EXPERIENCES OF IMPLEMENTING AND EXPANDING THE GENEXPERT MTB/RIF® ASSAY AND GXALERT IN ETHIOPIA

BACKGROUND

The quality and low sensitivity of acid-fast bacilli (AFB) smear microscopy has been a long-term problem for TB diagnosis in Ethiopia. GeneXpert MTB/RIF assay is near-patient, easy and safe to perform, rapid, and has the benefit of detecting rifampicin-resistance. Following the introduction of the GeneXpert MTB/RIF technology to Ethiopia between 2010-2012 by USAID's TB CARE I project, the International Organization of Migration (IOM), and different research projects in 25 sites across the country, the Ethiopian Public Health Institute (EPHI) performed a validation exercise which recommended national expansion of the technology. In December 2013, the Federal Ministry of Health (FMoH) officially launched the use of the GeneXpert MTB/RIF assay to diagnose TB and rifampicin-resistant TB (RR-TB) based on the available WHO recommendations and the results of the EPHI validation exercise. However, the test was only to be used for groups of patients as per the eligibility criteria or algorithm determined by the National TB Program (NTP) as shown in Figure 1 and rifampicin-resistant (RR) patients were referred to treatment initiating centers (TICs) to start the treatment for multidrug-resistant TB (MDR-TB).

USAID's Challenge TB project (CTB) was instrumental in the expansion of GeneXpert service across the country. The ultimate goal of the introduction and expansion of GeneXpert for the diagnosis of TB, was to bring a rapid diagnostic technology to diagnose TB and drug-resistant TB (DR-TB), improve the quality of TB diagnosis, and help to find more TB cases overall.

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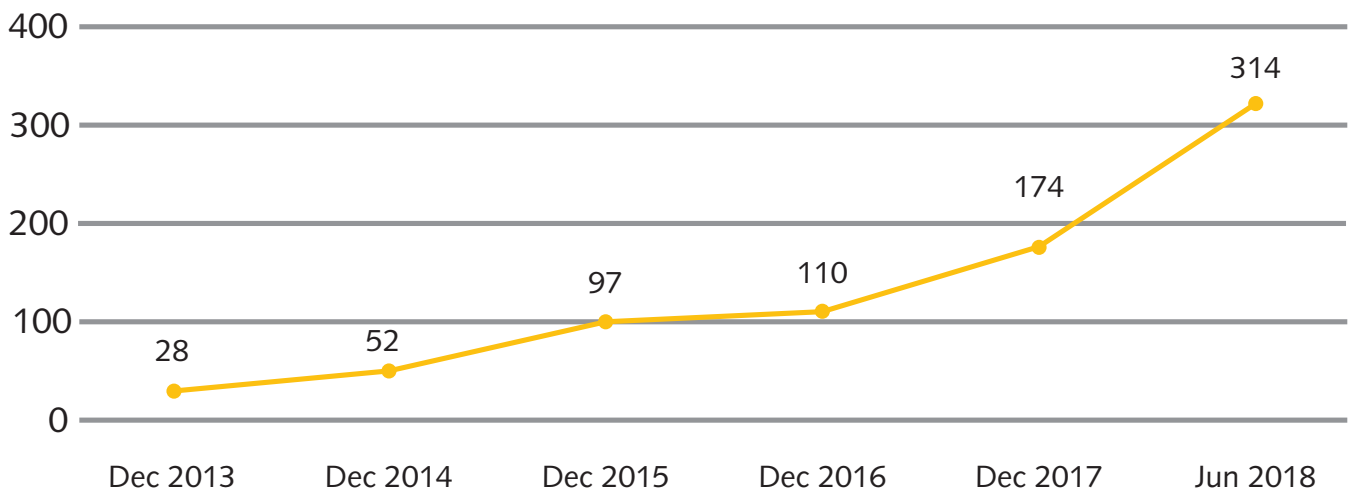
FIGURE 1: LIST OF PATIENT CATEGORIES TO TEST USING GENEXPERT, BASED ON THE NATIONAL TB DIAGNOSTIC ALGORITHM, 2014

- Previous TB treatment ≥1month
- Contact with RR-/MDR-TB case (presumed/proven)
- Patient from congregated setting, health facility, or other high MDR-TB prevalent settings.
- HIV positives/test not done
- Child ≤14yrs old
- Extra-pulmonary TB site

Almost all the machines procured and installed in the country were four-module systems, except two two-module machines, and one sixteen-module machine.

