


Burden of fungal infections in Kenya

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ABSTRACT

The burden of fungal infections has been on the rise globally and remains a significant public health concern in Kenya. We estimated the incidence and prevalence of fungal infections using all mycology publications in Kenya up to January 2023, and from neighbouring countries where data lacked. We used deterministic modelling using populations at risk to calculate the disease burden. The total burden of serious fungal infections is estimated to affect 6,328,294 persons which translates to 11.57% of the Kenyan population. Those suffering from chronic infections such as chronic pulmonary aspergillosis are estimated to be 100,570 people (0.2% of the population) and probably nearly 200,000 with fungal asthma, all treatable with oral antifungal therapy. Serious acute fungal infections secondary to HIV (cryptococcal meningitis, disseminated histoplasmosis, pneumocystis pneumonia, and mucosal candidiasis) affect 196,543 adults and children (0.4% of the total population), while cancer-related invasive fungal infection cases probably exceed 2,299 and those in intensive care about 1,230 incident cases, including *Candida auris* bloodstream infection. The burden of fungal infections in Kenya is high; however, limited diagnostic test availability, low clinician awareness and inadequate laboratory capacity constrain the country's health system in responding to the syndemic of fungal disease in Kenya.

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1. Introduction

The global burden of fungal infections is on the rise due to an increase in the number of people with associated risk factors such as HIV, cancer, and organ transplant as well as extremes of age (Maertens et al. 2001; Vallabhaneni et al. 2016). Fungal infections in Kenya are still a significant public health concern, thought to affect almost one in fifteen of the population at any point in time (Guto et al. 2016; Malwal et al. 2016). In order to prioritise healthcare, including training, provision of diagnostics and antifungal therapies, numerical estimates of disease burden are helpful.

The Kenyan population has also increased by an estimated 11 million people over the past decade (Commons 2022). This coupled with improved reporting rates for key health indicators, in tuberculosis and HIV, has led to a substantial increase in the population at risk of fungal infections (Samaranayake et al. 2002; Guarner 2017; Chepkondol et al. 2020; Ngugi et al. 2020). In 2016, it was estimated that about 7% of the Kenyan population was affected by a serious fungal infection, including

millions of children with tinea capitis (Guto et al. 2016). Since then, better fungal estimates and updated literature have been published.

The use of azole fungicides has in the recent past contributed to the thriving of triazole-resistant species of *Aspergillus fumigatus* species in some regions in Kenya (Kemoi et al. 2018). Hitherto, unreported cases of empyema necessitans due to *Aspergillus* are also being diagnosed in Kenya as well as reports of drug-resistant yeast infections (Brooks et al. 2019; Macharia et al. 2019). On the other hand, there is greater coverage of patients with HIV infection with antiretroviral therapy, although only modest progress on reducing tuberculosis mortality, which impacts the chronic pulmonary aspergillosis (CPA) caseload (Mohamed et al. 2022). Currently, about a dozen hospitals are offering kidney transplant services at a much-reduced cost compared to the cost of seeking such services abroad. The number of kidney transplants has therefore significantly increased with two of the dozen hospitals reporting about 400 transplants in the last decade (Ministry of Health Kenya

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2021; News 2021). These shifts in the demographics of the population and those at risk of fungal infections, ongoing gaps in diagnostic provision (GAFFI.org 2022) and new data propelled us into a thorough re-estimation of the incidence and prevalence of serious fungal infections in Kenya.

2. Materials and methods

Basic demographic data on the Kenya population was derived from Indexmundi.com (Mundi 2022) (Table 1). HIV data was taken from UNAIDS, and the assumption made that for those adults not on antiretroviral therapy (ART) it takes 7 years for the CD4 counts and

immunity to decline into the high-risk group. In children, it was assumed that all children were at risk, unless on ART. Furthermore, it was assumed that ART was failing in 12.3% of those on ART (Tsikhutsu et al. 2022). Pulmonary Tuberculosis (PTB) incidence was abstracted from the WHO 2020 annual report for Kenya (StopTB 2021). Asthma prevalence in adults was derived from a 2016 household survey (Turpin et al. 2019). Chronic obstructive pulmonary disease (COPD) was estimated from data from Rwanda, Tanzania, and Uganda, and admissions to hospital from Algeria (Hammond et al. 2020). Lung cancer and acute leukaemia were taken from the International Agency for Research in Cancer

Table 1. Demographics of Kenya, pertinent to fungal infections.

