FIND

LOOKING AHEAD

The TB Dx pipeline (some of it…)

Kavindhran Velen, PhD, MPH
Senior Scientist (TB Access)

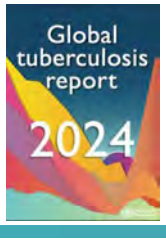
4 April 2025

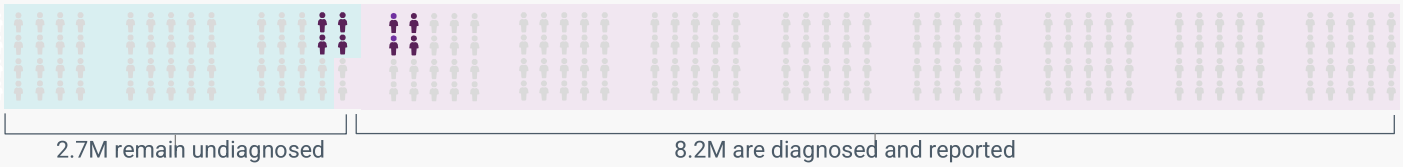
1.25 million deaths

Every year 10.8M people are estimated to get TB

= 50,000 people

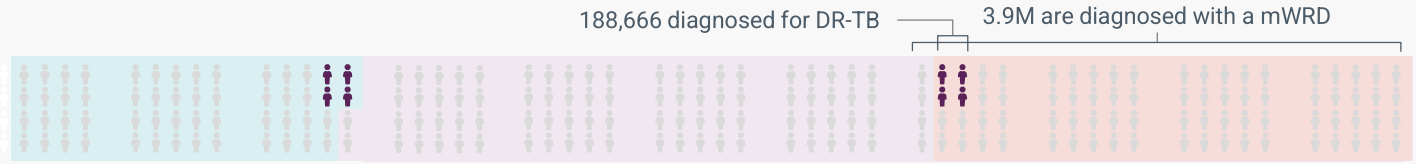
= 50,000 people





= 50,000 people

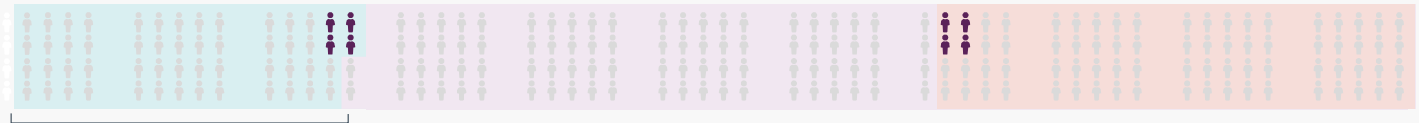
Global tuberculosis report 2024



= 50,000 people

WE NEED NEW AND IMPROVED DIAGNOSTICS TO DETECT MISSING CASES

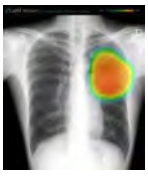
2.7M estimated missed cases

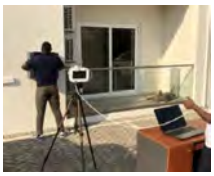


= 50,000 people

New tools to improve TB case detection

Non-sputum sample types + fast and accurate assays





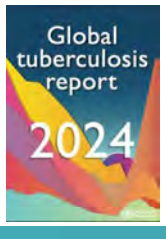
Fast and affordable screening tools

…AND NEW TOOLS TO REPLACE OLD AND INSUFFICIENT PRODUCTS

New (mainly) sputum based tools to replace microscopy, improve TB case detection and protect the drugs

4.3M detected but not reached by current available mWRDs

= 50,000 people

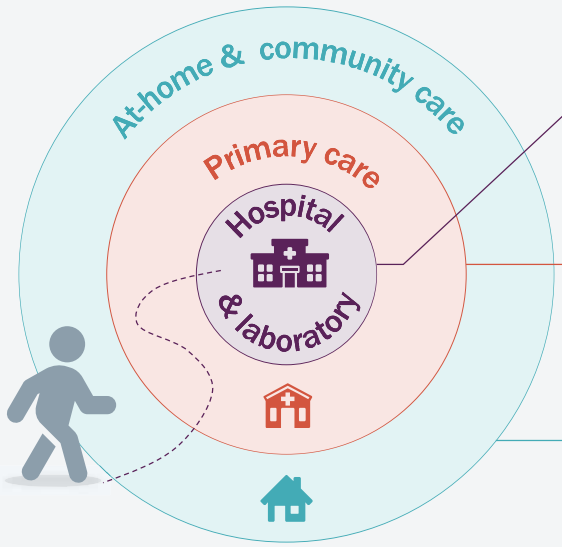


PATIENT-CENTRED CARE

DIFFERENT NEEDS AT EACH STEP OF THE PATIENT JOURNEY

WHAT NEEDS TO IMPROVE?

