

# CLAimHealth COLLABORATING, LEARNING, AND ADAPTING FOR IMPROVED HEALTH ACTIVITY

Good Practices and Promising Interventions, Technical Series No. 8: A Cost-Effectiveness Analysis of Mainstreaming Chest X-Ray Screening with Artificial Intelligence-Powered Computer-Aided Detection or Human Readers in Public Facilities

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# ACRONYMS

AI	artificial intelligence
ARMMC	Amang Rodriguez Memorial Medical Center
BatMC	Batangas Medical Center
ВСТВ	bacteriologically confirmed tuberculosis
CAD	computer-aided detection
CDTB	clinically diagnosed tuberculosis
CEA	cost-effectiveness analysis
СНО	city health office
CLAimHealth	Collaborating, Learning, and Adapting for Improved Health
COVID-19	coronavirus disease 2019
CXR	chest X-ray
DALY	disability-adjusted life-years
DOH	Department of Health
DSTB	drug-sensitive tuberculosis
ELTFU	early loss to follow-up
GPPI	good practices and promising interventions
GDP	gross domestic product
HR	human resources
НТА	Health Technology Assessment
ICER	incremental cost-effectiveness ratio
ICF	intensified tuberculosis case finding
JPR	Philippines Joint Program Review
LTFU	loss to follow-up
MTB/RIF	Mycobacterium tuberculosis complex and resistance to rifampin
NCR	National Capital Region
NTP	National Tuberculosis Control Program
NTPS	National Tuberculosis Prevalence Survey
ОН	Office of Health
OOP	out-of-pocket
PhilSTEP	Philippine Strategic Tuberculosis Elimination Plan
РНО	provincial health office
PLTFU	pretreatment loss to follow-up
ТАТ	turnaround time
ТВ	tuberculosis

TB IHSS	Tuberculosis Innovations and Health Systems Strengthening
TLTFU	treatment loss to follow-up
SA	screening alternative
SG	salary grade
S/s	signs and symptoms
USAID	United States Agency for International Development
WHO	World Health Organization
YLD	years lived with disability
YLL	years of life lost

# **EXECUTIVE SUMMARY**

Mainstreaming chest X-ray (CXR) screening with either artificial intelligence (AI) -powered computeraided detection (CAD) or human readers for intensified tuberculosis case finding (ICF) is a promising solution to some of the key limitations of the current ICF strategy in the Philippines, which relies on symptom-based screening as the primary screening tool. Shifting to CXR screening as the primary screening tool and expanding the capacity for ICF can help reduce delayed or missed tuberculosis (TB) case detection due to prolonged turnaround time (TAT). Recognizing this potential and the urgent need to find missing TB cases in the country, this study documents the health and socioeconomic benefits and cost-effectiveness of mainstreaming CXR screening in public facilities. This study, undertaken by the U.S. Agency for International Development's (USAID) Collaborating, Learning, and Adapting for Improved Health (CLAimHealth) Project in collaboration with USAID's TB Innovations and Health Systems Strengthening (TB IHSS) Project, builds on the initial pilot implementation of TB IHSS's innovative ICF model that involves CXR screening with AI-powered CAD in two large tertiary public hospitals.

The study estimates the incremental cost and health impacts of mainstreaming CXR screening over a period of ten years, vis-à-vis ICF by symptom-based screening (screening alternative I [SA1]). It considers all the additional capital and recurrent requirements of mainstreaming CXR screening with either AI-powered CAD (SA2) or human readers (SA3) per facility. It estimates the health impact of the two CXR screening alternatives, SA2 and SA3, based on the demand for CXR screening and TB diagnostic and treatment outcomes in pilot hospitals. Results suggest that mainstreaming CXR screening is very cost effective. Its incremental cost-effective ratio (ICER) is PHP 43,376 per disability-adjusted life-year (DALY) averted with AI-powered CAD and PHP 47,667 per DALY averted with human readers (see Table 1), both below the gross domestic product (GDP) per capita in 2020 (PHP 163,701). Both SA2 and SA3 remain very cost effective under different scenarios, such as higher discount rate, lower benefits, higher capital and recurrent costs, and a combination of lower benefits and higher capital and recurrent costs (see Figure 1).

Table I. Additional costs and benefits of mainstreaming CXR screening						
Indicator	SA2: with AI- powered CAD	SA3: with human readers				
ICER, PHP per DALY averted	43,376	47,667				
Additional cost per TB case screened, PHP	633	695				
Reduction in TB incidence, cases	1,197	same as SA2				
Productivity losses averted						
Due to early diagnosis and treatment, PHP million per year	34	same as SA2				
Due to early diagnosis and treatment, PHP per case treated	283,204	same as SA2				
Due to time savings, PHP per case screened and diagnosed	275.01	same as SA2				
Time savings, hours per case screened	8.3	same as SA2				

Table I. Additional costs and benefits of mainstreaming CXR screening						
Indicator SA2: with Al-SA3: wi powered CAD human real						
Cost savings (including out-of-pocket [OOP] cost savings and productivity losses averted), PHP per case screened and diagnosed	370.22	same as SA2				
Cost savings as percent of household income	1.04	same as SA2				





Using available data, the study also describes the socioeconomic benefits of mainstreaming CXR screening. Specifically, it estimates time savings, transport cost savings, and productivity losses averted from shorter CXR TAT due to either SA2 or SA3. It also estimates the productivity losses averted due to early diagnosis and treatment. Compared with ICF by symptom-based screening, mainstreaming CXR screening generates an additional time savings of 8.3 hours per case screened, transport cost savings of around PHP 95 per case screened and diagnosed, and productivity savings of about PHP 270 per case screened and diagnosed due to early CXR TAT. The estimated productivity savings due to early TB detection and treatment is about PHP 283,203 per case treated. By reducing direct and indirect costs of seeking TB care services by up to 1.04 percent of average monthly household income, mainstreaming CXR screening for ICF generates additional financial protection among patients. This eases the burden of catastrophic health expenditures for TB, especially among poor patients and their families. Although both CXR screening alternatives result in the same health and economic benefits, SA2 (with AI-powered CAD) requires less financial and human resources than SA3 (with human readers), making SA2 more cost-effective than SA3. From an efficiency perspective, SA2 is highly recommended in resource-limited settings, especially in those with high TB burden and a limited supply of registered radiologists.

The study draws mainly on reliable local data to provide evidence regarding the socioeconomic benefits and cost-effectiveness of mainstreaming CXR screening. Nonetheless, the study has some limitations due to its design and to data constraints. In addition to assessing the economic viability of mainstreaming CXR, it is important to mitigate the possible implementation risks of screening with AI-powered CAD. This requires detailed assessments of the following: (i) local adoption, feasibility, and user acceptability of AI-powered CAD; (ii) local affordability and financial sustainability of mainstreaming CXR screening with either AI-powered CAD or human readers; and (iii) securing potential PhilHealth funding and undergoing a comprehensive health technology assessment.

# I. BACKGROUND

Tuberculosis (TB) is one of the leading global public health problems. It is the world's tenth leading cause of death.<sup>1</sup> Globally, the Philippines remains one of the countries with the highest TB burden, with a TB incidence of 554/100,000 and a TB prevalence rate of 1,159/100,000 population.<sup>1,2</sup> Despite the severity of this burden, 43.9 percent of the 2016 National TB Prevalence Survey (NTPS) participants believed their TB symptoms were insignificant.<sup>2</sup> By 2019, 32 percent of persons with active TB in the country remained undetected or unreported.<sup>1</sup> Early TB diagnosis is essential for reducing the risk of transmission, improving disease control, and reducing morbidities and preventing premature deaths due to TB. Thus, finding persons with undetected TB—in health facilities and the community—is a priority for the National Tuberculosis Control Program (NTP) to achieve the vision of the Philippine Strategic TB Elimination Plan for 2017–2022 (PhilSTEP1) of a TB-free Philippines by 2035.

Several supply-and-demand factors contribute to low TB detection rates in the country. On the demand side, health care–seeking behavior of symptomatic individuals is low mainly because of perceived triviality of symptoms, travel costs to health facilities, and missed work or school days.<sup>3</sup> On the supply side, reliance on passive case detection using poorly sensitive diagnostic tools likely contributes to delayed or missed case detection and treatment.<sup>3</sup> According to the 2016 NTPS, TB detection rate is higher when traditional symptom screening is combined with rapid, highly sensitive screening and testing technologies (i.e., digital chest X-rays, Xpert Mycobacterium TB complex and resistance to rifampin [MTB/RIF] or GeneXpert, improved direct sputum smear microscopy with light-emitting diode fluorescent microscopy).

Aside from averting delayed or missed case detection, improving TB case detection rates also entails addressing high loss to follow-up (LTFU) across the TB diagnostics and care cascades (see Figure 1.1).<sup>4</sup> Some patients drop out of care at the onset of symptoms or during the screening and diagnostic process (early LTFU [ELTFU]); others drop out before initiating treatment (pretreatment LTFU [PLTFU]) or during treatment (treatment LTFU [TLTFU]).<sup>5</sup> For instance, according to a 2018 cross-sectional survey conducted across diagnostic and treatment health facilities in the Philippines, only 27 percent of patients diagnosed with drug-sensitive TB (DSTB) were cured and 62 percent of DSTB patients had completed treatment. The rest were either TLTFU (4 percent), had died (2 percent), or had an unknown outcome

<sup>&</sup>lt;sup>1</sup> World Health Organization. (2020). Global tuberculosis report 2020. Geneva: WHO. Retrieved from:

https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf

<sup>&</sup>lt;sup>2</sup> National TB Control Program, Department of Health, Philippines. (2018). *National Tuberculosis Prevalence Survey 2016 Philippines.* 

<sup>&</sup>lt;sup>3</sup> Lansang, M.A.D., Alejandria, M. M., Law, I., Juban, N. R., Amarillo, M. L. E., Sison, O.T., et al. (2021). High TB burden and low notification rates in the Philippines: The 2016 national TB prevalence survey. *PLOS ONE*, *16*(6), p.e0252240.

<sup>&</sup>lt;sup>4</sup> According to a 2018 cross-sectional national survey conducted across diagnostic and treatment health facilities in the Philippines, only 31 percent of patients with DSTB sought professional health care within a week after the onset of symptoms, 23 percent waited for one to two weeks, whereas 46 percent waited more than two weeks after the onset of symptoms before seeking care.

Alva, S. and Cloutier, S. (2019). Quality of Tuberculosis Services Assessment in the Philippines: Report. Chapel Hill, NC, USA: MEASURE Evaluation, University of North Carolina.

