

# Burden of fungal infections in Senegal

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## Summary

Senegal has a high rate of tuberculosis and a low HIV seropositivity rate and aspergilloma, life-threatening fungal infections, dermatophytosis and mycetoma have been reported in this study. All published epidemiology papers reporting fungal infection rates from Senegal were identified. Where no data existed, we used specific populations at risk and fungal infection frequencies in each to estimate national incidence or prevalence. The results show that tinea capitis is common being found in 25% of children, ~1.5 million. About 191 000 Senegalese women get recurrent vaginal thrush,  $\geq 4$  times annually. We estimate 685 incident cases of chronic pulmonary aspergillosis (CPA) following TB and prevalence of 2160 cases. Asthma prevalence in adults varies from 3.2% to 8.2% (mean 5%); 9976 adults have allergic bronchopulmonary aspergillosis (ABPA) and 13 168 have severe asthma with fungal sensitisation (SAFS). Of the 59 000 estimated HIV-positive patients, 366 develop cryptococcal meningitis; 1149 develop *Pneumocystis pneumonia* and 1946 develop oesophageal candidiasis, in which oral candidiasis (53%) and dermatophytosis (16%) are common. Since 2008–2010, 113 cases of mycetoma were diagnosed. In conclusion, we estimate that 1 743 507 (12.5%) people in Senegal suffer from a fungal infection, excluding oral candidiasis, fungal keratitis, invasive candidiasis or aspergillosis. Diagnostic and treatment deficiencies should be rectified to allow epidemiological studies.

**Key words:** Burden, estimation, fungi, senegal.

## Introduction

The annual incidence and prevalence of fungal infections is not well known in most countries especially in limited resource countries where the diagnosis is not often established due to a lack of specialists and diagnostic facilities. In Africa where tuberculosis and HIV have a high prevalence, secondary fungal infections

are probably common. Unfortunately despite the life-threatening nature of many of these infections, insufficient interest has been shown by public health authorities in these remediable infections.

Senegal is a West African country of about 14 million people.<sup>1</sup> The population is characterised by its youth and a high birth rate albeit decreasing in recent years. Most of the population lives on the threshold of poverty, the rate of illiteracy is also high particularly among girls. The healthcare system in Senegal (2010) has 34 hospitals, 89 health centres, 20 of which are in reality health posts acting as a health centre and 1195 health posts of which 1035 are functional, two psychiatric health centres, 76 private Catholic clinics and 1603 nurse-led clinics.<sup>2</sup> In terms of infrastructure coverage for health, Senegal has not yet reached the standards recommended by World Health Organization (WHO).<sup>2</sup>

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A starting point for improved care by doctors interested in fungal diseases is coherent estimates of the burden of infection both nationally and by underlying disease. Such estimates depend on epidemiological data, themselves inadequate as well as data on the impact of interventions in the population affected. The aim of this work was to synthesise existing data for fungal infections in Senegal, and where data are not available, make reasonable estimates of annual incidence and prevalence.

## Material and methods

All published epidemiology papers reporting fungal infection rates from Senegal were identified. The search was done in PubMed using the terms 'fungi', 'infections', 'Senegal', 'West Africa'. Where no data existed, we used specific populations at risk and fungal infection frequencies in those populations to estimate national incidence or prevalence, depending on the condition. We sourced the total Senegal populations from the national statistical institute,<sup>1</sup> and estimated the number of women between 15 and 50. The estimate of women with recurrent vulvovaginal candidiasis is a 'discounted' rate of 6% from Foxman *et al.* [3] and other papers.<sup>4,5</sup> The rate is discounted from ~9% as self-reported 'thrush' may reflect other disorders such as bacterial vaginosis. HIV-infected patient numbers were obtained from the UNAIDS 2013 report with numbers estimated up to 2012.<sup>6</sup> Estimates of cryptococcal meningitis (CM), *Pneumocystis pneumonia* and mucosal candidiasis were derived from local or regional data (see Results section). Patients with pulmonary tuberculosis were derived from the 2013 WHO country profiles.<sup>7</sup> It was assumed that about 10% of these patients died within a year of diagnosis according to the TB WHO annual (2014) report, but it is higher than that found in India.<sup>8</sup> Estimates of the annual incidence were derived as previously described assuming 22% had a residual cavity, and the rate of CPA was 22% in those with a cavity and 2% in those without.<sup>9</sup> The 5 year prevalence was calculated using a 15% annual death<sup>10,11</sup> or surgical rate. Other population numbers were sourced from references described in each section of the results.

