Diagnostic capacity for cutaneous fungal diseases in the African continent

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Abstract

Background Cutaneous fungal infections are very common, especially in poorer communities and with intercurrent HIV infection. Determining the fungal pathogen in skin-related fungal neglected tropical diseases (NTDs) determines optimal therapy. We undertook a country survey across many African countries to determine the diagnostic capacity for skin fungal diseases.

Methods A detailed questionnaire was delivered to country contacts to collect data on availability, frequency, and location of testing for key diagnostic procedures and followed up with 2 rounds of validation by video call and by confirmation of individual country data confirmation by email.

Results Of 47 countries with data, seven (15%) and 21 (45%) do not offer skin biopsy in the public or private sector, respectively, but 22 (46%) countries do it regularly, mostly in university hospitals. Direct microscopy is often performed in 20 of 48 (42%) countries in the public sector and not done in 10 (21%). Fungal cultures are often performed in 21 of 48 (44%) countries in the public sector but not done in nine (20%) or 21 (44%) in either public or private facilities. Histopathological examination of tissue is frequently used in 19 of 48 (40%) countries but not in nine (20%) countries in the public sector. The cost of diagnostics to patients was a major limiting factor in usage.

Conclusion Major improvements in the availability and use of diagnostic tests for skin, hair, and nail fungal disease are urgently needed across Africa.
Introduction

Africa, one of the world’s largest continents in terms of surface area and population, is largely made up of developing countries. The 1.3 billion African population do not yet have an effective health system that meets the standards required to achieve the objectives of Universal Health Coverage. Infectious and noninfectious skin diseases are significant public health problems, affecting about a billion people. Often ignored or underestimated compared with major communicable diseases such as HIV, tuberculosis, or malaria, skin fungal diseases may be primary, caused by trauma or implantation or linked to an immune deficit. Fungal or nonfungal diseases with deep involvement may have cutaneous signs that can clinically guide the diagnosis. Cutaneous signs can be the initial signs of deep fungal or nonfungal diseases. In Africa, there is an upsurge in fungal diseases ranging from mild and superficial to deep or systemic fungal infections, but prevalence is unavailable in most African countries owing to the lack of registers recording fungal disease.

Dermatophytosis is a superficial and often neglected fungal infection in Africa. Tinea capitis is the most common clinical form in children. The disease affects more than 20% of school-age children in West Africa and probably with a prevalence of about 138 million. In adults, tinea corporis is the most frequently encountered and is more common than tinea capitis, at least in tertiary centers in West Africa. Differentiating the correct diagnosis from others in skin disorders can be difficult due to the broad diagnostic possibilities. In South Africa for example, among 3,814 patients in several public hospitals, 4,424 diagnoses of dermatoses were found. Eczemas and papulosquamous eruptions accounted for 41.0%, followed by infections including dermatophytoses (16.5%), acne and rosacea (9%), dyschromias (7.5%), and connective tissue disorders (4.2%).

Fungal skin infections are also common in HIV-infected patients and may even be a clue to the diagnosis of HIV infection. In Burkina Faso, the overall prevalence of cutaneous mycosis in HIV infection was 19.9%, more frequent in women...
and in those with a CD4 count under 500 x 10^9/L.\textsuperscript{10} \textit{C. albicans} (22.4\%) and \textit{T. rubrum} (19.8\%) were the most isolated species.

Many healthcare systems in African countries lack adequate diagnostic capability, especially with regard to most microbiology tests, including mycology. Diagnostic errors and overtreatment with antimicrobials can be mostly prevented with adequate diagnostic and laboratory facilities for pathogen identification.\textsuperscript{11} Lack of ready accessibility to these services in primary health centers and hospitals is a major public health problem in many parts of Africa. Dermatologists per million population vary from less than one in several countries to 49 in Egypt.\textsuperscript{12} Only 5\% of gross domestic product (GDP) is spent on health in sub-Saharan Africa, which is half the world’s average.\textsuperscript{13} Sub-Saharan African countries spent on average $79 per person in 2018, and many spent ~$50.\textsuperscript{13} The low value of GDP leaves little room for investment or expenditure on the health sector, whose resources come from foreign aid, the state budget, and households who pay for all, or almost all, healthcare.\textsuperscript{14}

To assess the diagnosis of fungal skin infections in Africa, we conducted a survey of the availability of tests such as direct microscopy of skin, hair, nail samples, fungal culture, skin biopsy, and histopathology and fungal staining procedures in Africa. The survey was followed up with validation video conferences, email clarification of specific points, and individual country confirmation of country profiles.