FIGURE 2: EXPANSION OF GENEXPERT MTB/RIF ASSAY TESTING SERVICES, 2013-2019 (N = NUMBER OF MACHINES)



As of June 2019, a total of 314 functional GeneXpert machines had been distributed and installed in 285 health facilities (HFs). Among these HFs, five sites have three machines whilst 21 sites have two machines.

GENEXPERT SERVICE EXPANSION APPROACH

In order to improve access to quality TB diagnostic service, CTB supported the NTP to implement GeneXpert services across the country via the major activities shown in Table 1. The placement of the instruments was based on the HF workload of TB/HIV cases, accessibility by other HFs via a diagnostic laboratory referral network, and the availability of the necessary infrastructure at the respective HF.

TABLE 1: MAJOR ACTIVITIES SUPPORTED BY CTB TO ASSIST THE NATIONAL IMPLEMENTATION OF GENEXPERT SERVICES

Major Activity	Remarks
Procurement	Procured 12 four module machines, 44 Xpert check kits, 97 refurbished modules (procured to replace non-functional modules due to hardware failure), 67 inverters with batteries, and 55,000 Xpert cartridges.
Installation of Machines	Supported the installation of more than 90 percent of the GeneXpert machines (financially and technically)
Training	Trained 1,013 laboratory professionals and 1,473 clinicians were at Xpert trainings and awareness creation workshops
Maintenance	Assisted with the maintenance of the GeneXpert machines at the HF site level
Technical Support and Mentoring	Provided regular HF site level technical support and mentoring
Monitoring and Evaluation Activities	Supported the national and regional laboratories and the NTP in annual and strategic plan preparation, quarterly report collection, analysis, and reporting

