Check for updates

Received: 8 April 2021 | Revised: 1 June 2021 | Accepted: 10 June 2021

DOI: 10.1111/myc.13339

REVIEW ARTICLE

mycoses Diagnosis, Therapy and Prophylaxis of Fungal Diseases WILEY

Serious fungal diseases in Democratic Republic of Congo – Incidence and prevalence estimates

Guyguy K. Kamwiziku[1] | Jean-Claude C. Makangara[1] | Emma Orefuwa[2] | David W. Denning[2,3]

[1]Department of Microbiology, Kinshasa University Hospital, University of Kinshasa, Kinshasa, Democratic Republic of Congo

[2]Global Action Fund for Fungal Infections, Geneva, Switzerland

[3]Manchester Fungal Infection Group, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK

Correspondence
Guyguy K. Kamwiziku, Department of Microbiology, Kinshasa University Hospital, University of Kinshasa, Congo.
Email: drkamwiziku@gmail.com

Abstract

A literature review was conducted to assess the burden of serious fungal infections in the Democratic Republic of the Congo (DRC) (population 95,326,000). English and French publications were listed and analysed using PubMed/Medline, Google Scholar and the African Journals database. Publication dates spanning 1943–2020 were included in the scope of the review. From the analysis of published articles, we estimate a total of about 5,177,000 people (5.4%) suffer from serious fungal infections in the DRC annually. The incidence of cryptococcal meningitis, *Pneumocystis jirovecii* pneumonia in adults and invasive aspergillosis in AIDS patients was estimated at 6168, 2800 and 380 cases per year. Oral and oesophageal candidiasis represent 50,470 and 28,800 HIV-infected patients respectively. Chronic pulmonary aspergillosis post-tuberculosis incidence and prevalence was estimated to be 54,700. Fungal asthma (allergic bronchopulmonary aspergillosis and severe asthma with fungal sensitization) probably has a prevalence of 88,800 and 117,200. The estimated prevalence of recurrent vulvovaginal candidiasis and tinea capitis is 1,202,640 and 3,551,900 respectively.Further work is required to provide additional studies on opportunistic infections for improving diagnosis and the implementation of a national surveillance programme of fungal disease in the DRC.

KEYWORDS
aspergillosis, candidiasis, cryptococcosis, fungal infection, HIV/AIDS, Pneumocystis, tinea capitis, Tuberculosis

1 | INTRODUCTION

With a surface area of 2,345,000 km², DRC is the second largest country in Africa after Algeria. It has a population of around 95,326,000 inhabitants of which more than 60% live in rural areas.[1,2] The DRC shares 9,165 kilometres of border with 9 countries (Figure 1).[3] The country is currently ranks 176 out of 189 countries on the Human Development Index. In 2019, GDP per capita $545, a 2.13% decline from 2018.[4] With regards to health system architecture, the Ministry of Public Health is structured in the form of a 3-level pyramid. The national level has normative, regulatory and tertiary care provision responsibility. The provincial level provides technical supervision, monitoring and translation of directives and offers secondary reference health care. The operational level includes 516 Health Zones (HZ) with 393 General Reference Hospitals and 8,504 planned Health Areas (HA) of which 8,266 have a Health Centre. The function of this level is to implement the primary health care strategy. At this level, there are 2004 health centres for the detection and treatment of tuberculosis (CSDT) and 4,587 sites for the detection and treatment of HIV (SDT). In 2019, the DRC integrated 1752 existing CSDTs into the management of HIV-TB co-infection. A HZ is a geographically limited space covering a theoretical

 © 2021 Wiley-VCH GmbH.

population of 100,000 to 150,000 inhabitants with a general reference hospital (GRH). The health system also integrates private for-profit and not-for-profit sector health facilities (health services of non-governmental organisations and faith-based organisations). The majority of GRHs lack intensive care, laboratory services (with parasitology, biochemistry, bacteriology and haematology services) and imaging X-ray, ultrasound, electrocardiogram, non stress test, Optical coherent tomography, etc). In the same way, the three University Clinics are under-equipped to serve as tertiary reference facilities. The DRC has 29 pharmaceutical industry companies, and wholesale supply and distribution is provided by 150 authorised establishments.[5,6] There is an imbalance in the organisation of training courses and in the equitable distribution of health workers between rural and urban areas and between health structures. Health staff are concentrated in the capital Kinshasa and in the urban centres of the provinces. Health workforce indicators are low, using the benchmark ratio of 1 doctor per 10,000 inhabitants, only three out of ten provinces have staff numbers that meet or exceed international standards.[3] Communicable diseases with epidemic potential are an ongoing issue in the DRC.[3,4] The Director General for Disease Control has placed certain infectious diseases under epidemiological surveillance, including acute flaccid paralysis, cholera, leprosy, neonatal tetanus, plague, viral haemorrhagic fever, yellow fever, monkey-pox, measles, avian flu, bloody and simple diarrhoea, meningitis, malaria, typhus, pertussis, typhoid fever, acute respiratory infections, sexually transmitted infections, several neglected tropical diseases (NTDs), AIDS and tuberculosis (TB). Despite their known association with co-infections such as HIV and TB, fungal diseases are a glaring omission from the priority list of infectious diseases being surveilled. DRC is in a phase of epidemiological transition, characterised by an

