WHO Standard

Universal access to rapid TB diagnostics

Nazir Ismail
Team Lead, Diagnostic Team, GTB

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Diagnostics: Drug resistant TB Background

- Diagnostics are a key component of any TB strategy
  - *"If we cannot find TB, we cannot treat TB. And if we cannot treat TB, we cannot end TB."*
- Rapid detection of TB and drug resistance is essential to identify and select effective regimens
- Many diagnostic options are now available but scale up is severely lacking
- The Covid-19 has negatively impacted TB epidemic but has taught us important lessons of what can be achieved

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Diagnostic Gaps, 2021

Percentage of people estimated with TB disease who were notified	**60%**
Percentage of people newly diagnosed with TB who were initially tested with a WHO-recommended rapid test	**38%**
Percentage of people newly diagnosed with pulmonary TB who were bacteriologically confirmed	**63%**
Percentage of people diagnosed with bacteriologically confirmed TB who were tested for rifampicin-resistant TB	**70%**

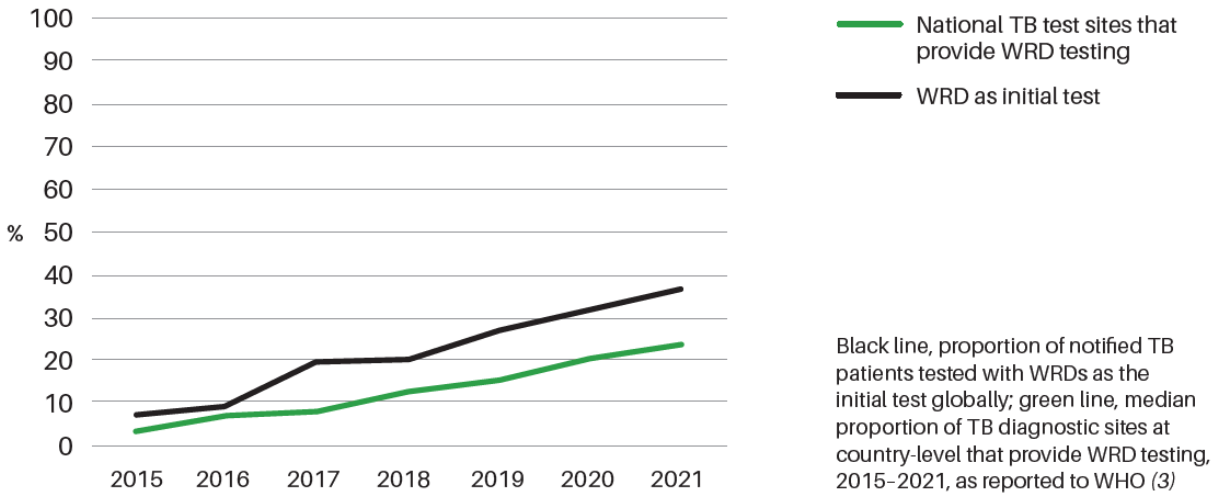
Target for 2025 – all notified cases tested with a WRD

Fluoroquinolone DST among MDR/RR-TB =49%
Bedaquiline & Linezolid DST much lower

2022 WHO Global TB Report

Access to WHO-recommended rapid TB Diagnostics

Fig. 1. Improving access to WRDs



Black line, proportion of notified TB patients tested with WRDs as the initial test globally; green line, median proportion of TB diagnostic sites at country-level that provide WRD testing, 2015–2021, as reported to WHO *(3)*

- >10 years since first recommendation
- Access is a major issue with only 25% of sites having a WRD in 2021
- Other diagnostic issues
  - Drug resistance detection
  - Timely reporting of results
  - Quality assurance of testing

Fig. 2. WHO-recommended rapid diagnostic testing platforms to be used as initial tests for TB, 2022

Xpert MTB/RIF & Ultra

Truenat MTB, MTB Plus & -RIF Dx

Loopamp™ MTBC detection

Abbott *RealTime MTB & MTB RIF/INH*

BD MAX MDR-TB

cobas® MTB & MTB-RIF/INH

FluoroType MTB & MTBDR

Several different products recommended by WHO to fit different contexts

WRDs refer to molecular tests and non-molecular tests but at present the former are the primary initial diagnostic tests

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The objectives of this *WHO standard* are to:

- improve **access** to and use of WRDs as initial tests for individuals with presumptive TB identified by active and passive case finding;
- increase detection of **bacteriologically confirmed** and **drug-resistant TB**; and
- reduce the **time to diagnosis**.

