The Global Fund / Andy Ball / Panos

The TB Quarterly Update
Innovations

AUGUST/SEPTEMBER 2024

THE GLOBAL FUND

Contents

About the TB Quarterly Update

The TB Quarterly Update is produced by the TB team at the Global Fund to share best practices, lessons learned and information on TB from countries supported by the Global Fund, partners and other stakeholders, as well as updates on new innovations and tools coming onto market. If you have any information you would like to share, please reach out to TBQuarterlyUpdate@theglobalfund.org.

1. What's New

Key learnings from exchange on innovations in artificial intelligence radiology

From 11 March to 13 March 2024, more than 200 participants from 37 countries gathered to exchange knowledge on the use of artificial intelligence (AI)-powered computer-aided detection (CAD) and digital chest X-ray (DCXR) for TB detection in Manila, Philippines. The meeting was organized by Stop TB Partnership (Stop TB) in collaboration with the Department of Health of the Republic of the Philippines, the United States Agency for International Development (USAID), the Global Fund and the private sector constituency of Stop TB's Board. Participants included:

- National TB program (NTP) representatives from high-burden countries.
- Clinicians from implementing countries.
- Non-governmental, technical and international organizations.
- Researchers.

The Global Fund sponsored the participation of countries, particularly those with significant DCXR investments in the current grants. During the exchange, 11 sessions were held over three days, focusing on the following topics:

1. Identifying needs for newer DCXR technologies and CAD and defining the use case and population to be screened.
2. Building human resource capacity and developing local resources to guide implementation (e.g., site selection, screening algorithms, standard operating procedures and guidelines).
3. Choosing appropriate products based on use case and population.
4. Procuring products and warranties.
5. Developing clear technical specifications.
6. Establishing systems for monitoring and feedback on equipment issues, including strengthening digital systems and developing interconnectivity to monitor utilization, identify errors and reinforce service-level agreements.
7. Understanding and planning for community needs during mass screening campaigns.
8. Ensuring close integration with local health facilities for follow-up of presumptive individuals identified in community campaigns and developing integrated and interconnected data systems with the necessary capacity for analysis.

This exchange was a good opportunity for countries to share experiences on the use of these new technologies and to address challenges related to DCXR and CAD, supporting implementers in their usage moving forward. Resources from this workshop are forthcoming.

Resources for X-ray systems and CAD

X-ray equipment test directory

There has been a significant increase in the number of smaller, lighter and ultraportable battery-operated X-ray systems. In 2024, 17 new models of equipment have been added; 2 models have version upgrades; 13 models offer integration with CAD as an optional package; and several X-ray systems are designed for uses beyond chest radiography (e.g., abdominal and skeletal). FIND provides a searchable directory of digital ultraportable and portable X-ray equipment that includes technical and practical information to inform and guide decisions about the use and/or procurement of equipment. Find out more about FIND's X-ray equipment test directory here.

TB CXR-CAD software

FIND and Stop TB co-manage an online directory of TB-CAD software, which can be found here. This resource is updated annually and reflects CAD software features, use cases and regulatory certifications. Global Fund Principal Recipients and other implementers can use this directory to learn more about current commercially available TB-CAD products.

In addition, WHO recently launched a call for expression of interest by manufacturers of software for CAD to submit products for WHO expert assessment. The assessment involves an independent evaluation of the software using a digital X-ray library hosted by FIND and the submission of regulatory and marketing documentation. More information about the process can be found here.

Validation platform for digital diagnostics
The FIND Validation Platform is a digital infrastructure for fast and standardized in-silico assessment (i.e., computer simulations) of digital diagnostics such as CAD software, rapid diagnostic test reader software, cough apps and AI-based sequencing interpretation software. The first use case is TB-CAD assessments. The current primary uses of the platform are to: (i) inform WHO prequalification (PQ) and policy, including independent performance evaluations of new TB-CAD software and versions; (ii) describe TB-CAD performance in line with the original technology class evaluation by the WHO; and (iii) generate evidence for new use cases of TB-CAD (i.e., children, people living with HIV), informing policy recommendations.

The platform also supports Global Fund Principal Recipients and other implementers to (i) compare the performance of different TB-CAD products; (ii) determine threshold selection of chosen TB-CAD products; and (iii) conduct exploratory analysis on TB-CAD in diagnostic research studies, such as sub-clinical TB, disease severity and novel diagnostics algorithm designs.