| Variable | Result | Source |
|-----------------------------------|---|---|
| Population characteristics | Total population: 54,685,051 Total Adult population: 33,357,881 Population under 15 years: 39% Annual population growth rate: 2.15% Population >60 years: 4% Percentage of females: 50% Number of children aged 5–14 years: 21,327,170 Proportion of population 15–55 years: 0.556 Number of women aged 15–55 years: 15,263,254 Total population of women aged 15–49: 13,355,347 | Mundi 2022 |
| Health status | Total number of functional health facilities: 9,064 Maternal mortality rate: 342 per 100,000 live births Infant mortality rate: 41.9 per 1000 live births Life expectancy at birth in 2021: 61.4 years Prevalence of underweight (Wt/Age) among children 6–59 months (2SD): 11% | Kenya Gazette Notice No 786; (Elephant 2022; UNICEF 2022a; UNDP 2022; UNICEF 2022b) |
| HIV | Total HIV/AIDS: 1,400,000 Children with HIV/AIDS: 86,000 Number of adults with HIV/AIDS: 1,314,000 of diagnosed cases not on ARVs: 14% Number of adults on ARVs: 1,160,570 Number of diagnosed adults not receiving ARVs: 153,430 Number of adult HIV patients with CD4 < 200/ μ l: 21,919 Percentage of adults with ARV failure: 11% Number of adult HIV patients at risk of OIs: 164,670 Number of children receiving ART: 69,390 Number of children at risk of OIs: 24,243 AIDS-related deaths: 19,000 Number of AIDS-related deaths in children: 3,100 | UNAIDS 2022 |
| TB | Total TB cases: 139,000 PTB annual incidence HIV+: 35,000 PTB annual incidence HIV-: 65,520 PTB annual incidence Total: 86,447 Pulmonary tuberculosis annual survivors: 73,480 | StopTB 2021 |
| Asthma, COPD, and Cystic Fibrosis | Asthma rate in adults: 10.00% Asthma number in adults: 3,335,788 COPD prevalence all GOLD stages: 7.8% COPD admissions to hospital per year: 388,665 (assumes 10.5% admissions per year) | Hammond et al. 2020 |
| Malignancies | Number of lung cancer deaths per 100,000 population: 729 Leukaemia rate per 100,000: 2.5 Leukaemia patients per year: 1,367 | IARC Kenya Factsheets (International Agency for Cancer on Research WHO 2022; Control UfIC 2014) |
| Transplant recipient | Allogenic haematologic stem cell transplant: 0 Renal transplants per year: 470 Liver transplants per year: 12 | IRODaT 2023 |

(International Agency for Cancer on Research WHO 2022) and acute myeloid leukaemia from a general WHO figure (Control UfIC 2014). Annual renal and hepatic transplant numbers were from 2019 (IRODaT 2023).

Searches for the incidence and prevalence of different fungal diseases were done. The following search terms were used, “Aspergillosis Kenya” “Candidiasis Kenya” “Pneumocystis Kenya” “Cryptococcus Kenya” “Histoplasmosis Kenya” “Mycetoma Kenya” “Chromoblastomycosis Kenya” “Sporotrichosis Kenya” “Tinea capitis Kenya”. The terms “incidence” and “prevalence” were used alongside the above terms. Where no data was found from Kenya, “Uganda”, “Sudan”, “Tanzania” and “Africa” were used. From these, and from existing papers in our libraries, we have estimated the proportion of people, with or without an underlying disease, who have a fungal disease. In many instances data was missing from Kenya, so nearby country estimates were used as proxy estimates, and if these were not available, then international data was used. All the assumptions and their sources for each fungal infection or disease are documented in Table 2.

Following this, calculations of annual incidence or prevalence were made using straightforward deterministic modeling using population(s) at risk (Table 2). These are estimated partly by underlying disease, where there well-established risk populations (i.e. advanced HIV disease) and by partly by individual fungal disease (i.e. fungal keratitis) on a population basis (Table 1). To use an example, 164,670 adults are at risk of a severe fungal infection (Table 1) and the point prevalence of cryptococcal antigenaemia is 6% to 7.5% (Table 2), so the annual incidence of cryptococcal disease (most with meningitis as there is very little screening) is 9,880 patients, using the lower percentage. The annual incidence of invasive aspergillosis (IA) comprised these underlying risk groups: acute myeloid leukaemia (AML) (13% risk) (Chen et al. 2020) plus an equal number for other moderate and high-risk haematological conditions (i.e. other leukaemia, multiple myeloma, and lymphoma), lung carcinoma (2.6%) (Yan et al. 2009), HIV deaths (4%) (Khoo SD 1994; Denning and Morgan 2022) and 1.3% of all those hospitalised (or severely ill) with a COPD exacerbation (Hammond et al. 2020) (Table 2). Chronic pulmonary aspergillosis (CPA) incidence and prevalence