https://apps.who.int/iris/bitstream/handle/10665/366854/9789240071315-eng.pdf

http://gh.bmj.com/cgi/content/full/bmjgh-2023-012666

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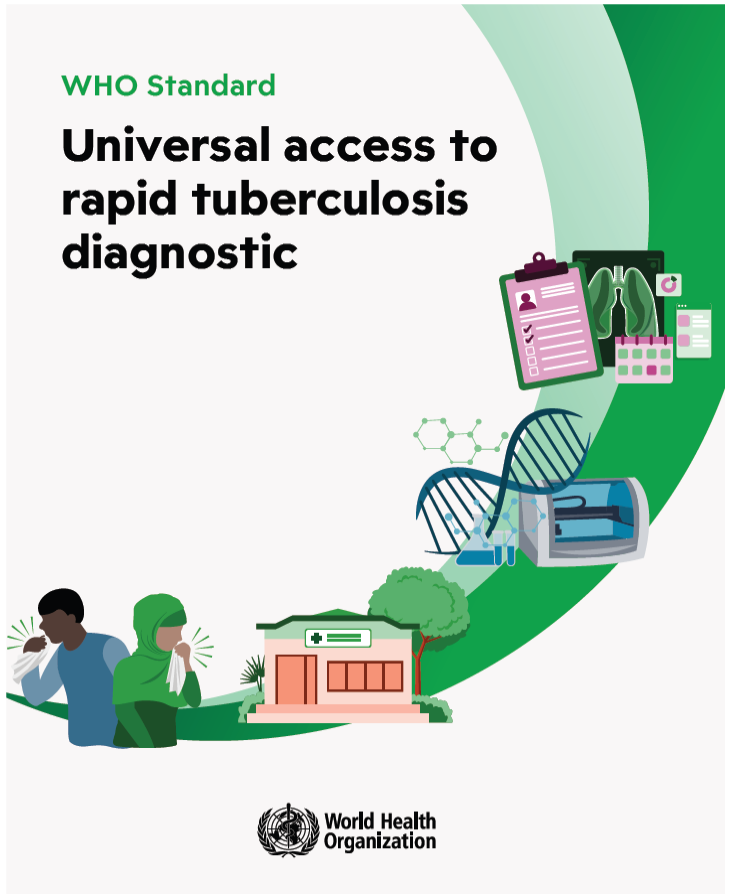

Principle	Interpretation
1. Strong political and financial commitment is available to ensure access to TB diagnosis.	Financial, technical, and human resources should be specified in planning documents, with additional support from the ministry of finance and from partners, donors, and civil society.
2. Diagnostic testing is equitable.	All individuals with presumptive TB in all sectors (public, private, non-NTP) should be eligible for WRD testing.
3. The most accurate, rapid tests are used to diagnose TB.	Transition from smear microscopy to WRDs as the initial test for TB diagnosis should be accelerated.
4. The diagnostic approach is patient centred.	Barriers that result in a negative patient experience and related costs should be minimized.
5. Diagnostic coverage reaches all levels of the health system and covers patients in private and other non-NTP sectors.	In accordance with plans for universal health coverage, WRDs should reach all primary health care facilities systematically and progressively in public, private, and non-NTP sectors.
6. Diagnostic results are provided in a timely manner in order to be useful for patient management.	On-site WRD testing should be provided in high-workload settings or where timely results cannot be obtained by sample referral. Sample referral systems should be strengthened for all other health facilities. Digital systems are used to improve timely access to results and analysis.
7. Diagnostic capacity is optimally used according to the local context.	All individuals with presumptive TB identified through passive and active case finding should have access to TB diagnostic testing including multi-disease testing (for, e.g. COVID-19, early infant diagnosis, and viral load for HIV), according to the local context.

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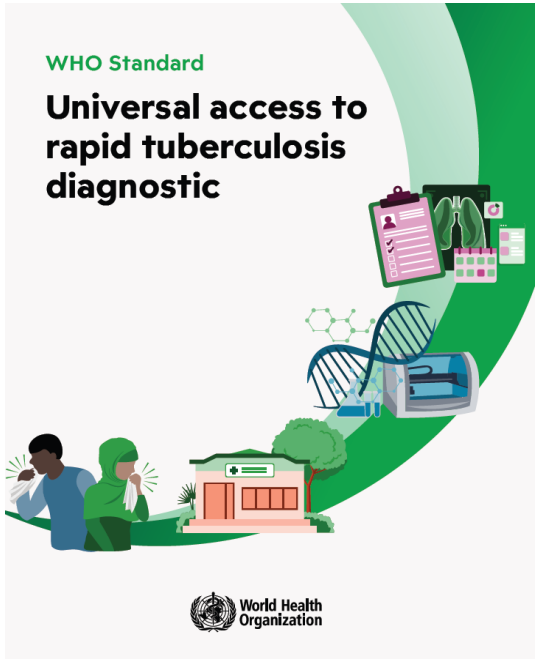

