



## Research Paper

## Estimated burden of fungal infections in Panama

Cristel Rodríguez-Vargas<sup>a</sup>, Ana Alastruey-Izquierdo<sup>b,c</sup>, David W. Denning<sup>b,d,\*</sup>, Ana Belén Araúz<sup>a</sup><sup>a</sup> Department of Infectious Diseases Hospital Santo Tomás, Panama<sup>b</sup> Global Action For Fungal Infections, 01564 Geneva, Switzerland<sup>c</sup> Mycology Reference Laboratory, National Centre for Microbiology, Instituto de Salud Carlos III, 28222 Madrid, Spain<sup>d</sup> Manchester Fungal Infection Group, The University of Manchester and Manchester Academic Health Science Centre, Manchester, UK

## ARTICLE INFO

## Article History:

Received 19 November 2023

Revised 15 February 2024

Accepted 16 February 2024

Available online 17 February 2024

## Keywords:

Histoplasmosis

Pneumocystis

Sporotrichosis

Paracoccidioidomycosis

Mucorales

## ABSTRACT

Data published on Panamanian fungal disease are scarce, mostly case reports. To date, there is no paper that compiles the burden of fungal disease. Here we estimate for the first time the incidence and prevalence of fungal diseases in Panama. Data on fungal disease were obtained from different search engines: PubMed, Google Scholar, Scielo and Lilacs. For population and at risk diseases, we used statistics from worldometer, UNAIDS, and WHO. Incidence, prevalence, and absolute numbers were calculated based on the population at risk. Panamanian population in 2022 was 4,429,739. We estimated that 85,530 (1.93 %) people suffer from fungal diseases. The most frequent fungal infection was recurrent *Candida* vaginitis (3285/100,000). There are 31,000 HIV-infected people in Panama and based on the number of cases not receiving anti-retroviral therapy (14,570), and previous reports of prevalence of opportunistic infections, we estimated annual incidences of 4.0/100,000 for cryptococcal meningitis, 29.5/100,000 for oral candidiasis, 23.1/100,000 for esophageal candidiasis, 29.5/100,000 for *Pneumocystis* pneumonia, 15.1/100,000, and for histoplasmosis. For chronic pulmonary aspergillosis (CPA) and fungal asthma we used data from Guatemala and Colombia to estimate COPD and asthma prevalence and WHO report for tuberculosis. We estimated annual incidences of 6.1/100,000 for invasive aspergillosis and prevalence of 31.5/100,000 for CPA, 60.2/100,000 for allergic bronchopulmonary aspergillosis, and 79.5/100,000 for severe asthma with fungal sensitisation. Other incidence estimates were 5.0/100,000 for candidaemia, 0.20/100,000 for mucormycosis, and 4.97/100,000 for fungal keratitis. Even though this report on burden of fungal disease is a forward step, more epidemiological studies to validate these estimates are needed.

© 2024 The Author(s). Published by Elsevier Masson SAS on behalf of SFMM. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

## Introduction

Panama is an isthmus located just north of the Equator, in the central part of the American continent (Fig. 1). It is the narrowest and most elongated territory of Central America. Located geographically within the septentrional low latitudes (7° 12' 07" and 9° 38' 46") and the 77° 09' 24" and 83° 03' 07" of western latitude. It is characterized by its tropical, hot, humid climate all year round. These features allow this country to serve as a home to multiple species of plants, animals, fungi, and microorganisms. Its population has grown by about 60 % over the last few years. The most important economic contributors are the Panama Canal, the airport activity and the Colon's Zona libre which is the main distribution center of merchandise in the hemisphere.

Serious fungal infections kill more than 3 million people and affect hundreds of millions of people, globally. They often occur because of predisposing diseases that affect the immune system or lungs such as AIDS, cancer, chronic pulmonary diseases, organ transplantation, corticosteroid therapy. Both predisposing diseases and fungal diseases continue to increase over the last years [1]. Despite this alarming data, serious fungal infections are neglected, causing pain, disability, and death.

It is well known that Panama is endemic to pathogens capable of causing serious fungal infections (including *Histoplasma* spp., and *Coccidioides* spp.), yet there are few epidemiologic data on punctual fungal diseases. With this study, we aim to estimate the incidence and prevalence of the most common fungal diseases, using national, regional, and international data in specific population at risk [2].

## Materials and methods

For the estimation of serious fungal infection's burden in Panama, we used the 2022 Worldometers total population [3] (Table 1). We

\* Corresponding author at: Professor of Infectious Diseases in Global Health, Manchester Fungal Infection Group, CTF building, Grafton Street, Manchester M13 9NT, UK.  
E-mail address: [ddenning@manchester.ac.uk](mailto:ddenning@manchester.ac.uk) (D.W. Denning).



Fig. 1. Topographical map pf Panama and its border areas.