Materials and methods

This survey was conducted in six phases: (1) questionnaire development in an Excel datasheet with later adaptation and improvement, (2) questionnaire completion by in-country respondents (usually collating responses from colleagues in other disciplines, such as radiology, respiratory medicine, dermatology, and ophthalmology), (3) questionnaire review and data analysis by the 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 the relevant topics (i.e., HIV/AIDS and laboratory coordination) and/or Ministry of Health representatives, where possible, (6) Africa Centres for Disease Control and Prevention (ACDC) validation webinars and direct contact with country leaders, using individual country profiles. The questionnaire consisted of seven sections, including information about the respondent and whether they were answering for the country (with consultation) or just their region or facility, availability of the WHO-recommended list of essential fungal diagnostics, the frequency of testing, reasons for not testing (i.e., cost, personnel, or unavailability of equipment), and individual responsible for payment for the tests and for skin biopsy procedure. Availability of diagnostics was classified by level of facility providing each test and regularity of use. The five levels of facility were classified as (a) diagnostic not available anywhere, (b) private centers, (c) specialist/university centers, (d) district hospitals, and (e) community health centers. The frequency of testing (how often tests are carried out in a particular facility or setting) was differentiated into: “often,” meaning daily or for less frequent tests such as skin biopsy done weekly; “occasionally” meaning done weekly or monthly (less frequent tests); and “rarely” meaning on special request, often as a referred assay.

Payment for testing was delineated into (i) patient pays, (ii) insurance pays, (iii) government or health service pays, and (iv) a charity/foundation pays.

To disseminate the questionnaire, a snowball sample was used, starting with GAFFI Ambassadors and existing networks of contacts. Respondents were encouraged to contact colleagues for tests or procedures where they did not have firsthand knowledge. 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 partially or fully completed questionnaire, an online video conference was held to provide clarification, as well as adding qualitative data, context, and narrative. Some questionnaires were completed during this meeting. In situations where there was still missing information, follow-up was carried out to collect additional data. Translators were used on video calls when necessary. Publications from countries were also checked to ensure that reported results were aligned with the questionnaire reports. Individual country profiles of diagnostics and basic data were shared with the local stakeholders and experts, to further verify data and correct any 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), to ensure an accurate picture of the current status of diagnostics in 2022 was obtained.

Data were compiled into Excel and visualized using QGIS software and Natural Earth vectors to design maps showing each diagnostic’s coverage across the continent.\textsuperscript{15} Population data were taken from the CIA World Factbook.\textsuperscript{16}

Results

Our survey yielded data on diagnostic test availability for cutaneous fungal diseases from 48 out of 49 African countries which have a population of over 1 million individuals. We were unable to garner any data from Lesotho. Countries with smaller populations were omitted from the survey included Cape Verde, Comoros, Djibouti, Sao Tome and Principe, Seychelles, and Western Sahara (six countries). In Somalia, we collected data separately for the states of Somaliland and Puntland. The Spanish enclaves Ceuta and Melilla and the French department Réunion island were not included. The questionnaire was completed by respondents linked to 72 health facilities distributed in the surveyed countries, some responding only for their institution and surrounding area, others nationally. Most respondents
collated results from colleagues in different disciplines, regions, and hospitals, and additional responses were received from most Ministries of Health as part of the validation processes.

The results are presented below (Table 1, Figures 1–4). The full report and individual country profiles are available online: https://gaffi.org/africa-diagnostic-reports.

