

Benefits of Artificial Intelligence versus Human-Reader in Chest X-ray Screening for Tuberculosis in the Philippines

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ABSTRACT

Background: Since 2017, the Philippines Business for Social Progress (PBSP) has implemented active case finding for Tuberculosis under their Advancing Client-centered Care and Expanding Sustainable Services for TB (ACCESSTB) project. This study aims to conduct a comparative analysis of a screening approach using AI for Chest X-ray (CXR) interpretation versus an approach relying solely on human-readers in three major regions of the Philippines.

Methods: This study undertook a retrospective analysis of data derived from two well-established and ongoing screening approaches. The data on number of people screened and the outcome of the screening at each stage of the screening process was extracted from quarterly reports provided by PBSP. Subsequently, the data was analysed to determine the diagnostic yield, the number needed to screen and the drop-out rates.

Results: The AI screening approach had a lower number needed to screen (26.3) compared to human-reader screening (41.5). The main reason driving this difference is the lower drop-out rate after CXR (16.6% in AI approach versus 43.1% in human reader approach). This lower drop-out rate is attributed to the quicker turnaround time for CXR results and this has an important public health benefit because a higher proportion of positive TB individuals participating in the screening will receive treatment in the AI screening approach (3.8% versus 2.4%).

Conclusion: The results illustrate that AI-powered CXR screening has clear benefits compared to screening with human readers. Further research is required to determine the comparative cost-effectiveness of the two screening approaches.

Keywords: tuberculosis, active case finding, CXR screening, artificial intelligence, benefit

INTRODUCTION

Tuberculosis (TB) ranks ninth globally among causes of death, with 10.6 million cases and 1.6 million deaths in 2021, including 187,000 HIV co-infections.^{1,2} In the WHO South-East Asia Region, over 4.3 million cases were reported in 2019, with the Philippines having 554,000 cases and 63,000 deaths in 2020.² The Global Burden

of Disease study shows TB caused 2,639 DALYs per 100,000 population in the Philippines in 2019, emphasizing the pressing need for ongoing efforts in TB prevention, diagnosis, and treatment.³ According to the Philippine Strategic Elimination Plan 2020-2023 (PhilSTEP1), the aim is to reduce TB deaths from 26,000 to 22,000 (a 15% decrease) and lower the

TB incidence rate from 554 to 488 per 100,000 (a 12% decrease).⁴ To achieve these targets, the country's National Tuberculosis Control Program (NTP) recommends active case finding (ACF), which involves systematic screening outside of healthcare facilities within specific communities.^{5,6} The proposed ACF strategy is mass chest X-ray (CXR) screening.⁴ In this regard, one of the objectives under the PhilSTEP1 is to screen at least 50 million people for TB using CXR.

Skilled radiologists are required for the interpretation of CXR images. However, the availability of radiologists in TB burdened resource-limited settings poses a significant challenge.^{7,8} Among qualified radiologists, inter- and intra-reader inconsistency is common due to factors like exhaustion and perceptual preconceptions which may lead to inaccuracies.⁹ In 2021, in light of these challenges, WHO endorsed computer-aided detection (CAD) as an alternative interpretation method to human readers during TB screening using plain digital CXRs.¹⁰ This recommendation followed three independent evaluations of CAD technologies in 2020, comparing sensitivity and specificity to human reader interpretation.¹⁰ The diagnostic accuracy and performance of the software were comparable to human reader interpretation.¹⁰

Two AI software solutions, CAD4TB and qXR, have been utilized and evaluated within the Philippines. In one study using CAD4TB on 12,256 CXRs from migrant TB screening programs, the system achieved 90.0% sensitivity at 80.0% specificity.¹¹ However, this study focused on migrant TB screening data, potentially limiting its generalizability to TB cases in the general population, and it lacked comparisons with human radiologists or other TB detection methods. Conversely, when assessed against human radiologists in a study involving 928 cases, qXR exhibited a higher sensitivity of 0.95 (0.83-0.99) in contrast to the radiologists' sensitivity of 0.87 (0.73-0.96).¹²

Furthermore, cost-effectiveness analysis has found that mainstreaming CXR screening with AI (specifically qXR) was more cost-effective, with an estimated cost per disability-adjusted life year (DALY) of PHP 43,376, compared to PHP 47,667 for human-reader-based screening during intensified case finding in public facilities.¹³ However, given the data for the study originated from only two government tertiary hospitals in the Luzon region, generalizability of the findings to other healthcare settings and geographical regions is limited.