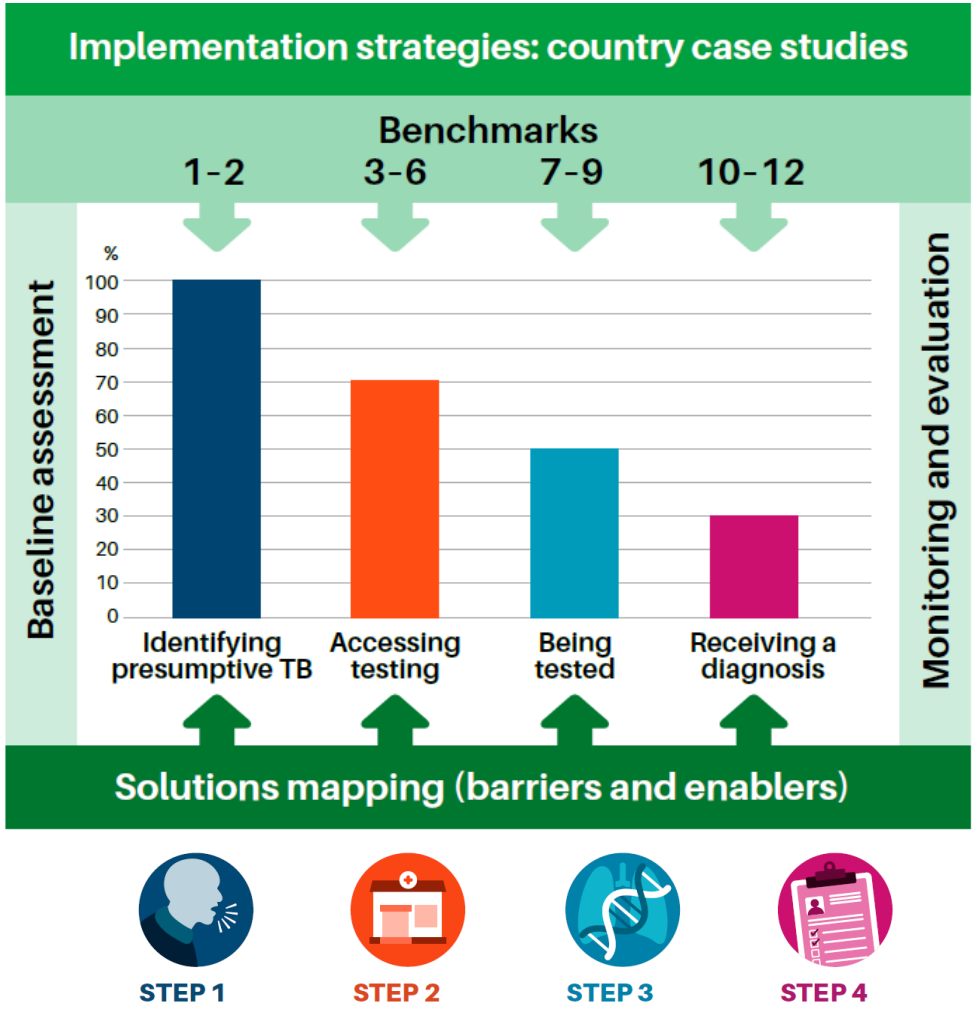

- Cascade of care framework
- Focused on access to diagnostics
- Broad consultative process
- Specific private sector considerations
- Mapping of enablers, strategies, solutions and case studies

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https://apps.who.int/iris/bitstream/handle/10665/366854/9789240071315-eng.pdf

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4 steps and
12 benchmarks

Operational measures of benchmarks include:

- ***Districts***
- ***Laboratories***
- ***Health facilities***
- ***Individuals***

STEP 1

Identifying presumptive TB

- Systematic screening of high-risk groups
- Chest X-ray for TB screening

STEP 2

Accessing testing

- Up-to-date diagnostic algorithms
- WRD access in primary health care
- Diagnostic coverage reaches all
- Testing capacity matches needs

STEP 3

Being tested

- Monitoring quality of testing
- All patients with presumptive TB tested with a WRD
- Universal DST provided

STEP 4

Receiving a diagnosis

- All pulmonary TB patients have a WRD result
- Test positivity rate monitored
- Timely delivery of results

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STEP 1

IDENTIFYING PRESUMPTIVE TB

Increase the number of people with presumptive TB in care

Private sector – risk populations e.g. HCW, miners

Screening high risk groups

- the groups at highest risk for developing TB.
- PLHIV, household contacts, others

Chest X-ray for TB screening

- the sensitivity of any cough or a cough of ≥ 2 weeks' duration for detection of TB disease is only 51% and 42%, respectively.
- Screening by chest radiography (CXR) (and CAD when available) is a highly sensitive (≥ 85%)

Benchmark 1

All household contacts, all PLHIV, and other locally relevant high-risk groups are screened for TB.

Benchmark 2

In all districts, chest X-ray is used regularly for TB screening.

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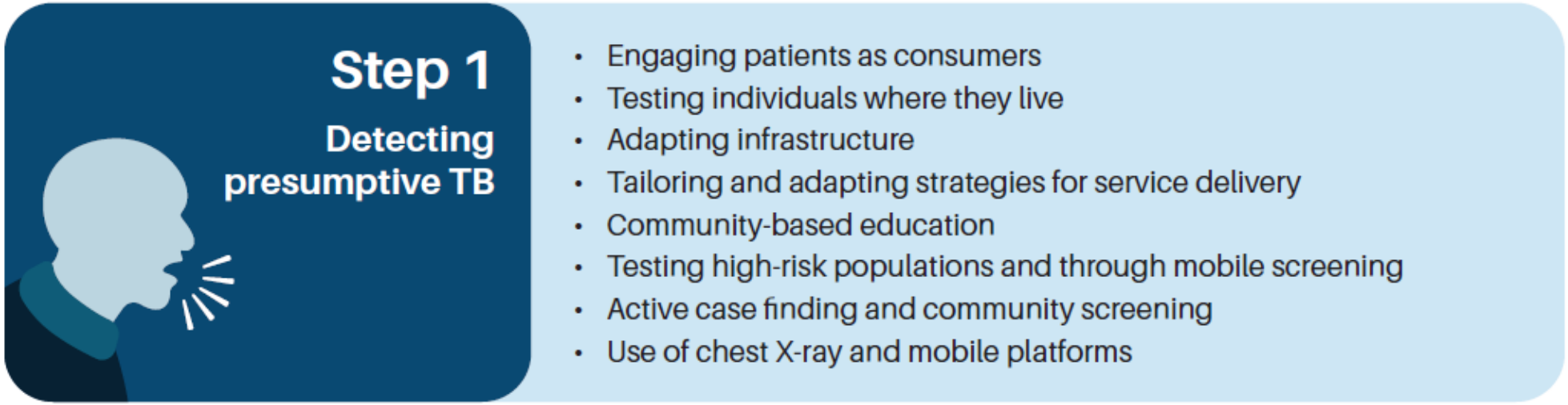
Fig. 7. Implementation solutions along the cascade of care from the systematic review



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STEP 2

ACCESSING TESTING

Increase access to WRDs

Private sector: Districts with private model: intermediary agencies or private laboratory engagement models

- Algorithms are the first step
- Diagnostic gaps persist for PLHIV, children and EPTB

- More than 80% of individuals with symptoms of TB enter at primary health care

- WRD as the initial test, 2017 - 2021 : 21%, 22%, 28%, 33% and 38%.

