 response rate below 25% in Africa. The low numbers of responders from Africa might reflect
171 the fact that there are few mycologists on the continent.⁸ However, the limited survey
172 responses revealed low access to susceptibility testing for both yeasts and moulds and
173 *Aspergillus* antigen detection. Apart from fluconazole which was available in 90% of African
174 institutions, access to other antifungals (also designated WHO essential medicines) such as
175 amphotericin B deoxycholate (available for 52.5% of institutions), liposomal amphotericin B
176 (17.5%) and the mould-active triazoles, itraconazole (52.5%), voriconazole (35.0%) and
177 posaconazole (5.0%) was also low. While more detailed and robust analysis still need to be
178 undertaken to understand the true extent of challenges faced, the current results are
179 sufficient to advocate for better diagnostic and therapeutic resources for IFDs in Africa.⁸

180 **Trending invasive fungal diseases in Africa**

181 *Candida auris*

182 *Candida auris*, which is classified as a critical pathogen on the WHO FPPL, was first reported
183 in 2009 and has now been documented in six African countries, namely; South Africa, Kenya,
184 Nigeria, Sudan, Egypt and Algeria.⁹⁻¹³ Due to the need for largely unavailable, sophisticated
185 laboratory tests (matrix-assisted laser desorption ionization–time of flight mass
186 spectrometry (MALDI-TOF) and/or ribosomal DNA (rDNA) sequencing of internal transcribed
187 spacer (ITS)/D1-D2 regions), the yeast is often misidentified in laboratories, a possible
188 reason for the paucity of data from the continent. Most reported cases appear sporadic;
189 however, confirmed outbreaks have been described in South Africa and Kenya. In South
190 Africa where the most cases have been recorded, *C. auris* is a leading cause of candidaemia

191 especially in private sector hospitals in Johannesburg, Gauteng province, South Africa and
192 protracted outbreaks have been reported from neonatal intensive care units within the
193 country.⁹ In 2019, 11 invasive cases of *C. auris* were identified in the intensive care and high-
194 dependency units of a hospital in Nairobi, Kenya.¹⁰ Multimodal interventions were instituted
195 including intensified infection prevention and control (IPC) measures, point prevalence
196 surveys to monitor on-going transmissions, admission and contact screening to promptly
197 detect colonized patients. Delegates from both South Africa and Kenya highlighted resource
198 challenges in implementing *C. auris* screening and instituting IPC measures for outbreak
199 control.

200 *Mucormycosis*

201 In contrast to *C. auris*, mucormycosis was first described in humans in the 1800s. It is caused
202 by mucoraceous fungi which are ubiquitous in nature and distributed globally. There
203 remains a paucity of data about mucormycosis in Africa. A recent review of published case
204 reports and series analysed 408 documented cases, most of which were reported from
205 North Africa, predominantly Egypt.¹⁴ Fewer than 10 cases were reported from each of the
206 East, West and Central African regions. The review also noted that only 38 isolates were
207 cultured suggesting a lack of laboratory capacity. Most cases were treated with
208 amphotericin B deoxycholate while only few received globally recommended antifungals
209 such as liposomal amphotericin B and posaconazole and some were managed with
210 inappropriate therapies such as ketoconazole and fluconazole. While mucormycosis appears
211 rare, an upsurge in cases was demonstrated during the COVID-19 pandemic and anecdotal
212 evidence provided during the conference also suggests that the disease may be
213 underreported in scientific literature. Knowledge and practice gaps noted include the true
214 prevalence of mucormycosis especially for clinical phenotypes besides rhino-orbitocerebral,

215 the species of mucoraceous fungi causing mucormycosis in Africa, and the ways to access
216 effective antifungal agents, such as posaconazole and liposomal amphotericin B, at
217 reasonable costs. Recommendations to bridge these gaps include knowledge, practice and
218 perception studies; research and development to develop rapid, point of care tests;
219 operating a disease registry and leveraging drug access programmes for other diseases, such
220 as HIV-related cryptococcal meningitis, for liposomal amphotericin B.

221 *Aspergillosis*

222 Aspergillosis is a spectrum of diseases caused by *Aspergillus* species. It mostly affects the
223 lungs and ranges from allergic to chronic and invasive forms. Despite the presence of risk
224 factors such as advanced HIV, escalating cancer burdens, and critical illnesses such as
225 COVID-19, invasive aspergillosis is rarely diagnosed in Africa. In their systematic review,
226 Yerbanga *et al* dispelled the notion of IA in Africa as a myth.¹⁵ This review identified case
227 reports and observational studies documenting IA in African countries. The prevalence of IA
228 approached 27% in haemato-oncology patients with a fatality rate of more than 60%
229 recorded. Invasive pulmonary aspergillosis was the most common clinical form of IA while
230 neutropenia, HIV/AIDS and renal transplant were the main predisposing conditions.
231 *Aspergillus flavus* and *A. niger* were the main species identified and *A. fumigatus* was
232 surprisingly uncommon. This species profile, distinct from developed countries where *A.*
233 *fumigatus* causes more than 80% of IA, has been observed in other tropical regions such as
234 the Indian sub-continent, and may be related to climate and geographic factors.
235 Management with antifungals was often started only after broad-spectrum antibiotic
236 therapy failed. Lack of qualified human resources in medical mycology, diagnostic tools,
237 clear diagnostic guidelines and therapeutic drug monitoring were among the barriers to
238 caring for patients with IA.

