Diagnostic options for pulmonary fungal diseases in Africa

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Shareable abstract (@ERSpublications)
Implementation of the WHO essential tests for pulmonary fungal diseases in Africa is a good start for improving respiratory health in the region. Training in spirometry, CT scanning and bronchoscopy is required in many countries. https://bit.ly/3HQ1sBN

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Abstract

Background Fungal lung diseases are global in distribution and require specific tests for diagnosis. We report a survey of diagnostic service provision in Africa.

Methods A written questionnaire was followed by a video conference call with each respondent(s) and external validation. To disseminate the questionnaire, a snowball sample was used.

Results Data were successfully collected from 50 of 51 African countries with populations >1 million. The questionnaire was completed by respondents affiliated with 72 health facilities. Of these 72 respondents, 33 (45.8%) reported data for the whole country while others reported data for a specific region/province within their country. In the public sector, chest X-ray and computed tomography are performed often in 49 countries (98%) and occasionally in 37 countries (74%), and less often in the private sector. Bronchoscopy and spirometry were done often in 28 countries (56%) and occasionally in 18 countries (36%) in the tertiary health facilities of public sector. The most conducted laboratory diagnostic assay was fungal culture (often or occasionally) in 29 countries (58%). In collaboration with the Africa Centre for Disease Control and Prevention, regional webinars and individual country profiles provided further data validation.

Conclusion This survey has found a huge disparity of diagnostic test capability across the African continent. Some good examples of good diagnostic provision and very high-quality care were seen, but this was unusual. The unavailability of essential testing such as spirometry was noted, which has a high impact in the diagnosis of lung diseases. It is important for countries to implement tests based on the World Health Organization Essential Diagnostics List.

Introduction

Inhalation of fungal spores of both opportunistic and true fungal pathogens affects both immunocompromised and immunocompetent people. The endemic fungi *Histoplasma capsulatum*, *Blastomyces* spp., *Coccidioides* spp., *Talaromyces marneffei* and *Paracoccidioides brasiliensis* are primary pulmonary pathogens in immunocompetent people [1, 2], with occasional infections caused by *Cryptococcus* spp. and *Sporothrix* spp. [2]. The commonest opportunistic fungi causing lung disease are *Aspergillus* spp., the mucoraceous fungi and *Pneumocystis jirovecii*, with the former two responsible for upper and lower respiratory tract infection [3]. *Aspergillus* spp., *Coccidioides* spp., *H. capsulatum* and Mucorales can cause chronic and ultimately fatal lung disease [4], including chronic pulmonary aspergillosis (CPA) and simple aspergilloma. Significant exposure to a large number of airborne fungi (notably *Aspergillus* spp., *Alternaria* spp. and *Cladosporium*) can precipitate the onset and exacerbation of asthma, chronic obstructive pulmonary disease (COPD) and allergic fungal rhinosinusitis.

The diagnosis of pulmonary fungal diseases rests on a combination of clinical, radiological, microbiological and serological findings, occasionally supported by histopathology [5, 6]. For example, invasive aspergillosis can be diagnosed by the detection of cavitary lesions with or without halo signs, consolidations or air crescent signs using computed tomography (CT) scanning and with galactomannan antigen detection in plasma, serum, bronchoalveolar lavage fluid or cerebrospinal fluid [7]. The detection of *Aspergillus* IgG is the cornerstone of CPA diagnosis and it is usually also detected in allergic bronchopulmonary aspergillosis and *Aspergillus* bronchitis in asthma, cystic fibrosis and bronchiectasis patients [5]. Pneumocystosis is diagnosed by detecting *P. jirovecii* DNA using quantitative real-time PCR in a respiratory tract specimen [7] or by direct microscopy, which is less sensitive than PCR.

Diagnosis of pulmonary fungal diseases remains challenging in Africa because most diagnoses are based on clinical presentation alone. Suspicion of pulmonary fungal diseases requires knowledge and experience because most clinical presentations are subtle; presenting with atypical signs and symptoms makes it easy to misdiagnose. Moreover, clinical presentation of pulmonary fungal diseases overlaps with that of other lung diseases/conditions, thus complicating the diagnosis [5]. The misdiagnosis or underdiagnosis of pulmonary fungal infections affects patient management and treatment outcomes. The mismanagement of patients includes unnecessary antibiotic treatment that might lead to antimicrobial resistance and associated complications (increased hospital stay and healthcare costs for patients and institutions, with regional and global impacts) and death. Undiagnosed lung fungal infection is often progressive with high mortality [8]. The Africa region has a high societal cost associated with undiagnosed fungal infections because it is estimated to have 70% of the global HIV-infected population [9], which is a key population at increased risk of opportunistic fungal infection, with limited capacity for fungi diagnosis [10, 11].

The capacity for proper fungal disease diagnosis in Africa is further complicated by the limited capacity for collecting recommended clinical samples for pulmonary fungal diseases, including bronchoalveolar lavage, tracheal aspirate and lung biopsy, which are all technically demanding procedures requiring highly trained personnel [12]. Achieving a diagnosis using histology is compromised by the limited number of specialists and the difficulty in obtaining appropriate biopsy samples [13, 14]. Antibody serology is generally poorly studied for fungal disease in Africa, with low specificity and uncertain sensitivity for some conditions. *Aspergillus* antigen testing in immunocompromised patients is also poorly studied in Africa, resulting in delayed diagnosis and an uncertain number of false positive results [15].