Table 2. Key assumptions to allow modelling of fungal disease incidence and prevalence in Kenya.

| Fungal Infection | Underlying condition | Assumptions | Reference(s) |
|---|---------------------------------|---|--|
| Recurrent <i>Candida</i> vaginitis ($\geq 4 \times$ /year) | None | 6% females aged 15–49 | Denning et al. 2018 |
| Candidaemia | Cancer, surgery critical care | 5/100,000 (mean of 2–11/100,000), with 33% occurring in critical care | Bongomin et al. 2017 |
| Intraabdominal candidiasis | Abdominal surgery, pancreatitis | 50% of the incidence of candidaemia in critical care | Montravers et al. 2011 |
| Oesophageal candidiasis | HIV/AIDS | 20% of new HIV/AIDS adults and 0.5% of adults on ARVs | Smith and Orholm 1990; Buchacz et al. 2010 |
| Cryptococcal meningitis | HIV/AIDS | 7.5% positive CrAg positives, 6% in HIV/AIDS adults with CD4 < 200/uL | Kanji et al. 2011; Meyer et al. 2013 |
| <i>Pneumocystis</i> pneumonia | HIV/AIDS | 15% of newly diagnosed HIV adults, 16% of children with HIV/AIDS | Chakaya et al. 2003; Bii et al. 2006 |
| Disseminated histoplasmosis | HIV/AIDS | 4.7% of advanced HIV | Ocansey et al. 2022 |
| Invasive aspergillosis (IA) | HIV/AIDS, respiratory, cancer | 13% of AML develop IA and an equal number of non-AML haematological conditions. 2.6% of lung cancer patients and 1.3% of COPD annual admissions, and 2% of renal transplant recipients. | Chen et al. 2014; Yan et al. 2009; Hammond et al. 2020 |
| Chronic pulmonary aspergillosis (CPA) with a TB-like presentation | Respiratory | 19% of HIV- and 10% of HIV+ clinically diagnosed PTB, 7% of HIV- and 3% of HIV+ proven PB and 1.5% annual rate after PTB cure. | Oladele et al. 2017; Page et al. 2019; Denning et al. 2023 |
| Chronic pulmonary aspergillosis – all | Respiratory | Assumes 67% of cases occur during or after pulmonary TB | Smith and Denning 2011 |
| Allergic bronchopulmonary aspergillosis (ABPA) | Respiratory | 2.5% of adult asthmatics | Denning et al. 2013; Kwizera et al. 2020 |
| Severe asthma with fungal sensitisation (SAFS) | Respiratory | 3.3% adult asthmatics, all with severe asthma | Kwizera et al. 2021 |
| Mucormycosis | Diabetes, leukaemia, trauma | 0.2/100,000 | Sharma and Goel 2022 |
| Fungal keratitis | Eye injury | 13.3/100,000 | Brown et al. 2021 |
| Tinea capitis | None | 23% of children 0–14 years | Bongomin et al. 2021 |

were estimated from 2020 pulmonary tuberculosis (PTB) data. We also assume that PTB is the underlying cause of CPA in 80% of all CPA cases (Smith and Orholm 1990). For several fungal infections, notably the skin fungal Neglected Tropical Diseases (NTD), a realistic estimate or burden was not possible.

3. Results

3.1. Kenya demographic profile

The Kenyan population in 2021 was estimated to be approaching 55 million (Table 1). This represents an increase of about 11 million people over the course of a decade. The current annual population growth rate stood at 2.15% in 2021. The proportion of the population aged between 15 and 55 years was 39%. The Gross-Domestic-Product (GDP) per capita is \$4,200 (CIA 2022), making Kenya a Lower Middle-Income Country (LMIC) (World Bank 2023).

Kenya is also categorised as having medium development, ranking 152 out of 191 countries in the 2021–2022 United Nations Human Development Index (UNDP 2022). According to the World Bank, the poverty level in Kenya is currently at 34.4%; poverty indices in Kenya have reduced over time.

