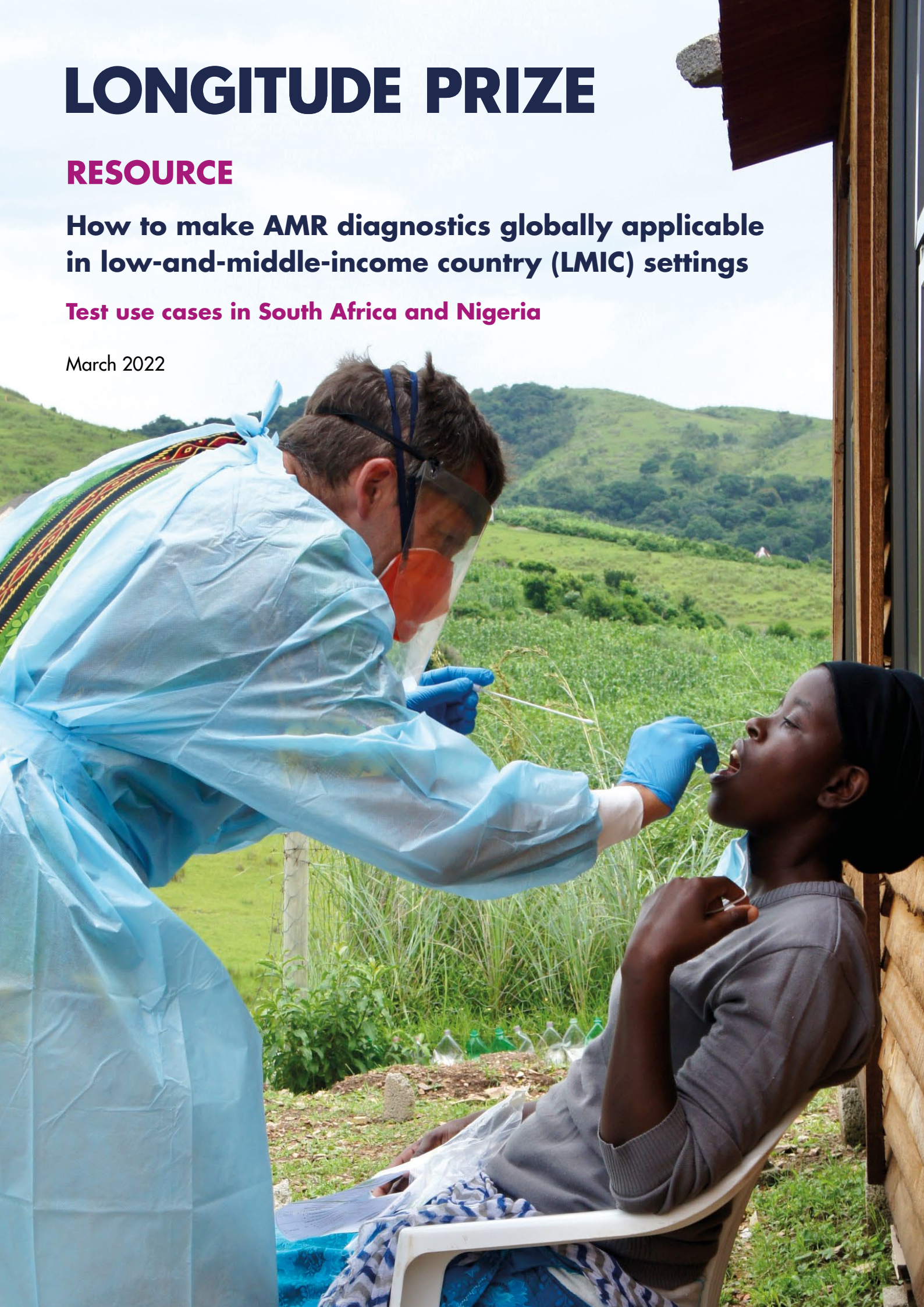
LONGITUDE PRIZE

RESOURCE

How to make AMR diagnostics globally applicable in low-and-middle-income country (LMIC) settings

Test use cases in South Africa and Nigeria

March 2022



LONGITUDE PRIZE

The Longitude Prize is a £10 million prize fund with an £8 million payout that will reward a competitor that can develop a point-of-care diagnostic test that will conserve antibiotics for future generations. The test must be accurate, rapid, affordable and easy-to-use anywhere in the world. The Longitude Prize is run by Nesta Challenges, part of Nesta, the UK's innovation foundation, with funding from Innovate UK.

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EXECUTIVE SUMMARY

Nesta Challenges (NC) commissioned technical advice from Market Access Africa (MAA) to support diagnostic developers focus on making their point-of-care diagnostic tests for Antimicrobial Resistance (AMR) globally applicable. MAA assessed profiles of tests within the Longitude Prize cohort in relation to clinical and public health needs in Nigeria and South Africa – and identified pathways for marketing them.

The findings and practical recommendations presented in this resource aim to support Longitude Prize teams to create product commercialisation plans for marketing their tests in Nigeria, South Africa, and LMIC settings more broadly.

The project found that there is demand for the profiles of tests being developed as part of the Longitude Prize in Nigeria and South Africa. Products are expected to offer value in terms of cost, patient and health system impact if they can enter the market early in the healthcare pathway.

Practical recommendations

AMR diagnostic developers considering the South African or Nigerian market in their future product commercialisation plans, should consider the following practical recommendations:

- Conduct **evaluation studies** to validate the performance and clinical impact of the test, compared to the gold-standard.
- Commission a **cost-benefit analysis** of the test to understand its impact with a defined price point in mind.
- Prevent off-label use, by ensuring Quality Assurance (QA).
- Engage early with Key Opinion Leaders (KOLs) in the target markets to help streamline market entry.
- Secure regulatory approval from SAPHRA (South Africa) and NAFDAC (Nigeria).
- Generate provider and caregiver demand.
- Build operational capabilities.

Diagnostic products can enter each market via four pathways:

- Direct to consumer (DTC) marketing and sales.
- Private and/or public sector lab services or chains.
- Private sector pharmaceutical distributors.
- Private or public medical insurers.

Further detail on the practical recommendations and an appraisal of the pathways to market can be found in section 1.5.2. Recommendations for teams.

BACKGROUND

The Longitude Prize is looking for diagnostic tests that can be used safely and effectively at point-of-care settings globally, including in low-and-middle-income countries (LMICs). The seven mandatory criteria to win the Longitude Prize include 'Easy-to-Use' and 'Affordable,' within which is 'Globally Applicable'. Please see the Longitude Prize Rules on our website for more details.

Diagnostic developers often focus on developing tests that suit high-income countries, entering revenue-driven markets to achieve commercial success and build a sustainable business. Entering LMIC markets can be challenging to navigate, particularly for small, early-stage companies.

To support Longitude Prize teams focus on making their point-of-care tests globally applicable, NC commissioned technical advice from Market Access Africa (MAA) – a consultancy specialising in market access strategies for point-of-care diagnostics in African countries. MAA assessed, using publicly available information, profiles of tests within the Longitude Prize cohort in relation to clinical and public health needs in two LMICs, namely Nigeria and South Africa – and identified pathways for marketing them.

This document is a **resource** to support Longitude Prize teams to make their products globally applicable, by providing practical **recommendations** which can be used to shape teams' **product commercialisation plans** for marketing tests in different global settings. It is recommended that teams focus on section 1.5.2. Recommendations for teams.

INTRODUCTION

MAA conducted primary and secondary research, consulting a wide range of key opinion leaders (KOLs) in Nigeria and South Africa, from policymakers and regulators to health insurers, pharmaceutical distributors and research institutes – to provide practical recommendations and useful contacts to support Longitude Prize teams with market entry in both settings.

The research was carried out in three phases:

Primary research and landscaping	Interviews with country-level experts to understand: • The current treatment and diagnostic standard of care. • Patient pathways to care. • Pros and cons of product use cases. • Regulatory and policy considerations. Please see Annex 2 for a list of organisations that were represented during the interviews.
Secondary research	Further secondary research included reviewing scientific literature, country-specific reports, guidelines and data from the National Institute of Communicable Diseases (NICD), National Centre for Disease Control (NCDC), South African Health Products Regulatory Authority (SAPHRA), National Agency for Food and Drug Administration and Control (NAFDAC), World Health Organization (WHO) and other documents.
Analysis and report development	Analysis of primary and secondary research data to deliver the final report and recommendations for Longitude Prize teams.