In the recent decade there has been marked improvement in the diagnosis of pulmonary fungal diseases worldwide using CT [10], PCR [16] and detection of circulating galactomannan or *Aspergillus* antigen [17]. However, none of these tests is routinely used in African settings for clinical management of patients. This survey was carried out to document the availability, accessibility and usage of different fungal diagnostic methods in Africa.

Methodology

The survey was conducted in six phases: 1) questionnaire development with later adaptation and improvement; 2) questionnaire completion by in-country respondents; 3) questionnaire review and data analysis by a Global Action for Fungal Infections (GAFFI) team and then video conference call with respondent(s); 4) external validation from public or private sources; 5) country validation *via* video conference call with country leaders in relevant topics (*i.e.* HIV/AIDS, laboratory coordination) and/or Ministry of Health representatives, where possible; and 6) collaboration with Africa Centres for Disease Control and Prevention (Africa CDC) in regional webinars and a further round of country validation using country diagnostic availability profiles.

Questionnaire development

The final iteration of the questionnaire consisted of seven sections. Part 1 covered the respondent(s), including their role, facility and whether their country had a biosafety level 3 (BSL-3) laboratory with or without protocol for handling pathogenic fungi. Part 2 covered the World Health Organization (WHO)-recommended list of essential fungal diagnostic tests. The availability of diagnostic tests was classified in two ways: type of facility providing the diagnostic test and regularity of use. Facility type was classified as 1) not available anywhere, 2) private centre, 3) specialist/university centre, 4) district hospital or 5) community health centre. For each diagnostic test, respondents were asked to select how often it was performed at each type of facility, responding "often", "occasionally", "rarely" or "never". This provided a granular, multidimensional view of the availability of each diagnostic test. There were also two further fields to provide additional context regarding availability of diagnostic tests and frequency of use: one for any comments, including reasons that procedures are not performed regularly (*e.g.* broken equipment, lack of trained personnel); and one asking about payment, using four classifications, for which respondents were asked to list any that apply: 1) patient pays, 2) insurance pays, 3) government/health service pays or 4) a charity or foundation pays. The final part of the questionnaire covered essential clinical procedures and radiology and used the same tabular structure as Part 2, recording the level of facility undertaking the test, the regularity with which it was done and who pays for it, along with a comments section. We also asked for approximate costs of several diagnostic tests/procedures. Additional open questions regarding additional fungal diagnostic tests used in the respondent's country and any other comments completed the survey (supplementary file 1).

Questionnaire completion in country

All African countries with populations of >1 million were contacted. To disseminate the questionnaire, a snowball sample was used, involving GAFFI Ambassadors and existing networks of contacts. Respondents were encouraged to reach out to colleagues in areas where they did not have first-hand knowledge. It proved difficult to find medical or laboratory professionals willing to complete the questionnaire in a few countries. In order to ensure thorough coverage, additional responses were sought from the larger countries, in most cases from different parts of the country. After receipt of a completed questionnaire, online meetings were organised to provide clarification, as well as qualitative data and narrative. In some cases, the questionnaire was filled in during this meeting. Translators were used when necessary. Publications from countries were also checked to ensure that reported results aligned with questionnaire responses.

Data compilation and display

Data were compiled and visualised using QGIS software and Natural Earth vectors (www.naturalearthdata.com) to design maps showing each diagnostic test's coverage across the continent. Population estimates were taken from the Central Intelligence Agency World Factbook (www.cia.gov/the-world-factbook).

In-country validation

Collected data and country profiles were distributed to relevant local stakeholders and experts with the purpose of verifying data and/or correcting inaccuracies. Online validation meetings were held with stakeholders, including representatives of the Ministry of Health and the national laboratory service, as well as the initial questionnaire respondent(s), and again with the participation of Africa CDC.

Results

Health institution and reporting

Availability and usage frequency data of key diagnostic tests for fungal diseases were successfully collected from 50 of 51 African countries (98%) with populations >1 million (including Somaliland, a self-declared but not widely recognised country that is claimed by Somalia and Puntland, an autonomous state within Somalia). Countries omitted from the survey were Cabo Verde, Comoros, Djibouti, Sao Tome and Principe, Seychelles and Western Sahara (plus several territories of France and Spain such as Réunion and Melilla) and we were unable to glean any data from Lesotho. The questionnaire was completed by respondents affiliated to 72 health facilities distributed in the surveyed countries (supplementary figure S1). The number of responses varied between countries, with Tanzania having the highest with seven respondents, followed by Nigeria and Democratic Republic of Congo with four respondents each; Cameron and Guinea-Bissau with three respondents each; Angola, Egypt, Gabon, Mauritania and South Africa with two respondents each; and the remaining countries with one respondent each. A total of 33 of 72 respondents (45.8%) reported data for the whole country while others reported data on the specific region of the affiliated health facility. Of the 72 respondents involved in this survey, 40 were medical laboratory professionals and 22 were medical doctors, physicians, pathologists or Centre directors. The collected data were from different levels of health facilities (private centres, specialist/university centres, district hospitals and health centres). Online participation with the Africa CDC involved 191 stakeholders