239 Unlike the invasive form, chronic pulmonary aspergillosis (CPA) has been recognised as a
240 post-TB lung disease since the 1960s but remained a neglected condition in Africa until
241 recently. Reporting of CPA cases in Africa has risen progressively since the turn of the
242 century, an indication of increasing recognition of its public health importance brought
243 about by awareness creation championed by GAFFI and collaborators.¹⁶ CPA affects patients
244 with structural lung defects. Since pulmonary TB heals with scarring, fibrosis, or cavity
245 formation, it is one of the commonest at-risk conditions for CPA, and is responsible for 1.2
246 million of the estimated 3 million CPA cases globally.¹⁶ As Africa has several high-TB burden
247 countries, the prevalence of post-TB CPA is expectedly high. Nigeria's TB burden is ranked as
248 the largest in Africa and sixth largest globally. In 2021, Nigeria accounted for 4.4% of the
249 global number of TB cases, with 590,000 new cases of TB reported, an increase from the
250 452,000 reported in 2020. In a prospective longitudinal study to determine at what stage
251 post-treatment for TB that patients would develop CPA, the prevalence at recruitment was
252 31.2% but increased steadily to 31.9%, 34.8% and 36.2% at 3, 6 and 9 months respectively
253 (Davies *et al*, unpublished data). In a population-based study of previously treated PTB
254 patients in Uganda, another country where TB is endemic and diagnosing CPA presents a
255 dilemma, about 6.5% of the participants developed CPA within 2 years of TB treatment.¹⁷ A
256 more recent study in Uganda revealed that 20% of persons with persistent respiratory
257 symptoms after 2 months of standard anti-TB treatment had CPA.¹⁷ According to data from
258 the National tuberculosis and leprosy programme in Tanzania, only 34% of all new TB cases
259 were bacteriologically confirmed in 2020 and 43% of all cases were clinically diagnosed.
260 Despite recommendations of the WHO for molecular diagnostics as the preferred first-line
261 testing option, only 63% of all notified cases were bacteriologically confirmed using any
262 method. This gap in bacteriologically confirmed TB may very well point to the burden of CPA

263 in Tanzania. Additional research is obviously needed to fully elucidate the burden and
264 impact of CPA, especially post-TB treatment, on individual and public health. A systematic
265 inclusion of CPA monitoring in TB programmes was recommended where persons suspected
266 and confirmed to have TB are investigated for CPA during and after the completion of anti-
267 TB therapy. Challenges encountered in all settings, whether while managing CPA or
268 conducting research studies, include low level of clinicians' awareness, similarities of clinical
269 signs and symptoms with TB and unavailability of *Aspergillus*-specific serological diagnostics
270 in most African countries (*Aspergillus* IgG antibody testing was reported to be regularly
271 done only in Morocco; occasionally done in Tunisia, Niger and Chad; and never done in 39
272 countries).¹⁸

273 Aspergillosis is most commonly managed using mould-active azoles including itraconazole
274 and voriconazole. Azole resistance is a globally emerging phenomenon which can severely
275 hamper treatment. It often occurs following treatment but could also arise de novo in
276 environmental isolates of *Aspergillus fumigatus* which have been exposed to azole
277 containing fungicides used in the agricultural sector. Despite large agrarian communities
278 and poor antimicrobial, including antifungal, stewardship, there is paucity of data on azole
279 resistance in Africa, especially since many laboratories lack the capacity to perform
280 antifungal susceptibility testing. Pooling all available data from Africa in a systematic review,
281 Amona et al estimated an overall prevalence of triazole resistance of 17.1% in
282 environmental isolates and 1.3% in clinical isolates.¹⁹

283 *Overarching recommendations*

284 Overall, there is an urgent need for intensive surveillance in order to better understand the
285 burden of these trending fungal diseases in the continent. Effective surveillance requires
286 considerable resources; thus, African countries need to invest in efficient disease

287 surveillance mechanisms. South Africa possesses the most established fungal disease
288 surveillance system in Africa owing to decades of investment into a national diagnostic
289 laboratory network and integration of a mycology reference laboratory into the country's
290 national public health institute. This infrastructure is currently being leveraged to facilitate a
291 sub-regional surveillance network. In Nigeria, surveillance is currently being undertaken at
292 sentinel sites under the auspices of Nigerian Fungal Disease Surveillance and Capacity
293 Building (NIFUSCAB) with support from the US CDC and Nigeria Centre for Disease Control
294 (NCDC). These two models show that despite the challenges, surveillance for fungal disease
295 is feasible in Africa.

296 **AIDS and Mycoses**

297 Africa accounts for majority of global deaths from advanced HIV and a substantial number
298 of these deaths are caused by AIDS-related mycoses.²⁰ Two of these fungal killers-
299 histoplasmosis and cryptococcosis- were spotlighted.

