July 17th, 2025

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Community Webinar: Tests for TB and Drug Resistance

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AN ACTIVIST'S GUIDE TO DIAGNOSTIC TOOLS *FOR TUBERCULOSIS*

July 2025

Launched:
10th July

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TB: Back to #1 on the charts

- Leading cause of mortality from an infectious disease
  - estimated 1.25 million deaths in 2023
- Estimated 10.84 million people developed TB globally in 2023
  - Only 8.16 million were diagnosed and reported
  - Diagnostic gap of 2.7 million "missing" cases*
    *“Missing cases” - individuals who remain undiagnosed, untreated, and/or unreported by health systems

In 2023, 10 countries collectively accounted ~50% of the global gap - India (16%), Indonesia (11%), Pakistan (7.8%), China (6.5%) and Myanmar (6.5%)

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Terminology

BOX 1: ASSESSING THE ACCURACY OF A TEST

The accuracy of a test is evaluated by two key measurements: sensitivity and specificity.

- Sensitivity is how well a test correctly identifies people who have TB. It measures the proportion of true positives — meaning the test gives a positive result when someone actually has TB.
- Specificity is how well a test correctly identifies people who do not have TB. It measures the proportion of true negatives — meaning the test gives a negative result when someone actually does not have TB.

In simple terms:

- Sensitivity answers: "If someone has TB, how likely is the test to detect it?"
- Specificity answers: "If someone doesn't have TB, how likely is the test to say they don't have it?"

While sensitivity and specificity are important for understanding how accurate a test is, other factors also matter, such as: How many people can access the test? How quickly does the test provide results? Does the test use sample types that are easy for most people to provide? All these aspects together help determine how impactful a test will be in real-world settings.

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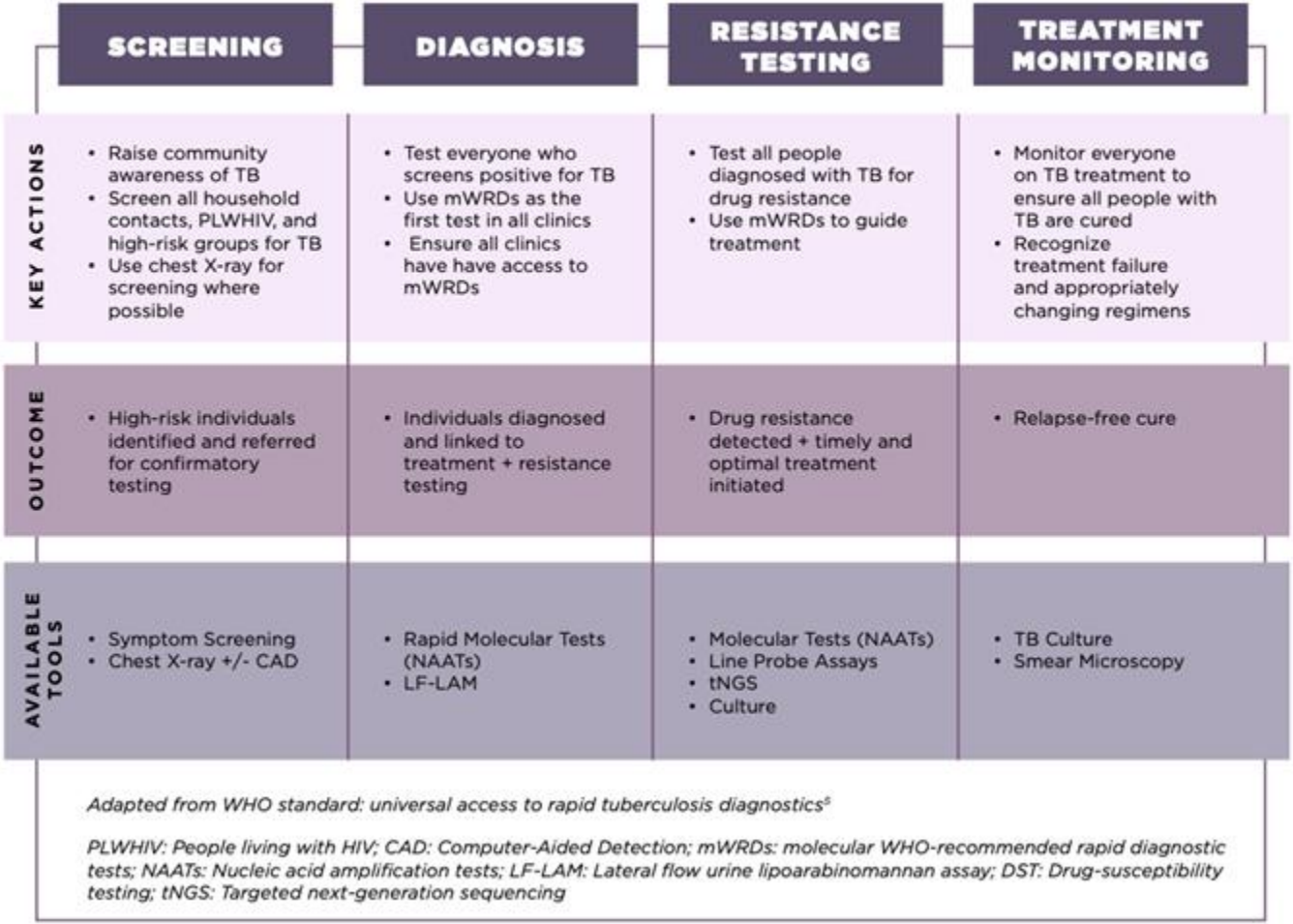
FIGURE 1: KEY ACTIONS, OUTCOMES, AND AVAILABLE TOOLS ALONG THE TB DIAGNOSTIC PATHWAY