TABLE 1 Pattern of pulmonary fungal disease key diagnostic tests per regularity of use in different levels of health facilities in the surveyed area from 50 countries or states surveyed

Frequency of testing	Public sector n (%)	Population (millions)	Private sector n (%)	Population (millions)
Chest X-ray				
Often	46 (92)	1336.9	35 (70)	1039.4
Occasionally	3 (6)	31.7	4 (8)	128.2
Rarely	1 (2)	2.0	3 (6)	25.2
Countries use	50 (100)	1370.5	42 (84)	1192.8
Countries never use	0	0	8 (16)	177.7
CT				
Often	27 (54)	577.8	23 (46)	613.0
Occasionally	10 (20)	526.4	12 (24)	530.0
Rarely	5 (10)	200.0	3 (6)	36.9
Countries use	42 (84)	1304.1	38 (76)	1201.9
Countries never use	8 (16)	66.4	12 (24)	168.6
Radiologist report				
Often	35 (70)	1088.7	31 (60)	674.9
Occasionally	6 (12)	211.1	3 (6)	169.5
Rarely	5 (10)	59.8	5 (10)	105.4
Countries use	46 (92)	1354.7	39 (78)	940.7
Countries never use	4 (8)	15.9	11 (22)	429.8
Bronchoscopy				
Often	15 (30)	320.0	13 (26)	340.1
Occasionally	13 (26)	421.1	9 (18)	274.6
Rarely	11 (22)	499.0	6 (12)	438.1
Countries use	39 (78)	1239.6	28 (56)	1052.8
Countries never use	11 (22)	130.9	22 (44)	317.7
Spirometry				
Often	13 (26)	286.1	12 (24)	285.9
Occasionally	5 (10)	110.6	8 (16)	208.0
Rarely	11 (22)	736.1	7 (14)	570.7
Countries use	29 (58)	1132.8	27 (54)	1064.6
Countries never use	21 (42)	237.7	23 (46)	305.9
Fungal culture				
Often	22 (44)	747.9	13 (26)	418.2
Occasionally	7 (14)	173.3	7 (14)	240.6
Rarely	11 (22)	374.1	7 (14)	371.4
Countries use	39 (78)	1289.4	27 (54)	1030.3
Countries never use	10 (20)	60.2	23 (46)	335.4
***Aspergillus* antibody**				
Often	1 (2)	51.4	2 (4)	98.0
Occasionally	3 (6)	52.8	4 (8)	70.6
Rarely	7 (14)	347.2	6 (12)	261.8
Countries use	11 (22)	495.0	12 (24)	474.0
Countries never use	39 (78)	875.5	38 (76)	896.5
***Pneumocystis* PCR**				
Often	3 (6)	118.6	2 (6)	133.5
Occasionally	4 (6)	77.6	2 (4)	13.4
Rarely	4 (14)	123.6	3 (6)	126.5
Countries use	11 (22)	261.4	9 (18)	214.9
Countries never use	39 (78)	1109.1	41 (82)	1155.6

CT: computed tomography.

from 43 African countries, including representatives of Ministries of Health, civil society organisations, mycology experts, dermatologists, and lung disease and HIV/AIDS/tuberculosis (TB) care providers.

Radiological procedures

In the public sector, chest X-ray, CT, radiology reporting, bronchoscopy and spirometry procedures were not available in 0, 8, 6, 11 and 21 countries, respectively. In the private sector, chest X-ray, CT, radiology

reporting, bronchoscopy and spirometry were not available in 8, 12, 13, 22 and 23 countries, respectively (table 1 and supplementary figure S2).

Chest X-ray was used often in 92% of countries at some level of the health system, but only occasionally in three countries (6%) and rarely in Guinea-Bissau (2%) (table 1 and figure 1a). In Guinea-Bissau, there was only a single portable X-ray system and in Gabon and Cameroon chest X-rays were performed infrequently. By contrast, CT scanning in the public sector was unavailable in eight countries (16%) (Angola, Equatorial Guinea, Guinea-Bissau, Sierra Leone, Somalia (including Somaliland and Puntland) and South Sudan) and rarely used in another five countries (12%) (Burkina Faso, Ethiopia, Malawi, Namibia and Uganda) (table 1). In the private sector, the most conducted radiological procedure was chest X-ray (78%), followed by CT scan (70%). In terms of usage regularity, chest X-ray was performed often in 93%, 80%, 70% and 50% of specialist/university centres, private centres, district hospitals and health centres, respectively. A chest X-ray varied in price from $4 in Uganda to $200–$300 in Puntland, but with an average of $13–$40 including the report. CT scanning was more expensive (including the report), varying from $15–$20 in Eritrea and Mali up to $300 in Morocco and Puntland. We did not ask about the use of digital *versus* conventional radiology techniques.

Reporting by radiologists in the public sector was done often in 35 countries (70%, population 1089 million) and occasionally in another six (12%, population 211 million) (table 1 and figure 1b). Reporting by a radiologist was not undertaken in the public sector in Angola, Equatorial Guinea, Guinea-Bissau or South Sudan (population 16 million) and was rare in Burundi, Rwanda, Cameroon, Namibia and Somaliland (population 60 million). We did not enquire about the use of computer-aided diagnosis, principally used for TB, because none of these systems has been developed for diagnosing fungal lung disease.