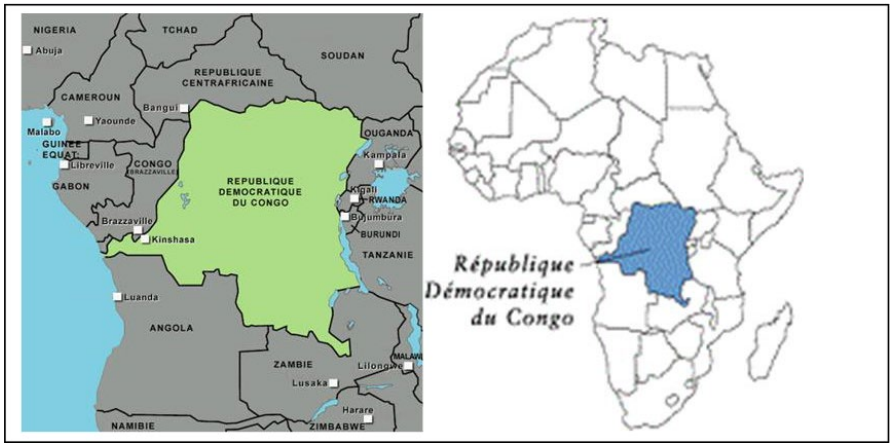

FIGURE 1 Map of the Democratic Republic of Congo with the neighbouring countries

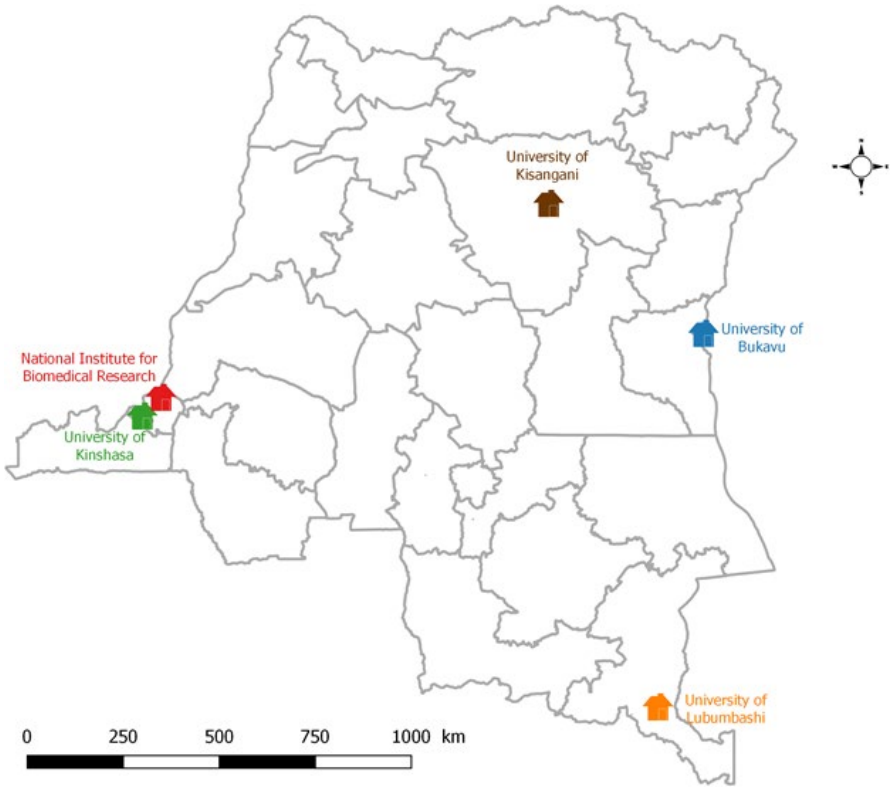

FIGURE 2 localisation of main institutions publishing articles in Democratic Republic of Congo

increase in the incidence of non-communicable diseases such as cancer and diabetes which heighten the need to address fungal infections as a public health issue of growing significance.

There is no surveillance programme for fungal diseases in the DRC.[6] Given the poor availability and accessibility of diagnostics in the DRC, fungal infections unfortunately remain grossly underestimated. Despite the paucity of data, some studies have been conducted in DRC which allow for baseline modelling to be carried out. The aim of this literature review is to take stock of the current incidence and prevalence of fungal infections in DRC.

2 | MATERIALS AND METHODS

This literature review was based on articles about fungal infections using the Google Scholar and PubMed/Medline search engines, African newspapers, health reports, epidemiological journals in DRC and WHO reports (Figure 2). The articles searched were mostly in English. The keywords searched were: fungal infection, opportunistic disease, HIV/AIDS, tuberculosis, chronic pulmonary, cryptococcosis, histoplasma, all associated with DRC. The oldest article retrieved was from 1943 and the most recent was from 2020. There are few studies on fungal diseases in the DRC and many of them are more than a decade old so we extended our searches to studies in border countries that have already estimated the burden of some fungal infections. We first considered Central African Countries and then, other sub-Saharan African countries. The countries chosen were those that are close to the four major universities in the DRC that use published articles. Where no article was found from the DRC or neighbouring countries, we used data from other countries within Africa and if this was not available, then data from other countries outside the African region. The socio-demographic data were taken from the National Health Development Plan 2016-2020 reports and the 2017 reports of the National Statistics Institute (Table 1). The HIV prevalence and deaths were taken from the 2019 UNAIDS report. To evaluate the incidence of children and adults at risk of developing the OIs, we have assessed different factors impacting on OI incidence in the literature.[7] Considering that people living with HIV infection (PLWHIV) who are not on ART generally develop profound immunodeficiency over 7 years for adults and 5 years for children and that the rate failure of ART is 11%, we estimated the population of PLWHIV at risk.[8] TB rates were taken from the WHO Global report 2019, and we derived the pulmonary TB survivors. Asthma prevalence in adults living in Kinshasa was assumed to apply to the whole country.[9] Chronic obstructive pulmonary disease (COPD) prevalence was taken from the Cameroon [10] and it was assumed that 10.5% were admitted to hospital each year, as in Algeria.[11] Lung cancer was taken from Global cancer observatory (Globocan) [12] and acute myeloid leukaemia from the WHO expert committee.[13] No stem cell or organ transplantation procedures are done in the DRC. We used the various populations and denominators and estimated prevalence or incidence of different fungal diseases using information from multiple sources, all described in Table 2. The assumptions used to compute annual incidence or prevalence are also shown.

3 | RESULTS

3.1 | Country's profile

In the DRC, endemic diseases have a high mortality: malaria is the leading cause of death with a prevalence of 23%. HIV/AIDS and TB are also common. The DRC is among 30 countries with the highest burden of TB ranking 11th in the world and 3rd in Africa. It is also one of 13 countries facing the dual challenge of HIV-TB co-infection and drug resistance at the same time.[3,14] Although HIV prevalence is declining in the DRC, at 0.8%, its epidemiology is complex. It is higher among women in some provinces and four times higher in urban areas. Apart from HIV and TB co-infection, which are well supported and documented, the prevalence and incidence of other opportunistic infections is not known due to the lack of any diagnostic capability in most health facilities.

3.2 | Review of serious fungal infections

The scarcity of articles on fungal infections has prompted us to use prevalence or incidence from other countries to estimate the burden in the DRC. The summary shown in Table 2 and 3 is derived from the various populations at risk and the rate per 100,000 inhabitants. Each year in DRCongo approximately 5,079,278 people are affected by fungal diseases, 5.32% of the whole population.

3.2.1 | Fungal skin infections: Tinea capitis and neglected tropical diseases

In children, tinea capitis is the most common superficial fungal infection. Our estimation is 3,551,862 children have tinea capitis, a rate of 3,726 per 100,000. An old study (1959) gave a disparate prevalence of tinea capitis by region, the lowest prevalence was 2.9% in the middle part of the DRC and the high was 20% in the East part.[42,43] No recent study is published, but it is a common problem. Neglected tropical skin fungal diseases have not been reported recently. An old study from the Belgian Congo (currently DRC) found 9 cases of mycetoma in 1954.[44] A strain of *Catenulostroma chromoblastomycosum* is deposited with the information that it is from a case of chromoblastomycosis from Zaire (currently DRC).[45] *Sporothrix schenckii* is a ubiquitous fungus, causing mostly non-life-threatening localised infections of the skin and subcutaneous tissues - only one case is reported from DRC in an HIV patient.[46] No data was found for *basidiobolomycosis*, *chromoblastomycosis*, *rhinoporidioisis or Conidiobolus* or Emergomyces infections. They are probably rare.

TABLE 1 The basic demographics of the country

Data	Number	Reference	Comments
Population	95 326 400	[2]	2019
HIV infection	520 000	[15]	Prevalence 2019
Pulmonary tuberculosis	233 520	[16]	Annual incidence 2019
Asthma numbers in adults	3 551 860	[2]	With 2019 population
Acute myeloid leukaemia	380	[17]	Annual incidence

Abbreviation: HIV, Human Immunodeficiency Virus.