Adapted from WHO standard: universal access to rapid tuberculosis diagnostics[5]

PLWHIV: People living with HIV; CAD: Computer-Aided Detection; mWRDs: molecular WHO-recommended rapid diagnostic tests; NAATs: Nucleic acid amplification tests; LF-LAM: Lateral flow urine lipoarabinomannan assay; DST: Drug-susceptibility testing; tNGS: Targeted next-generation sequencing

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TB Screening

TB Screening

- Screening identifies individuals who may have active TB disease
  - enabling timely diagnosis and treatment initiation
- Screening methods include symptom assessment and chest X-ray
- Screening may be integrated into routine care at health facilities or in communities
  - similar to screening for NCDs like diabetes or hypertension
- Screening should prioritize people at high risk for TB*
- A positive screening result is not a diagnosis and must be followed by confirmatory diagnostic testing and evaluation.

***High-risk groups**

- Household and close contacts of people with active TB
- People Living With HIV (PLWHIV)
- Individuals in prisons or detention centers
- Miners exposed to silica dust
- People with clinical risk factors (diabetes/ chronic lung disease/ malnutrition/ history of TB)
- Limited access to healthcare (urban slums/ refugees/ migrants/ unhoused individuals)

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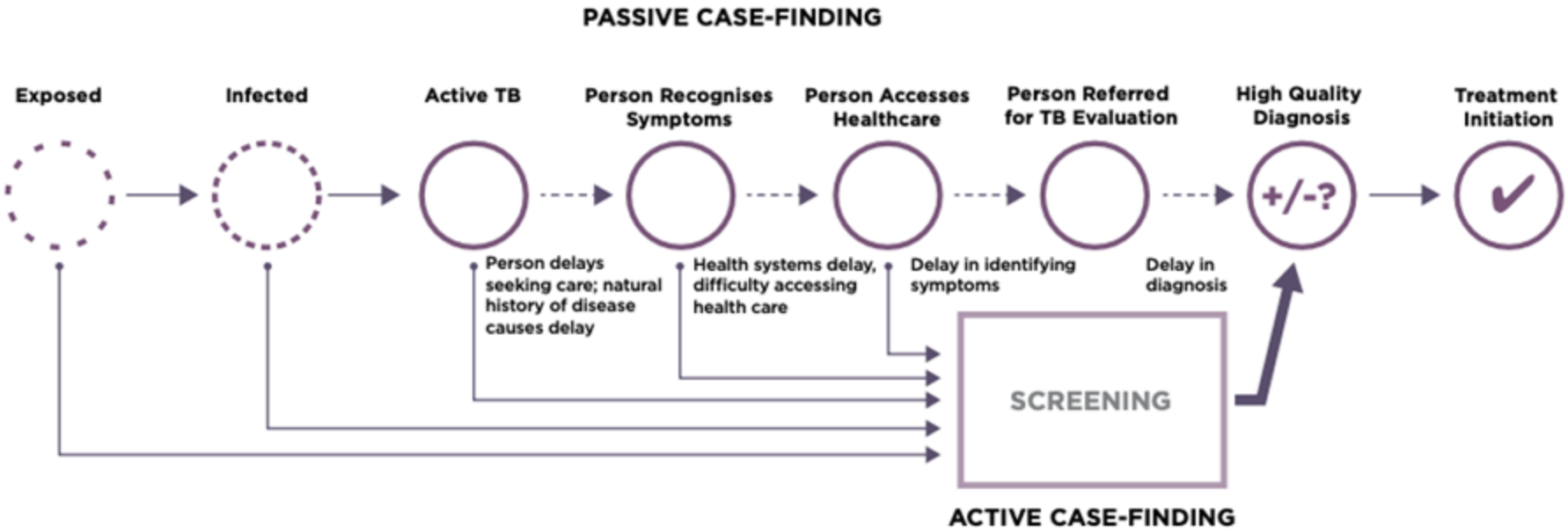
FIGURE 2: ACTIVE VERSUS PASSIVE CASE FINDING



Adapted from WHO image Comparison of patient-initiated and provider-initiated screening pathways for the diagnosis and treatment of tuberculosis (TB)[8]

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How to Screen

1. Symptom Screening

2. Chest X-ray +/- Computer-Aided Detection

Note: Positive symptom screens or abnormal X-ray findings both require confirmatory diagnostic testing

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Symptom Screening

- Classic symptoms of pulmonary TB - cough (of any duration), night sweats (drenched), weight loss, fever (low grade), and hemoptysis (coughing up blood).

- A positive symptom screen typically prompts further evaluation (i.e., chest X-ray or diagnostic testing)

- Low sensitivity:
  - Will miss people with asymptomatic TB and/or people with early TB disease who have yet to develop symptoms
  - Symptoms could also be the result of another illness

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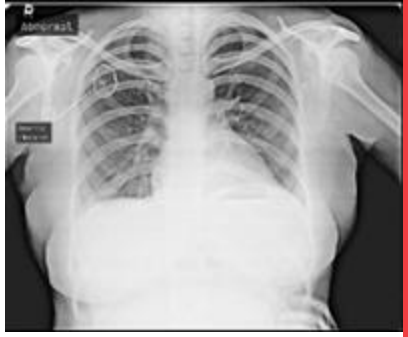
Chest X-Ray (CXR)



- Radiographic imaging to produce an image of the internal structures of the lungs
  - Helps identify any lung abnormalities that may be suggestive of TB

- Air in the lungs appears as black space and lung abnormalities (such as lesions caused by TB) appear as gray or white shadows.