## Results

### Country profile

The estimated population in Senegal is around 14 million, with adults comprising 56.7% and children

(<16 years) 43.3% of the population. The female proportion is 50.14%.<sup>1</sup> Table 1 shows the total burden of fungal infections, and the number of infections classified according to the main risk factors as well as the rate per 100 000 inhabitants. The per capita GDP in 2013 was \$1047.

### Respiratory infections

Both infectious and non-communicable respiratory infectious diseases are significant public health problems in Senegal, including tuberculosis and asthma. Rates of these problems vary substantially across sub-Saharan African countries.<sup>12,13</sup> Tuberculosis (TB) is a public health priority in Senegal and the programme dedicated to its control includes screening the population mainly by microscopy and treating affected

**Table 1** Assumptions used in the calculations of burden.

Fungal disease	Prevalence	Annual incidence
Respiratory conditions		
CPA after TB	15% annual mortality/ surgical resection.	22% of those with a residual cavity and 2% of those without.
Total CPA	80% of CPA cases occur after TB	NE
ABPA	2.5% of adult asthmatics	NE
SAFS	33 of 10% adult asthmatics	
Fungal infections complicating HIV infection		
Cryptococcal meningitis	NA	7% of new AIDS patients
<i>Pneumocystis pneumonia</i>	NA	22% of new AIDS patients
Oesophageal candidiasis	NA	22% of new AIDS patients and 5% of remainder of HIV-positive people
Other serious fungal infections		
Candidaemia	NA	NE
Invasive aspergillosis	NA	NE
Mucormycosis	NA	1.2 cases per million
Mucosal, skin and superficial fungal infections		
rVVC	6% in women 15–50 years	NA
Dermatophytosis	12% of population	NE
Tinea capitis	24.9% of children age <15	NE
Mycetoma	NE	NA
Fungal keratitis	NA	NE

NE, not estimated; NA, not appropriate to estimate.

patients for free. In 2013, 11 568 cases of pulmonary TB were reported to the national authorities,<sup>7</sup> mostly in HIV-negative people; only 818 were infected with HIV. Based on previously published assumptions,<sup>9</sup> it is estimated that 685 new cases of CPA occurred following TB and that the 5-year period prevalence is 2160 cases (15.3/100 000). Chronic pulmonary aspergillosis (CPA) (including aspergilloma) occurs in Senegal as a series of 22 cases with aspergilloma was described by Ade *et al.* in 2011 [14]. We have assumed that TB is the underlying pulmonary problem in CPA for 80% of patients given a prevalence of about 2700 patients. The COPD prevalence of all GOLD (Global initiative for chronic Obstructive Lung Disease) stages was 22.9% of adults diagnosed with pulmonary problems other than TB attending hospital<sup>15</sup> supports this estimate, but there is no COPD population estimate.

The prevalence of asthma is moderate in Senegal. In children, the prevalence was 3% in a children's hospital in Dakar with 1% mortality.<sup>16</sup> In adults, data collected in one hospital showed a prevalence of 8.2%,<sup>17</sup> whereas another study done in workplaces found 3.2%.<sup>18</sup> The World Health Survey in 2002–2003 identified an asthma rate in adults of 3.72% and the incidence of wheezing of 8.4% in a sample of 2845 subjects.<sup>13</sup> We have therefore used an asthma prevalence in adults of 5% (369 200) and assuming 2.5% of adult asthmatics have ABPA,<sup>19</sup> 9976 patients with ABPA are likely (Table 2). SAFS was estimated by assuming that 33% of the worse 10% of adult asthmatics are sensitised to one or more fungi (Table 2), such as *Aspergillus fumigatus*, *Alternaria* spp., *Cladosporium* spp., *Candida albicans*, *Penicillium* spp. or *Trichopyton* spp., as common examples.<sup>20</sup> The SAFS estimate is 13 168 patients (Table 1). There may be some overlap between ABPA and SAFS, depending on the severity of asthma in ABPA and its definition, and the relative frequency of *Aspergillus* IgE or radioallergosorbant test (RAST) test positivity in SAFS.<sup>21</sup>

### Other serious fungal infections

In 2011 in Senegal, the precise number of patients with HIV was estimated at 59 000.<sup>22</sup> Among them, 18 032 were on ARVs, the number presenting with AIDS was 5224 and the estimated number with CD4 cell counts  $<350 \times 10^6 \mu\text{l}^{-1}$  (i.e. needing antiretroviral therapy based on 2010 WHO guidelines) was 19 000.<sup>23</sup> The numbers of patients starting ARVs were 3320 in 2011,<sup>3</sup> and the AIDS-related deaths in 2010 were 2600<sup>22</sup> and 1900 in 2012 (UNAIDS report).<sup>24</sup>