Figure 1: FIND's Validation Platform
Source: FIND

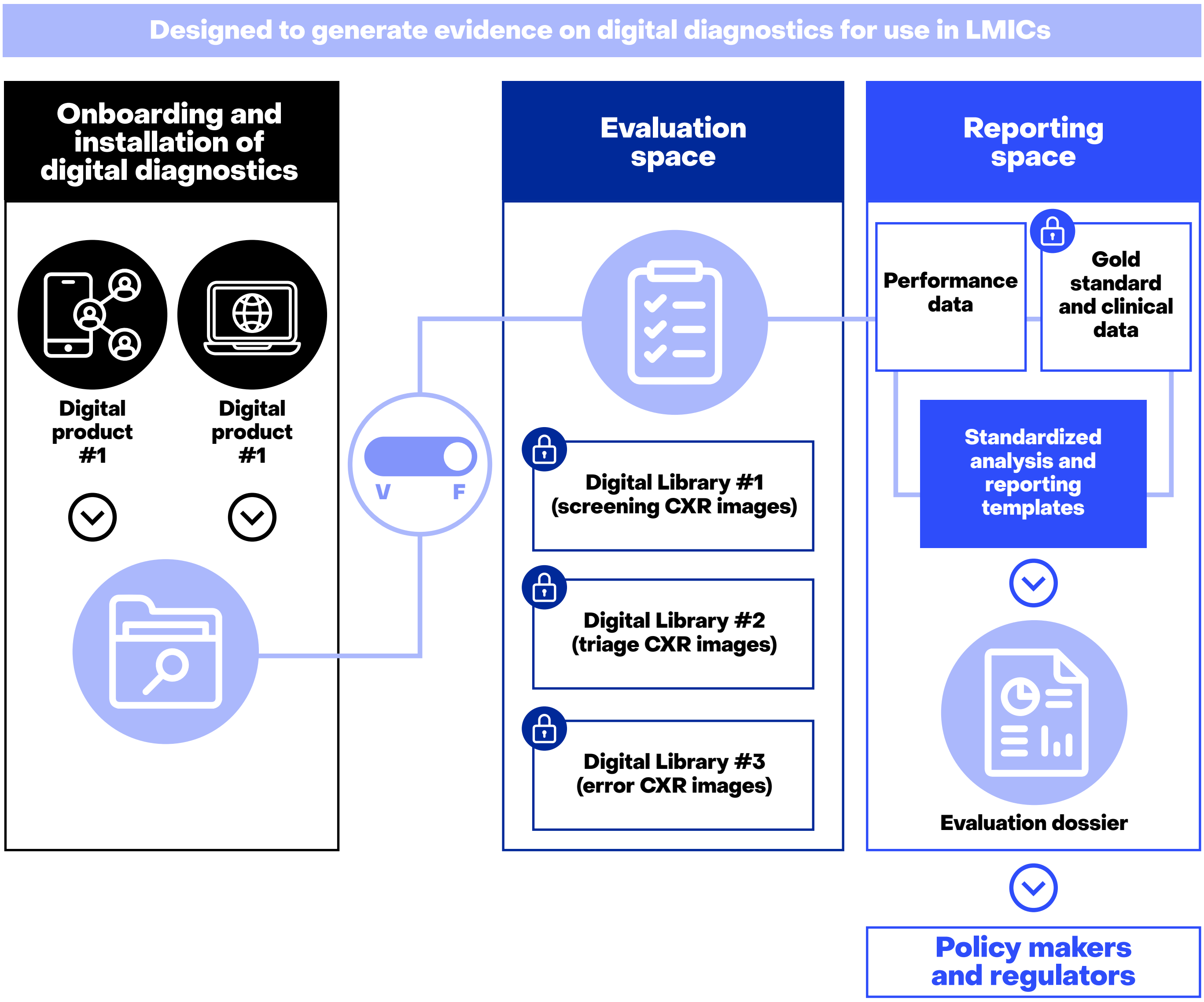
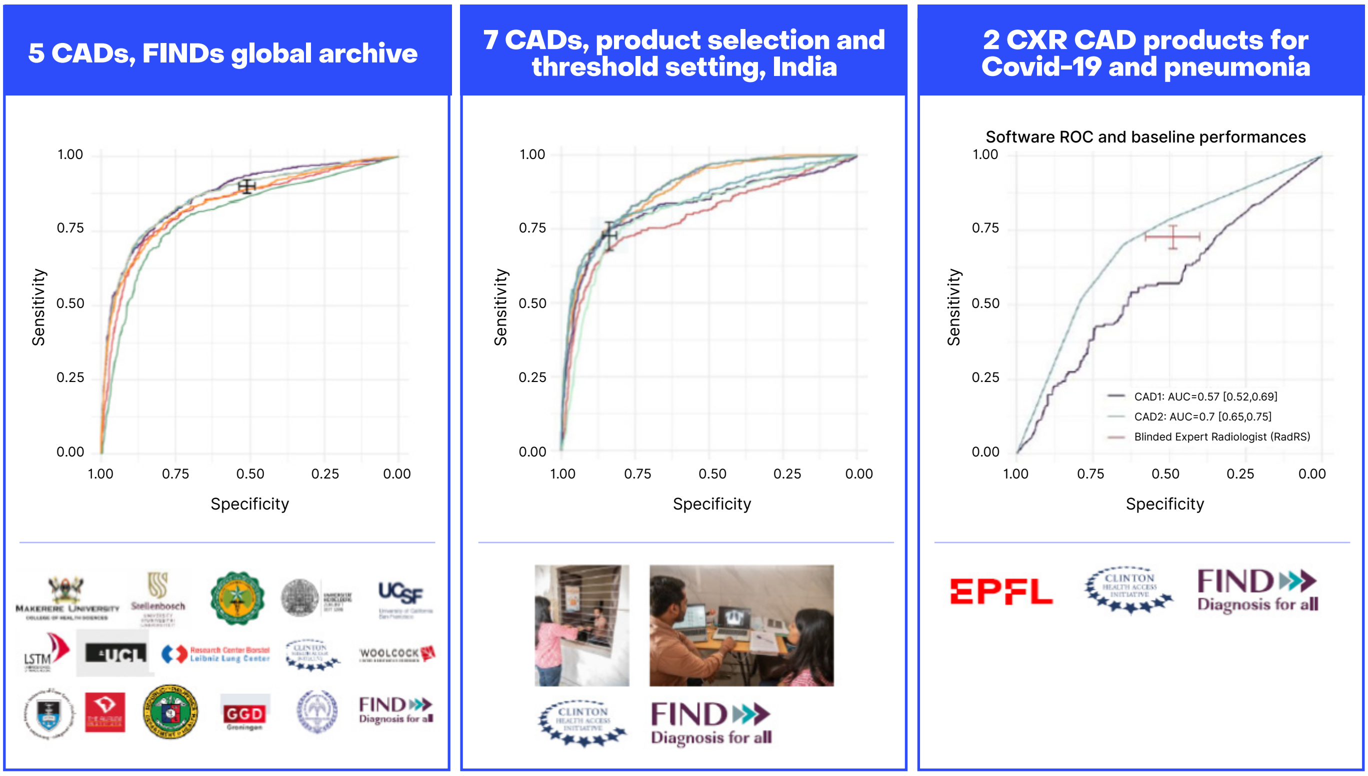


Figure 2: Recent results from CAD evaluations

Source: FIND



Kik et al unpublished

Sandra Kik and Swati Goel, publication in prep

Arentz et al publicatrion in prep

Learn more about FIND's approach to AI detection and validation for TB in this report and in this video.