**Table 1**  
Population and rates used to calculate burden of serious fungal infections in Panama.

Population	Number	Prevalence and annual rates	References
Total Panamanian population	4408,939		Worldometers 2022 [14]
Total adult population	3258,206	73.9 %	
HIV population 2022	31,000	0.7 %	UNAIDS [15]
HIV population at risk of opportunistic infection	2903		Assumes a 7 year fall in CD4 count to <200×10 [6], and 5 % non-adherence/resistance rate in those taking ART
TB total annual incidence	2100	47/100,000	WHO TB country profile, 2022 [16]
Asthma prevalence in adults	106,700	2.42 %	Guatemala rate from 2003 World Health Survey [7]
COPD prevalence	122,125	2.77 %	Colombia rate from PREPOCOL study (2008) [8]
COPD admissions to hospital	15,880	13 %	Data from Trinidad and Tobago [9]
Acute myeloid leukaemia	132	3/100,000	Global Cancer Observatory, 2020. [10]
Lung cancer	340		Global Cancer Observatory, 2020. [10]
Solid organ transplant 2014	40		Evolución De Los Trasplantes De Componentes. Rev Med Panama. 2014 [11,13]
Allogeneic haematopoietic stell cell transplant	59		2016. Experiencia del ION en trasplante de células madre hematopoyéticas. [12,13]

WHO = World Health Organization; HIV = human immunodeficiency virus; TB = tuberculosis; COPD = Chronic Obstructive Pulmonary Disease.

included at risk population: people living with HIV/AIDS (PLWHA), people living with pulmonary tuberculosis, patients with asthma, chronic obstructive pulmonary disease (COPD), patients with hematologic neoplasms, lung cancer, hematopoietic stem cell transplantation recipients, solid organ transplantation recipients. Data on PLWHA were obtained from the HIV/AIDS UNAIDS country factsheet [4]. Tuberculosis data were obtained from the World Health Organization (WHO) 2020 profile on Panama [5]. Current asthma and COPD data from the basic indicators of the country report of 2016 [6] were substantially too low as based on partial voluntary reporting. Therefore, asthma prevalence in adults was taken from the 2003 World Health Survey in Guatemala [7] and COPD prevalence from a multicenter study in Colombia [8]. Annual admissions to hospital were taken from data from Trinidad and Tobago [9]. Leukemia and lung cancer incidence, and absolute patient numbers, were obtained from the International Agency for Research on Cancer of the WHO [10]. Solid organ transplant and HSCT were obtained from two reports that compiled the experience of these treatments in our country [11,12,13]. Assumptions about specific risk populations are shown in Table 1.

A literature review was made about fungal infections in Panama. We used PubMed, Google Scholar, Scielo and Latin American and Caribbean Health Sciences Literature search engines with the following keywords: “mycoses, cryptococcal meningitis, histoplasmosis, pneumocystis pneumonia, invasive pulmonary aspergillosis, pulmonary aspergillosis, allergic bronchopulmonary aspergillosis, neuroaspergillosis, candidemia + Panama”. We also searched the national indicators report provided by the Ministry of Health. Where no article was found from Panama, we used data from countries with similar population characteristics.

Estimations were done in Excel, using proportions of at risk patients having a specific fungal condition. In some instances, incidence was calculated, notably invasive aspergillosis, HIV-related opportunistic infections and fungal keratitis. For other conditions, prevalence was estimated, notably recurrent vulvovaginal candidiasis, fungal asthma and chronic pulmonary aspergillosis. Burden per 100,000 population was then estimated. The estimate of chronic pulmonary aspergillosis (CPA) assumes the following: the proportion of newly presenting pulmonary ‘TB’ patients with CPA is 19 % and 10 % in clinically diagnosed HIV un-infected and infected patients and 3 %

and 7 % in cases of proven pulmonary TB in HIV un-infected and infected patients respectively [17]. In addition, 10 % of patients completing anti-tuberculous therapy are estimated to develop CPA within the year of TB diagnosis. These groups represent annual incidence. Following cure of TB, an estimated 1.5 % annually will develop CPA, which we have estimated for 5 years as a period prevalence. Furthermore, we have assumed a 20 % year one and a 7.5 % annual mortality of CPA thereafter. As smoking and lung cancer rates are low in Panama, we have assumed that the proportion of CPA cases linked to TB is 80 % of the total [18].

This research did not involve human subjects or clinical charts, there are no confidentiality or personal information that needs to be protected. Regarding the ethics aspects, we have ensured that the information herein described is truthful and will help in the decision-making of better healthcare programs, not only to the country studied, but the global initiative to decrease the fungal burden.

## Results

The current population of Panama is 4,429,739 as of Monday, March 14, 2022, of whom 1,150,733 (26.1 %) are children, 36.9 % are adults above 40 years old; 1,694,267 are adult women of whom 10 % are over 60 years (Table 1) [3]. Total expenditure on health was 5.86 % of gross domestic product and 67.5 % of that was public expenditure [19].

