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Early View

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Diagnostic Options for Pulmonary Fungal Diseases in Africa

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Running head: Diagnosis of fungal lung disease in Africa

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 to 72 health facilities, of whom 33 of 72 respondents (45.8%) reported data for the whole country while others reported data for a specific region/province. In the public sector, chest X-ray and CT scan are done often or occasionally in 49 (98%) and 37 (74%) countries, and less often in the private sector. Bronchoscopy and spirometry were often or occasionally done in 28 (56%) and 18 (36%) of countries in the tertiary health facilities of public sector. The most conducted laboratory diagnostic assay is fungal culture (often or occasionally) in 29 (58%) countries.

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 is unusual. The unavailability of essential testing such as spirometry was noted which has high impact in lung diseases diagnosis. It is important for countries to implement tests basing on the WHO Essential Diagnostic List.

Research in context

Evidence before this study

Both acute and chronic respiratory infection and airways disease are common in Africa, in all age groups. Fungal lung disease includes life-threatening infection in immunocompromised and critically ill patients, chronic pulmonary aspergillosis complicating and mistaken for TB, and allergy, including fungal asthma, which is responsive to inexpensive antifungal therapy. Diagnostic capacity for COPD and asthma, lung cancer and fungal disease has not been mapped previously in the African continent.

Added value

This survey of capacity to diagnose lung disease, including fungal lung infections finds major deficiencies. CT scanning is unavailable in 8 countries and rarely done in 5. Spirometry is unavailable or rarely done in 21 and 11 countries respectively. Bronchoscopy is never or rarely done in 11 and 11 countries, respectively. Diagnosing *Pneumocystis* pneumonia and chronic pulmonary aspergillosis require *Pneumocystis* PCR and *Aspergillus* IgG antibody, unavailable in 78% of countries.

Implication of the findings

Many gaps in diagnostic capacity exist in Africa. Implementation of the WHO Essential tests would be a good start. Training in spirometry, CT scanning and bronchoscopy is required in many countries. Clinician awareness about fungal lung disease, supported by technical training of healthcare workers would improve respiratory health in Africa.

Introduction:

Inhalation of fungal spores of both opportunistic and true fungal pathogens affect 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 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. *Cladosporium* and others) can precipitate the onset of and exacerbate asthma, chronic obstructive pulmonary disease (COPD) and allergic fungal rhinosinusitis.

The diagnosis of pulmonary fungal diseases rests on the combination of clinical, radiological, microbiological and serological findings; occasionally supported by histopathology [5, 6]. For example, invasive aspergillosis (IA) can be diagnosed by the detection of cavitary lesions with or without halo signs, consolidations, or air crescent signs using CT scanning, with galactomannan antigen detection in plasma, serum, BAL, or CSF [7]. The detection of *Aspergillus* immunoglobulin (Ig) G is the cornerstone of CPA diagnosis and is usually also positive in allergic bronchopulmonary aspergillosis (ABPA) and *Aspergillus* bronchitis in asthma, cystic fibrosis and bronchiectasis patients [5]. Pneumocystosis is diagnosed by detecting *Pneumocystis jirovecii* DNA using quantitative real-time polymerase

chain reaction (PCR) in a respiratory tract specimen [7], or direct microscopy which is less sensitive than PCR.

Diagnosis of pulmonary fungal diseases remains challenging in Africa as most diagnoses are based on clinical presentation alone. Suspicion of pulmonary fungal diseases requires knowledge and experience as most clinical presentations are subtle; presenting with atypical signs and symptoms making it easy to misdiagnose. Moreover, clinical presentation of pulmonary fungal diseases overlaps with other lung diseases/conditions and thus complicate the diagnosis [5]. The misdiagnosis or underdiagnosis of pulmonary fungi infections impact in patients' management and treatment outcome. The mismanagement of patients include unnecessary antibiotic treatment that might lead to antimicrobial resistance and associated complications (increase in hospital stay and health care cost for both patients, institutions, regional and global at large) and death of the patients. Furthermore, undiagnosed lung fungal infection is often progressive with a high mortality [8]. The Africa region shares the high societal cost associated with undiagnosed fungi infections as it is estimated to have 70% of global HIV infected population [9] (one key population at increased risk of opportunistic fungi infection) with limited capacity for fungi diagnosis [10, 11].