2. Knowledge Sharing and Learning Resources

CASE STUDY: Scale-up of digital chest X-rays (DCXR) and CAD in Kenya

Background

The first ever UN High Level Meeting on TB in 2018 resulted in several global TB targets endorsed by heads of state and aimed at accelerating efforts to end TB. In the 2023 follow up meeting, these targets were further updated with the commitment to provide treatment for up to 45 million people between 2023 and 2027. To achieve this, the UN declaration reiterated the importance of promoting equitable, affordable and timely access to the benefits of research and innovation by rapid deployment of recently approved tools. In 2022, Kenya began implementing the Introducing New Tools (iNTP) Project, a collaboration between Stop TB and USAID that rolled out a package of the latest innovations in diagnostics, treatments and digital health technologies. The iNTP Project aimed to improve detection of TB in hard-to-reach populations facing barriers to accessing services in Kenya. Through its implementation, multiple products have been introduced, including eight ultra-portable digital chest X-rays (DCXR) with CAD that can be used in community field settings. Other investments include the purchase of:

- Four DCXR to support the TB prevalence survey, which were mounted on trucks and used for outreach post-prevalence survey (no CAD).
- Ten DCXR stationed at health facilities, which were financed through the Global Fund grant (no CAD).
- One hundred and ninety-seven DCXR procured by the Ministry of Health (MoH) for county and subcounty hospitals (facility-based, no CAD).

Figure 3: Kenya TB case notification trend, 2011-2023

Source: The National Leprosy, Tuberculosis and Lung Disease Programme

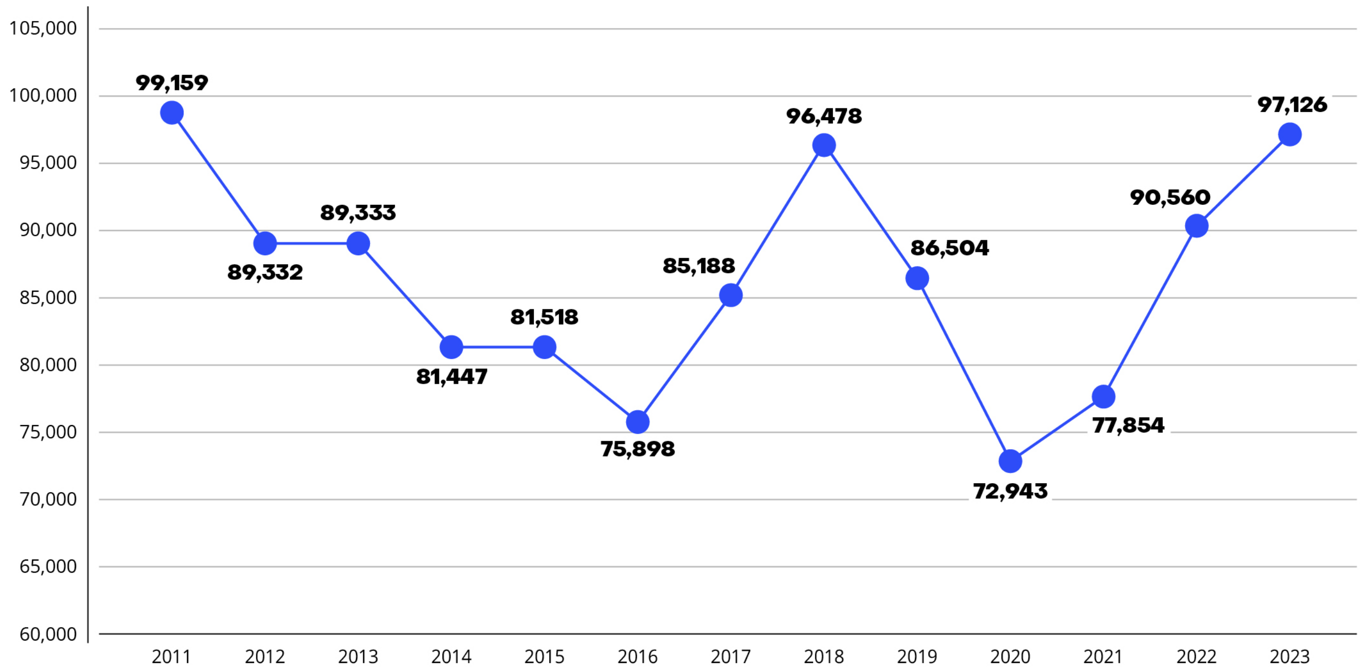
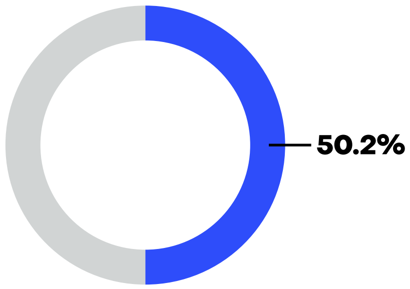
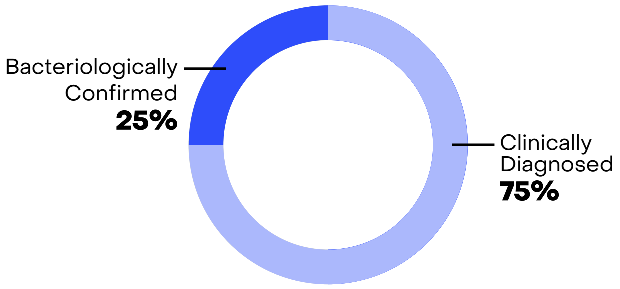


Figure 3 (continues): Kenya TB case notification trend, 2011-2023

Source: The National Leprosy, Tuberculosis and Lung Disease Programme





Implementation

iNTP site selection was informed by an analysis of various data points, including facility workload, burden of TB and HIV, availability of other molecular diagnostic platforms, and facility human resources for health (HRH). Additional criteria was later considered when selecting sites to implement the iNTP Project. These included ease of access (easy, medium and hard-to-reach) to TB services, facility ownership (i.e., public/private/faith-based organization) and the use of DCXR with CAD. A site assessment tool was developed and used together with other pre-existing tools (e.g., DxGeoMap) for the accessibility assessment. Prioritization and assessment of sites included the considerations in Box 1 and was followed by a pre-installation assessment.

BOX 1: Considerations for DCXR with CAD

Placement in low level health facilities (level 2 and 3)
- Limited access to X-ray services.
- Targeted community screening and outreach.
- Primary health care/universal health coverage (integrated use).