Clinical procedures

Spirometry is a key investigation for breathlessness, and can establish the diagnosis of asthma, COPD and post-TB obstructive lung disease. Spirometry was regularly undertaken in 13 countries in public facilities (population 286 million) and in 12 countries in private clinics and hospitals (table 1 and figure 2a). Five other countries did spirometry occasionally (population 111 million). However, 21 countries in Africa did no spirometry at all in the public health service (population 238 million), and it was rarely undertaken in another 11 countries (combined population 736 million). In some countries, spirometry was only undertaken in the public sector (*i.e.* Algeria, Rwanda and Eritrea) and the converse was true in Burkina Faso, Equatorial Guinea, Somalia, Sudan and Zimbabwe. The cost of spirometry varied from $5 (in Eritrea) to ∼$100 (in Liberia and Morocco).

There were 15 countries providing a routine or frequent bronchoscopy service in the public sector, covering a population of 320 million people, and another 13 countries with an occasional service, covering about 421 million people (table 1 and figure 2b). In some countries, *e.g.* Cameroon, Equatorial Guinea and Somalia, this service was provided exclusively by the private sector. These three countries and eight others had no public sector bronchoscopy service (population 131 million). An additional 11 countries rarely did bronchoscopy in the public sector (population 498 million). This was mirrored in the private sector in most of these countries, including Botswana, Ethiopia, Nigeria and Tanzania. A total of 32 private centres (44.5%) and 46 specialist centres (63.9%) reported conducting bronchoscopy. In terms of usage regularity, bronchoscopy was the most-often performed test by 14 private centres (43.8%) and 21 specialist/university centres (45.7%) (table 1). Bronchoscopy procedure costs ranged from $10 in Eritrea to $60–$300 in Morocco.

The respondents identified many common obstacles preventing more procedure use including equipment shortage, lack of trained personnel to perform tests, lack of awareness among physicians of the value of a particular diagnostic test, low demand for some appropriate tests and high costs. A total of 58 facilities (80.6%) mentioned the payment method for radiological and clinical procedures while 14 (19.4%) did not. In 19 of the 58 facilities (32.8%) the patients paid the full charge, in three facilities (5.2%) the costs were covered by the government, and in one facility (1.7%) costs were covered by insurance. In 35 facilities (60.3%) the procedure cost was partially paid by the patient and the remaining amount handled by another agent (government, insurance, foundations).

WHO-recommended essential in vitro *diagnostics*

The WHO-recommended essential laboratory diagnostics for pulmonary fungal disease diagnosis were used in both public and private sectors in the surveyed countries with varying frequencies. In the private sector, the most conducted diagnostic procedure was fungal culture (40%). In terms of usage regularity, fungal culture was the most frequently performed test, at 53.1%, 50%, 21.4% and 33.3% of tests for specialist/university centres, private centres, district hospitals and health centres, respectively. Ten countries