INCREASED TESTING THROUGH INCREASED AVAILABILITY



Technologies suitable to testing infrastructures

Near POC
- Basic lab equipment requirements
- Benchtop/desktop units, mains power
- Semi-automated testing processes

True POC
- No laboratory equipment requirements
- Portable, battery-operated devices
- Kits including disposable sample materials
- Fully automated testing process

Instrument free POC
- No instrument or power requirements
- Kits including disposable sample materials
- Fully automated testing processes

Increasing accessibility

WHEN YOU REPLACE NOTHING WITH SOMETHING – WE MAY ALREADY BE 'GOOD ENOUGH'

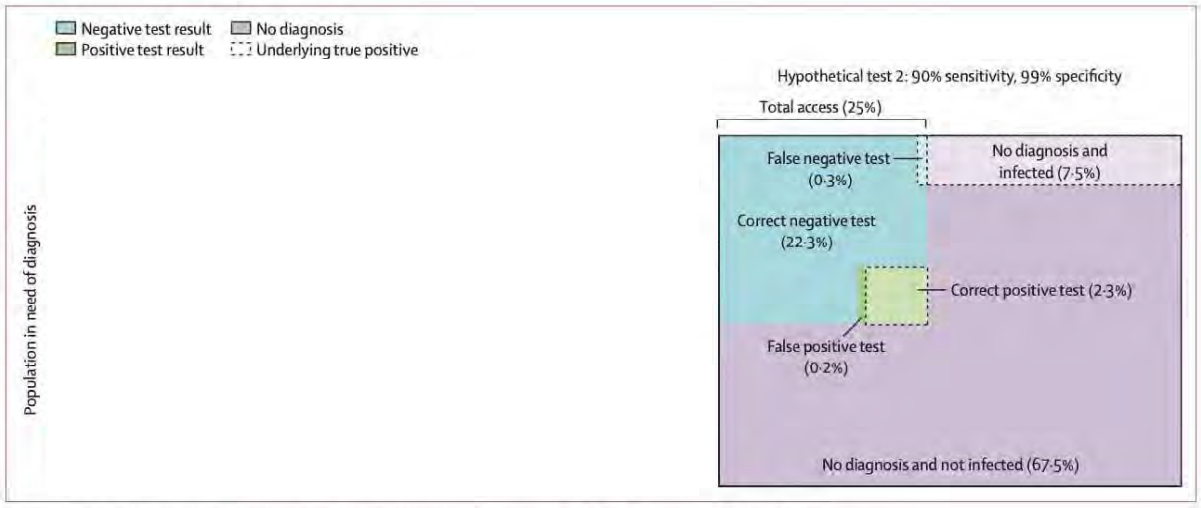


Figure 1: **Trade-off between test accuracy and test access, assuming an underlying disease prevalence of 10%**

71.5% of the entire population with a correct diagnosis

24.6% of the entire population with a correct diagnosis

Lancet Glob Health 2024; 12: e1139–48

Trade-offs between clinical performance and test accessibility in tuberculosis diagnosis: a multi-country modelling approach for target product profile development