<sup>&</sup>lt;sup>5</sup> MacPherson, P., Houben, R.M., Glynn, J.R., Corbett, E.L. and Kranzer, K. (2013). Pre-treatment loss to follow-up in tuberculosis patients in low-and lower-middle-income countries and high-burden countries: a systematic review and meta-analysis. *Bulletin of the World Health Organization*, 92:126-138.

(5 percent).<sup>4</sup> The literature classifies the factors affecting LTFU into three categories: (i) patient-related factors (lack of understanding, time); (ii) health system factors (long waiting times/delays); and (iii) disease-related factors (weakness, fatigue).



Figure 1.1. LTFU across diagnostic and care cascades for TB<sup>6</sup>

### Systematic Screening for Active TB in Health Facilities and Communities and Its Challenges

Systematic screening for active TB in health facilities and communities can help discover persons with undetected TB.<sup>7</sup> In the Philippines, according to NTP, all health facilities are required to perform systematic screening (via intensified tuberculosis case finding [ICF]) for all clients visiting the facility, along with accompanying persons, regardless of the reason for consult.<sup>8</sup> Symptom-based screening, or screening using any of the four cardinal signs and symptoms (S/s) of TB (i.e., at least two weeks of cough, unexplained fever, unexplained weight loss, and night sweats), is the primary screening tool recommended by NTP for ICF (see Figure 1.2). Cases having any of the above signs and symptoms for at least two weeks are identified as presumptive TB. Those that are not presumptive by signs and symptoms are offered chest x-ray (CXR) screening, except for patients who have undergone it in the past year. NTP recommends annual CXR screening for all health facility consults. A case is then identified as presumptive TB if the CXR finding is suggestive of TB.

<sup>&</sup>lt;sup>6</sup> MacPherson, P., Houben, R.M., Glynn, J.R., Corbett, E.L. and Kranzer, K. (2013). Pre-treatment loss to follow-up in tuberculosis patients in low- and lower-middle-income countries and high-burden countries: a systematic review and meta-analysis. *Bulletin of the World Health Organization*, 92:126-138.

<sup>&</sup>lt;sup>7</sup> Available evidence suggests that compared with passive case finding, systematic TB screening is associated with early diagnosis, lower deaths among risk groups, lower patient costs, but higher PTLTFU and no difference in treatment success (Telisinghe et al. 2021). A study by Muyoyeta et al. (2017) demonstrates that defining presumptive TB cases based on S/s only would miss 42 percent of patients who are TB-positive.

Muyoyeta, M., Kasese, N. C., Milimo, D., Mushanga, I., Ndhlovu, M., Kapata, N., et al. (2017). Digital CXR with computer aided diagnosis versus symptom screen to define presumptive tuberculosis among household contacts and impact on tuberculosis diagnosis. *BMC infectious diseases, 17(1),* 1-8.

Telisinghe, L., Ruperez, M., Amofa-Sekyi, M., Mwenge, L., Mainga, T., Kumar, R., et al. (2021). Does tuberculosis screening improve individual outcomes? A systematic review. *EClinicalMedicine*, 40, 101127.

<sup>&</sup>lt;sup>8</sup> National TB Control Program, Department of Health. (2020). *Manual of Procedures 6th edition*. Manila: Department of Health.

Several patient and facility factors, however, influence a patient's decision to avoid CXR screening. The 2019 Philippines Joint Program Review (JPR) observed that insufficient TB screening is currently conducted in the health care setting.<sup>9</sup> Although most patients are accompanied during their hospital visit, their companions are rarely included in routine TB screening activities, missing many potential TB cases. According to the 2019 JPR, CXR is available only in select hospitals and primary care centers, and this lack of access to CXR limits the capacity to conduct effective TB screening efforts in the country. In facilities where CXR is available, heavy caseloads, limited supply of health professionals, and lack of state-of-the-art equipment limit effective CXR screening (see Figure 1.3). For instance, the radiology departments of Batangas Medical Center (BatMC) in Region IV-A and Amang Rodriguez Memorial Medical Center (ARMMC) in the National Capital Region (NCR) are both operating at maximum capacity, serving about 150–200 patients per day.<sup>10</sup> These characteristics highlight the need to augment capacity to adequately support ICF efforts in these facilities. Furthermore, according to the 2019 JPR, complicated screening algorithms in health facilities, which sometimes entail referrals to outside facilities, contribute to further delays and LTFU.



SM = smear microscopy, TB LAMP = loop-mediated isothermal amplification

# Figure 1.2. Systematic screening for pulmonary PTB in adults ≥15 years old with unknown human immunodeficiency virus (HIV) infection status in health facilities<sup>11</sup>

To help avert delayed or missed case detection, the World Health Organization (WHO) and NTP recommend active case finding (ACF)—systematic screening outside health facilities—by bringing the screening examination/procedures, such as CXR, to targeted community, workplace, and congregate settings.<sup>7,12</sup> ACF efforts since 2017 have focused on targeted risk groups either through mobile van-

<sup>&</sup>lt;sup>9</sup> National Tuberculosis Control Program, Department of Health, Philippines. (2020). *Review report: 2019 Philippines TB Joint Program Review.* 

<sup>&</sup>lt;sup>10</sup> TB Innovations and Health System Strengthening System, FHI 360. (2021). Draft Report: ICF Among Outpatients and their Companions by A.I-Read Chest X-ray for Tuberculosis Triaging. Unpublished.

<sup>&</sup>lt;sup>11</sup> National Tuberculosis Control Program, Department of Health. (2020). *Manual of Procedures 6th edition*. Manila: Department of Health.

<sup>&</sup>lt;sup>12</sup> WHO. (2015). Systematic screening for active tuberculosis, An Operational Guide. Geneva: WHO. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/181164/9789241549172\_eng.pdf

based CXR or the CXR voucher system. The 2019 JPR, however, found that a high proportion of persons identified as presumptive TB by CXR through these methods were lost early, before completing bacteriological confirmation. Only 35–48 percent of those who had an abnormal CXR in mobile vanbased TB screening were tested with Xpert MTB/RIF, 37 percent in CXR voucher program, and 67 percent in prison. According to the 2019 JPR, these losses were mainly due to a combination of lack of Xpert cartridges and prolonged CXR turnaround time (TAT). Improving case detection approaches and reducing screening and diagnostic TAT by intensifying and expanding new strategies for more sensitive, rapid case-finding and patient-centered care can help avert delayed or missed TB case confirmation and treatment. Improving active case detection and promoting rapid treatment initiation not only help reduce TB burden by directly reducing active TB cases and reducing premature deaths but they also help reduce transmission to others by treating patients.



# Figure 1.3. Role of ICF and CXR with AI-powered computer-aided detection (CAD) in finding missing TB cases

# ICF through CXR Screening with AI-Powered CAD

NTP recognizes the need to mainstream CXR screening and adopt new rapid diagnostic tools that have better TB detection accuracy (e.g., Xpert MTB/RIF) to expand TB screening and diagnostic efforts.<sup>7,8</sup> Artificial intelligence (AI)-powered CAD, studied and used in many parts of the world, is a promising solution to augment limited CXR capacity and shorten CXR TAT and improve the sensitivity of CXR, thus helping avert ELTFU and improve TB case detection. By automatically detecting and localizing abnormalities, AI-powered CAD in CXRs can save time for radiologists. Recent evaluation and systematic reviews of the diagnostic accuracy of AI software for radiologic abnormality identification by CXR for TB found AI interventions to be a promising practice, especially in settings with high TB burden.<sup>13,14</sup> For instance, CAD4TB and qXR—commercially available AI software for reading CXR—

<sup>&</sup>lt;sup>13</sup> Harris M., Qi A., Jeagal L., Torabi N., Menzies D., Korobitsyn A., Madhukar. P., et al. (2019). A systematic review of the diagnostic accuracy of artificial intelligence-based computer programs to analyze chest x-rays for pulmonary tuberculosis. *PLOS ONE 14(9)*, e0221339. https://doi.org/10.1371/journal.pone.0221339.

<sup>&</sup>lt;sup>14</sup> Qin, Z. Z., Ahmed, S., Sarker, M. S., Paul, K., Adel, A. S. S., Naheyan, T., et al. (2021). Tuberculosis detection from chest xrays for triaging in a high tuberculosis-burden setting: an evaluation of five artificial intelligence algorithms. *The Lancet Digital Health, 3(9),* e543–e554.

have consistent sensitivity of more than 95 percent while maintaining specificity above 82 percent with an overall accuracy of more than 85 percent against laboratory diagnosis by Xpert MTB/RIF (a sputum test that simultaneously detects *Mycobacterium tuberculosis* complex and resistance to rifampin [MTB/RIF]).<sup>15</sup> The WHO found that the diagnostic accuracy and overall performance of AI-powered CAD was similar to the interpretation of digital CXR by a human reader, both in screening and triage contexts.<sup>16</sup> The updated WHO TB screening guidelines recommends CAD software in place of human readers for analysis of digital CXR for TB screening and triage in individuals over 15 years. A performance evaluation of five commercially available AI algorithms—including CAD4TB (version 7), InferRead DR (version 2), Lunit INSIGHT CXR (version 4.9.0), JF CXR-1 (version 2), and qXR (version 3)—concluded that all five algorithms significantly outperformed registered radiologists in Bangladesh when reading CXRs for TB, reducing the number of Xpert tests required by 50 percent while maintaining a sensitivity above 90 percent.<sup>12</sup>

With the endorsement of NTP, the Tuberculosis Innovations and Health Systems Strengthening Project (TB IHSS) developed and implemented an innovative model for TB case finding in two large Philippine public hospitals: BatMC (between August 2019 and February 2020) and ARMMC (between September 2019 and March 2020).<sup>17</sup> TB IHSS works to assist the Department of Health (DOH) to actively identify, develop, test, and scale up innovative technologies and approaches for TB case detection, treatment-seeking, and treatment adherence interventions for vulnerable and high-risk populations. Initial results of the TB IHSS ICF model demonstrate that using AI-powered CAD in tertiary hospitals can shorten CXR TAT and improve ELTFU rates, improve laboratory test rates, and diagnose more TB cases (see Section 2 for more details).

### Good Practices and Promising Interventions

The Collaborating, Learning and Adapting for Improved Health (CLAimHealth) activity provides monitoring, evaluation, and learning support to the United States Agency for International Development (USAID)/Philippines' Health Project (2017–2023), which seeks to improve health outcomes for underserved Filipinos. CLAimHealth, one of nine current activities in USAID's Health Project, generates and uses high-quality monitoring and evaluation data, documents good practices and promising interventions (GPPIs), and conducts implementation research.

