Stop TB Partnership

Recommended Truenat Operational Research Questions

The introducing New Tools Project (iNTP)

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Background

The introducing New Tools Project (iNTP), a collaboration between the Stop TB Partnership and USAID, is the largest multi-country roll-out of Truenat technology **(9 countries in Africa and Asia)**. The project aims to support countries in improving patient access to new diagnostic and digital health tools and increasing the detection and treatment of TB and rifampicin-resistant TB. Implementing Truenat testing near the point of care is expected to lead to improvements in the entire TB care cascade.

In order to demonstrate the impact of Truenat implementation and document the findings and lessons learned, countries are encouraged to develop operational research projects that investigate the acceptability and feasibility of Truenat testing, its impact on patient-important outcomes (e.g., time to diagnosis and treatment initiation), its ability to affect access to rapid diagnosis, its diagnostic accuracy using non-sputum samples, and its costs and cost-effectiveness. The table below describes potential topics countries can address in operational research projects.

1.

Acceptability and Feasibility

Determine the operational facilitators and barriers to implementing Truenat testing for the detection of TB and rifampicin resistance.

- Includes semi-structured interviews, focus group discussions, and key informant interviews with various stakeholders.
  - Examples of studies using focus group discussions can be found here as models[1,2,3]

What are the perspectives of lab technicians and managers on the ease of use of Truenat instruments:

- If Truenat sites were previously microscopy sites, how easy was it for the microscopist to upskill and if they feel competent to process samples, do basic preventative maintenance, quality control, and troubleshooting
- Include questions on competency requirements, troubleshooting, ability to ensure optimal instrument uptime and responsiveness of local agents
- Compared to other rapid molecular tests

What are the perspectives of lab technicians and clinicians (including doctors, nurses, and community health workers) around time to results and perceived benefit of the Truenat instruments, including compared to referring specimens off-site for rapid molecular testing?

Feasibility and effectiveness of the use of the diagnostic connectivity functionalities (sending of electronic results) may also be explored.

What are the perspectives of people receiving care for TB around time to results and perceived benefit of Truenat testing?

What are the perspectives of lab and program managers, as well as local and national decision-makers around the placement of Truenat instruments in the diagnostic algorithm, cost, and robustness of the instruments?

- Benefits, challenges, and challenges of decentralization of rapid molecular testing versus referral to more centralized sites may be explored; multiplexing of instruments for different disease testing may also be explored

What are the facilitators and barriers for implementing Truenat testing in different settings: facility-based testing or community active case finding or testing hard-to-reach populations?[4]

What are the perspectives on the ideal training requirements for lab technicians using the tests?

- How long should training be and what is the optimal frequency for site-based mentorship and refresher training?
- What are the quality management training requirements?

1. Mathabire-Rucker S et al, 2022. Feasibility and acceptability of using the novel urine-based FujiLAM test to detect tuberculosis: A multi-country mixed-methods study. 10.1016/j.jctube.2022.100316
2. Hermann Y et al, 2022. User perspectives and preferences on a novel TB LAM diagnostic (Fujifilm SILVAMP TB LAM) - a qualitative study in Malawi and Zambia. 10.1371/journal.pgph.0000672
3. Asiimwe C et al, 2012. Early experiences on the feasibility, acceptability, and use of malaria rapid diagnostic tests at peripheral health centers in Uganda-insights into some barriers and facilitators. doi.org/10.1186/1748-5908-7-5
4. Codeiro-Santos M et al 2020. Feasibility of GeneXpert® Edge for Tuberculosis Diagnosis in Difficult-to-Reach Populations: Preliminary Results of a Proof-of-Concept Study. 10.4269/ajtmh.20-0326

2. Case Finding and Rifampicin Resistance Detection

Determine the impact of Truenat testing on standard WHO indicators on TB and RR-TB case detection, bacteriological confirmation, and access to rapid molecular diagnosis

- The comparator ideally should be historical data from the same site (e.g., when only smear microscopy was available at the site and a rapid molecular test was available only at a referral facility) comparing the period before and after Truenat implementation. Collecting monthly data for the comparisons would be ideal.

What is the impact of Truenat testing on:

- Number and proportion of new/relapse TB cases tested with a rapid molecular test as an initial diagnostic (collected as part of quarterly M&E for iNTP)
- Number and proportion of new/relapse TB cases that were bacteriologically confirmed (collected as part of quarterly M&E for iNTP)
- Number of rifampicin-resistant TB cases notified at a facility
- Number of new/relapse TB cases notified at a facility

3. Impact on the TB Care Cascade

Determine the impact of improved access to molecular TB testing using Truenat on the TB cascade, from identification of people being investigated for TB to completion of TB treatment.