UNAIDS estimated that the current number of people with HIV/AIDS diagnosis was 31,000. Of these, 16,430 (53 %) are on antiretroviral therapy (ARV), 14,570 are not receiving ARV, and a minimum of 1800 are at risk of opportunistic infections (Table 1). Late presentation to care of newly identified HIV patients is common – 72 % with 54.5 % having advanced HIV disease [20]. There are less than 500 AIDS-related deaths annually [4].

The total pulmonary tuberculosis annual incidence by 2020 was 1400 (32 per 100,000 population), of whom 350 (8.2 per 100,000 population) are HIV positive. The TB case fatality ratio was 21 % [5]. Pulmonary tuberculosis had an annual incidence in 2022 of 1764, of whom 361 have concurrent HIV infection. The absolute number of adults and children diagnosed with asthma by 2016 was 30,290. [6], but we have used the population estimate from Guatemala generated by the 2003 World Health Survey of 2.42 % of adults with asthma (Table 1) [7]. The absolute number of people with COPD by 2016, according to the country indicators of the Ministry of Health was 2794. An prevalence estimate from Colombia of 2.77 % (Table 1) is similar to BOLD study data from Mexico of 3.1 % of the population – a total of 122,125 patients [8]. We have assumed that 13 % of these patients are admitted to hospital each year [9].

The leukemia frequency per 100,000 habitants is 5.6 and the absolute number of AML per year is estimated to be 132 [10]. The absolute number of people with lung cancer was 340 in 2020 [10]. The transplant activity in Panama is in constant evolution. The procedures practiced are corneal, renal, hematopoietic cells, liver, and heart transplant. The annual mean is between 40 and 50 but it was reduced to zero because of the COVID-19 pandemic, restarting in 2020. The last record obtained was from 2014, with 38 renal transplants from dead donors and 10 from live donors, for a total of 48 renal transplant procedures [11]. In 2016, 59 allogeneic stem cell transplant procedures were done [12]. Regarding liver transplants, the number of procedures practiced each year varies from 5 to 16, with 2018 being the most active year [13]. Currently, there are 350 intensive care unit beds across the country.

Overall, we estimate that there are 85,580 people suffering from serious fungal infections in Panama. This is approximately 1.93 % of the total population. The predominant fungal infection is recurrent *Candida* vaginitis.

### HIV-related fungal diseases

In patients living with HIV/AIDS, there were estimated to be 145 cases of cryptococcal meningitis annually, with an incidence of 3.3 per 100,000 person-years (Table 2). This estimation was obtained from the assumption that 5 % of patients with AIDS have a positive cryptococcal CSF antigen, described on a multicenter study performed in Latin-American countries, Panama included [21]. The mortality of AIDS patients with cryptococcal meningitis is about 50 % in 30 days and 60 % at one year, according to local data [22]. A recent global analysis indicated an additional 23 % of cryptococcal cases in non-AIDS patients (33 patients), so a total of 178 patients with this disease [23].

There were 1306 estimated PCP cases in PLHIV/AIDS annually, with an incidence of 29.5 per 100,000 person-years, based on the assumption that 46 % of new AIDS patients with respiratory symptoms had evidence of PCP in bronchoalveolar lavage in Panama [24]. As to oral candidiasis there were 1306 cases, which represent an incidence of 29.5 per 100,000 person-years, based on the assumption that 90 % of PLHIV nor on ARV suffers from this fungal infection [25]. There were 1022 cases of esophageal candidiasis annually, with an incidence of 23.1 per 100,000 person-years, based on the assumption that 20 % of PLHIV not on ARVs and 0.5 % of those on ARVs suffer from the disease [26].

Our country and histoplasmosis have been long interlinked. Histoplasmosis was first reported from Panama by Samuel Darling in 1906, while examining smears from lungs, spleen and bone marrow in a case that was thought to be miliary TB [27]. Other investigations of

**Table 2**

Estimated burden of fungal pathogens/disease in Panama.

Fungal pathogen/disease	Predominant risk groups	Incidence /100,000 annually	Prevalence /100,000	Total cases/year
Esophageal candidiasis	HIV/AIDS	23.1	–	1022
<i>Pneumocystis jirovecii</i> pneumonia	HIV/AIDS	29.5	–	1306
Oral candidiasis	HIV/AIDS	29.5	–	1306
Histoplasmosis	HIV/AIDS	15.1	–	668
Cryptococcal meningitis	HIV/AIDS	4.0	–	178
Chronic pulmonary aspergillosis	Chronic respiratory diseases	13.2	–	584
Chronic pulmonary aspergillosis	Chronic respiratory diseases	–	31.5	1396
Severe asthma with fungal sensitization	Chronic respiratory diseases	–	79.5	3521
Allergic bronchopulmonary aspergillosis	Chronic respiratory diseases	–	60.2	2668
Invasive aspergillosis	Critical care + surgery	6.1	–	270
Candidemia	Cancer + immunocompromised	5.0	–	220
Mucormycosis	Cancer + immunocompromised	0.2	–	9
Recurrent <i>Candida</i> vaginitis	No underlying disease.	–	3285*	72,760
Fungal keratitis	No underlying disease	4.97	–	220