While a CXR can identify potential TB-related lesions, provide information about their location, nature and extent, it demonstrates a specificity of 75% for TB, risking false positive results for individuals without TB.^{14,15} This can be attributed, in part, to CXR's ability to detect various lung abnormalities associated not only with TB, but other conditions such as those related to cardiovascular disease.¹⁶

Considering the modest specificity of the CXR, there is a need for follow-up microbiological testing that has high sensitivity and specificity for TB, such as molecular tests, smear microscopy or liquid cultures, to confirm the diagnosis after an abnormal CXR.¹⁷ The most accurate of these are molecular tests such as the Xpert MTB/RIF assay. This nucleic acid amplification-based test employs real-time Polymerase Chain Reaction to detect specific *Mycobacterium TB* DNA sequences in sputum samples.¹⁸ The sensitivity and specificity to detect TB of Xpert MTB/RIF are high at 88% and 99% respectively.¹⁹

The WHO recommends the Xpert MTB/RIF assay after CXR examination within what is known as an algorithm to improve sensitivity, provide a definite diagnosis and detect drug resistance.²⁰ The algorithm combining any TB symptom (chronic cough, sputum production, hemoptysis, fever, night sweats and weight loss) followed by CXR and Xpert MTB/RIF testing increases true-positive results. In a

retrospective cohort study in India among 5553 contacts, Xpert testing after symptoms screening identified 20 cases, while the combination of symptoms and CXR followed by Xpert testing detected 35 cases, showing a 75% increase compared to symptoms and Xpert alone.²¹

PBSP and the ACCESS TB Project

The Philippines' Department of Health and National Tuberculosis Program receives support for its tuberculosis control initiatives from international development partners and non-governmental organizations, including the Philippine Business for Social Progress (PBSP). PBSP, with funding from the Global Fund, is implementing The Advancing Client-centered Care and Expanding Sustainable Services for TB (ACCESS TB) project.²² This initiative strives to enhance the detection and treatment of TB in alignment with the national objective of achieving a TB-free Philippines by 2035.¹²

As part of this initiative, CXR screening is conducted using mobile X-ray vans, targeting populations such as the urban and rural poor, elderly, and those in congregate settings. The strategy to target high risk groups reduces access barriers among vulnerable populations and decreases the risk of community transmission.²³ This The

ACCESS TB project is conducted in the three regions: National Capital Region (population: 13.48 million), CALABARZON (population: 16.20 million), and Central Luzon (population: 12.42 million).

Since 2018, the PBSP has introduced AI-powered CXR screening with qXR to reduce turnaround time of CXR reading.²² PBSP commissions other organizations to conduct ACF using mobile vans relying solely on human readers. Mobile vans are often positioned at municipal council offices of the target barangay (the most local level of government), where community health workers inform and invite individuals to the screening.

For the human-reader screening approach, a standardized checklist is utilized to gather demographic information, symptoms, and the patient's TB history. Subsequently, individuals at risk of TB undergo CXR screening and the X-ray images are emailed to a radiologist for interpretation. In cases where the X-ray is suggestive of TB, patients are referred for gene Xpert testing. A sputum sample is collected and transported to the nearest equipped rural health unit (RHU) for processing within 1-3 days depending on the existing workload. Once TB is confirmed, the patients are enrolled in a TB treatment program.

