CHALLENGE TB TECHNICAL BRIEF

OPTIMIZING AND UNDERSTANDING THE USE OF XPERT MTB/RIF® TESTING

SUMMARY

Molecular testing for tuberculosis (TB) and rifampicin (RIF) resistant TB using the Xpert MTB/RIF® assay has been a game changer since its endorsement by the World Health Organization (WHO) in 2010. While it has been rolled-out in high burden countries at large-scale, many challenges remain, including accessibility and the availability of services.

Using examples from Nigeria and Tajikistan, we describe successful approaches to optimize Xpert MTB/RIF® testing by expanding access and service availability and discuss limits, remaining challenges, and solutions supported by KNCV through the USAID-funded Challenge TB project.

Furthermore, we present additional indicators and analysis approaches, which can provide important additional perspectives on the effect of optimization activities and can guide in the interpretation of whether the test is optimally used and utilized.

OUTLINE

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CHALLENGE TB

INTRODUCTION

XPERT MTB/RIF AND ITS GLOBAL ROLL-OUT

The Xpert MTB/RIF® assay from Cepheid Inc. (hereafter called Xpert) was endorsed by WHO in 2010 to be used as the initial diagnostic test for HIV-associated TB and people at risk for multidrug-resistant (MDR) TB[1]; policy updates included the use of Xpert for pulmonary and extrapulmonary TB in adults and children and recommended the use of Xpert as initial diagnostic test for all presumptive TB cases,[2,3] hereafter called the 'Xpert4All' policy. Following the WHO endorsement, high-burden countries implemented and expanded their GeneXpert (GX) instrument networks at a large scale: Six years after the initial endorsement, 130 countries (eligible for reduced instrument and cartridge prices[4]) had procured a total of 29,865 modules (6,659 instruments).[5]

CHALLENGES, PRIORITIES, AND APPROACHES

Although many improvements have been made, numerous countries still face challenges with regards to ensuring accessibility and availability of Xpert testing. In a survey among 29 high burden countries conducted in 2016, only 52 percent of surveyed countries reported adopting the Xpert4All recommendations in their national guidelines; and only 40 percent of those have actually been able to make Xpert testing practically widely available for all presumptive TB cases.[6]

Bottlenecks, such as the geographic accessibility of respective laboratories for all populations through an efficient laboratory network, uptake of and demand for Xpert testing from individual facilities, unavailability of Xpert testing services due to instrument breakdowns or cartridge supply interruptions, limited the availability of Xpert testing in countries. Consequently, many countries reported GX instruments whose full capacity was not effectively used, i.e., were underutilized.

Building on the previous support provided under USAID/TB CARE I, which was primarily focused on the initial implementation and roll-out of Xpert in high burden countries, USAID/Challenge TB has been focusing on optimizing access and availability of Xpert testing. Tightly connected to support provided by other partners such as Global Fund (GF), key approaches have been to expand the Xpert laboratory network and/or to increase population access, for example by connecting peripheral sites through a specimen transportation system (STS). At the same time, substantial efforts have been made in countries to improve the functionality of Xpert instruments and laboratory support systems, including, but not limited to, ensuring timely instrument service and maintenance, functional cartridge supply systems, and human resources management.

NIGERIA - SUCCESSFUL XPERT OPTIMIZATION USING A PACKAGE APPROACH

BACKGROUND

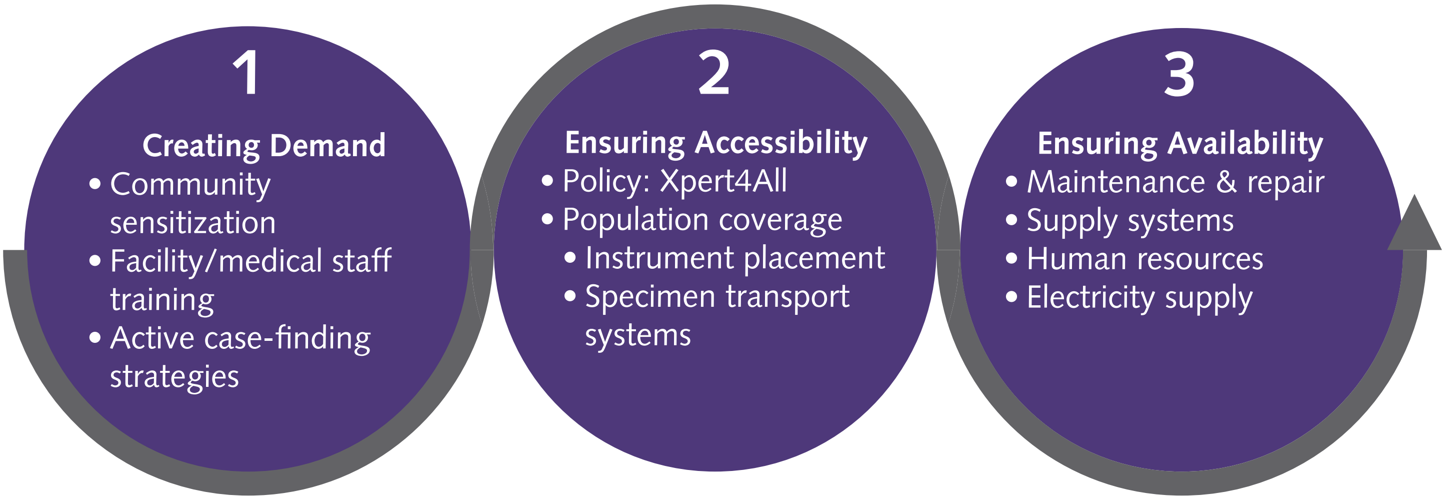
Nigeria was among the first countries that implemented Xpert testing soon after the WHO endorsement. By the end of 2018, 394 Xpert instruments had been installed.