De Nooi, Lancet GH 2024

IMPACT OF ON-SITE TESTING

SAME DAY TEST-AND-TREAT IS FEASIBLE

FIND

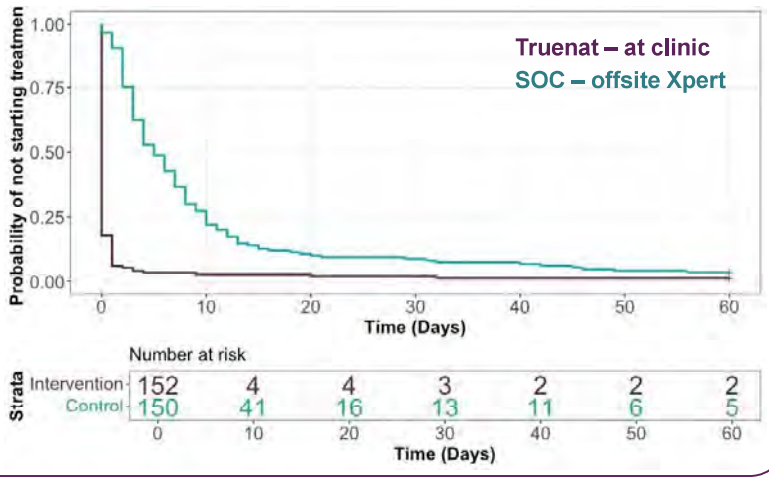
Impact of point-of-care implementation of the Truenat MTB assays on TB diagnosis and treatment initiation.

Intervention:

On-site Truenat at PHC clinics + rapid communication of results vs SOC (off-site Xpert testing in all clinics and on-site smear microscopy when available).

Main results:

- Placement of molecular diagnostics in primary health care clinics is feasible
- Majority can initiate Rx on day 0 at PHC



TB-CAPT consortium submitted. TB-CAPT.org

EDCTP

TB-CAPT

IFAKARA HEALTH INSTITUTE

cism centro de investigação em saúde de manhiça

SWABS IN ACTIVE CASE FINDING, HOUSEHOLD CONTACTS, RSA

SWAB BASED STRATEGY INCREASES SAMPLE AND DIAGNOSTIC YIELD

Duncan Village Informal Settlement, BCM Health District

In home sputum testing on Xpert lead to 86% linkage to care, with median 1 day time-to-clinic presentation

Interim results (Nov 2024):

- Eastern Cape, South Africa
- 957 household contacts enrolled across 445 households
- **Sample yield:** sputum 293 (32%, test on site) and 943 swabs* (98%, test in lab)
- **Positivity rate:** Sputum 29/288 (10%), swabs 61/868 (7%)
- **Yield: - Sputum alone = 3.03%**
- **- Swabs alone = 6.37%**
- **- Sputum or Swab = 6.69%**
- **Added value:** 32 of 664 (4.8%) who could not produce sputum tested positive on swab assay