- Only 25% of TB diagnostic sites have access. Increased capacity leads to better access.

Benchmark 3

In all facilities in all districts, the TB diagnostic algorithm requires the use of a WRD as the initial diagnostic test for all individuals with presumed TB, including children and PLHIV (combined with lateral flow lipoarabinomannan [LF-LAM]) and extrapulmonary TB.

Benchmark 4

All primary health-care facilities have access to WRDs (on site or through sample referral).

Benchmark 5

All individuals with TB have access to a WRD as the initial diagnostic test.

Benchmark 6

WRD testing capacity meets expected needs, including surge capacity, according to the latest data.

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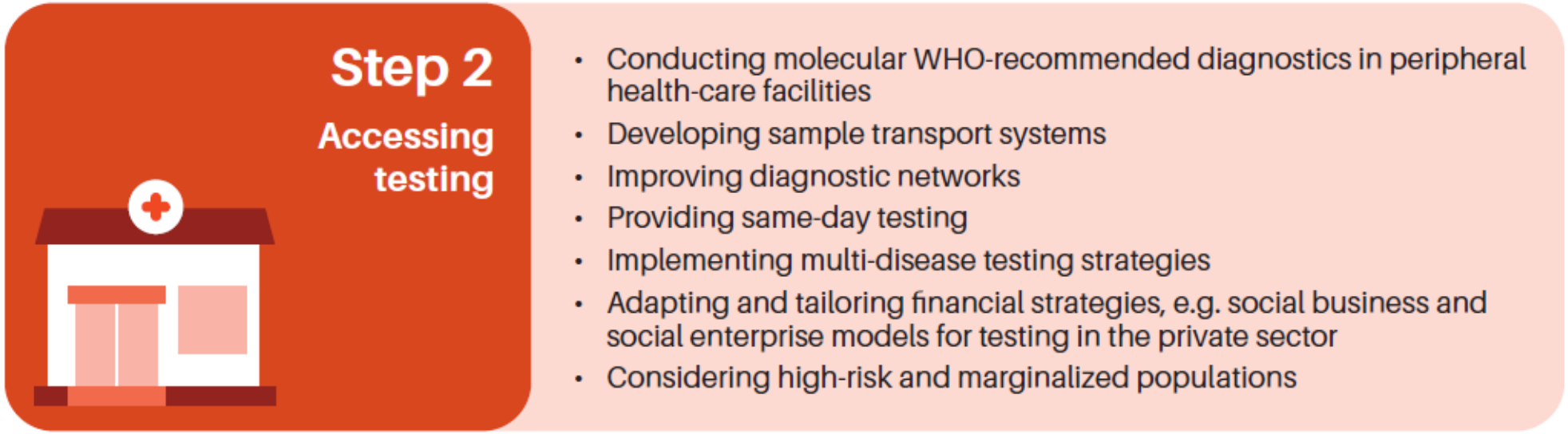
Fig. 7. Implementation solutions along the cascade of care from the systematic review



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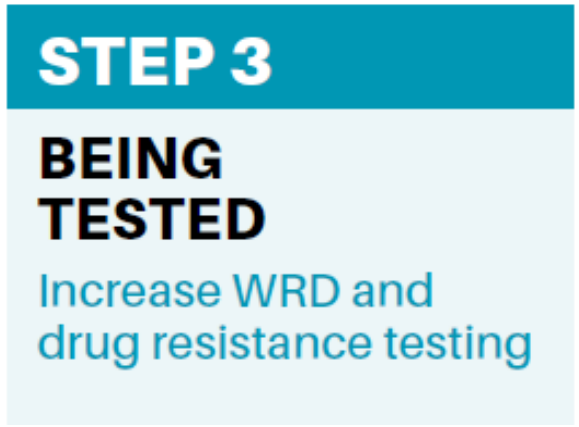

Private sector: Private laboratory reporting on universal DST

Major concerns of instrument failures and maintenance. Only three of the ten countries reporting data achieved the Global Laboratory Initiative target of 3%.

A large proportion of individuals with bacteriologically confirmed TB are still diagnosed by smear microscopy.

Only 70% of all bacteriologically confirmed TB cases were tested for resistance at least to RIF. FQ resistance testing 49%
Group A drugs (e.g. bedaquiline and linezolid) much lower.

Benchmark 7

All functional instruments have an error rate ≤ 5%.

Benchmark 8

All individuals with presumptive TB are tested with a WRD.

Benchmark 9

All patients with bacteriologically confirmed TB undergo universal drug susceptibility testing.

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Fig. 7. Implementation solutions along the cascade of care from the systematic review

Step 3

Being tested

- Engaging clinicians as consumers
- Providing longitudinal training to health-care workers
- Using evaluative and iterative strategies to redesign clinical, laboratory, and pharmacy workflows
- Using quality improvement feedback to improve care
- Servicing and maintaining equipment regularly
- Integrating multi-disease testing to improve access
- Facilitating broader engagement of the health system

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STEP 4

RECEIVING A DIAGNOSIS

Increase WRD-based diagnosis

Private sector: Disaggregation by bacteriologically confirmed versus clinically diagnosed

Only 63% of pulmonary TB cases notified globally in 2021 were bacteriologically confirmed

The median test-positivity rate in 2021 was 17% (IQR 9–26) globally and 11% in the African Region, and 27% in the Western Pacific Region.