The observed challenges in Nigeria have been frequent instrument breakdowns (often caused by harsh climatic conditions), and creating testing accessibility for the majority of the population. Based on detailed assessments, a 'package of interventions' has been developed to close these gaps and optimize the use and utilization of existing machines.

Country Profile[7]
- 180 million people
- High burden of TB, TB/HIV, and MDR TB
- Estimated incidence TB: 219/100,000 (143-311)
- Estimated incidence MDR/RR TB: 12/100,000 (7.3-19)
- Notified/estimated TB incidence: 24% (17-38)
- First Xpert installed in 2011
- Xpert4All introduced at the beginning of 2016
- 394 Xpert (1,576 modules) installed by Dec 2018

THE OPTIMIZATION PACKAGE

The key pillars of the package interventions are creating demand, ensuring accessibility, and availability of testing. With support from Challenge TB, this approach has been now implemented for several years, the individual activities and results are outlined in detail below.



1 - CREATING DEMAND FOR XPERT TESTING

Sensitizing Communities
Knowledge and understanding of TB is key to improving the health-seeking behavior of the population. Therefore, Challenge TB has been supporting community sensitization activities, which focused on creating awareness about the signs and symptoms of TB and informing about available health services and referral processes. That was achieved through meetings with the communities directly. For certain events, community sensitization has been combined with on-the-spot sputum collection and Xpert testing, so called outreach events. National and/or regional level approaches included radio messages, bulk SMS's, and the establishment of a toll-free call center for questions and answers about TB.

Sensitization & training of health care workers
Facility-based activities for demand creation included training and orientation of health care worker on national policies and standard operating procedures (SOPs) on the identification and management of presumptive TB and DR TB. This is usually conducted during a short half day events at the peripheral clinics, laboratories and/or different departments of hospitals.

Active case-finding
In some areas, proprietary and patent medicine vendor (PPMVs) and community pharmacists (CPs) were trained to recognize the signs and symptoms of TB among people visiting their shops to purchase over-the-counter drugs. Those with TB signs and symptoms are encouraged to visit the nearest health facility. The PPMVs and CPs receive incentives for every complete referral made as well as any positive case diagnosed from their referral.

The FAST strategy (**F**inding, **A**ctively, **S**eparating, and **T**reating) aims to rapidly identify, diagnose, separate and treat TB patients in hospital settings and thereby reduce transmission. This approach can also increase the number of patients screened and tested for TB and has been implemented in many facilities in Nigeria.

2 - ENSURING ACCESSIBILITY TO XPERT TESTING

Population coverage – Specimen transportation systems
If Xpert machines can't be placed at every clinic, specimen transportation systems are an essential part of ensuring accessibility to testing for peripheral sites. In Nigeria, three different models for specimen transportation are used:

1. Courier model
The contracted courier model employs the services of a company to transport sputum specimens and results on a daily basis between peripheral facilities and Xpert sites. This system is flexible and responsive: i.e., before delivering the samples to a facility, the courier checks with the facility if the instrument is functional. If not, samples are brought to a nearby facility instead, and the courier also ensures the results are returned to the correct requesting health center.

2. Incentivized health care worker (HCW) model
The HCW model uses hospital staff or volunteers to transport specimens and results, which functions on a financial incentive basis. Practical experience shows that the HCW model is less expensive, while the courier model is more efficient in terms of responsiveness, workload, and turnaround times.

3. Combining different mechanisms
Currently, a nationwide integrated system is established to transport any clinical specimens (blood, sputum, and others) for the three disease areas (HIV, TB, and malaria) via a third-party logistics company. It is expected that this system will be more efficient and less costly when compared to independent and disease-specific transport systems.

Highlight - Community Involvement

In Bateriko, the community health center with the Xpert instrument used to suffer from frequent power outages. The neighboring petrol station owner offered to provide electricity from his own business to fill the gap. With support from Challenge TB, an electricity line was installed that now ensures an uninterrupted power supply for Xpert testing.

3 - ENSURING AVAILABILITY OF XPERT TESTING

Maintenance and repair
Cepheid has established a regional service and repair center in Nigeria to ensure more rapid repair of, for example, faulty modules, which previously needed to be sent to France. This center also serves neighboring countries in West Africa. In addition, Nigeria has trained so-called 'superusers', which include more than 100 staff members from the national and local ministries and implementing partners. A toll-free hotline has been established where laboratory staff can receive distance support from superusers to help identify technical problems and provide troubleshooting. Superusers can also help with the replacement of modules and facilitate the prompt generation of mandatory documents for the timely launch of the repair process by Cepheid.

Uninterrupted power supply
Power outages are a big challenge in Nigeria, especially those whose length exceeds the capacity of the installed batteries. Therefore, some Nigerian laboratories have installed solar panels, and at the same time, faulty inverters and batteries have been repaired or replaced.