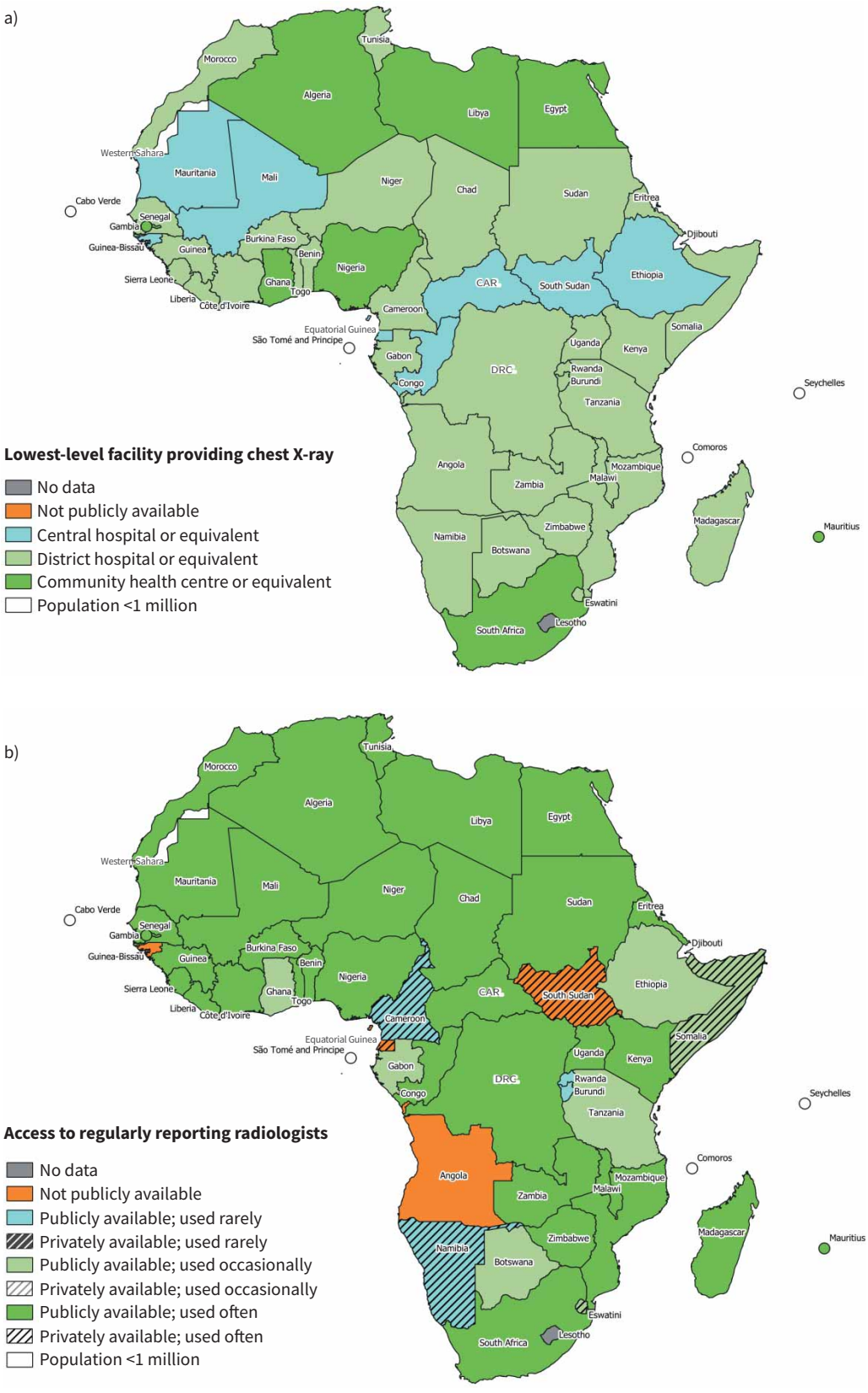


FIGURE 1 a) Provision of chest X-ray in different setting, using a hierarchical approach: seven countries (*e.g.* Ethiopia) only use chest X-ray at central teaching hospitals, 33 countries (*e.g.* Benin) use chest X-rays at these hospitals and at district hospitals, and 10 countries (*e.g.* Ghana) provide chest X-rays at these facilities and in

community clinics. b) Access to regularly reporting radiologist. CAR: Central African Republic; DRC: Democratic Republic of the Congo.

never performed fungal culture in the public sector, although in Equatorial Guinea and Liberia it was available in the private sector. In Angola and Tanzania, it was rarely done in the public sector, but more often in the private sector. The survey did not ask about fungal identification or susceptibility testing, or the cost of fungal culture.

The survey did collect data about BSL-3 laboratories. The survey found that 45 facilities/countries (63.9%) had a BSL-3 operating laboratory; however, only 14 of these (31.1%) had a protocol to handle pathogenic fungi, several of which are BSL-3 organisms (figure 3). One university teaching hospital from Mozambique had fungal disease diagnosis protocols in a level two health laboratory and two respondents reported not knowing about the availability of any BSL-3 protocol. Most health facilities with BSL-3 laboratories used them for TB and viral diagnosis, without a protocol for fungal cultures.

Pneumocystis PCR was reported to be conducted in 11 private centres (15.3%) and 17 specialist centres (23.6%). However, it was not available in 39 countries in the public sector and 41 countries in the private sector (table 1). In Kenya and Zimbabwe, it was only available in the private sector. In terms of usage regularity, *Pneumocystis* PCR was the most frequently performed test in six private centres (54.5%) and four specialist/university centres (5%).

Aspergillus IgG antibody testing was reported to be regularly done only in Morocco; occasionally done in Tunisia, Niger and Chad; and never done in 39 countries in either the public or private sector (table 1). Overall, *Aspergillus* IgG antibody testing was performed in 13 private centres (18.1%) and 14 specialist centres (19.4%). We did not survey the use of *Aspergillus* IgE antibody.

Several commonly encountered obstacles were identified: shortage of equipment in some laboratories, difficulty in ordering and paying for kits and reagents, the lack of trained laboratory personnel to perform each test, the lack of awareness among physicians leading to low demand for appropriate tests and the high cost. A total of 52 facilities (72.2%) mentioned the payment method for the diagnostic cost, while 20 (27.8%) did not. In 13 of the 52 facilities (25%) the patients paid the full charge, in three facilities (5.8%) costs were covered by the government, in two facilities (3.8%) costs were covered by insurance and in 34 facilities (65.4%) the diagnostics cost was partially paid by the patient and the remaining amount handled by another agent (government, insurance, foundations).