TABLE 2 Assumptions underlying the assessment of serious fungal diseases burden

Fungal disease	Underlying condition	Assumptions made	References
Cryptococcal meningitis	HIV/AIDS	12.2% of AIDS patients	[18]
Pneumocystis pneumonia	HIV/AIDS	10% PCP as newly diagnosed HIV/AIDS adults over 2 years	[19]
Disseminated histoplasmosis	HIV/AIDS	1.5% of advanced HIV disease	[20,21]
Invasive aspergillosis	HIV/AIDS; COPD; Leukaemia; lung cancer	10% of AML patients develop IA. Rate in non-AML same as in AML. 1.3% of admitted COPD patients, 2.6% of lung cancer patients and 4 per 1000 HIV/AIDS patients develop IA	[22-26]
Chronic pulmonary aspergillosis (CPA)	Tuberculosis, COPD	22% of TB survivors with cavities, 2% of those without cavities and assumed pulmonary TB is the underlying diagnosis in 80% of all CPA cases	[27-29]
Allergic Broncho pulmonary aspergillosis (ABPA)	Asthma	2.5% of adult asthmatics	[30] [31]
Severe asthma with fungal sensitisation (SAFS)	Severe asthma	33% of worst 10% of adult asthmatics.	[32]
Candidaemia		5/100,000 (mean of 2-11/100,000) with 30% in ICU (critical care and post-surgical patients) and 70% in cancer and other immunocompromised patients	[33]
Candida peritonitis	Pancreatitis, major abdominal surgery	1 patient with hospital-acquired (almost all post-operative) *Candida* peritonitis for every 2 patients with candidaemia, in ICU	[34]
Oral candidiasis	HIV/AIDS	90% of untreated HIV patients	[35,36]
Oesophageal candidiasis	HIV/AIDS	20% of patients not on ARVs and 0.5% of those on ARVs	[37,38]
Recurrent candida vaginitis (≥4x/year)		6% of adult women	[39]
Mucormycosis		Affects 2 per million of the population based on data from Europe	[40]
Tinea capitis		7.38% of school-age children	[41]

Abbreviations: AML, Acute myeloid leukaemia; ARV, antiretroviral; COPD, Chronic obstructive pulmonary disease; HIV/AIDS, Human Immunodeficiency Virus/ Acquired ImmunoDeficiency Syndrome; IA, invasive aspergillosis; ICU, Intensive Care Unit; PCP, *Pneumocystis* pneumonia; TB, Tuberculosis.

3.2.2 | *Candida* diseases

No data on recurrent vulvovaginal candidiasis (rVVC), candidaemia and *Candida* peritonitis were found. The prevalence of rVVC is thought to be 2523/100 000, using a 6% proportion of women aged between 15 and 54, or to affect about 1.2 million women.[39] Other data from Cameroon found 34.8% of women had vaginal candidiasis, suggesting this problem is more frequent than in Europe and the USA, and likely to be underestimated by our estimate.[47] Although blood culture is fairly widespread in DRC, there are no data on the frequency of candidaemia. Using a low average country incidence, of 5/100 000,[48] we estimate ~4,770 patients annually. In France, the ratio of candidaemia to intra-abdominal candidiasis

TABLE 3 Estimate of serious fungal infections in Republic Democratic of Congo

Serious Fungal Infection	Estimate	No underlying disease	HIV/AIDS	Respiratory disease	Cancer +immunocompromised	Critical care +surgery	Rate/100,000	Total Burden
Cryptococcal meningitis	I	–	6168	–	–	–	6.5	6168
Pneumocystis pneumonia adult	I	–	2800	–	–	–	2.9	2800
Pneumocystis pneumonia children	I	–	595	–	–	–	0.6	595
Pneumocystis pneumonia total	I	–	3016	–	–	–	3.2	3016
Invasive aspergillosis	I	–	380	2560	123	–	3.2	3063
CPA post TB	I	–	–	11,580	–	–	12.1	11,580
CPA post TB	P	–	–	36,500	–	–	38.3	36,500
CPA – all	P	–	–	54,700	–	–	57.4	54,700
ABPA	P	–	–	88,800	–	–	93.2	88,800
SAFS	P	–	–	117,200	–	–	123	117,200
Candidaemia	I	–	–	–	3340	1430	5.0	4770
Candida peritonitis	I	–	–	–	–	715	0.8	715
Oral candidiasis	I	–	50,470	–	–	–	52.9	50,470
Oesophageal candidiasis	I	–	28,800	–	–	–	30.2	28,800
Recurrent Candida vaginitis (>4x/year)		1,202,640	–	–	–	–	2523	1,202,640
Mucormycosis	I	–	–	–	190	–	0.2	190
Histoplasmosis	I	–	–	840	–	–	0.9	840
Fungal keratitis	I	12,680	–	–	–	–	13.3	12,680
Tinea capitis	P	3,551,900	–	–	–	–	3726	3,551,900
Total burden		4,767,220	92,229	312 180	3653	2145		5,177,427

Abbreviations: ABPA, Allergic bronchopulmonary aspergillosis; CPA, Chronic pulmonary aspergillosis; I, incidence; P, prevalence; SAFS, Severe asthma with fungal sensitisation; TB, tuberculosis.

is 2:1, in intensive care.[49] On this basis, we anticipate on 715 cases (0.8/100,000), but this could be erroneous as there are few intensive care beds, but conversely many patients present with severe acute abdominal emergencies.

Oral candidiasis and oesophageal candidiasis as opportunistic infections in HIV are common. We estimated an annual incidence of 52.9/100 000 and 30.2/100,000 respectively. This equates to over 50,000 oral candidiasis patients in those with CD4 <200/μl [35,50] and 28,800 oesophageal candidiasis cases.[37] In addition, a local cross-sectional report from 1988 found 24% of HIV patients to have oral candidiasis.[51]

3.2.3 | HIV-associated infection fungal disease

In 2019, 258,610 of 520,000 people living with HIV/AIDS (PLWHIV) are on ART, that is ~50%, with 15,000 deaths, 9,600 in adults.[15] There were an estimated 56,074 at risk of acquiring an opportunistic infection, based on a 7 year decline in CD4 counts to <200 μl in those not on ART, and assuming an 11% ART failure rate in those on ART Ian the literature many opportunistic fungal infections are described in PLWHIV in those not on ART and immunocompromised. In the DRC, none of these infections are well documented. Considering *Pneumocystis* pneumonia (PCP) occurred an annual rate of 5% in at risk PLWHIV,[19] we estimate ~2804 episodes in adults and 595 in children, a total of 3,400 or 3.6 per 100,000. Cryptococcal meningitis (CM) was estimated at a rate of 11% in at risk PLWHIV, based on a study in the east of the DRC [52] an annual incidence 6168 or 6.5 per 100 000. The related species *Histoplasma capsulatum* have two variety: capsulatum and *duboisii* cause important deep mycoses and have been reported in PLWHIV. In the DRC mainly *duboisii* variety infections are reported. One study mentioned five cases.[53] So, we tentatively estimate 840 annual cases or 0.9 per 100 000 people.