Human resources: An extra pair of hands
Some facilities lacked personnel to operate Xpert instruments and process specimens in a timely manner. Other facilities are supported by qualified staff in addition to routine laboratory personnel. Their payment is based on performance, i.e., in addition to their basic salary, staff receive incentives for the number of samples tested.

This performance graded payment instills commitment and motivates staff to perform optimally. It has been also observed that incentive systems lead to a greater likelihood that faulty instruments are reported more promptly. However, an incentivized payment system does require additional time and effort to limit the possibilities for exploitation. Measures implemented include a regular cross-checking of clinic and lab registers to match the numbers of presumptive TB cases, the number of tests conducted in the laboratory, and the number of patients started on treatment.

RESULTS AND LESSONS LEARNED

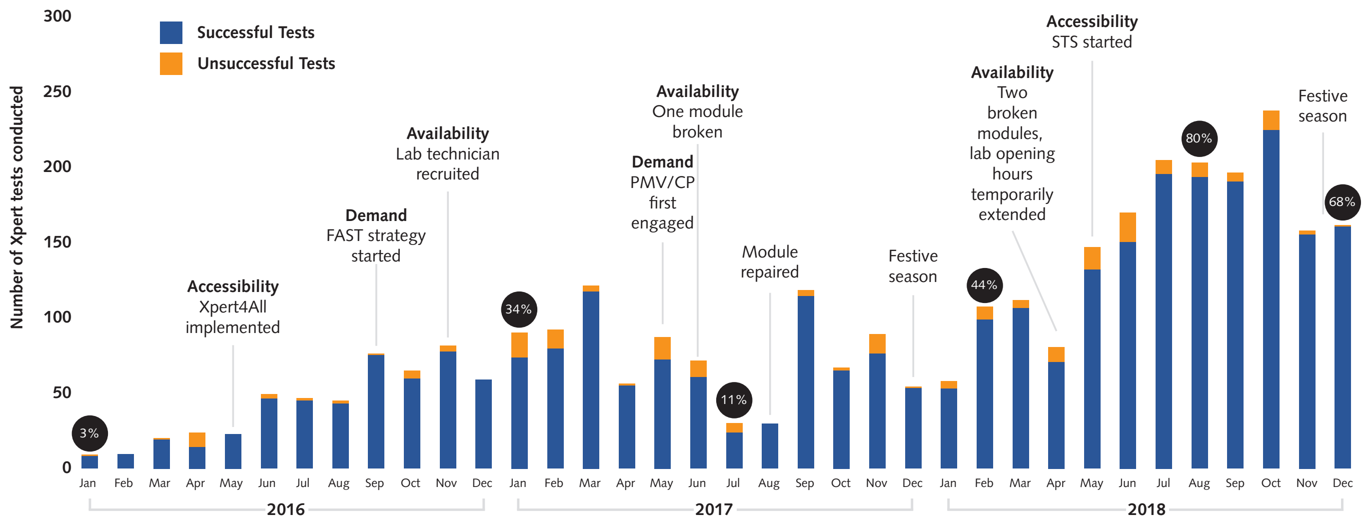
Using two selected sites as examples, we illustrate the effect of the aforementioned interventions on Xpert testing volumes over a period of three years (January 2016 – December 2018). The data sources were the routine laboratory data (from GxAlert) as well as Challenge TB records of interventions and events.

In both facilities (Figure 1), the optimization package activities led to a marked increase in the number of people tested for (DR-)TB on a monthly basis: starting with an average of 14 tests per month (Q1 2016), Eastern Nigeria Medical Centre (Enugu) conducted an average of 202 tests per month in Q4 of 2018, which corresponds to 5 percent and 74 percent of the maximum instrument utilization, respectively. In the same time frame, the average monthly testing volume was doubled in Sir Muhd Sansui Hospital (Kano).

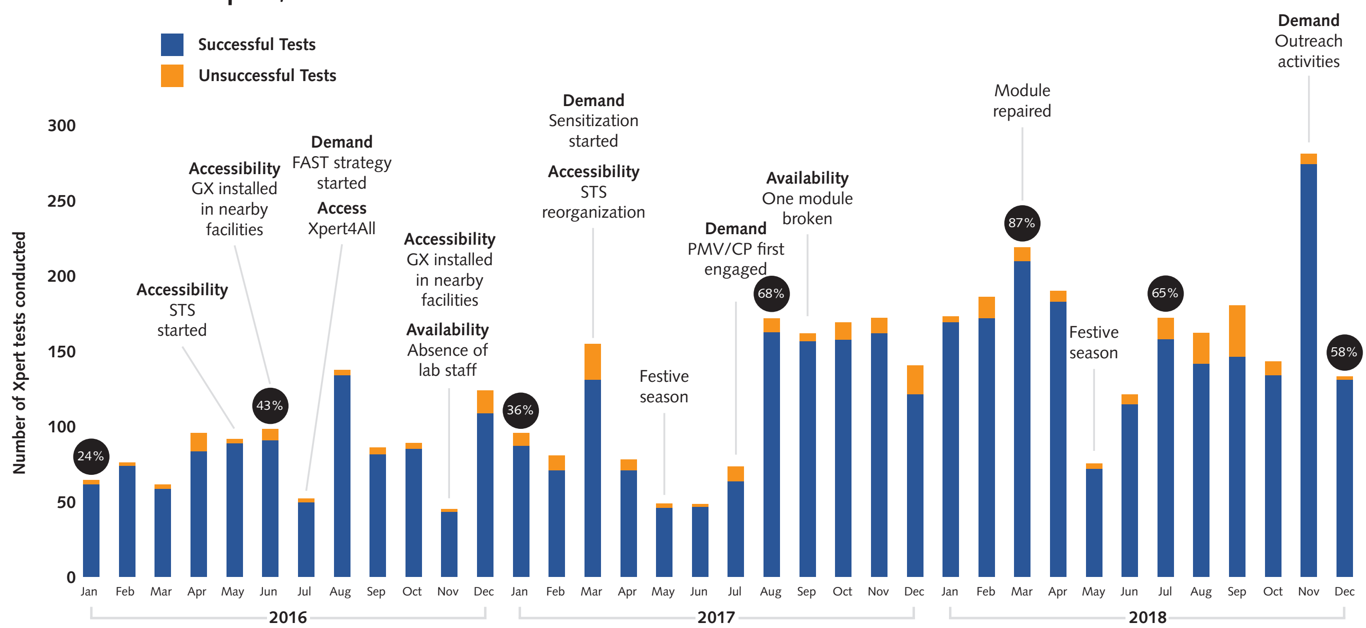
Figure 1: Xpert test statistics & optimization activities