In both the South African and Nigerian markets, the scope of the project was to review:

1. Current disease management, treatment and patient pathway
   - The current management and treatment of respiratory tract infections (RTIs), bloodstream infections (BSIs) and urinary tract infections (UTIs) – and opportunities to improve the current standard of care.
   - The current workflows and diagnostic testing models at different levels of the health system (Level 0 to Level 4).
   - The use-cases of test profiles within the Longitude Prize cohort, to understand their potential to address identified gaps and workflow needs.

2. Competitive and commercial landscape
   - The competitive landscape, including identifying existing products offering greater value with respect to cost, patient and health system impact.
   - The types of clinics or labs the test types would be sold in.
   - The distribution networks (the wholesalers/ agents selling diagnostic products to the clinics and the labs servicing private clinics).
   - The current price point of similar tests.
   - The commercial drivers for adoption.

FINDINGS

1.1. AMR research and development (R&D) priorities for diagnostics in Africa

According to the WHO, the following clinical syndromes present some of the most pressing needs for R&D in AMR diagnostics and testing in low-and-middle-income countries (LMICs).[1]

- Fever of unknown source.
- Sore throat/cough, upper respiratory infections (URTIs).
- Pneumonia/lower respiratory tract infections (LRTIs).
- Urinary tract infections (UTIs).
- Bloodstream infections (BSIs) and Sepsis.

A lack of diagnostic tools that address these needs poses severe challenges for tackling AMR[2] in Africa where more than one-third of African countries do not have data on AMR (although available data indicate that AMR is increasing).[3]

There is an alarming increase in **drug resistance** to **commonly prescribed antibiotics** including aminoglycosides, sulphadoxine pyrimethamine and ampicillin in hospital outpatients and higher levels of AMR seen in inpatient care, including moderate to high rates of resistance to third-generation cephalosporins. There are currently very limited second-line treatment options and standardisation, and quality of microbiological identification and susceptibility testing methods needs to be improved to allow national and international organisations to monitor the extent of AMR.[2,3]

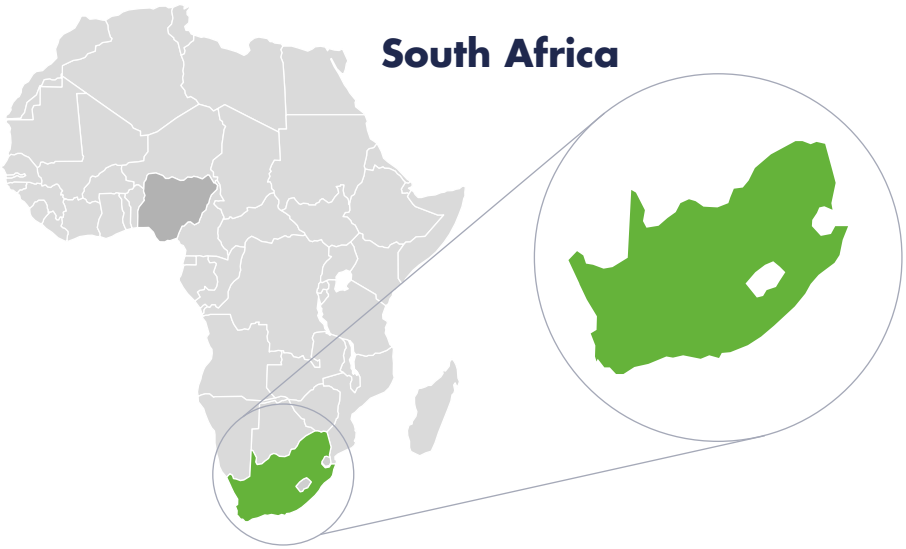
The need for quality assured diagnostics in LMICs has been ongoing for many years as lack of access to quality diagnostics remains a major contributor to the burden of disease. In 2003, the WHO Special Programme for Research and Training in Tropical Diseases (WHO/TDR) published a set of criteria for the ideal test at all levels of the healthcare system in LMICs. Its purpose is to guide treatment and clinical management decisions for infectious tropical diseases and sexually transmitted infections. These criteria are known by the acronym **ASSURED** (affordable, sensitive, specific, user-friendly, rapid, equipment-free, delivered), and have become widely accepted as the benchmark for an ideal test that can be used at the point of care (POC).

Future diagnostics should take into account rapid advances in digital technology and mobile health (m-health), to allow for **REASSURED** diagnostic systems that can inform disease control strategies in real-time, strengthen the efficiency of healthcare systems and improve patient outcomes. Longitude Prize teams are encouraged to use the REASSURED criteria to consider their tests, which encompasses **real-time connectivity** and **ease of specimen collection**.

1. WHO. Technical consultation on in vitro diagnostics for AMR, 27–28 March 2019, WHO Headquarters, Geneva: meeting report. WHO 2019. Report No.: WHO/MVP/EMP/IAU/2019.08. https://apps.who.int/iris/handle/10665/326481
2. Tadesse BT et al. Antimicrobial resistance in Africa: a systematic review. BMC Infectious Diseases. 2017;17(1):616. doi: 10.1186/s12879-017-2713-1
3. Ndihokubwayo et al. Antimicrobial resistance in the African region: issues, challenges and actions proposed. WHO Regional Office for Africa 2013. Link

1.2. South Africa and Nigeria landscape

1.2.1. Snapshot of South African landscape



Overview of South African healthcare fundamentals

Population	Total population (2019)	58 million
	Population growth rate (2019)	1.3%
Health economics	Health spend/capita (2018)	US$525
	Health spend/GDP (2018)	8.2%
	Private health expenditure (2018)	44%
	Pharma market size (2019)	US$3B

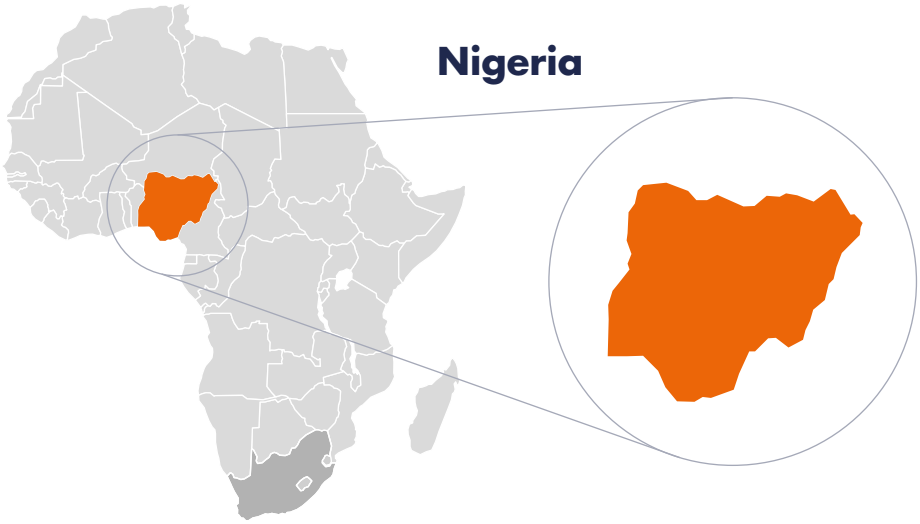
Regulatory body: SAPHRA.

Health system overview:

- Three-tiered decentralised service delivery system.
- Tertiary care (managed by the National Department of Health).
- Secondary care (managed by Provincial Health Departments).
- Primary care (managed by the Municipal Health Departments).

Please see Annex 4 for a detailed overview of the AMR Strategy in South Africa. Annex 6 contains details of the public and private health systems in Nigeria and South Africa.

1.2.2. Snapshot of Nigerian landscape



Overview of Nigerian healthcare fundamentals

Population	Total population (2019)	210 million
	Population growth rate (2019)	3%
Health economics	Health spend/capita (2018)	US$84
	Health spend/GDP (2018)	3.89%
	Private health expenditure (2018)	77%
	Pharma market size (2019)	US$600–1B

Regulatory body: NAFDAC.