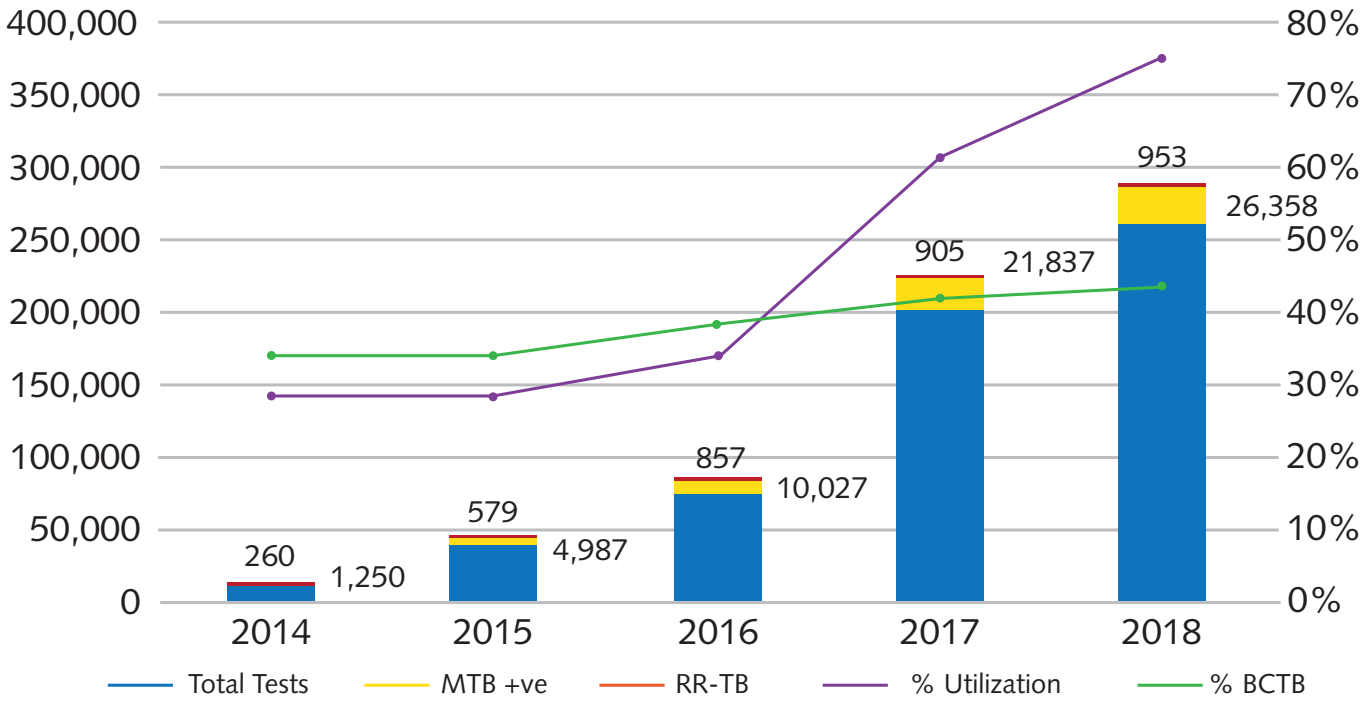
RESULTS

ENHANCED DETECTION OF BACTERIOLOGICALLY CONFIRMED AND DR-TB CASES

Since the second year of the project, CTB has been engaged to improve service expansion and utilization of new technologies (GeneXpert access) with efficient sample transportation and lab networking to ensure access for first and second-line drug susceptibility testing (DST) in the country. The Ministry of Health, partners and donors have invested in GeneXpert availability, for instance, from just 28 machines in 2013, GeneXpert availability progressively scaled up reaching a total number of machines of 314 in 2018. CTB's role was significant in terms of functionality of machines (from installation to maintenance), training and mentoring of staff, procurement of accessories, cartridges, connectivity solutions (GxAlert), etc.

The trend in utilization rate has improved from 28 percent in 2014 to 78 percent in 2018 (July-Dec 2018) for existing GeneXpert machines, therefore, the proportion of bacteriological confirmed TB cases has improved proportionally from 34 percent to 41 percent. Similarly, the notification of confirmed RR-TB cases has also increased (Figure 3).