3.2.4 | Fungal asthma and aspergillosis

There are approximately 3,551,860 adults with asthma in the DRC, 6.9% of the adult population in 2019.[9,54] According to the only African study on allergic bronchopulmonary aspergillosis (ABPA) from South Africa, we estimated that 2.5% (88,800 people) of these asthmatics developed ABPA.[30] Severe asthma with fungal sensitisation (SAFS) prevalence is estimated at 117,211 adults.[27] The incidence of TB in the DRC in 2019 was 278,000 with 233,520 with pulmonary disease. Only 30,000 people developed TB with HIV. Given a 12.8% mortality, there were 180,920 PTB.[16] After pulmonary TB, we estimate a prevalence of chronic pulmonary aspergillosis (CPA) over five years of 36,500 people (a rate of 38.3 per 100 000) and annual incidence was 11,579 (a rate of 12.1 per 100 000). Assuming that pulmonary TB comprises 67% of the cases, the total prevalence estimate for CPA is 54,700. To estimate invasive aspergillosis (IA), we started with a likely annual incidence of 380 (22%) acute myeloid leukaemia (AML) patients per year of a total of 1723 leukaemia excluding myelodysplastic syndrome.[17] In this group of patients 76 IA patients are a conservative estimate.[26,55] Globocan estimate 1811 lung cancer cases in the DRC,[12] of which a 2.6% are thought to develop IA (47 patients). No transplant programmes (solid organ and haematopoietic cell) are ongoing in the country. We also estimated that 4% of the 9,600 HIV deaths are linked to IA, a total of 380 patients. For chronic obstructive pulmonary disease (COPD) there are 193,007 admissions to hospital per year (10.5% of the total COPD population) and 1.3% develop IA, a total of 2,510 patients.[56] Overall, IA annual incidence is estimated at 3.2 per 100 000 (3016 people). Mucormycosis was estimated 0.2 per 100,000 patients. So, 190 people were affected.

3.2.5 | Other fungal diseases and immunocompromised status

Fungal keratitis was not recorded in any publication. However corneal disease and opacities are relatively frequent, some due to parasites such as in onchocerciasis. In one study of 750 people in an area hyperendemic for onchocerciasis, visual loss was found in 8.5%, of which 2.2% had monocular blindness with a corneal scar found in nearly 10% of patients.[57] Many of these cases are likely to be due to unrecognised fungal keratitis. We have estimated an annual incidence of 13/100,000 from data from other parts of Africa and 12,678 people are affected.[58] There is no nationwide registry of surgeries but 75 abdominal surgeries annually were reported in a local university hospital in Southeastern DRC.[59]

4 | DISCUSSION

This study is the first to comprehensively estimate the burden of fungal diseases in the DRC. Our burden estimate of 5,177,427 people affected by serious fungal disease (>5.5% of the population) indicates significant morbidity and probably mortality in the DRC.

Extended on both sides of the Equator, the DRC has four microclimates, including a hot and humid equatorial climate in the centre, a tropical climate in the South and North, an oceanic climate at the mouth of the Congo River and a temperate climate in the east. Rainfall varies from 800 mm on the shores of Lake Tanganyika to over 2,500 mm in the mountainous regions west of Lake Kivu. The hydrographic network is dense, with a large river running through the whole country. Surface water resources (river, streams and lakes) represent 52% of the continent's reserves, covering 86,080 Km^2 or 3.8% of the country's surface area. Most of the lakes are in the East: Tanganyika, Kivu, Albert, Moero and Edouard and Upemba (in the middle of Katanga).[3] This climate is conducive to the sustainability of several endemic diseases: Malaria, enteric diseases, TB, cholera and a diverse population of mostly unknown and undiagnosed endemic and opportunistic fungal pathogens.[42] Fungal infections are frequent opportunists in HIV infection and observed clinically in the DRC.[60] The most common are oral and oesophageal candidiasis, PCP, cryptococcal meningoencephalitis and histoplasmosis. In addition, TB is the most common predisposing factor for the development of CPA. The clinical presentation of PCP, histoplasmosis and CPA is similar to TB and often mistaken. Among those who die, there is currently no indication of any fungal aetiologies, because it is not looked for and autopsy is rarely done.[15]

From 2016, current policy is to "test and treat" HIV care in order to achieve the 90-90-90 targets, reducing transmission and progression to advanced HIV disease and death. These targets were to ensure that by 2020, 90% of people living with HIV know their HIV status, 90% of these people are on antiretroviral treatment (ART) and 90% of people on ART have an undetectable viral load. In 2020, all these targets are missed.[61,62]

Oesophageal candidiasis is common with HIV and was frequently reported with oral candidiasis. Our estimates place it as the most common opportunistic infectious disease in HIV after oral candidiasis, but we have not estimated the prevalence of cutaneous dermatophyte infections which are also common in HIV. The prevalence of HIV-associated esophageal candidiasis in sub-Saharan Africa was 12%, with a range from 1% to 52% across individual studies.[41] However, oesophageal candidiasis can also be diagnosed in otherwise healthy people such as those receiving antibiotic therapy which promotes the overgrowth of *Candida*.[63]

Pneumonia is one of the leading causes of mortality and morbidity in children under five years. In low and middle-income countries, poverty, poor living conditions, inadequate health services, malnutrition and HIV are the risk factors for pneumonia. The risk of death is highest in HIV-infected children with pneumonia in Sub-Saharan Africa.[7] In the DRC, lethality is estimated at 4.9% without distinction of aetiologies.[64] PCP occurs in children and other immunocompromised persons and is a common cause of severe pneumonia in HIV children. *Pneumocystis jirovecii*, which causes PCP, was classified as a protozoan, but now is identified as a fungus. Rates of 3.6 to 11% were described for Tanzania, Congo and Ivory Coast in the first decade of the AIDS epidemic.[65-67] PCP remains the most important AIDS opportunistic infection in the developed countries; by contrast

tuberculosis is the most frequent in sub-Saharan Africa countries. The incidence of PCP among 18 sub-Saharan African countries was 15.4%.[68] We have estimated a conservative incidence of 595 children with PCP and HIV infection, which is almost certainly an underestimate given 5,000 paediatric HIV deaths in 2019. Our estimate of only 2,804 adult cases of PCP is also conservative, given 9,600 AIDS deaths and only a 70% response rate for PCP in Africa,[69] if treated. Trimethoprim-sulfamethoxazole (TMP-SMX) resistance has emerged and leads to treatment failure increasing death.[70] The case fatality ranges from 10% to 27% in sub-Saharan Africa countries.[71]

Cryptococcal meningitis is a common problem in advanced HIV disease in the DRC, with an 11% incidence documented. This translates into over 6000 cases annually, a similar figure to a 2017 global and national estimate.[72] With only India ink available for diagnosis (~80% sensitivity) [73] and fluconazole available for therapy,[74] at least 80% of these patients will die currently.

Disseminated histoplasmosis has been described in the Cameroon caused by both species of *Histoplasma*. The prevalence of histoplasmosis in advanced HIV infection in Cameroon is 13% and is documented more in HIV positive patients than negative patients.[20] Histoplasmosis was previously reported sporadically in the DRC.[75] Based on these limited data, we have assumed a 1.5% annual rate of disseminated histoplasmosis in the DRC in advanced HIV disease. This needs confirmation with antigen (or PCR) diagnosis.