Health system overview:

- Three-tiered decentralised service delivery system.
- Tertiary care (managed by the Nigeria Federal Ministry of Health (FMoH)).
- Secondary care (managed by Nigeria State Ministry of Health (SMoHs)).
- Primary care (managed by the state Primary Healthcare Boards but overseen centrally by the National Primary Healthcare Development Agency (NPHCDA)).

Please see Annex 5 for a detailed overview of the AMR plan in Nigeria.

1.2.3. South Africa and Nigeria: Findings on antibiotic misuse

In South Africa, RTIs and UTIs account for at least 60% of antibiotic misuse/over-prescription. Contributory factors include prescriber practice and the cost of antibiotics, especially in the private sector. The interviews found that many social factors also contribute, for example:

- Patients or their families do not believe they will recover until they are prescribed antibiotics.
- The patient's employer denies sick leave.
- Patients are less likely to return to doctors that do not prescribe antibiotics.

> *"STIs, URTIs, LRTIs, UTIs and infective diarrhoea are major conditions seen at primary healthcare, without doctors sending for tests, and instead treating based on symptoms… leading to over-treatment sometimes. We could reduce antibiotic use if there was a test to help decide that this is not a bacterial infection, or if an STI, which it is – assuming people acted on the results."*
>
> **Senior Clinician, South Africa**

Similarly, the interviews found that in Nigeria, some patients believe that they have not been treated unless they are prescribed antibiotics, leading to over-treatment. If a clinician does not prescribe antibiotics, the patient may instead purchase them from a community pharmacist or a patent and proprietary medicine vendor (PPMV).

In South Africa, 70% interviewees responded that misuse of antibiotics is greater in the private sector than public, as there are broader baskets of antibiotics available to the sector. In both countries, the public sector is more limited by the budget available for purchase of antibiotics compared to the private sector. When not available in the public sector, antibiotic prescriptions and lab orders are given to patients to purchase or order from the private sector. Public and private medical insurers do not strictly oversee the prescription of antibiotics. If patients can afford the prescriptions, they are billed according to the limits of the health insurance benefits plan they are enrolled in.

At health facilities in Nigeria generally, the clinical diagnostic index of suspicion amongst clinicians is high, due to the long time-to-result. Antibiotic susceptibility testing (AST) with an automated system may provide prelliminary results in 24 hours and full results in 7 days. Many laboratories still use manual systems, and due to the patient workflow, turnaround time, lack of reagents and lack of funds from patients to pay out of pocket (OOP) – results are sometimes available to support clinical management in 2 – 3 weeks. Many clinicians therefore prefer to order complete blood count tests (where they receive results in less than 24 hours) to support immediate clinical management, rather than completing blood or urine microscopy/ culture/ sensitivity testing (m/c/s).

1.3. Current disease management (according to recommended guidelines) and reality of practice

In both South Africa and Nigeria, 70% interviewees responded that syndromic management is the primary patient pathway, where clinical decisions are made based on the symptoms and signs presented by the patient.

1.3.1. South Africa

Interviews found that in South Africa, the following is the order of prioritisation in public health: UTI < LRTI < URTI < BSI – and that public health including lateral flow tests, simple finger prick assays and blood pressure measurement should be able to be performed by a lay health worker.

Standard treatment guidelines			Comments	Challenge/gaps
UTIs (L0-L1)	Empirical or syndromic management.	Public sector: Urine dipstick (none at L0; limited use at L1).	Antibiotics are prescribed >80% of the time with no follow-up unless patient relapses. A wider basket of antibiotics is available in the private sector.	• Challenges: Collection of "good quality urine samples"as clean urine collection is difficult. • Gaps: POC tools to provide differential diagnosis between viral, bacterial and/or fungal infection.
		Private sector: Urine dipstick/POC automated urinalysis and CBC, CRP is done in facilities where available.		
		Public and private sector: Where available, suspected cases are tested for the presence of bacteria and AST is conducted to determine the course of antibiotic to use.		
UTIs (L2-L4)	Public and private sector: Suspected cases are tested for the presence of bacteria and AST before or alongside empirical management commences.		CBC, CRP and Procalcitonin (but mostly in the private sector where available). A wider basket of antibiotics is available in the private sector.	
RTIs (L0-L1)	Empirical or syndromic management in public and private facilities. CBC tests are also used in the private sector.		Antibiotics are prescribed >80% of the time with no follow-up unless patient relapses. A wider basket of antibiotics is available in the private sector.	• Gaps: POC tools to provide differential diagnosis between viral, bacterial and/or fungal infection.
RTIs (L2-L4)	Public and private sector: Throat swab culture and AST are ordered before or alongside empirical management.		CBC, CRP, and Procalcitonin (but mostly in the private sector where available). Antibiotics are widely prescribed even if a viral infection is suspected. A wider basket of antibiotics is available in the private sector.	• Gaps: A diagnostic tool with a shorter turnaround time (the current standard culture test takes ~7 days).
BSIs (L0-L1)	Empirical or syndromic management in public and private facilities.		Antibiotics are prescribed >80% of the time with no follow-up unless patient relapses. A wider basket of antibiotics is available in the private sector.	• Gaps: POC tools to differentiate viral, bacterial and/or fungal infections.
BSIs (L2-L4)	Public and private sector: Blood culture and AST are ordered before or alongside empirical management.		Treatment for BSIs is dependent on the level of facility. A wider basket of antibiotics is available in the private sector. Other tests include CBC, CRP and Procalcitonin (but mostly in the private sector where available).	• Gaps: A diagnostic tool with a shorter turnaround time to enable swift management (the current standard culture test takes ~7 days).