The health system in Kenya is composed of public and private health-care service providers whose total currently stands at 9,064 health facilities. The public health system in Kenya was devolved a decade ago and is now run by (regional) county governments. This has led to a more responsive healthcare administration that is closer to the people.

The maternal mortality rate in Kenya is 342 per 100,000 live-births (UNICEF 2022a), and the infant mortality rate is at 41.9 per 1000 live-births. The life expectancy at birth is currently 61.4 years, a ten-year improvement from two decades ago at the height of the HIV pandemic mortality in Kenya (Guto et al. 2016; UNDP 2022).

3.2. HIV-related fungal disease in Kenya

UNAIDS reports that 1,400,000 Kenyan adults and 86,000 children were living with HIV/AIDS in 2021. This number has remained nearly constant over the last 10 years. The number of adults on ARVs has in the same period more than doubled, from 548,588 in 2012 (Guto et al. 2016) to 1,160,570 in 2021. About

150,000 HIV-positive diagnosed adults are at risk of opportunistic infections, as are 24,243 children. AIDS-related deaths have reduced threefold over the last decade, from 57,000 in 2012 to 19,000 in 2021.

3.2.1. Cryptococcal meningitis

A recent global estimate put cryptococcal antigen (CrAg) prevalence for eastern and southern Africa at 3.7% (96% CI 3.6–3.8), with Kenya having a prevalence of about 7% (95% CI 5–10) (Rajasingham et al. 2022). Cryptococcal meningitis is rare in children with HIV, so only adults are included in the risk population. This yielded a total annual incidence of about 9,000 cases (Table 3). This estimate was informed by a 6% proportion of patients with CrAg positive with a CD4 < 200 (Kanji et al. 2011; Meyer et al. 2013).

3.2.2. Disseminated histoplasmosis

Histoplasmosis was recognised early as an AIDS-defining illness (Kalata et al. 2019) and has other underlying causes (Ekeng et al. 2021). We only found one case report of disseminated histoplasmosis (Macharia and Walong 2019). However, we assumed a 4.7% incidence in advanced HIV disease (based on data from Ghana) that yielded an estimation of 2,244 incident cases, possibly a conservative estimate, bearing in mind other underlying causes.

3.2.3. *Pneumocystis pneumonia* (PCP)

The prevalence of PCP in children was estimated to be 17%, from a study conducted on Kenyan children who died following severe respiratory infections (Mirza et al. 2018). The proportion of adults found to present with PCP and a CD4 count of less than 200 cells/mm³ was estimated at 16%. This translated to 17,000 incident cases and a rate of 43 per 100,000 persons (Bii et al. 2006). In the present study, we estimated a PCP annual incidence of 7.1 per 100,000 in children and 46.5 per 100,000 people in adults in Kenya (Table 3).

3.2.4. Mucosal candidiasis in those infected with HIV

We assumed an oral candidiasis attack rate of 90% of at-risk HIV patients over 2 years. This resulted in an incidence of 67,312 cases annually. To estimate oesophageal candidiasis, we assumed that adults affected comprise 20% of new HIV/AIDS patients and 0.5% of those HIV patients on ARVs (Table 2). This yielded an annual incidence of 87,945 cases. There is uncertainty

Table 3. Incidence and prevalence of serious fungal infections in Kenya.