The CPA spectrum includes aspergilloma, chronic cavitary pulmonary aspergillosis and chronic fibrosing pulmonary aspergillosis. The literature notes some of the highest burdens of CPA after TB in some African countries. Ahead is Nigeria (120,747) followed by Uganda (18,000), Kenya (12,927) and Tanzania (10,437).[33] As pulmonary TB is relatively common in the DRC, we estimate an annual incidence in cured TB patients of over 11,000 patients, and a 5 year period prevalence of ~36,500 patients. Without *Aspergillus* IgG antibody detection, most will go undiagnosed and so inappropriately treated with antibiotics and anti-TB therapy, but not antifungal therapy. The mortality of CPA in Africa has been well described, but in other countries is 50%-80% over 5 years in non-HIV patients.[76]

ABPA is an uncommon complication of asthma or cystic fibrosis usually caused by *Aspergillus fumigatus*. The estimated prevalence derives from South Africa. In Africa, the highest burden is found in Algeria (310,310) followed by Nigeria (93,649), Tanzania (18,987), Uganda (18,700), Kenya (17,696) and Senegal (9976).[33]

Severe asthma has a heterogeneous nature. Depending on the definition used, 5% to 15% of all patients with asthma are classified as severe and a large proportion have poorly controlled disease. The mortality due to asthma in Africa was 0.7% in 2017.[32] In Africa, the diagnosis of asthma is still a challenging issue. No African country has registered yet with the International Severe Asthma Registry. Data about severe asthma deaths are scarce.[77,78] SAFS is uncertain as this disease has been recently described, it was conservatively estimated that 30% of patients with severe asthma have or develop SAFS in the world. In Africa the highest burden was described in Egypt (176,661) and the lowest is Kenya (23,359).[33] Antifungal therapy for SAFS is effective and mostly affordable in Africa, unlike many of the new monoclonal agents used in Europe and the USA.[79]

Tinea capitis is a public health problem caused by the dermatophytes *Epidermophyton*, *Microsporum* and *Trichophyton* spp. Without a recent review of dermatophytes in DRC, studies from other countries have been used to estimate the prevalence in school-age children. Biguet's study in 1943 demonstrated that the prevalence varied from one region to another in the DRC.[43] Bongomin made the same observation in Tanzania where this pathology had a correlation with socio-economic conditions and in Rwanda it was demonstrated that different species of dermatophytes predominated in different regions.[41] In a large epidemiological study involving 15,000 people, *M langeronii* (renamed *M audouinii*) (41.8%) and *T violaceum* (32.3%) have been reported as the main causative agents of tinea capitis in Congo, Rwanda and Burundi.[41]

No recent report of fungal NTDs diseases has been published in the DRC. Some cases were reported decades ago. The lack of epidemiological data does not exclude their presence in the DRC. A systematic review of blastomycosis from 25 African countries and 5 from middle eastern countries reported a total of 172 cases with only one isolate from the DRC.[80]

No data on fungal keratitis are published from the DRC, but diagnosis with routine eye examination including visual acuity testing, slit-lamp biomicroscopy and direct ophthalmoscopy can all contribute. The key tests include corneal scraping with direct microscopy and fungal culture. Adequate microbiology laboratories are only present in tertiary hospitals, some private hospitals and GRH's (Table 4). Clinical features alone may be suggestive of a fungal aetiology of corneal ulcer, but are not perfect.[81,82]

The WHO recommended Essential in vitro Diagnostics list now includes rapid tests for *Histoplasma* antigen, *Crypotococcus* antigen, *Aspergillus* antigen, *Aspergillus* antibody and *Pneumocystis* PCR, the latter three tests being added in 2021.[84] Without access to these diagnostics, patients suffering from serious fungal infections nearly always die. A recent survey of WHO EDL in DRC revealed that only four of the recommended nine diagnostic modalities for fungal disease are available in the DRC and of those that do exist, availability and penetration are variable across the country. None of the newer recommended rapid tests are present in the country outside of the limited confines of small scale research studies. Vulnerable patients are underserved in this regard and this invariably leads to a high level of preventable mortality for a significant proportion of the population. Of the WHO recommended antifungal drugs that are critical for providing optimal treatment for fungal disease, only 30% of the required minimum set of antifungal medication is available in the DRC. For HIV patients, flucytosine and amphotericin B when used in combination with each other and coupled with an accurate diagnosis of cryptococcal meningitis and therapeutic interventions increase survival chances of the estimated 6,170 HIV patients with cryptococcal meningitis by up to 70% [74] Neither flucytosine or amphotericin B are available in DRC. For TB patients, itraconazole and

TABLE 4 Essential diagnostics and antifungal agents in Democratic Republic of Congo

WHO recommended Essential in vitro Diagnostics	WHO recommended Essential antifungal Medicines
Available	**Available**
Direct microscopy	Fluconazole
Blood culture [a]	Griseofulvin
Histopathology	Nystatin
Fungal culture [a, b]	Ketoconazole (withdrawn internationally) [83]
Unavailable	**Unavailable**
Histoplasma antigen	Amphotericin B
Aspergillus antigen	Itraconazole
Aspergillus antibody	Voriconazole
Pneumocystis PCR Cryptococcal antigen (CrAg)	Flucytosine
	Natamycin eye drops
	Capsofungin
	Micafungin
	Anidulafungin

Abbreviations: PCR, Polymerase chain reaction; WHO, World Health Organization.

its alternative, voriconazole are essential antifungal drugs currently unavailable in the DRC which, if made available, could treat an estimated 54,745 people currently living with the debilitating effects of invasive or chronic aspergillosis, and many more with fungal asthma. Natamycin, an effective treatment usually available in high-income countries could contribute significantly to saving the eyesight of 12,680 people who are at risk of blindness due to undiagnosed fungal keratitis. Without significant redress, the high numbers of people dying or living with a severely impaired quality of life from fungal disease in DRC will remain and with emerging threats such as antifungal resistance, and the rise of non-communicable diseases, could be set to increase. Efforts should be made to ensure the provision of access to essential diagnostics and treatment, underpinned by increased surveillance, research and capacity building of health professionals. The implementation of dedicated programmes to integrate fungal disease care pathways into the health system must be prioritised by public health authorities and donors.

CONFLICT OF INTEREST

No COI for the authors.

AUTHOR CONTRIBUTIONS

Guyguy Kamwiziku: Investigation (equal); Methodology (supporting); Writing-original draft (lead). **Jean Claude Makangara:** Methodology (supporting); Writing-original draft (supporting). **Emma Orefuwa:** Investigation (equal); Writing-original draft (supporting). **David Denning:** Conceptualization (lead); Methodology (lead); Writing-review & editing (lead).