- High sensitivity for detecting lung abnormalities suggestive of TB
  - But low specificity, as other diseases can produce similar abnormalities

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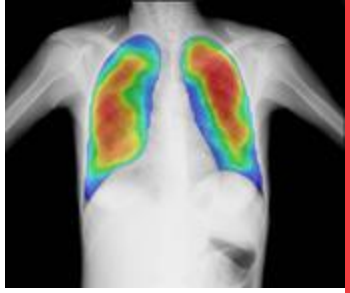
Computer-Aided Detection (CAD)



- In 2021, WHO recommended the use of CAD software for automated interpretation of digital CXRs
  - Among people aged 15 years and older
- CAD leverages artificial intelligence (AI) to help identify TB-related abnormalities
  - useful in places with few trained radiologists
- Multiple types of proprietary CAD software available that can automatically read digital CXRs and determine the likelihood of TB disease
  - Helps health workers determine if someone should be referred for further diagnostic evaluation
- Performance comparable to a human reader
  - Recommended as an alternative to human interpretation of CXR for TB screening
  - Specialist interpretation remains important for complex cases

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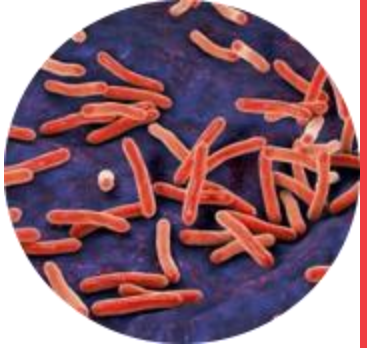
TB Diagnosis

What is Diagnosis?



Diagnosis is the confirmation that a person has active TB, and results in the clinical decision to initiate treatment.

- Diagnosis can be determined following:
  - **Microbiological confirmation:** detecting the presence of MTB* in a sample using a WHO-recommended diagnostic test; or
  - **Clinical judgement**: based on signs and symptoms and other risk factors of TB, even in the absence of a positive TB diagnostic test result (especially among children and PLWHIV for whom current tests aren't as accurate)

- Following a positive TB diagnosis, further drug-susceptibility testing is required to identify the most appropriate drugs/ treatment regimen

*MTB: Mycobacterium Tuberculosis
(The full name of the bacteria that causes TB)

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Technologies for Microbiological Confirmation

1. Molecular Tests or Nucleic Acid Amplification Tests (NAATs) (Genotypic)

2. Culture (Phenotypic)

Cheat Code:

Genotypic – Multiplies the DNA
→ doesn't grow live bacteria—just amplifies and analyzes their genetic material

Phenotypic – Grows the bacteria
→ actually grows live TB bacteria to visually inspect it

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Molecular Tests or Nucleic Acid Amplification Tests (NAATs)

- **Genotypic** molecular tests that detect the presence of MTB in a sample by amplifying the TB bacteria's DNA, even if there's only a small amount present in the sample
- How it works:
  1. Sample collected (typically sputum)
  2. The sample is prepared and genetic material (DNA) of the TB bacteria is extracted
  3. The extracted genetic material is amplified - many copies are made using techniques like polymerase chain reaction (PCR)
  4. The amplified genetic material is then detected, indicating the presence of the TB bacteria
- NAATs are highly sensitive and specific tests that can produce results within a few hours, and may be used for both - TB detection and resistance testing (detection of DNA mutations associated with resistance to certain drugs)

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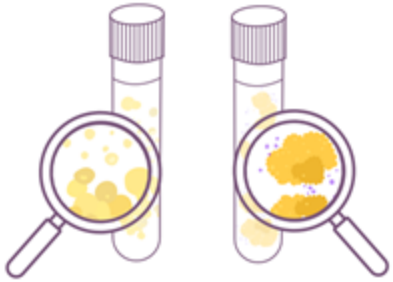
TB Culture



- **Phenotypic** test that physically grows TB bacteria from samples using a liquid or solid medium in order to visually detect it
- How it works:
  1. The sample is collected (typically sputum sample) and put into a tube with a substance that helps the bacteria grow (culture medium)
  2. The sample is incubated under controlled conditions (temperature, atmosphere) to allow the bacteria to multiply
  3. After a period of time, the culture is visually inspected to confirm the presence/growth of TB
- Takes between 2 to 6 weeks for results (as TB grows very slowly)
  - not appropriate as an initial TB test
- 'Gold standard': The most sensitive (~98–99%) and specific (80–93%) TB test
  - Used as the reference standard for determining the sensitivity and specificity of other TB tests (microbiological reference standard)
- TB culture is also used for drug-susceptibility testing and treatment monitoring

Categories of tests:

1. Initial tests for TB diagnosis with drug-resistance detection

2. Initial tests for TB diagnosis without drug-resistance detection

3. Follow-on tests for detection of TB drug resistance

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Initial Tests for TB Diagnosis with Drug-Resistance Detection

Low-Complexity Automated NAATs

- WHO recommends GeneXpert (Cepheid) and Truenat (Molbio) tests as initial tests for detection of TB and rifampicin (RIF) resistance
- Automated tools, placed in decentralized laboratories
  - Enables testing at the peripheral levels of the healthcare system
  - Ideal for resource- limited settings with basic laboratory infrastructures in place
- Uses software and hardware (such as computers) to report results
- Require basic lab infrastructure with stable power supplies and temperature control
  - But without other specialized equipment
- Require basic technical skills to operate

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Low-Complexity Automated NAATs

Xpert MTB/RIF Ultra (Cepheid, USA)