300 Disseminated histoplasmosis in Africa's advanced HIV disease (AHD) population has
301 remained neglected for more than three decades of the HIV pandemic.²¹ Poor awareness
302 and lack of context-appropriate diagnostic tools present the major challenges to the
303 diagnosis and management of the disease. Greater public health focus on tuberculosis
304 which is endemic in many parts of Africa also confounds the diagnosis of histoplasmosis.
305 Culture of the causative organism, *Histoplasma capsulatum* is 100% specific and regarded as
306 the gold standard for diagnosis but it is slow, has poor sensitivity and often, facilities for
307 culture are not available.²² For this reason, the Pan American Health Organization and WHO
308 guidelines recommend antigen detection assays for diagnosing disseminated histoplasmosis
309 in persons with HIV. Only recently, a study conducted using antigen detection assays,
310 determined a 7.7% prevalence of disseminated histoplasmosis in Nigeria.²³ These assays,

311 however, are still not readily available in most African countries. In Nigeria, an enzyme
312 immunoassay-based technique has been piloted but challenges have been experienced with
313 respect to required equipment and personnel training. Moreover, requirements for sample
314 batching have resulted in prolonged turnaround times for results, delayed treatment and
315 fatal outcomes in some instances. As a matter of urgency, highly accurate rapid diagnostic
316 tests (RDTs) need to be made accessible, through better government-sponsored health
317 insurance packages, at facilities providing AHD care, as they could be life-saving in the
318 resource-limited context characteristic of African countries.

319 Unlike histoplasmosis, cryptococcosis is a well-researched and well-documented AIDS-
320 related mycosis with much of the evidence about the disease generated in Africa. Much
321 progress regarding diagnosis and treatment has been made over the years: a simple,
322 efficient diagnostic tool, the IMMY Crag lateral flow assay, has been in use for over a decade
323 and effective treatment regimens have been determined following rigorous clinical trials.²⁴
324 Nonetheless, translating this evidence into routine practice remains problematic in Africa.
325 Some of the barriers to effective management of CM include deferral of diagnostic and
326 therapeutic lumbar punctures either due to reluctance of local clinicians to perform the
327 procedure or high refusal rates amongst patients, and the pervading lack of access to
328 antifungals like liposomal amphotericin B and flucytosine. The practice gaps in CM care
329 underscore the need for implementation science and research as well as health systems
330 strengthening without which deaths from CM will remain high in the continent. As an
331 example, the Driving Reduced AIDS-associated Meningo-encephalitis Mortality (DREAMM)
332 implementation science project adapted standard operating procedures from CM clinical
333 trials for use in routine care settings in Africa. This reduced all-cause 2-week mortality from

334 49% to 24% among people living with HIV presenting to public hospitals in Africa with
335 suspected HIV-related CNS infection.²⁵

336 **Laboratory and point of care tests; current realities and future perspectives**

337 IFDs often present with non-specific symptoms and require laboratory tests for
338 confirmation. At the same time, diagnostic delays are associated with an increased risk of
339 death while early diagnosis and the institution of appropriate antifungal therapy are directly
340 linked to improved survival. The pivotal role of quick and accurate diagnostics can thus not
341 be overstated. As emphasised in preceding sections, diagnostic capabilities are sub-par in
342 Africa but not totally absent. The session on laboratory and point of care tests created an
343 opportunity for some functional mycology laboratories in Africa to share their approach to
344 offering mycology diagnostic services despite limitations. The Lagos University Teaching
345 Hospital diagnostic laboratory emphasized their focus on improving basic specimen
346 processing and simple diagnostic tools such as microscopy and minimum requirements for
347 fungal culture. The Centre for Healthcare-Associated, Antimicrobial Resistance and Mycoses
348 (CHARM) team from South Africa's National Institute for Communicable Diseases (NICD)
349 shared their wealth of experience in antifungal sensitivity testing which is offered in a
350 reference laboratory setting.

351 Rapid and point of care tests for fungal diseases (which allow for the detection of antigen or
352 antibody depending on the disease) have come of age and are increasingly available in
353 immunochromatographic and lateral flow formats, although access remains challenging in
354 many parts of Africa. Massively rolling out these tests, through government-sponsored
355 health insurance packages, to health facilities catering for at-risk populations could
356 revolutionise mycology practice in the region since they satisfy the ASSURED criteria of
357 'Affordability, Sensitivity, Specificity, User friendliness, Robustness, Equipment-free and

358 Delivered', to varying degrees.²⁶ Additional criteria proposed in 2019, namely real time
359 connectivity and ease of sample collection/environmental friendliness, are particularly
360 useful features for a point of care or rapid diagnostic test for IFDs. Real time connectivity
361 could result in faster reporting of test results for prompt action while also encouraging
362 better disease surveillance and quality assurance monitoring. Ease of sample collection is
363 especially desirable in Africa where invasive sampling procedures such as lumbar punctures
364 and bronchoalveolar lavage are seldom undertaken. Besides these desirable criteria, the
365 need for clarity on who performs which test, where it is performed and how it is reported
366 was discussed. With the exception of *Aspergillus* galactomannan lateral flow RDT which
367 requires sample pre-treatment steps and some laboratory equipment, the other lateral flow
368 assays like Crag and *Aspergillus* antibody tests could be conducted by all cadres of health
369 worker provided they have been properly trained. Nevertheless, who performed the test
370 and where it was conducted may differ depending on local context and this should be taken
371 into consideration when assigning roles. The need for implementation research to
372 determine the best way of operationalising the conduct of these tests in African settings
373 was underscored. Finally, the use of RDTs does not obviate the need for quality assurance.
374 Experienced laboratory personnel still need to provide oversight function irrespective of
375 where the test is conducted to ensure there is no compromise to quality care and
376 documentation. Future research and development in the field could be targeted at
377 molecular point of care tests for IFDs as has been done for tuberculosis with the Xpert
378 MTB/RIF and loop mediated isothermal amplification tests.