- This would be an indirect effect of improving access to TB diagnosis using sensitive diagnostic tools at near point-of-care, compared to referral for rapid molecular testing.
- The comparator would be the period prior to Truenat implementation.

What is the impact of Truenat testing on the TB cascade:

- The proportion of the population that has access to a rapid molecular test within a 5 km distance
- Number and proportion of estimated people with TB that are evaluated for TB at a health facility
- Number and proportion of people being investigated for TB for whom a request for TB test is made
- Number and proportion of people being investigated for TB for whom a request for TB test is made and who provide a specimen for testing
- Number and proportion of people being investigated for TB for whom a specimen is collected and received at the testing facility
- Number and proportion of people being investigated for TB that have been tested with a rapid molecular test as an initial diagnostic test
- Number and proportion of people being investigated for TB for whom a test is conducted and whose results are reported to the clinician
- Number and proportion of people being investigated for TB for whom a test is conducted and whose results are reported to the clinician and are started on TB treatment
- Number and proportion of people with TB who complete TB treatment
- Time from sample collection to TB diagnosis
- Time from sample collection to TB treatment initiation, and from diagnosis to treatment initiation, with and without connectivity (sending electronically patient results)

4.

Impact of the Use of Truenat in Active Case Finding Activities

Including as a confirmatory test after screening by digital chest X-ray with software for the computer-aided detection (CAD) of TB.

- What is the impact of Truenat testing in community active case finding on case detection (yield) and time to treatment initiation
- What are lessons learned from using Truenat in community case finding
- What proportion of patients tested with Truenat in community active case finding are lost to follow-up vs those linked to care?

5.

Cost and Cost-effectiveness[5,6,7,8,9]

Determine the cost and cost-effectiveness of implementing Truenat testing

- This analysis can compare the costs associated with Truenat testing at peripheral sites or in community active case finding compared to that of another rapid molecular test used at higher level in the health system.
- Countries can partner with academic researchers in order to address this question.

- What are the costs associated with implementing Truenat testing, including compared to other rapid molecular testing?
  - Consider different use cases: facility-based or community active case finding, onsite testing vs sample referral
  - Can include costs of the test (reagents and consumables, warranty, and maintenance), costs associated with staffing, connectivity (data transfer costs), training, sample collection, and transport, biosafety, quality assurance requirements, and utilities (water and electricity)
- What is the incremental cost-effectiveness ratio for use of Truenat as a replacement of another rapid molecular test per additional TB or rifampicin-resistant case detected?
- What is the cost-effectiveness of Truenat compared to other rapid molecular tests?
  - Event-based cost per case detected / case tested
  - Cost-utility analysis (DALY / QALY, depending on what data may be available in the country)
  - By implementation strategy: facility vs active case finding models

5. Kaso WA et al 2021. Costs and cost-effectiveness of GeneXpert compared to smear microscopy for the diagnosis of pulmonary TB using real-world data from Arsi zone, Ethiopia. PlosOne https://doi.org/10.1371/journal.pone.0259056
6. Vassall A et al 2017. Cost-effectiveness of Xpert MTB/RIF for tuberculosis diagnosis in South Africa: a real-world cost analysis and economic evaluation. Lancet Global Health https://doi.org/10.1016/S2214-109X(17)30205-X
7. Ejalu DL et al 2022. Cost-effectiveness of GeneXpert Omni compared with GeneXpert MTB/Rif for point-of-care diagnosis of tuberculosis in a low-resource, high-burden setting in Eastern Uganda: a cost-effectiveness analysis based on decision analytical modeling. BMJ Open 10.1136/bmjopen-2021-059823
8. Donkeng-Donfack VF et al 2022. A cost-benefit algorithm for rapid diagnosis of tuberculosis and rifampicin resistance detection during mass screening campaigns. BMC Infect. Dis https://doi.org/10.1186/s12879-022-07157-0
9. Thompson RR et al 2023. Multicomponent strategy with decentralized molecular testing for tuberculosis in Uganda: a cost and cost effectiveness analysis. The Lancet Global Health https://doi.org/10.1016/S2214-109X(22)00509-5

6.

Diagnostic Accuracy of Truenat for Pediatric and Extra-pulmonary TB Diagnosis

The Truenat test can be used on non-sputum samples as per the manufacturer. Still, there is currently insufficient evidence on diagnostic accuracy to allow for WHO recommendations. The comparator would be Xpert MTB/RIF Ultra and culture.