- Initial test for TB and RIF resistance for all people being evaluated for pulmonary TB
  - also recommended for adults and children with signs of extrapulmonary TB
- High sensitivity, imperfect specificity:
  - detects TB bacteria when it is present in a sample at very low quantities
  - Sometimes gives a positive result when live TB isn't present (in people who have previously recovered from TB or are currently improving on treatment)
- Can detect TB using many different sample types
  - Sputum, stool, gastric aspirate, nasopharyngeal aspirate, cerebrospinal fluid, lymph node samples, and other body fluids (lung, abdomen, heart)
- Cartridge-based, fully automated test, run on GeneXpert instruments
  - Requires continuous electricity
- Test costs US$7.97 per test
- Time to result: <2 hours (for both TB and rifampicin resistance)

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Low-Complexity Automated NAATs

Truenat MTB Plus and MTB-RIF Dx (Molbio, India)

- Initial test for TB and RIF resistance for all people being evaluated for pulmonary TB
- Reflex testing (sequentially):
  - separate test chips for TB and RIF resistance
  - MTB Plus chips - to detect TB bacteria, MTB-RIF Dx chip - to detect RIF resistance
- Rapid, portable, lightweight, semi-automated
  - Can be battery operated (~8 hours)
- Designed for use in places with basic laboratories (at the peripheral level) and minimal infrastructure
  - Further decentralizable than Xpert Ultra
- Currently validated only for sputum samples, not recommended for other sample types
- Test costs US$7.90 per test
- Time to result: <2 hours (for both TB and RIF resistance)

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Moderate-Complexity Automated NAATs

- Initial test for the detection of TB and resistance to RIF and INH (simultaneously)
  - follow-on testing for fluoroquinolones (specifically levofloxacin)
- Slightly more complex: sample preparation stage
  - Requires higher level of technical skill (than Xpert or Truenat tests)
- Rapid provision of accurate results
  - Run on larger instruments that can test multiple samples simultaneously
  - Ideal for areas with high population density and/or rapid sample referral systems
- Requires well-established laboratory infrastructure (usually test-specific equipment) and skilled personnel with training in laboratory procedures
  - Placed in district-level laboratories
- Companies that have WHO-approved platforms for this class of technology:
  - RealTime MTB, RealTimeMTB RIF/INH (Abbott)
  - BD MAX MDR-TB (Becton Dickinson)
  - cobas MTB, cobas MTB-RIF/INH (Roche)
  - FluoroType MTB, Fluorotype MTBDR (Hain Lifesciences/ Bruker)

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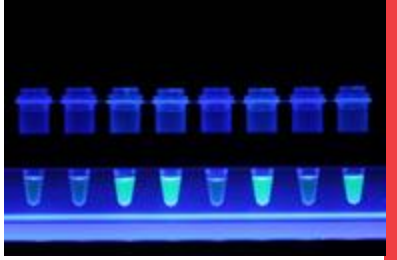
Initial Tests for TB Diagnosis without Drug-Resistance Detection

Low-Complexity Manual NAATs



TB-LAMP (Loop-mediated isothermal amplification)

- Used in basic laboratories at the peripheral level of the healthcare system
  - Requires basic equipment only
- Test-tube- based molecular test (loop-based NAAT)
  - Targets TB bacterial DNA and multiplies DNA sequences to detect TB
- Difference from Xpert and Truenat
  - Done at a single temperature
  - TB detected visually using an ultraviolet (UV) lamp
  - Less expensive (~US$6)
  - Time to result: 40 minutes
  - Lower sensitivity
  - Cannot detect drug resistance
- WHO recommended as an initial test for the detection of TB only in areas with low prevalence of drug-resistant TB

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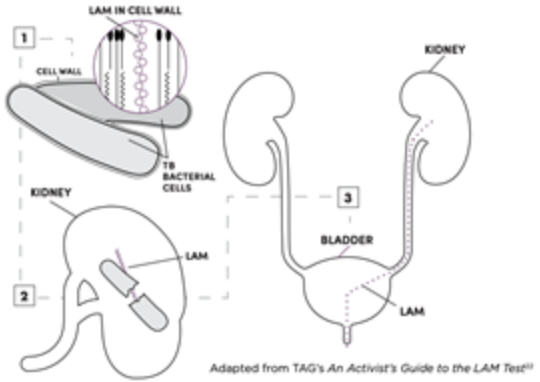
Antigen-Based Lateral Flow Tests



Urine-based lipoarabinomannan (LAM) test

- WHO-recommended for detecting TB in PLWHIV
- Only TB diagnostic proven to reduce mortality
  - by enabling faster diagnosis and earlier treatment initiation among PLWHIV (especially those with advanced disease)
- Antigen-based test detects the presence of LAM in urine
  - LAM - a component of the TB bacteria's cell wall
  - Released into the urine when TB spreads throughout the body
- Abbott Determine TB LAM Ag test (only available LAM test)
  - Test cost: US$3.70
  - Time to result: 25 minutes (rapid)
  - Instrument free, true point-of-care test (no lab or equipment required) - similar to a pregnancy test
  - Higher sensitivity in people with advanced HIV (sensitivity increases as CD4 count decreases

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Follow-on Tests for Detection of TB Drug Resistance

What makes TB ‘drug resistant’?