Portability and durability
- Ease of carrying in targeted community screening and outreaches.
- Able to withstand long travel times and difficult terrain.

CAD (AI) software
- Limited number of radiologists at level 4 and 5.
- Allow teleradiology-improved access.
- Remote quality assurance and quality control (QA/QC).
- Multiple conditions diagnosed (integrated use).

Source: The National Leprosy, Tuberculosis and Lung Disease Programme

Further assessments will be completed for existing DCXR to better understand site readiness required for CAD installation. This will involve evaluating the current hardware and software capabilities of the DCXR units to determine if they meet the technical requirements for AI applications. The assessment will include a review of system performance, connectivity options and compatibility with AI algorithms, which aims to identify any upgrades or modifications needed to support seamless AI integration, ensuring that the DCXR systems can effectively leverage AI for enhanced diagnostic accuracy and efficiency.

The selected sites began iNTP implementation, which involved the following activities:
- Prioritization and planning of equipment need.
- Review and adoption of existing guidelines on DCXR and CAD, including WHO guidelines on use of DXCR.
- Demonstrations and discussions on available systems/platforms with a committee of experts.
- Development of recommendations on specifications for DCXR and CAD based on review of systems, envisioned use, pre-existing equipment and lessons learned.

BOX 2: Other implementation considerations

- **Import and clearance processes:** Coordination with customs authorities in handling documentation, tariffs and any import duties. Verification that the import permits and certifications were in place and that the equipment adhered to the relevant safety and quality standards. These processes faced significant delays.
- **Product registration:** Submission of detailed technical specifications, safety data and clinical efficacy evidence to relevant health authorities and regulatory bodies for registration.
- **Regulatory landscape and compliance:** QA and QC procedures included regular inspections, maintenance routines and adherence to guidelines set by regulatory agencies to ensure reliability of diagnostic results and protection of patient's safety.
- **Associated accessories (i.e., dosimeters, patient shields, lead aprons and thyroid shield and battery chargers/back up):** Selection and use of accessories to promote a safer diagnostic environment and enhanced the overall functionality of the DCXR equipment.
- **Sustainability and maintenance:** Warranty, existence of in country support and parts replacement.
- **Staff capacity development:** Training programs focusing on operating equipment, understanding AI functionalities and interpreting diagnostic results. This has been an on-going process through on-the-job training, mentorship and support supervision.

Source: The National Leprosy, Tuberculosis and Lung Disease Programme

Monitoring and evaluation goals included interoperability for seamless data exchange, opportunities for teleradiology to access expert opinions and data dashboards for real-time performance.

iNTP implementation was collaborative and included national and subnational TB control teams, radiologists and other TB experts (Chest X-ray Committee of Experts), along with site assessments for CXR replacement, capacity development of staff, deployment and monitoring and evaluation. Specific innovations during implementation included:

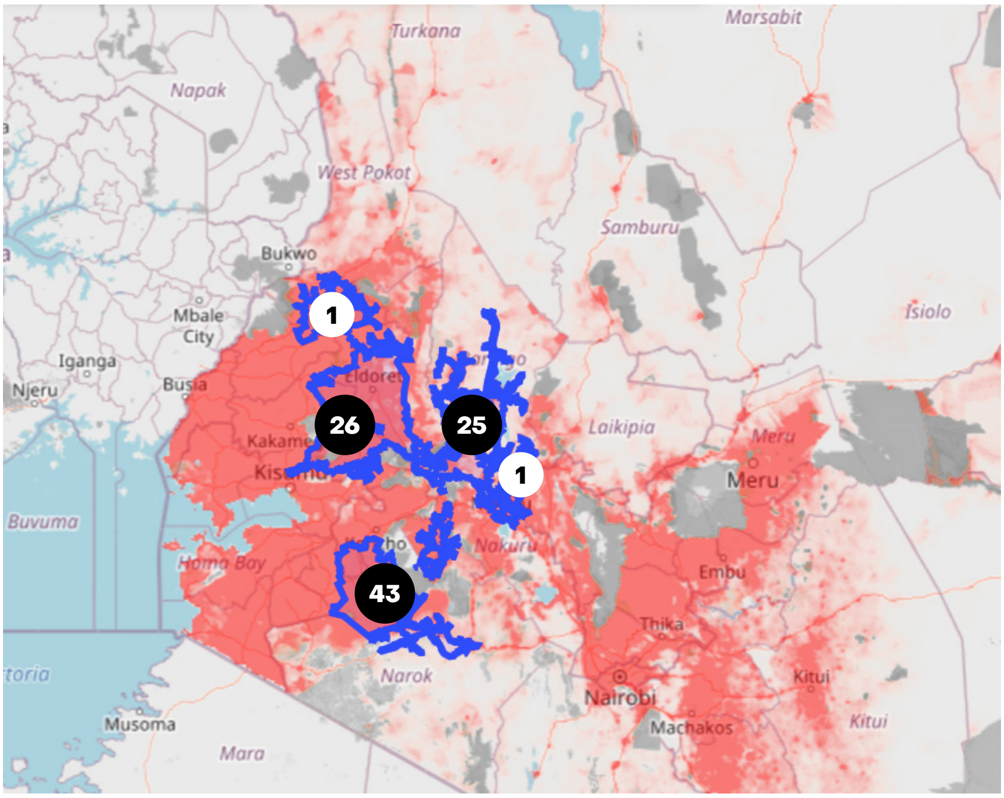
- **Development of an application programming interface (API)** that retrieves data from the internal storage of eight DCXR-CAD devices for storage in the national TB data repository (TIBULIMS), making it more shareable and accessible to different stakeholders.
- **Engagement of radiologists** for second level reading following AI analysis as a QA/QC measure and also to inform non-TB findings.
- **Engagement of various technical experts** in a sub-committee mandated to plan for the implementation of the roll-out the new technology.
- **Buy-in and ownership** from the county teams through engagement and involvement in the early planning stages.

Results

Population accessibility was analyzed using DxGeoMap. Software was used to create an area around each testing location within the chosen time frame and transport mode. If the individuals can travel to the nearest health facility within a given timeframe (15, 30, 60, or 90 minutes), the testing location was deemed accessible. (See Figures 4 and 5).