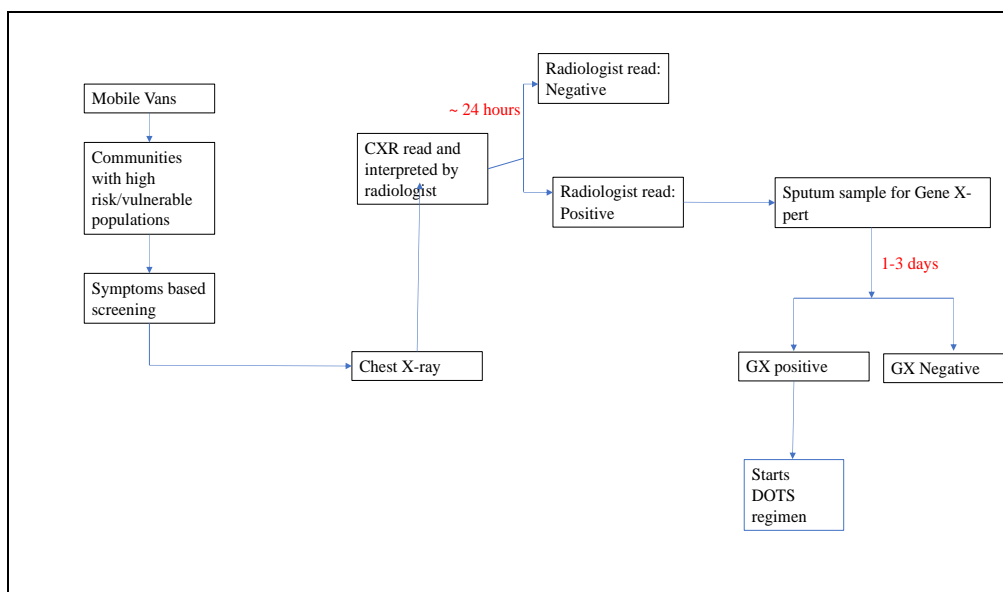


Figure 1: Chart depicting the Human-Reader Screening Process

The AI-screening approach similarly involves a standardized symptom checklist followed by conducting a CXR examination. The difference is that the X-ray images are processed using qXR, an AI-based technology.¹² With qXR, the CXR results turnaround time improves significantly from up to 24 hours to a minute. Upon obtaining the results, the health worker is promptly notified, enabling them to immediately collect sputum samples from presumptive TB cases during the same visit.¹² Then again, similar to the conventional approach, sputum samples are transported to the nearest equipped RHU for gene X-pert testing that is typically completed within 1-3 days depending on the

backlog at the facility. By removing one step and eliminating the need to recontact the patient after radiologist confirmation, this process enables earlier intervention and initiation of treatment, possibly leading to better patient outcomes.

X-rays flagged as presumptive TB cases by the AI undergo verification by a radiologist. This practice is undertaken for legal reasons given the absence of approval from the Philippines Food and Drug Administration for AI to function as a standalone TB screening tool. However, it is important to note that the additional radiologist reading adds an extra layer of expertise but is not required for the Gene X-pert screening (as noted in figure 2).