379 **Capacity building programs and initiatives**

380 In Africa, capacity building is required in the areas of clinical and laboratory personnel
381 knowledge, laboratory infrastructure and networks as well as operating disease registries

382 and conducting quality health research for IFDs. While many challenges remain, a few
383 ongoing initiatives within the region and in regions with similar socioeconomic profiles are
384 noteworthy and could serve as primers to catalyse action. An example of laboratory capacity
385 building was presented from Morocco where the mycological panel in the diagnostic
386 laboratory was gradually upgraded and adapted to local epidemiology and financial
387 resources based on mapping of the expected fungal infections from medical units and
388 patient populations.

389 In Nigeria, NIFUSCAB, with support from CDC, conducted clinician training to improve
390 requests for mycological testing while also training laboratory scientists to conduct the tests
391 and providing diagnostics, namely Crag LFA, *Aspergillus* galactomannan, *Aspergillus*
392 antibody and *Histoplasma* enzyme immunoassay. This three-pronged approach (clinician
393 training, laboratory personnel training and provision of diagnostic test kits) resulted in
394 significant increases in testing for IFDs at the six sentinel sites. Furthermore, in order to
395 reach a wider group of trainee doctors, NIFUSCAB has engaged the National Postgraduate
396 Medical College of Nigeria to host training modules in the form of freely available online
397 webinars on the College's website. These webinars would be accessed by trainees and
398 certificates of completion awarded after scoring a pass mark on the post-course
399 assessment. At the time of the conference, NIFUSCAB was in the process of co-creating the
400 webinars with indigenous specialists, a strategy expected to ensure buy-in from both
401 trainers and trainees. Disease entities selected for development as modules were
402 dependent on at-risk patient groups likely to be seen by each clinical specialty (Table 2).
403 Diagnostic specialties, namely radiology and histopathology, which cut across all risk groups,
404 were also targeted for module development.

405 Despite its importance, clinician training takes a long time to yield dividends and can be
406 influenced by many variables, including the quality of the teaching system and health
407 worker turnover/attrition rates.²⁷ As a stop-gap measure, diagnostic laboratory hubs (DLH)
408 have the potential to significantly impact the diagnosis of key IFDs in certain target
409 populations when implemented in settings where there is limited clinical expertise in fungal
410 diseases. GAFFI established such a laboratory capacity building partnership in Guatemala,
411 implementing a package of care to screen for cryptococcosis, histoplasmosis and
412 tuberculosis in persons living with HIV. Specimens are sent in to the DLH from a network of
413 laboratories. The centralization of tests at the DLH provides a cost-effective approach that
414 assures the quality of a local laboratory service especially when the incidence of fungal
415 diseases is relatively low. Results can be sent electronically to clinicians for prompt
416 institution of therapy, thus improving outcomes.²⁷

417 Using eumycetoma as a case study, the mycetoma research centre (MRC), a WHO
418 collaborating centre in Khartoum, Sudan emphasised the need to build capacity for research
419 and development. Mycetoma was recognized as a neglected tropical disease in 2016.²⁸ Lack
420 of access to diagnostics (i.e., trained microscopists, culture techniques, or PCR methods),
421 the unavailability of a point-of-care test and effective antifungals for eumycetoma are some
422 of the challenges faced in mycetoma care. Research and development priorities, thus
423 include updating the global burden and mapping of cases; developing novel point of care
424 tests for use in low resource settings, developing new treatment solutions including drug
425 discovery and susceptibility testing, ascertaining the mode of transmission and determining
426 the role of the host and the pathogen in mycetoma. To date, itraconazole is the only drug
427 used for mycetoma treatment because despite good in vitro activity of voriconazole and
428 posaconazole, their use is limited by longer treatment duration, high cost, and the relative

429 lack of studies regarding their response.²⁸ A landmark achievement of the MRC was the
430 recent conclusion of a clinical trial comparing the efficacy of fosravuconazole, a prodrug of
431 ravuconazole, to itraconazole for treatment of eumycetoma. This double-blinded,
432 randomized clinical trial sponsored by the Drugs for Neglected Diseases Initiative (DNDi) and
433 partners, is the first of its kind in mycetoma research.²⁹ The trial demonstrated no significant
434 difference in efficacy rates between both drugs. However, fosravuconazole offers several
435 advantages over itraconazole like reduced pill burden, once weekly dosing, and minimal
436 drug-drug interactions, thus presenting a more patient-friendly option for mycetoma
437 treatment. Challenges to building research capacity and conducting the trial in Africa were
438 highlighted by the delegate representing DNDi including the civil unrest on-going in Sudan.