Number of Xpert tests and interventions in Eastern Nigeria Medical Centre (Enugu) (first graph) and Sir Muhd Sansui Hospital (Kano) (second graph) between 01/16 and 12/18. Unsuccessful tests include error/invalid/no result. The percentages depict the utilization of maximum instrument capacity. Repeated activities, e.g., gradual expansion events, are not shown. Sensitization in Eastern Nigeria Medical Centre started in 2015 (not shown). The festive season in Kano 2016 was in June (not shown).

Eastern Nigeria Medical Centre, Enugu State



Sir Muhd Sansui Hospital, Kano State



XPERT OPTIMIZATION IS A PACKAGE APPROACH

It is interesting to note that most single-interventions, such as implementing the Xpert4All policy in early 2017, had a relatively small effect on the number of monthly tests in both facilities (Figure 1). Others, such as setting up and expanding an STS appear to lead to a larger increase in monthly tests. This is expected as the interventions depend on each other: the Xpert4All policy has little effect if not brought to scale by establishing a large network of peripheral facilities connected via an STS. Even both together are expected to only have a small effect if the clinicians at the facilities do not create demand because they are not aware of Xpert in the national policies or trained on its use. And finally, none of the interventions will have any effect if there is no responsive troubleshooting mechanism for technical instrument problems, as the test statistics for both facilities illustrate.

The concept that Xpert implementation is a programmatic approach (and thus requires a package of interventions) has already been established in the first years of its initial roll-out in countries, e.g., under TB CARE I. The facilities analyzed here both show a successful optimization of Xpert use when consistently applying the same concept. While the specific interventions to optimize Xpert testing certainly depend on the individual circumstances and requirements of each facility and country, experience from Nigeria shows that the key pillars and important interventions of the Xpert optimization are demand, accessibility, and availability.

In contrast to the package approach for early implementation, more emphasis needs to be put on creating demand and ensuring accessibility, specifically with regards to population coverage. Other aspects, such as ensuring availability through service and maintenance, supply systems, and human resources still remain a key priority and challenge for many countries, which is discussed in the next section.

THE LIMITATIONS AND CHALLENGES OF THE PACKAGE OPTIMIZATION

The package approach presented here was implemented in most Challenge TB-supported Xpert sites, and while many reported a positive effect, some sites reported only small increases in the number of monthly tests. Among the limiting factors observed for optimization was, for example, the health seeking behavior of the population, either influenced by long travel distances or the costs incurred to reach even the most peripheral clinics with sputum collection points. Another limiting factor might also be a very small catchment population size that cannot be practicably expanded but simply does not have a high number of (presumptive) TB patients. This particular aspect is presented and discussed in the next section.

ATTRIBUTING CAUSE AND EFFECT: KEEPING THE BIG PICTURE IN MIND

The pitfalls of attributing causes and effects are a well-known challenge and, if planned outside of thoroughly designed research settings, it is almost impossible to draw conclusions on the effect of one single intervention. The two presented facilities clearly demonstrate this: individual interventions were started within a few months of each other, overlapped, and/or were gradually expanded.

While the optimization activities require a package approach, it is very important to extend this concept to the data analysis too. Due to overlapping activities, which strongly depend on each other (such as the Xpert4All policy and STS), increased utilization cannot be attributed to one intervention. Conversely: just because the Xpert4All policy did not show a major effect in the month it was implemented, this does not necessarily mean it had no effect. In reality, the simple reason might be that it had not been brought to scale, e.g., with an STS.

Instead of attempting a pre-post intervention comparison, it will be more informative to mark events on a timeline, as we illustrated for the two facilities. This could be a simple but more accurate way for laboratory and program managers to link Xpert use and utilization to interventions and understand their effect. A detailed analysis of the cause and effect of single interventions requires well-designed research studies.

TAJIKISTAN - ENSURING ACCESS TO XPERT MTB/RIF TESTING

BACKGROUND

Tajikistan has a mountainous terrain, and the population is widely dispersed, as a consequence, access to health care is a key challenge.

Ensuring accessibility to rapid TB diagnostics has been a priority in the past years, and approaches that have been taken by the National TB Program (NTP) and partners included the expansion of the TB diagnostic network by increasing the number of facilities which offer rapid (DR-)TB testing, relocating Xpert instruments from low-demand to high-demand locations and implementing a wide specimen transportation network.