Capacity for proper fungal disease diagnosis in Africa is further complicated by the limited capacity of collecting recommended clinical samples for pulmonary fungal diseases including bronchoalveolar lavage, tracheal aspirate, and lung biopsy 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 by using, computed tomography scanning (10), PCR [16], and detection of circulating galactomannan or *Aspergillus* antigen [17]. However, none of these tests are 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 GAFFI team and then video conference call with respondent(s), 4) external validation from public or private sources and 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, 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 BSL-3 lab with or without protocol for handling pathogenic fungi. Part 2 covered the WHO-recommended list of essential fungal diagnostics. Availability of diagnostics was classified in two ways: type of facility providing the diagnostic, and regularity of use. The five levels of facility used were 1) not available anywhere, 2) private centers, 3) specialist/university

centers, 4) district hospitals and 5) community health centers. For each diagnostic, respondents were asked to select how often it was performed at each type of facility, responding as often, occasionally, rarely or never. This provided a granular, multi-dimensional view of the availability of each diagnostic. There were also two further fields to provide additional context regarding availability of diagnostics 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, of which respondents were asked to list any that apply: 1) patient pays, 2) insurance pays, 3) government/health service pays and 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 diagnostics/procedures. Additional open questions completed the survey regarding additional fungal diagnostics used in the respondent's country and any other comments, 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 with GAFFI Ambassadors and existing networks of contacts. Respondents were encouraged to reach out to colleagues in areas where they didn't 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 organized in order 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 were aligned with the questionnaire reports.

Data compilation and display

Data was compiled and visualized using QGIS software and Natural Earth vectors (www.naturalearthdata.com) to design maps showing each diagnostic's coverage across the continent. Population estimates were taken from CIA World Factbook (https://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 participation of Africa CDC.

Results:

Health institution and reporting

The data of availability and usage frequency of key diagnostics for fungal diseases were successfully collected from 50 of 51 (98%) African countries with populations >1 million (including Somaliland, a self-declared but not widely recognized country which 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 responses varied from one country to another with Tanzania being the highest with 7 respondents, followed by Nigeria and Democratic Republic of Congo with 4 respondents each, Cameron and Guinea-Bissau with 3 respondents each, followed by Angola, Egypt, Gabon, Mauritania and South Africa with two respondents each, and the remaining countries with 1 respondent each as illustrated in (Figure 1). A total of 33 (45.8%) of 72 respondents reported data for the whole country while others reported data on the specific region of health facility affiliated. Of the 72 respondents involved in this survey, 40 were medical laboratory professionals, 22 were either medical doctors, physicians, pathologists or Centre directors. The collected data were from different level of health facilities (private centers, specialist/university centers, district hospital and health centers). Online participation with the Africa CDC, involved 191 stakeholders from 43 African countries including representatives of Ministries of Health, civil society organizations, mycology experts, dermatologists, lung disease and HIV/AIDS/tuberculosis (TB) care providers.

Radiological procedures

In the public sector, chest X ray, CT scan, radiology reporting, bronchoscopy, and spirometry procedures are not available in 0, 8, 6, 11, and 21 countries respectively, while in private sector chest X ray, CT scan, radiology reporting, bronchoscopy, and spirometry are not available in 8, 12, 13, 22, and 23 countries respectively (Table 1 and Figure S2).

Chest X-ray is utilized often in 92% of countries at some level of the health system, but only occasionally in 3 countries (6%) and rarely in Guinea Bissau (2%) (Table 1) (Figure 1A). In Guinea Bissau, there is currently only a single portable X-ray system and in Gabon and Cameroon chest X-rays are done infrequently. In contrast, CT scanning in the public sector is unavailable in 8 countries (16%) (Angola, Equatorial Guinea, Guinea-Bissau, Sierra

Leone, Somalia (including Somaliland and Puntland) and South Sudan) and rarely used in another 5 countries (12%) (Burkina Faso, Ethiopia, Malawi, Namibia and Uganda) (Table 1). In the private sector, the most conducted radiological procedure is the chest X-ray (78%), followed by CT scan (70%). In terms of usage regularity, chest X-ray is performed often in 93%, 80.4%, 70% and 50% of specialist/university centers, private centers, district hospitals and health centers, respectively. A chest X-ray varied in price from $4 in Uganda to $200-300 in Puntland, usually $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.

Table 1: **Pattern of pulmonary fungal diseases key diagnostics per regularity of use in different level of health facilities in surveyed area from 50 countries or states surveyed.**

Test	Frequency of testing	Public sector (%)	Population (millions)	Private Sector (%)	Population (millions)
Chest X-ray	Often	46 (92)	1,336.9	35 (70)	1,039.4
	Occasionally	3 (6)	31.7	4 (8)	128.2
	Rarely	1 (2)	2.0	3 (6)	25.2
	Countries use	**50 (100)**	**1,370.5**	**42 (84)**	**1,192.8**
	Countries never use	**0**	**0**	**8 (16)**	**177.7**
CT-Scan	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)**	**1,304.1**	**38 (76)**	**1,201.9**
	Countries never use	**8 (16)**	**66.4**	**12 (24)**	**168.6**
Radiologist report	Often	35 (70)	1,088.7	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)**	**1,354.7**	**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)**	**1,239.6**	**28 (56)**	**1,052.8**
	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)**	**1,132.8**	**27 (54)**	**1,064.6**
	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)**	**1,289.4**	**27 (54)**	**1,030.3**
	Countries never use	**10 (20)**	**60.2**	**23 (46)**	**335.4**
Aspergillus Ab	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)**	**1,109.1**	**41 (82)**	**1,155.6**