Cryptococcal meningitis is a frequent opportunistic infection in AIDS patients; and due to the simplicity of the test, diagnosis is not a problem anymore even in developing countries. CM was the cause of early mortality in HIV-infected patients accounting for between 13% and 44% in developing countries.<sup>25</sup> Several studies carried out in teaching hospitals in Dakar, reported that the prevalence of *Cryptococcus* infection in HIV-infected patients increased over time, from 2% to 7.8%<sup>26</sup> (between 1999 and 2003),<sup>27</sup> and we have used a 7% rate for the purposes of calculation (Table 1). This results in a total estimated number of CM of 366 cases (Table 2). In Senegal, 5400 (4300–6900) children aged between 0 and 14 years were HIV infected in 2013<sup>6</sup>; the CM prevalence is lower among children, but as this total is <10% of the adult number of cases and we have not adjusted the estimate downwards. One study showed 11 cases of CM in patients without HIV infection,<sup>26</sup> but the risk factors were unknown as the authors stated. We also estimated that as many as 1149 (22%) (Tables 1 and 2) of new AIDS patients develop *Pneumocystis pneumonia*.<sup>28</sup> Likewise 20% of new AIDS patients and 5% of those on ARVs develop oesophageal candidiasis.

The reported prevalence of mucormycosis is 0.2/100 000 inhabitants;<sup>29</sup> so, we have provisionally estimated the number of mucormycosis cases as 8–28 patients nationally. As we did not find any prevalence in Africa, our calculation was based on a population estimate from the United States of two cases of mucormycosis per million<sup>29</sup> and from France of 0.6 per million.<sup>30</sup> If the actual frequency is as high as in India (13/100 000), where diabetes is also common,<sup>31</sup> the actual number affected in Senegal could be as high as 1690.

### Skin infections

Cutaneous fungal infections are common in tropical areas and a main cause of medical consultation in Senegal. Some local prevalence studies are published in different areas of the country among school children and varied between 22% and 28.6% in the regions of Dakar and Thiès,<sup>32,33</sup> while in the South and the River Valley prevalence are lower 3.1% to 14.8%.<sup>34,35</sup> More recently, in 2002 a dermatophytosis rate in adults of 26.4% was found.<sup>36</sup> Based on these data and a conservative figure of 12%, we estimate that 1 560 000 people are affected by a cutaneous fungal infection (Table 2).

In addition, a study among women who use bleaching which is a method to make the skin lighter, by

using chemical products such as corticoids and hydroquinone (creams and lotions), showed that dermatophytic infection was the most common with 30% of women being infected, followed by candidiasis and nonspecific intertrigo and tinea versicolour.<sup>37</sup> In HIV-infected patients, onychomycosis was found in 4.6% and dermatophyte infection prevalence varied between studies (16%<sup>38</sup> and 23%<sup>39</sup>).

Children have a high rate of tinea capitis; 24.9% (average of two studies).<sup>32,33</sup> Those children who live in poor communities are most at risk. For all children across Senegal, we estimate that 1 523 700 children have tinea capitis (Table 2).

A series of 113 mycetomas were observed in LeDantec hospital (Dakar), 70% of fungal aetiology and 30% actinomycotic mycetoma.<sup>40</sup> It is not possible to make a population estimate as there is no risk factor denominator to make a viable estimate.

### Mucosal infections

Mucosal infections with *Candida* spp. are very common especially in women who often present with recurrent vulvovaginal candidiasis (rVVC).<sup>3–5</sup> Recurrent vaginal candidiasis is defined as more than three episodes by year.<sup>41,42</sup> But in Senegal no study has been published yet in this area. According to our calculation, rVVC occurs four times a year or more often ~191 228 women at the rate of 2712/100 000 females using a 6% proportion (Table 1). As a problem, rVVC is probably underappreciated in Senegal as rural women in rural areas do not often go to the hospital for clinical examination where they have to pay for their analysis. The prevalence found in a study done with pregnant

women and sex worker women recruited in different regions of Senegal reported a prevalence of 24%.<sup>43</sup> In HIV-infected patients, the prevalence of gastrointestinal candidiasis is reported as 4.6%.<sup>39</sup>

Assuming that 22% of those presenting with late stage HIV infection<sup>44</sup> (New AIDS patients) and those with CD4 counts under  $200 \times 10^6 \text{ l}^{-1}$  have oesophageal candidiasis and that 0.5% of those on ARVs<sup>45</sup>, we estimate 1946 cases in HIV patients (14/100 000) (Tables 1 and 2). This figure ignores all the non-HIV related cases, estimated to be an incidental finding in 0.13% of patients undergoing endoscopy in Korea.<sup>46</sup> In HIV-infected patients, oropharyngeal candidiasis (OPC) is the most common fungal infection,<sup>47</sup> but it was difficult to estimate with any precision.