Various interventions to support Xpert use and utilization have been conducted by Challenge TB and other implementing partners, similar to the activities described from Nigeria. However, here we focus on the detailed description and analysis of Tajikistan's strategy for and results of ensuring accessibility to Xpert testing.

Country Profile[7]

- Population 8.93 million
- High MDR TB burden
- Estimated incidence TB: 85/100,000 (65-106)
- Estimated incidence MDR/RR TB: 26/100,000 (18-35)
- Notified/estimated TB incidence: 78% (62-100)
- First GeneXpert instrument installed in 2013
- 46 GeneXpert (124 modules) installed by the end of Jan 2019
- Xpert4All policy introduced in 2017

APPROACH TO ENSURING ACCESSIBILITY

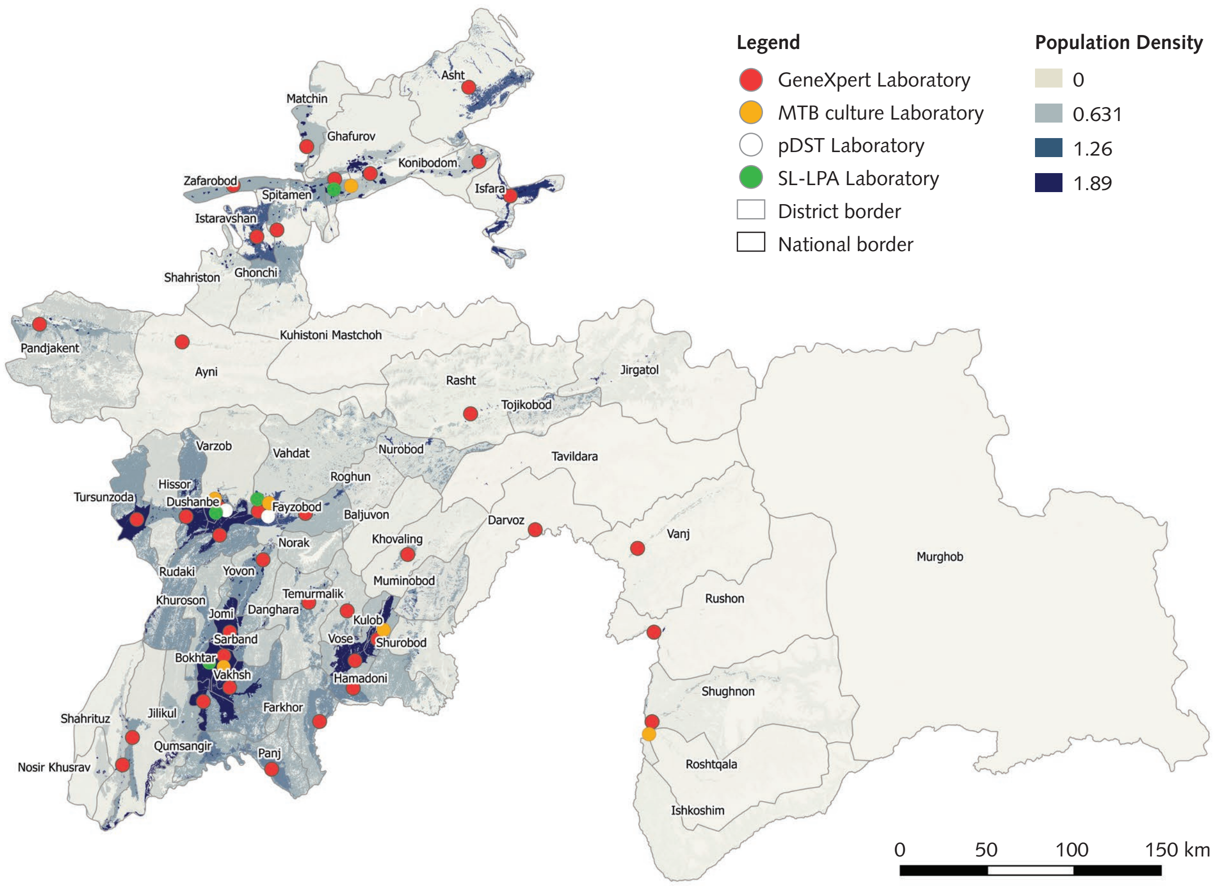
With support from the GF, USAID, and other partners, the NTP expanded the Xpert laboratory network from 15 instruments in 2015 to 46 instruments at the end of January 2019.

Xpert placement strategies

The placement of new instruments and the relocation of some existing machines have been part of a national diagnostic network redesign. The primary criteria for the placement of Xpert instruments have been population size and the burden of drug-susceptible and MDR/RIF resistant TB. Due to the aforementioned challenges with geography, accessibility to health services for the population, especially in the winter time, has been another important criterion, i.e., some instruments were specifically placed in extremely remote and hard-to-reach populations with a higher disease burden.

