

Briefing Note:

Chest Radiography and Computer-aided Detection (CAD) Solutions for Tuberculosis Programs

8 September 2021

1. Purpose

This document has been developed for Global Fund staff when supporting Principal Recipients in the selection of X-ray and computer-aided detection (CAD) software.

2. Use of Chest X-rays and CAD Software in Tuberculosis Programs

Chest X-ray (CXR) has been used by tuberculosis (TB) programs as a screening tool for detecting TB disease particularly among subpopulations that are at higher risk. A summary of WHO recommendations on use of chest X-ray¹ for screening and other purposes is presented in Box 1. Limited access to high diagnostic quality digital CXR imaging and a shortage of trained radiologists to interpret the images are key barriers faced by programs, particularly in low resource settings. Advances in digital imaging technologies have led to the development of better digital CXR devices including portable and ultra-portable battery-operated equipment. In addition, computer-aided detection artificial intelligence (CAD/AI) software packages have been developed and introduced to automate the interpretation of digital CXR images. The use of portable digital CXR devices equipped with CAD/AI software solutions to interpret CXRs is gaining interest in the context of an integrated response to COVID-19 and TB and after the release of WHO consolidated guidelines on systematic screening for tuberculosis². Some of the recommendations on tools for screening for TB are:

- Among individuals aged 15 years and older in populations in which TB screening is recommended, systematic screening for TB disease may be conducted using a symptom screen, chest X-ray or molecular WHO-recommended rapid diagnostic tests, alone or in combination.

- Among individuals aged 15 years and older in populations in which TB screening is recommended, computer-aided detection software programmes may be used in place of human readers for interpreting digital chest X-rays for screening and triage for TB disease.
- Among individuals younger than 15 years who are close contacts of someone with TB, systematic screening for TB disease should be conducted using a symptom screen including any one of cough, fever or poor weight gain; or chest radiography; or both.

Box 1. Summary of WHO Recommendations on using CXR for TB.

Source: WHO, Chest Radiography in TB Detection, 2016

CHEST X-RAY: AN ESSENTIAL TOOL TO END TB

CXR IS A SENSITIVE TOOL FOR SCREENING FOR ACTIVE TB

Reference: Systematic screening for active tuberculosis: principles and recommendations (4)

- CXR has higher sensitivity for pulmonary TB than screening for TB symptoms.

AN ABNORMAL CXR IS AN INDICATION FOR FULL DIAGNOSTIC EVALUATION

Reference: International standards for tuberculosis care (20)

- All patients with unexplained findings suggestive of TB on CXR should be evaluated for TB with a bacteriological diagnostic test.
- CXR can be used as a supplementary diagnostic aid, although the specificity is low.
- A bacteriologically confirmed diagnosis is always preferred.

CXR IS AN IMPORTANT TOOL FOR DIAGNOSING CHILDHOOD TB

Reference: Guidance for national tuberculosis programmes on the management of tuberculosis in children (22)

- CXR is useful in diagnosing pulmonary and extrapulmonary TB in children in combination with history, evidence of TB infection and microbiological testing.

CXR CAN IMPROVE THE EFFICIENCY OF USING THE XPRT MTB/RIF ASSAY

Reference: implementation manual for the Xpert MTB/RIF assay (3)

- CXR and further clinical assessment can be used to triage who should be tested with the Xpert MTB/RIF assay to reduce the number of individuals tested and the associated costs, as well as to improve the pre-test probability for TB and, thus, the predictive value of the Xpert MTB/RIF assay.

CXR CAN ASSIST IN DIAGNOSING TB AMONG PEOPLE LIVING WITH HIV

Reference: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection (23)

- CXR can assist in diagnosing TB among people living with HIV. It is particularly useful for ruling out TB disease before providing treatment for latent TB infection.

CXR HELPS RULE OUT ACTIVE TB BEFORE TREATING LATENT TB INFECTION

Reference: Guidelines on the management of latent tuberculosis infection (24)

- CXR used in combination with symptom screening has the highest sensitivity for detecting TB and, thus, should be used to exclude active TB before initiating treatment of latent TB infection.
- Individuals with any radiological abnormality or TB symptoms should be investigated further for active TB and other conditions.

CXR IS AN ESSENTIAL TECHNOLOGY FOR PREVALENCE SURVEYS

Reference: Tuberculosis prevalence surveys: a handbook (21)

- CXR is a necessary screening tool to identify survey participants eligible for bacteriological examination; in recent surveys, CXR has proven essential for detecting a large proportion of prevalent TB cases.

3. Considerations of Quality and Regulatory Aspects, including Global Fund Quality Assurance Policy on Diagnostics

Technical specifications for portable digital radiography system have been published by WHO and IAEA to support decision-making regarding the selection, incorporation, allocation and use of portable X-ray systems.³

The Global Fund's Quality Assurance Policy for Diagnostics Products (the "QA Policy")⁴ is currently applicable to imaging equipment used in Global Fund-financed programs for diagnosis, screening, surveillance or monitoring purposes. Software is currently not covered under this policy.