ORCID

Guyguy K. Kamwiziku https://orcid.org/0000-0001-6770-3999
Jean-Claude C. Makangara https://orcid.org/0000-0002-1791-2247
David W. Denning https://orcid.org/0000-0001-5626-2251

REFERENCES

1. Deuxième enquête démographique et de santé (EDS-RDC II 2013-2014) - Democratic Republic of the Congo. ReliefWeb. Accessed January 10, 2021. https://reliefweb.int/report/democratic-republic-congo/deuxi-me-enqu-te-d-mographique-et-de-sant-eds-rdc-ii-2013-2014
2. République démocratique du Congo • Fiche pays • PopulationData.net. Accessed February 20, 2021. https://www.populationdata.net/pays/republique-democratique-du-congo/
3. Mise en œuvre du PNDS 2016-2020 de la République Démocratique du Congo : tenue à Kinshasa de la revue annuelle 2016 du secteur de la santé avec l'appui de l'OMS et du Groupe inter bailleurs de la Santé (GIBS). Regional Office for Africa. Accessed January 10, 2021. https://www.afro.who.int/fr/news/mise-en-oeuvre-du-pnds-2016-2020-de-la-republique-democratique-du-congo-tenue-kinshasa-de-la
4. rdc-css-2017-2021.pdf. Accessed January 10, 2021. https://www.who.int/emergencies/crises/cod/rdc-css-2017-2021.pdf?ua=1%20Accessed%20December%2019th%202020
5. UCOP-Observatoire-_-Rapport-annuel-2019.pdf. Accessed January 10, 2021. https://www.ucopplus.org/media/2019/05/UCOP-Observatoire-_-Rapport-annuel-2019.pdf
6. IDSR-Technical -Guidelines-2010_French _final.pdf. Accessed January 10, 2021. https://www.afro.who.int/sites/default/files/2017-06/IDSR-Technical%20-Guidelines-2010_French%20_final.pdf
7. Frigati L, Archary M, Rabie H, Penazzato M, Ford N. Priorities for Decreasing Morbidity and Mortality in Children With Advanced HIV Disease. *Clin Infect Dis*. 2018;66(suppl_2):S147-S151. https://doi.org/10.1093/cid/ciy013
8. Haas AD, Radin E, Hakim AJ, et al. Prevalence of nonsuppressed viral load and associated factors among HIV-positive adults receiving antiretroviral therapy in Eswatini, Lesotho, Malawi, Zambia and Zimbabwe (2015 to 2017): results from population-based nationally representative surveys. *J Int AIDS Soc*. 2020;23(11):e25631. https://doi.org/10.1002/jia2.25631
9. Obel KB, Ntumba KJM, Kalambayi KP, Zalagile AP, Kinkodi KD, Munogolo KZ. Prevalence and determinants of asthma in adults in Kinshasa. *PLoS One*. 2017;12(5):e0176875. https://doi.org/10.1371/journal.pone.0176875
10. Musafiri S, van Meerbeeck J, Musango L, et al. Prevalence of atopy, asthma and COPD in an urban and a rural area of an African country. *Respir Med*. 2011;105(11):1596-1605. https://doi.org/10.1016/j.rmed.2011.06.013
11. Polatli M, Ben Kheder A, Wali S, et al. Chronic obstructive pulmonary disease and associated healthcare resource consumption in the Middle East and North Africa: The BREATHE study. *Respir Med*. 2012;106:S75-S85. https://doi.org/10.1016/S0954-6111(12)70016-1
12. 900-world-fact-sheets.pdf. Accessed January 10, 2021. https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf
13. WHO Expert Committee on specifications for pharmaceutical preparations. *Rev Inst Med Trop São Paulo*. 2008;50(3):144. https://doi.org/10.1590/S0036-46652008000300013
14. Murhula Kashongwe I, Mawete F, Anshambi N, et al. Challenge to treat pre-extensively drug-resistant tuberculosis in a

