INTRODUCTION OF TRUENAT™ MTB PLUS AND MTB RIFAMPICIN (RIF) DX ASSAYS AT THE PERIPHERAL LEVEL: CHALLENGES AND EARLY LESSONS LEARNED

Tuberculosis (TB) is a major cause of illness and was the leading cause of death worldwide by an infectious agent prior to the COVID-19 pandemic (World Health Organization, 2021). Furthermore, it is estimated that 47 percent of the global population has little or no access to diagnostics (Fleming et al., 2021). The Truenat™ rapid molecular diagnostic tool was developed to provide timely access to high-quality molecular diagnostic testing for TB and other pathogens near point-of-care in resource-limited settings.

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BACKGROUND

The United States Agency for International Development's Infectious Disease Detection and Surveillance (IDDS) project, in collaboration with the Stop TB Partnership implementing the introducing New Tools Project[2], is supporting the introduction of more than 300 Truenat™ instruments and tests for nearly 585,000 people in 9 high-TB burden countries in Africa and Southeast Asia to improve access and timeliness of TB detection. The World Health Organization (WHO) has recommended that sputum smear microscopy, the initial test for TB in many laboratories, be replaced with one of the WHO-recommended rapid molecular diagnostic tests such as Truenat™. The Truenat™ testing system uses portable, battery-operated devices to rapidly detect *Mycobacterium tuberculosis* complex bacteria and rifampicin resistance. The system uses room temperature stable reagents (Trueprep™ AUTO Sample Pre-treatment and Prep kits) and Truenat™ micro-polymerase chain reaction (PCR) chips. The system is designed to be operated

[2] www.stoptb.org/accelerate-tb-innovations/introducing-new-tools-project

in peripheral laboratories with minimal infrastructure and is therefore the first WHO-recommended molecular test for TB that can be operated near point-of-care. Furthermore, Truenat™ is capable of integrated testing for other priority pathogens such as SARS-CoV-2.

To support effective introduction and scale-up of the Truenat™ rapid molecular diagnostic tool, the Stop TB Partnership and IDDS developed an implementation guide and a series of six training modules covering test system overview, introduction to the diagnostic algorithm, operational aspects, order planning and quality assurance, monitoring and evaluation, and specimen collection and biosafety practices. These training modules were recently endorsed by the Global Laboratory Initiative network and are available to all countries implementing Truenat™ instruments.

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IMPLEMENTATION OF TRUENAT™

INDIA EXPERIENCE

India was the first country to implement Truenat™, with approximately 1,600 instruments introduced in 2019 to support the national TB control program. Many of these instruments were repurposed shortly after introduction to decentralize diagnostic testing for the COVID-19 pandemic. Now in 2022, there are more than 4,500 Truenat™ instruments, including 2,500 supporting the TB program, that take advantage of the multiple disease testing capabilities to support SARS-CoV-2, sexually transmitted infections, HIV, and TB detection. Truenat™ testing has been successfully integrated into the diagnostic algorithm and replaced nearly 8,000 direct microscopy centers. For TB, the high sensitivity compared to smear microscopy has improved TB case detection. For example, analysis of operational research data from the Andhra Pradesh state showed that Truenat™ introduction improved the TB case notification rate by 30 percent, compared to smear microscopy (Jeyashree et al., 2020).

NIGERIA AND ZIMBABWE EXPERIENCES

Truenat™ MTB Plus and RIF Dx assays were introduced for the first time in Nigeria and Zimbabwe in 2021, with instruments placed in 20 peripheral-level laboratories throughout Zimbabwe and 38 laboratories in 14 states in Nigeria, with support from two implementing partners—Institute of Human Virology, Nigeria, and Royal Netherlands Chemical Society-Nigeria—to decentralize and provide rapid molecular diagnostic testing for TB to underserved areas. Most of the laboratories in which Truenat™ instruments were placed had previously relied on sputum microscopy for diagnosis of TB and had limited experience with rapid molecular diagnostic tools. Prior to implementation, centralized multi-day trainings using the Global Laboratory Initiative-endorsed Truenat™ modules were conducted for TB program and laboratory managers to introduce them to the new diagnostic tool. In addition, an initial half-day training was provided to an end user at each laboratory (mostly microscopists) by the local Molbio agent during the placement of the instrument at the site, and each user demonstrated competency before testing was initiated. In Zimbabwe, a refresher training (offered as a hybrid format with in-person and virtual components) was held for end users to introduce quality practices as well as provide an opportunity for the end users to share challenges and best practices with Truenat™.

KEY CHALLENGES

Challenges encountered when implementing a new rapid molecular diagnostic tool such as Truenat™ for the first time at the peripheral level were not unexpected. Most of the sites had little or no experience using rapid molecular diagnostic tools. The most frequent challenges identified included poor specimen quality, need for additional hands-on training and practice pipetting, inability to attend virtual trainings due to poor Internet connection, lack of sensitization to good biosafety practices, prolonged power outages that affected the ability to recharge the Truenat™ instruments, unavailability of trained staff to cover leaves of absences because only one user was trained to perform the Truenat™ testing, and low number of specimens received. Some performance problems with the Trueprep extraction device were also reported, which were investigated in a timely manner and resolved by the local agent. Some of these problems were anticipated; for example, initial high non-determinate result (e.g., invalid/error) rates due to difficulties with specimen processing and micro-PCR chip lot-specific performance issues were documented when Ethiopia implemented Truenat (Meaza et al., 2021). Performance of the micro-PCR chips were impacted when storage temperatures exceeded 30^{0}C for prolonged periods. A key observation from site visits carried out at the end user laboratories in Zimbabwe were gaps in quality management system (QMS) awareness, biosafety, and waste management practices. There was no evidence of standard operating procedures, maintenance and quality control logs, or quality improvement records. A review of performance indicator data, including external quality assessment (EQA) panel results, identified challenges such as sites with low usage and poor performance of some laboratories.