Figure 2: Tajikistan's laboratory network

Georeferenced map of TB diagnostic laboratories and the respective available tests (including GeneXpert, MTB culture and phenotypic DST as well as LPA, but not microscopy), overlaid with the population



Instrument sizes

Tajikistan used either 2- or 4-module devices, depending on the estimated workload considering population size and disease burden. For some sites, 2-module devices were installed, although technically, a one-module device would have been sufficient to cover the anticipated testing needs. The device size selection was specifically done to ensure uninterrupted services: Tajikistan does not yet have a local authorized service provider, hence repairs can take up to 30 days, especially in sites that are also very hard to access during winter time, where a breakdown of a single module instrument would result in a complete interruption in service for extended periods of time, e.g. if a replacement module cannot be transported to the site when the roads are blocked by snow. To avoid this, a second module was installed at those sites.

Specimen transportation network

Laboratory network planning included an analysis of road networks and possible specimen transportation routes. In the 40 Challenge TB-supported districts, a dedicated vehicle visits peripheral health facilities at least once a week to collect samples. Schedules and SOPs have been developed, and the staff has been trained. While the digital connectivity system, which will also automatically return results to all facilities, is operating in test mode, the STS vehicle also returns hard copy Xpert results to the respective facilities. All the districts that do not yet have an Xpert laboratory are also linked to Xpert testing via the STS.

The strategic approach also included ensuring availability and accessibility to drug sensitivity testing (DST) using phenotypic and genotypic TB diagnostic methods, such as C/DST and Line Probe Assay (LPA). Given the high burden of drug-resistant TB, rapid DR-TB diagnosis and treatment are essential for appropriate TB treatment and care. Therefore, specimens are transported at least once a week from the Xpert sites to the nearest laboratories that offer testing for C/DST and/or LPA.

RESULTS

Tajikistan's Xpert network strategy was analyzed by assessing the aspects of: a) the effectively available Xpert testing capacity, b) the provided Xpert testing services for the respective catchment population, and c) the geographic accessibility of services.

We used three Xpert sites (Figure 3), which were selected based the following criteria: Xpert and specimen transportation are functional for 12 months (timeframe of analysis February 18 to January 19) and started at the same time (all in January 2018). Furthermore, sites needed to be connected to GxAlert to have access to real-time raw data. In addition to the GxAlert data, the population figures of each catchment area were compiled by the KNCV country team based on census data from 2016.

EFFECTIVELY AVAILABLE CAPACITY & UTILIZATION

The standard Xpert instrument capacity is a routinely used indicator to (theoretically) quantify the Xpert testing service provided. While this is great for comparing aggregate data and to compare different countries, it is also worth calculating the maximum available capacity (as well as the respective utilization) (see Box 1 for definitions). As this considers real laboratory opening times and working days, it gives a more realistic picture of the maximum available capacity. We have also defined the effectively available capacity, which considers health service interruption events, such as instrument breakdowns and cartridge supply interruptions and therefore helps to understand potential losses in capacity due to weak or non-functional lab support systems (see Box 1 for definitions).

Effectively available capacity
In the three selected sites, the effectively available Xpert capacity was 100 percent in the previous 12 months, which showed that instruments and laboratory support systems functioned well enough to ensure the full availability of Xpert testing services.

Utilization of maximum capacity
Comparing the three selected sites, only Kulob Xpert site showed a high utilization of the maximum available capacity (85%), while Hamadoni and Khovaling only achieved 37 percent of utilization. Limiting the analysis to only the instrument utilization rate would suggest that two of the three sites operate ineffectively, however, additional analysis of the population served, reveals a very different picture.

ACTUAL PROVIDED XPERT TESTING SERVICE FOR THE CATCHMENT POPULATION

All three instruments in the selected sites serve different catchment population sizes, ranging from 56,328 to 353,081 people (Figure 3). To analyze the actual service provided for the population, the number of Xpert tests per 100,000 catchment population per year was determined as a surrogate for population coverage.

The best coverage was observed in Khovaling as this site conducted more than 1,400 tests per 100,000 in the past 12 months, which is more than double that of Hamadoni (Figure 3) or the national average, which was calculated as 590 tests per 100,000 population (Challenge TB database). This finding would suggest that a seemingly underutilized instrument, such as the instrument in Khovaling, could still serve its catchment population very well.

Since both Khovaling and Hamadoni had a second module installed to ensure uninterrupted services in case of a module failure, the utilization is expected to be low; hence, this example illustrates the importance of going beyond the utilization rate when interpreting how efficiently an instrument is used. However, in addition to this analysis, it is also of utmost importance to understand who is tested.

TARGET POPULATION

In order to assess the implementation of any Xpert policy and the actually tested eligible target groups, many countries designed their manual or digital data systems in such a way to reflect the eligibility criteria. While these data can be incomplete, or contain misclassifications or data entry errors, determining who is actually tested is very important to understand Xpert use.

A simplified way of assessing Xpert implementation, which can serve as a quick-check (in the absence of data on patient characteristics), is to analyze the percentage of MTB positive Xpert results among successful Xpert tests, which can be easily extracted from GxAlert.

A closer analysis of the Xpert testing results in the three selected sites revealed that the percentage of MTB positive Xpert tests remarkably differs in Khovaling, i.e., is only 2 percent compared to 8 percent and 11 percent at the two other sites. A possible reason can be the application of indiscriminate eligibility criteria, and indeed, a rapid investigation revealed that the clinical team in Khovaling is very active in finding and testing patients, which might partly explain the high number of tests per population but requires further investigation.