Reports of results received after 7 days are common in many settings and TAT is not consistent

Benchmark 10

All patients with pulmonary TB receive an initial WRD result to inform their diagnosis.

Benchmark 11

All districts monitor the test positivity rate to optimize the impact of screening and testing strategies.

Benchmark 12

All TB testing laboratories achieve a turn-around time of ≤ 48 h for ≥ 80% of samples received for WRD testing.

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Fig. 7. Implementation solutions along the cascade of care from the systematic review

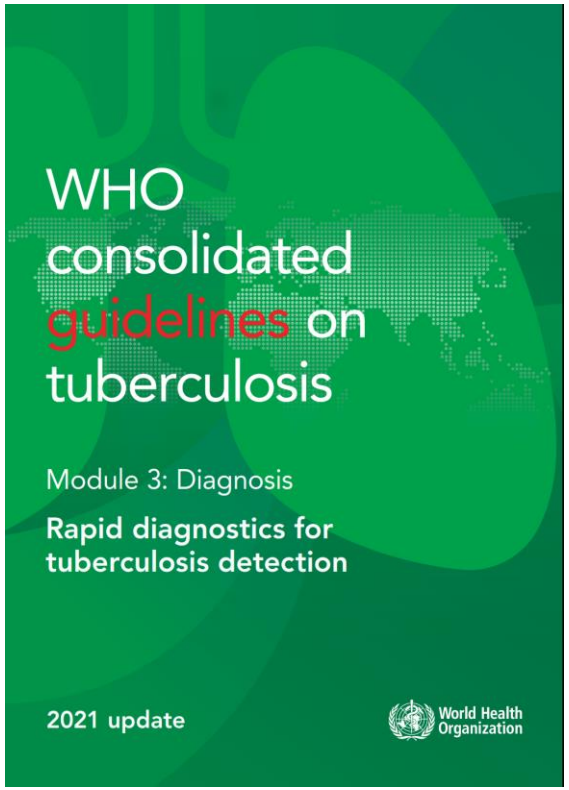
Step 4

Receiving a diagnosis

- Linking patients and clinicians
- Adapting and tailoring delivery of molecular WHO-recommended diagnostics results
- Changing infrastructure, including electronic data systems and mHealth solutions
- Using interactive assistance
- Building partnerships with the private sector and using mHealth tools
- Supporting clinicians by longitudinal engagement
- Using evaluative and iterative strategies to improve services
- Adapting financial strategies