Skin biopsy

About 617 million people, living in 22 countries (Morocco, Senegal, Tunisia, Liberia, Cote d’Ivoire, Togo, Benin, Niger, Nigeria, Central African Republic, Gabon, Sudan, Eritrea, Namibia, South Africa, Zimbabwe, Uganda, Rwanda, Burundi, Malawi, Madagascar, and Mauritius) had regular access to skin biopsy in the public sector and in 10 of these countries in the private sector as well (Table 1, Figure 1). However, the situation in Madagascar is probably mirrored in many countries: skin biopsies are only performed in university centers and in some private centers all located in the major cities, Antananarivo or Fianarantsoa, because of the lack of laboratories and/ or pathologists available to perform histological analysis. In Malawi, for instance, district hospitals (level d) and community (level e) settings do not analyze biopsies but only collect samples and send to facilities at specialist/university (level c) or private facilities. There are only three laboratories equipped to analyze biopsy samples in the country: one private laboratory, one government hospital, and one teaching institution. In Nigeria, Mozambique, and Mali, skin biopsies are only performed in teaching hospitals and rarely in private practice in Nigeria. Skin biopsies were rarely done in the community in a few countries, where it was more available in hospital settings.

Skin biopsy was publicly available and used occasionally in Burkina Faso, Cameroon, Chad, Mauritania, Republic of Congo, DRC, Egypt, Ethiopia, Ghana, and Tanzania, representing a collective population of about 494 million people.

In eight countries, skin biopsy was publicly available but used rarely in a few centers, for example, Angola, The Gambia, Mali, Sierra Leone, Mozambique, Kenya, Botswana, and Eswatini; private services offered this diagnostic procedure in Eswatini and Kenya. So, about 151 million people have very limited access to skin biopsy.

In Guinea, Guinea Bissau, Algeria, Libya, South Sudan, Somalia, and Equatorial Guinea, the test was not publicly available or performed privately, with the exception of the State of Puntland and Equatorial Guinea, where it was occasionally carried out in the private sector. These territories have a total population of 89 million.

There were no data available for Zambia and Lesotho.

Table 1 Provision of fungal disease tests in 48 countries in Africa, 47 for skin biopsy

<table>
<thead>
<tr>
<th></th>
<th>Skin biopsy N (%)</th>
<th>Skin, hair, nail microscopy N (%)</th>
<th>Fungal culture N (%)</th>
<th>Histopathology N (%)</th>
</tr>
</thead>
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<tr>
<td>Not publicly available</td>
<td>7 (15)</td>
<td>10 (21)</td>
<td>9 (20)</td>
<td>9 (20)</td>
</tr>
<tr>
<td>Not privately available</td>
<td>21 (45)</td>
<td>20 (42)</td>
<td>21 (44)</td>
<td>25 (52)</td>
</tr>
<tr>
<td>Publicly available, used rarely</td>
<td>8 (17)</td>
<td>9 (18)</td>
<td>10 (21)</td>
<td>8 (17)</td>
</tr>
<tr>
<td>Privately available, used rarely</td>
<td>6 (13)</td>
<td>5 (10)</td>
<td>7 (15)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Publicly available, used occasionally</td>
<td>10 (21)</td>
<td>9 (18)</td>
<td>8 (17)</td>
<td>12 (25)</td>
</tr>
<tr>
<td>Privately available, used occasionally</td>
<td>9 (20)</td>
<td>10 (21)</td>
<td>7 (15)</td>
<td>8 (17)</td>
</tr>
<tr>
<td>Publicly available, used often</td>
<td>22 (46)</td>
<td>20 (42)</td>
<td>21 (44)</td>
<td>19 (40)</td>
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<tr>
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<td>10 (21)</td>
<td>13 (27)</td>
<td>13 (27)</td>
<td>10 (21)</td>
</tr>
<tr>
<td>No data (Zambia)</td>
<td>1 (2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

N represents the number of countries doing the test.

Direct microscopy of dermatological samples

In 20 countries, direct microscopy of skin, hair, and nail samples was rated as being carried out often in the public sector, representing a population of 708 million people (Table 1, Figure 2). In 13 of these countries, it was also done often in the private sector, and Namibia is the only country where it is often available in the private sector but rarely performed in the public health facilities. In only five countries was direct microscopy available in the community (Algeria, Burundi, Nigeria, Rwanda, and Somaliland) and in 13 only in district or regional hospitals. In some countries where there were multiple responses, there was variability in the stated testing frequency in different facilities and regions.

In nine countries, direct microscopy for dermatological samples is occasionally carried out in the public sector (for a total population of 208 million people). In 11 countries, occasional direct microscopy was available in the private sector, and in Angola, DRC, and Puntland, this was the most frequent means of obtaining testing.