Fungal keratitis also occurs in Senegal and five cases were reported by a team at Dantec hospital caused by *C. albicans* in four patients and *Acremonium* in one.<sup>48</sup>

### Discussion

Tuberculosis is often diagnosed in communities living in low socioeconomic conditions, where the close proximity promotes the dissemination of the infection. The National TB programme provides diagnosis and free treatment, and patients are reviewed every 2 weeks to monitor treatment. Although TB is probably the most common disease underlying CPA, numerous other conditions such as COPD and asthma are frequent in Senegal and could reasonably double the overall CPA estimate. Unfortunately CPA is not often diagnosed in TB patients, due to a lack of testing capability, although two recent surgical series clearly indicated a

**Table 2** Estimate of the burden of fungal diseases in Senegal.

Infection	Number of infections per underlying disorder per year			Total burden	Rate /100 K
	None	HIV/AIDS	Respiratory		
Oesophageal candidiasis	–	1946	?	1946	14
Recurrent vaginal candidiasis ( $\geq 4 \times$ /year)	191 228	–	–	191 228	2712 <sup>1</sup>
ABPA	–	–	9976	9976	71
SAFS	–	–	13 168	13 168	93
Chronic pulmonary aspergillosis	–	–	2700	2700	19
Mucormycosis	–	–	–	26	0.2
Cryptococcal meningitis	?	366	?	366	2.6
Pneumocystis pneumonia	–	1149	?	1149	8.2
Tinea capitis	1 523 700	?	?	1 523 700	10 806
Total burden estimated	1 714 959	2704	25 844	1 743 507	

ABPA, allergic bronchopulmonary aspergillosis; SAFS, severe asthma with fungal sensitisation.

<sup>1</sup>Females only.

local problem with CPA.<sup>14,17</sup> Diagnosis methods need to be adopted in Senegal, as there is no public laboratory doing *Aspergillus* serology, and many clinicians rely only on clinical findings and radiology only to make a diagnosis. As *Aspergillus* are common fungi in the environment, a positive culture do not always mean they are responsible for the pathology. This emphasises the need in Senegal for alternative diagnostic strategies.

Asthma appears to be more a problem in urban areas of most African countries unlike rural areas,<sup>49</sup> but this generalisation could be skewed because the rural population does not often go to the hospital for diagnosis. On the other hand, most African cities have pollution problems, and this could be one trigger for asthma. Severe asthma exacerbations and emergencies are not always well handled in Senegal and so many patients probably die of this pathology without being diagnosed. In Senegal more studies are need to be done in order to assess the prevalence of severe and brittle asthma to identify possible solutions, including antifungal therapy for SAFS patients.

Cryptococcal meningitis is now often diagnosed in immunocompromised patients in Senegal as direct examination with India ink and culture is relatively simple and does not require expensive equipment. Thus, the reasons for the low rate of CM before 1999 probably reflect a lack of research, which underestimated the prevalence. This single incidence figure also ignores any cases that might be identified by screening in the community. There could be also some duplication of cases between these two populations of patients with CM, possibly 10%, but on the other hand we have not estimated community cases not treated in hospitals. Now a routine research of *Cryptococcus* is available for HIV-positive patients. Although a study reported CM in three non-immunocompromised patients,<sup>50</sup> we have not attempted to estimate the annual incidence in non-AIDS patients.

The estimate of *Pneumocystis pneumonia* is from the early 1990s and may overestimate the annual incidence as co-trimoxazole prophylaxis is more common 20 years later. On the other hand, the annual number of new AIDS cases is high at >5000 and the proportion estimated to have PCP is low compared with other countries and based on relatively insensitive diagnostic techniques. Clearly an updated estimate is required. Our PCP estimate (Table 2) ignores other patients developing PCP including malnourished children and other severely immunocompromised patients.