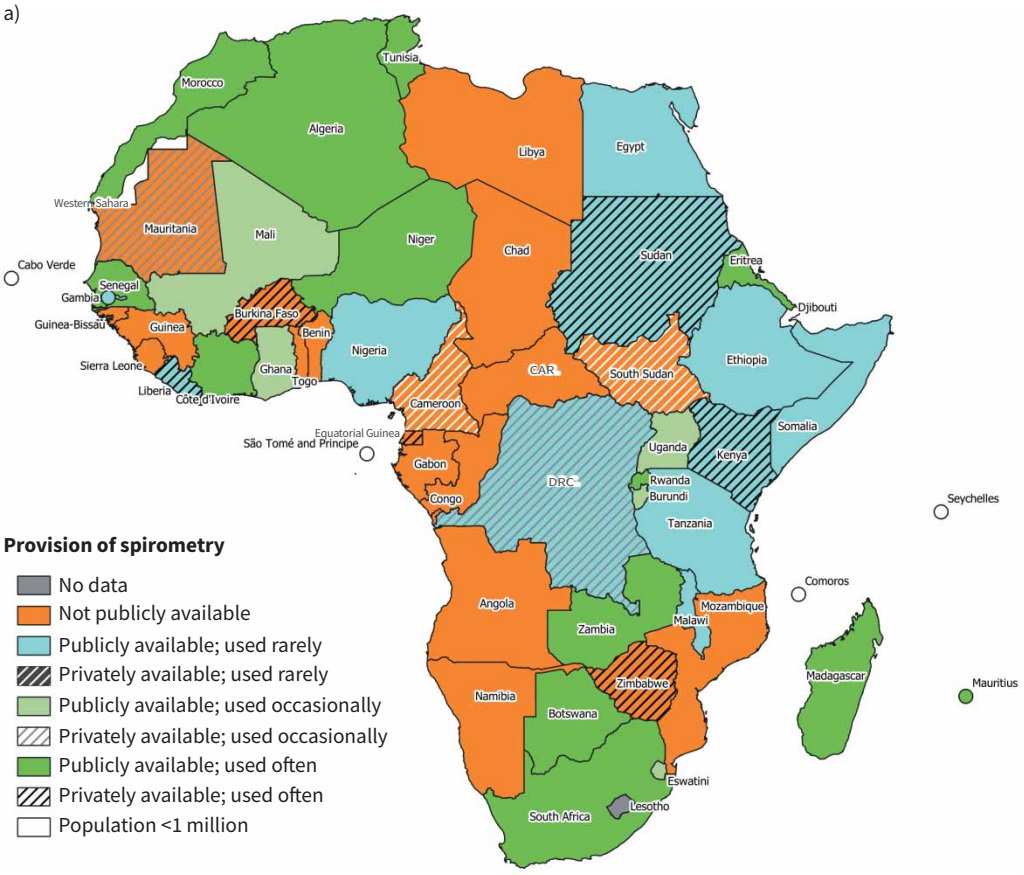
Discussion

All countries in Africa are classified as low-income and middle-income countries, and these countries encompass more than 1.2 billion people. Multiple predisposing factors expose people to infectious diseases, including fungal diseases. Because most people in Africa live in rural areas, they are directly in contact with environmental fungi [18–21]. Pulmonary diseases (notably asthma, COPD and TB) are prevalent in Africa and can be complicated by fungal disease, especially aspergillosis, pneumocystosis, mucormycosis and endemic mycoses, all reported either in global or country-based epidemiology reports [22–26]. The true burden of fungal diseases is incompletely estimated (partly because of inadequate diagnostics) in Africa, despite the magnitude of these fungal diseases usually exceeding healthcare capabilities [23, 24]. In this context, the collected data in this survey reveal that there is a great shortage of key diagnostic tools for pulmonary fungal diseases.

Concerning radiological procedures, CT is completely unavailable in the public sector of 16% and in the private sector of 24% of surveyed countries. Moreover, even if available, usage frequency does not exceed 68.6% in the best conditions, which reflects a lack of awareness of its importance (or unaffordability) not only for radiographic diagnosis of pulmonary fungal diseases but also for other conditions. In terms of clinical procedures, bronchoscopy and spirometry are completely unavailable in the public sector in 22% and 42%, respectively, and in the private sector in 44% and 46%, respectively, of the surveyed countries. These results indicate weak healthcare systems in a considerable number of African countries and an inability to adequately care for a well-known risk group of patients susceptible to fungal diseases, especially those with COPD and asthma.

Other rapid diagnostic tools like *Aspergillus* antibody testing and *Pneumocystis* PCR are not available in 78% of surveyed countries. The lack of *Pneumocystis* PCR greatly impacts on the diagnosis of pneumonia