With respect to GPPIs, a good practice is defined as an intervention, technology, or methodology that, through a rigorous process of peer review and evaluation, clearly links positive effects to the practice, has been shown to be effective in a specific city and/or province, and can be replicated. A promising intervention, on the other hand, has strong quantitative and qualitative data that show positive outcome(s) but does not yet have enough evidence to support generalizable positive health outcomes and the potential for scale-up. The context, process, and outcomes of these interventions should be

<sup>&</sup>lt;sup>15</sup> Qin, Z. Z., Sander, M. S., Rai, B., Titahong, C. N., Sudrungrot, S., Laah, S. N., et al. (2019). Using artificial intelligence to read chest radiographs for tuberculosis detection: A multi-site evaluation of the diagnostic accuracy of three deep learning systems. *Scientific Reports*, *9*(*1*), 1–10.

<sup>&</sup>lt;sup>16</sup> WHO. (2021). WHO consolidated guidelines on tuberculosis. Module 2: screening–systematic screening for tuberculosis disease. Geneva: WHO.

<sup>&</sup>lt;sup>17</sup> USAID's TB IHSS Project. (2021). Good practices and promising interventions: Intensified case finding among outpatients and their companions by artificial intelligence-read chest x-ray for tuberculosis triaging. Draft Report.

assessed according to a standard set of criteria; namely, a good practice or high-impact intervention should meet most, if not all, of the following seven identified evaluation criteria: effectiveness, replicability, commitment, alignment, integration, inclusiveness, and resources.<sup>18–19</sup> Their effectiveness should be linked to the achievement of goals of the USAID Office of Health (OH) and the Health Project's high-level indicators.

For the duration of its contract (2018–2022), CLAimHealth will identify and document, on an ongoing basis, potential GPPIs of current and future USAID OH implementing partners (IPs). Collectively, these documents are designed to validate whether the recommended interventions are indeed GPPIs that should be replicated and scaled up at the national level. This report is the eighth of a technical series of selected GPPIs documented over the life of the Health Project. Figure 1.4 shows the selection process for this TB IHSS GPPI.



# Figure 1.4. Selection Process for Good Practices and Promising Interventions

 <sup>&</sup>lt;sup>18</sup> Ng E, de Colombani P. (2015). Framework for Selecting Best Practices in Public Health: A Systematic Literature Review. Journal of Public Health Research, 4(3):577. Retrieved from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4693338/</u>
 <sup>19</sup> Adamou B, et al. (2014). Guide for Monitoring Scale-Up of Health Practices and Interventions. MEASURE Evaluation PRH.

Retrieved from: https://www.measureevaluation.org/resources/publications/ms13-64

<sup>&</sup>lt;sup>19</sup> WHO. (2017). A Guide to Identifying and Documenting Best Practices in Family Planning Programmes. Geneva: World Health Organization. Retrieved from: https://www.who.int/reproductivehealth/publications/family\_planning/best-practices-fp-programs/en/

#### Assessing the Cost-Effectiveness of Mainstreaming CXR Screening

CLAimHealth recognizes the need to address the challenges of TB screening, particularly in health facilities, and the potential of mainstreaming CXR screening with AI-powered CAD to reduce the number of undetected TB cases. This study, in collaboration with CLAimHealth and TB IHSS, documents the health and socioeconomic benefits and cost-effectiveness of mainstreaming CXR screening with either AI-powered CAD or human readers. Section 2 of this report provides a brief background on the key features of TB IHSS's ICF model and key highlights of its pilot implementation. This pilot implementation provides important lessons and insights for mainstreaming CXR screening in tertiary hospitals. Section 3 presents the objective of this study and the learning questions it addresses. It outlines the assessment framework and methodology of this study. Finally, Section 4 presents the results of the study and their policy implications. Annexes I-4 describe the detailed process and assumptions used to estimate the cost-effectiveness of mainstreaming CXR screening and to describe its socioeconomic benefits.

# 2. TB IHSS's INTENSIVE CASE FINDING BY CXR SCREENING WITH AI-POWERED CAD

As shown in Figure 2.1, the key features of the TB IHSS ICF model include health promotion activities before and during implementation, the use of CXR screening with AI-powered CAD among outpatients and their companions, on-the-spot sputum sample collection, and use of Xpert MTB/RIF for TB diagnosis.<sup>15</sup> Unlike symptom-based screening (see Figure 1.2), the TB-IHSS ICF model offers CXR screening to all patients and their companions, regardless of the presence of any TB sign or symptom. Depending on their CXR finding, clients (i.e., patients and their companions) are either referred to undergo an Xpert MTB/RIF test (i.e., if either they are symptomatic or their CXR result is suggestive of TB) or they are discharged (i.e., asymptomatic and CXR result not suggestive of TB). If *Mycobacterium tuberculosis* without rifampicin resistance (MTB+/-RR/TB) is detected, the client will be recommended to initiate treatment and the DOH will be notified of the case. Otherwise, the client will be endorsed for further clinical examination. To offer CXR screening and accommodate all willing patients and their companions, the project provided additional staff and equipment during its pilot implementation.



Figure 2.1. TB IHSS ICF algorithm<sup>20</sup>

### CXR Screening Caseload

During the pilot implementation, TB IHSS conducted screening activities in BatMC and ARMMC four days a week, usually from Monday until Thursday, excluding holidays. Over seven months, the screening activities served a total of 12,277 clients.<sup>21</sup> Around 64 clients per day (including their companions) were

<sup>&</sup>lt;sup>20</sup> Source: TB IHSS

<sup>&</sup>lt;sup>21</sup> According to TB IHSS, 15 percent of clients attributed their participation to poster advertisements via social media and public announcements at the outpatient department of the study hospitals.

screened in BatMC (between August 2019 and February 2020) and 76 clients per day in ARMMC (between September 2019 and March 2020). Patient companions represent a substantial share of these numbers (i.e., BatMC: 43.8 percent; ARMMC: 47.4 percent). Figure 2.2 shows the average daily number of patients screened per week in the two pilot hospitals during implementation. The greatest number of clients screened in a day was 171 in ARMMC (November 19, 2019) and 128 in BatMC (August 20, 2019), whereas the least number was 20 in ARMMC (October 3, 2019) and 7 in BatMC (August 16, 2010).<sup>22</sup> With the start of the coronavirus disease 2019 (COVID-19) pandemic in February 2020, the government assigned ARMMC as a major COVID-19 referral hospital and priority was given to COVID-19 response. Despite this, the average number of clients screened in ARMMC remained high at around 89 per day in February 2020 and around 91 per day in the first half of March 2020, prior to the implementation of enhanced community quarantine, effective March 15, 2020. However, the temporary closure of outpatient departments was subsequently implemented to limit the spread of COVID-19.



Clients include patients and their companions screened. ARMMC data are from September 2019 to March 2020. BatMC data are from August 2019 to February 2020.

#### Figure 2.2. Average daily number of clients screened in TB IHSS pilot hospitals<sup>23</sup>

#### Additional TB Cases Diagnosed and TAT

Among 12,277 clients screened in the two pilot hospitals, 3,377 or 27.5 percent (BatMC: 24.9 percent; ARMMC: 30.3 percent) were identified as presumptive TB cases (see <u>Table 2.1</u>). Among patients screened, 1,963 or 29.3 percent and 1,414 or 25.3 percent among companions screened were identified as presumptive TB cases. Of them, only 2,840 (84.1 percent) submitted sputum samples for diagnostic purposes. Sputum submission rates were similar for both patients (84.6 percent) and their companions (83.4 percent) and were much higher than the sputum submission rate among ICF programs organized via mobile CXR van-based (35–48 percent) and CXR voucher (37 percent) screening activities. Of the 2,840 people tested by Xpert MTB/RIF, 196 people (127 patients; 69 companions) were bacteriologically

<sup>&</sup>lt;sup>22</sup> Caseload was especially low during some operating days because of some unavoidable circumstances, such as implementation of project activities (e.g., dry run), volcanic eruption (Taal volcano), technical issues, low outpatient attendance, or majority had already been screened.

<sup>&</sup>lt;sup>23</sup> Source: TB IHSS database

confirmed as having TB (BCTB). Of the 196 BCTB cases, 98 or half had at least one TB sign/symptom, whereas the other half were asymptomatic. Of them, almost 65 percent, or 127, were patients and 35 percent, or 69, were companions. Albeit lower than the BCTB yield rate among patients (1,914 per 100,000), the yield rate among patient companions (1,235 per 100,000) was more than twice the national TB incidence (554 per 100,000), confirming the need to include them in screening activities. The inclusion of companions in the TB IHSS ICF model serves as a community outreach activity.

Of the 3,377 presumptive cases, 484 were clinically diagnosed with TB (CDTB). These cases did not fulfill the criteria for bacteriological confirmation but were diagnosed by the attending physicians based on clinical findings, X-ray abnormalities, suggestive histology, or other biochemistry or imaging tests.

This brings the total number of TB cases diagnosed to 680 (BatMC: 225; ARMMC: 455). The overall TB detection rate among all screened clients in the two hospitals was high, at around 5,539 per 100,000 (BatMC: 3,501 per 100,000; ARMMC: 7,776 per 100,000). This is almost ten times the estimated national TB incidence (0.55 percent or 554 per 100,000 population) and almost five times the national TB prevalence (1,159 per 100,000). However, only 264 (BatMC: 124; ARMMC: 140) or 38.8 percent of all patients with a diagnosed TB case initiated treatment within 20 days of their initial consultation. This is lower than the expected treatment initiation rate.<sup>24</sup> Nonetheless, without the intervention, most of the TB cases that were detected and initiated to treatment would have been missed or diagnosed later. All initiated treatments were notified in the national TB database, increasing the total number of notified cases in the two facilities in the same period.

<sup>&</sup>lt;sup>24</sup> Among the factors that TB IHSS identified as possible reasons for the low treatment initiation rate were: the delay in diagnostic TAT, which was often over one month because of overloaded laboratories in the hospitals during the initial period of the project; lack of communication between hospital laboratory staff, hospital management teams, and project staff; and inability to trace patients due to incorrect phone numbers.