1.3.2. Nigeria

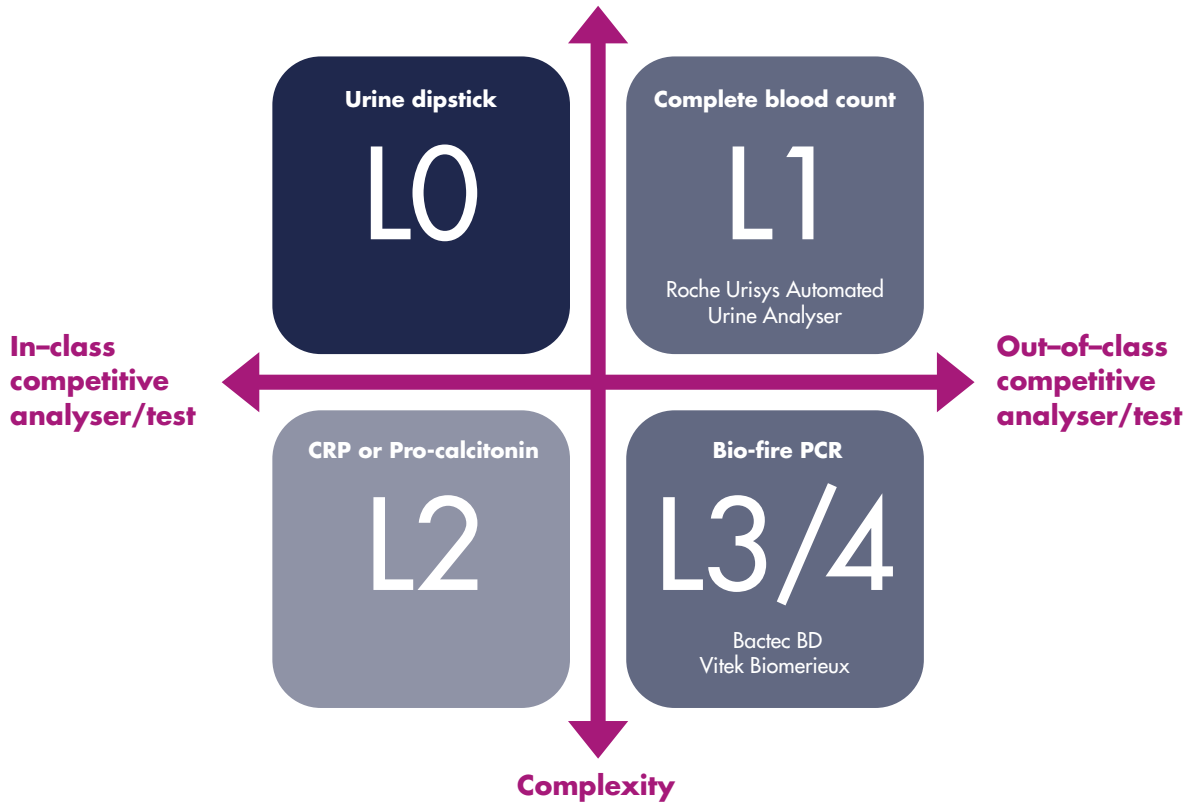
Standard treatment guidelines			Comments	Challenge/gaps
UTIs (L0-L1)	Empirical or syndromic management.	Public sector: Urine dipstick (none at L0 limited use at L1).	Antibiotics are prescribed >80% of the time with no follow-up unless patient relapses. A wider basket of antibiotics is available in the private sector.	• Challenges: Collection of "good quality urine samples"as clean urine collection is difficult. • Gaps: POC tools to provide differential diagnosis between viral, bacterial and/or fungal infections.
		Private sector: Urine dipstick/POC automated urinalysis and CBC is done in facilities where available.		
		Public and private sector: Where available, urine microscopy, culture and sensitivity (m/c/s) tests are done to determine the course of antibiotic to prescribe.		
UTIs (L2-L4)	Public and private sector: Urine m/c/s investigations are ordered before or alongside empirical management commences.		CBC (but mostly in the private sector where available). A similar basket of antibiotics is available in the public and private sector. In this instance, antibiotic over-prescription is driven more by prescriber practice and cost, rather than availability or accessibility.	
RTIs (L0-L1)	Empirical or syndromic management in public and private facilities. CBC tests are also used in the private sector.		Antibiotics are prescribed >80% of the time with no follow-up unless patient relapses. A wider basket of antibiotics is available in the private sector.	• Gaps: POC tools to provide differential diagnosis between viral, bacterial and/or fungal infections.
RTIs (L2-L4)	Public and private sector: Throat swab m/c/s are ordered before or alongside empirical management.		CBC (but mostly in the private sector where available). Antibiotics are widely prescribed even if viral infection is suspected. A similar basket of antibiotics is available in the public and private sector. In this instance, antibiotic over-prescription is driven more by prescriber practice and cost, rather than availability or accessibility.	• Gaps: A diagnostic tool with a shorter turnaround time (the current standard culture test takes ~7 days).
BSIs (L0-L1)	Empirical or syndromic management in public and private facilities.		Antibiotics are prescribed >80% of time with no follow-up unless patient relapses. A wider basket of antibiotics is available in the private sector.	• Gaps: POC tools to differentiate viral, bacterial and/or fungal infections.
BSIs (L2-L4)	Public and private sector: Blood m/c/s are ordered before or alongside empirical management.		Treatment for BSIs is dependent on the level of facility. A similar basket of antibiotics is available in the public and private sector. In this instance, antibiotic over-prescription is driven more by prescriber practice and cost, rather than availability or accessibility. Other tests include CBC, CRP, Procalcitonin where available but mostly in the private sector.	• Gaps: A diagnostic tool with a shorter turnaround time (current standard culture test takes ~7 days).

“ You want a test that has a very good negative predictive value (NPV) – so reliably tells you that although the patient may look sick, you can be 99.9% sure they don’t have bacterial sepsis so you can withhold antibiotics and look for differential diagnoses like TB, cryptococcal meningitis, autoimmune diseases, etc. Most clinicians would not be confident with a NPV of 85% enough to withhold antibiotics. The default is usually ‘if I’m not sure I’ll prescribe antibiotics’ as opposed to ‘if I’m not sure I’ll wait. ”

Senior Academic and Microbiologist, South Africa

1.4. Competitive and commercial landscape

The competitive landscape in both target countries remains uncrowded as commercially available diagnostic products reside at higher facility levels (from Level 2 upwards).



‘In-class’ products provide the same ‘result type’ for an equal investment. At Level 0, the current in-class solution is a urine dipstick which can be used interoperably with a lateral flow urine test. An example of an ‘out-of-class’ product would be an automated analyser at Level 1 which would not be comparable to a lateral flow test for UTIs, but instead a handheld or benchtop point-of-care device.

1.4.1. Market Landscape: Five product categories

The market landscape can be grouped into five product categories with distinct features and characteristics – and corresponding product methods.

Product categories	Manual biomarker tests	Haematology tests	Clinical chemistry tests	DNA-based tests	Microscopy, culture and AST‡
	are used for UTIs to detect LE and Nitrites as measures of infection in Urine	WBC count is used as a proxy measure of infection for UTIs, RTIs and BSIs	are used for UTIs, RTIs and BSIs to detect (high-sensitivity) CRP or PC* as measures of acute inflammation or infection in Blood (Serum)	are used for BSIs to detect and identify nucleic acid material of causative micro organisms and AST in Blood	are used for UTIs, RTIs and BSIs to detect the causative microorganisms and AST in Urine, Blood and Throat Swabs
Product types or methods	Combi dipsticks, POC automated analysers	Complete blood count	Point of care and lab based assays	Lab based non POC and near POC PCR devices	Manual methods and advanced methods with automated analysers
Key metrics†**					
Affordability	Low cost		Varies		High cost
Ease of use	Easy-to-run		Varies		Complex-to-run

Definitions

- Affordability: Tests are affordable to OOP end-users (benchmark <US$2 at point of care).
- Easy-to-use: Test is easy to perform in a few steps, requiring minimum training and no power requirements.
- LE: Leucocyte Esterase.
- CRP: C-Reactive Protein.
- PC: Pro-Calcitonin.
- AST: Antimicrobial Sensitivity Testing.
- WBC: White Blood Cell.

* In South Africa, PC is a cost-effective biomarker test to distinguish between viral and bacterial infections.

** The layout of the key metrics has no direct correlation with the layout of the product categories.

† Data on the unique performance of these tests in the target market landscape was inaccessible and unavailable.

‡ Microscopy, culture and AST tests are commonly ordered and done together in South Africa and Nigeria, hence why they are included together in same category.

1.4.2. Mapping commercially available diagnostics

The diagrams below are non-exhaustive maps of commercially available diagnostic tools for UTIs, RTIs and BSIs at the various levels of care in South Africa and Nigeria, grouped by the five product categories in 1.4.1.

South Africa

	Manual biomarker tests	Haematology tests	Clinical chemistry tests	DNA-based	Microscopy, culture and AST
Commercially available products	Micro Essential Roche Machery-Nagel Bio Rad	Sysmex Beckman Coulter	Roche Abbot	Roche Qiagen Biomérieux Applied Biosystems	Biomérieux BD Bio Rad

Nigeria

	Manual biomarker tests	Haematology tests	Clinical chemistry tests	DNA-based	Microscopy, culture and AST
Commercially available products	Micro Essential Roche Machery-Nagel	Sysmex	Roche	Roche Biomérieux	Biomérieux BD

1.4.3. Price points of diagnostic test products in South Africa and Nigeria

The landscape in South Africa and Nigeria consists of diagnostic test products with varying price points. The diagram below presents consumer cost prices in the private sector in both countries.[4] C-Reactive Protein (CRP) tests are used for RTI differentiation (i.e. distinguishing viral vs bacterial RTIs) in both countries.

	South Africa				Nigeria			
	Example products	Consumer cost price ($USD)*			Example products	Consumer cost price ($USD)*		
		Lowest	Average	Highest		Lowest	Average	Highest
Urinalysis	Roche	N/A	N/A	41.00	Micro Essential	2.43	3.16	4.86
Throat Swab Culture	BD	N/A	N/A	45.00	BD	7.29	10.88	13.60
CRP†	Roche	14.00	N/A	4.55	Roche	10.93	11.90	16.76
Pro-Calcitonin	Roche	42.00	52.00	61.00	Roche	N/A	N/A	N/A
Complete Blood Count	Sysmex	N/A	N/A	16.00	Sysmex	4.86	7.39	8.50
Blood Culture and AST	Biomérieux	N/A	N/A	55.00	BD	14.57	23.85	35.21

1.4.4. Commercial landscape: Supply chain, distribution networks and drivers

In South Africa and Nigeria, all products are sold by an appointed **in-country distributor** or via the **foreign manufacturer** directly to private labs, clinics, hospitals or dispensaries/pharmacies. In general, it is more cost effective to use a small existing in-country distributor to manage the business because of the cost of running a business in either market. It is critical to have service and technical personnel (see 1.5.2. Recommendation 5) as first line in-country to secure confidence from the market and a quick turnaround time to repair.