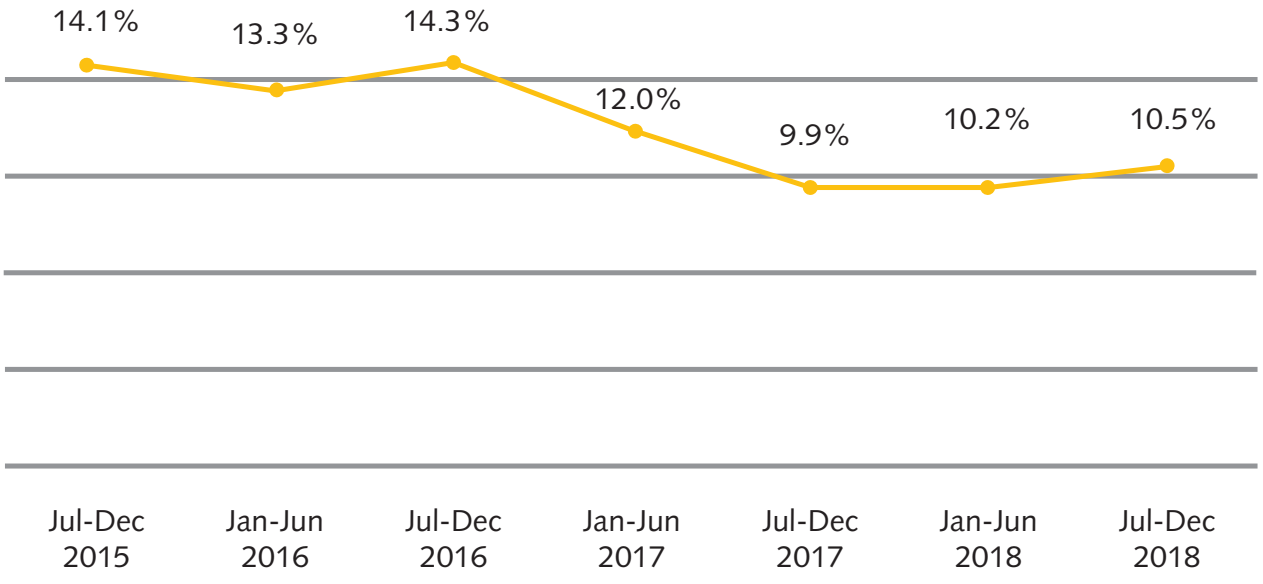
FIGURE 3: TRENDS IN GENEXPERT UTILIZATION AND CONFIRMED MTB AND RR-TB CASES



NATIONAL GENEXPERT POSITIVITY RATE

The TB positivity rate of GeneXpert tests showed a declining trend over the years (Figure 4). From a peak of 19.1 percent (2,962) in June 2016, it had decreased to 10.4 percent (12,795) by the end of 2018. However, the absolute number of positive TB test results increased. This decline in the positivity yield was due to a change in the national algorithm which allowed all presumptive TB cases to be tested by GeneXpert test (i.e., implementation of 'Xpert for all'). This increased the number of tests significantly, but the percentage of positives declined as those patients tested included more patients with a lower index of suspicion for TB.

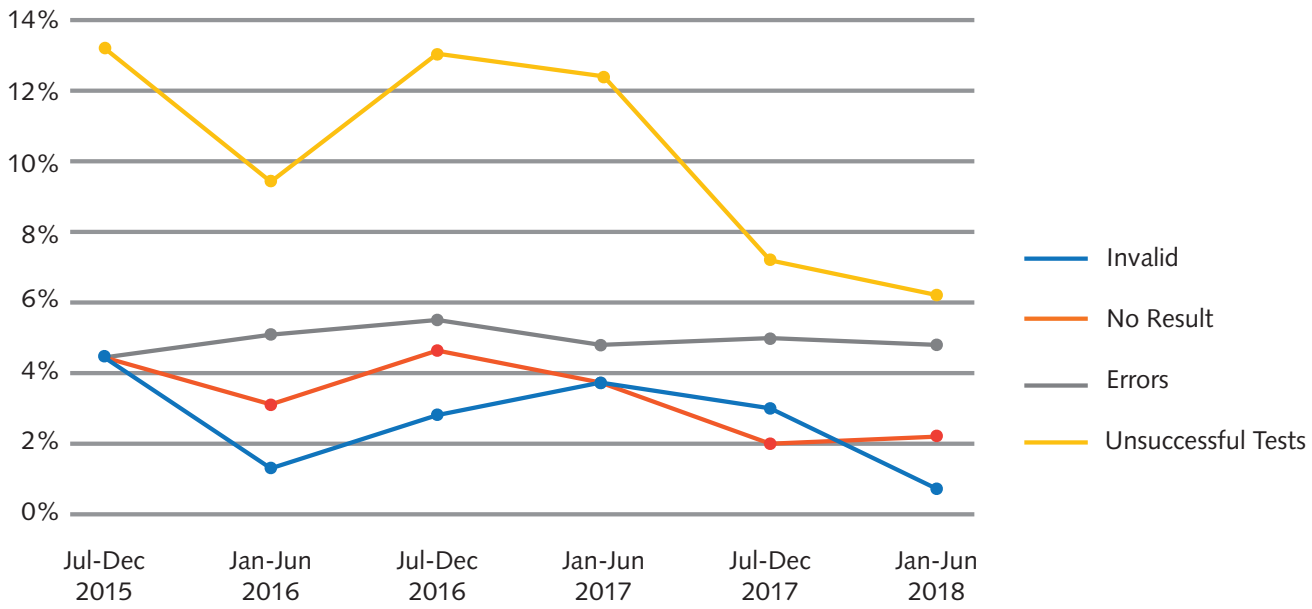
FIGURE 4: GENEXPERT POSITIVITY RATE, 2015 - 2018