439 **Synopsis of technical sessions**

440 Despite pervasive challenges- lack of tools, trainings and surveillance- improving the field of
441 medical mycology in Africa is possible with concerted efforts. Participants iterated the need
442 for a change in the way research is conducted in Africa to include a wider scope of partners
443 and the adoption of more robust methodologies. It was agreed that researchers need to
444 partner with governments and civil society organisations to facilitate stakeholder buy-in.
445 Similarly, to gain more insight and achieve greater impact, research methods need to
446 incorporate health economics, social science and health systems strengthening. The
447 relevant professionals from these disciplines should be part of research teams. Adequate
448 investments in capacity building for health workers and access programmes are also needed
449 before embarking on research. This enables the smooth uptake of research findings and
450 swift adoption of evidence into practice. Notable mycology research collaborations driven
451 by African leadership which embody these principles were highlighted including DREAMM,²⁵
452 and a National Institute for Health Research-funded Global Health Research Group on HIV-

453 associated Fungal Infections (acronym: IMPRINT). The need to expand laboratory diagnostic
454 access across the continent by embracing modern technologies from telemedicine to
455 artificial intelligence was emphasised. Local manufacturing of point of care tests also
456 requires broader consideration. The potential impact of establishing mycology reference
457 laboratories at national or sub-regional levels was discussed in detail. These laboratories
458 could serve as training centres, and given their robust organisational structure, they could
459 serve as hubs for international collaboration within and outside the continent. However,
460 reference laboratories stand the risk of becoming 'ivory towers' that fail to impact grassroots
461 patient care. This is preventable by maintaining close links with and providing diagnostic
462 support for a network of clinical or health facility laboratories.

463 **Meeting resolutions - The Nairobi Declaration**

464 At the close of the two-day meeting and based on the deliberations, the consortium agreed
465 on the following action points:

- 466 1. To catalogue existing free online educational resources to accelerate the work of
467 raising awareness about IFD. At the same time, country delegates and national
468 societies will pursue local initiatives within country to raise awareness and conduct
469 local training programmes.
- 470 2. To build strong collaborations between clinical and laboratory teams. The PAMWG
471 will facilitate exchange programmes to build clinical and laboratory capacity to
472 diagnose and treat IFDs. The group will undertake a detailed mapping of African
473 reference laboratories and what they offer to provide information to clinicians and
474 laboratorians seeking particular skillsets or capacities. Other facilities outside the
475 continent, such as European Excellence Centres in Medical Mycology affiliated with

476 ECMM and centres affiliated with ISHAM, would be similarly catalogued as possible
477 resources for training.

478 3. To spearhead improved surveillance for IFDs at national and sub-regional levels. Best
479 practices and lessons learned from current surveillance initiatives will be curated and
480 used as advocacy, training and implementation blueprints for establishing
481 sustainable systems in additional countries.

482 4. To champion advocacy for the provision of high-quality POC and conventional
483 laboratory testing for IFDs using available tools such as the WHO Essential
484 Diagnostics List and domesticated national versions of this list, and leveraging
485 existing programmes such as HIV and TB treatment programmes.

486 5. To advocate for the availability of antifungals at the level of the African Union and
487 Africa CDC as well as global funders such as Unitaid, Global Fund and US President's
488 Emergency Plan for AIDS Relief (PEPFAR).

489 6. To build research capacity especially for clinical trials and implementation science
490 research that will further elucidate best practices for managing fungal diseases in
491 Africa.