Figure 4: Accessibility view – 60 minutes driving

Source: The National Leprosy, Tuberculosis and Lung Disease Programme



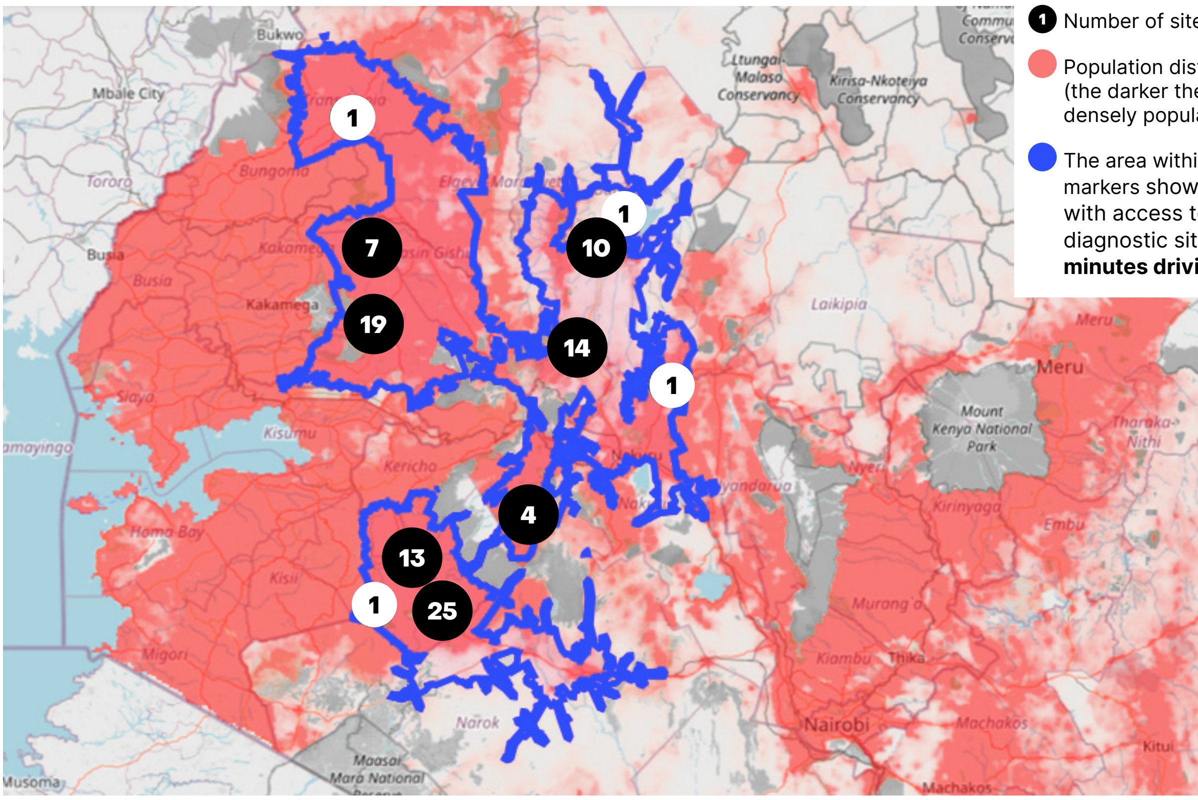
1 Number of sites per region

Population distribution (the darker the color, the more densely populated the area is)

The area within the blue markers shows the population with access to the nearest diagnostic sites **within 60 minutes driving**. The area outside shows the population that cannot reach a diagnostic site within 60 minutes driving.

Figure 5: Accessibility view – 90 minutes driving

Source: The National Leprosy, Tuberculosis and Lung Disease Programme



1 Number of sites per region

Population distribution (the darker the color, the more densely populated the area is)

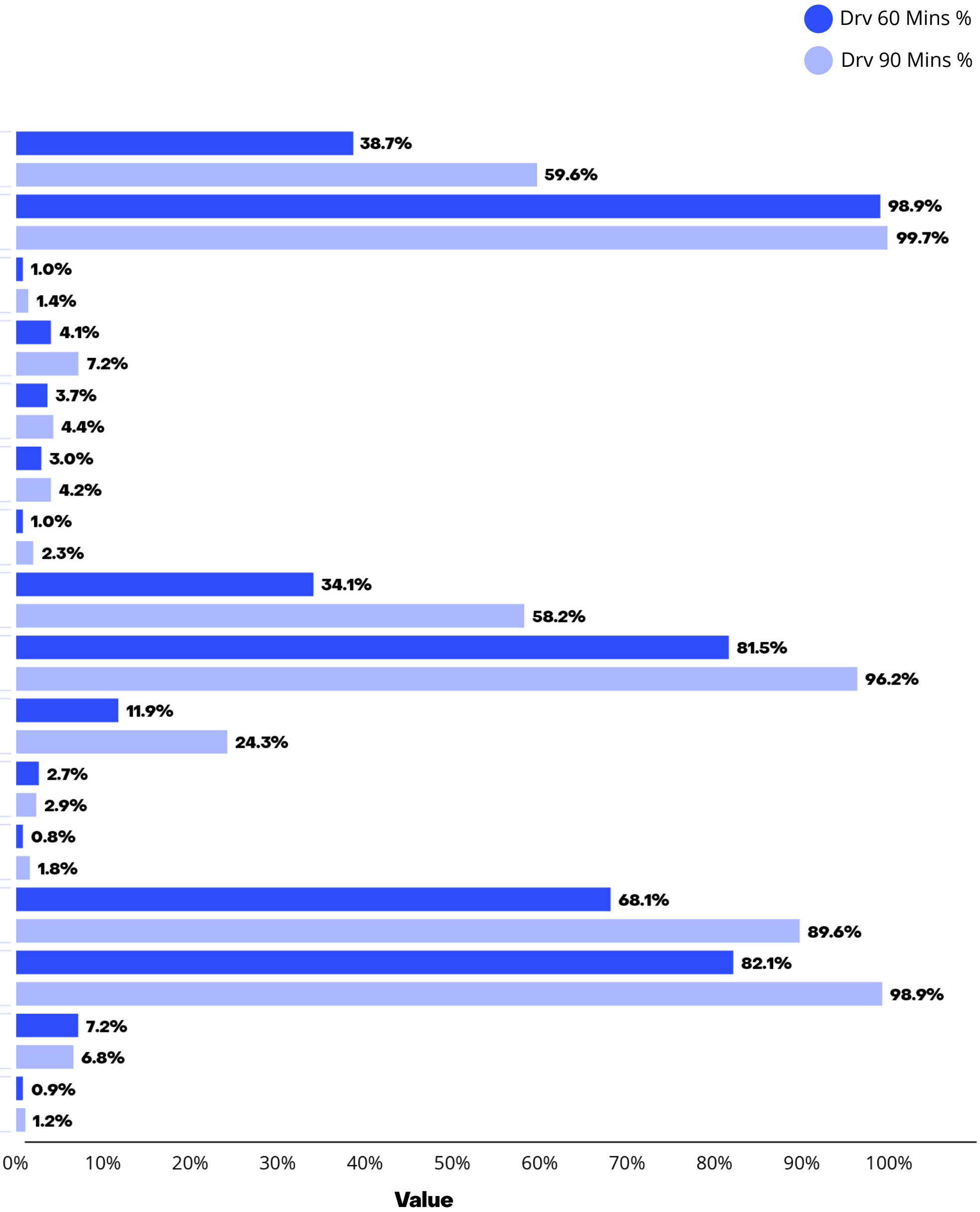
The area within the blue markers shows the population with access to the nearest diagnostic sites **within 90 minutes driving**.