| Infection | Incidence or prevalence | Number of infections per underlying disorders per year | | | | | Rate/ 100 K | Total burden |
|--|-------------------------|--|----------|-------------|--------|-------|-------------|--------------|
| | | None | HIV/AIDS | Respiratory | Cancer | ICU | | |
| PCP in adults | I | - | 25,429 | - | - | - | 46.5 | 25,429 |
| PCP in children | I | - | 3,879 | - | - | - | 7.1 | 3,879 |
| Cryptococcal meningitis | I | - | 8,975 | - | - | - | 16.4 | 8,975 |
| Histoplasmosis | I | - | 2,244 | - | - | - | 4.1 | 2,244 |
| Oesophageal candidiasis | I | - | 87,945 | - | - | - | 161 | 87,945 |
| Chronic pulmonary aspergillosis-Post TB | I | - | - | 17,738 | - | - | 32.4 | 17,738 |
| Chronic pulmonary aspergillosis-Post TB | P | - | - | 80,456 | - | - | 147 | 80,456 |
| Chronic pulmonary aspergillosis-all | P | - | - | 100,570 | - | - | 184 | 100,570 |
| Allergic bronchopulmonary aspergillosis (ABPA) | P | - | - | 83,395 | - | - | 153 | 83,395 |
| Severe asthma with fungal sensitisation (SAFS) | P | - | - | 110,081 | - | - | 201 | 110,081 |
| Candidaemia | I | - | - | - | 1,914 | 820 | 5.0 | 2,804 |
| Candida peritonitis | I | - | - | - | - | 410 | 0.8 | 410 |
| Oral candidiasis | I | - | 67,312 | - | - | - | 123 | 67,312 |
| Recurrent vaginal candidiasis (>4 times/year) | P | 915,795 | - | - | - | - | 3,349* | 915,795 |
| Tinea capitis | I | 4,905,249 | - | - | - | - | 8,970 | 4,905,249 |
| Fungal keratitis | I | 7,929 | - | - | - | - | 14.5 | 7,929 |
| Mycetoma | P | ND | - | - | - | - | - | - |
| Invasive aspergillosis | I | - | 760 | 5,053 | 385 | - | 11.33 | 6,198 |
| Mucormycosis | I | 109 | - | - | - | - | 0.20 | 109 |
| Total burden estimated | | 5,829,083 | 196,543 | 299,099 | 2,299 | 1,230 | | 6,328,294 |

Note: *females only
ND- No Data

about the frequency of oesophageal candidiasis in children.

3.3. Aspergillosis

Aspergillosis is a condition that affects individuals who have an underlying pulmonary disease and is highly prevalent in immunocompromised populations (Fosses Vuong and Waymack 2022). Tuberculosis (TB) prevalence in Kenya was found to be higher than previously estimated (Enos et al. 2018) where approximately half of those who contract the disease annually are missed. The PTB incidence in HIV was estimated to be 35,000. This represents about 40% of the annual PTB incidence in Kenya (Table 1) (UNAIDS 2022).

3.3.1. Chronic pulmonary aspergillosis

We estimated the incidence and prevalence of CPA from 2020 WHO pulmonary TB figures. Misdiagnosis of CPA as TB probably occurs in 5,490 HIV-negative and 1,842 HIV-positive people annually, with an additional 2,396 people presenting with dual infection with TB and CPA. An additional 8,424 patients who successfully complete anti-tuberculous therapy develop CPA during that therapy or in the few months following it. An additional 13,918 people develop CPA in the two to five years following TB

cure, with an overall annual incidence of 32,070. Some of these patients will die and so the five-year period prevalence is estimated at 88,015 patients, with an annual mortality related to CPA of 9,172. We have also assumed that 80% of CPA cases are linked to TB, leading to a total prevalence of >110,000 cases.

3.3.2. Invasive aspergillosis and mucormycosis

There is paucity of data on cancers and transplants in Kenya. Available sources have estimated the number of lung cancer deaths at 729 per 100,000 persons (International Agency for Cancer on Research WHO 2022). Approximately 1,367 new leukaemia patients are seen annually, with an annual incidence rate of 2.5/100,000. A total of 470 renal transplants and 12 liver transplants are done each year in Kenya. COPD prevalence for at GOLD stages 2–4 stood at 7.8%, or 3.7 million, of whom an estimated 388,665 are admitted to hospital or die at home (Hammond et al. 2020).

Mucormycosis is a rarely diagnosed condition in Kenya. We used a conservative estimate of 0.2 per 100,000, which gave an annual burden of 109 cases. One of its biggest risk factors is diabetes mellitus. In Kenya, only 20% of those with diabetes were found to have received treatment, and less than 10% of those who knew their diabetes status had their blood

glucose under control (Mohamed et al. 2018). This means the actual number of cases could be significantly more than our estimates.

For IA annual incidence, we assumed a 13% incidence in AML and an equal number of other patients with haematological malignancy and lymphoma (355 cases annually), 2.6% of lung cancer patients (21 cases), 1.3% of COPD admissions (5,053 cases annually), 2% and 4% of renal and liver transplant recipients respectively (10 cases). An estimated 760 HIV/AIDS patients died of invasive aspergillosis each year and 385 cases from cancer and other immunosuppressive conditions, including transplantation. Our annual incidence estimate for invasive aspergillosis incidence 6,198 cases.