The Global Fund requirements outlined in section 6 of the QA Policy on clinical standards for the use of computer aided software for TB screening in individuals aged 15 years and older are aligned with WHO guidelines on tuberculosis, specifically module 2 on systematic screening for tuberculosis.

In addition, equipment for chest radiography considered as imaging equipment must comply with Section 7.i. of the QA Policy and must be manufactured at a site compliant with the requirements of ISO 13485 or an equivalent Quality Management System recognized by one of the Regulatory Authorities of the Founding Members of the Global Harmonization Task Force.

Computer-aided detection artificial intelligence (CAD/AI) software has a medical purpose as it is intended to process, analyze, create or modify medical information and can be qualified as a medical device.

If CAD/AI is included in the hardware of an imaging equipment it is part of the category of "imaging equipment". In this case, Section 7.i of the QA Policy applies as per the above, in addition to Sections 5 and 6 (compliance with applicable laws and regulations, and WHO guidance or national guidelines).

There is no specific requirement in the QA Policy for CAD/AI software that are not included in the hardware, other than (1) complying with applicable laws and regulations and (2) being consistent with WHO guidance or complying with national guidelines (Sections 5 and 6 of the QA Policy recalled above).

All other provisions of the QA Policy, in particular Sections 10 to 15, apply in both instances.

After QA due diligence, information on products compliant with QA Policy will be made publicly available through the QA list published on the Global Fund website.

The Global Fund will update its current guidance to reflect innovations highlighted on this briefing.

4. Equipment Available in the Market and through the Global Drug Facility

FIND published a [technology landscape analysis](#) on digital chest radiography and CAD solutions for TB diagnostics in 2021⁵. It covers an overview of CXR technology including analog retrofit digital radiography, consideration for X-ray equipment selection, overview of commercially available CAD solutions for TB programs, complete range of stationary (facility-based) X-ray equipment for CXR imaging, and early adopter experience with CXR CAD implementation for TB diagnosis.

The [FIND publication](#) also includes a product comparison sheet⁶ listing 21 portable X-ray equipment along with the picture, specification of X-ray generator and detector, digital radiography workstation, software including CAD/AI integration option, regulatory approval received (FDA or CE), operating conditions, installation and training, service and maintenance, and estimated cost for some of the products. This is provided for information purposes only, see footnote.*

At present, the Stop TB Partnership's Global Drug Facility includes two ultra-portable digital X-ray systems and two CAD software packages in their [product catalogue](#).⁷ A practical guide to help facilitate uptake of these new technologies is also available.⁸

In summary, digital X-rays and CAD/AI are important tools to improve TB screening and promote earlier diagnosis of TB. Digital X-rays can also be used for other conditions and diseases including COVID-19. Chest X-ray equipment, including portable and digital devices as well as CAD/AI software are eligible for procurement using Global Fund grant funds. Refer to the Global Fund website ([see here](#)) for a list of eligible products.

For further information, please contact the TAP/TB team or SO/QA team.

* This is provided for information purposes only. The Global Fund gives no warranty and accepts no responsibility or liability for the accuracy, or the completeness of the information and materials contained in this document. Implementing partners remain obliged to comply with the relevant grant agreement (including Article 5 of the Grant Regulations).

5. References

1. Chest Radiography in Tuberculosis Detection; Summary of current WHO recommendations and guidance on programmatic approaches. WHO. 2016. Available at: <https://apps.who.int/iris/bitstream/handle/10665/252424/9789241511506-eng.pdf?sequence=1>
2. WHO consolidated guidelines on tuberculosis Module 2: Screening – Systematic screening for tuberculosis disease. WHO. 2021. <https://www.who.int/publications/i/item/9789240022676>
3. Portable digital radiography system: technical specifications. Geneva: World Health Organization; 2021. <https://www.who.int/publications/i/item/9789240033818>
4. Global Fund Quality Assurance Policy for Diagnostics products as amended on 4 May 2017. https://www.theglobalfund.org/media/5885/psm_qadiagnostics_policy_en.pdf
5. Digital chest radiography and computer-aided detection (CAD) solutions for TB diagnostics - technology landscape analysis. FIND. 2021. Link: <https://www.finddx.org/wp-content/uploads/2021/04/FIND-CXR-CAD-solutions-for-TB-diagnosis-7Apr2021-2pg-spread.pdf>
6. Product comparison sheet: full range of available products in the market for portable and ultra-portable x-ray equipment. FIND. 2021. Link: https://www.finddx.org/wp-content/uploads/2021/03/FIND-CADAI-Solutions_Annex2_24Mar2021.pdf
7. Global Drug Facility Diagnostic Catalogue - July 2021. Stop TB Partnership. Link <http://stoptb.org/assets/documents/gdf/drugsupply/GDFDiagnosticsCatalog.pdf>
8. Practical Guide on the Screening and Triage for TB using Computer-Aided Detection (CAD) Technology and Ultra-portable X-Ray Systems. Stop TB Partnership. 2021. Link: <http://www.stoptb.org/dhthub/practicalguide.asp>