EARLY LESSONS LEARNED

Implementation of Truenat™ has been successful despite these key challenges. India has successfully integrated Truenat™ into the diagnostic algorithm, and it has become a standard of diagnostics and was key to increasing diagnostic testing capacity for SARS-CoV-2 and TB. In Zimbabwe and Nigeria, key performance indicator (KPI) data for error/invalid rates demonstrated performance improvement over time and increasing usage rates. The first cycle of EQA performance using Truenat™ in Zimbabwe showed that 70 percent of laboratories successfully reported results within the cycle deadline. Furthermore, 43 percent achieved a perfect score. Early lessons learned after implementation included the following:

1. Integration and Planning
    a. Development of a stepwise implementation roadmap with the national TB programs and stakeholders helped minimize hurdles.
    b. A pre-installation site survey ensured that selected sites are suitable for Truenat™ testing.
    c. Training materials should be localized to include updated diagnostic algorithms, specimen collection and referrals, and stock management procedures.
2. Supervision, Mentorship and Sustainability
    a. A cadre of superusers to perform site visit supervision and mentorship is essential to support implementation of a QMS, strengthen biosafety and waste management practices, provide troubleshooting assistance, ensure adherence to guidance and standard operating procedures, and resolve local issues.
    b. Inclusion of national TB reference laboratory staff, district managers, and other TB diagnostic network stakeholders as superusers is important to build sustainable technical capacity to support Truenat™ testing after IDDS support ends.
    c. Competency assessments should be integrated with site visits and re-training provided based on site needs.
    d. Establishment of an end-user WhatsApp group was beneficial because it provided an opportunity for sharing challenges, troubleshooting, and best practices among the users.

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3. Monitoring and Evaluation
   a. Weekly facility reporting helped quickly address challenges.
   b. Regular KPI data collection to monitor performance helped identify sites experiencing high error/invalid rates and low usage so additional technical support could be targeted.
   c. EQA performance reports successfully identified laboratories experiencing problems with the testing system and informed national laboratory stakeholders so additional support could be directed to low-performing laboratories.
4. In-person Training
   a. Challenges with unstable Internet connections highlighted the importance of providing initial hands on in-person training.
   b. Follow-up end-user in-person "refresher" training is essential to introduce good molecular laboratory practices, EQA processes, and QMS sensitization. This also provided a valuable opportunity for the Truenat™ users to share experiences and best practices.
   c. Demand creation workshops and specimen collection training to engage local health care workers and the community to increase awareness and utilization and improve specimen quality are important.
   d. Additional training of end-user staff at each laboratory is necessary to ensure continuity of operations in case of staff absences or turnover.
5. Introducing Quality Management
   a. Peripheral-level laboratory sensitization to QMS is essential.
   b. Truenat™ training modules discussed quality control practices; however, laboratories lacked equipment including timers, micropipettes, and consumables to implement quality control processes. These laboratories need to be supported with additional materials to ensure quality control.
   c. Truenat™ is an open platform test system with multiple steps that requires periodic environmental monitoring for contamination.
6. Instrumentation and Consumables
   a. Prolonged power outages hindered the ability of some sites to recharge the Truenat™ instruments, highlighting the importance of alternative methods of charging, including solar.
   b. The use of surge protectors to guard against instrument damage is important for sites with unstable power.
   c. Regular preventive maintenance procedures, including flushing of Trueprep, reduced error rates.
   d. Truenat™ instruments have initially proven to be resilient in the field for the first 6 months, with the most frequent problem associated with failure of the Trueprep component, seen with 5 of the 58 units in Zimbabwe and Nigeria.
   e. Each Truenat™ instrument procured through the introducing New Tools Project included a no-cost replacement extended warranty, which was key to avoid disruptions in testing services.
   f. Implementing acceptance testing for new lots of micro-PCR tests and where storage temperatures exceed 30^{0}C is necessary to verify performance to ensure high-quality results.

HOW IDDS IS RESPONDING TO CHALLENGES

IDDS is actively responding to the challenges and early lessons learned from the Truenat™ placements at the peripheral laboratories to improve and ensure successful implementation of these new molecular diagnostic tools in all countries. For example, IDDS is supporting initial monthly superuser site visits to provide mentorship and supervision support to the end-users. IDDS country teams are working with end-users to help collect and report KPI data to monitor performance. IDDS has collaborated with SmartSpot Quality to provide short instructional videos that can be shared through mobile phone applications, such as WhatsApp, to support end-users who have difficulty attending virtual training sessions. In addition, IDDS has created a superuser training package that includes training modules with translations, job aids, and quality logs that can be shared with countries and localized to facilitate in-person trainings and strengthen QMS and biosafety practices at facilities hosting the Truenat™ instruments These materials were refined and updated after feedback from the pilot superuser training workshop. Furthermore, IDDS is developing end-user refresher training materials and working with the local Molbio agents to host end-user in-person training workshops to train additional users, introduce quality systems and good laboratory practices, strengthen biosafety practices, and provide an opportunity to share challenges and best practices with other end-users. These materials are informing IDDS' support of Truenat™ implementation across additional countries, including Bangladesh, Cambodia, the Democratic Republic of the Congo, Kenya, Philippines, Uganda, and Vietnam.

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