\* Females only.

the source of *Histoplasma capsulatum* var. *capsulatum*, and its linkage with bats are done in the early 1960's in Panama. Martha Shacklette, Fred Diercks and Nathan Gale published the first ever report of *H. capsulatum* isolated from a bat in 1962. They were working in the Middle America Research Unit in Balboa Heights and sampled, bats, soil with guano from a building at Madden Airfield. Nine of 14 (64.3 %) of *Chilonycteris rubiginosa fusca* as well as soil were positive, using mouse inoculation to find the organism [28]. The same year, Robert Taylor, Shacklette and Harlan Kelly found *H. capsulatum* in a few (3.3 %) of 426 soil samples in animal burros and leaf-cutting ant waste [29]. In 1965, additional investigations by PD Klite and Robert Young of soil from a bat roost in a tree yielded *H. capsulatum* [30], as well as an extensive survey of 15 species of bats from 31 sites in Panama [31]. Previous study of exposure to *Histoplasma*, using histoplasmin skin tests, found a 30 % population prevalence, confirming the endemicity and burden of this pathogen in Panama [32]. We estimated that there were 668 cases linked to HIV infection annually, with an incidence of 15.1 per 100,000 person-years (Table 2), based on previous data stating that 23 % of PLHIV at risk of opportunistic infection has a positive *Histoplasma* urine antigen in Panama [21].

#### Fungal infections associated with lung disease

The prevalence of both asthma and COPD in Panama is uncertain. For asthma we have used data from the World health Survey from 2003 in Guatemala (3275/100,000 adults), which is almost certainly a significant underestimate, based on clinical experience. COPD prevalence is probably relatively low because smoking is uncommon in Panama. We have used the lowest prevalence from Latin America, from neighboring Colombia (2.77 %, 122,125 people) as our baseline estimate.

Allergic bronchopulmonary aspergillosis prevalence is estimated to be 60.2 per 100,000 habitants and severe asthma with fungal sensitization incidence is estimated to be 79.5 per 100,000 habitants (Table 2) [33]. This was based on the assumption that 33 % of patients with asthma can develop severe asthma and 10 % of the adult asthmatic population have severe asthma.

In patients with chronic lung conditions, CPA is a most important fungal disease, with an incidence of 584 cases and a prevalence of approximately 1396 31.5 per 100,000 habitants (Table 2). We also estimate 123 deaths annually. We have not estimated chronic pulmonary histoplasmosis, which is likely in some patients. People with residual cavities after pulmonary TB are at much greater risk for CPA [34].

*Candida auris* was first identified in Panama in 2016, mandating surveillance by the Ministry of Health. Up until 2018 there were 37 cases of *C. auris* in a third level hospital of Panama City, highlighting its importance [35].

The incidence of invasive aspergillosis is estimated to be 6.1 per 100,000 habitants (Table 2), considering 4 % of those who die of HIV/AIDS [36], lung cancer patients [9], COPD [37], and those with leukaemia or after transplantation [38]. Those with co-morbid chronic lung pathology are at greater risk. We have not estimated cases in general intensive care or those with severe influenza or COVID-19, although frequent [23].

#### Other important fungal infections

The estimated annual incidence of candidemia is thought to be ~5.0 per 100,000 inhabitants, without supporting local data (Table 2). The associated risk factors are cancer, diabetic and immunocompromised patients, estimated to be 154 annually and another 66 cases in critical care annually [39]. The incidence of *Candida* peritonitis is estimated to be 0.75 per 100,000, accounting for 33 people which risk factor is critical care and surgery [40]. The incidence of recurrent *Candida* vaginitis is estimated to be 3285 per 100,000 habitants, for an

absolute number of 72,760 women affected usually without a specific predisposing factor (Table 2) [41].

#### Sporotrichosis, chromoblastomycosis and eumycetoma

*Sporothrix* spp. complex is a pathogenic, thermally dimorphic fungus, found worldwide, ubiquitous in soil, plants, and decaying vegetables. It is responsible for causing sporotrichosis in humans and some domestic animals. Risk factors for getting the disease are leisure and occupational activities such as agriculture and floriculture. Zoonotic transmission has been reported in urban areas. Clinical presentation depends on the host's immune system, with fixed cutaneous and lymphocutaneous sporotrichosis being the most common, whereas disseminated sporotrichosis is reported in the immunocompromised hosts [42]. To our knowledge there have been three reports of sporotrichosis in Panama, the first two in 1962 [43] and the most recent one in 2018, was found to be a zoonosis after exposure to a cat [44].

Chromoblastomycosis has been reported from Panama, starting in 1946. Overall, there have been 8 reported cases up to 2021 [45]. Equally long ago (1945), one case of eumycetoma has been reported from Panama [46].

These few cases reported throughout the years highlight the fact that these three neglected tropical diseases exist in Panama, probably to a greater extent than we know, but infrequently diagnosed or reported.