Figure 6 (below) shows the population accessibility by county. This information allows us to infer that counties like Bomet, Nandi and Trans Nzoia have good accessibility while Bungoma, Kisumu and Kericho have poor accessibility and require further analysis. Identifying potential sites and placing devices in these low accessibility counties will improve accessibility.

Figure 6: Kenya TB case notification trend, 2011-2023

Source: The National Leprosy, Tuberculosis and Lung Disease Programme

Name	Total population in country	Drv 60 Mins %	Drv 90 Mins %
Baringo	775,953	38.7%	59.6%
Bomet	1,293,772	98.9%	99.7%
Bungoma	1,767,539	1.0%	1.4%
Elgeyo-Marakwet	537,774	4.1%	7.2%
Kakamega	2,137,210	3.7%	4.4%
Kericho	843,163	3.0%	4.2%
Kisumu	1,206,752	1.0%	2.3%
Nakuru	2,298,101	34.1%	58.2%
Nandi	1,097,669	81.5%	96.2%
Narok	1,242,346	11.9%	24.3%
Nyamira	741,383	2.7%	2.9%
Nyandarua	731,762	0.8%	1.8%
Trans Nzoia	1,175,423	68.1%	89.6%
Uasin Gishu	1,308,444	82.1%	98.9%
Vihiga	709,426	7.2%	6.8%
West Pokot	735,644	0.9%	1.2%

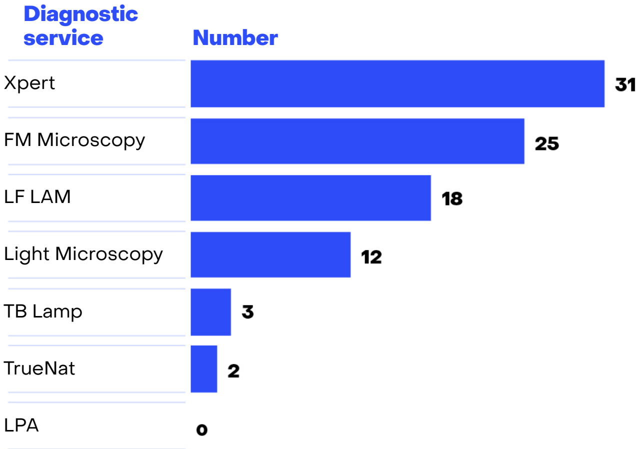


The site assessments of 35 health facilities (24 level-2 facilities and 11 level-3 facilities) located in 34 sub-counties in (23 counties) further revealed that 34 out of 35 facilities had at least one functional X-ray machine, with 71% of the total number of X-ray machines (70 out of 99) functional. While 100% of facilities assessed had a designated X-ray room, 63% (22/35) of them had valid X-ray operating licenses, 97% (34/35) of them had a radiographer and 71% (24/35) had a radiologist. (See Figures 7, 8 and 9).

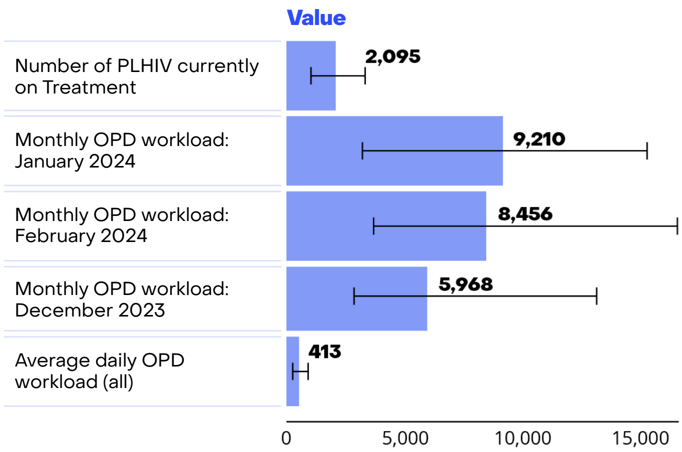
Figure 7: Machines, infrastructure and HR assessment