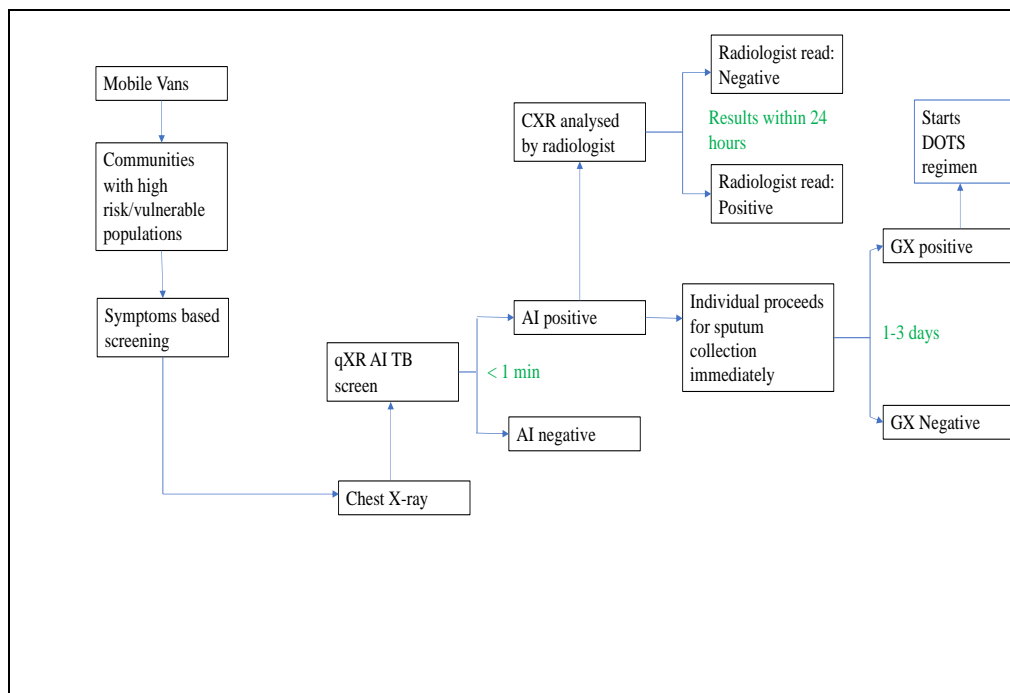


Figure 2: Chart depicting the AI Screening Process

Research gap and significance of the study

While some AI-powered tools, specifically qXR and CAD4TB, have undergone accuracy comparisons with human-readers and cost-effectiveness evaluation in health facilities in the Philippines, there is limited evidence of the cost-effectiveness in the context of ACF in communities.^{13,24,25} Clear evidence on the cost-effectiveness of AI-powered chest X-ray in ACF would better inform the adoption of this screening

approach as an alternative to the conventional radiologist dependent model. To address this research gap, this study aims to evaluate the benefits of AI-powered CXR screening compared to human-reader screening during ACF.

MATERIALS & METHODS

This comparative analysis examines data from the Philippine Business for Social Progress (PSBP) TB active case-finding program in the Philippines between 2021

and 2022. The study was conducted over a five-month period from March to July 2023, with onsite visits carried out in May and June 2023. The research focused on regions that actively conducted ACF for a minimum of two years and had complete data for both AI-powered CXR screening and human-reader CXR screening. The 2-year interval was chosen because there was a disruption in the program during the COVID-19 pandemic and the new technology was only fully adopted and utilized from 2021.

Number of Cases Detected in both the AI powered and Human-reader ACF

The study quantified the number of cases detected by AI screening and by human-reader screening as confirmed by Gene Xpert and clinically. This key metric provides insight into the program's ability to identify and diagnose individuals affected by TB. Data on number of cases detected was found within the quarterly monitoring and evaluation reports. These reports were consolidated to give the total number of individuals that were diagnosed with TB over the study period. The accuracy and completeness of this data depends on the

quality of the organizational reporting process.

Other operational indicators of AI-powered and Human-reader ACF

In addition to the number of cases detected, the quarterly monitoring and evaluation reports provided information on the number of individuals screened at each stage of the screening process. This information facilitated the assessment of other operational indicators, offering deeper insights into the performance of each screening programme. These included:

- Diagnostic yield: The proportion of individuals screened who are diagnosed with TB.²⁶
- Number needed to screen (NNS): The number of individuals that need to be screened to identify one new case of TB.⁶
- Drop-out rate: The proportion of cases that are detected as positive on the initial CXR screening for TB but are not subsequently tested using the GeneXpert diagnostic test.²⁷

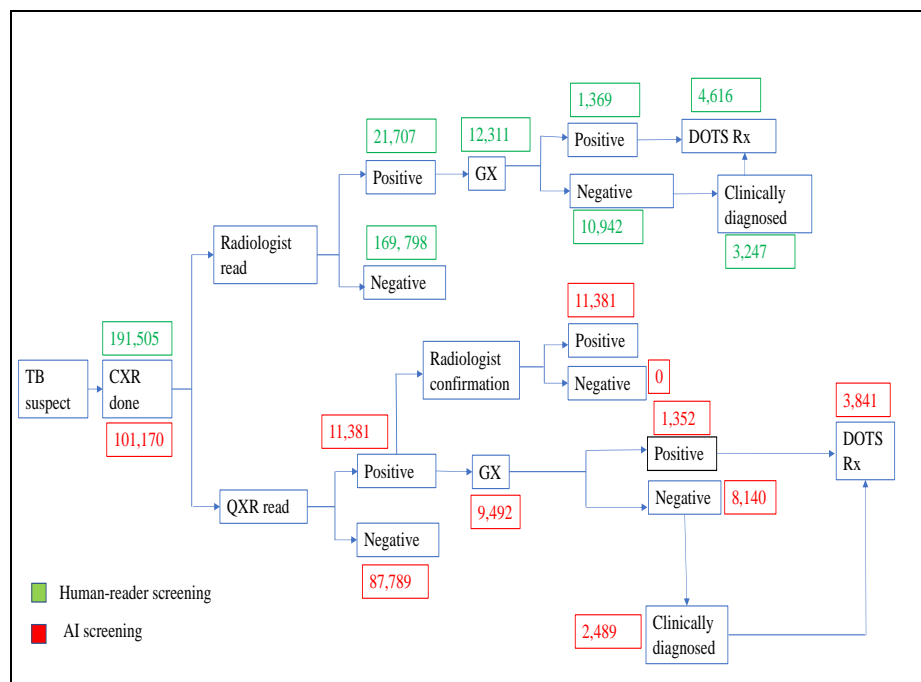


Figure 3: Comparison of patient numbers at the different points of screening in the two approaches