UTI tests for the private sector, South Africa

Exploring the UTI market for the private sector in South Africa is complex due to the model of service delivery in the private hospital network. However, there may be opportunities for AMR diagnostic developers to engage with private sector networks in relation to medical insurance clients – and options for out of pocket or co-payments for 'convenience and return to work' motivations.

The complexity lies in the reimbursement model. All hospital services (excluding in-patient services) are out-sourced, including diagnostics services unless provided at point-of-care. The reimbursement would form part of hospital services and capped at the maximum threshold for medical insurance cover. There may also be co-payments if the cost exceeds the reimbursement rate. Out of pocket is highly likely but South Africa offers 'gap cover medical insurance' to close the gap between hospital reimbursement and out of pocket payments, although this is costly and only applies to a small number of insured patients.

In general, all private laboratory chains have a depot or lab within the hospital and the diagnostic could be covered under lab reimbursement. Diagnostics that are not provided at point of care or that require more than a lateral flow or 'finger prick' are likely to be placed within these small labs.

4. Sources: Nigeria: Surjen Online Marketplace was used for laboratory tests. These prices were corroborated with prices from interviews with Nigerian KOLs. South Africa: Prices sourced from interviews with private pathology labs. Not all consumer prices could be obtained.

1.5. Further insight and recommendations for Longitude Prize teams

Products within the Longitude Prize cohort are expected to offer value to LMICs in terms of cost, patient and health system impact if they can enter the market early in the healthcare pathway – to serve Level 0 and Level 1 needs.

1.5.1. Value proposition of POC diagnostics for AMR

Across Nigeria and South Africa, four themes were identified describing the overall value proposition of test use-cases.

- **Decentralisable** and **deployable** but also **quality assured** to the lowest levels of the health systems where they are most needed (Level 0 and Level 1).
- The **price point** should be lower than the current standard of care, which costs anywhere between $2-$61 USD depending on location and device type.
- **Empirical patient management** is the current standard of care in the public sector which is more price conscious than the private sector, which is more time-conscious.
- Tests should be **easy to ship, stock** and **manage** (battery powered, limited need for electricity or power generators and not internet-dependent) with limited cold chain requirement, etc.

NB. Although participants stated that the price point of novel diagnostics must be lower than the current standard of care, Nesta Challenges' position is that innovations will inevitably enter the market at a higher price point than the current standard, and this will reduce over time. Nesta Challenges encourages diagnostic innovators to stress the economic impact of their test in reducing AMR within health systems as a means to communicate their value.

1.5.2. Recommendations for teams

1.0. Evaluate suitable pathways for market entry

Products can enter the market in South Africa and Nigeria via four pathways. An appraisal of these pathways can be found below.

Product entry pathways	Advantages	Disadvantages
Direct-to-consumer (DTC) marketing and sales Using private sector GPs and/ or nurse practitioners (NPs) where patients pay OOP for these tests.	• Most insured patients are motivated by convenience and a return to work mindset. • Potential OOP payment, co-payment or fully covered under prescribed minimum benefit (PMB).	• Insured population is a fraction <10-20% of national need. Public sector remains largely un-insured where the need is greater. • Longitude Prize teams would be expected to support marketing and sales (M&S) activities (at a minimum co-finance).
Private and/or public sector lab services/chains Labs can maintain Quality Control (QC) of sample collection, etc.	• Sample quality and patient trust is linked. • Established sample transport network for potentially batched tests or those collected at L0 but tested at L2. • Most labs have depots in all private hospitals (for larger POC instruments or batch testing).	• Need to ensure adequate coverage of services (real access for last mile patients). • Investment required into sample transport if none exists. • If sample collection is more complex than finger prick, phlebotomist is required by law (in South Africa).
Private sector pharmaceutical distributors Do DTC marketing of products to patients via community pharmacies, PPMVs, etc.	• Well-established in both countries and could easily accommodate novel platforms. • Removes logistical hurdles. • Carriage paid to (CPT) or Free Onboard (FOB)[5] agreements may be simple to execute.	• Non-exclusive agreements may increase competitive pressure. • Inclusion of margins may price Longitude Prize diagnostics out of segments – it is likely co-financing will be necessary at a minimum.
Private or public medical insurers Avoids patients having to pay OOP for tests as they would be covered in insurance packages.	• If included in PMB and simple to run, it could be a niche entry to market approach. • Larger client base (not just medically insured).	• South Africa has a greater medically insured population than Nigeria, but the public sector need is equally great in both markets.

5. These are Incoterms related to shipping/logistics. FOB means that the seller ships the goods to the nearest port, and the seller is responsible for transportation after that. CPT is where the seller pays for the goods to be shipped to the import port that the buyer chooses. https://www.cosmosourcing.com/blog/incoterms-defined-fob-exw

2.0. Complete evaluation studies

Evaluation studies would help Longitude Prize teams to validate:

- Test **performance**, in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV);
- **Clinical impact**, for example impact on time to treatment/turnaround time, hospitalisation, antibiotic consumption, treatment and long-term resistance, change in prescribing behaviour, etc. of these tests compared to the gold standard of culture and AST. Clinical benefit was identified as a gate-keeper to new market entrants in both countries.

These studies will also bolster **dossiers** for **licensing and registration**. NC and MAA can support Longitude Prize teams with **introductions to relevant organisations** who are well-suited to conduct the evaluations in each country. .

3.0. Commission a cost-benefit analysis

Cost-benefit analyses would provide Longitude Prize teams with greater awareness on the cost-components of implementing diagnostic tests at **scale**. They can also serve as an **advocacy tool**/economic investment case to convince LMIC governments and the private sector to adopt tests.

4.0. Engage early with KOLs

It is recommended that Longitude Prize teams engage early with well-connected key opinion leaders that were interviewed as part of the project. This could support teams to **streamline market entry** in these markets.

5.0. In Nigeria, take steps to prevent widespread informal testing and treatment.

Off-label use in lab systems, refers to where reagents or detergents are replaced in the diagnostic workflow with those from another manufacturer that might not be approved. The research found this to be prevalent in Nigeria.

Diagnostic manufacturers should:

- Build control mechanisms into the assay.
- Ensure the test has Quality Assurance (QA). Participate in external QA, or build robust QA into the assay.
- Understand the operating limits of the test, for example temperature range or humidity for product stability.

Laboratories can also be accredited with annual re-training programmes, which comes at a cost to the manufacturer – and this investment is less likely to be made with regards to technical personnel in rural areas.

General recommendations for driving commercialisation and adoption in LMICs:

6.0. Secure regulatory approval

Ensure all necessary studies required by national regulatory authorities and Ministries of Health are in place. National regulators and technology assessors may require additional studies on their local needs in addition to clinical trial results. Health economics studies may also prove useful to augment existing data. Insufficient studies is a key risk factor impacting the market-strategy in LMICs – as is poor clinical trial results.

If clinical trial results indicate poor performance against bench-marked technologies, national authorities will be hesitant to adopt the product.

For South Africa and Nigeria, regulatory approval from SAPHRA and NAFDAC respectively would be key to introducing products into both markets.

7.0. Generate provider and caregiver demand

Take steps to improve the knowledge and skill sets of health providers, and create awareness among end-users and caregivers.

Lack of demand generation is a key risk factor impacting go-to-market strategy. Market development (e.g. demand creation, provider awareness) could be an expensive undertaking however, and will require public sector partners with funding and interest in the relevant disease areas.

8.0. Build operational capabilities

Regarding procurement and the supply chain, ensure widespread availability of high-quality, affordable and optimal supply through public and private sector channels.