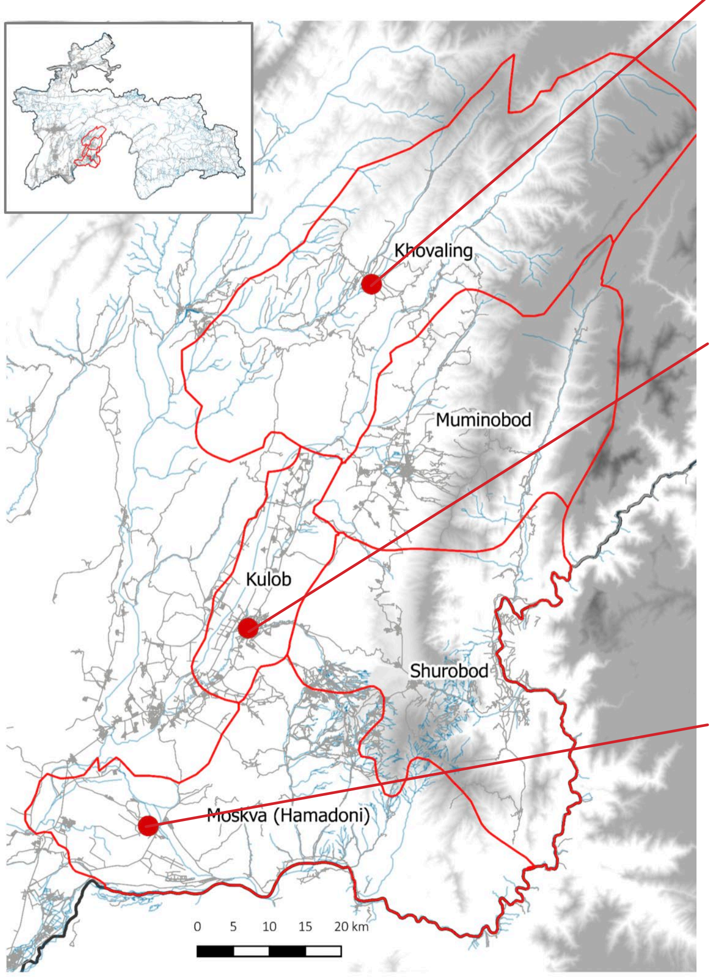
PROXIMITY TO XPERT TESTING SERVICE

For all districts, a large number of peripheral clinics have sputum collection points established (Figure 3) that are visited at least weekly. Driving distances between the Xpert sites and respective STS points can be as short as 4 km but can be as high as 150 km, e.g., for Kulob. The latter example illustrates the limitations of ensuring accessibility through strategic instrument placement and STS in certain geographic areas, especially if the means and resources for an STS are limited.

Ideally, this analysis would include the average distance calculation for, e.g., 80 percent of the population, but due to the lack of GIS village maps and the respective population data, this was not possible.

Figure 3: Xpert testing service availability, coverage and accessibility

Topographic map of five districts in Tajikistan, respective location of Xpert sites (red circles), road network (gray lines), rivers (blue lines), district administrative boundaries (red lines).



Khovaling

- District level facility that serves Khovaling only
- Catchment population 56,328, STS points: 22
- 2 module device (3.6 modules per 100,000 population)
- Distance to farthest collection point: 50km

Utilization of maximum instrument capacity:	37%
Tests per 100,000 population per year:	1477
% MTB positive/successful Xpert:	2%

Kulob

- Regional level facility, serves Kulob, Muminobod & Shurobod
- Catchment population 353,081, STS points 51
- 4 module device (1.1 modules per 100,000 population)
- Distance to farthest collection point: 150km

Utilization of maximum instrument capacity:	85%
Tests per 100,000 population per year:	1074
% MTB positive/successful Xpert:	11%

Hamadoni

- District level facility that serves Hamadoni only
- Catchment population 143,706, STS points 23
- 2 module device (1.4 modules per 100,000 population)
- Driving distance to farthest collection point: 35km

Utilization of maximum instrument capacity:	37%
Tests per 100,000 population per year:	581
% MTB positive/successful Xpert:	8%

Box 1: How to calculate Xpert instrument capacity and utilization

Standard instrument capacity & utilization

- Calculated regardless of module functionality and excluding temporary service interruption events
- Assuming standard service availability of 8 hours/day (3 tests per day and module) and 240 working days per year
- Standard utilization = Number of tests conducted/Standard instrument capacity

→ This is useful when analyzing aggregate data, e.g., annual or national-level data, and when comparing different countries.

Maximum instrument capacity & utilization

- Calculated regardless of module functionality and excluding temporary service interruption events
- Considering actual service availability: opening hours per day and working days per week, considering the actual day of installation for the instrument
- Utilization of maximum capacity = Number of tests conducted/Maximum instrument capacity

→ This is useful for analyzing what a specific site should realistically be able to achieve if all the diagnostic support systems, such as repair and supply are provided.

Effectively available instrument capacity

- Calculated considering module functionality and other temporary service interruption events that lasted longer than two weeks. This includes only health system related events (e.g., the supply interruption, absence of facility staff) but not interruptions due to political events such as elections
- Considering actual service availability with regards to opening hours and working days
- Percentage of effectively available capacity = Available testing capacity of instrument/maximum instrument capacity.

→ This is useful to quantify the losses in capacity due to non-functional diagnostic support systems.