#### Paracoccidioidomycosis

Paracoccidioidomycosis is a fungal infection caused by thermally dimorphic fungus from the genus *Paracoccidioides*. *P. brasiliensis* and *P. lutzii* are considered the most important species to cause human infection. Paracoccidioides is endemic in Central and South America. 80 % of the cases have been reported in Brazil, followed by Colombia, Venezuela and Ecuador. It is an occupational disease related to farmers who live in rural areas and workers of coffee and tobacco crops. In children, adolescents and immunocompromised hosts, the infection progresses rapidly after inhalation of the conidia, to systemic disease. In immunocompetent hosts and adults, the disease is often chronic, with lymphatic dissemination after several years. Inoculation through skin is another form of getting the disease, though it is less frequent [47]. In our clinical experience, cases of paracoccidioidomycosis had been diagnosed in Panama, however there are no recent case reports or epidemiological studies. In 1989 a prevalence of 21.95 % exposure (measured skin testing) of *P. brasiliensis* infection was reported in the whole republic [48].

#### Fungal keratitis

Fungal keratitis is a severe sight-threatening condition, most prevalent in tropical and subtropical locations and has been estimated to account for 20–60 % of all culture-positive corneal infections in these areas. It follows minor ocular trauma, in young, healthy individuals. It is often an occupational disease, affecting agricultural or outdoor workers. The diagnosis is made by culture and microscopy. More than 300 different fungal species are known to cause fungal keratitis. It is estimated that the incidence in our country is 4.97 per 100,000 habitants, which corresponds to 220 people affected (Table 2). However, this data assumes that the incidence is similar to neighbor countries such as Colombia and southern USA [49]. There is no published research in Panama assessing this important fungal disease.

#### Mucormycosis

Rhinocerebral mucormycosis is a devastating infection with lethal capacity. Diabetes is the most common predisposing factor for



mucormycosis, but not usually uncontrolled diabetes and it is also associated with immunosuppression such as leukaemia organ transplant, trauma, burns and corticosteroid therapy. Few mucormycosis cases have been reported in Panama. A recent case with a successful treatment was published in 2019, but no surveillance research is available [50]. We estimated that in our country, the incidence is about 0.2 per 100,000 habitants for a total of 9 cases per year (Table 2).

## Discussion

This is the first attempt to summarize epidemiological data on the burden of serious fungal diseases in Panama. There are few papers about incidence, prevalence, or mortality of serious fungal diseases in Panama, and the ones that were found during this meticulous literature search were from one of the third level medical care facilities, omitting the rest of the country's population at risk, which sets a clear selection bias.

Our estimation of the total burden of fungal diseases in Panama is 1.95 %, which is similar to American countries reports such as Argentina (2.01 %), Canada (1.8 %), Colombia (1.5 %), Chile (1.9 %) and Dominican Republic (2.2 %). [35–39] We believe there is underestimation of the total burden of fungal diseases because they are not part of the epidemiological surveillance in Panama, which means they do not require obligatory notification. Our estimates also omit some entities, such as invasive aspergillosis in ICU, oesophageal candidiasis in non-HIV patients, mycetoma and others we could not estimate.

As in other burden reports, our most common fungal infection is recurrent *Candida* vaginitis (more than 4 episodes per year), accounting for 73,192 women without underlying predisposing factors. As stated in the literature reviewed, the infection is caused mostly by *Candida albicans* in 85–95 % and the rest being accounted for by non-*albicans* species. The clinical picture of both etiologies is indistinguishable, with the difference that non-*albicans* species tend to be more resistant to treatment than *albicans* species [41].

The lack of data on candidemia may have lead to an underestimation at 5/100,000. In Ecuador the rate was 7.2/100,000 [51], in Colombia was 12/8/100,000 [52], in Brazil 14.9/100,000 [53] and much higher in Uruguay at 16.4/100,000 [54]. Our clinical impression is that this is a relatively frequent cause of sepsis in Panama. The recent emergence of *C. auris* infections, which are now relatively frequent, demands high quality diagnostics in hospital microbiology laboratories. Surveillance is required.

Other fungal infections estimations were predominantly associated with HIV/AIDS patients. In our experience, PCP, histoplasmosis and cryptococcal meningitis are not rare in HIV/AIDS patients, although sometimes the diagnosis is made based up on clinical judgement or clinical response to specific treatment. We found few reports of these fungal infections in HIV/AIDS patients, the most recent reports being 23 % of positive *Histoplasma* antigen in AIDS patients and 5 % of positive cryptococcal plasma antigen in Panama [22]. PCP diagnosis in public hospitals is based mainly on sputum stains and clinical improvement of patients after PCP treatment. PCP incidence in Panama was much higher than in many other countries, and indeed one of the highest in the world, as there are many patients with advanced HIV disease and the attack rate of PCP was documented at 45 % (although clinically diagnosed). These burdens may be underestimated based on the lack of rapid, point of care diagnostic tests. The mortality of these diseases is thought to be as high as 50 % in 30 days and 60 % at one year for cryptococcal meningitis [18].