TREND IN UNSUCCESSFUL TEST PERFORMANCE OF GENEXPERT MACHINES FROM 2015 TO 2018

The level of unsuccessful performance of GeneXpert tests has been decreasing over time from 13.1 percent in 2015 to 6.2 percent in 2018 (Figure 5). The decline is the result of strong site-level mentoring by CTB zonal, regional, and national level laboratory advisors with their government counter parts, staff training, and power back-up distribution and installation. Government counterparts at all levels participated in the capacity-building of lower level laboratory personnel working with GeneXpert. The number of 'No result' errors (mainly due to power interruption) has significantly decreased (from 5.1 percent to 0.4 percent) due to the installation of inverters by CTB and uninterruptible power supplies by the FMoH, and plays a significant role in the overall decline in the number of unsuccessful tests. The other significant change is related to 'Invalid' test results which have been decreased by technical corrections and training of laboratory staff. They decreased from 4.4 percent in 2015 to 1.9 percent in 2018. There is no significant change observed in 'Error' results which are mainly due to instrument, cartridge, and technical issues. However, they also declined from 4.5 percent in 2015 to 3.8 percent in 2018.

FIGURE 5: THE DECLINE IN UNSUCCESSFUL GENEXPERT TEST RESULTS FROM 2015 TO 2018



GENEXPERT MAINTENANCE

CTB has worked to keep every GeneXpert machine in the country functional. Maintenance data from the sites were collected through GxAlert and the zonal officers, and preventive and curative maintenance was undertaken in collaboration with the EPHI and the local service provider (Medica Pharma). Preventive maintenance was supported by the CTB zonal, regional and national laboratory officers and advisors. In addition, CTB procured 97 refurbished modules to replace failed modules. In order to hand over this activity, CTB organized four rounds of training focused on advanced GeneXpert training. In addition, over the last six months, CTB staff have intensified their mentoring of counterpart staff on maintenance issues, so that this area is sustained after the CTB project closes out.

GXALERT

BACKGROUND

Collection of the relevant data required for improved laboratory management via the paper-based TB laboratory reports, has been a challenging procedure. Therefore, the EPHI, National TB Program, and Implementing partners, rolled out 'GxAlert' for the GeneXpert machines and expanded services. GxAlert is used to transmit (i) Program data to regional and national TB programs, (ii) Inventory reports for logistic officers (for quantification purposes at NTP level), (iii) Maintenance reports for biomedical engineers at regional laboratories and EPHI; (iv) Data on DR-TB for MDR-TB program managers at national/NTP and sub-national levels; (v) Information on GeneXpert machines that report high error that can be used for troubleshooting because real time information is obtained through GxAlert. It helps all Xpert devices to communicate in an optimal manner to improve outcomes at all levels.