492 Progress made in realising these resolutions will be evaluated in the next biennial meeting.

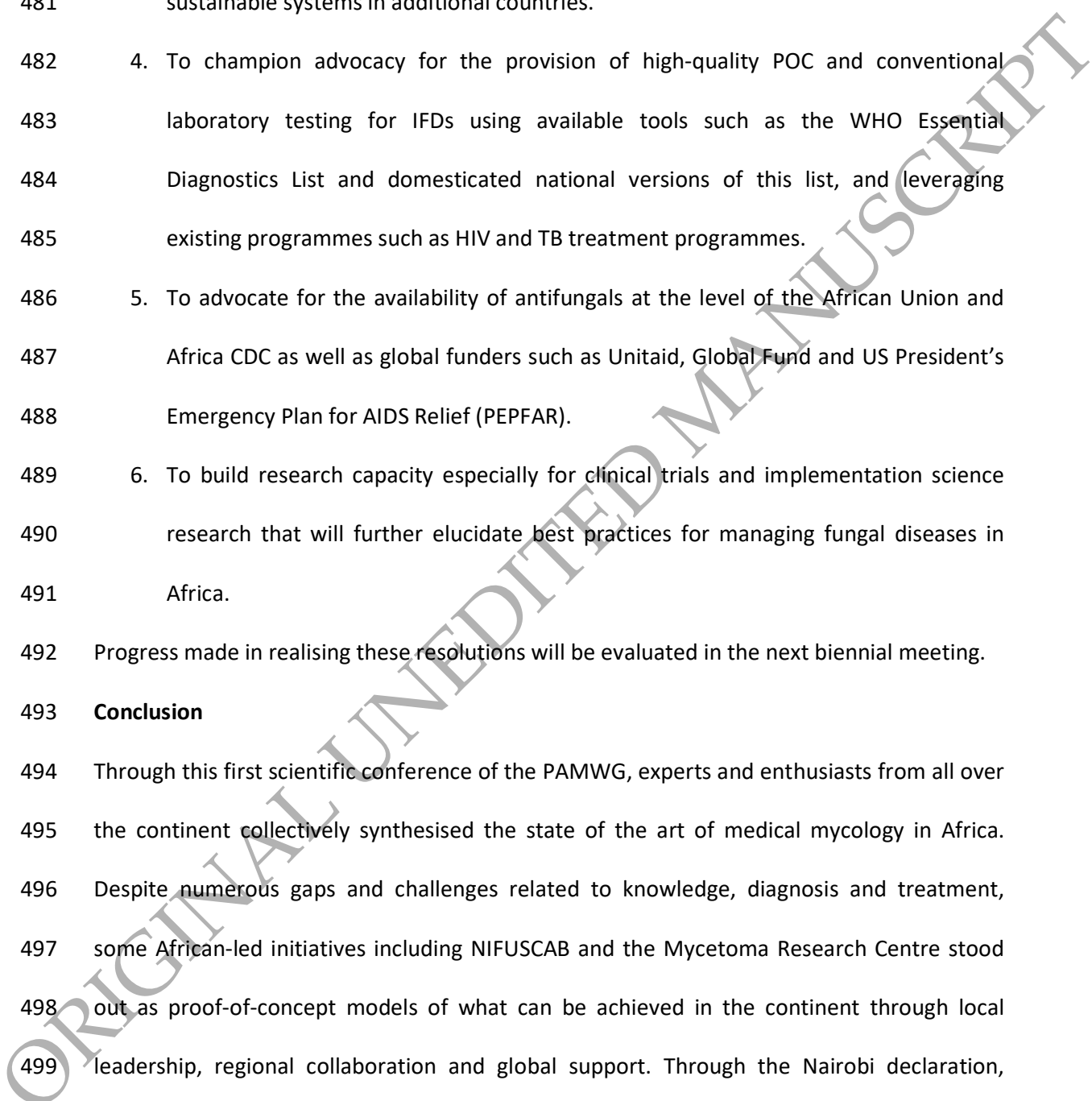
493 **Conclusion**

494 Through this first scientific conference of the PAMWG, experts and enthusiasts from all over
495 the continent collectively synthesised the state of the art of medical mycology in Africa.

496 Despite numerous gaps and challenges related to knowledge, diagnosis and treatment,
497 some African-led initiatives including NIFUSCAB and the Mycetoma Research Centre stood

498 out as proof-of-concept models of what can be achieved in the continent through local

499 leadership, regional collaboration and global support. Through the Nairobi declaration,



500 delegates committed to galvanising action in a uniform direction. This is expected to address
501 and provide sustainable solutions to the menace of neglected, life-threatening fungal
502 diseases in Africa.

503

504 **Acknowledgements**

505 We acknowledge all participants at the first scientific meeting of the Pan African Mycology
506 Working Group who contributed to the various sessions.

507

508 **Conflict of Interest**

509 None.

510

511 **Disclaimer:** The findings and the conclusions in this report are those of the authors and do
512 not necessarily represent the views of the Centers for Disease Control and Prevention or any
513 other institution.

514 **References**

515 1. Oladele RO, Akase IE, Fahal AH, Govender NP, Hoenigl M, Gangneux JP et al. Bridging
516 the knowledge gap on mycoses in Africa: Setting up a Pan-African Mycology Working
517 Group. *Mycoses*. 2020; 63(3):244-249. doi: 10.1111/myc.13044.

518 2. World Health Organization. WHO Fungal Priority Pathogens List to Guide Research,
519 Development and Public Health Action. World Health Organization; Geneva,
520 Switzerland: 2022

521 3. Bongomin F, Kibone W, Okot J, Nsenga L, Olum R, Baluku JB. Fungal diseases in
522 Africa: epidemiologic, diagnostic and therapeutic advances. *Ther Adv Infect Dis*.
523 2022; 9:20499361221081441. doi: 10.1177/20499361221081441.

- 524 4. Global Action for Fungal Infections. Country fungal disease burdens. Available at
525 <https://gaffi.org/media/country-fungal-disease-burdens/>. Accessed on July 15, 2023.
- 526 5. Rajasingham R, Govender NP, Jordan A, Loyse A, Shroufi A, Denning DW et al. The
527 global burden of HIV-associated cryptococcal infection in adults in 2020: a modelling
528 analysis. *Lancet Infect Dis.* 2022; 22(12):1748-1755. doi: 10.1016/S1473-
529 3099(22)00499-6.
- 530 6. Salmanton-García J, Au WY, Hoenigl M, Chai LYA, Badali H, Basher A et al. The
531 current state of laboratory mycology in Asia/Pacific: A survey from the European
532 Confederation of Medical Mycology (ECMM) and International Society for Human
533 and Animal Mycology (ISHAM). *Int J Antimicrob Agents.* 2023; 61(3):106718. doi:
534 10.1016/j.ijantimicag.2023.106718.
- 535 7. Salmanton-García J, Hoenigl M, Gangneux JP, Segal E, Alastruey-Izquierdo A, Arikan
536 Akdagli S et al. The current state of laboratory mycology and access to antifungal
537 treatment in Europe: a European Confederation of Medical Mycology survey. *Lancet*
538 *Microbe.* 2023; 4(1):e47-e56. doi: 10.1016/S2666-5247(22)00261-0.
- 539 8. Driemeyer C, Falci DR, Oladele RO, Bongomin F, Ocansey BK, Govender NP et al. The
540 current state of clinical mycology in Africa: a European Confederation of Medical
541 Mycology and International Society for Human and Animal Mycology survey. *Lancet*
542 *Microbe.* 2022; 3(6): e464-e470. doi: 10.1016/S2666-5247(21)00190-7.
- 543 9. Govender NP, Magobo RE, Mpembe R, Mhlanga M, Matlapeng P, Corcoran C, Govind
544 C, Lowman W, Senekal M, Thomas J. *Candida auris* in South Africa, 2012-2016. *Emerg*
545 *Infect Dis.* 2018; 24(11):2036-2040. doi: 10.3201/eid2411.180368