a)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Mauritania
Mali
Niger
Chad
Sudan
Eritrea
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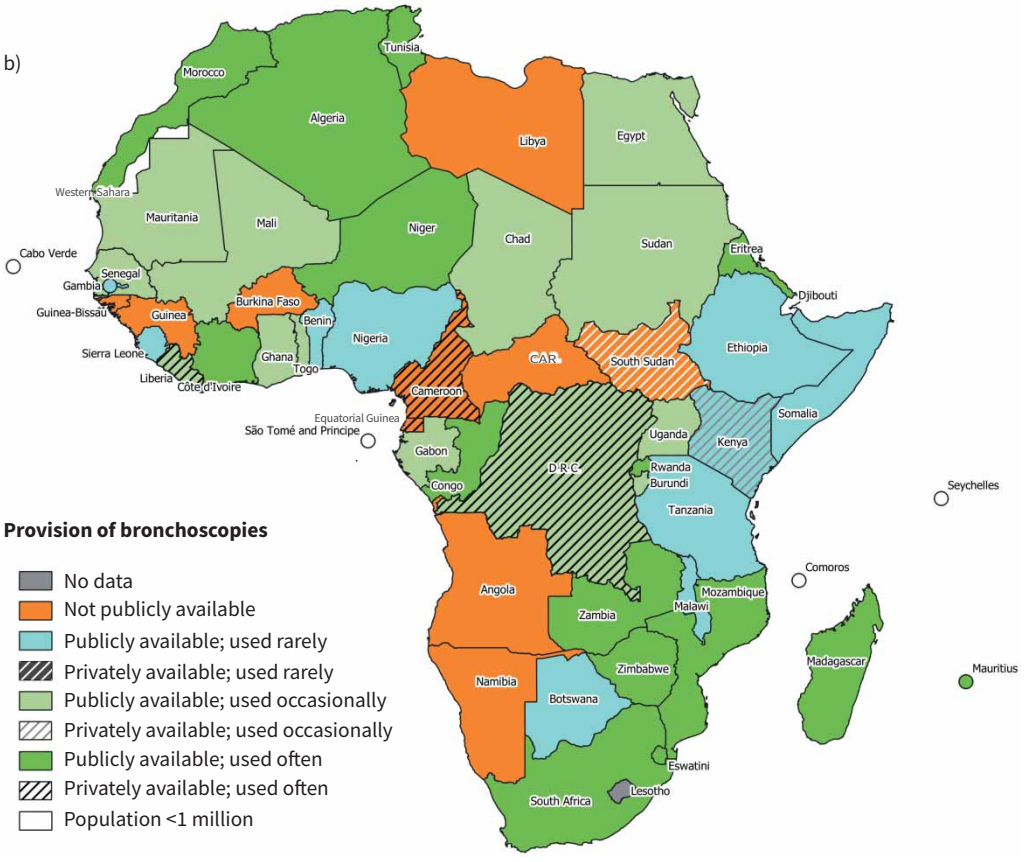
Senegal
Gambia
Guinea-Bissau
Guinea
Burkina Faso
Benin
Nigeria
Ethiopia
Sierra Leone
Liberia
Côte d'Ivoire
Ghana
Togo
CAR
South Sudan
Cameroon
Somalia
Equatorial Guinea
São Tomé and Príncipe
Uganda
Kenya
Gabon
DRC
Rwanda
Burundi
Congo
Seychelles
Tanzania
Comoros
Angola
Mozambique
Malawi
Zambia
Madagascar
Mauritius
Zimbabwe
Namibia
Botswana
Eswatini
Lesotho
South Africa
Provision of spirometry
No data
Not publicly available
Publicly available; used rarely
Privately available; used rarely
Publicly available; used occasionally
Privately available; used occasionally
Publicly available; used often
Privately available; used often
Population <1 million

b)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Senegal
Gambia
Guinea-Bissau
Guinea
Burkina Faso
Benin
Nigeria
Ethiopia
Sierra Leone
Liberia
Côte d'Ivoire
Ghana
Togo
CAR
South Sudan
Cameroon
Somalia
Equatorial Guinea
São Tomé and Príncipe
Uganda
Kenya
Gabon
DRC
Rwanda
Burundi
Congo
Seychelles
Tanzania
Comoros
Angola
Mozambique
Malawi
Zambia
Madagascar
Mauritius
Zimbabwe
Namibia
Botswana
Eswatini
Lesotho
South Africa
Provision of bronchoscopies
No data
Not publicly available
Publicly available; used rarely
Privately available; used rarely
Publicly available; used occasionally
Privately available; used occasionally
Publicly available; used often
Privately available; used often
Population <1 million

FIGURE 2 a) Provision of spirometry. b) Frequency of bronchoscopy in tertiary health facilities. CAR: Central African Republic; DRC: Democratic Republic of the Congo.

in children, often in the context of advanced HIV disease. The generally low suspicion index for fungal infection among clinicians has led to limited use of fungal culture even when available. In this survey, fungal culture as a diagnostic tool was available in 78% of the surveyed countries. This low suspicion index is further emphasised by the fact that most respondents assume that fungi mainly cause skin infection and culture would only be requested by dermatologists, which reflects the absence of suspicion of invasive and chronic pulmonary fungal diseases among African physicians.

This survey confirms that few facilities (31% of those with a BSL-3 laboratory, which were available in 64% of surveyed institutions) in Africa are able to handle highly pathogenic fungi. This is significantly lower than what has been reported in Asia, where ~80% of hospitals have a (BSL-3) mycology laboratory [27]. The limited availability of BSL-3 laboratories with pathogenic fungi-handling protocols is a proxy indicator for a lack of mycology-trained specialists in the surveyed countries.

With the exception of countries with universal health insurance like Rwanda, Tunisia and Algeria, where coverage is reported to be >80% [28], health insurance coverage in Africa is reported to be very low, at <20% [29]. This forces most patients and families to cover their healthcare costs privately and consequently often leads to delays in seeking proper health services. These findings were also observed in the current survey: ~25–32.8% of patients fully covered the costs of diagnostic, radiological and clinical investigations privately, and ~62–70% reported partial cover. Only 5% were fully covered by either government or health insurance.