- Drug-resistant TB (DR-TB) means a strain of MTB has mutated (changed) in a way that helps it escape or resist being killed by a specific drug(s)
- Resistance to TB drugs can be transmitted and/or develop over time from inadequate or irregular TB drug exposures, e.g., from:
    - **Incorrect prescription** by healthcare provider
    - **Poor quality drugs** resulting in inadequate drug levels / exposures
    - **Drug shortages** resulting in treatment interruption / discontinuation
    - **Lack of adherence** to the treatment - common due to toxicity/side effects/ lack of counseling
- Most DR-TB is transmitted (primary resistance) rather than developed (secondary resistance)
- Treatment for DR-TB is **longer, more expensive, and harder to tolerate** than treatment for drug-sensitive TB (DS-TB)
- DR-TB is generally separated into four groups, defined by the medicine(s) to which TB bacteria are resistant

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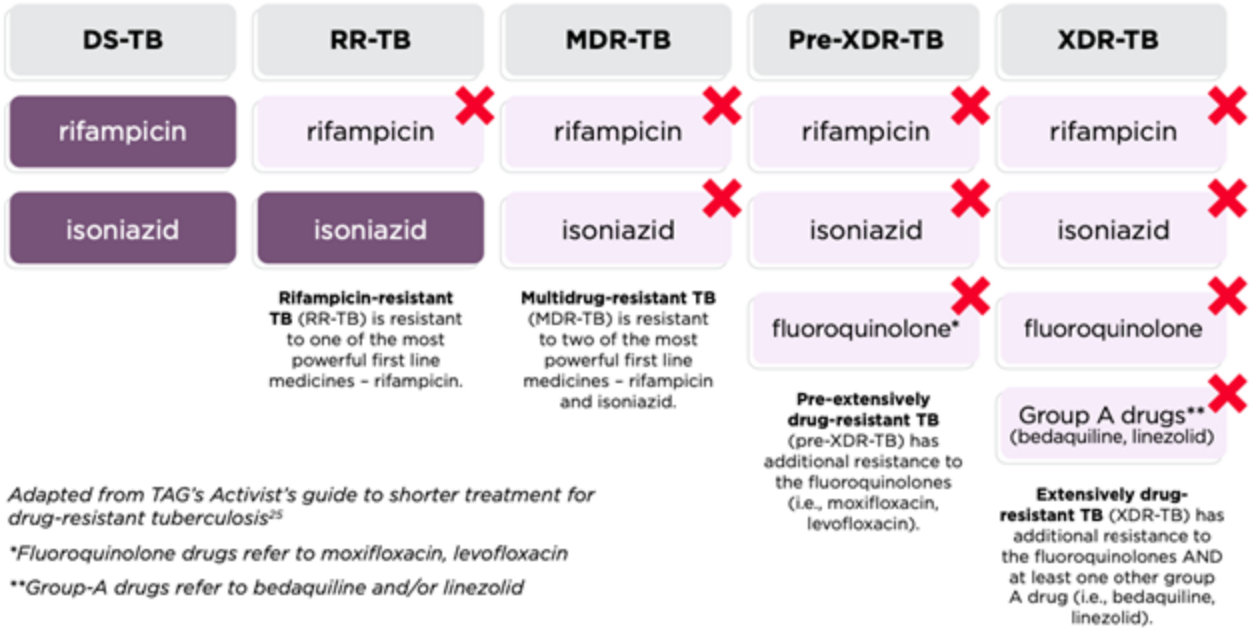
Defining DR-TB in the context of treatment regimens

FIGURE 7: DRUG-RESISTANT TB IN THE CONTEXT OF TREATMENT REGIMENS



Adapted from TAG's Activist's guide to shorter treatment for drug-resistant tuberculosis[25]

**Fluoroquinolone drugs refer to moxifloxacin, levofloxacin*

***Group-A drugs refer to bedaquiline and/or linezolid*

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Importance of Drug-Sensitivity Testing

- DR-TB is harder to cure, requires longer treatment and risks transmission of resistant strains
- Accurate diagnosis of DR-TB is critical for effective treatment and reducing transmission
- WHO recommendation: Test *all* TB patients for at least rifampicin resistance
- Recent advancements in molecular diagnostics and updated WHO guidelines have reshaped testing strategies and treatment protocols
- Misdiagnosis leads to undertreatment, increased mortality, and community transmission
- **Universal drug-susceptibility testing** means that all people being evaluated for TB should also receive DST as part of the initial TB test, with follow-up DST as needed

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Low-Complexity Automated NAATs

Xpert MTB/XDR

- WHO-recommended in 2021 as a follow-on test
  - to detect resistance to INH and FQs in people with TB, and resistance to ethambutol (ETH) and amikacin (AMK) in people with RR-TB
- Placed at peripheral healthcare centers (at the same level as Xpert Ultra and Truenat tests)
- Can differentiate between low- and high-level resistance to INH and FQs
  - Low-level resistance: TB bacteria can survive lower doses of a drug; high-level resistance: bacteria can survive even the highest safe doses
- Time to result: <90 minutes
- High test cost (US$14.90) - limits widespread scale-up and adoption in countries
- Single cartridge to analyze sputum samples that have already tested positive for TB and RR-TB
  - requires a newer model GeneXpert instrument or an expensive upgrade to older model GeneXpert instruments
- High sensitivity and specificity for detecting resistance to these drugs

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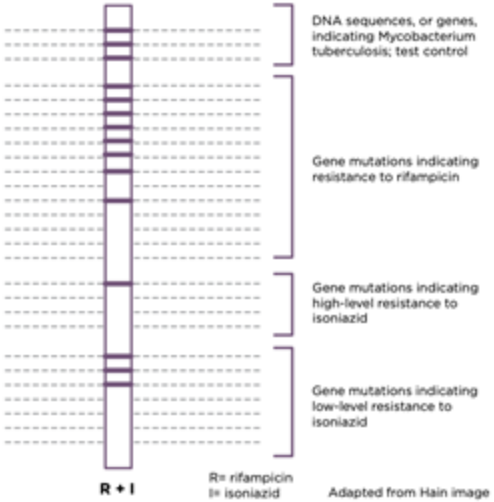
Line Probe Assays