We must consider that the reality of our country is that we do not have these novel diagnostic techniques available throughout the year, attributable to several factors. First, there is little industry interest in this relatively small market. Second, a cumbersome process must be overcome to get registration from the Minsa or the

Ministerio de Salud so that hospitals can actually undertake the tests. Third and finally, the hospitals' budgets which are always overstretched.

Invasive aspergillosis estimates were made based on assumptions of previous epidemiological data and the burden of lung disease such as pulmonary TB, COPD, and asthma in Panama. Aspergillosis diagnosis is based on clinical and radiological suspicion, antigen or antibody assays and in at least some of the cases, isolation of the organism in bronchoalveolar lavage specimens. In the public practice, Panama lack's rapid antigen techniques such as galactomannan quantification.

Even though there are robust databases on neoplastic diseases, we lack information of infectious diseases affecting patients with cancer. Moreover, little is known about opportunistic infections in the non-HIV population such as organ transplant recipients. Thus, the data herein presented for those populations is based on previous epidemiological data published. For cancer and immunocompromised patients, the associated fungal infections were invasive aspergillosis and candidemia.

Other endemic mycoses such as paracoccidioidomycosis and sporotrichosis are scarcely reported in our country, either by single case reports or by reports of several decades ago. Because of the constant turnover and characteristics of our population, the lack of reports cannot be accepted as the actual truth. This leads us to the conclusion that newer prevalence and incidence studies must be done to state the actual burden of these diseases and to update the knowledge we already have. Some of the earliest cases of histoplasmosis and coccidioidomycosis were described from Panama (before HIV/AIDS), and such endemicity is unlikely to have disappeared.

Fungal lung disease may be more common than our estimates suggest, particularly with regard to asthma. We have used a prevalence of 2.42 % in adults based on data from Guatemala in 2003. A later study in adolescents in Panama found 20.5 % had asthma and 22.9 % had current asthma [55], although prevalence of asthma falls in adulthood. In the Global Burden of Disease report on years lived with disability, asthma was number 6 in Panama, after back pain, depression, diabetes, hearing loss and anxiety [56]. However fungal asthma, and ABPA in particular, seems unrecognized in the country, as evidenced by a recent consensus report on how to manage severe asthma in Latin America, which only mentions the biologics [57]. As antifungal therapy is effective for fungal asthma and much less costly than biologics, this seems like a missed opportunity.

The limitations of this study are several. First we used external data not necessarily representing the country. Second, the lack of mandatory notification of any of these diseases (as is the case in most countries) makes them difficult to track. Lastly, the lack of non-culture diagnostic tests will likely overlook these infections in at risk populations. However, with this report we place Panama on the map in terms of fungal diseases and create awareness of the importance of fungal infections in our country, and should support the need for better diagnostic tests. Hopefully we open the gate for local epidemiologic surveillance of fungal diseases.

## Conclusions

In this work we present the burden of fungal diseases in Panama for the first time, taken from reports of the most important fungal diseases that affect our population and estimates from similar countries. The most frequent fungal infection is recurrent *Candida* vaginitis which affects women without predisposing factors of childbearing age. The most affected at-risk population are HIV/AIDS patients which represent the vast majority of histoplasmosis, cryptococcosis and PCP infections. Other relatively common diseases assessed were *Aspergillus*-associated conditions, which primarily affect people with underlying lung disease or non-HIV immunocompromised patients.

## Declaration of competing interest

The authors declare no conflict of interest with the contents of this paper.