Reporting by radiologists in the public sector was often done in 35 countries (70%, population 1,089 million) and occasionally in another six (12%, 211 million) (Table 1) (Figure 1B). Reporting by a radiologist is not undertaken in the public sector in Angola, Equatorial Guinea, Guinea-Bissau, or South Sudan (population 16 million) and is 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 tuberculosis, as none of these systems have 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 is regularly undertaken in 13 countries in public facilities (population 286 million) and in 12 countries in private clinics and hospitals (Table 1) (Figure 2A). Five other countries occasionally do spirometry (111 million). However, 21 countries in Africa do no spirometry at all in the public health service (population 238 million), and it is rarely undertaken in another 11 countries with a combined population of 736 million. In some countries, spirometry is only undertaken in the public sector (i.e., Algeria, Rwanda and Eritrea) and the converse is 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 are 15 countries providing a routine or frequent bronchoscopy service in the public sector covering a population of 320 million people, and another 13 with an occasional service, covering about 421 million people (Table 1, Figure 2B. In some countries such as Cameroon, Equatorial Guinea and Somalia, this service is provided but exclusively by the private sector. These three countries and eight others have no public sector bronchoscopy service (population 131 million). An additional 11 countries rarely do bronchoscopy in the

public sector (population 498 million), and this is mirrored in the private sector in most of these countries including Botswana, Ethiopia, Nigeria and Tanzania. A total of 32 (44.5%) and 46 (63.9%) private and specialist centers, respectively reported conducting bronchoscopy. In terms of usage regularity, bronchoscopy is the most often performed test by 14 (43.8%), and 21 (45.7%) private centers, specialist /university centers, respectively (Table 1) (Figure 6). Bronchoscopy procedure costs ranged from $10 (Eritrea) to $60-300 in Morocco.

The respondents identified many common obstacles preventing more procedure use including the shortage in equipment, the lack of trained personnel to perform tests, the lack of awareness among physicians of the value of particular diagnostic test, low demand for some appropriate tests and the high cost. A total of 58 (80.6%) of facilities mentioned the payment method for radiological and clinical procedures cost while 14 (19.4%) did not. In 19 (n=58, 32.8%) facilities the patients paid the full charge, in 3 (5.2%) facilities the costs were covered by the government, and in one facility (1.7%) costs were covered by insurance. In 35 facilities (n=58, 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 are used in both public and private sectors in the surveyed countries with varying frequencies. In the private sector, the most conducted diagnostic procedure is fungal culture (40%). In terms of usage regularity, fungal culture is the most often performed test by 53.1%, 50%, 21.4% and 33.3% specialist/university centers, private centers, district hospital and health centers, respectively. Ten countries never do fungal culture in the public sector, although in Equatorial Guinea and Liberia it is available in the private sector. In

Angola and Tanzania, it is 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.

However, the survey did collect data about biosafety level 3 (BSL3) laboratories. The survey found that 45 (63.9%) facilities/countries had a biosafety level 3 (BSL3) operating laboratory, however only 14 of these (31.1%) have a protocol to handle pathogenic fungi, several of which are BSL3 organisms (Figure 3). One university teaching hospital from Mozambique had fungal diseases diagnosis protocols in a level two health laboratory and two respondents reported not knowing about the availability of any BSL3 protocol. Most health facilities with BSL3 laboratories used them for tuberculosis and viral diagnosis, without a protocol for fungal cultures.

Pneumocystis PCR was reported to be conducted in 11 (15.3%) private centers and 17 (23.6%) specialist centers. However, it is not available in 39 countries in the public sector and 41 countries in the private sector (Table 1). In Kenya and Zimbabwe it is only available in the private sector. In terms of usage regularity, *Pneumocystis* PCR is the most often performed test by 6 (54.5%), and 4 (23.5%) private centers, specialist/university centers, respectively.

Aspergillus IgG antibody was reported to be regularly tested only in Morocco, occasionally in three (Tunisia, Niger and Chad), and never done in 39 countries in either the public or private sector. (Table 1, Figure 4). Overall, *Aspergillus* IgG antibody test was reported to be done in 13 (18.1%) private centers and 14 (19.4%) specialist centers. We did not survey the use of *Aspergillus* IgE antibody.

Several commonly encountered obstacles were identified: shortage of equipment in some laboratories, difficult 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 (72.2%) facilities mentioned the payment method for the diagnostic cost, while 20 (27.8%) did not. In 13 (n=52, 25%) facilities, the patients paid the full charge, in 3 (5.8%) facilities costs were covered by the government, and in 2 (3.8%) facilities costs were covered by insurance; in 34 (n=52, 65.4%) facilities, the diagnostics cost was partially paid by the patient and the remaining amount handled by another agent (s) (government, insurance, foundations).

Discussion:

All countries of Africa are classified into low- 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. Since most people in Africa live in rural areas, they are directly in contact with environmental fungi [18-21]. Pulmonary diseases (notably asthma, COPD, 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 that the magnitude of these many fungal diseases usually exceeding health capabilities [23, 24]. In this context, the collected data in this survey reveals that there is a great shortage of the key diagnostics for pulmonary fungal diseases.