The data collected also included information on the number of patients at various stages of the patient process flow such as the number of patients that had Gene X-pert test done and the number of patients that were clinically diagnosed. This dataset was incorporated into Figure 3 above to conduct a comprehensive analysis of these outcome variables.

RESULT

Outcomes of screening of AI versus human reader approach

As depicted in figure 3, the AI screened a total of 101,170 patients, out of which 11,381 tested positive on QXR screening (11.2%). Among the positive cases, 9,492 patients (83.4%) underwent confirmation sputum testing using Gene X-pert, leading to the enrollment of a total of 3,841 TB cases. Of the enrolled TB cases, 2,489 (64.8%) were clinically diagnosed. This subset of clinically diagnosed patients constituted 30.6% of those who initially tested negative on the Gene-Xpert.

In comparison, the human-reader involved the screening of 191,505 patients, with

21,707 patients identified as positive during the initial screening (11.3%). Among those with positive results, 12,311 individuals (56.7%) received Xpert testing, resulting in the enrollment of 4,616 TB cases. Of the enrolled TB cases, 3,247 (70.3%) were clinically diagnosed. This subset of clinically diagnosed patients constituted 29.7% of those who initially tested negative on the Gene-Xpert.

Figure 4 shows that the proportion of presumptive cases flagged by the initial CXR screening was comparable between the two approaches (11.2% versus 11.3%). However, in the AI approach a higher proportion of the presumptive cases were subsequently tested with gene X-pert following a positive CXR, as compared to the human-reader screening. (83.4% versus 56.7%) Among those tested with gene X-pert, a slightly higher percentage, 40.5%, were enrolled into TB treatment in the AI approach, as opposed to 37.5% in the human-reader approach. It's crucial to highlight that the AI approach and the human-reader approach were not implemented on same sets of X-rays.

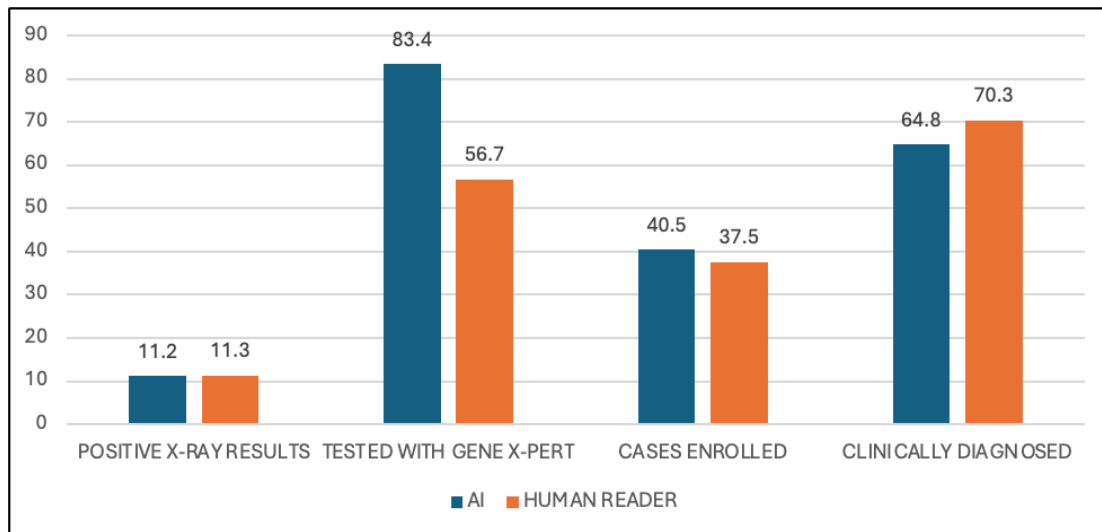


Figure 4: a graph showing the relative percentage of patients in each approach that had positive X-ray results, of those what percentage were tested for gene X-pert, of those what percentage were enrolled on TB treatment and of those what percentage were clinically diagnosed

Operational indicators

Drop-out rates (DR)

The drop-out rate for each screening approach was calculated by dividing the number of Positive X-ray Cases not tested

with GeneXpert by the number tested with GeneXpert and multiplying it by 100. The drop-out rate in the AI approach was 16.6% and the drop-out rate in the human reader approach was 43.1%.