Operational capability building (e.g. commercialisation, distribution, procurement) will be critical to Longitude Prize teams looking to capitalise on the potential market size in LMICs.

Close

Although it is not a requirement for Longitude Prize teams to have marketed their tests in different global settings in order to meet the criteria to win the prize, the findings and recommendations presented in this resource aim to support diagnostic developers to create product commercialisation plans for marketing their tests in Nigeria, South Africa, and LMIC settings more broadly.

ANNEXES

Annex 1: Acronyms

AMR: Antimicrobial Resistance

AMS: Antimicrobial Stewardship

ANC: Antenatal Care

AST: Antimicrobial Susceptibility Testing

CBC: Complete Blood Count

CRP: C-reactive Protein

CPT: Carriage paid to

DoH: South Africa Department of Health

DTC: Direct To Consumer

FAO: Food and Agriculture Organisation

FMoH: Nigeria Federal Ministry of Health

FOB: Free Onboard

GARP: Global Antibiotic Resistance Partnership

GEMS: Government Employees Medical Scheme

GP: General Practitioner

HTA: Health Technology Assessment

KOL: Key Opinion Leader

LMICs: Low- and Middle-Income Countries

LUTH: Lagos University Teaching Hospital

MAC: Ministerial Advisory Committee

M/c/s: Microscopy/culture/sensitivity testing

M&S: Marketing and Selling

NAFDAC: National Agency for Food and Drug Administration and Control

NCDC: Nigeria Centres for Disease Control and Prevention

NIMR: Nigeria Institute of Medical Research

NP: Nurse Practitioner

NICD: National Institute of Communicable Diseases

NPV: Negative Predictive Value

OIE: The World Organisation for Animal Health

OOP: Out of Pocket

PC: Pro Calcitonin

POC: Point of Care

PPMV: Patent and Proprietary Medicine Vendor

PPV: Positive Predictive Value

QC: Quality Control

SADC: Southern African Development Community

SALDA: Southern African Laboratory Diagnostics Association

SMoH: Nigeria State Ministry of Health

WHO: World Health Organization

Annex 2: Participant organisations

30 experts at over 21 organisations were interviewed, representing Ministries of Health and government agencies, academics, private sector insurers, labs and hospitals. Interviewees in **South Africa** represented the following institutions, 12% of which were directly patient-facing.

Category	Institution	Description
National regulator	South African Health Products Regulatory Authority	SAHPRA is a federal agency tasked with regulating (monitoring, evaluating, investigating, inspecting and registering) all health products including drugs, complementary medicines, medical devices and in vitro diagnostics (IVDs)
National research institute	National Health Laboratory Service	NHLS is a national network of public health and research laboratories that offers laboratory and diagnostic services across South Africa.
National research institute	National Institute for Communicable Diseases	NICD is a national research institute providing public health research to support the government's response to communicable disease threats.
Public health insurer	Government Employees Medical Scheme	GEMS is a public sector insurer created specifically to meet the healthcare needs of Government Employees.
National academic and public health research institute	University of Cape Town	The department of infectious diseases and HIV medicine at UCT offers inpatient and outpatient health services and is world renown for clinical research in HIV, Tuberculosis and AMR. It also contributes to policy development for infectious diseases and AMR strategy at the Provincial and National level.
Private health insurer	Discovery Health	Discovery is South Africa's leading private medical insurer providing managed care services to over 3.3 million beneficiaries with a market share of over 40%.
Pharmaceutical Distributor	Southern African Laboratory Diagnostics Association	SALDA represents multinational and local companies who distribute In Vitro Diagnostic tests.
Private lab diagnostics group	Lancet Laboratories	Lancet Laboratories offer a wide range of pathology services across South Africa with a staff strength of over 90 specialist pathologists performing over 3,700 separate pathology tests.
National academic and public health research institute	University of Kwazulu-Natal	The pharmaceutical sciences department at UKZN has an AMR unit and their research influences national health policy in terms of amendments to standard treatment guidelines (STGs) and the Essential Drugs List (EDL).
National academic and public health research institute	Stellenbosch University	The medical microbiology and immunology department's NHLS affiliated laboratories at the University of Stellenbosch offer diagnostic services in western cape town, South Africa.
National academic and public health research institute	University of the Witwatersrand, Johannesburg	The medical microbiology and immunology department's NHLS affiliated laboratories at the University of Witwatersrand offer diagnostic services in western cape town, South Africa.

Interviewees in **Nigeria** represented the following institutions. 10% of which were directly patient-facing.

Category	Institution	Description
National policy maker	Federal Ministry of Health	FMoH is the federal ministry responsible for developing and implementing health related policies. It is headed by two Ministers appointed by the President, assisted by a Permanent Secretary, who is a career civil servant.
National regulator	National Agency for Food and Drug Administration and Control	NAFDAC is a federal agency responsible for regulating and controlling the manufacture, importation, exportation, advertisement, distribution, sale and use of drugs and medical devices in Nigeria.
National research institute	Nigeria Centre for Disease Control	NCDC is a national public health institute, with the mandate to lead the preparedness, detection and response to infectious disease outbreaks and public health emergencies.
National research institute	Nigerian Institute of Medical Research	NIMR is a national public health institute carrying out applied and operational research for the promotion of national health and development.
National tertiary medical institution	Lagos University Teaching Hospital	LUTH is a federal tertiary teaching hospital affiliated with the University of Lagos College of Medicine.
Private health insurer	AXA Mansard Health Limited	AXA Mansard Health Limited is the Health Maintenance Organization (HMO) arm of the AXA Mansard group of companies providing personal, family and corporate health insurance plans.
Pharmaceutical distributor	ISN Pharmaceuticals Limited	ISN Pharmaceuticals Limited is a private supplier of medical diagnostic products and services.
Private lab diagnostics group	Medicaid Laboratories Limited	Medicaid Laboratories Limited is a private sector lab and radio diagnostic company with various centres in Nigeria's capital city.
Private hospital group	Lily Hospitals	Lily group of hospitals is a network of private service institutions across southwest Nigeria providing integrated medical and diagnostic services.
Pharmaceutical distributor	Dozie and Dozie's Pharmaceuticals Limited	Dozie and Dozie's Pharmaceuticals Limited is a private sector supplier of medical and diagnostic supplies.

Annex 3: REASSURED criteria[6]

30 experts at over 21 organisations were interviewed, representing Ministries of Health and government agencies, academics, private sector insurers, labs and hospitals. Interviewees in **South Africa** represented the following institutions, 12% of which were directly patient-facing.

Acronym	Criteria	Disadvantages
R	Real-time connectivity	Tests are connected and/or a reader or mobile phone is used to power the reaction and/or read test results to provide required data to decision-makers.
E	Ease of specimen collection	Tests should be designed for use with non-invasive specimens.
A	Affordable	Tests are affordable to end-users and the health system.
S	Sensitive	Avoid false negatives.
S	Specific	Avoid false positives.
U	User-friendly	Procedure of testing is simple — can be performed in a few steps, requiring minimum training.
R	Rapid and robust	Results are available to ensure treatment of patient at first visit (typically, this means results within 15 min to 2 hours); the tests can survive the supply chain without requiring additional transport and storage conditions such as refrigeration.
E	Equipment free or simple Environmentally friendly	Ideally the test does not require any special equipment or can be operated in very simple devices that use solar or battery power. Completed tests are easy to dispose and manufactured from recyclable materials.
D	Deliverable to end-users	Accessible to those who need the tests the most.

6. Land KJ et al. REASSURED Diagnostics to Inform Disease Control Strategies, Strengthen Health Systems and Improve Patient Outcomes. Nature Microbiology 4 (1): 46–54; 2019. doi: https://doi.org/10.1038/s41564-018-0295-3

Annex 4: South Africa AMR strategy framework 2014-2024[7]

Background

In 2011, the Situation Analysis report generated awareness of AMR and highlighted that South Africa has a quadruple burden of resistant infectious diseases: multidrug resistant TB; drug resistant HIV; malaria; and AMR.

In October 2014, the Minister of Health launched the National AMR Strategy Framework spanning 10 years (2014-2024), which outlines the country's plan for the management of AMR and the improvement of patient outcomes.