The implications of these results are profound for the African continent. There is an urgent need to increase reliance on CT of the lungs because it is the preferred method for radiographic diagnosis of fungal diseases

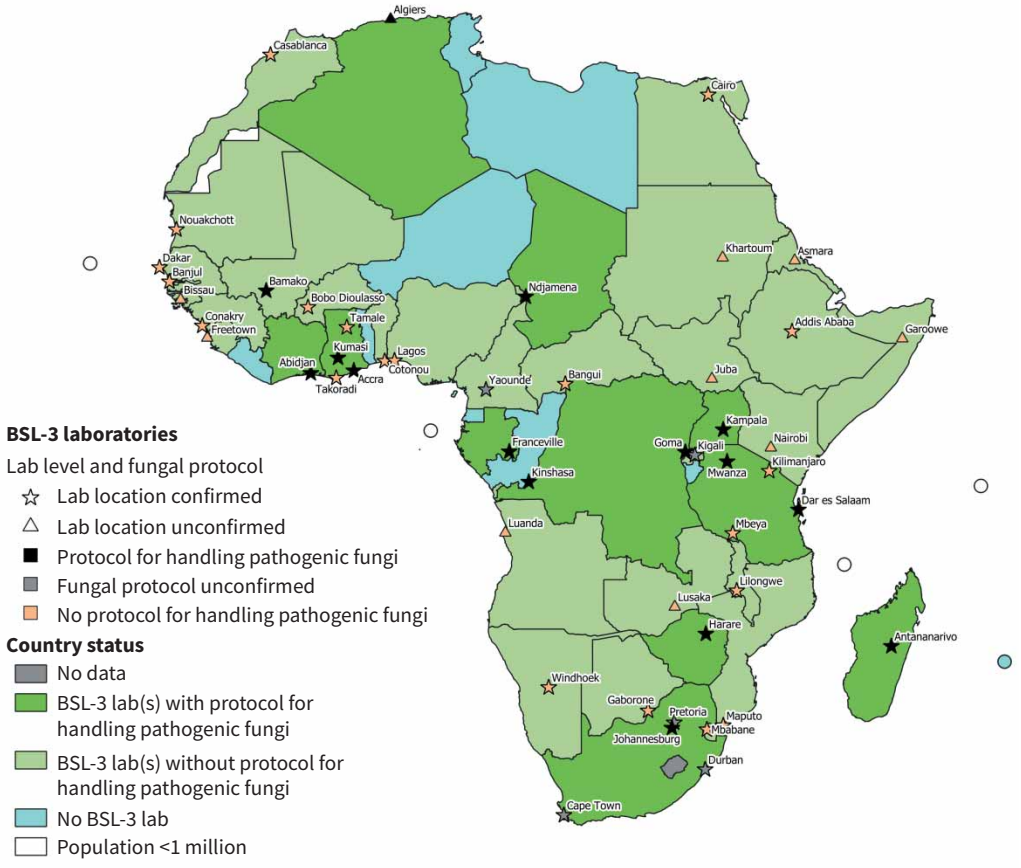

FIGURE 3 Biosafety level 3 (BSL-3) laboratories.

and important differential diagnoses such as lung cancer, and other structural or inflammatory conditions [7, 30]. Provision of spirometry and bronchoscopy equipment is also needed, with linked training for healthcare workers in their use. They are important in the diagnosis of asthma, COPD, interstitial lung disease and cancer and enable the evaluation of known or suspected respiratory infections and recurrent or unresolved pneumonia as well as the assessment of infiltrates in immunocompromised patients [31, 32].

There is clearly a major need to implement the simpler and low-cost antigen and antibody tests across the continent. In parallel with this, more mycology specialists are required to provide expertise, particularly in fungal identification and interpretation. Pulmonary TB is known to be the major risk factor for respiratory fungal diseases including CPA and aspergillus bronchitis in the context of bronchiectasis. Sub-Saharan Africa has the largest burden of pulmonary TB globally [33], with 16 of the 30 high-burden countries located there [34]. Misdiagnosis of CPA as pulmonary TB can lead to a fatal outcome. *Aspergillus* antibody (IgG) testing is the cornerstone of CPA diagnosis, and the new lateral flow assay can be used as a screening tool, which means that it can be easily used in TB clinics and their laboratories alongside GeneXpert/mAFB microscopy [35]. Owing to the emergence of the COVID-19 pandemic and the concerted efforts of the WHO and African countries, all African countries were able to diagnose COVID-19 using PCR by June 2020 [36]. Therefore, it should be possible to leverage the ubiquity of nucleic acid extraction and PCR machines in health centres for the diagnosis of *Pneumocystis* pneumonia, given the provision of the kits. *Pneumocystis* PCR is not only more sensitive than microscopy in detecting *P. jirovecii*, but also can be performed on other samples, such as nasopharyngeal aspirates in small children.

The main limitation to this survey is that the majority of the data presented were from one health facility or one region within each country, which is less important for the smaller countries but may be significant for the larger countries. The method used to capture the data might have not have reliably covered the rural settings with limited internet access, although country feedback did compensate for this in most countries. Some responses were probably subjective and so diagnostic availability is likely less than reported here, especially in rural and remote areas. Fungal diagnostic capacity in Africa might differ in locations and facilities in ways not captured in this survey.

Conclusion

This survey has found a huge disparity of diagnostic test capability across the African continent, mostly between countries, but also within countries. There are some good examples of good diagnostic provision and very high-quality care as a result, but this seems to be the exception rather than the rule. The unavailability of essential testing such as spirometry was noted, which has a large impact in lung diseases diagnosis. A concerted effort is required to train clinicians on fungal disease differential diagnosis, which tests to do and how to utilise the results, if the testing is new to them. It is also important for countries to implement tests on the WHO Essential Diagnostics List.

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