Source: The National Leprosy, Tuberculosis and Lung Disease Programme

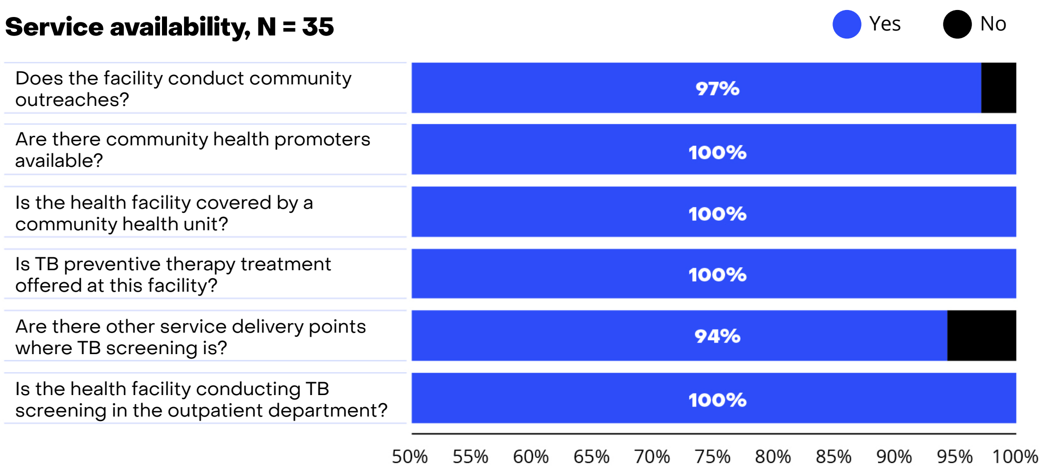
Diagnostic capacity of the visited health facilities



Workload of the visited health facilities



Service availability, N = 35



- Genexpert available in 89% of the visited HFs
- Average daily workload is 413 (IQR: 250–782)
- TB and TB related services are available

Figure 8: Machines, infrastructure and HR assessment

Source: The National Leprosy, Tuberculosis and Lung Disease Programme

Readiness for TB screening using digital X-ray and computer-aided software

Characteristic	N = 35[1]
Is electricity available from the grid?	35 (100%)
Are there sufficient sockets available for battery charging of essential devices?	35 (100%)
Is there a power backup solution including solar? (optional)	
· Yes	28 (80%)
· No	7 (20%)

1 Median (IQR) or Frequency (%)

Figure 9: Machines, infrastructure and HR assessment

Source: The National Leprosy, Tuberculosis and Lung Disease Programme

Readiness for TB screening using digital X-ray and computer-aided software

Characteristic	N = 35[1]
How much do they pay for CXR services?	520 (400, 1000)
How many CXR are done monthly?	330 (175, 502)
Who is responsible for reading the CXR at the referral site?	
· Resident radiologist	21 (60%)
· Outsourced radiologist	4 (11%)
· Clinical officers	10 (29%)
What is the turnaround time for getting the results back to the clinicians?	
· 10 - 30 minutes	21 (60%)
· 1 hour	1 (2.9%)
· 24 hours	5 (14%)
· 3 days	1 (2.9%)
· 45 minutes	4 (11%)
· Emergency case one day. Normal one week.	1 (2.9%)
· One week for reported result	1 (2.9%)
Are clinicians at this facility (the facility being assessed) trained on CXR reading?	25 (71%)
Is there secured storage for X-ray machines?	35 (100%)

1 Median (IQR) or Frequency (%)

Lessons learned and next steps

Lessons learned during scale up of DXCR with CAD include: (i) the importance of comprehensive training, sensitization, and mentorship for radiographers, clinicians, and TB coordinators; (ii) the integration of DCXR-CAD activities into routine service delivery to minimize disruption and optimize resource utilization; and (iii) thorough site assessments and selection to ensure screening efforts are targeted, efficient and tailored to the specific needs of the at-risk populations and the capacities of the selected sites.

Programs should prioritize technology interoperability when implementing new digital health tools. By integrating CAD4TB with the existing TIBULIMS platform, the project was able to streamline data management, enhance access to comprehensive patient information and facilitate robust reporting. Country-specific regulations and requirements related to radiation safety should also be considered prior to procurement of new radiation equipment. Ensuring reliable and consistent availability of commodities for follow-on diagnostic testing after the DCXR-CAD screening was also crucial.

Challenges included: (i) difficulties in moving the machines, which required more than one person to move and impacted mobility and ease of use; (ii) the lack of general-purpose imaging as the machine is only suitable for special purposes (chest) imaging and is not recommended for other body parts; (iii) the lack of digital communication between the laptop and generator, requiring radiographers to manually set exposures, leading to potential inefficiencies; and (iv) fragility and maintenance due to the multiple detachable parts and no in-country distributors. As replacement parts were shipped in from the Netherlands, this affected operations in some sites.

In terms of next steps, the NTP is currently due to acquire DCXR with CAD using Global Fund support through COVID-19 financing and grant funds from 2020-2022 and 2023-2025 allocation periods. To address the lessons learned as the program continues to scale, the following activities are currently underway:

1. Development of a DCXR-CAD handbook to guide the installation and operationalization of the equipment and software in the country. This will include factors to consider when procuring the equipment, what constitutes a complete installation package (including accessories), how to assess facilities for readiness and how to ensure quality of service in the course of operationalization.
2. Assessment of the health facilities with existing DCXR for suitability of CAD deployment and assessment of proposed sites for readiness for DCXR deployment.

CASE STUDY: Use of connectivity solutions to link digital chest X-ray screening and lab diagnosis in Uganda

Background

Significant investments have been made in recent years in many high TB burden countries to establish diagnostics connectivity solutions that make use of digital data produced by newer TB screening and diagnostic tools. These solutions can send, aggregate and process data from multiple instruments. This data can then be used remotely to monitor performance of instrument networks in real-time and troubleshoot use or maintenance problems, facilitate reagent forecasting and stock management, and also enable test results to be sent to clinicians quickly. It is both a WHO and Uganda National TB and Leprosy Programme (NTP) priority for all molecular diagnostic testing sites to have a data connectivity system that electronically transmits results to clinicians and patients and data to the Ministry of Health (MoH).