IMPLEMENTING THE WHO STANDARD

WHO GUIDANCE ON TB DIAGNOSIS



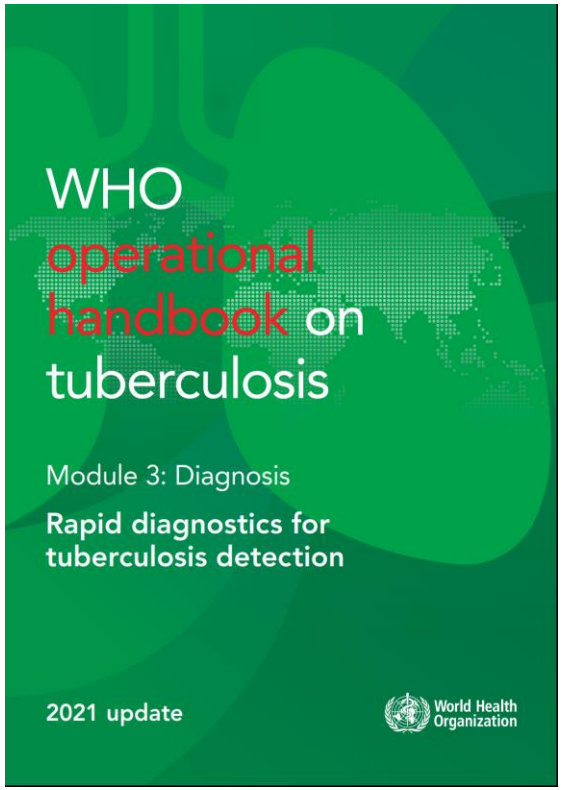


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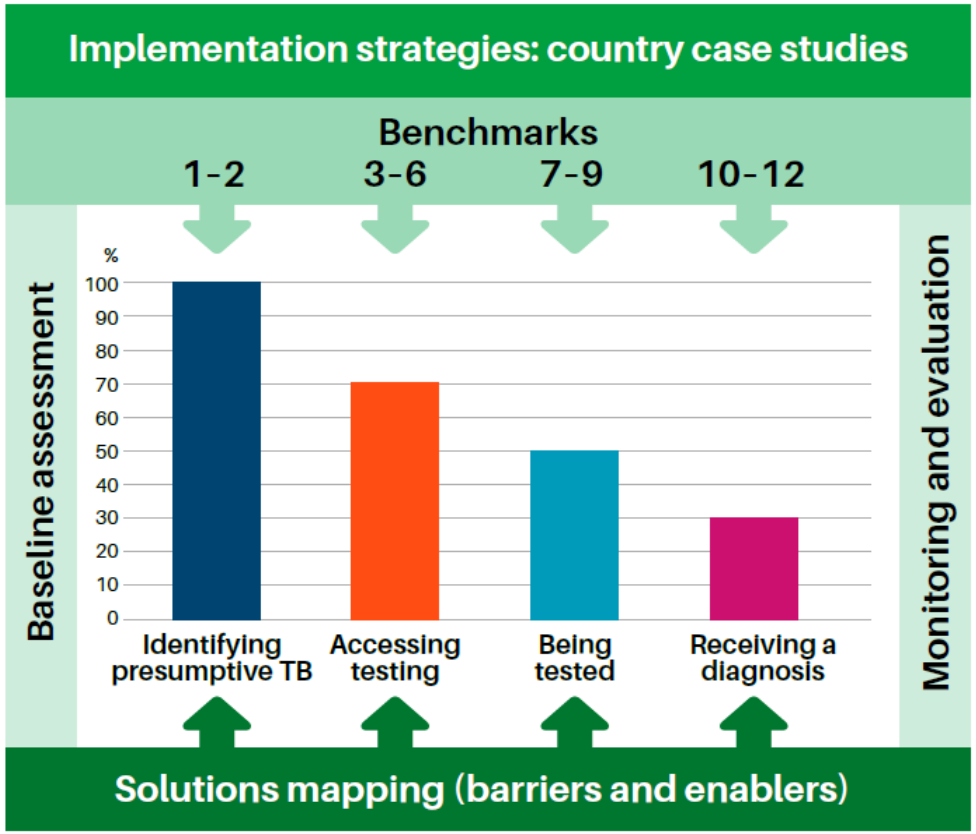
Fig. 5. Illustrative example of the WHO standard: universal access to rapid tuberculosis diagnostics and implementation components



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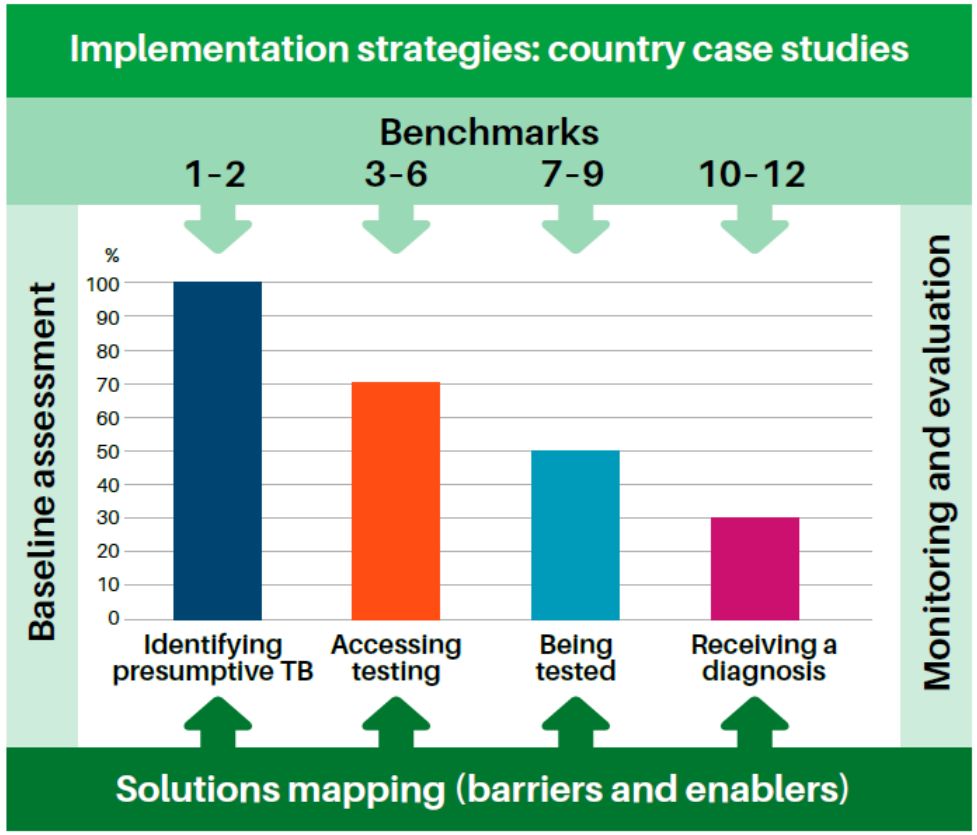
BARRIERS, ENABLERS, APPROACHES AND STRATEGIES FOR SCALING UP ACCESS TO AND USE OF WRDS



Key findings from the systematic review and stakeholder consultations

1. Equitable access and person-centred diagnosis and care are core components of optimization.
2. Multicomponent strategies for WRD implementation are enablers.
3. Strong communication among stakeholders and creation of fora in which stakeholders can exchange solutions ensure continuous improvement and targeted responses.
4. Multi-disease testing approaches can increase access, lower costs and strengthen health systems.
5. Longitudinal, accessible training for stakeholders can facilitate implementation of multicomponent WRDs.
6. Integration and movement of samples, information and patients between public- and private-sector services increase access and improve the quality of services in both sectors.
7. Use of data management and communication software in laboratory systems allows strong monitoring and rapid delivery of results to patients.
8. Iterative improvement of the diagnostic network can increase access and efficiency.
9. Strengthened global, national and subnational resource mobilization and national research capacity accelerate expansion of WRD services.