Concerning radiological procedures; CT-scan 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, both bronchoscopy and spirometry are completely unavailable in 22% and 42% respectively in the public sector of the surveyed countries, while in private sector they are completely unavailable in 44% and 46% respectively. These results indicate weakness of health 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 COPD and asthma.

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

diagnosis of pneumonia in children, often in the context of advanced HIV disease. The generally low suspicion index of fungal infection among clinicians has led to limited use of fungal culture even when available. This is observed in this survey where fungal culture as a diagnostic tool is available in 78% of the surveyed countries. This is further emphasized 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-laboratory (64% of surveyed institutions)) in Africa possesses the capability of handling highly pathogenic fungi which is significantly lower than what has been reported from Asia where around 80% of hospitals in Asia had 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 to countries with universal health insurance like Rwanda, Tunisia and Algeria where coverage is reported to be more than 80% [28], health insurance coverage in Africa is reported to be very low, below 20% [29]. This forces most patients and families to cover their health cost services privately and consequently often leads to delay in seeking proper health services. These findings were also observed in the current survey whereby about 25% to 32.8% of patients fully cover the diagnostic, radiological and clinical investigations' cost privately while about 62% to 70% reported partial cover. Only 5% are 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 scan of the lungs as it is the preferred method for radiographic diagnosis of fungal diseases and important differential diagnoses such as lung

cancer, and other structural or inflammatory conditions [7, 30]. Provision of spirometry and bronchoscopy equipment linked to training of healthcare workers to use. They are important to in diagnoses of asthma, COPD interstitial lung disease and cancer and enable evaluation of known or suspected respiratory infections, recurrent or unresolved pneumonia and 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 assist in interpretation. Pulmonary tuberculosis (PTB) 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 PTB globally [33], with 16 out of 30 high burden countries there [34]. Misdiagnosis of CPA as PTB can lead to a fatal outcome. *Aspergillus* antibody (IgG) 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]. Due 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 centers 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 ones. 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, 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 high impact in lung diseases diagnosis. A concerted effort is required to train clinicians about fungal disease differential diagnosis, which tests to do and how to utilize the results, if the testing is new to them. It is also important for countries to implement tests on the WHO Essential Diagnostic List.

Declarations

Conflict of interest

All authors declare no conflict of interest

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The full report is available at https://gaffi.org/africa-diagnostic-reports/

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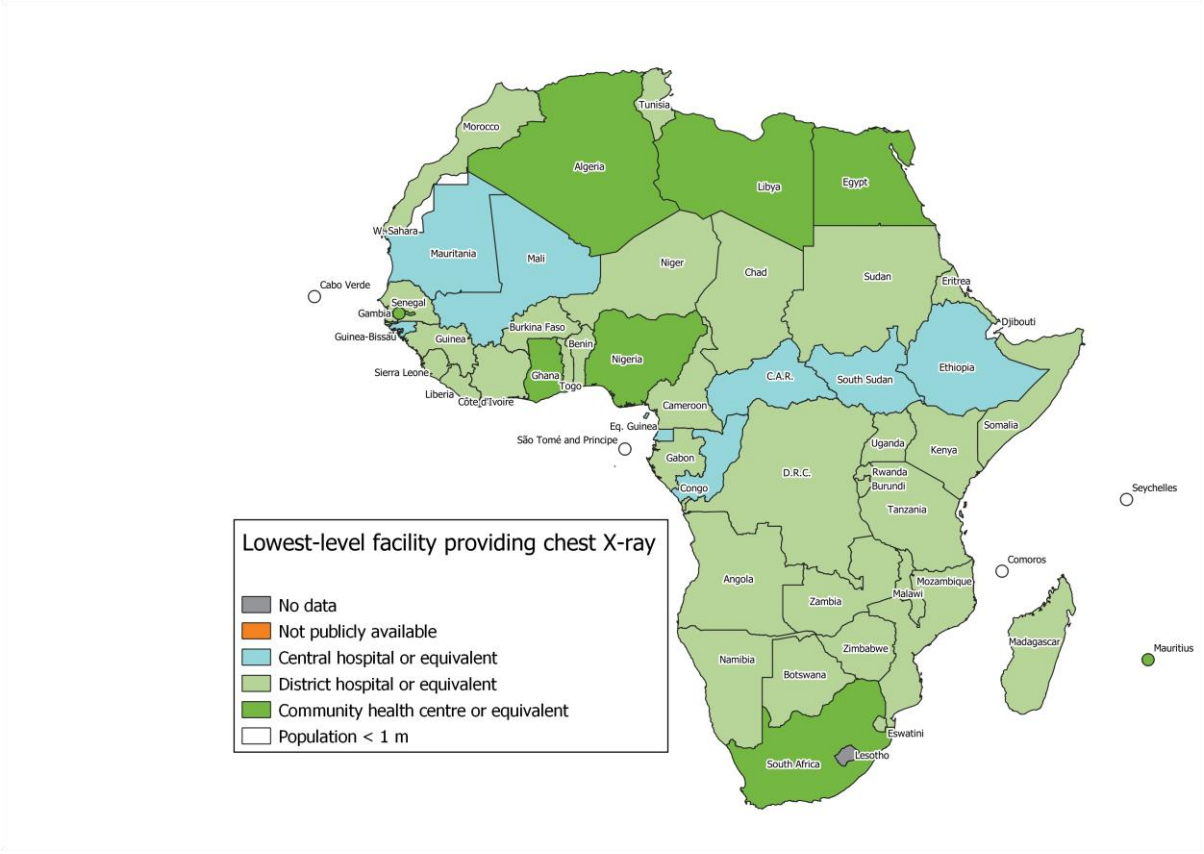
Figure legends