START-UP AND ROLL-OUT OF GXALERT

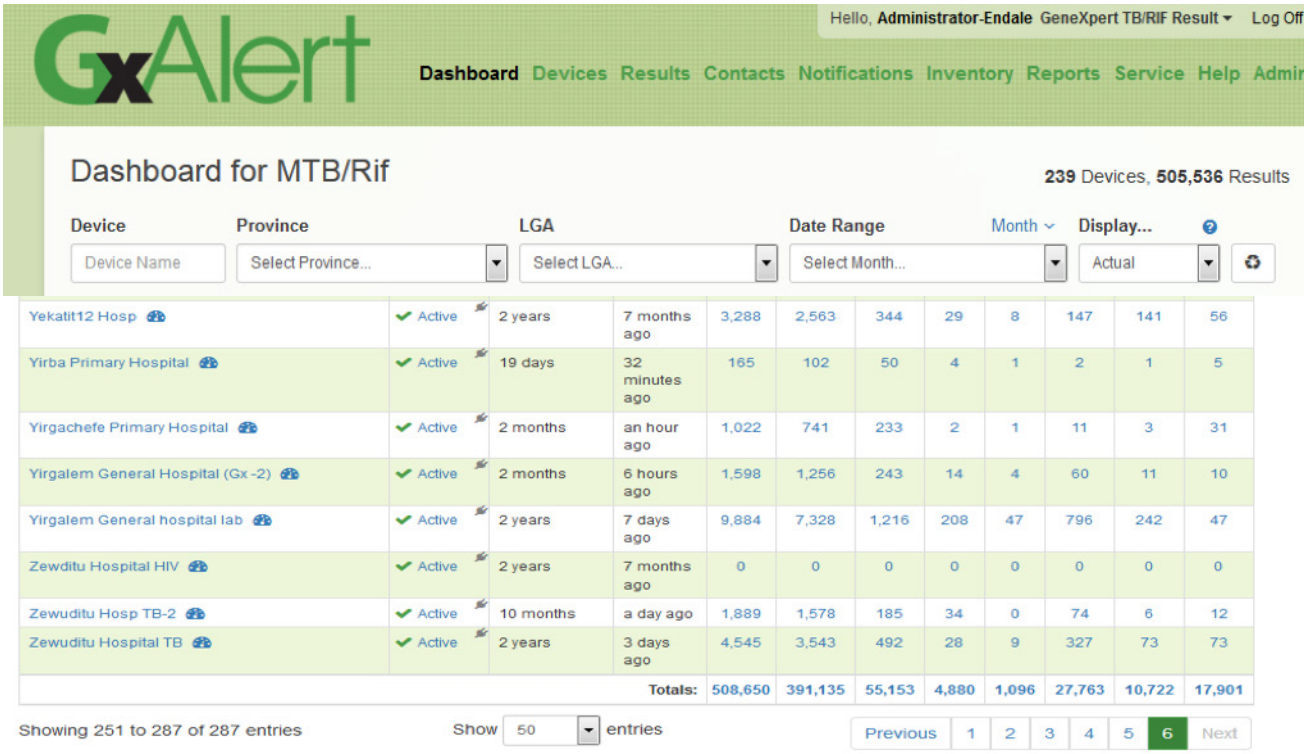
The complete package of CTB support that was implemented for both the preparation and roll-out phases of introduction of GxAlert is provided in Table 2 below.

TABLE 2: MATERIALS PROCURED AND DISTRIBUTED FOR THE IMPLEMENTATION OF GXALERT

Major Activity	Status
Procurement of 320 3G and 4G Internet Modems (3G 85 and 4G 34)	Procured and donated to EPHI
Procurement of 400 3G and 4G Internet package only SIM Cards	Procured and donated to EPHI
Training on installation for five teams composed of three individuals	15 staff were trained on installation and as trainers
Providing GxAlert training for all end users and program staff	450 staff were trained on GxAlert, focusing on how to use the data obtained from the system and how to work with it
Installation of GxConnect Software	Software installed in 239 out of 285 Xpert sites. All the connected sites are reporting to the EPHI secure server
Budgeting and paying for annual internet costs	One GB internet only package was procured from Ethio Telecom for monthly consumption

All the above procurement, training, installation, and mentoring activities were financially and technically supported by CTB. The budget covered the running cost for internet payment for implementation up until July 30 2019. As part of the transition of the CTB provided support, this payment was handed over to the EPHI in order to sustain the service. The participants who attended the training on GxAlert were from regional health bureaus, regional reference laboratories, and GeneXpert site-level staff. Figure 6 shows a screenshot of the current GxAlert implementation from the secured local server of the EPHI.