Table 2.1. Cases screened and diagnosed <sup>25</sup>							
Indicator	Total	BatMC (Aug 2019– Feb 2020)	<b>ARMMC</b> (Sept 2019– Mar 2020)				
Clients screened (patients and their companions)	12,277	6,426	5,85 I				
Presumptive TB (both by CXR and S/s)	3,377	1,602	1,775				
Percent of clients screened	27.5	24.9	30.3				
BCTB cases	196	95	101				
Percent of clients screened	1.6	1.5	1.7				
Yield by CXR presumptive only	98	49	49				
Percent of clients screened	0.8	0.8	0.8				
Yield by S/s presumptive only	22	14	8				
Percent of clients screened	0.2	0.2	0.1				
Yield by S/s and CXR presumptive	76	32	44				
Percent of clients screened	0.6	0.5	0.8				
CDTB cases	484	130	354				
Percent of clients screened	3.9	2.0	6.1				
Total TB cases diagnosed	680	225	455				
Percent of clients screened	5.5	3.5	7.8				
Treatment initiation	264	124	140				
Percent of clients screened	2.2	1.9	2.4				
Percent of TB cases diagnosed	38.8	55.I	30.8				

Note: Percentage values may not add up because of rounding.

Table 2.2 shows the TAT at different stages of TB care in the two hospitals. With AI-powered CAD, it takes less than a day to undergo CXR screening and get results. CXR screening with AI-powered CAD for TB, which also allows same-day sputum collection, reduces ELTFU by eliminating the need for a second visit to receive the CXR result, which entails additional time and cost for the patients and their companions. Likewise, by reducing the frequency of visits per patient, it would reduce the existing TBrelated caseload in the radiology department of these hospitals. This may result in a shorter waiting time for other patients without TB who require X-ray service, which indicates that the model has potential as a good practice worth investing in and scaling up.

<sup>&</sup>lt;sup>25</sup> Source: TB IHSS database

Table 2.2 TAT at different stages of cascade of care (in days) <sup>26</sup>							
	Total	B	at <b>MC</b>	ARMMC			
Stage of care		Patient	Companion	Patient	Companion		
CXR screening to Xpert MTB/RIF results	4.73	3.23	4.73	6.41	5.03		
Screening to CXR results	<	<	<	<	<		
CXR screening to sputum collection	0.42	0.45	0.72	0.32	0.22		
Sputum submission to Xpert result	3.96	2.81	4.06	5.63	3.90		
Lab results to treatment initiation	13.8	15.97	13.58	11.43	9.40		
CXR screening to treatment initiation	20.30	18.47	22.08	20.54	21.30		

BatMC data include the period between August 2019 and February 2020. ARMMC data include the period between September 2019 and March 2020.

Estimates by the TB IHSS suggest that, for the pilot implementation at BatMC and ARMMC, the cost per BCTB case detected with an "official" CXR reading is USD 1,358 or without an "official" CXR reading is USD 996 (see Table 2.3). Estimates by the TB IHSS suggest that the cost per BCTB case detected is USD 1,358 with a CXR reading by a radiologist or USD 996 without an official CXR reading (see Table 2.3). Interestingly, although the health promotion activities represent only less than 0.7 percent of the total cost of the TB IHSS ICF model, 15 percent of the clients attribute their participation to print and social media posters. Meanwhile, 43 percent of clients attributed their participation to hospital staff, whereas 39.5 percent attributed theirs to project screeners.

Table 2.3 Pilot implementation unit costs (in PHP) <sup>27</sup>						
Item	Cost per case screened	Cost per BCTB case diagnosed				
CXR official reading cost	300	18,696				
AI CAD software license (Qure.ai)	47	2,953				
Xpert test (PhilSTEP: PHP 1,500)	347	21,624				
Communications cost	2	104				
Professional services (screener, team lead)	32	1,996				
Health promotion	8	472				
Mobile x-ray service	367	22,871				
Others (laptop, meetings, trainings)	24	1,470				
Total	1,126	70,187				
(in USD at USD 1 : PHP 51.7)	USD 22	USD 1,358				
Total cost without official reading	826	51,491				
(in USD)	USD 16	USD 996				

<sup>&</sup>lt;sup>26</sup> Source: TB IHSS database.

<sup>&</sup>lt;sup>27</sup> Source: TB IHSS database

# 3. LEARNING OBJECTIVES AND METHODOLOGY

# 3.1. Learning Objectives

Building on TB IHSS's initial work, this study addresses the following policy and learning questions about mainstreaming CXR screening through an in-depth cost-effectiveness analysis (CEA) and a descriptive analysis of its socioeconomic benefits.

Policy question I: Is mainstreaming CXR screening with either AI-powered CAD or human readers cost-effective?

• Learning questions: As compared to symptom-based screening, what is (1a) the additional cost of CXR screening per case; (1b) the cost per disability-adjusted life year (DALY) averted; and (1c) the estimated reduction in TB incidence and mortality?<sup>28</sup>

Policy question 2: As compared to symptom-based screening, how well will mainstreaming CXR screening result in improved financial risk protection for patients?

• Learning questions: As compared to symptom-based screening, how well will CXR screening compare in terms of (2a) patient time, (2b) out-of-pocket (OOP) costs, (2c) productivity losses, and (2d) potential for reduction of TB-related catastrophic costs among patients?

Using reliable local data, this study provides evidence regarding the health and socioeconomic benefits and cost-effectiveness of mainstreaming CXR screening with either AI-powered CAD or human readers. This can help fill the gap in the literature, support national and local policy decision-making, promote of the use of AI-powered CAD and similar interventions, and expand future adoption of CXR screening in the Philippine setting.

# 3.2. Analytical Framework

This study follows the U.S. Government's Assessment Methodology for Economic Analysis, WHO's Guide to CEA, and DOH's Health Technology Assessment (HTA) Method Guide.<sup>29–30</sup> It compares the additional costs, intermediate health outcomes (i.e., TB cases detected, initiated to treatment, and treated), and other socioeconomic benefits (i.e., transport cost savings, time savings, and productivity losses averted) of the two CXR screening alternatives (SAs) for TB ICF with symptom-based screening as the base screening alternative without intervention or status quo:

- SAI: Symptom-based screening (status quo),
- SA2: Expanded CXR screening with AI-powered CAD, and
- SA3: Expanded CXR screening with human readers.

<sup>&</sup>lt;sup>28</sup> Quality-adjusted life-year (QALY) is another composite measure that is more frequently used in developed countries and has limited application in developing countries. Lack of data limit the ability to reliably calculate QALY.

<sup>&</sup>lt;sup>29</sup> U.S. Government Accountability Office. (April 2018). Assessment Methodology: Economic Analysis.

<sup>&</sup>lt;sup>31</sup> WHO. (2003). Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: WHO.

<sup>&</sup>lt;sup>30</sup> Health Technology Assessment Unit, Department of Health–Philippines. (2020). Philippine HTA Methods Guide.

### Screening Alternatives

SAI (symptom-based screening), which serves as the base screening alternative in this study (i.e., no intervention), entails no additional investment. It refers to the systematic screening of patients using the four signs and symptoms of TB as the primary screening tool for TB in health facilities (see Figure 3.1). It identifies a case as presumptive TB based on the presence of any of the four signs and symptoms for at least two weeks. It will then refer asymptomatic patients for optional CXR screening, except those who have already undergone testing in the past year. However, given the current limited capacity of radiology units in health facilities, only a small fraction of patients opt for CXR screening, and many are lost early because of long TAT (i.e., more than one day). SAI identifies patients who are either symptomatic or asymptomatic but with CXR finding suggestive of TB as presumptive cases and recommends them for Xpert MTB/RIF testing. It discharges patients otherwise and recommends those diagnosed with TB for treatment.



Figure 3.1. Decision tree: TB screening alternatives

SA2 refers to mainstreaming the use of CXR screening with AI-powered CAD. It also entails the assessment of TB signs and symptoms as in SA1, but instead of symptom-based screening, CXR screening is the primary screening tool for ICF under SA2. All patients and their companions undergo CXR screening under SA2 regardless of whether they present any TB S/s or not (see Figure 3.1). It identifies presumptive TB cases as those who are either symptomatic or asymptomatic but with CXR findings suggestive of TB. It recommends them for Xpert MTB/RIF testing. It will discharge patients otherwise. In compliance with the standard TB screening procedure, a registered radiologist will review and certify all CXR findings. Finally, as in SA1, SA2 will recommend treatment for patients diagnosed with TB. Unlike SA1, SA2 requires additional capital investment (i.e., digital CXR and AI-powered CAD) and human resources (HR, including screeners or nurses, a radio technician, and a radiologist) to accommodate more patients and their companions. To maximize the benefits from the investment,

patients and their companions will be encouraged to avail of the TB screening service through costeffective health promotion strategies. Figure 3.2 illustrates the health impact of mainstreaming CXR screening. By expanding the capacity for CXR screening, SA2 can accommodate additional cases and find missing cases in health facilities. As demonstrated by the TB IHSS project in BatMC and ARMMC, it can reduce CXR TAT to less than a day (supply-side effect), as well as ELTFU rates (demand-side effect). SA2 can detect more TB cases than SA1 and refer them for treatment. As a result, it can avert more morbidities and premature deaths due to TB compared with SA1.



Figure 3.2. Health impact of mainstreaming CXR screening

SA3 (expanded CXR screening with human readers) also entails mainstreaming the use of CXR screening for all patients and their companions as in SA2 (see Figure 3.1). However, human readers are, deployed instead of an AI-powered CAD. Like SA2, SA3 also entails symptom screening for all patients and their companions. SA3 will also identify those who are symptomatic as presumptive cases, as well as those asymptomatic but with CXR findings suggestive of TB. SA3 will recommend them for Xpert MTB/RIF testing. It will discharge patients otherwise. A radiologist will certify all CXR findings before diagnosis. Finally, as in SA1 and SA2, SA3 will recommend treatment for patients diagnosed with TB. Like SA2, SA3 requires additional capital, HR, and health promotion campaigns to encourage and accommodate more patients and their companions. However, unlike SA2, SA3 requires digital CXR only and instead deploys only two radiologists to read, interpret, and generate CXR findings for all patients and their companions.<sup>31</sup> Overall, SA3 will have similar supply-side and demand-side effects and intermediate health impact as SA2 (see Figure 3.2). Specifically, SA3 can likewise result in more cases screened, lower CXR TAT, and lower ELTFU rates. It can detect more TB cases than SA1 and recommend them for treatment. As a result, it can avert more morbidities and premature deaths due to TB compared with SA1.