Figure 1: A. Provision of chest X-ray in different setting, using a hierachical appraoch: 7 countries (ie Ethiopia) only use chest X-ray at centralor teaching hospitals, 33 countries (ie Benin) use chest X-rays at these hospitals and at district hospitals and 10 countries provide Chest X-rays at these facilities and in community clinics (ie Ghana). B. Access to radiologist reporting at different frequency.

Figure 2: A. Provision of spirometry; B. Frequency of bronchoscopy in tertiary health

facilities

Figure 3. Biosafety level 3 laboratories


Lowest-level facility providing chest X-ray
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Not publicly available
Central hospital or equivalent
District hospital or equivalent
Community health centre or equivalent
Population < 1 m
Tunisia
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Algeria
Libya
Egypt
W. Sahara
Mauritania
Mali
Niger
Chad
Sudan
Eritrea
Djibouti
Cabo Verde
Senegal
Gambia
Guinea-Bissau
Guinea
Burkina Faso
Benin
Nigeria
Ethiopia
Sierra Leone
Liberia
Côte d'Ivoire
Ghana
Togo
C.A.R.
South Sudan
Cameroon
Somalia
Eq. Guinea
São Tomé and Príncipe
Uganda
Kenya
Gabon
D.R.C.
Rwanda
Burundi
Congo
Tanzania
Seychelles
Comoros
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Eswatini
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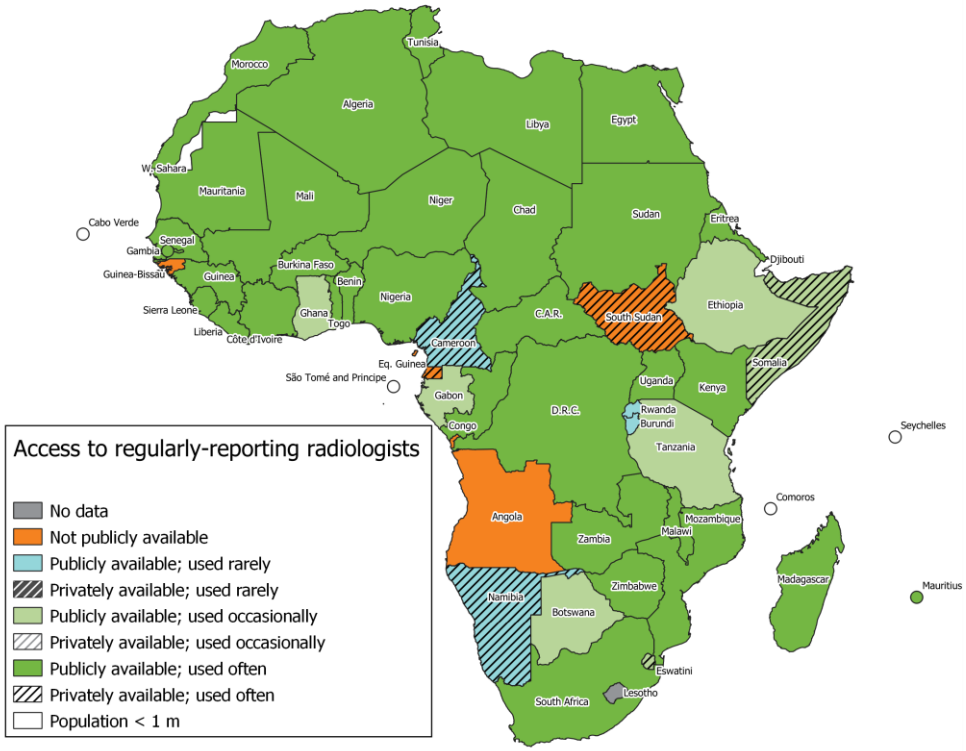
South Africa