In Senegal, other opportunistic diseases are also seen in immunocompromised patients such as

candidaemia, invasive aspergillosis, mucormycosis and histoplasmosis, but their prevalence is likely to be underestimated because many clinicians do not suspect them and *Aspergillus* antigen tests are not available. Malignant haematological conditions are diagnosed in Senegal but the incidence is not well known, and fungal infections are not often searched for in these patients. Fungal opportunistic infections are more common in West Africa that it seems, and so the diagnosed cases probably represent the tip of an iceberg.

Nosocomial infections due to fungi are also not well known in Senegal and studies need to be done in patients hospitalised for a long period of time in high-risk services like intensive care for adults, neonates and paediatrics, oncology, renal medicine, burns, orthopaedics and others. Studies are needed to better clarify the frequency of fungal infections in some of these risk patients. In Dantec hospital, the qualitative fungal flora composition was determined by our laboratory; and *C. albicans* and *A. fumigatus* were isolated at 15.5% and 11.1%, respectively.<sup>51</sup>

Recurrent mucosal infections especially vaginal have a high incidence in high-risk populations including sex workers and pregnant women. *Candida albicans* is the most prevalent species in vaginal infections diagnosed in Senegal but this is based on the blastese (germ tube test) test which cannot differentiate *C. albicans*, *C. africana* and *C. dubliniensis*. A study done in Fann Hospital (Senegal) showed the presence of the recently described *C. africanum*, using molecular testing; not routinely used in laboratory diagnosis in Senegal.<sup>52</sup>

In HIV-positive patients, the point prevalence of oral candidiasis was 53%,<sup>38</sup> but in reality is more common than this over a period of a year, typically 90% in those with CD4 cell counts under  $200 \times 10^6 \text{ l}^{-1}$ . We would therefore expect over 13 500 patients with HIV to develop oral candidiasis. We cannot estimate with any certainty the number of non-HIV-infected people with oral candidiasis, including newborns, denture stomatitis, following antibiotic or inhaled corticosteroid therapy or complicating cancer, malnutrition and general debility.

Skin infections are common in immunocompetent patients. Fungal agents responsible are usually the dermatophytes and *C. albicans*. Prevalence based on laboratory diagnosis may underestimate burden as direct examination and culture are not very sensitive. The climate and the conditions of hygiene in Senegal could be the reasons of high prevalence. Tinea capitis is often diagnosed in children mostly living in poor

hygienic conditions making the contamination and the propagation very easy and recurrent. In Senegal, skin bleaching is used by around 25% of women<sup>53</sup> and causes economic and health problems. In fact it costs women 1 081 658 CFA (US \$2207) monthly, ~20% of their total income.<sup>54</sup> Skin bleaching is responsible for many skin disorders including infections (49%).<sup>37</sup> While fungal infections are common in women using bleaching, more studies need to be done to assess the real burden of fungal infections in that population.

Mycetomas are present in Senegal and mostly in rural areas; unfortunately the diagnosis is usually late, because of the chronic nature of the infection and the absence of healthcare specialist in those areas. The two forms of mycetomas are diagnosed in our laboratory. The most clinical forms are localised in the foot and when severe they are complicated by bacterial infection and chronic ill health. As they are usually diagnosed in young people who are working, like farmers, fishermen, these uncommon infections are economically severe.

## Conclusion

These results demonstrate that fungal infections are a cause of public health concern in Senegal and need to be more studied to determine their prevalence in the overall population. To do so, clinicians need to be trained and to be made aware of these infections, in order to improve the diagnosis and treatment. This article provides the first estimate of the burden of the major serious fungal infections in Senegal. Some of the data used here are not recent or are inferred using information from outside Senegal and therefore epidemiological studies are required to determine the exact incidence and prevalence of these infections and trends over time.

## Conflict of interest

ASB and DN declare no conflict of interest. DWD holds Founder shares in F2G Ltd a University of Manchester spin-out antifungal discovery company, in Novocyt which markets the Myconostica real-time molecular assays and has current grant support from the National Institute of Allergy and Infectious Diseases, National Institute of Health Research, NorthWest Lung Centre Charity, Medical Research Council, Astellas and the Fungal Infection Trust. He acts as a consultant to T2 Biosystems, GSK, Sigma Tau, Oxon Epidemiology and Pulmicort. In the last 3 years, he has been paid for talks on behalf of Astellas, Dynamiker, Gilead,

Merck and Pfizer. He is also a member of the Infectious Disease Society of America Aspergillosis Guidelines and European Society for Clinical Microbiology and Infectious Diseases Aspergillosis Guidelines groups. He is also President of the Global Action Fund for Fungal Infections.

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