### Assessment Indicators

<u>Table 3.1</u> summarizes the indicators this study uses to address the policy and learning questions presented earlier. The study retrospectively estimates the incremental cost-effective ratios (ICERs) of mainstreaming CXR screening in health facilities, which entails shifting to CXR screening as the primary screening tool and expanding screening capacity. It estimates the additional investment costs and health outcomes for the two CXR screening alternatives, SA2 and SA3, compared with symptom-based

<sup>&</sup>lt;sup>31</sup> CXR with human readers, or SA3, requires two radiologists to meet same demand for CXR and maintain the same CXR TAT as with AI-powered CAD or SA2.

screening (SA1) or the status quo scenario over an economic life of ten years.<sup>32</sup> It also describes and compares the likely socioeconomic impact of mainstreaming CXR screening among patients in terms of patient waiting and travel time reductions and financial risk protection relative to no intervention. It considers potential reductions in OOP costs, labor productivity losses, and catastrophic TB-related costs—OOP expenditures and indirect costs exceeding a given threshold of household income (e.g., 20 percent). Sections 3.3 and 3.4 outline the methodology for estimating these indicators while Annexes I—3 discuss them in more detail.

Table 3.1 Indicators for addressing learning questions					
Learning Questions	Indicators				
1. Is mainstreaming CXR screening with either Al- powered CAD or human readers cost-effective? As compared to symptom-based screening, what is (1a) the additional cost of CXR screening per case; (1b) the cost per DALY averted; and (1c) the estimated reduction in TB incidence and mortality?	<ul> <li>ICERs of CXR screening with either Alpowered CAD or human readers/additional cost per DALY averted</li> <li>Additional cost per case screened</li> <li>Estimated reduction in TB incidence and mortality</li> </ul>				
2. As compared with symptom-based screening, how well will mainstreaming CXR screening with either Al- powered CAD or human readers result in improved financial risk protection for patients? How well will CXR screening with either Al-powered CAD or human readers compare in terms of (2a) patient time, (2b) OOP costs, (2c) productivity losses, and (2d) potential reduction in TB-related catastrophic costs among patients?	<ul> <li>Time savings per case screened</li> <li>OOP costs savings per case screened</li> <li>Productivity losses averted per case screened and TB case treated</li> <li>Cost savings as a percent of household income per case screened and TB case treated</li> </ul>				

# 3.3 Cost-Effectiveness Analysis

### Cost-Effectiveness Indicator

CEA compares the costs and outcomes of alternative interventions or policy options (e.g., SA2 and SA3). ICERs are the main results of a CEA and can be used as a basis for selecting the intervention with the least cost for every unit of health impact.<sup>33</sup> The formula for measuring ICER or cost per DALY is as follows:

<sup>&</sup>lt;sup>32</sup> According to the European Society of Radiology, radiological equipment has an average useful life of five to ten years with annual maintenance and updates. Beyond this period, equipment is no longer state-of-the art and replacement is essential. Aside from high risk of failures and breakdowns, which might cause delays in diagnosis and treatment, operating costs of older equipment will be higher than new equipment.

European Society of Radiology (ESR). (2014). Renewal of radiological equipment. *Insights into imaging*, 5(5), 543-546. <sup>33</sup> Bertram, M. Y., Lauer, J. A., De Joncheere, K., Edejer, T., Hutubessy, R., Kieny, M. P., and Hill, S. R. (2016). Cost-effectiveness thresholds: pros and cons. *Bulletin of the World Health Organization*, 94(12), 925.

$$ICER_i = \frac{C_i - C_a}{H_i - H_a}$$

where:

C is the cost of intervention, H is the health outcome expressed in terms of years of DALY, i refers to intervention, and a refers to baseline comparator or status quo (i.e., SAI).

According to WHO and Commission on Macroeconomics and Health,<sup>34</sup> an intervention is considered:

- a) Not cost effective if ICER > gross domestic product (GDP) per capita x3,
- b) Cost effective if ICER < GDP per capita x3, and
- c) Very cost effective if ICER < GDP per capita.

This study uses a time discount rate of 3 percent to discount the economic costs of the intervention and DALYs averted to be consistent with the Commission on Macroeconomic on Health.<sup>35</sup> It also used a 7 percent time discount rate in its sensitivity analysis.

#### **Economic Costs**

Assuming SAI as the status quo, the study estimates the incremental or additional economic costs that each of the two CXR screening interventions, SA2 and SA3, entails over a period of ten years. It considers the following additional direct costs for mainstreaming CXR screening and maintaining it: (i) capital investment costs (excluding taxes) and (ii) recurrent or maintenance and operating expenses. All prices are expressed in 2021 prices and exclude taxes. Capital investment costs include costs of a digital X-ray system, laptop, and training of staff for both SA2 and SA3. In addition, SA2 requires licensed CAD software. The recurrent costs for both interventions include HR complement, support and maintenance, health promotion and communications, and other operating costs, including supplies, electricity, and contingencies. SA2's HR requirements include two screeners/nurses to accommodate additional patients, a radio technician to operate the digital X-ray system, and a registered radiologist to certify the CXR findings. SA3 requires the same set of HR plus an additional registered radiologist. Unlike SA2, SA3 relies on two radiologists to read, interpret, and generate CXR findings for all patients and their companions. Annex I provides a detailed description of each cost item, including data sources, assumptions, and the rationale for including them. Because the study measures health impacts based on the number of TB patients treated, it also adjusts for the additional costs for diagnostic and treatment using TB IHSS data and other relevant studies.

<sup>&</sup>lt;sup>34</sup> WHO Commission on Macroeconomics and Health & World Health Organization. (2001). *Macroeconomics and health: investing in health for economic development: executive summary / report of the Commission on Macroeconomics and Health.* World Health Organization. Retrieved from <u>https://apps.who.int/iris/handle/10665/42463</u>

<sup>&</sup>lt;sup>35</sup> This implies that a year of life gained today will be valued more than a year of life gained next year.

### Health Impact

The study quantifies the incremental health impact  $(H_i - H_a)$  for each intervention (SA2 and SA3) relative to the status quo (SA1) by converting the number of additional patients screened, diagnosed, and treated under the intervention over a period of ten years in terms of DALY.

 $H_i - H_a = (h_i - h_a) \times DALY$  per case detected

where  $(h_i - h_a) = \Delta h_i$  represents the number of additional TB cases diagnosed.

The number of additional cases screened and TB cases diagnosed under SA2 and SA3 relative to SA1 are estimated using TB IHSS data, with some adjustments related to other interventions, which are beyond the scope of this study. In addition, the number of additional cases screened under SA3 are subject to the capacity of human readers and target CXR TAT. Annex 2 provides more details on how the study measures the health impact of each intervention and summarizes its data requirements.

DALY is a composite indicator that combines both morbidity and mortality impacts into a single measure. It is the number of years lost due to ill-health, disability, or premature death. It is the sum of years of life lost (YLL) and years lived with disability (YLD).

DALY = YLL + YLD

where  $YLL = N \times L$  and  $YLD = I \times DW \times d$ .

YLL is derived by multiplying the number of disease-specific deaths by age (*N*) with the standard life expectancy at the age of death (*L*). This study estimates TB deaths by age by applying the national TB death rate to age-disaggregated population data.<sup>36</sup> It uses data on population and standard life expectancy at the age of death, *L*, from the United Nation's Department of Economics and Social Affairs World Population Prospects 2019 database.<sup>37</sup> To measure YLD, the number of TB cases diagnosed (*I*) is multiplied by the average duration of the disease (*d*) and a disability weight factor (*DW*) that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead).<sup>38</sup> The study relies on WHO database for the country's TB incidence or number of cases diagnosed and the Global Burden of Disease Collaborative Network's estimate for the disability weight factor (*DW* = 0.333).<sup>39,40</sup> Duration data (*d* = two years)—the average duration of untreated TB minus the treatment duration—is based on other

<sup>&</sup>lt;sup>36</sup> According to WHO (2020), there are 25 TB-related deaths in the Philippines per 100,000 population. Age-disaggregated TB death rate is unavailable.

<sup>&</sup>lt;sup>37</sup> United Nations Department of Economic and Social Affairs (UNDESA), Population Dynamics. (2019). World Population Prospects 2019. Retrieved from https://population.un.org/wpp/Download/Standard/Population

<sup>&</sup>lt;sup>38</sup> In the burden of disease literature, the term disability is used broadly to refer to departures from good or ideal health. <u>https://www.who.int/quantifying\_ehimpacts/publications/en/9241546204chap3.pdf</u>.

<sup>&</sup>lt;sup>39</sup> WHO. (2020). WHO TB incidence estimates disaggregated by age group, sex, and risk factor. Retrieved from https://www.who.int/teams/global-tuberculosis-programme/data

<sup>&</sup>lt;sup>40</sup> Global Burden of Disease Collaborative Network. (2020). *Global Burden of Disease Study 2019 (GBD 2019) Disability Weights*. Seattle, USA: Institute for Health Metrics and Evaluation (IHME). Retrieved from: <u>http://ghdx.healthdata.org/record/ihme-data/gbd-2019-disability-weights</u>

studies.<sup>41,42</sup> This study omits the long-term impacts of TB on those who will recover from the disease and on their communities through a possible reduction in community infection rates, which could be a subject of a different study. This simplifies computation, but it will most likely underestimate YLD, albeit by a relatively small amount given its unit of analysis (i.e., hospital). Finally, to get the average DALY per case detected and treated, we divided the estimated DALY for TB by the total number of TB cases in the country (see <u>Annex 3</u> for more details).

#### Sensitivity Analysis

To assess how possible changes in key variables will affect the cost-effectiveness of mainstreaming CXR screening with either AI-powered CAD or human readers, the study performs a sensitivity analysis by varying the following key variables: discount rate, utilization rate, and recurrent costs. The DOH's HTA Method Guide recommends a 7 percent discount rate. Compared to a lower discount rate, a higher discount rate values future costs and life gained less. The ratio of the percentage change in ICER to the percentage change in the variable tested (e.g., sensitivity indicator) measures the responsiveness of the intervention's cost-effectiveness to key variable changes. To further aid future program planning and decision-making, the study computes the switching value of key variables—the value at which the incremental cost-effectiveness of CXR screening becomes marginal (i.e., ICER = GDP per capita x3).

### 3.4 Descriptive Analysis of the Possible Socioeconomic Costs and Benefits of Mainstreaming CXR Screening with Either AI-Powered CAD or Human Readers

Because of data constraints, the study does not perform a comprehensive quantitative assessment of the socioeconomic benefits of mainstreaming CXR screening with either AI-powered CAD or human readers. Nonetheless, it describes the socioeconomic benefits of SA2 and SA3 among patients (demand side), which will mainly flow from the additional life years saved or productivity losses averted due to increased early diagnosis and treatment of TB and other savings in terms of patient time and OOP expenses. These cost savings translate into a reduction in financial burden or additional financial protection among patients with TB. Because SA2 and SA3 will result in the same reduction in CXR TAT and an increase in cases screened, these interventions will generate equal socioeconomic benefits.