- 546 10. Adam RD, Revathi G, Okinda N, Fontaine M, Shah J, Kagotho E et al. Analysis of
547 *Candida auris* fungemia at a single facility in Kenya. *Int J Infect Dis.* 2019; 85:182-187.
548 doi: 10.1016/j.ijid.2019.06.001. Epub 2019 Jun 8. PMID: 31185293
- 549 11. Oladele R, Uwanibe JN, Olawoye IB, Ettu AO, Meis JF, Happi CT. Emergence and
550 Genomic Characterization of Multidrug Resistant *Candida auris* in Nigeria, West
551 Africa. *J Fungi (Basel).* 2022; 8(8):787. doi: 10.3390/jof8080787.
- 552 12. Badri AM, Sherfi SA. First Detection of Emergent Fungal Pathogen *Candida auris* in
553 Khartoum State, Sudan. *Am J Biomed Sci & Res.* 2019; 6(1): AJBSR.MS.ID.000982.
554 DOI:
555 10.34297/AJBSR.2019.06.000982
- 556 13. Zerrouki H, Ibrahim A, Rebiahi SA, Elhabiri Y, Benhaddouche DE, de Groot T et al.
557 Emergence of *Candida auris* in intensive care units in Algeria. *Mycoses.* 2022;
558 65(7):753-759. doi: 10.1111/myc.13470.
- 559 14. Osaigbovo II, Ekeng BE, Davies AA, Oladele RO. Mucormycosis in Africa:
560 Epidemiology, diagnosis and treatment outcomes. *Mycoses.* 2023; 66(7):555-562.
561 doi: 10.1111/myc.13581.
- 562 15. Yerbanga IW, Nakanabo Diallo S, Rouamba T, Denis O, Rodriguez-Villalobos H,
563 Montesinos I, Bamba S. A systematic review of epidemiology, risk factors, diagnosis,
564 antifungal resistance, and management of invasive aspergillosis in Africa. *J Mycol*
565 *Med.* 2023; 33(1):101328. doi: 10.1016/j.mycmed.2022.101328.
- 566 16. Olum R, Osaigbovo II, Baluku JB, Stemler J, Kwizera R, Bongomin F. Mapping of
567 Chronic Pulmonary Aspergillosis in Africa. *J Fungi (Basel).* 2021; 7(10):790. doi:
568 10.3390/jof7100790.

- 569 17. Namusobya M, Bongomin F, Mukisa J, Olwit WK, Batte C, Mukashyaka C, Mande E,
570 Kwizera R, Denning DW, Rhein J, Prasad S, Sekaggya-Wiltshire C. Chronic pulmonary
571 aspergillosis in patients with active pulmonary tuberculosis with persisting symptoms
572 in Uganda. *Mycoses*. 2022; 65(6):625-634. doi: 10.1111/myc.13444.
- 573 18. Mushi MF, Zaki SM, Penney ROS, Bamba S, Ngouanom Kuate MP, Kasamba EL et al.
574 Diagnostic options for pulmonary fungal diseases in Africa. *ERJ Open Res*. 2023;
575 9(2):00397-2022. doi: 10.1183/23120541.00397-2022.
- 576 19. Amona FM, Oladele RO, Resendiz-Sharpe A, Denning DW, Kosmidis C, Lagrou K et al.
577 Triazole resistance in *Aspergillus fumigatus* isolates in Africa: a systematic review.
578 *Medical Mycology*. 2022; 60(8): myac059
- 579 20. Lakoh S, Kamudumuli PS, Penney ROS, Haumba SM, Jarvis JN, Hassan AJ et al.
580 Diagnostic capacity for invasive fungal infections in advanced HIV disease in Africa: a
581 continent-wide survey. *Lancet Infect Dis*. 2023; 23(5):598-608. doi: 10.1016/S1473-
582 3099(22)00656-9.
- 583 21. Oladele RO, Ayanlowo OO, Richardson MD, et al. Histoplasmosis in Africa: an
584 emerging or a neglected disease? *PLoS Negl Trop Dis* 018; 12: e0006046. doi:
585 10.1371/journal.pntd.0006046
- 586 22. Kuate MPN, Nyasa R, Mandengue C, Tendongfor N, Bongomin F, Denning DW.
587 Screening for acute disseminated histoplasmosis in HIV disease using urinary antigen
588 detection enzyme immunoassay: A pilot study in Cameroon. *J Microbiol Methods*.
589 2021; 185:106226. doi: 10.1016/j.mimet.2021.106226.
- 590 23. Oladele RO, Osaigbovo II, Akanmu AS, Adekanmbi OA, Ekeng BE, Mohammed Y et al.
591 Prevalence of Histoplasmosis among Persons with Advanced HIV Disease, Nigeria.
592 *Emerg Infect Dis*. 2022; 28(11):2261-2269. doi: 10.3201/eid2811.220542