Following on closely to the World Health Assembly (WHA) endorsing the Global Action Plan in 2015, South Africa developed and published an Implementation Plan for the AMR Strategy Framework to guide the implementation of the strategy. Since then they have been working actively with animal health and environmental colleagues to update the AMR Strategy Framework, and incorporate more relevant interventions from these sectors. The Ministerial Advisory Committee (MAC) received support from professional societies and organisations from and outside of South Africa, such as Global Antibiotic Resistance Partnership (GARP).

Strategic objectives to achieve targets

- Strategic objective 1: Strengthen, coordinate and institutionalise interdisciplinary and intersectoral efforts through national and provincial One Health governance structures which encompasses human, animal, and environmental health experts.
- Strategic objective 2: Diagnostic stewardship to improve the appropriate use of diagnostic investigations to identify pathogens and guide patient and animal treatment and antimicrobial management whilst strengthening quality laboratory systems for the detection of disease.
- Strategic objective 3: Optimise surveillance and early detection of AMR and antimicrobial use to enable reporting of local, regional, and national resistance patterns to optimise empiric and targeted antibiotic choice.
- Strategic objective 4: Enhance infection prevention and control and biosecurity to prevent the spread of resistant microbes to patients in healthcare settings and between animals, farms and countries. Reduced use of antimicrobials by disease prevention and community measures include wide-reaching vaccination programmes, improvements in water and sanitation, and improved biosafety.
- Strategic objective 5: Promote appropriate use of antimicrobials in human and animal health through antimicrobial stewardship (AMS) practices and controlled access to antimicrobials to ensure availability.

7. Antimicrobial Resistance National Strategy Framework; A One Health Approach 2018 – 2024. Departments of Health and Agriculture, Forestry and Fisheries for the Republic of South Africa. South Africa 2017. Link Other sources: Zwarenstein M. The structure of South Africa's health service. Afr Health. 1994 Mar;(Spec No):3–4; The World Bank South Africa Profile. https://data.worldbank.org/country/south-africa

The validation of the AMR Strategy, initiated in 2018 by the Southern African Development Community (SADC) Secretariat with support from the tripartite alliance (WHO, OIE & FAO), was a major step towards a collective approach in fighting the spread of AMR.

Decision-makers	Local influencers	International influencers
Department of Health, Republic of South Africa	Department of Agriculture, Forestry and Fisheries, Republic of South Africa Department of Basic Education, Republic of South Africa South African Veterinary Association The Pharmaceutical Society of South Africa (PSSA) South African Association of Community Pharmacists (SAACP) South African Medical Association	World Health Organisation FIND Medical Research Council (MRC) Center for Disease Dynamics, Economics and Policy (CDDEP) Global Antibiotic Resistance Partnership (GARP) Centers for Disease Control and Prevention

8. National Action Plan for Antimicrobial Resistance 2017 – 2022 Nigeria. Federal Ministries of Agriculture and Rural Development, Environment and Health 2017. Link. Other sources: National Population Commission (NPC), Nigeria, and ICF. 2019. 'Nigeria Demographic and Health Survey 2018'. https://dhsprogram.com/publications/publication-fr359-dhs-final-reports.cfm The World Bank Nigeria Profile. https://data.worldbank.org/country/NG

Annex 5: Nigeria AMR strategy framework[8] 2017-2022

Background

Following the WHA resolution in 2015 requesting countries to develop or adopt country specific AMR action plans, in line with the Global Action Plan on AMR, the Nigerian Minister of Health in 2016 approved the establishment of Nigeria's National AMR Coordinating Body at the NCDC. A National AMR Technical Working Group (AMR-TWG) was created comprising stakeholders from human ¬¬health, animal health, food animal production and environmental sectors. In 2017, the TWG was first tasked with developing a situational analysis and later that year developed an AMR National Strategic Plan (2017 – 2022).

Strategic objectives to achieve targets:

- Strategic objective 1: Increase awareness and knowledge of AMR and related topics.
- Strategic objective 2: Build a 'One Health' AMR Surveillance System.
- Strategic objective 3: Intensify Infection Prevention and Control in Tripartite Sectors.
- Strategic objective 4: Promote Rational Access to Antibiotics and Antimicrobial Stewardship.
- Strategic objective 5: Invest in AMR Research and Development.

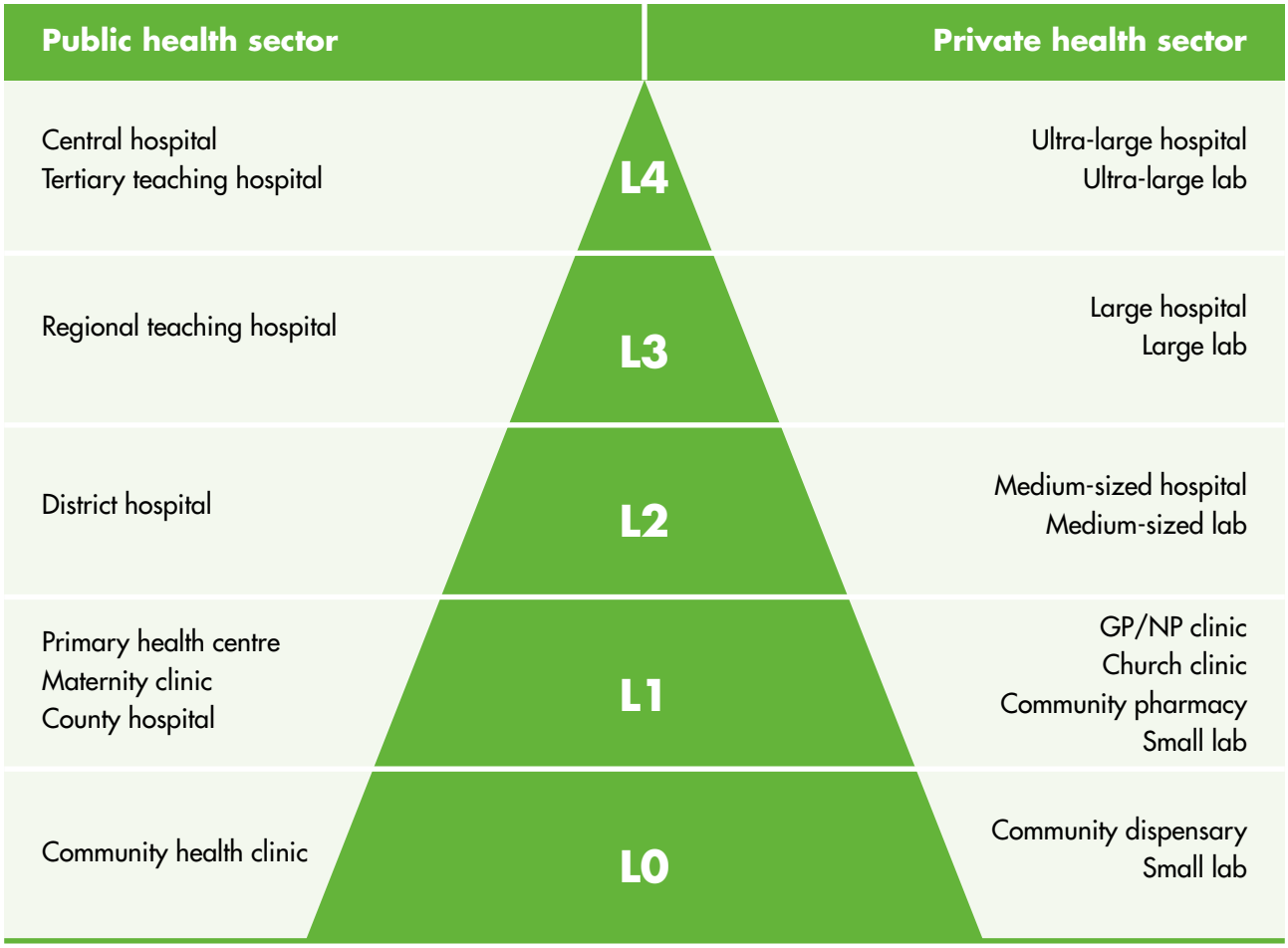
Antimicrobial stewardship (One Health approach)

A major gap identified is 'One Health' coordination of animal and human national disease surveillance systems. The strategic plan incorporates the One Health approach and aims at implementing proposed actions by strengthening and utilising existing national systems or by creating new structures where they do not exist. The focus is on setting up a national AMR surveillance system using a One Health approach and strengthening institutional capacities (e.g. laboratories) for early AMR detection.