3.3.3. Fungal asthma and allergic aspergillosis

Kenya has an asthma prevalence of 10% in adults according to findings from a national survey. Translating to a total burden of 3,335,788 adult cases. Allergic bronchopulmonary aspergillosis (ABPA) was found to have a prevalence of an estimated 83,395 cases almost all with asthma, usually poorly controlled asthma. Cystic fibrosis is barely recognised in Kenya. We also estimated severe asthma with a fungal sensitisation prevalence of 110,081 cases with severe disease. The underlying assumption here was that 33% of 10% adult asthmatics had severe asthma (Denning et al. 2014), and there is some overlap with ABPA. We have not been able to estimate allergic fungal rhinosinusitis in the absence of any data.

3.4. Candidiasis and candidemia

To estimate the annual incidence of candidemia, we assumed a rate of 5/100,000, this being the mean of 2–11/100,000 persons (Arendrup 2010; Bongomin et al. 2017). This translated to a burden of 1,914 cases of individuals with cancer and other immunocompromising conditions and 820 cases from surgery and critical care, summing up to a total figure of 2,734 cases. One 12-month study of 378 patients admitted to intensive care in Nairobi in 2019–2020 found 31 (8.2%) to have a bloodstream *Candida* infection. The commonest 2 species were *Candida auris* (29%) and *Candida albicans* (26%) (Solomon et al. 2021). These data don't allow a national extrapolation as there are

very few intensive care beds in public hospitals in Kenya.

For *Candida* peritonitis, we estimate an annual incidence of 0.75 per 100,000 persons, yielding a total burden of 410 cases among those who are critically ill and have undergone surgical procedures. This is based on a ratio of 2 cases of candidaemia for every case of intraabdominal candidiasis in intensive care (*Candida* peritonitis) (Montravers et al. 2011).

Recurrent *Candida* vaginitis is characterised by four or more episodes of vulvovaginal candidiasis over a year (Lakoh et al. 2021). To estimate the annual incidence we assumed that 6% of females aged between 15 and 49 years are affected (Denning et al. 2018). This gave a total burden of 915,795 cases almost all in individuals with no underlying disease.

3.5. Fungal keratitis

Fungal keratitis is rarely diagnosed in Kenya, although the Ministry of Health collects annual data on microbial keratitis (Brown et al. 2021). Using data from other African countries for the ratio of bacterial to fungal keratitis, we conservatively estimate an annual incidence of 14.5 per 100,000 persons, translating to 7,929 people whose eyes are affected, most losing their sight.

3.6. Tinea capitis and other serious skin fungal diseases

Tinea capitis is a fairly ubiquitous condition in Kenya that affects a large number of rural and urban dwellers, primarily school-going children. The most prevalent aetiological agents in Kenya are *Trichophyton* spp, *Epidermophyton* spp, and *Microsporum* spp. which occur singly, dually, or as a triple infection (Moto et al. 2015). We estimated the annual prevalence of 4,905,249 cases almost all without any underlying disease.

Mycetoma was reported relatively frequently in the 1960s (Cameron et al. 1973a). This case series of 155 cases provided data on both Actinomycetoma and Eumycetoma. The cultures were often negative, but 34 cases were attributed to *Madurella mycetomatis*. We were unable to find any epidemiological studies on chromoblastomycosis, but there is one published case (Cameron et al. 1973b). No studies on sporotrichosis were found.

The total burden of serious fungal infections is estimated to affect 6,328,294 persons which translates to 11.57% of the Kenyan population.

4. Discussion

The last decade saw Kenya's economic status raised to the lower middle-income level. This had significant implications for health-related parameters including the type and number of fungal infections in the country. It also means more and more people can afford basic amenities and have higher expectations of health services (The Kenya Institute for Public Policy Research and Analysis 2020; Chepkondol et al. 2020). There are now more healthcare facilities, more healthcare workers, and improved diagnostics across board. Research outputs also improved within the same period, allowing for more up-to-date fungal burden estimates.

An increase in the number of people affected with non-communicable diseases in Kenya has significantly increased as well. The number of cancer cases, especially has gone up, as has the number of kidney transplants conducted in Kenya. The number of immunocompromised individuals has also increased, in part, due to an increase in the screening and diagnosis of cancer in Kenya, particularly breast and cervical cancer.

The period also saw a transition of the country's health system, from a centralised national system to a more regional, devolved county system. This in effect meant perennially experienced stock-outs of drugs including antifungals were mitigated more swiftly at the local level.