<sup>&</sup>lt;sup>41</sup> Studies of the natural history of TB disease in the absence of treatment, the duration of pulmonary tuberculosis from onset to cure or death is approximately three years (Tiemersma et al. 2011). A more recent study by Ragonnet et al. (2021) suggests that sputum smear–positive pulmonary TB (SP-TB) has an average duration of 1.57 years, whereas it is 5.35 years for culture-positive pulmonary TB (but smear-negative). SP-TB comprises around 75–80 percent of pulmonary TB (PTB), which represents 85 percent of global TB cases. This implies that the average duration of untreated TB is around 2.3–2.7 years.

Ragonnet, R., Flegg, J. A., Brilleman, S. L., Tiemersma, E. W., Melsew, Y. A., McBryde, E. S., and Trauer, J. M. (2021). Revisiting the natural history of pulmonary tuberculosis: A Bayesian estimation of natural recovery and mortality rates. *Clinical Infectious Diseases*, 73(1), e88–e96.

Tiemersma, E. W., van der Werf, M. J., Borgdorff, M. W., Williams, B. G., and Nagelkerke, N. J. (2011). Natural history of tuberculosis: duration and fatality of untreated pulmonary tuberculosis in HIV negative patients: a systematic review. *PLOS ONE*, 6(4), e17601.

<sup>&</sup>lt;sup>42</sup> According to WHO (2020), a six-month regimen of four first-line drugs (i.e., isoniazid, rifampicin, ethambutol, and pyrazinamide) is the currently recommended treatment for drug-susceptible TB.

WHO. (2020). Global Burden of Disease Study 2019. Geneva: World Health Organization; 2020. Licens.0e: CC BY-NC-SA 3.0 IGO. Retrieved from: <u>https://www.who.int/teams/global-tuberculosis-programme/data</u>

#### Time Savings

Without intervention (SA1), TB screening and diagnosis in hospitals may require two or more visits. The initial hospital visit entails symptom screening and CXR as needed. The second hospital visit entails retrieving CXR findings and providing a sputum sample as needed. By causing the same improvements in CXR TAT, both SA2 and SA3 can equally save the patients undergoing TB screening and their companions a second hospital visit.<sup>43</sup> Same-day release of CXR findings can reduce travel time and costs for patients and their companions (e.g., family, guardians, or significant others). This study estimates the roundtrip travel and waiting time savings per patient screened, along with their companion, using data from the TB IHSS database and Google maps (see <u>Annex 4</u> for more details). Because studies measuring the actual duration of patient visits in Philippine health facilities are rare, this study computes for time savings per patient by assuming each visit will take an average of around four hours, including waiting in line but excluding travel time to and from the facility.<sup>44,45</sup>

#### Productivity Losses Averted

As mentioned earlier, the study also estimates the economic value of productivity losses averted under SA2 and SA3 based on DALYs averted due to early diagnosis and treatment and time savings per case screened. It estimates the former by multiplying the estimated DALYs averted (see Section 3.3) by the average GDP per capita. It then estimates the economic losses averted during screening by multiplying the waiting and travel time savings per case by the average wage, and regional employment rates (for more details, see Annex 4). For both the patients and their companions, shorter wait and travel times due to faster CXR TAT imply less time away from productive activities, such as their jobs or household chores. If not averted, such losses represent indirect patient costs.

### **OOP Cost Savings**

In addition to indirect cost savings, shorter CXR TATs may also generate travel and other direct cost savings. Due to lack of data, the study only estimates the travel cost savings per case screened using data from TB IHSS database and public fare matrix (see <u>Annex 4</u> for more details).

<sup>&</sup>lt;sup>43</sup> In primary care facilities, more than one additional visit may be necessary before TB treatment initiation, bringing the average number of trips to 2.4 visits (Tomeny et al., 2020).

Tomeny, E., Mendoza, V. L., Marcelo, D. B., Barrameda, A. J. D., Langley, I., Abong, J.M., et al. (2020). Patient-cost survey for tuberculosis in the context of patient-pathway modelling. *International Journal of Tuberculosis and Lung Disease*, 24(4), 420-427. <sup>44</sup> Dayrit, M.M., Lagrada, L.P., Picazo, O.F., Pons, M.C., and Villaverde, M.C. (2018). *The Philippines health system review*. World Health Organization. Regional Office for South-East Asia.

<sup>&</sup>lt;sup>45</sup> A national study of public hospitals in Malaysia indicates that while an actual outpatient consultation with a medical professional takes only around 15 minutes, the waiting time for patients can take more than two hours from the time of registration (Pillay et al., 2011).

Pillay, D.I., Ghazali, R.J.D.M., Abd Manaf, N. H., Abdullah, A. H. A., Bakar, A. A., Salikin, F., et al. (2011). Hospital waiting time: the forgotten premise of healthcare service delivery? *International Journal of Health Care Quality Assurance*, 24(7), 506-522.

#### **Financial Protection**

Finally, the study considers a possible reduction in TB-related catastrophic costs among patients at the screening and diagnostic stages of care due to either SA2 and SA3. It estimates the direct and indirect cost savings per case as a proportion to average household income (see <u>Annex 4</u> for more details).

### 3.5 Scope and Limitations

As discussed earlier, the study focuses on the cost-effectiveness of mainstreaming CXR screening with either Al-powered CAD or human readers. Evaluation of the incremental cost-effectiveness of the TB IHSS ICF intervention ("CXR screen-all approach") in the two hospitals, which is beyond the scope of this study, entails additional data and analysis aside from TB IHSS data.<sup>46</sup> This study considers most of the additional input costs during pilot implementation (excluding mobile X-ray services and some professional services; Section 3.3). In addition, it considers the treatment costs required to achieve the intervention's intermediate impact but which were beyond the scope of the pilot implementation. Daily caseload during the pilot implementation serves as a basis for computing demand or caseload in this study. It estimates the health impact based only on the additional TB cases diagnosed because of the intervention. It excludes the proportion of the TB cases diagnosed through the intervention that could have been found even without the intervention (SAI). Detailed assessment of factors (e.g., feasibility, user and social acceptability, adoption, appropriateness, reach, affordability, and sustainability of mainstreaming CXR screening) with either AI-powered CAD or human readers, which may pose implementation risks for either CXR screening alternative (i.e., with Al-powered CAD or human readers) are likewise beyond the scope of this study. This study recommends these important factors for further investigation. Also, this study does not assess the affordability of mainstreaming CXR screening at the local level, but it should be considered according to varying local incomes and budgets. Nonetheless, to aid decision-making, Section 4.1 presents how much it will cost to install and maintain a CXR screening package for ICF in a public hospital.

The study draws mainly on reliable local data, but it has certain limitations due to its design and some data constraints. Interpretation of findings must consider the study's scope and limitations. First, the study focuses only on the immediate and direct impacts of mainstreaming CXR screening for ICF on the health of patients with TB. It did not estimate the possible long-term contribution of mainstreaming CXR screening to local control of TB transmission, which limits the interpretation timeframe of the study findings. This can be significant when the intervention is implemented on a large scale.<sup>47</sup> Second, because the data used were mostly from the two government tertiary hospitals in Luzon, the study's estimates for the base scenario do not reflect other health care settings (e.g., primary and secondary health care settings, private sector settings) and other geographical regions. Cost differences in adopting the same technology across health care settings are likely. Nonetheless, the results of this study's sensitivity analysis provide insights into the cost-effectiveness of the intervention in other settings.

<sup>&</sup>lt;sup>46</sup> For instance, it may require a retrospective analysis of caseload and total implementation cost (from screening to treatment) associated with the current ICF model in the two study hospitals.

<sup>&</sup>lt;sup>47</sup> Available data to forecast the long-term effects of active case-finding, such as costs, are limited and measured differently. Sohn, H., Sweeney, S., Mudzengi, D., Creswell, J., Menzies, N. A., Fox, G. J., et al. (2021). Determining the value of TB active case-finding: current evidence and methodological considerations. *The International Journal of Tuberculosis and Lung Disease*, *25(3)*, 171–181.

Cost-effectiveness is sensitive to regional variations in demand for health services and local supply of inputs. For instance, health-seeking behavior and treatment success may be significantly different in Visayas, Mindanao, or even in other parts of Luzon. Section 4.1 discusses how the main results of this study apply to other similar settings and how the results of the sensitivity analysis can capture other settings.

Another limitation is that the study does not consider the prevalence of human immunodeficiency virus (HIV) and other severe infections (e.g., COVID-19). As such, it may slightly underestimate the costeffectiveness of mainstreaming CXR screening interventions. Because of the unavailability of site data, the base scenario of this study's CEA does not account for the COVID-19 pandemic impact on caseload. Nonetheless, given the findings of another study on the impact of COVID-19–related disruptions on TB services in the country, <u>Section 4.1</u> discusses the likely impact of the COVID-19 pandemic on the costeffectiveness of the intervention, along with the results of this study's sensitivity analysis.<sup>48</sup> Finally, the full benefits of mainstreaming CXR screening are significantly higher. As discussed in <u>Section 3.4</u>, this study does not quantify several benefits, including improvements in quality of care and quality of life among patients and their families, which are not easily quantifiable.

# 3.6 Legal and Ethical Considerations

All data collection, processing, and analysis in this study observed Republic Act No. 10173, otherwise known as the Data Privacy Act. As the study relies on secondary data and did not use any confidential or private information, the study did not require any institutional review board approval. All data sets used were anonymized. Presentation and reports only include aggregate data. The consultant team signed a non-disclosure agreement specifying that they cannot discuss or share matters about the documentation with persons or institutions not connected with the study, published, or posted on social media platforms, broadsheets, other publications, and mass media outlets.

<sup>&</sup>lt;sup>48</sup> Klinton, J.S., Heitkamp, P., Rashid, A., Faleye, B. O., Htat, H. W., Hussain, H., *et al.* (2021). One year of COVID-19 and its impact on private provider engagement for TB: A rapid assessment of intermediary NGOs in seven high TB burden countries. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases, 25*.

# 4. **RESULTS AND RECOMMENDATIONS**

Health interventions entail additional investment but bring important health and economic benefits, as demonstrated in this study. To optimize the use of public resources, it is important to assess which among the feasible alternatives represents the most efficient or cost-effective option for achieving the intended impact.