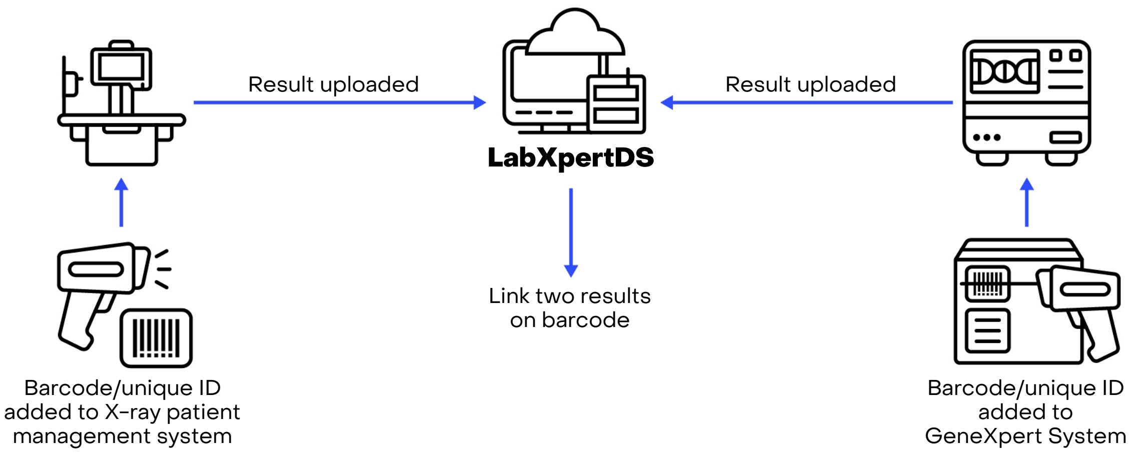
Implementation

LabXpert is a web-based system that supports automated data capture from the GeneXpert, Truenat, Afinion and DCXR machines to enable real-time reporting and feedback. The system supports monitoring of equipment use, equipment functionality, inventory management and linkage of patients to treatment by sending alerts to patients and clinicians. To link DCXR and laboratory results, three requirements need to be met: (i) a unique patient identifier; (ii) internet access for both DCXR and laboratory equipment; and (iii) a central system that enables data to be retrieved from both systems (See Figure 10).

After screening is complete, if the patient is eligible for laboratory testing, their details are edited in the CAD system to include a barcode. The updated details

Figure 10: Process of linking lab and DXCR results

Source: The National TB and Leprosy Programme



are then automatically uploaded to LabXpertDS, the barcode is attached to the sputum container and sent to the laboratory, and the laboratory team scans the barcode as a specimen ID while creating a test. After the laboratory test is complete, the results are automatically uploaded to LabXpertDS, which verifies if the uploaded results have a barcode, checks for a corresponding DCXR result and displays the information to the clinician on one screen. LabXpertDS enables health care workers to link the laboratory testing to the DCXR screening, ensuring that they have access to the DCXR and laboratory results on one interface.

Results

LabXpertDS has been installed on 300 GeneXpert machines in 15 TB regions in Uganda, including more than 100 districts. While this integration is still in the beta stages, all GeneXpert sites, 291 in total, are configured to report on LabXpertDS. However, not all DCXR sites are connected. This connectivity solution has improved access of test results to clinicians as LabXpertDS uses an SMS function to send results to requesting clinicians, reducing the result dispatch turnaround times.

Lessons learned and next steps

Linking laboratory and DCXR screening requires barcodes or unique patient identifiers. However, barcodes used for samples are expensive because they must be able to withstand the cold temperature at which samples are stored. Therefore, there is a need to bring down the costs. Efforts are underway to create a virtual barcode to replace the more expensive, physical ones. With all TB sites in Uganda covered, other next steps include scaling this solution to other disease programs. The Ministry of Health of Uganda is currently planning to install LabXpert on all m-PIMA machines throughout the country, which are used for HIV viral load and HIV early infant diagnosis (EID) testing.

Figure 11: Instruments connected in Uganda

Source: The National TB and Leprosy Programme

99,399 GeneXpert Results

7,883 TrueNat Results

1,040 Afinion Results

259 X-ray Results

3. Additional Updates

Regional meeting of francophone countries

Stop TB held a regional meeting on "Advancing community, rights and gender for an equitable response to tuberculosis in French-speaking Africa" from 11 June to 13 June 2024 in Yaoundé, Cameroon. The objectives of this meeting were to build a common understanding of community, rights and gender (CRG) in the response to TB, launch the Francophone Africa chapter of TB Women and promote and ensure gender-sensitive and transformative responses to TB in the Francophone Africa region. The meeting also provided an opportunity for participating countries to align CRG approaches and interventions, ensure coordination and support around the multisectoral accountability framework to end TB (MAF-TB) and gain further clarity on the Stop TB Partnership Challenge Facility for Civil Society (CFCS) grant and support mechanism.

Stop TB Partnership

Stop TB Partnership

Recent WHO guidance

- TB surveillance: Consolidated guidance on tuberculosis data generation and use: module 1: tuberculosis surveillance
- Target product profile: Target product profile for tuberculosis diagnosis and detection of drug resistance
- Social protection: Guidance on social protection for people affected by tuberculosis
- TB and comorbidities: WHO operational handbook on tuberculosis: module 6: tuberculosis and comorbidities, 2nd ed

4. Voices on Innovation

Innovations herald the dawn of a new era—revolutionizing TB control through rapid diagnosis and providing shorter, high-quality, effective treatment and prevention regimens for a TB-free future. The rapid adoption and scale of innovative solutions are key to accelerating our progress towards achieving the End TB goals.

Dr. Immaculate Kathure,
Acting Head, Division of Tuberculosis and Lung Health,
Ministry of Health, Kenya

Stepping up innovations in community access and diagnosis are revolutionizing the fight against TB. By leveraging technology and community engagement, we can break down barriers by reaching the most vulnerable populations. These solutions empower individuals, promote early detection, and ensure timely treatment—driving us closer to a TB-free world.

Dr. Annie Bisso,
NTP Manager,
National TB Programme, Cameroon

The Global Fund / Jiro Ose

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About the NextGen Market Shaping Strategic Initiative

The NextGen Market Shaping Strategic Initiative, financed by the Global Fund, will support the implementation of innovative approaches and mechanisms for the introduction and scale up of new tuberculosis tools in Global Fund-supported countries. This initiative is part of the Global Fund NextGen Market Shaping approach, which outlines a holistic set of interventions to shape innovation and accelerate new product introductions at scale, promote capacity building for regional manufacturing and drive environmentally sustainable procurement and supply chains.