low-income country: A report of 12 cases. *J Clin Tuberc Mycobact Dis*. 2020;21:100192. https://doi.org/10.1016/j.jctube.2020.100192
15. UNAIDS data 2019 | UNAIDS. Accessed January 10, 2021. https://www.unaids.org/en/resources/documents/2019/2019-UNAIDS-data
16. Organisation mondiale de la santé. *Global Tuberculosis Report 2019*. World health organization; 2019.
17. Nkanga MSN, Longo-Mbenza B, Vandenberghe P, et al. Feasibility of iFISH patterns in hematologic malignancies among Congolese patients at Kinshasa University clinics. *Asian Pac J Trop Biomed*. 2017;7(12):1116-1119. https://doi.org/10.1016/j.apjtb.2017.10.014
18. Desmet P, Kayembe KD, Vroey CD. The value of cryptococcal serum antigen screening among HIV-positive/AIDS patients in Kinshasa, Zaire. *Aids*. 1989;3(2):77-78. https://doi.org/10.1097/00002030-198902000-00004
19. GAFFI-annual-report-2017.pdf. Accessed January 10, 2021. https://www.gaffi.org/wp-content/uploads/GAFFI-annual-report-2017.pdf
20. Mandengue C, Denning D. The burden of serious fungal infections in Cameroon. *J Fungi*. 2018;4(2):44. https://doi.org/10.3390/jof4020044
21. Oladele EA, Badejo OA, Obanubi C, et al. Bridging the HIV treatment gap in Nigeria: examining community antiretroviral treatment models. *J Int AIDS Soc*. 2018;21(4):e25108. https://doi.org/10.1002/jia2.25108
22. Chen LS, Bose P, Cruz ND, et al. A pilot study of lower doses of ibrutinib in patients with chronic lymphocytic leukemia. *Blood*. 2018;132(21):2249-2259. https://doi.org/10.1182/blood-2018-06-860593
23. Antinori S, Nebuloni M, Magni C, et al. Trends in the postmortem diagnosis of opportunistic invasive fungal infections in patients with AIDS: a retrospective study of 1,630 autopsies performed between 1984 and 2002. *Am J Clin Pathol*. 2009;132(2):221-227. https://doi.org/10.1309/AJCPRAAE8LZ7DTNE
24. Guinea J, Torres-Narbona M, Gijón P, et al. Pulmonary aspergillosis in patients with chronic obstructive pulmonary disease: incidence, risk factors, and outcome. *Clin Microbiol Infect*. 2010;16(7):870-877. https://doi.org/10.1111/j.1469-0691.2009.03015.x
25. Yan X, Li M, Jiang M, Zou L, Luo F, Jiang Y. Clinical characteristics of 45 patients with invasive pulmonary aspergillosis: Retrospective analysis of 1711 lung cancer cases. *Cancer*. 2009;115(21):5018-5025. https://doi.org/10.1002/cncr.24559
26. Lortholary O, Gangneux J-P, Sitbon K, et al. Epidemiological trends in invasive aspergillosis in France: the SAIF network (2005–2007). *Clin Microbiol Infect*. 2011;17(12):1882-1889. https://doi.org/10.1111/j.1469-0691.2011.03548.x
27. Denning DW, Pleuvry A, Cole DC. Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. *Med Mycol*. 2013;51(4):361-370. https://doi.org/10.3109/13693786.2012.738312
28. Smith NL, Denning DW. Underlying conditions in chronic pulmonary aspergillosis including simple aspergilloma. *Eur Respir J*. 2011;37(4):865-872. https://doi.org/10.1183/09031936.00054810
29. Page ID, Byanyima R, Hosmane S, et al. Chronic pulmonary aspergillosis commonly complicates treated pulmonary tuberculosis with residual cavitation. *Eur Respir J*. 2019;53(3):1801184. https://doi.org/10.1183/13993003.01184-2018
30. Benatar SR, Keen GA, Naude WDT. Aspergillus hypersensitivity in asthmatics in Cape Town. *Clin Htmlent Glyphamp Asciiamp Exp Allergy*. 1980;10(3):285-291. https://doi.org/10.1111/j.1365-2222.1980.tb02109.x
31. Denning D, Pleuvry A, Cole D. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bull World Health Organ*. 2011;89(12):864-872. https://doi.org/10.2471/BLT.11.089441
32. Kwizera R, Musaazi J, Meya DB, et al. Burden of fungal asthma in Africa: A systematic review and meta-analysis. Barac A, ed. *PLoS One*. 2019;14(5):e0216568. https://doi.org/10.1371/journal.pone.0216568
33. Bongomin F, Gago S, Oladele R, Denning D. Global and multinational prevalence of fungal diseases—estimate precision. *J Fungi*. 2017;3(4):57. https://doi.org/10.3390/jof3040057
34. Montravers P, Boudinet S, Houissa H. Candida and severe acute pancreatitis: We won't be fooled again. *Crit Care*. 2013;17(3):137. https://doi.org/10.1186/cc12613
35. Low A, Gavriilidis G, Larke N, et al. Incidence of opportunistic infections and the impact of antiretroviral therapy among hiv-infected adults in low- and middle-income countries: a systematic review and meta-analysis. *Clin Infect Dis*. 2016;62(12):1595-1603. https://doi.org/10.1093/cid/ciw125
36. Mushi MF. Oral candidiasis among African human immunodeficiency virus-infected individuals: 10 years of systematic review and meta-analysis from sub-Saharan Africa. *J Oral Microbiol*. 10.
37. Smith E, Orholm M. Trends and patterns of opportunistic diseases in Danish AIDS patients 1980–1990. *Scand J Infect Dis*. 1990;22(6):665-672. https://doi.org/10.3109/00365549009027119
38. Buchacz K, Baker RK, Young B, Brooks JT. Changes in the Use of HIV Antiretroviral Resistance Testing in a Large Cohort of U.S. Patients, 1999 to 2006. *JAIDS*. 2010;53(5):625-632. https://doi.org/10.1097/QAI.0b013e3181bf1dd2
39. Denning DW, Kneale M, Sobel JD, Rautemaa-Richardson R. Global burden of recurrent vulvovaginal candidiasis: a systematic review. *Lancet Infect Dis*. 2018;18(11):e339-e347. https://doi.org/10.1016/S1473-3099(18)30103-8
40. Prakash H, Chakrabarti A. Global Epidemiology of Mucormycosis. *J Fungi*. 2019;5(1):26. https://doi.org/10.3390/jof5010026
41. Bongomin F, Olum R, Nsenga L, Baluku JB. Burden of tinea capitis among children in Africa: protocol for a systematic review and meta-analysis of observational studies, 1990–2020. *BMJ Open*. 2020;10(9):e041230. https://doi.org/10.1136/bmjopen-2020-041230
42. Nweze EI, Eke IE. Dermatophytes and dermatophytosis in the eastern and southern parts of Africa. *Med Mycol*. 2018;56(1):13-28. https://doi.org/10.1093/mmy/myx025
43. Biguet J, Deblock S, Cochet G, Ouadraogo P. Première contribution à l'étude des Teignes en Haute Volta. Revue des dermatophyties et des Dermatophytes en Afrique noire. *Ann Parasitol Hum Comparée*. 1959;34(5–6):694-727. https://doi.org/10.1051/parasite/1959345694
44. 1956asbm0479.pdf. Accessed January 10, 2021. http://lib.itg.be/open/asbmt/1956/1956asbm0479.pdf
45. Chromoblastomycosis - PubMed. Accessed February 20, 2021. https://pubmed.ncbi.nlm.nih.gov/25395928/
46. Callens SFJ, Kitetele F, Lelo P, et al. Pulmonary cystic disease in HIV positive individuals in the Democratic Republic of Congo: three case reports. *J Med Case Reports*. 2007;1(1):101. https://doi.org/10.1186/1752-1947-1-101
47. Kengne M, Shu SV, Nwobegahay JM, Achonduh O. Antifungals susceptibility pattern of *Candida spp*. isolated from female genital tract at the Yaoundé Bethesda Hospital in Cameroon. *Pan Afr Med J*. 2017;28: https://doi.org/10.11604/pamj.2017.28.294.11200
48. Arendrup MC. Epidemiology of invasive candidiasis. *Curr Opin Crit Care*. 2010;16(5):445-452. https://doi.org/10.1097/MCC.0b013e32833e84d2
49. Montravers P, Mira J-P, Gangneux J-P, Leroy O, Lortholary O. A multicentre study of antifungal strategies and outcome of Candida spp. peritonitis in intensive-care units. *Clin Microbiol Infect*. 2011;17(7):1061-1067. https://doi.org/10.1111/j.1469-0691.2010.03360.x
50. Matee M, Scheutz F, Moshy J. Occurrence of oral lesions in relation to clinical and immunological status among HIV-infected adult