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Enablers identified by key stakeholders

Use of solar panels:

As electricity was the single most commonly discussed barrier, solutions to the problem were proposed frequently. They included generators, inverters and high-capacity solar panels. One implementer reported:

> For facilities where we could see that the air-conditioning is now optimal, and the refrigerators are in order and they have high-capacity solar panels, we saw that those facilities are working optimally without problems. But for those that are yet to be upgraded, we still have the same issues. My machine broke down today. It's breaking down again tomorrow. Then the refrigerator is not working because there is no power to our refrigerators ... All these are power dependent. So, without an ultimate power backup plan, we're not making any headway.

Refresher training and incentives:

Video-based refresher training, which was introduced in response to COVID-19-related travel restrictions, also overcame some of the challenges created by staff turnover and idiosyncratic instrument operation. Several countries reported lower error rates after video-based modular training provided by test suppliers.

Some stakeholders reported that paying a small bonus to laboratory staff for effective performance of WRD tests helped to reduce user error and the TAT, and that laboratory staff were willing to run a test that might require staying after their normal working hours.

> We give incentive of about [US$ 0.11] per test. That has really, really, really increased the testing that we have in country by WRD in the last year. Testing has increased astronomically because of that little money we give [to the lab technician] for a successful[ly run] test.

Market diversification:

Stakeholders suggested that diversification of the tools used and their availability on the market might make users less vulnerable to shifts in the market that resulted in changes in the prices or availability of instruments. One participant suggested that production of new instruments in high-burden countries might both stabilize the market and keep costs down. He said,

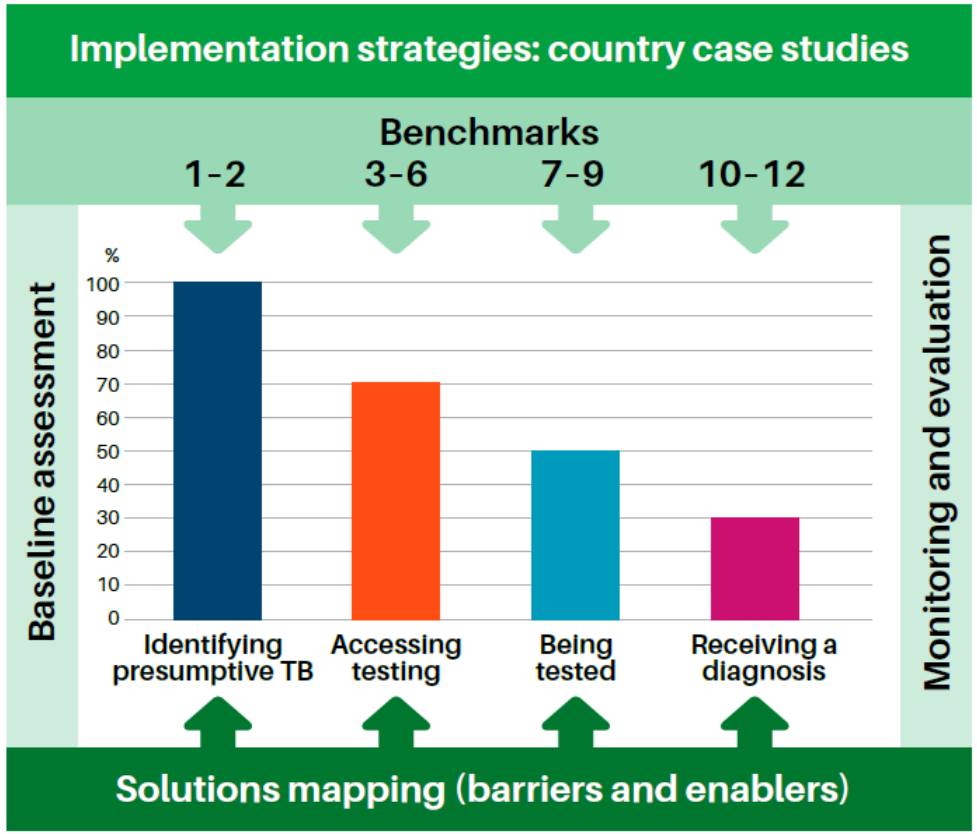
> Let's provide that opportunity for other platforms as well to be tested and be adopted in the lab system. There are risks to one platform, as we saw...during the pandemic when there's cartridge stockouts, they have to ration cartridge orders to countries. ... [high burden] countries will be in a disadvantaged position once those things happen.

Integrating the public and private sectors:

In many contexts, NTPs, in collaboration with donors, have placed WRD instruments in private-sector hospitals and laboratories, reimbursed the tests conducted or brought the prices of instruments and consumables into an affordable range for private laboratories and patients. One civil society stakeholder explained the importance of this flexibility for positivity rates:

> We have established 28 Xpert sites in private-sector. We have engaged the large private hospitals in the private sector and established 28 Xpert sites there. Where the machines are established, we see a proportion of the positive cases, that is more than 50%. We have established a specimen transportation mechanism and in 50 districts, so specimens are transported to Xpert sites to the private-sector, where the machines are established in private-sector. If the machines are not established at private-sector, the specimens are transported to the public sector machines.