The number of HIV cases has remained fairly constant over the last five years, owing largely to aggressive campaigns targeting HIV diagnosis and recruitment to and retention in care of many more HIV-positive people. Both new HIV infections and mortality have decreased benefitting from multifaceted biomedical and social HIV prevention strategies and the integration of HIV services into the public health system in Kenya. However, evidence points to an increased HIV mortality risk, owing to HIV-positive individuals starting antiretroviral therapy late with progressive HIV disease (Silverman et al. 2019).

Cryptococcal meningitis diagnosis relied on culture but more sensitive and cost-effective techniques such as the lateral flow antigen immunoassay are

increasingly being used in Kenya (Abassi et al. 2015; Gitonga et al. 2019; Lakoh et al. 2022). The overall burden of cryptococcosis has decreased in Kenya compared to the last estimates from 11,900 to 8,975 (Guto et al. 2016). This could be attributed to more conservative estimates used previously as informed by the existing evidence at the time.

In 2015, histoplasmosis was added to Kenya's list of "zoonotic diseases of public health concern" (Munyua et al. 2016). Chest X-rays of Suk (Chok or Chuk) tribesman in 1949 (northeast of Eldoret) showed some with calcification, characteristic of prior resolved histoplasmosis. In 1951, Dr. Hugh Stott skin-tested 768 gold miners (east of Lake Victoria) and male prisoners in the goal in Nakuru (mostly from the Rift Valley) with histoplasmin (Stott 1954). He found 65 (8.5%) to be positive, with the miners having a 14.6% positivity rate and prisoners 5.3%. Chest X-ray calcification was found in 34.8% of those with a positive histoplasmin reaction compared with those with negative tests (9.8%). *Histoplasma capsulatum* was first isolated from soil in the village of Darajani, East Kenya in 1964 near the Chyulu Hills National Park, home to some huge lava tubes (caves) (al-Doory and Kalter 1967). These caves house huge numbers of bats. This was the second isolation of *H. capsulatum* from east Africa, the other being from Tanzania in 1960. Histoplasmosis clearly is present in Kenya, with very few case reports only. *Histoplasma* antigen testing of urine and serum (the most sensitive assay for disseminated histoplasmosis) is not available in Kenya (Lakoh et al. 2022).

PCP has a higher incidence (25,429 cases in adults and 3,879 cases in children) than previously estimated (17,000) (Guto et al. 2016). This corroborates the evolving epidemiological trends that showed an increase in incidence over a recent five-year period (Kolbrink et al. 2022). PCP fatalities are probably also linked with cancer and autoimmune diseases. Currently, most diagnoses are made clinically, but the broader at-risk population and frequent bacterial co-infection in babies with PCP underlines the need to implement *Pneumocystis* PCR diagnosis across the country (Morrow et al. 2014). *Pneumocystis* PCR (a WHO Essential diagnostic) is not done in any public facility in Kenya (Lakoh et al. 2022).

Oral and oesophageal candidiasis still pose a significant health challenge in Kenya. The burden

of infection reduced significantly from the last estimate and this is largely due to the widespread use of HIV opportunistic infection prevention medications in the country. Recurrent vaginal candidiasis cases with no underlying cause increased by 50% from the last estimation (using the same 6% proportion), making it the second most burdensome fungal infection in Kenya. This increase reflects changing population demographics in Kenya. The risk of infection increases with a history of bacterial vaginosis, diabetes, wearing panty liners, drinking acidic juices such as cranberry juice, antibiotic use, having intra-uterine devices, and a short ano-vaginal distance, among others (Patel et al. 2004; Guzel et al. 2011).

CPA is being increasingly recognised in Kenya. Data from across Africa reveals growing interest in CPA as documented from South Africa, Senegal, and Morocco (Olum et al. 2021). Most recently in Kenya, serological evidence of *Aspergillus* infection from HIV-positive patients with difficult-to-treat tuberculosis found at least 46 cases (Mohamed et al. 2022). Our current estimate is nearly eight-fold higher than previously reflecting a better understanding of CPA internationally, supported by national data. Our estimate of over 100,000 prevalence emphasises the need to incorporate *Aspergillus* IgG antibody testing into TB programmes across Kenya. Likewise, with invasive *aspergillosis* mortality in Africa exceeding 60% (Yerbanga et al. 2023), the inclusion of *Aspergillus* antigen testing into leukaemia and intensive care would be appropriate. Ongoing work on fungal adhesins points to a promising potential for addressing invasive fungal infections in immunosuppression both preventively and therapeutically, this will lead to better estimates in future (Kumari et al. 2021).