- WHO-recommended in 2016 as the initial DST for first-and second-line TB drugs
- Molecular tests that use PCR to amplify TB bacteria DNA sequences
  - Then use strip-based technology with binding patterns that indicate the presence of certain genetic mutations linked to drug resistance
  - If these target DNA sequences are present in the solution, they bind to the probes and form colored bands on the strip, indicating a positive result for resistance to specific TB drugs
- Can detect resistance to first-line (RIF, INH) and second-line drugs (FQs, AMK) and provide mutation data for common variants
  - Sensitivity limited to prominent resistance mutations
- More complex - placed in district/central laboratories
  - Requires well-equipped labs with multiple instruments and trained technicians
  - Results in 1-2 days (sample transport to central labs + ~5 hours turnaround time)
- Companies that have WHO-approved platforms for this class of technology:
  - *GenoType MTBDRplus* and *GenoType MTBDRsl* (Hain Lifescience)

FIGURE 8: LINE PROBE ASSAYS



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Targeted Next Generation Sequencing (tNGS)

- WHO-recommended in 2024 for follow-on detection of resistance to a broad range of TB drugs after the initial detection of TB and/or RIF-resistance
- Comprehensive resistance detection to modern treatment regimens
  - Can detect resistance to ≤ 16 drugs from a simple sample
  - Including second-line drugs not included in other NAATs or LPAs (such as BDQ, LZD, CFZ)
- Placed in central laboratories
  - Requires complex lab infrastructures and highly skilled lab technicians
  - Time to result: 1-2 days
- High accuracy for commonly used TB drugs (such as INH, RIF)
  - Lower sensitivity for new and repurposed drugs
  - Mycobacterial **culture still required** to rule out resistance to new drugs (such as **BDQ, DLM, Pa, CS, LZD**)
- Companies that have WHO-approved platforms for this class of technology:
  - *Deeplex Myc-TB* (GenoScreen)
  - *amPORE TB* (Oxford Nanopore)
  - *TBseq* (ShenTing)

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FIGURE 9: THE TNGS PROCESS EXPLAINED

COLLECT SPUTUM SAMPLE

DNA EXTRACTION

Purification of DNA sample from sample

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Processing DNA sample for compatibility with sequencing system

SEQUENCE

Analysis of TB genome sequences

ANALYZE DATA

Bioinformatics process to identify Mtb as well as drug resistance mutations

REPORT RESULTS

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Treatment Monitoring

- Important to regularly monitor response to TB medication
  - Detecting signs of poor response to treatment allows for prompt treatment adjustment and improve chances of cure
- Currently available molecular diagnostics (NAATs, LPAs, tNGS) cannot be used for treatment monitoring
  - Cannot differentiate between live and dead TB bacteria
  - May remain positive even when treatment is working
- Two phenotypic tools currently recommended:

1. Smear Microscopy:
   - Rapid results but low sensitivity (~50%)
   - Poor performance when small amounts of TB bacteria present in sample
2. Mycobacterial Culture:
   - Gold standard (high accuracy) but very slow (2-6 weeks for results)
   - Conversion of samples from culture-positive to culture-negative - important evidence of the efficacy of TB treatment - but takes place after 2-3 months of treatment

FIGURE 4: COMPLEXITY OF THE CLASSES OF TB TECHNOLOGIES

COMPLEXITY	LC-ANAAT	LC-MNAAT	LF-LAM	MC-ANAAT	LINE PROBE ASSAYS	TNGS
Equipment & Infrastructure	Basic laboratory; Minimal equipment; basic power supply; no special infrastructure required	Basic laboratory; Manual assay; basic power supply; no special infrastructure required	No equipment or laboratory infrastructure; true point-of-care test	Specialized machines and infrastructure; stable power requirements; manual specimen preparation	Molecular laboratory; special infrastructure required;	Centralized, molecular laboratory; special infrastructure
HR Skill Level	Basic technical skills (e.g. basic pipetting, precision not critical)	Basic technical skills (e.g. basic pipetting, precision not critical)	Minimal training (health workers); potential use as a self-test	Moderate technical skills (i.e., multiple sample or reagent handling steps, precision pipetting and molecular workflows may be required)	Advanced technical skills (i.e., multiple sample or reagent handling steps, precision pipetting, molecular workflows may be required)	Highly skilled lab personnel with specialized skills
Results Reporting	Automated	Automated or manual	Manual; visual interpretation of results	Automated	Manual	Automated
WHO-recommended products	Xpert MTB/RIF Ultra, Xpert MTB/XDR (Cepheid), Truenat MTB, MTB Plus and MTB-RIF Dx (Molbio)	TB LAMP (Eiken Chemical)	Determine TB LAM Ag (Alere/Abbott)	RealTime (Abbott), BD MAX (Becton Dickinson), Cobas (Roche), FluoroType (Hain Lifesciences)	GenoType MTBDRplus, GenoType MTBDRsl (Hain Lifescience), Genoscholar NTM+MDRTB II, Genoscholar PZA TB II (Nipro)	Deeplex Myc-TB (GenoScreen), amPORE TB (Oxford Nanopore), TBseq (ShenTing)

Adapted from WHO Consolidated guidelines on tuberculosis: module 3: diagnosis: rapid diagnostics for tuberculosis detection, 3rd ed.[14]
LC-aNAAT: Low-complexity automated NAATs; LC-mNAAT: Low-complexity manual NAATs; LF-LAM: Lateral Flow urine lipoarabinomannan assay; MC-aNAAT: Moderate-complexity automated NAATs; tNGS: Targeted next-generation sequencing; HR: Human resource

Placement of Screening and Diagnostic Tests

FIGURE 10: PLACEMENTS OF TB SCREENING AND DIAGNOSTIC TOOLS AT DIFFERENT LEVELS OF HEALTH SYSTEMS

PERIPHERAL HEALTH CENTER

- Symptom screening
- Chest X-ray +/- CAD
- Rapid molecular tests (LC-aNAATs and LC-mNAATs)
- LF-LAM tests for PLWHIV
- C-reactive protein for PLWHIV
- Sample referral for complex DST
- Smear Microscopy

DISTRICT HOSPITAL

- MC-aNAATs
- Line probe assays for DST
- Mycobacterial culture for DST

CENTRAL HOSPITAL

- tNGS for DST

Adapted from TAG's Community-led Monitoring for Access to Tuberculosis Screening and Diagnostic Testing.[35]
Note: This figure indicates the lowest level of the health system where a tool can be implemented.