- 593 24. Temfack E, Lortholary O. Access to flucytosine for the treatment of HIV-associated
594 cryptococcal meningitis in Africa. *Lancet Infect Dis.* 2022; 22(9):1262-1264. doi:
595 10.1016/S1473-3099(22)00315-2
- 596 25. Mfinanga S, Kanyama C, Kouanfack C, Nyirenda S, Kivuyo SL, Boyer-Chammard T et
597 al. Reduction in mortality from HIV-related central nervous system infections in
598 routine care in Africa (DREAMM): A before-and after- implementation study. *The*
599 *Lancet HIV.* 2023; 10(10): E663-E673. doi: [https://doi.org/10.1016/S2352-](https://doi.org/10.1016/S2352-3018(23)00182-0)
600 [3018\(23\)00182-0](https://doi.org/10.1016/S2352-3018(23)00182-0)
- 601 26. Osaigbovo II, Bongomin F. Point of care tests for invasive fungal infections: a
602 blueprint for increasing availability in Africa. *Ther Adv Infect Dis.* 2021;
603 8:20499361211034266. doi: 10.1177/20499361211034266.
- 604 27. Medina N, Alastruey-Izquierdo A, Mercado D, Denning DW, Arathoon E, Rodriguez-
605 Tudela JL. Diagnostic Mycology Laboratories Should Have a Central Role for the
606 Management of Fungal Disease. *J Fungi (Basel).* 2022; 8(12):1285. doi:
607 10.3390/jof8121285.
- 608 28. Fahal AH, Ahmed KO, Saeed AA, Elkhawad AO, Bakhiet SM. Why the mycetoma
609 patients are still neglected. *PLoS Negl Trop Dis.* 2022; 16(12): e0010945. doi:
610 10.1371/journal.pntd.0010945.
- 611 29. Fahal AH, Bakhiet SM, Mohamed EW, Ahmed ES, Bakhiet OE, Yousif AA et al. A
612 randomized, double blind phase II proof-of-concept superiority trial of
613 fosravuconazole 200 mg or 300 mg weekly dose versus itraconazole 400 mg daily, all
614 three arms in combination with surgery, in patients with eumycetoma in Sudan—top
615 line results. *Med Mycol.* 2022; 60(Suppl 1): myac072S45a.

617

618 **Table 1: Proposed strategies to bridge gaps in understanding the burden of mycoses in**
619 **Africa**

Recommendation	<i>Modus operandi</i>
Popularising the WHO FPPL through various media channels	Highlights fungi of critical or high importance to human health, providing pathways for action such as engagement with policy makers
Providing diagnostics and setting up surveillance systems	Provides data on disease burden and antifungal susceptibility patterns.
Implementation science research in medical mycology	Improves uptake of diagnostics and public-health interventions targeting IFDs, thereby improving case-finding.
Investing in and increasing pre-service and in-service trainings for HCP of all categories	Makes HCP knowledgeable to promptly detect IFDs

620

621

622

623

624

625

WHO= World Health Organisation; FPPL= Fungal Priority Pathogens List; HCP= Healthcare personnel; IFD= Invasive fungal disease

ORIGINAL UNEDITED MANUSCRIPT

626
627
628

Table 2: Fungal diseases targeted for educational webinars based on at-risk groups seen by clinical specialties in Nigeria

Clinical specialty	Patient groups at risk	Fungal infections targeted for module development
Dermatology	Immunocompetent and PLHIV	<ul style="list-style-type: none"> • Dermatomycosis: <i>Tinea capitis</i>; <i>Tinea corporis</i>; Onychomycosis • Fungal neglected tropical diseases (mycetoma, chromoblastomycosis, sporotrichosis) • Systemic mycoses: cryptococcosis, histoplasmosis
Infectious diseases	PLHIV	<ul style="list-style-type: none"> • Candidiasis: Oral and oesophageal • Cryptococcosis, • Pneumocystosis • Disseminated histoplasmosis
Intensive care	Central venous line in situ, Mechanical ventilation, COVID-19	<ul style="list-style-type: none"> • Invasive candidiasis • Invasive aspergillosis
Haemato-oncology	AML, HSCT, Cancer patients receiving radiotherapy	<ul style="list-style-type: none"> • Invasive candidiasis • Invasive aspergillosis • Mucormycosis
Pulmonology	TB, COPD, Asthma	<ul style="list-style-type: none"> • Chronic pulmonary aspergillosis • Allergic bronchopulmonary aspergillosis
Otorhinolaryngology	Immunocompetent, Diabetic patients	<ul style="list-style-type: none"> • Otomycosis • Fungal invasive rhinosinusitis

629 *PLHIV: Persons living with HIV; AML: Acute Myeloid Leukemia; HSCT: Hematopoietic stem cell*
630 *transplantation; TB: Tuberculosis COPD: Chronic Obstructive Pulmonary Disease*

631
632
633

ORIGINAL UNEDITED MANUSCRIPT