# 4.1 Cost-Effectiveness of Mainstreaming CXR Screening

Annex I presents the estimated incremental costs of mainstreaming CXR screening vis-a-vis symptombased screening, while Annex 2 and Annex 3 respectively present the estimated incremental demand (cases screened) and DALYs averted thanks to such mainstreaming.<sup>49</sup> Results show that the ICER of mainstreaming CXR screening in public facilities with AI-powered CAD (SA2), at a 3 percent discount rate, is PHP 43,376 per DALY, which is lower than the ICER of mainstreaming CXR screening with human readers (SA3: PHP 47,667 per DALY). This means that SA2 is more cost-effective than SA3 since a lower ICER indicates a higher cost-effectiveness. Both ICERs are less than 30 percent of the country's GDP per capita in 2020 (PHP 163,701), which confirms that both SA2 and SA3 are very cost-effective alternatives (ICER < GDP per capita). Although SA2 has greater capacity than SA3, as discussed in section 3, both SA2 and SA3 yield the same number of cases per year (12,277) by serving the same demand (276 cases per week) and achieving the same CXR TAT (<I day). As a result, more TB cases (617) can be diagnosed each year, increasing the number of TB cases treated by around 120 per year (see Annex 2 for more details). Over a period of 10 years, this translates into a reduction in TB incidence by about 1,197 cases (a 0.2% reduction in national TB incidence) and around 55 deaths. Given the same expected treatment initiation and success rates, both SA2 and SA3 can generate the same incremental DALYs averted over a period of 10 years (1,770 DALY), as shown in Figure 4.1 (see Annex 3 for more details). Achieving the same health impact entails a lower incremental cost with SA2 than SA3, as shown in Figure 4.1 (see Annex 1 for more details). The discounted incremental cost of mainstreaming CXR screening with AI-powered CAD or SA2 is estimated at PHP 76.8 million per facility (in 2021 prices), which is slightly lower than with human readers (SA3: PHP 84.4 million per facility). As discussed in section 3, this incremental cost includes capital and recurrent costs, as well as diagnostic and treatment costs required to achieve intended health impact. Among these cost items, the additional recurrent cost of human readers that SA3 entails accounts for this cost difference. Beginning in Year 1, SA2 entails an additional capital cost (CAD software) every five years, but this is much lower than the annual recurrent cost of an additional human reader.

It is important to note that the projected demand (in cases screened per year) for both CXR screening alternatives are below their respective maximum capacities or optimal levels of utilization, given their capital and human resource complements. SA2 has greater excess capacity than SA3 since it can accommodate more cases per day than SA3. That is, while SA3 has only an excess capacity of 16 percent, or an average of nine cases per day, SA2 can expand its screening operations to five days a week and accommodate at least an additional 25 percent more cases, or 69 cases per week, without

<sup>&</sup>lt;sup>49</sup> Mainstreaming CXR screening in health facilities entails shifting to CXR screening as the primary screening tool and expanding screening capacity for intensified case finding.

delaying the release of screening results or requiring additional screening resources. The average daily cases it can serve can be expanded beyond 69 cases per day, as demonstrated by the TB IHSS pilot implementation. These additional cases only entail diagnostic costs for presumptive cases and treatment costs for those who will be initiated to treatment. This implies that, in areas with higher demand than the base scenario, the ICERs for both interventions can be higher. Furthermore, since SA2 can accommodate more clients than SA3, the difference between their cost-effectiveness can be wider in areas where the caseload is over 16 percent greater caseload than the base scenario. The continuous development and possible release of more affordable CAD software is another factor that could further increase the cost-effectiveness of SA2, albeit marginally.



Figure 4.1. Cost-effectiveness of mainstreaming CXR screening with either AI-powered CAD or human readers

### Sensitivity Analysis

As shown in Figure 4.2 and Table 4.1, mainstreaming CXR screening (SA2 or SA3) remains cost-effective at a 7 percent discount rate. Although a higher discount rate increases the ICERs to PHP 43,688 per DALY under SA2 and PHP 47,890 per DALY under SA3, the ICERs remain below the high costeffectiveness threshold (GDP per capita in 2020: PHP 163,701). Mainstreaming CXR screening remains cost-effective with a decline in benefits, increase in capital and recurrent costs, or both, even under a 7 percent discount rate. This demonstrates that the cost-effectiveness of mainstreaming CXR screening with either Al-powered CAD or human readers is robust to cost increases and benefit reductions. The ICERs of mainstreaming CXR screening are highly sensitive to changes in benefits, as shown by the high sensitivity indicator values, under both SA2 (8.77) and SA3 (7.98). A 20 percent reduction in benefits raises its ICER to PHP 54,220 per DALY at a 3 percent discount rate, and PHP 54,610 per DALY at a 7 percent discount rate, under SA2. Under SA3, its ICER is PHP 59,584 per DALY (at 3 percent) and PHP 59,863 per DALY (at 7 percent). Nonetheless, the intervention remains very cost-effective (ICER < GDP per capita) under both SA2 and SA3. A lower-benefit scenario implies higher investment cost per patient and a lower overall health impact. For instance, it may entail a lower-than-expected utilization rate or higher PTLTFU, which may be due to prolonged diagnostic TAT. Lockdown and social distancing policies and low acceptability among radiologists and clinicians are also likely to lower CXR screening utilization. This likely scenario emphasizes the economic importance of having adequate HR and strong health promotion activities and a well-functioning TB diagnostic and treatment referral network, to

support the expansion of CXR screening, while maintaining a shorter CXR TAT than the status quo. Note, however, that these inputs are necessary but not sufficient to achieve the same health impact as mainstreaming CXR screening. Given these resources, activities, and network improvements, some presumptive TB cases can be missed or lost when symptom-based screening is the primary tool and not all targeted people undergo CXR screening.



# Figure 4.2. Cost-effectiveness of mainstreaming CXR screening with either AI-powered CAD or human readers under various scenarios

Table 4.1. Sensitivity analysis							
Comparia	ICER (F DA	PHP per LY)	Switching	Sensitivity			
Scenario	3 percent	7 percent	percent)	Indicator			
SA2: Expanded CXR screening with AI- powered CAD							
Base scenario	43,376	43,688	_	_			
Higher capital and recurrent costs (by 20 percent)	52,051	52,425	1,024.12	0.82			
Lower benefits (by 20 percent)	54,220	54,610	91.10	8.77			
Higher capital and recurrent costs and lower benefits (by 20 percent)	65,064	65,532	78.37	-			
SA3: Expanded CXR screening with human readers							
Base scenario	47,667	47,890	_				

Table 4.1. Sensitivity analysis							
Secretia	ICER (F DA	PHP per LY)	Switching	Sensitivity			
Scenario	3	7	values (in	Indicator			
	percent	percent	percent				
Higher capital and recurrent costs (by 20	57,200	57,468	925.48	0.82			
percent)							
Lower benefits (by 20 percent)	59,584	59,863	90.25	7.98			
Higher capital and recurrent costs and	71,500	71,835	78.14	-			
lower benefits (by 20 percent)							

Note: Switching values are the values at which the intervention becomes marginally cost-effective (i.e., ICER = GDP per capita x 3) at a 7 percent discount rate; these values are lower at 3 percent. Sensitivity indicator is the ratio of the percentage change in ICER to the percentage change in the variable tested. "-" denotes not applicable.

Meanwhile, the ICERs of mainstreaming CXR screening are less sensitive to cost increases (sensitivity indicator < 1). A 20 percent increase in capital and recurrent costs raises the ICER to PHP 52,051–52,425 per DALY under SA2, and PHP 57,200–57,468 per DALY under SA3. While higher costs reduce the intervention's cost-effectiveness by raising the average unit cost of screening, both SA2 and SA3 remain very cost-effective under this scenario. A concurrent reduction in benefits and increase in costs is also likely. Table 4.1 shows that a combination of a 20 percent reduction in benefits and a 20 percent increase in costs raises the ICER to PHP 65,064–65,532 per DALY under SA2, and PHP 71,500–71,835 per DALY under SA3, but the values are still below average GDP per capita.

As mentioned in Section 3, cost-effectiveness can be sensitive to regional variations in local demand for health services and the supply of inputs. Switching values of key variables, or the values at which the incremental cost-effectiveness becomes marginal, provide insights as to how the results here may apply to other settings. They provide useful inputs to future program planning and decision-making, especially when considering areas with lower health utilization and higher local prices than that in the base scenario. Table 4.1 presents the switching values associated with SA2 and SA3. Mainstreaming CXR screening will remain cost-effective (i.e., ICER < GDP per capita x 3) as long the changes in the key variables are below these switching values; otherwise, it will become cost-ineffective (i.e., ICER > GDP per capita x 3). On the one hand, with Al-powered CAD, ICER is three times the GDP per capita (PHP 491,104), or marginally cost-effective, at a 7 percent discount rate with either a 10.2-fold increase in costs, a 91.1 percent reduction in benefits, or a 78.4 percent increase in cost and a proportional reduction in benefits. On the other hand, as shown in Table 4.1, switching values are lower for SA3 at the same discount rate: a 9.3-fold increase in costs, a 90.3 percent reduction in benefits, or a 78.1 percent increase in costs and reduction in benefits. These suggest that mainstreaming CXR screening

remains very cost-effective even after accounting for the estimated 20–25 percent impact of COVID 19– related disruptions on TB services. 50, 51, 52

### Local Investment Cost

Table 4.2 presents the financial investment required to fully cover the installation and maintenance of an expanded CXR screening for ICF with either AI-powered CAD or human readers. This includes capital and annual recurrent costs per public facility. On the one hand, SA3 entails lower capital costs than SA2: PHP 3.5 million in Year I and an additional capital cost of PHP 0.1 million in Year 6, compared with PHP 4.3 million in capital cost in Year I and PHP 0.9 million in Year 6 for SA2. On the other hand, SA3 entails higher recurrent costs (PHP 3.6 million–4.3 million per year) than SA2 (PHP 2.6 million–3.2 million per year). Annex I provides a detailed discussion on what each cost item entails.