Access to regularly-reporting radiologists
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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 m
Tunisia
Morocco
Algeria
Libya
Egypt
W. Sahara
Mauritania
Mali
Niger
Chad
Sudan
Eritrea
Djibouti
Cabo Verde
Senegal
Gambia
Guinea-Bissau
Guinea
Burkina Faso
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Nigeria
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South Sudan
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Somalia
Eq. Guinea
São Tomé and Principe
Gabon
Uganda
Kenya
Rwanda
Burundi
D.R.C.
Congo
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Comoros
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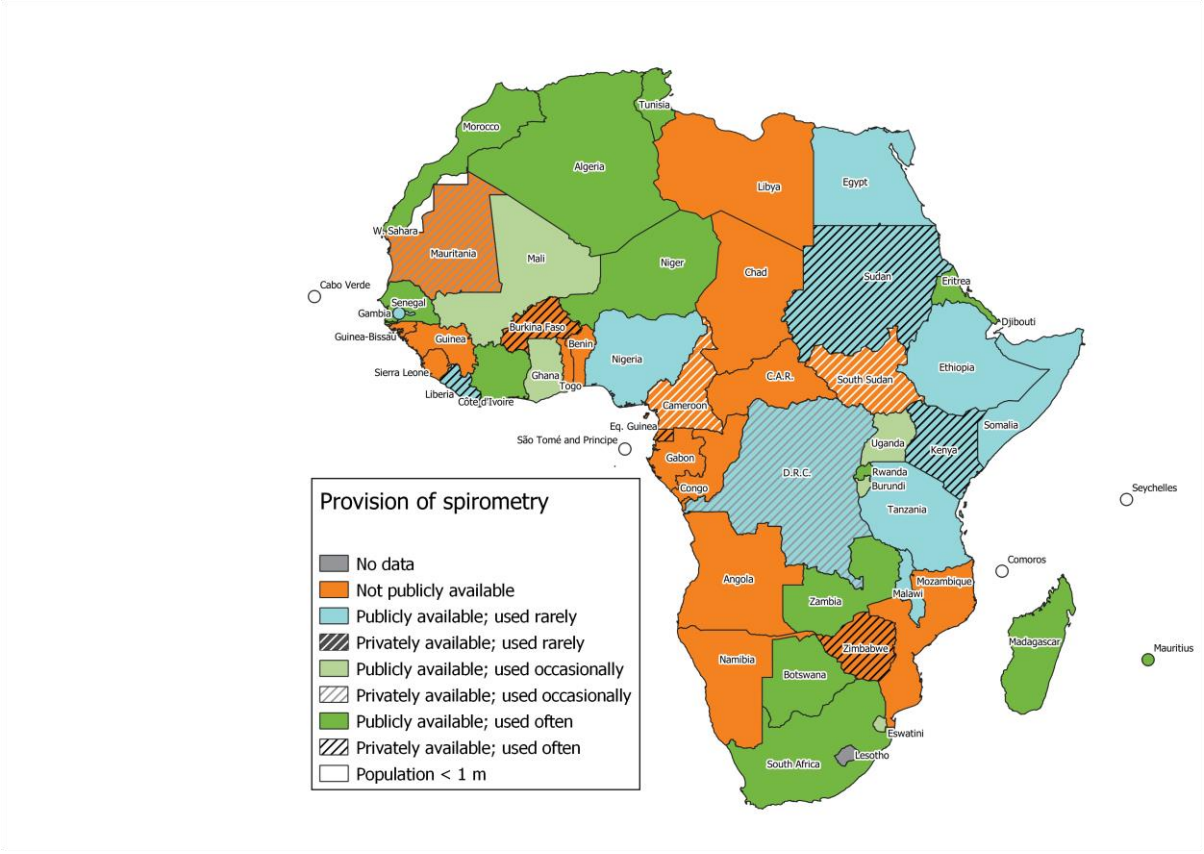
Lesotho
South Africa