** Tested with in-house PCR.*

DESMOND TUTU HEALTH FOUNDATION

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FIND Diagnosis for all

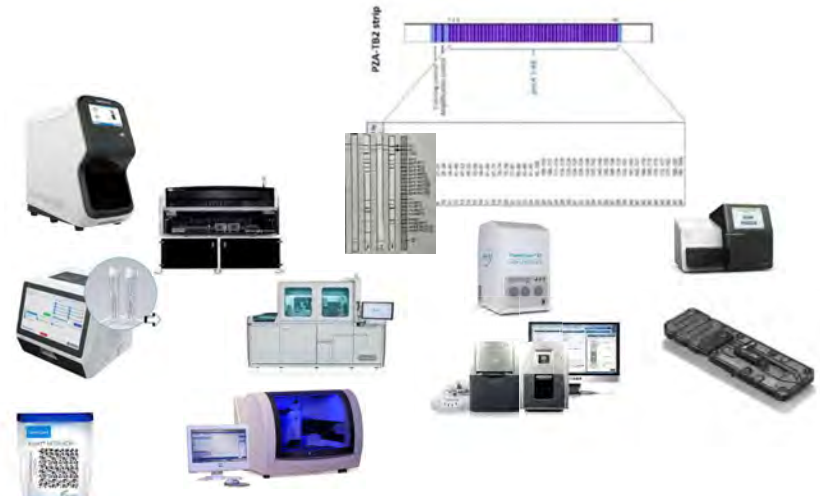
A BUSY PIPELINE OFFERING MANY NEW DIMENSIONS TO HOW TB COULD BE DIAGNOSED

Near POC MDx

non sputum
TB or no TB

Low complexity NAAT

Busy pipeline giving cepheid a run for their money



Moderate complexity NAAT

Rolled out in RSA

tNGS

WHO endorsed in 2023

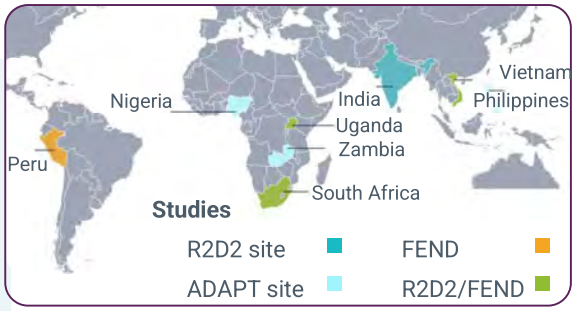
KEY CHARACTERISTICS OF NEAR POC TOOLS

Characteristic	Minimal requirements
Form	Tests can be instrument based, with the instrument preferably being battery operated and thus not requiring any special infrastructure
Intended purpose	A diagnostic test to detect pulmonary TB, at the peripheral level, to support initiation of TB therapy during the clinical encounter or on the same day in peripheral settings
Target use	Health workers with basic technical skills (e.g. non-precision pipetting and minimal sample processing)
Setting (level of healthcare system)	Peripheral microscopy centres and primary health clinics
Cost	Instrument ≤$2000 Test ≤$6 (Optimal = ≤$4)
Performance	85% (Sputum) 75% (Non-sputum)
Time to result	<60 minutes (Optimal ±15mins)

DRIVING ACCESS WITH SIMPLE SAMPLES + AFFORDABLE PCR INSTRUMENTS

STATUS OF SWABS AS ALTERNATIVE SAMPLE TYPE ON EXISTING PLATFORMS

JOINED FORCES ASSESS STANDARDIZED SWAB PROTOCOL



Tongue swabs on Xpert Ultra
N =1732 participants across 8 countries
Culture reference standard
Sensitivity = 66% Specificity = 99%
Smear sensitivity = 49%

protocols.io

30 seconds

Consensus tongue swab collection and Xpert Ultra process protocol

Jul 29, 2024

Consensus standard operating procedure for collection of tongue swabs for TB diagnostics

DOI
dx.doi.org/10.17504/protocols.io.kxygxyw54l8j/v1

Alfred Andama[1], Amy E Steadman[2], Charlotte Ahls[3], Gerard Cangelosi[4], Anura David[5], Margaretha de Vos[6], Karen Heichman[7], Midori Kato-Maeda[8], Adam Penn-Nicholson[6], Alaina Olson[4], Lesley Scott[2], Lindsey Turnbull[3], Rachel Wood[4], Kris Weigel[4], Adithya Cattamanchi[9]

Jul 29, 2024

Xpert MTB/RIF Ultra testing from tongue swabs – Diluted SR method

DOI
dx.doi.org/10.17504/protocols.io.14egn69nyl5d/v1

Charlotte Ahls[1], Anura David[2], Gayatri Shankar Chilambi[3], Adithya Cattamanchi[4], Margaretha de Vos[5], Kelsey Heard[1], Karen Heichman[6], Adam Penn-Nicholson[5], Lesley Scott[2], Amy E Steadman[1], Lindsey Turnbull[1], David Alland[3]

Dilute SR buffer with PB 2:1

Dilute 2 parts Sample Reagent (SR) in 1 part phospate buffer (PB) to create SR:PB

Scale as needed for the appropriate number of tests (700uL per sample). Prepare fresh each day.

Vortex and load in Xpert Ultra with PB preloaded

Dry tongue swab

Add 700uL SR:PB

Vortex for 5-10 seconds or invert 10 times to mix the sample. Incubate for **15 minutes**. Between 5-10 minutes, vortex again for 5-10 seconds or invert 10 times.

Prepare cartridge by adding 1.5mL of phosphate buffer.

Add the entire sample (approximately 500uL) to the cartridge.

dx.doi.org/10.17504/protocols.io.kxygxyw54l8j/v1
dx.doi.org/10.17504/protocols.io.14egn69nyl5d/v1

Novel Swab-based Molecular Diagnostic – Example 1

Platform: Truelab® Duo Real Time Quantitative micro PCR Analyzer & TrueLyse
Assay: Truenat MTB Ultima
Technology holder: Molbio Diagnostics, India

Workflow

Collect Sample → Mix Sample → Lyse Sample → Transfer 6uL and Incubate → Transfer and Run Test

Operational characteristics

Time-To-Result	Hands-On-Time	Battery Operation	Cost per Test	Cost per Device
~40 min	<5 min	Yes	$8	$10,000