## References

- [1] Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases—estimate precision. *J Fungi* 2017;3(4):1–29.
- [2] Rodrigues ML, Nosanchuk JD. Fungal diseases as neglected pathogens: a wake-up call to public health officials. *PLoS Negl Trop Dis* 2020;14(2):1–9.
- [3] Worldometers. Panama Demographics 2020 (Population, Age, Sex, Trends) - Worldometer [Internet]. 2022 [cited 2022 Mar 14]. Available from: <https://www.worldometers.info/demographics/panama-demographics/>
- [4] Panamá | ONUSIDA [Internet]. [cited 2022 Mar 14]. Available from: <https://www.unaids.org/es/regionscountries/countries/panama>
- [5] World Health Organization WH. Tuberculosis profile 2020. Available from: [https://worldhealthorg.shinyapps.io/tb\\_profiles/?\\_inputs\\_entity\\_type=%22country%22&lan=%22EN%22&iso2=%22PA%22](https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_entity_type=%22country%22&lan=%22EN%22&iso2=%22PA%22)
- [6] INEC. Indicadores Básicos de Panamá 2016. Minist Salud [Internet]. 2016;1–24. Available from: [http://www.minsa.gob.pa/sites/default/files/publicacion-general/indicadores\\_basicos\\_de\\_salud\\_2016.pdf](http://www.minsa.gob.pa/sites/default/files/publicacion-general/indicadores_basicos_de_salud_2016.pdf)
- [7] To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health* 2012;12(1):204.
- [8] Caballero A, Torres-Duque CA, Jaramillo C, Bolívar F, Sanabria F, Osorio P, et al. Prevalence of COPD in five Colombian cities situated at low, medium, and high altitude (PREPOCOL study). *Chest* 2008;133(2):343–9.
- [9] Thorington P, Rios M, Avila G, Henry J, Haynes C, Pereira LMP, et al. Prevalence of chronic obstructive pulmonary disease among stable chronic disease subjects in primary care in Trinidad, West Indies. *J Thorac Dis* 2011;3:177–82.
- [10] International Agency for Research on Cancer. <https://gco.iarc.who.int/media/globocan/factsheets/populations/591-panama-fact-sheet.pdf> Accessed August 1st 2023
- [11] Cuero C. Evolución De Los Trasplantes De Componentes. *Rev Med Panama* 2014;34(3):19–22.
- [12] Franceschi J. Trasplante de células hematopoyéticas. 15 años de experiencia del ION. *Rev Med Panama* 2016;36(2):9–19.
- [13] IRODaT - International Registry on Organ Donation and Transplantation [Internet]. [cited 2022 Sep 22]. Available from: <https://www.irodat.org/?p=database&c=PA&year=2018#data>
- [14] Worldometers. <https://www.worldometers.info/world-population/panama-population/> Accessed September 12th 2023
- [15] UNAIDS. <https://www.unaids.org/en/regionscountries/countries/panama> Accessed 10th August 2023
- [16] World Health Organization. [https://worldhealthorg.shinyapps.io/tb\\_profiles/](https://worldhealthorg.shinyapps.io/tb_profiles/) Accessed 5th August 2023.
- [17] Denning DW, Cole C, Ray A. New modeling approach for chronic pulmonary aspergillosis (CPA) in the context of pulmonary tuberculosis – revised burden for India. *Int J Infect Dis Regions* 2022;6:7–14.
- [18] Smith NL, Denning DW. Underlying conditions in chronic pulmonary aspergillosis including simple aspergilloma. *Eur Respir J* 2011;37(4):865–72.
- [19] PAHO. Health in the Americas - country profile Panama. <https://hia.paho.org/en/countries-22/panama-country-profile>. 2022. Accessed 2nd November 2023.
- [20] Robles MA, Ortiz AY, Zaldivar Y, Castillo J, Gondola J, Mewa JC, Moreno A, Burgos R, Chavarria O, Castellero O, Gonzalez C, Pascale JM, Martínez AA. Evolution of late presentation to care and advanced HIV in newly HIV diagnosed subjects in the Republic of Panama: 2012–2017. *Int J STD AIDS* 2020;31(8):791–9.
- [21] Caceres D, Arauz AB, Flores C, Santiago E, Montoya S, Saenz C, et al. Implementation of rapid diagnostics assays for detection of histoplasmosis and cryptococcosis in central American people living with HIV. *Mycoses* 2021;64:1396. – 140.
- [22] González E, Araúz AB, Rodríguez French A. Meningitis por *Cryptococcus neoformans* en pacientes con SIDA. *Rev Med Panama* 2013;33(2):3–7.
- [23] Denning DW. Global incidence and mortality of severe fungal disease. *Lancet Infect Dis* 2024 S1473-3099(23)00692-8. doi: 10.1016/S1473-3099(23)00692-8.
- [24] De Armas Rodríguez Y, Wissmann G, Müller AL, Pederiva MA, Brum MC, Brackmann RL, et al. Pneumocystis jirovecii pneumonia in developing countries. *Parasite* 2011;18:219–28.
- [25] Matee MI, Scheutz F, Moshy J. Occurrence of oral lesions in relation to clinical and immunological status among HIV-infected adult Tanzanians. *Oral Dis* 2000;6(2):106–11.
- [26] Smith E, Orholm M. Trends and patterns of opportunistic diseases in Danish AIDS patients 1980–1990. *Scand J Infect Dis* 1990;22(6):665–72.
- [27] Darling ST. A protozoan general infection producing pseudotubercles in the lungs and focal necroses in the liver, spleen and lymphnodes. *JAMA* 1906:1283–5.