Provision of spirometry
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Not publicly available
Publicly available; used rarely
Privately available; used rarely
Publicly available; used occasionally
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Publicly available; used often
Privately available; used often
Population < 1 m
Tunisia
Morocco
Algeria
Libya
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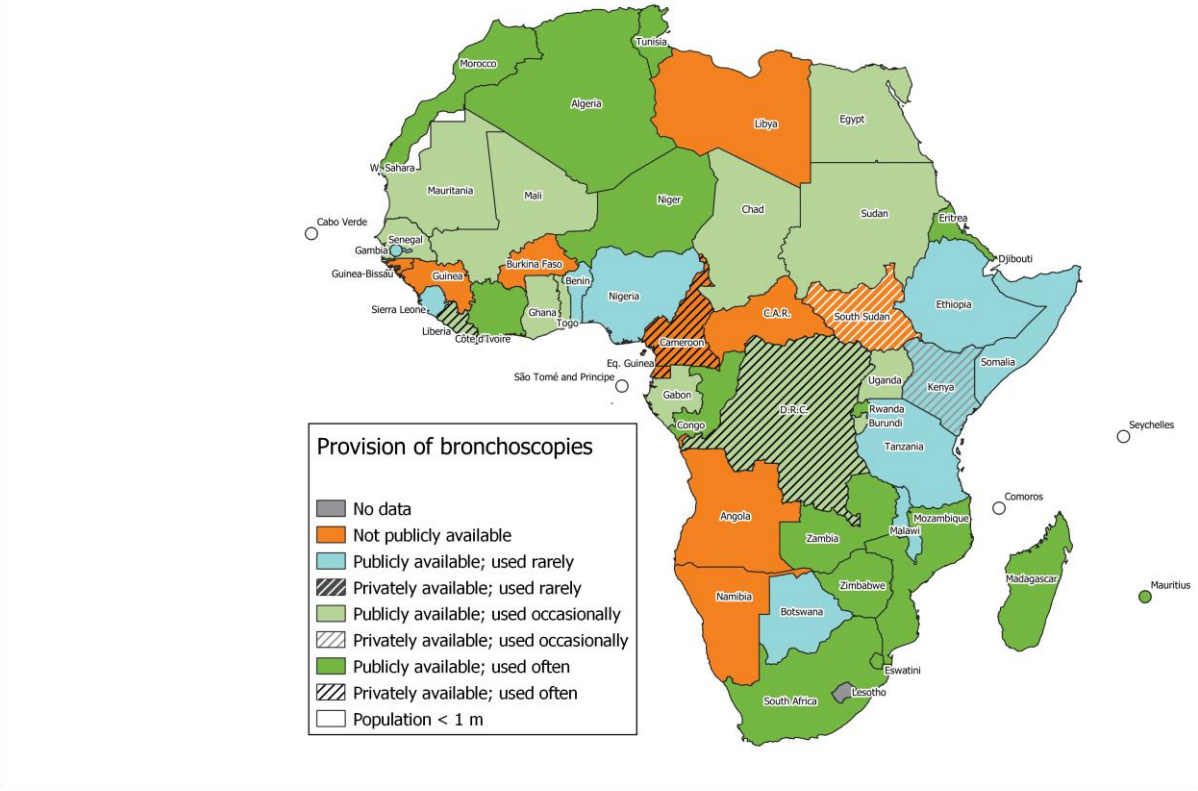
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Zambia
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Zimbabwe
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Botswana
Eswatini
Lesotho
South Africa
Provision of bronchoscopies
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Publicly available; used often
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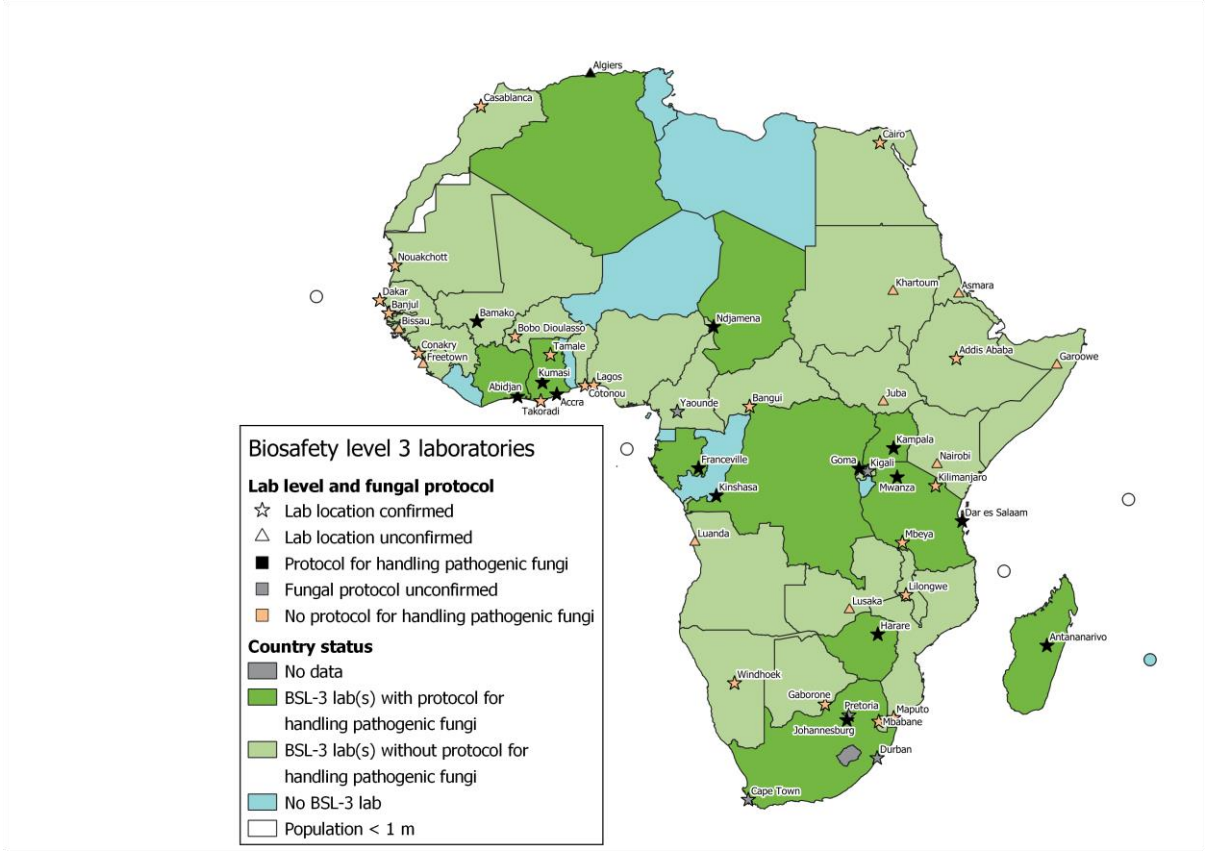
Population < 1 m