A substantial number of Kenyan patients were found to have severe persistent asthma; 10% of adults compared with a 2003 estimate used previously of 3.12%. These patients presented with higher rates of adult-onset asthma and lower rates of rhinosinusitis, among other comorbidities (Kirenga et al. 2020). A significant increase in the number of ABPA and SAFS cases was established in this study, a five-fold increase from the last estimate. Fungal asthma in Africa recently quantified by Kwizera et al. found a relatively high prevalence of fungal sensitisations

in asthmatics (3%-52%) and a substantially high prevalence of ABPA estimated at 1.6%-21.2% (Kwizera et al. 2019). More cases are being diagnosed in Kenya than before. More focus should now be put on antifungal treatment as an alternative to long-term prednisolone or biologics to improve asthma control (Moss 2014).

Fungal rhinosinusitis (FRS) is poorly diagnosed and not documented in Kenya, it is divided into invasive and non-invasive FRS. Most of the former are captured in IA and mucormycosis, these are life-threatening and life-altering for survivors because of (usually) extensive surgery (Searyoh et al. 2020). Non-invasive FRS includes sinus fungal ball and fungus-related eosinophilic FRS (Chakrabarti et al. 2009). Invasive fungal rhinosinusitis. More awareness of fungal rhinosinusitis in Kenya is required.

Candida auris is less virulent but as a cause of invasive *candidiasis* may pose a significant challenge to eliminate from Kenyan patients (Adam et al. 2019). Studies have shown the existence of diversity in both genetic and biological characteristics of different *Candida auris* clades that are resistant to at least one antifungal drug (Bing et al. 2022). Our estimate of *Candida* bloodstream infection has increased in line with an increasing population size (5/100,000).

The estimate for invasive *aspergillosis* is substantially higher than the previous estimate. This reflects the addition of deaths from AIDS being included (4%), COPD as an underlying disease being added and increased numbers of renal transplant procedures and lung cancer cases.

We have included an estimate of fungal keratitis incidence, which was absent previously. We know that microbial keratitis is relatively common in Kenya (based on annual County reports), but distinction between bacterial and fungal keratitis is only occasionally made (Brown et al. 2021).

Azole resistant *Aspergillus* is present in nearly all continents, and some variants have a high fatality rate even in Kenya (Jeanvoine et al. 2020; Burks et al. 2021). The drug used, clinical setting and patient characteristics including gene alterations such as *cyp51* gene, all lead to varied levels of resistance (Chowdhary et al. 2017; Guegan et al. 2020).

Tinea capitis was the most burdensome condition accounting for 77% of all fungal infections in Kenya. Mostly affecting school-going children, this

contagious disease spreads quickly among young children who intimately interact with each other during child play. The pooled prevalence in Africa was found to affect more than one in five school-aged children (Bongomin et al. 2021). In the prior estimate, 1.7 million children were thought to be affected (Guto et al. 2016); our current estimate is 4.9 million. This new estimate reflects the large increase in children in Kenya from 17.1 to 21.3 million over 7 years and the use of a more up to date estimate of the proportion affected – from 10% to 23%. Treatment options available in Kenya include griseofulvin, itraconazole, terbinafine, and fluconazole (Alkeswani et al. 2019), most of which are readily available.

Skin fungal infections were excluded from this study due to data paucity occasioned by human resource capacity challenges. Most regions in sub-Saharan Africa have less than 1 dermatologist per million people. This coupled with limited training in dermatology makes it difficult to accurately diagnose skin fungal NTDs (Mosam and Todd 2021). Promising advances in collaborative skin research shine a ray of hope for future quantification of fungal skin NTDs in Kenya and Africa at large (Verschoore and Dlova 2022).

The national infection prevention and control guidelines in Kenya were last updated more than a decade ago. Lack of interventions and measures specifically targeting fungal conditions in Kenya are obviated by the lack of mycology treatment guidelines. This significantly lowers the suspicion indices by healthcare workers, delaying the diagnosis and treatment of fungal infections (Sangoi et al. 2009; Caudron de Coquereaumont et al. 2021) in Kenya.

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Author contributions

SNR: Concept design and development, data acquisition, drafting the article, data analysis and interpretation, final approval of the version to be published.

DWD: Concept design and development, data acquisition, drafting the article, data analysis and interpretation, revising critically for important intellectual content, final approval of the version to be published.

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