FIGURE 6: DASHBOARD AND DEVICE FUNCTION TABS FROM GXALERT



RESULTS

In the initial phase of implementation, a total of 21 machines were evaluated. Currently, with an expansion of implementation, a total of 239 out of 285 (83%) Xpert sites have been connected through CTB support via the EPHI secure server. As of April 30 2019 a total of 505,536 test results have been reported through GxAlert. Table 3 shows the results of the data collected through GxAlert in real-time.

TABLE 3: ANALYSIS OF DATA COLLECTED THROUGH GXALERT

Years	Utilization Rate	Positivity Rate	% of Unsuccessful Tests	% Invalid	% No Result	% Errors
July-Dec 2015	28%	14%	13%	4.0%	4.0%	4.0%
Jan-June 2016	28%	13.3%	9.4%	1.4%	3.0%	5.1%
July-Dec 2016	34%	14.3%	12.9%	2.8%	4.6%	5.5%
Jan-June 2017	61%	12.0%	12.3%	2.6%	2.6%	3.3%
July-Dec 2017	75%	9.9%	7.1%	2.2%	2.2%	2.7%
Jan-June 2018	78%	10.2%	6.3%	1.0%	0.4%	4.9%
July-Dec 2018	41%	10.5%	6.2%	1.8%	0.4%	3.7%

CHALLENGES

CHALLENGES FACED DURING IMPLEMENTATION

- Lengthy procedures required for Cepheid to replace failed modules.
- Training gap for laboratory staff and clinicians on GeneXpert national implementation strategy and algorithm.
- Current underutilization of Xpert test due to cartridge shortage and the lack of clinician sensitization workshops at newly installed sites or referring HFs network.
- Weak implementation of the integrated specimen referral system established throughout the country.
- Poor internet connectivity in the country.

CHALLENGES THAT WILL CONTINUE AFTER CLOSEOUT

- Insufficient national stock of Xpert cartridges due to a budget shortage and delays in the procurement process.
- Budget gap for replacement module procurement (until now all of the module procurement costs have been covered by CTB).
- Inadequate availability of backup power systems at GeneXpert laboratories.
- Inadequate number of GeneXpert machines to provide universal DST to the community.
- Lack of clear and easy reporting mechanism in the government laboratory tier system
- Budget gap for technical support, monthly internet package payment and to address installation cost at 45 new sites for GxAlert (until now all of the GxAlert costs have been covered by CTB).
- Delays in postal sample transportation and turnaround time for GeneXpert results

LESSONS LEARNED AND NEXT STEPS

The rapid GeneXpert MTB/RIF assay service expansion and GxAlert implementation significantly increased the quality of TB diagnosis, increased access, and real-time data reporting to decision-makers. A series of measures – addressing power outage by providing inverters and batteries, strong Xpert site mentoring, the provision of gap-filling training for laboratory staff, and the installation of GxAlert at almost all sites – accelerated the reduction in unsuccessful tests, whilst increasing utilization, functionality, and data access for the NTP.

However, gaps in financial support remain for the current network, and the service requires support for further expansion to the lower levels of the health services as planned in the NTP's strategic plan. There is also a need to address the training gap for the newly installed GeneXpert sites, and the technical support needed to increase the GeneXpert MTB/RIF assay utilization and monitor implementation. The installation of GxAlert needs to be completed for all GeneXpert systems in the country and its functionality supported via technical assistance to ensure increased yield and performance of the

GeneXpert equipped health facilities. Additional in-country capacity needs to be built for the maintenance and repair of GeneXpert machines and to ensure the functionality of the GeneXpert network.

The FMoH and EPHI, in collaboration with the regional health bureaus, need to strengthen the TB laboratory teams and assign a focal person for each initiative at each administrative level as CTB support ends. In addition to this, it is recommended that the NTP and EPHI mobilize resources and integrate activities for efficient utilization of resources in order to maintain site-level mentoring, GxAlert expansion, GeneXpert module procurement, TB laboratory equipment maintenance and certification.

CONCLUSIONS, LESSONS LEARNED AND NEXT STEPS

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