Biosafety level 3 laboratories
Lab level and fungal protocol
Lab location confirmed
Lab location unconfirmed
Protocol for handling pathogenic fungi
Fungal protocol unconfirmed
No protocol for handling pathogenic fungi
Country status
No data
BSL-3 lab(s) with protocol for handling pathogenic fungi
BSL-3 lab(s) without protocol for handling pathogenic fungi
No BSL-3 lab
Population < 1 m
Algiers
Casablanca
Cairo
Nouakchott
Dakar
Banjul
Bissau
Bamako
Bobo Dioulasso
Conakry
Freetown
Tamale
Kumasi
Abidjan
Lagos
Cotonou
Accra
Takoradi
Ndjamena
Khartoum
Asmara
Addis Ababa
Garoowe
Yaounde
Bangui
Juba
Kampala
Nairobi
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Kigali
Kilimanjaro
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Franceville
Kinshasa
Dar es Salaam
Luanda
Mbeya
Lilongwe
Lusaka
Harare
Antananarivo
Windhoek
Gaborone
Pretoria
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Johannesburg
Durban
Cape Town

Mushi et al, Diagnostic Options for Pulmonary Fungal Diseases in Africa

Supplementary data

Figure S1: Location and breadth of initial survey response

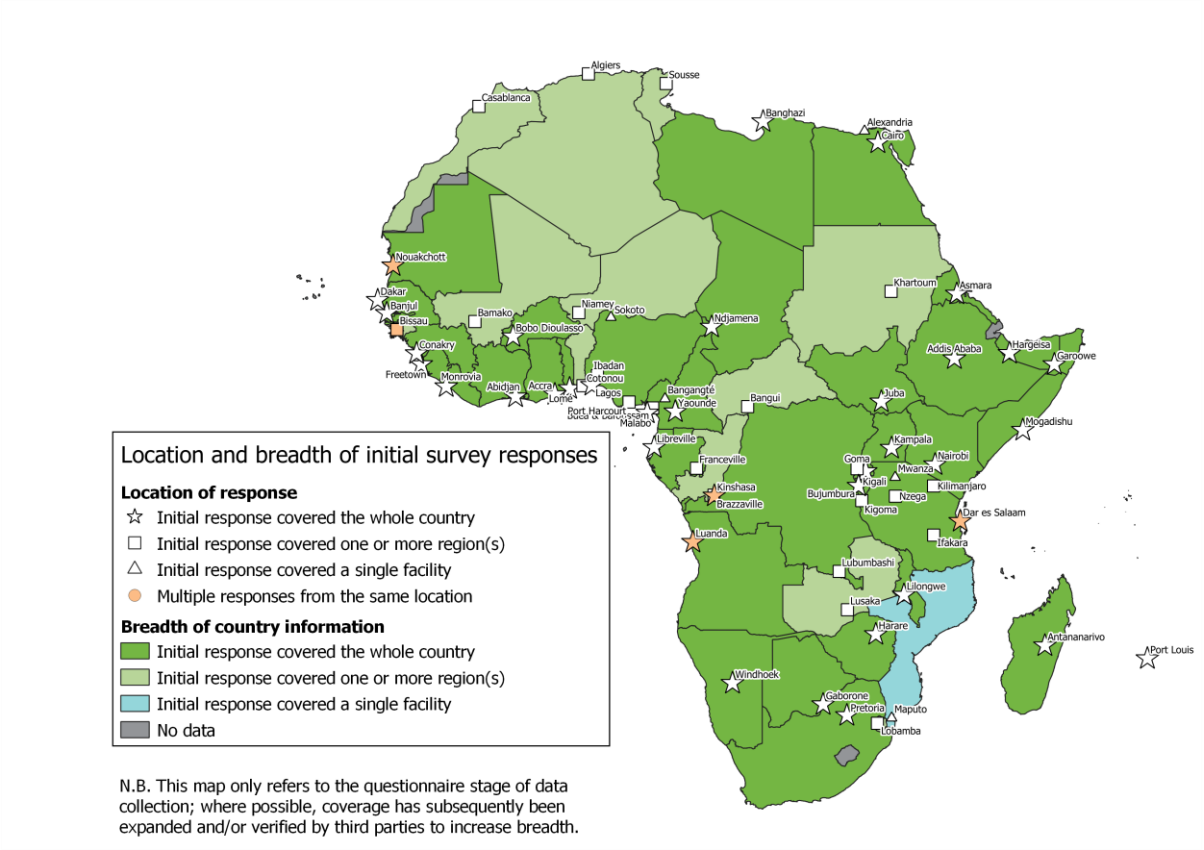

Figure S2: **Frequency of key diagnostics' unavailability in surveyed countries (n=50)**