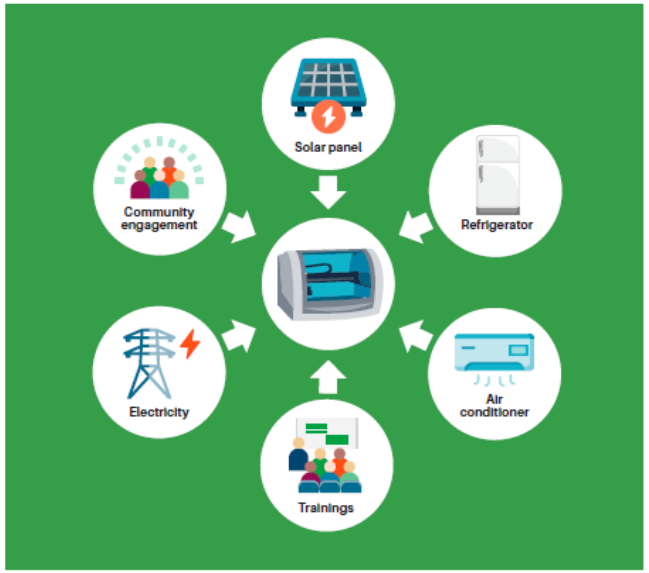
COUNTRY CASE STUDIES



Nigerian case study
Beyond the instrument

Summary

Fig. 8. The WRD package in Nigeria



Philippines case study
Building the diagnostic network

Fig. 9. A STRider in action

Photo credit: Courtesy of Philippine Business for Social Progress TB Project

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INVESTING IN UNIVERSAL ACCESS TO TB DIAGNOSTICS

The benefit–cost ratio for TB

- median cost–benefit ratio of TB control is even higher than those of HIV, hepatitis B, hypertension and diabetes in low- and medium-income countries .

Lessons from programmes for the control of other priority diseases

- In one quarter of 2020, the COVID-19 Diagnostic Consortium received orders from 44 countries for over 17 million PCR tests >>>TB after 10 years
- To date billions of Covid-19 tests performed

Price reductions as volumes increase

- price of tests for HIV viral load dropped by 40–60% when the volume increased from 2 to 10 million tests
- Concessional pricing for high-burden countries not be limited to public or nongovernmental sectors

Proportion of spending on TB diagnostics in overall health-care spending

- diagnostics account for less than 3% of the US$ 5.3 billion spent annually on TB and overall health care
- even a 10-times increase in spending on WRDs in LMICs for TB at current prices would still represent < 0.15% of total health-care spending .

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WHO Standard: Universal Access to TB diagnostics Conclusion

- Adoption of this WHO standard will increase the number of
  - Individuals offered an accurate and rapid diagnostic test
  - the number of bacteriologically confirmed TB cases, which represent the pool of infectious cases that are a priority for testing
  - increase testing for RIF resistance, an important step towards universal DST and quality-assured testing.
- Up-front investment will accelerate
  - universal health coverage,
  - result in better health for all and
  - reduce the unacceptable rate of morbidity and mortality due to a curable, preventable disease such as TB.
- Participation of all role players – implementers, funders, civil society and private sector across each step of the cascade to reach the ultimate objectives

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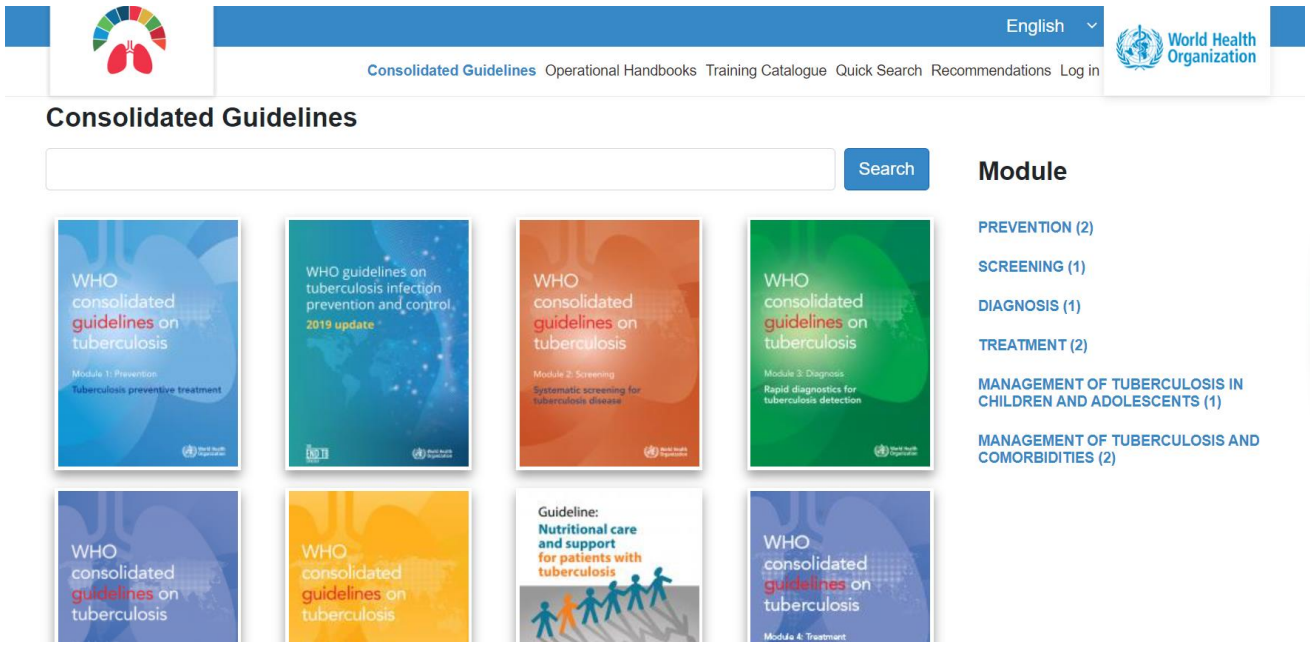
Thank you



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