Diagnostic Yield

The diagnostic yield for each screening approach was calculated by dividing the number of positive diagnoses by the total number of individuals screened and multiplying it by 100. The number of cases detected includes both the Gene X-pert positive and clinically diagnosed. In figure 4, for the AI screening, out of a total of 101,170 individuals screened, 3,841 cases were detected as Gene X-pert positive, resulting in a diagnostic yield of 3.8%. In the Human-reader screening, out of a total of 191,505 individuals screened, 4,616 cases were detected as Gene X-pert positive, resulting in a diagnostic yield of 2.4%.

Number Needed to Screen (NNS)

The NNS represents the ratio of the total number of individuals screened to the total number of newly identified TB cases. For the AI approach, a total number of 101,170 individuals were screened and there were 3,841 identified TB cases, resulting in a number needed to screen of 26.3. For the human-reader approach, a total of 191,505 individuals were screened, resulting in the identification of 4,616 identified TB cases. Hence, the NNS for the human-reader arm was 41.5.

DISCUSSION

Clinical Benefits of AI-Powered CXR Screening for ACF in the Philippines

A higher drop-out rate in the human-reader screening than in the AI approach (43.1% versus 16.6%) indicates a larger proportion of patients who did not proceed with further diagnostic steps after a positive CXR result. This higher drop-out rate leads to missed opportunities for earlier TB diagnosis, and positive TB cases may cause further community spread. The lower dropout rate observed in the AI screening approach can be attributed to the quicker turnaround time for X-ray results. As highlighted in the description of the AI integration in the ACCESS TB project, the duration for sputum collection decreased significantly, from up to 24 hours before the adoption of

qXR to less than one minute after its incorporation into the program.¹²

When contextualizing these findings in the global landscape, particularly in countries like Zimbabwe, India, and Pakistan, where pre-diagnostic drop-out rates with human readers range from 6% to 30%^{28,29,30}, the AI approach not only outperforms but also holds promise for addressing healthcare challenges in regions where accessibility and efficiency are critical factors in combating diseases such as TB. However, we must consider the subsequent increased burden on already overburdened health facilities with the increased referral of cases for gene X-pert.

Despite the significantly lower drop-out rates, further investigation is needed to identify the reasons for incomplete sputum collection in the AI approach. Considering that AI-analyzed CXR results are obtainable within a minute, and the protocol states to immediately acquire sputum samples from individuals labeled as presumed cases, the drop-out rate should be closer to zero percent rather than the 16.6% identified. A potential factor contributing to the drop-out rate observed between the screening phase and final diagnosis could be that these patients were unable to produce sputum as observed in a 1/3 of TB-HIV co-infected patients³¹ making a gene X-pert difficult to conduct. Nevertheless, further research is required to confirm this hypothesis.

A notable observation is the considerable proportion of TB cases enrolled on treatment in both AI-based and human-reader screening through clinical diagnosis. Clinical diagnosis based on clinical presentation and CXR findings is considered reasonable in individuals where TB cannot be ruled out despite negative bacteriological tests, as recommended by WHO.¹⁵ This approach is especially important for groups where confirming TB diagnosis with bacteriological tests is challenging, such as individuals with HIV or other immune-compromising conditions.²⁷

Within the AI screening, 64.8% of the enrolled cases were through clinical diagnosis, while in the human-reader screening, an even higher proportion of 70.3% of enrolled cases were through clinical diagnosis. However, when it came to the rate of transition from a negative GeneXpert test to clinical diagnosis, both screening programmes were comparable. (30.6% versus 29.7%). This suggests that, in some instances, both AI and human-reader screening miss cases that are later diagnosed through clinical evaluation. This is expected given the sensitivity of qXR versus radiologists (0.95 and 0.87 respectively).¹²