TABLE 1: AN ALGORITHM, DETAILING THE DIFFERENT TESTS THAT CAN BE USED FOR DIFFERENT SCENARIOS OF DIAGNOSTIC AND DRUG-SUSCEPTIBILITY TESTING

Scenario	Purpose	Recommended Test
Initial Screening	Identify high-risk individuals and refer for further confirmatory testing	• Symptom Screening • Chest X-ray +/- CAD
Initial Diagnosis	Detect TB + RR	• Low-complexity automated NAATs (Xpert MTB/RIF Ultra, Truenat MTB Plus, and Truenat MTB-RIF Dx) • Moderate-complexity automated NAATs
Confirmed RR-TB	Detect resistance to INH, FQs	• Low-complexity automated NAATs (Xpert MTB/XDR) • Moderate-complexity automated NAATs • LPAs
Presumptive XDR-TB (Confirmed FQ-R TB)	Detect resistance to other group-A drugs	• tNGS • Culture
Treatment monitoring	Evaluate treatment success	• Smear Microscopy • Culture

Note: Diagnostic tools without DST ability are not included in this algorithm because they are recommended to be used in very specific situations or populations. Low-complexity manual NAATs (TB-LAMP) can be used as a replacement for smear microscopy in low-burden settings. In PLWHIV, C-reactive protein, a blood-based test, can be used for screening and LF-LAM can be used for initial diagnosis.

Ensuring Access to TB Tests

Special Populations - PLWHIV

- High risk - TB is the leading cause of death among PLWHIV (~161,000 deaths in 2023)
- Shortfalls of current tests:
  - Lower sensitivity of TB diagnostic tests due to disseminated TB or paucibacillary TB
  - Difficulty producing sputum
- Recommended diagnostic test: Urine-based LF-LAM test
  - Low accuracy, but proven mortality benefits - faster diagnosis and treatment initiation
- Recommended screening test: C-reactive protein test (CRP)
  - Non-specific marker of inflammation - measured in the blood
  - Elevated CRP levels - associated with active TB
  - Quick, inexpensive, done at point-of-care

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Special Populations - Children

- High-risk population, underserved by current TB diagnostics
- More likely than adults to progress to active TB and develop extrapulmonary TB
- Lower sensitivity of current tests - low bacterial load in children
- WHO-recommended treatment decision algorithm (<10 years):
  - Combine clinical assessment, history of contact with a person with TB, CXR findings, results from available lab tests
  - To ensure children at high risk can start treatment promptly
  - Allows diagnosis even if lab tests are not possible or produce negative results but clinical indicators of TB are present

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Special Populations - Extrapulmonary TB

- TB infection present outside the lungs
  - Affecting lymph nodes, pleural cavity, brain, spinal cord, bones, joints, abdominal cavity
  - Sputum samples - not useful
  - Alternate samples collected from affected body sites for testing
- WHO's recommended treatment decision algorithm:
  - Combines clinical evaluation, imaging (ultrasound / X-ray), lab testing of samples from affected area with rapid molecular tests (Xpert Ultra)
  - Helps support timely and accurate diagnosis

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Concurrent Testing

- WHO updated guidelines in April 2025 for high-risk populations
  - Recommended concurrent testing
- Using more than one type of tests/sample simultaneously
  - To increase chances of timely and accurate diagnosis
  - Helps find TB in people who might have otherwise been missed
  - Increases diagnostic yield among high-risk groups
- PLWHIV:
  - Molecular test on a respiratory sample (like sputum) and a urine-based LAM test
- Children:
  - molecular test on a respiratory sample together with a stool test
- Children living with HIV:
  - all three — a molecular test on a respiratory sample, a stool test, and a urine LAM test — at the same time

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Fair and affordable pricing

- Critical to improving access, especially in resource-limited settings
- Increased competition brings new and improved tests, but prices still remain high
  - Due to factors beyond manufacturing costs (distributor markups, sales and marketing expenses, supply chain inefficiencies)
- Cost-of-goods-sold (COGS)-plus pricing model
  - Prices set based on transparent production costs + reasonable profit margin
- Time for $5 campaign - power of collective advocacy
  - Drove Cepheid to lower price of Xpert MTB/RIF test from $9.98 to $7.97
  - 20% price reduction saves US$32 million - additional 3.6 million tests

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Adequate and Sustainable Funding

- TB programs remain chronically underfunded
- Current political and global health funding landscape
  - Additional strain on already limited resources
- Urgent need for alternative, sustainable financing solutions
  - To help countries strengthen health systems, expand laboratory capacity, procure essential tests at scale
- Close the gap and maximize impact of TB program efforts
  - Increased investment from domestic budgets and global donors
  - Innovative financing mechanisms
  - More efficient use of available funds

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Call to Action: Demanding Accountability

Country Governments

- Increase domestic funding for NTPs and invest in health system infrastructure
- Update NTP policies in line with the latest WHO recommendations
- Integrate TB screening and diagnostic testing at all levels of care
- Prioritize comprehensive training for health workers on new diagnostic tools and algorithms

Global Donors

- Boost financial support to help countries strengthen health systems
- Invest in R&D for new diagnostics, making funding conditional on commitments to cost transparency and fair pricing
- Leverage collective procurement power to help drive down prices and improve access
- Invest in local manufacturing and technology transfer