LESSONS LEARNED

Optimal placement and use of Xpert testing

The example from Tajikistan shows the achievements and limitations in ensuring accessibility to Xpert testing through strategic placements in combination with a wide specimen transportation network. The instrument in Kulob, for example, was able to conduct a comparatively high number of tests per served catchment population in combination with a very high utilization of instrument capacity, suggesting that this instrument is optimally placed and used.

However, using all available resources, the maximum driving distance within the STS for this site is 150 km, which is still very far. It is an obvious logistical and financial challenge for many countries to bring this to scale, let alone setting up an even closer STS network – or alternatively, place substantially more Xpert instruments in order increase accessibility. Possible solutions could be either additional resources, different transport mechanisms or ideally, new diagnostic tests that can be brought closer to the community at lower costs.

A different perspective on analyzing 'optimal use' of Xpert

Routinely, we only use the standard Xpert instrument utilization to draw conclusions on the optimal use of Xpert. However, the additional, simple indicators presented here show that a lot of additional understanding about the use of Xpert in routine settings can be gained. The maximum utilization and the effectively available capacity can give laboratory and program managers a better understanding of potential losses due to non-functional laboratory support systems. Calculating the number of tests per catchment population could be a useful indicator to understand population coverage of testing. If detailed information on the characteristics and eligibility criteria are unknown, analyzing the positivity rate among all Xpert tests can provide additional insight into target groups.

While two of the three sites show a rather low utilization of maximum capacity, the actual number of tests conducted per catchment population are either similar or higher compared to the national average suggesting that both instruments serve the population well. However, in the case of Khovaling, the low positivity rate among Xpert tests requires further investigation; potentially the additional use of Xpert for screening could explain at least partly the higher number of tests.

While an in-depth analysis of the use and utilization of Xpert is still required, these indicators could serve as a kind of 'quick-check' for laboratory and program managers, and focus attention on priority sites, i.e., those in which the results deviate from the average and might require further support and investigation. This targeted analysis of specific sites can direct the focus towards important programmatic questions on the use of Xpert according to the policies and efficiency of its use.

SUMMARY AND FINAL REMARKS

Nigeria and Tajikistan illustrate successful approaches, as well as the remaining bottlenecks to optimal use and utilization of Xpert MTB/RIF testing in the routine diagnosis of TB:

- Xpert implementation and optimization are a package approach, key pillars are creating demand, ensuring accessibility and availability of testing services. We present here successful strategies and interventions from two countries; however, it is important to assess and address individual country- or facility requirements. For planning and selecting interventions, the dependency of activities needs to be kept in mind, i.e., changing to the Xpert4All policy might have little effect on the volume of testing if not implemented in conjunction with activities that bring this to scale, i.e., increase accessibility.

- Assessing the optimal use and utilization of Xpert, within the selected strategies, has to go beyond analyzing the utilization of instrument capacity and has to include the catchment population, i.e., the number of tests conducted by 100,000 catchment population as well as an analysis of applied eligibility criteria. Geographic and programmatic choices have to be included as well in order to understand the full picture. Focusing only on instrument utilization alone could be potentially misleading if used to plan and adjust activities and project planning. Similarly, the analysis from Nigeria shows the effect and interdependency of individual interventions, that may be overlapping. This specifically highlights the risk of biased conclusions when only focusing on pre-post analysis using routine data and needs to be kept in mind in project assessments and planning for future activities.

- The here presented simple and informative approaches to better monitor the effectiveness of interventions and strategic choices can serve as useful 'quick-check' indicators for immediate action, but these do not replace thorough and detailed evaluations: following several years of Xpert implementation and expansion, detailed evaluations of Xpert in light of the specific network strategies should be made a priority in the coming years. These evaluations should be conducted as part of a national diagnostic network assessment to provide thorough evidence on results and guide country-specific approaches for strong programmatic integration of diagnostics.

- Both country examples clearly illustrate the need for a target value for Xpert testing volume, which is urgently required to interpret achievements and identify gaps for Xpert and other diagnostic tests. Most countries use a combination of estimates from prevalence surveys and notification rates to estimate targets. However, prevalence surveys are usually powered at the national level and not the district level. Notification rates can be strongly influenced by the functioning of the local health system, for which we do not have an accurate measure to correct for. Subsequently, both measures are not accurate enough to estimate testing targets at the regional or district level but are urgently needed for planning and resource allocation. In the analysis of data from Tajikistan, we have therefore not estimated a target but suggest as a measure a deviation from the national average. However, it is of the utmost importance that better ways are developed to estimate the burden of disease at the regional or local levels, e.g., through an adjustment of prevalence survey designs or modeling approaches.

LIMITATIONS

The findings and conclusions presented here are based on a selected set of facilities from both countries. This limited analysis harbors the risk of bias and does not allow a generalization of findings within or across countries. It is, therefore, recommended to conduct an expanded analysis including more sites per country and secondly compare across countries, ideally within the framework of project evaluations or diagnostic network assessments.

To provide a simple and practical approach to data analysis that can be easily replicated in other settings, we used extracts from GxAlert only. The data are individual test data and not individual patient data. For one site in Nigeria, we were able to confirm that the number of repeat/duplicate tests per individual patient is negligible, and no such analysis was possible for other locations, which has to be kept in mind when interpreting the data and findings.

In some countries, recent population and/or catchment population figures by facility might not be available. Nigeria's most recent census was conducted in 2006, and more recent figures are extrapolated from those. In these situations, the analysis and interpretation of the proposed population coverage indicator have to be conducted with care.

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