Decision-makers	Local influencers	International influencers
Nigeria Centre for Disease Control Federal Ministry of Health	Pharmacists Council of Nigeria Veterinary Council of Nigeria Association of General and Private Medical Practitioners of Nigeria (AGPMPN) - Lagos State Nigerian Medical Association Guild of Medical Directors (GMD) Medical and Dental Council of Nigeria Association of Medical Laboratory Scientists of Nigeria	World Health Organisation FIND Medical Research Council (MRC) Center for Disease Dynamics, Economics and Policy (CDDEP) Global Antibiotic Resistance Partnership (GARP) Centers for Disease Control and Prevention (CDC) National Institute for Health and Care Excellence (NICE)

Annex 6: Overview of public and private sector health system

South Africa



Hospitals

- Small district hospitals (~50-150 beds).
- Regional hospitals serve patients based on referrals from district hospitals (~200-800 beds).
- Tertiary hospitals receive referrals from regional hospitals, and provide supervised specialist and intensive care services (~400-800 beds).
- Central hospitals provide tertiary and central referral services and many provide national referral services.

There are more than ~200 private hospitals offering ~30,000 beds, and more than 60 private clinics. 3 hospital groups dominate the private hospital market and have equivalent numbers of beds.

Laboratories

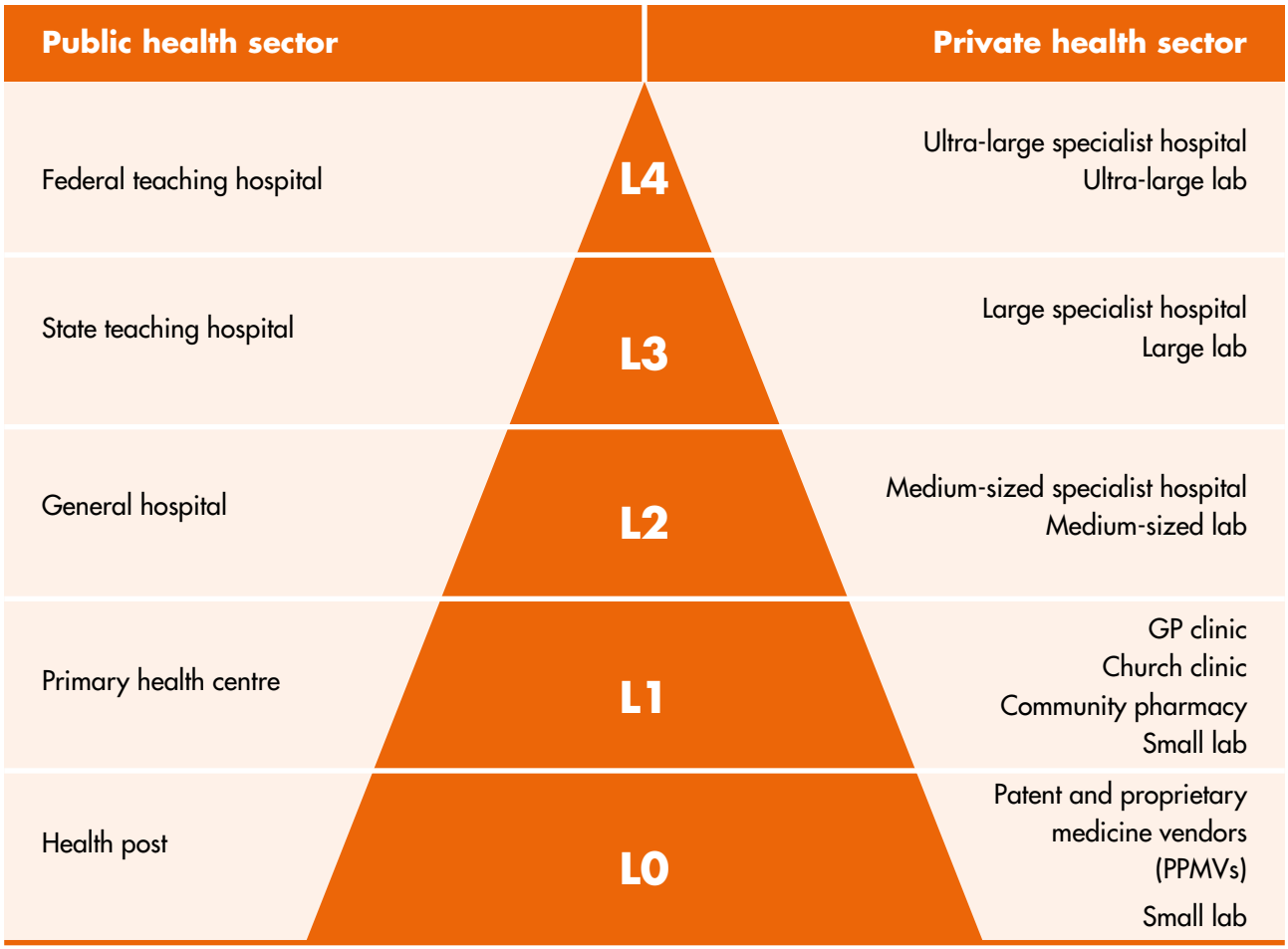
The public sector has a National Health Lab Service (NHLS). Labs are a single national resource located across the 9 provinces. Choice of diagnostic tests in the public sector is based on centralised and competitive bid prices. In the private sector, several labs exist but are organised in large groups. Private hospital groups are serviced by a range of separate independent labs but organised in corporate structures. There are 3 large corporate labs like AMPATH, Lancet Labs and a plethora of small practices and individual pathologists.

Insurance

There are 78 different private insurers who offer 3 – 4 benefit options. Approximately 8 million people who are insured are split into 200 different risk pools; 3 million of those are insured by the single largest insurer – Discovery Health. Discovery Health has a whole range of benefit options from hospital only to comprehensive coverings for almost anything a patient wants.

~84% of the population use the public health system and ~14% of the population use the private health system. 50% of healthcare expenditure is in the private sector serving 14% of the population and 84% of the population make up the remaining 50% of healthcare expenditure. The private sector is largely stagnant and the total number of insured individuals has not grown considerably over the years. Growth has predominantly been in the uninsured population due to the growing population alongside a stagnant insured pool.

Nigeria



Community pharmacies, patent and proprietary medicine vendors (PPMVs) and other drug retail outlets are also a first point of contact for many patients seeking healthcare. There are at least 40,226 operational health facilities: 73.1% are managed by the federal, state and local ministries of health whilst 26.9% are managed by private providers. Private facilities mimic the 3 tiered health system depending on the level of funding, infrastructure and human resources available. 93% of healthcare is paid for out of pocket. Insurance coverage is about 5%.

Annex 7: Note on the role of regulators and health technology assessments in South Africa

Health technology assessment (HTA) is a critical process in research and scientific methodology. It outlines the medical (laboratory-based), social, financial and ethical issues related to the use of a health technology in order to ensure safe, effective health policies in the interest of the patient.

A Health Technology Assessment (HTA) unit functions within the National Health Lab Service (NHLS) Quality Assurance Department. The primary objective of this unit is to focus on in vitro diagnostic laboratory technologies with particular reference to diagnostic reagents, analysers and point-of-care testing (POCT) technologies.

The NHLS HTA unit promotes and facilitates access to safe, reliable and appropriate diagnostic technologies and laboratory services in an equitable manner through:

- Prequalification of diagnostics for in vitro diagnostic devices in pathology services.
- Capacity building of national regulatory authorities (SAPHRA) and national reference laboratories.
- Facilitation of procurement of affordable and appropriate diagnostics.
- Policy, guidance and advocacy to NHLS and the national Department of Health as well as the Southern African Development Community (SADC) region.
- Collaboration with The International Network of Agencies for Health Technology Assessment (INAHTA) as middle-income developing country.
- HTA training and technical support including internal and external participants.

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