Operational Benefits of AI-Powered CXR Screening for ACF in the Philippines

The Number Needed to Screen (NNS) in each screening method serves as an indicator for the level of effort required in a screening programme. A lower NNS signifies a more efficient screening process, as fewer patients need to undergo screening to find each positive case. The NNS in the AI screening approach is substantially lower at 26.3, compared to the human-reader's NNS of 41.5. The high NNS in the human-reader approach is largely due to the high drop-out rate (43.1%). The AI screening achieves a higher detection rate in the screened population and optimizes resource utilization by requiring fewer screening efforts to identify each positive case. These findings underscore AI's potential benefits in large-scale community based ACF screening scenarios.

However, it's crucial to consider a recent systematic review comprising 58 studies conducted in medium or high TB incidence settings among individuals living with HIV.³² In this extensive analysis, which exclusively involved human readers, the weighted mean NNS for active TB was remarkably lower, at 14 for abnormal CXRs and 17 for CXRs suggestive of TB. This indicates a notable proficiency of human readers in TB detection through CXR interpretation, presenting a nuanced

perspective on the choice between AI and human readers in TB screening strategies.

Nevertheless, considering the high TB-burden in countries such as the Philippines and the need for community based ACF, CAD emerges as a viable alternative. This will, however, require consideration of the upfront costs (software, hardware, and staff training) associated with acquiring and integrating AI technology into existing healthcare infrastructure.

The calculated diagnostic yield provides a quantitative measure of the effectiveness of different screening approaches in identifying cases of interest. The data show that the AI screening demonstrated a higher diagnostic yield (3.8%) compared to the human-reader screening (2.4%). However, the diagnostic yield of a screening algorithm is also influenced by the prevalence of the disease in the population being screened. The higher the prevalence of the disease, the higher the diagnostic yield of the screening approach.³³ Because the prevalence of the different screening locations was unknown, we cannot draw any conclusions from this indicator.

Limitations of the Study

This study involved the retrospective analysis of data from two established and ongoing screening approaches. There was no radiologist screening of those identified as negative by qXR so there may have been some false negatives. The two screening approaches were implemented in different barangays which could have different prevalence of TB. In addition, there was no randomization of individuals to one of the two approaches and the screenings were performed by different teams. In addition, since the patients were screened by healthcare workers using a symptom screening questionnaire, there is a possibility of bias in the selection of individuals for X-ray. All these factors could have influenced the diagnostic yield.

CONCLUSION

The integration of AI into the screening process allows for swift availability of actionable information, facilitating early detection and minimizing dropout rates, thereby optimizing testing procedures in the diagnostic process. Furthermore, considering the high TB-burden in countries such as the Philippines, AI emerges as a viable alternative for implementing CXR for ACF at scale.

By needing lower numbers to screen (NNS), AI-driven CXR screening may offer governments and healthcare providers the ability to allocate their limited resources more effectively. This could result in the expansion of TB screening programmes to reach a larger population, especially in high TB-burden countries like the Philippines, where scaling up screening efforts is crucial for early case detection. In addition, the lower drop-out rates in the AI screening approach, provide a significant public health benefit by reducing the spread of TB infections.

This study presents a foundation for further research into the cost-effectiveness of ACF using AI versus human readers. Performing a prospective study within the same geographical region for both a human and an AI could effectively mitigate potential confounding variables such as TB prevalence. Furthermore, to eliminate other confounding variables related to execution of the screening approach, this prospective study should use the same clinical team for the two approaches. This minimizes confounding factors such as differing sputum collection approaches that may affect GeneXpert test results. Finally, cost and outcome data on the TB treatment would be needed.

Declaration by Authors: We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship that are not listed. We further confirm that the order of authors listed in

the manuscript has been approved by all of us.

Ethical Approval: No primary data collection was conducted for this study. As this study is based on secondary data and does not involve any confidential or private information, institutional review board approval was not required. All presentations and reports only present aggregated data, ensuring that no individual-level information is disclosed. Additionally, any discussions about the study documentation were limited to authorized individuals or institutions directly involved in the research.

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Conflict of Interest: The data that was analysed in this study was extracted by the Philippine Business for Social Progress monitoring and evaluation team. This team was consulted during the analysis of the data.

Conflict of Interest: The authors declare no conflict of interest.

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