What is the sensitivity and specificity of Truenat testing on non-sputum samples:

- Stool, gastric aspirates, and nasopharyngeal aspirates for pediatric TB diagnosis
- Urine, fine needle aspirates/tissue biopsies, gastric aspirates, CSF, synovial fluid and other body fluids for extrapulmonary TB diagnosis

Instrument Key Performance

The following are standard KPIs that should be monitored at site level:

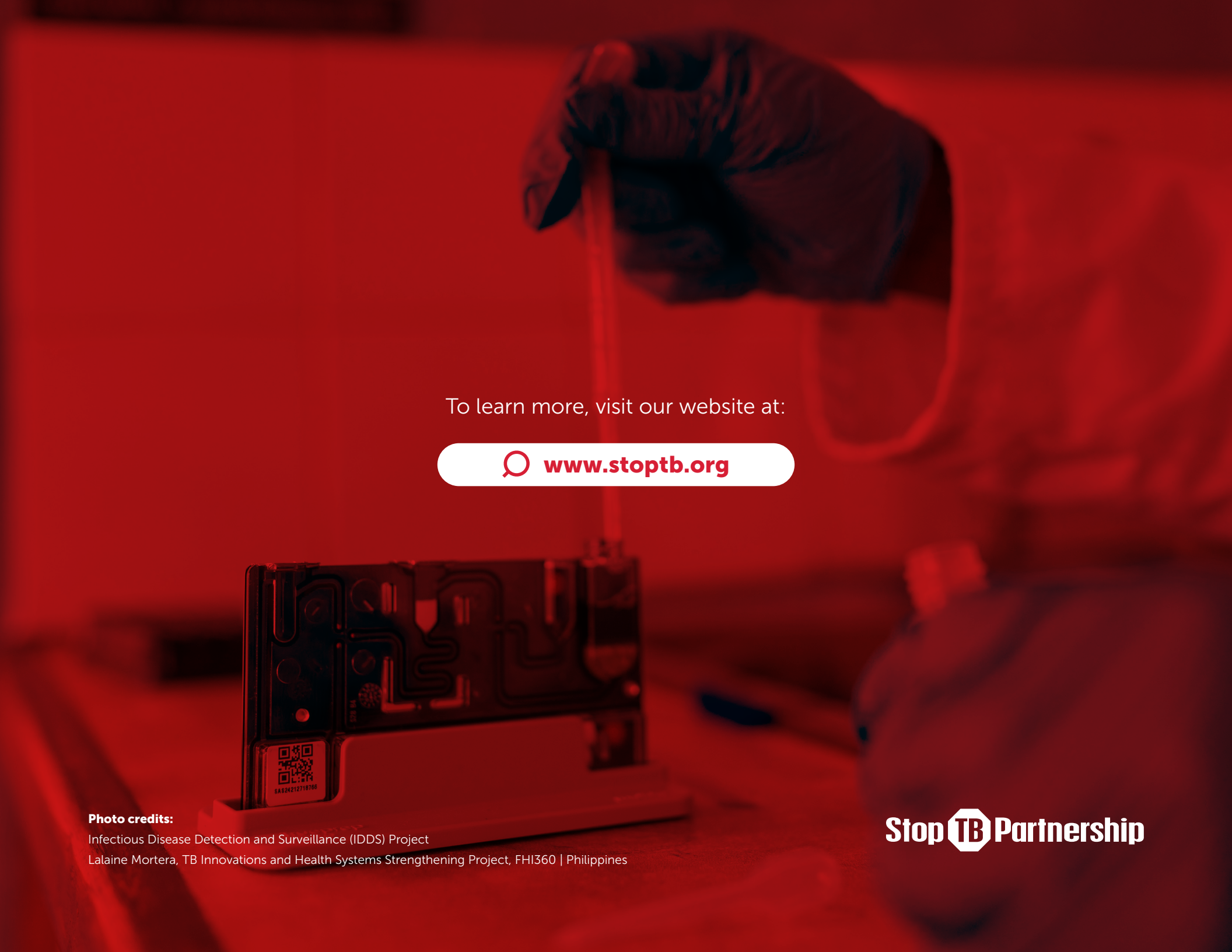
i. Number and proportion of specimens with MTB detected
   - Monitoring the MTB positivity rate by site allows for identification of challenges in effective case finding or following the established algorithm for testing of all people on-site with Truenat as an initial diagnostic test
   - Referrals from other sites should be analyzed separately

ii. Number and proportion of MTB-positive specimens with rifampicin resistance detected

iii. Number and proportion of samples with unsuccessful results (errors, invalid, no results) for Trueprep and Truelab steps, stratified by specific errors

iv. Number and proportion of samples with rifampicin indeterminate results

v. Laboratory turnaround time: time between receipt of specimen at the laboratory and result reporting



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