Tanzanians. *Oral Dis*. 2008;6(2):106-111. https://doi.org/10.1111/j.1601-0825.2000.tb00110.x
51. Colebunders R, Lusakumuni K, Nelson AM, et al. Persistent diarrhoea in Zairian AIDS patients: an endoscopic and histological study. *Gut*. 1988;29(12):1687-1691. https://doi.org/10.1136/gut.29.12.1687
52. J. KM, S. M, D. BM, T. MK. HIV screening among patients followed for cryptococcal meningitis in developing countries: Data from Bukavu in the Democratic Republic of Congo. *Afr J Microbiol Res*. 2014;8(7):721-723. https://doi.org/10.5897/AJMR2013.5420
53. Carme B, Hayette MP, Ngaporo AI, et al. Histoplasmose Africaine à histoplasma duboisii (Histoplasma capsulatum var. Duboisii): quatorze cas congolais observés en 10 Ans (1981-1990):7.
54. To T, Stanojevic S, Moores G, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health*. 2012;12(1):204. https://doi.org/10.1186/1471-2458-12-204
55. Perkhofer S, Lass-Flörl C, Hell M, et al. The Nationwide Austrian Aspergillus Registry: a prospective data collection on epidemiology, therapy and outcome of invasive mould infections in immunocompromised and/or immunosuppressed patients. *Int J Antimicrob Agents*. 2010;36(6):531-536. https://doi.org/10.1016/j.ijantimicag.2010.08.010
56. Hammond EE, McDonald CS, Vestbo J, Denning DW. The global impact of Aspergillus infection on COPD. *BMC Pulm Med*. 2020;20(1):241. https://doi.org/10.1186/s12890-020-01259-8
57. Kayembe DL, Kasonga DL, Kayembe PK, Mwanza J-CK, Boussinesq M. Profile of eye lesions and vision loss: a cross-sectional study in Lusambo, a forest-savanna area hyperendemic for onchocerciasis in the Democratic Republic of Congo. *Trop Med Int Health*. 2003;8(1):83-89. https://doi.org/10.1046/j.1365-3156.2003.00957.x
58. Brown L, Burton MJ, Gichangi M, Denning D. The global incidence of fungal keratitis. *SSRN Electron J Published online*. 2019. https://doi.org/10.2139/ssrn.3466994
59. Kalau WA, Dinganga N, Ngoie E, Odimba E, Detry O. First steps of laparoscopic surgery in Lubumbashi: problems encountered and preliminary results. *Pan Afr Med J*. 2015;21. https://doi.org/10.11604/pamj.2015.21.210.6689
60. Amona FM, Denning DW, Moukassa D, Hennequin C. Current burden of serious fungal infections in Republic of Congo. *Mycoses*. 2020;63(6):543-552. https://doi.org/10.1111/myc.13075
61. Sidibé M, Loures L, Samb B. The UNAIDS 90–90-90 target: a clear choice for ending AIDS and for sustainable health and development. *J Int AIDS Soc*. 2016;19(1):21133. https://doi.org/10.7448/IAS.19.1.21133
62. 2020 Global AIDS Update — Seizing the moment — Tackling entrenched inequalities to end epidemics. Published online 2020:384.
63. Choi JH, Lee CG, Lim YJ, Kang HW, Lim CY, Choi J-S. Prevalence and risk factors of esophageal Candidiasis in healthy individuals: a single center experience in Korea. *Yonsei Med J*. 2013;54(1):160. https://doi.org/10.3349/ymj.2013.54.1.160
64. Birindwa AM, Manegabe JT, Mindja A, Nordén R, Andersson R, Skovbjerg S. Decreased number of hospitalized children with severe acute lower respiratory infection after introduction of the pneumococcal conjugate vaccine in the Eastern Democratic Republic of the Congo. *Pan Afr Med J*. 2020;37:211. https://doi.org/10.11604/pamj.2020.37.211.22589
65. Dhingra D, Mandal A, Singh A. Pneumocystis jirovecii Pneumonia in Children. *J Pediatr Infect Dis*. 2018;13(01):002-009. https://doi.org/10.1055/s-0037-1604337
66. De Armas RY, Wissmann G, Müller AL, et al. *Pneumocystis jirovecii* pneumonia in developing countries. *Parasite*. 2011;18(3):219-228. https://doi.org/10.1051/parasite/2011183219
67. Theodoratou E, Al-Jilaihawi S, Woodward F, et al. The effect of case management on childhood pneumonia mortality in developing countries. *Int J Epidemiol*. 2010;39(suppl_1):i155-i171. https://doi.org/10.1093/ije/dyq032
68. (PDF) Burden of pneumocystis pneumonia in HIV-infected adults in sub-Saharan Africa: A systematic review and meta-analysis. Accessed January 28, 2021. https://www.researchgate.net/publication/307978597_Burden_of_pneumocystis_pneumonia_in_HIV-infected_adults_in_sub-Saharan_Africa_A_systematic_review_and_meta-analysis
69. Lowe DM, Rangaka MX, Gordon F, James CD, Miller RF. Pneumocystis jirovecii Pneumonia in Tropical and Low and Middle Income Countries: A Systematic Review and Meta-Regression. Vermund SH, ed. *PLoS One*. 2013;8(8):e69969. https://doi.org/10.1371/journal.pone.0069969
70. Morris A, Lundgren JD, Masur H, et al. Current epidemiology of *Pneumocystis* pneumonia. *Emerg Infect Dis*. 2004;10(10):1713-1720. https://doi.org/10.3201/eid1010.030985
71. Fisk DT, Meshnick S, Kazanjian PH *Pneumocystis carinii* Pneumonia in Patients in the Developing World Who Have Acquired Immunodeficiency Syndrome. *Clin Infect Dis*. 2003;36(1):70-78. https://doi.org/10.1086/344951
72. Rajasingham R, Smith RM, Park BJ, et al. Global burden of disease of HIV-associated cryptococcal meningitis: an updated analysis. *Lancet Infect Dis*. 2017;17(8):873-881. https://doi.org/10.1016/S1473-3099(17)30243-8
73. Tang MW, Clemons KV, Katzenstein DA, Stevens DA. The cryptococcal antigen lateral flow assay: A point-of-care diagnostic at an opportune time. *Crit Rev Microbiol*. 2016;42(4):634-642. https://doi.org/10.3109/1040841X.2014.982509
74. Shroufi A, Chiller T, Jordan A, et al. Ending deaths from HIV-related cryptococcal meningitis by 2030. *Lancet Infect Dis*. 2021;21(1):16-18. https://doi.org/10.1016/S1473-3099(20)30909-9
75. Pakasa N, Biber A, Nsiangana S, et al. African Histoplasmosis in HIV-Negative Patients, Kimpese, Democratic Republic of the Congo. *Emerg Infect Dis*. 2018;24(11):2068-2070. https://doi.org/10.3201/eid2411.180236
76. Lowes D, Al-Shair K, Newton PJ, et al. Predictors of mortality in chronic pulmonary aspergillosis. *Eur Respir J*. 2017;49(2):1601062. https://doi.org/10.1183/13993003.01062-2016
77. FitzGerald JM, Tran TN, Alacqua M, et al. International severe asthma registry (ISAR): protocol for a global registry. *BMC Med Res Methodol*. 2020;20(1):212. https://doi.org/10.1186/s12874-020-01065-0
78. Adeloye D, Chan KY, Rudan I, Campbell H. An estimate of asthma prevalence in Africa: a systematic analysis. *Croat Med J*. 2013;54(6):519-531. https://doi.org/10.3325/cmj.2013.54.519
79. Rapeport WG, Ito K, Denning DW. The role of antifungals in the management of patients with severe asthma. *Clin Transl Allergy*. 2020;10(1):46. https://doi.org/10.1186/s13601-020-00353-8
80. Schwartz IS, Muñoz JF, Kenyon CR, et al. Blastomycosis in Africa and the Middle East: A Comprehensive Review of Reported Cases and Reanalysis of Historical Isolates Based on Molecular Data. *Clin Infect Dis*. 2020:ciaa1100. https://doi.org/10.1093/cid/ciaa1100
81. Mwanza J-CK, Kayembe DL. Uveitis in HIV-Infected Patients. *Eur J Ophthalmol*. 2001;11(1):53-56. https://doi.org/10.1177/112067210101100110
82. Thomas PA, Kaliamurthy J. Mycotic keratitis: epidemiology, diagnosis and management. *Clin Microbiol Infect*. 2013;19(3):210-220. https://doi.org/10.1111/1469-0691.12126
83. Répertoire des produits pharmaceutiques enregistrés et autorisés par la DPM en RDC, Edition 2020 – Autorité Congolaise de Réglementation Pharmaceutique. Accessed February 20, 2021. https://www.acorep.gouv.cd/download/repertoire-des-produits-pharmaceutiques-enregistres-et-autorises-par-la-dpm-en-rdc-edition-2020/

84. WHO Technical Report Series, No. 1031,2021: The selection ad use of essential in vitro diagnostics TRS 1031: http://www.who.int/publications/item/9789240019102-RechercheGoogle. Accessed February 12, 2021. https://www.google.com/search?client=opera&q=WHO+Technical+Report+Series%2C+No.+1031%2C2021%3A+The+selection+ad+use+of+essential+in+vitro+diagnostics+TRS+1031%3A+http%3A%2F%2Fwww.who.int%2Fpublications%2Fitem%2F9789240019102&sourceid=opera&ie=UTF-8&oe=UTF-8

How to cite this article: Kamwiziku GK, Makangara J-CC, Orefuwa E, Denning DW. Serious fungal diseases in Democratic Republic of Congo – Incidence and prevalence estimates. *Mycoses*. 2021;00:1–11. https://doi.org/10.1111/myc.13339