In contrast, direct microscopy for skin, hair, and nail samples was rarely performed in nine countries (357 million population) and in 10 countries was not performed at all in the public sector (97 million people). In 20 countries, there was no service in the private sector for direct microscopy.
Reasons given for not undertaking direct microscopy include infrequent requests from clinicians or lack of trained personnel and reagents. It is usual practice for patients to pay for the analysis. In Ghana, as an example, direct microscopy of dermatological samples is a common procedure in most urban centers due to the availability of KOH. Most rural laboratories lack KOH, and the laboratory health professionals who are posted to these areas are usually unfamiliar with the process. A similar comment was made in Mauritius – samples are collected at smaller centers, but microscopy takes place at the regional hospitals/laboratories. In Morocco, most microscopy is performed only at university hospitals. In Guinea Bissau, urine microscopy was frequently done but no microscopy of skin, hair, or nails. In Zimbabwe, most diagnoses are made clinically and patients treated empirically.

Fungal culture

Fungal culture was publicly available and used often in 21 countries representing a population of 728 million (Table 1, Figure 3). In 13 of these countries, fungal culture was rarely, occasionally, or (in three countries) often done in district or regional hospitals. Angola, Kenya, Eswatini, and Namibia offered a frequent or regular fungal culture service. In the private sector in Namibia, Angola, Eswatini, and Kenya, fungal culture was privately available and used often. In Algeria, fungal culture is not available in community centers or small cities. In Cameroon, superficial samples only are cultured in Bangangté, but in Yaoundé (Level 2) all requests are processed. In The Gambia, fungal culture is only available in the Medical Research Council laboratories. In Togo, two laboratories offer fungal culture. In Niger and Morocco, fungal culture is done at university centers. Almost all...
countries charge patients for diagnostic tests, including fungal culture, with the notable exceptions of Algeria, Libya, South Africa, Mauritius, and Malawi, with some subsidy provided by nongovernmental and charitable hospitals.

In eight countries, Burundi, Cameroon, Chad, Republic of Congo, DRC, Guinea Bissau, Madagascar, and Namibia, the test was publicly available and used occasionally. These countries have a collective population of 199 million.

In Mauritania, Ghana, Sudan, Ethiopia, Kenya, Tanzania, Gabon, Ethiopia, Malawi, Angola, and Eswatini, fungal culture was publicly available but used rarely. These 10 countries have a population of 368 million. Private services offered culture in Kenya, Tanzania, and Angola. A lack of requests by clinicians probably contributes to this in several countries, as mentioned for DRC and Liberia. In Mauritania, no laboratory was set up to do this.

Fungal culture was not publicly available in nine countries, namely Guinea, Sierra Leone, Liberia, Equatorial Guinea, Eritrea, Libya, South Sudan, Somalia, and Zambia, but was privately available in Liberia. These countries have a total population of 81 million people.

**Histopathology**

In 19 countries (population 664 million), histopathology was publicly available and used often, and in 10, it was frequently used in the private sector as well (Botswana, Egypt, Mauritius, Morocco, Mozambique, Niger, South Africa, and Zimbabwe as well as Kenya and Madagascar; Table 1, Figure 4). However, in Nigeria, only the university centers provided a histopathology service; it was rarely done in regional or district hospitals and occasionally in private practice. In 13 countries, there was some provision (usually rare
Histopathology was publicly available and used occasionally in 12 countries, namely Algeria, Burkina Faso, Ghana, Cameroon, Gabon, Chad, Sudan, Ethiopia, DRC, Tanzania, Namibia, and Eswatini. These countries have a population of 474 million.

In Senegal, Mauritania, Guinea, Togo, Angola, Kenya, Madagascar, and Malawi, histopathology is publicly available but used rarely (176 million people), although it was readily available privately in Kenya and Madagascar, and in Mauritania, at least for skin biopsies.

There was a significant disparity between public and private availability for histopathological examination of tissue. Nine countries had no public histopathology service (population 56 million), but 25 countries offered no private histopathology service. So, Libya, Guinea Bissau, Central Africa Republic, Eritrea, Sierra Leone, Somalia, and South Sudan had no histopathology service at all, and Equatorial Guinea and Liberia had only private histopathology services.