Diagnostic Companies

- Invest in the developing tools that address testing gaps and involve affected communities and vulnerable populations early in the R&D process
- Commit to transparent, fair pricing (reflecting COGS) and ensure accessibility in all HBCs
- Provide affordable service and maintenance plans
- Scale up manufacturing to meet global needs

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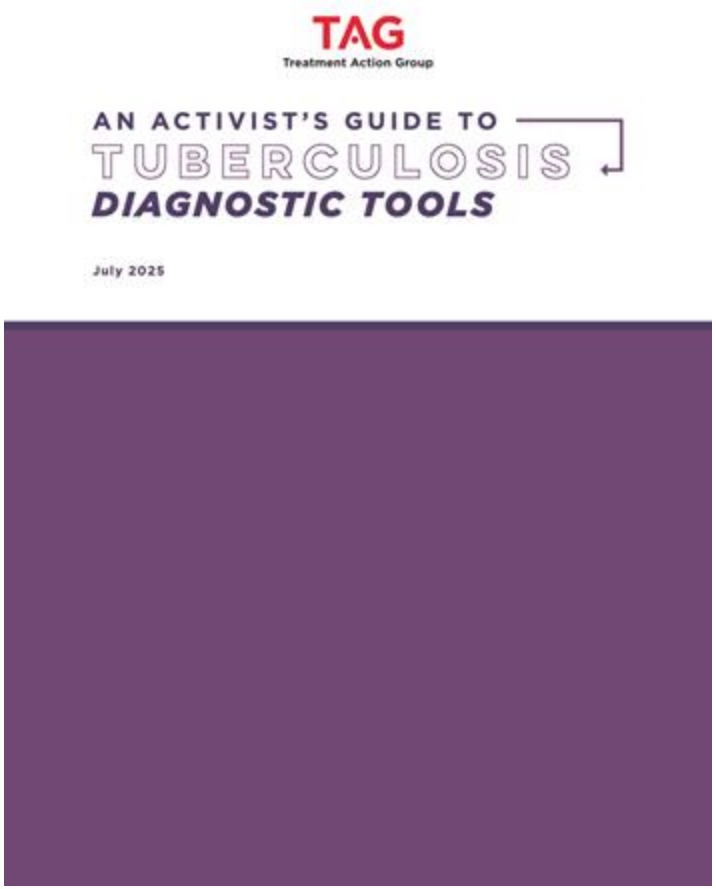

[An Activist's Guide to Diagnostic Tools for Tuberculosis 2025]

Thank you!

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Other TAG resources:

1) Cheat Sheets for Tuberculosis Activists
   a) WHO-Recommended TB Screening & Diagnostic Tools
   b) TB Screening & Diagnostic Tools Pipeline
2) An Activist's Guide to Shorter Treatment for Drug-Resistant Tuberculosis
3) An Activist's Guide to Rifapentine – TB Preventive Treatment: 3HP and 1 HP

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WHO-RECOMMENDED TB SCREENING & DIAGNOSTIC TOOLS*

Developed by:
Erin McConnell & David Branigan

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KEY

POPULATION:

- Children
- Adolescents and adults
- People living with HIV

LEVEL OF THE HEALTH SYSTEM:

- Primary care center
- District laboratory
- Central laboratory

ABBREVIATIONS:

TB/MTB: tuberculosis
RIF: rifampicin
INH: isoniazid
LAM: lipoarabinomannan
FQ: fluoroquinolones
AGaminoglycosides
CAP: capreomycin
PZA: pyrazinamide

** As of June 2024*
***Only for HIV-negative people over 5 years*
****To be implemented concurrently with rapid molecular testing*
*****Mycobacterial culture still required to rule out resistance to new and repurposed drugs bedaquiline, linezolid, clofazimine, etc.*

People at risk of TB

TB SCREENING

- **Symptom screening**
- **Chest X-ray**
- **Ultraportable chest X-ray**
- **Computer-aided detection (CAD)**
- **C-reactive protein**
- **Rapid molecular tests**

People with signs and symptoms of TB or positive TB screening result

TB DIAGNOSIS

- **Rapid molecular tests for TB and RIF resistance**
  - Xpert MTB/RIF Ultra
  - Truenat MTB Plus & MTB-RIF
- **Rapid molecular test for TB**
  - TB-LAMP
- **High-throughput molecular tests for TB and RIF/INH resistance**
  - RealTime MTB RIF/INH, BD MAX MDR-TB, cobas MTB-RIF/INH, FluoroType MTBDR Version 2.0
- **Urine-LAM lateral flow test**
  - Determine TB LAM Ag***

Screening/ diagnostic testing required to rule out active TB before TPT initiation

TB INFECTION TESTING**

- **Tuberculin skin test**
- **Next-generation TB-specific skin test**
  - Cy-TB, Diaskintest, C-TST
- **Interferon-gamma release assays**
  - QuantiFERON-TB Gold Plus, T-SPOT.TB

People diagnosed with active TB

DRUG-SUSCEPTIBILITY TESTING

- **Rapid molecular tests for TB and INH/FQ/AG resistance**
  - Xpert MTB/XDR
- **Targeted next-generation sequencing for comprehensive DST**
  - Deeplex Myc-TB, AmPORE-TB, TBseq
- **Line probe assays**
  - GenoType MTBDR (RIF/INH) & MTBDRsl (FQ/AG/CAP), Genoscholar MDRTB II (RIF/INH) & PZA TB II
- **Mycobacterial culture****
  - MGIT liquid culture broth microdilution, solid culture

People on TB treatment

TB TREATMENT MONITORING

- **Smear microscopy**
- **Mycobacterial culture**
  - MGIT liquid culture , solid culture