- [28] Shacklette MH, Diercks FH, Gale NB. *Histoplasma capsulatum* recovered from bat tissues. *Science* 1962;135(3509):1135.
- [29] Shacklette HBK, Taylor RL. Isolation of *Histoplasma capsulatum* and *Microsporium gypseum* from soil and bat guano in Panama and the Canal Zone. *Am J Trop Med Hyg* 1962;11:790–5.
- [30] Klite PD, Diercks F. *Histoplasma capsulatum* in fecal contents and organs of bats in the canal zone. *Am J Trop Med Hyg* 1965;14(3):433–9.
- [31] Klite PD, Young R. Bats and Histoplasmosis A Clinico-epidemiologic study of two human cases. *Ann Intern Med* 1965;62(6):1263–71.
- [32] Tucker H. Histoplasmin, Tuberculin and Coccidioidin sensitivity on the isthmus of panama: preliminary report of 500 patients. *Am J Trop Med Hyg* 1950;30(6):865–70.
- [33] 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;51:361–70.
- [34] Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bull WHO* 2011;89:864–72.
- [35] Ramos R, Caceres DH, Perez M, Garcia N, Castillo W, Santiago E, et al. Emerging multidrug-resistant *Candida duobshaemulonii* infections in panama hospitals: importance of laboratory surveillance and accurate identification. *J Clin Microbiol* 2017;56(7):1–6.
- [36] Denning DW, Morgan EF. Quantifying deaths from aspergillosis in HIV positive people. *J Fungi* 2022;8:1131.
- [37] Hammond EE, McDonald CS, Vestbo J, Denning DW. The global impact of *Aspergillus* infection on COPD. *BMC Pulm Med* 2020;20:241.
- [38] Lortholary O, Gangneux JP, Sitbon K, Lebeau B, de Monbrison F, Le Strat Y, et al. Epidemiological trends in invasive aspergillosis in France: the SAILF network (2005–2007). *Clin Microbiol Infect* 2011;17(12):1882–9.
- [39] Arendrup MC. Epidemiology of invasive candidiasis. *Curr Opin Crit Care* 2010;16(5):445–52.
- [40] Montravers P, Mira JP, Gangneux JP, 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):1061–7.
- [41] Denning DW, Kneale M, Sobel JD, Rautemaa-Richardson R. Global burden of recurrent vulvovaginal candidiasis. *Lancet Infect Dis* 2018;18:e339–47.
- [42] Carlos IZ, Batista-Duarte A. Sporotrichosis: an emergent disease. Sporotrichosis: new developments and future prospects. Springer; 2015. p. 1–23.
- [43] Calero C, Tapia A. Two cases of sporotrichosis in the Isthmus of Panama. *Am J Trop Med Hyg* 1962;11:676–7.
- [44] Rios ME, Suarez J, Moreno J, Vallee J, Moreno JP. Zoonotic sporotrichosis related to cat contact: first case report from Panama in Central America. *Cureus* 2018;10(7):1–5.
- [45] Santos DWCL, de Azevedo CMPES, Vicente V, Queiroz-Tellez F, Rodrigues A, de Hoog G, Denning DW, Colombo AL. The global burden of chromoblastomycosis. *PLoS Negl Trop Dis* 2021;15(8):e0009611.
- [46] Calero C. Madura foot (Mycetoma): first report from the isthmus of panama. *Arch Dermatol Syphilol* 1947;55(6):761–71.
- [47] Cordova LA., Torres J. Paracoccidioidomycosis. StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. 2022 Sep 19. <https://www.ncbi.nlm.nih.gov/books/NBK563188/>
- [48] de Martín MC, Suárez M. [Infection caused by *Paracoccidioides brasiliensis* in people living in Coclé and Veraguas, Republic of Panamá]. *Rev Med Panama* 1989;14(2):112–5.
- [49] Brown L, Leck AK, Gichangi M, Burton MJ, Denning DW. The global incidence and diagnosis of fungal keratitis. *Lancet Infect Dis* 2021;21(3):e49–57.
- [50] Pecchio M. Mucormycosis - dual therapy with prolonged survival. *J Refug Glob Heal* 2019;2(1):1–4.
- [51] Zurita J, Denning DW, Paz-Y-Miño A, Solís MB, Arias LM. Serious fungal infections in Ecuador. *Eur J Clin Microbiol Infect Dis* 2017;36:975–81.
- [52] Alvarez-Moreno CA, Cortes CA, Denning DW. Burden of fungal infections in Colombia. *J Fungi* 2018;4:41.
- [53] Giacomazzi J, Baethgen L, Carneiro LC, Millington MA, Denning DW, Colombo AL, Pasqualotto AC. The burden of serious human fungal infections in Brazil. *Mycoses* 2016;59:145–50.
- [54] Macedo-Viñas M, Denning DW. Estimating the burden of serious fungal infections in Uruguay. *J Fungi* 2018;4:37.
- [55] Mallol J, Solé D, Baeza-Bacab M, Aguirre-Camposano V, Soto-Quiros M, Baena-Cagnani C. Regional variation in asthma symptom prevalence in Latin American children. *J Asthma* 2010;47(6):644–50.
- [56] Global Burden of Disease Collaborative Network. Global burden of disease study 2015 (GBD 2015) life expectancy, all-cause and cause-specific mortality 1980–2015 [Internet]. Seattle, United States of America: Institute for Health and Evaluation (IHME). 2016. Available from: <https://ghdx.healthdata.org/record/ihme-data/gbd-2015-life-expectancy-all-cause-and-cause-specific-mortality-1980-2015>
- [57] García G, Bergna M, Vázquez JC, Cano Salas MC, Miguel JL, Celis Preciado C, et al. Severe asthma: adding new evidence – Latin American Thoracic Society. *ERJ Open Res* 2021;7(1):00318–2020.