**Diagnostic costs**

The procedure cost for a skin biopsy varies from $3 to $150, depending on the country; higher costs are seen in Nigeria and Liberia and a low cost in Eritrea. Skin biopsy as a procedure is rarely supported by government or national health service insurance. Almost all countries charge patients for diagnostic tests, including fungal culture, with the notable exceptions of Algeria, Libya, South Africa, Mauritius, and Malawi, with some subsidy.
provided by nongovernmental and charitable hospitals and in some countries for some tests. Histopathology costs from $15 to $150, with high costs in Liberia and DRC.

**Discussion**

The objective of this study was to investigate the availability of cutaneous fungal tests such as direct microscopy of skin, hair and nails, fungal culture, skin biopsy, and histopathology in Africa. Skin fungal infections are frequent globally. 2,5 African countries are no exception; however, due to a lack of accurate clinical diagnosis and diagnostic tools the prevalence is mostly not known. A program of estimating the incidence and prevalence of serious fungal diseases in each country (N > 80 countries) has routinely assessed tinea capitis because of its potential for serious complications such as kerion, but in some countries such as Algeria and Senegal more comprehensive estimates have been done. 17-19 Most data published on fungal skin diseases are on dermatophytosis, 3, 9, 10, 20 and mycetoma, which is reported in countries with desert or semidesert climates such as Sudan, Mauritania, and Senegal. 19-24 Although dermatophytosis is among the most diagnosed skin fungal disease in Africa, the numbers are underestimated 4, 25 for a variety of reasons, including the limited availability of diagnostic tests. A strikingly high frequency of onychomycosis in those with diabetes of 51% was recently described in Cameroon. 26

More serious are the implantation or subcutaneous endemic mycoses in Africa, such as chromoblastomycosis, sporotrichosis, mycetoma, and histoplasmosis (including African histoplasmosis caused by H. capsulatum var. duboisii) as well as...
systemic mycoses that can disseminate to the skin. Substantial geographical variation in the frequency of these generally neglected mycoses has been noted. Chromoblastomycosis prevalence in northeastern Madagascar (1.47/100,000 persons) was higher than in the south (0.8/100,000 persons), both probably much commoner than in other locations. Sporotrichosis has been reported in miners in South Africa but is especially common in the central highland of Madagascar where the prevalence was 0.21/100,000 inhabitants. Africa is crossed by the mycetoma belt. The highest global number of cases has been found in Sudan (at least 10,608), while Sudan’s neighbor Chad and Egypt reported only 154 and 59 cases, respectively. Senegal and Uganda reported their multyear experience based on pathological confirmation with 337 cases over 18 years with regional variation in Senegal and 279 cases over 70 years in Uganda. For many other countries, only individual cases were reported, including Burundi and Namibia.

Skin biopsy is an essential procedure for the diagnosis of many skin disorders, including skin cancer and subcutaneous fungal infections such as chromoblastomycosis. Detailed guidance on site selection, likely diagnosis, biopsy technique, and sample handling are published but do not include examples of likely deep fungal skin infection. Skin/tissue biopsy is also required to diagnose secondary infections such as secondary filamentous fungal infection of burns or ulcers. The indications for and complementary testing of skin lesions of possible fungal origin, including disseminated fungal infections, are outlined by the Infectious Disease Society of America and American Society of Microbiology. The most used test for diagnosing deep cutaneous fungal infections is skin biopsy, which is available mostly in public health facilities and often in the private sector for a little more than a third of the countries. Skin biopsy requires histopathological interpretation, and some countries and cities lack histopathology services. Most histopathologists’ work is carried out in teaching hospitals and is concentrated in capital cities; so, countries may have both equipped facilities and well-trained personnel but these are often available in only 1 or 2 centers. It is likely that the frequency of skin biopsy is a proxy indicator for the number of specialists in dermatology (where there is also histopathology). Training, recruiting, and retaining experienced dermatology specialists are clearly of major importance in addressing current diagnostic gaps.

Generally, in Africa, fungal infection tests are more often available in the public health service compared with private facilities. Nearly half of the countries in Africa serving over 700 million people have at least some access to direct microscopy and fungal culture. The health system in Africa is generally organized in a pyramidal fashion, consisting of dispensaries, health huts, health posts, health centers, district and regional hospitals, and university hospitals at the top level, where most of the clinical, surgical, and biological specialties are generally located. Clinicians and dermatologists are insufficient generally but especially in remote areas. So often the first diagnostics steps in the clinical diagnosis of skin mycoses are difficult, even before confirmation by mycology and other testing. Mobile phone cameras combined with artificial intelligence software could assist in providing guidance to nonspecialists, especially when referral to a major hospital is impractical.

Most African countries lack specialists in the field of mycology. The few specialists there tend to be employed in the public sector and usually in universities, research centers, and teaching hospitals. In some countries, such as Senegal and other smaller countries, the facilities and well-trained personnel are available but only in a few health facilities. As diagnostic access appears better for skin fungal disease (and fungal disease generally) in the public sector, at least in cities and university hospitals, building on these strengths is critical. Barriers remain however in well-appointed public sector facilities because of procurement delays, other bureaucracy, and limited funds. In many African countries, it is common that the same laboratory specialists perform both public and private activities. In some places, diagnostic interventional procedures (such as skin biopsy) that cannot be done in public healthcare facilities are transferred to the private sector.

Histopathology and mycology are the most neglected laboratory specialties in African countries. Histopathology is performed mostly in public health facilities where most specialists work. Not many histopathologists work in Africa; for example, in Tanzania there are only 15 pathologists for the entire country, a situation common in the African continent, although there is now a growing African dermatopathology special interest group. Direct microscopy is the most easily available test in these countries and is mainly used in public facilities. The reason may be the simplicity of the test which does not require a lot of equipment and reagents but sufficient training to identify yeasts and fungal hyphae. In addition, direct microscopy is also used to diagnose other neglected tropical diseases (NTDs) such as leprosy and leishmaniasis, so there is an opportunity for integration of diagnostic methods. Likewise, fungal culture is also widely available in most of Africa, but in most countries the culture is only performed for superficial samples in university centers or regional hospitals.

The lack of many diagnostic tests in most African countries also means that reagent distributors do not have reagents available in the country because demand is low. This becomes a vicious cycle because demand stays low because of lack of availability. When diagnostic kits and reagents are purchased, they are often expensive and the delivery time is long. Even simple reagents such as stains or dyes are difficult to obtain in many developing countries. Many laboratories performing these tests struggle with costs and continuous availability.

Direct microscopy, histopathology, and fungal identification are all skilled procedures. The number of specialists that can perform these tests is limited in all African countries, which in turn limits the number of laboratories both able and willing to offer these tests. Therefore, clinicians often treat cutaneous fungal infections based on clinical appearance and
symptomatology, which can lead to inappropriate treatment, poor response rates, and complications. For example, it may encourage the use of readily available topical combinations of strong corticosteroids with topical antibiotics and antifungals as a “catch-all” treatment for skin conditions, which can often be purchased without prescription or monitoring. This ready availability of topical antifungal preparations has contributed to the growth of terbinafine-resistant \textit{T. indotinea} in India.\textsuperscript{36}

The incidence of antifungal drug resistance is increasing for most fungi, including dermatophytes.\textsuperscript{36,37} Addressing this growing problem will require a combination of clinical expertise, laboratories able to culture and identify fungi, including dermatophytes, and the first introduction of dermatophyte susceptibility testing.\textsuperscript{38} These specialized healthcare elements will require public health coordination and data dissemination.

The data presented here were obtained through a questionnaire addressed to specialists in each country. The limitations of this study include (1) the exclusion of countries with a population of <1 million and (2) the partial nature of the information obtained for some countries where the information was obtained only for the localities where the respondent practiced rather than the whole country, or was actually addressed via additional validation with country leaders through Africa CDC. The emergence of terbinafine resistance in \textit{Trichophyton} species may require dermatophyte susceptibility testing in at least some facilities, a question that was not addressed in the survey. Inevitably, the full picture regarding diagnostic access needs to be documented in each country, especially in larger countries with a diverse and complex healthcare ecosystem. The WHO’s efforts to address skin-related NTDs should contribute to improved diagnostic capability.\textsuperscript{39} One of the challenges set out in this framework document, in addition to the need for enhanced diagnostic facilities and training, is how best to utilize the expertise of the small number of local experts and laboratories to maximum effect.

Acknowledgments

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