Table 4.2 Financial cost estimates for mainstreaming CXR screening         (in 2020 PHP million)										
Intervention and	Year									
Cost Item		2	3	4	5	6	7	8	9	10
SA2 (with AI- powered CAD)	6.9	2.9	2.9	3.0	3.0	4.0	3.1	3.1	3.1	3.2
Capital	4.3	-	-	-	-	0.9	-	-	-	-
Recurrent	2.6	2.9	2.9	3.0	3.0	3.1	3.1	3.1	3.1	3.2
SA3 (with human readers)	7.1	4.0	4.0	4.1	4.1	4.2	4.2	4.2	4.2	4.3
Capital	3.5	-	-	-	-	0.1	-	-	-	-
Recurrent	3.6	4.0	4.0	4.1	4.1	4.2	4.2	4.2	4.2	4.3

# 4.2 Socioeconomic Benefits of Mainstreaming CXR Screening

As discussed earlier, mainstreaming CXR screening (SA2 or SA3) in health facilities results in early TB diagnosis and treatment, reducing TB-related morbidities and mortalities. This can help avert productivity losses of about PHP 283,204 per case treated, or PHP 34 million per year (in 2020 prices) (see <u>Table 4.3</u>).<sup>53</sup> In addition, by reducing the CXR TAT and generating waiting and travel time savings (SA2 or SA3: 8.3 hours per case screened and diagnosed), mainstreaming CXR screening can avert an

<sup>51</sup> A simulation study suggests that COVID 19–related disruptions caused a 25 percent global reduction in expected TB detections. WHO. (2020). World Health Organization (WHO) Information Note: COVID-19: Considerations for tuberculosis (TB) care. Retrieved from: <a href="https://www.who.int/docs/default-source/documents/tuberculosis/infonote-tb-covid-19.pdf">https://www.who.int/docs/default-source/documents/tuberculosis/infonote-tb-covid-19.pdf</a>

<sup>&</sup>lt;sup>50</sup> Klinton, J.S., Heitkamp, P., Rashid, A., Faleye, B. O., Htat, H. W., Hussain, H., et al. (2021). One year of COVID-19 and its impact on private provider engagement for TB: A rapid assessment of intermediary NGOs in seven high TB burden countries. Journal of Clinical Tuberculosis and Other Mycobacterial Diseases, 25.

<sup>&</sup>lt;sup>52</sup> In the Philippines, according to Klinton et al., 2021, due to COVID 19–related disruptions, there was a 20–25 percent decline in all TB care services in the country in 2020 compared to 2019. About 60–80 percent of private clinics had to shut down during the initial lockdown. In addition, COVID-19 test results were required for each client in some Xpert test sites, further delaying the TAT. Klinton, J.S., Heitkamp, P., Rashid, A., Faleye, B. O., Htat, H. W., Hussain, H., et al. (2021). One year of COVID-19 and its impact on private provider engagement for TB: A rapid assessment of intermediary NGOs in seven high TB burden countries. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases, 25*.

<sup>&</sup>lt;sup>53</sup> This amount also includes the effect of early treatment. Although it can be argued that these TB cases will be lost if left undiagnosed, caution must be exercised when using this argument to perform cost-benefit analysis (i.e., cost of treatment must be considered).

additional PHP 275 in productivity losses per case screened and diagnosed. Mainstreaming CXR screening (SA2 or SA3) can also help generate at least PHP 95 travel cost savings per case screened. These bring the total direct and indirect cost savings to PHP 370 per case screened and diagnosed, equivalent to 1 percent of the average monthly household income, or 0.1 percent of the average annual income in 2018 in the national capital region and CALABARZON region (PHP 35,566).<sup>54</sup> This amount excludes the productivity losses averted due to early diagnosis and treatment to avoid overestimation, since these losses also reflect diagnostic and treatment outcomes. This amount can help provide additional financial protection, especially among poor TB patients. Costs related to TB diagnosis and treatment, often compounded by transport costs and forgone income, can drive families below the poverty line, entrenching them in a vicious poverty-disease cycle.<sup>55</sup> A recent study of TB patients in Cavite by Tomeny et al. (2020) suggests 80 percent of multidrug-resistant TB patients and 28 percent of DSTB patients in their study experienced catastrophic expenditures, or expenditures exceeding 20 percent of their annual household income, due to treatment of their illness.<sup>35</sup> The 20 percent threshold captures the point at which the patients and their families must forego basic sustenance expenditures to afford treatment.<sup>45</sup>

Table 4.3. Socioeconomic benefits of mainstreaming CXR screening					
ltem	Value				
Time savings per case screened					
Travel time (hours)	0.96				
Waiting time (hours) – for presumptive cases only					
Productivity losses averted					
Due to early diagnosis and treatment, PHP per case diagnosed and treated					
Due to time savings, PHP per case screened and diagnosed	275.01				
OOP cost savings, PHP per case screened	95.21				
Financial cost protection, PHP per case screened and diagnosed <sup>2</sup>	370.22				
Financial cost protection per case diagnosed, as a percent of monthly household income <sup>2</sup>	1.04				

<sup>1</sup> Same for AI-powered CAD and human readers.

<sup>2</sup> Excludes productivity losses averted due to early diagnosis and treatment.

### 4.3 Lessons Learned and Recommendations

Table 4.4 summarizes the key lessons learned from this study.

#### Policy question 1: Is mainstreaming CXR screening with either AI-powered CAD or human readers cost-effective?

Results of the study confirm that mainstreaming CXR screening in tertiary public facilities, with either AI-powered CAD or human readers, is very cost-effective vis-a-vis symptom-based screening.<sup>41</sup> As compared to symptom-based screening, the ICER of mainstreaming CXR screening with either AI-powered CAD or human readers (PHP 43,376 per DALY and PHP 47,667 per DALY averted

<sup>55</sup> WHO. Tuberculosis Patient Cost Surveys: A Handbook. Geneva: WHO.

<sup>&</sup>lt;sup>54</sup> Philippine Statistics Authority (PSA). (2020). 2018 Family Income and Expenditure Survey. Quezon City: PSA. Retrieved from: https://psa.gov.ph/sites/default/files/FIES%202018%20Final%20Report.pdf

https://apps.who.int/iris/bitstream/handle/10665/259701/9789241513524-eng.pdf

respectively) is less than GDP per capita (PHP 163,701). Compared with symptom-based screening, mainstreaming CXR screening entails an additional cost of around PhP 633 per case screened with Alpowered CAD (SA2) and PhP 695 per case screened with human readers (SA3). In terms of health outcomes, SA2 and SA3 result in the same reduction in TB incidence of about 1,197 cases (0.2% reduction in national TB incidence) and around 55 deaths over a period of 10 years. Mainstreaming CXR screening remains very cost-effective under different likely adverse scenarios considered, such as higher discount rate, lower benefits, higher capital and recurrent costs, and a combination of lower benefits and higher capital and recurrent costs.

Table 4.4. Learning questions and lessons learned						
Learning Questions	Lessons Learned					
I. Is mainstreaming CXR screening with either AI-powered CAD or human readers cost-effective? Learning questions: As compared to symptom-based screening, what is (Ia) the additional cost of CXR screening per case, (Ib) the cost per DALY averted, and (Ic) the estimated reduction in TB incidence and mortality?	<ul> <li>Mainstreaming CXR screening with either Al-powered CAD or human readers is very cost-effective.</li> <li>As compared to symptom-based screening, mainstreaming CXR screening entails (1a) an additional cost of around PHP 633 per case screened with Al-powered CAD (SA2) and PHP 695 per case screened with human readers (SA3), or (1b) around PHP 43,376 per DALY averted with SA2 and PHP 47,667 per DALY averted with SA3. In terms of (1c), SA2 and SA3 result in the same reduction in TB incidence, by 1,197 cases and around 55 deaths over a 10-year period.<sup>1</sup></li> </ul>					
2. As compared to symptom-based screening, how well will mainstreaming CXR screening with either AI-powered CAD or human readers result in improved financial risk protection for patients? Learning questions: As compared to symptom-based screening, how well will CXR screening with either AI- powered CAD or human readers compare in terms of (2a) patient time, (2b) OOP costs, (2c) productivity losses, and (2d) potential reduction in patient catastrophic costs?	<ul> <li>Mainstreaming CXR screening with either AI-powered CAD or human readers results in additional financial risk protection for patients.</li> <li>As compared to symptom-based screening, mainstreaming CXR screening saves about (2a) 8.3 hours in waiting and travel time per case screened, and (2b) PHP 95 OOP costs per case screened.</li> <li>It can avert productivity losses amounting to at least (2c) PHP 2,200 per case screened and diagnosed plus PHP 283,203 per case screened and TB case treated.</li> <li>Finally, patient time and OOP cost savings bring potential reduction in patient catastrophic costs of at least about (d) 0.5 percent of patients and their families' average annual household income.<sup>2</sup></li> </ul>					

<sup>1</sup> The reduction per facility represents a 0.2 percent reduction in national TB incidence.

<sup>2</sup> Excludes productivity losses averted due to early diagnosis and treatment.

Policy question 2: As compared to symptom-based screening, how well will mainstreaming CXR screening result in improved financial risk protection for patients?

The study also confirms that, compared with symptom-based screening, mainstreaming CXR screening generates time and OOP cost savings among patients, and results in productivity savings due to early TB detection and treatment and early CXR TAT. By reducing the direct and indirect costs of seeking TB care services by up to 1.04 percent of monthly household income, mainstreaming CXR screening for

ICF can help generate additional protection from catastrophic health expenditures for TB, especially among poor patients and their families. It can also help reduce the risk of impoverishment from expenses and loss of income associated with undiagnosed or untreated TB and premature deaths.

Because there are unquantified benefits such as improvements in quality of care and quality of life among patients and their families and possible reductions in community transmissions overt time, the full benefits of mainstreaming CXR screening are expected to be significantly higher, particularly in high TB burden areas. It is also important to highlight that, while both SA2 and SA3 result in the same health and socioeconomic benefits, SA2 or CXR screening with AI-powered CAD (1) is more cost-effective, (2) requires less financial and human resources than with human readers (SA3), and (3) has greater potential for broader service expansion.

### Recommendations for Next Steps

From an efficiency perspective, mainstreaming CXR screening with AI-powered CAD or SA2 is highly recommended, especially in resource-limited settings with high TB burden and a limited supply of registered radiologists. Nonetheless, the socioeconomic benefits and cost-effectiveness of mainstreaming CXR screening only indicate its economic viability for achieving the intended health impact. Accelerating access to AI-powered CXR screening, while mitigating possible implementation risks, requires detailed assessments of the following: (i) feasibility, local adoption, and user acceptability of AI-powered CAD; (ii) local affordability and financial sustainability of mainstreaming CXR screening with either AI-powered CAD or human readers; and (iii) securing potential PhilHealth funding and undergoing a comprehensive HTA, which also covers (i) and (ii).

The feasibility of mainstreaming CXR screening will be subject to local availability of additional health care professionals, such as radiologists and radio technicians. It will likely be complicated by the need to navigate the complexities of rolling out the intervention in the context of a COVID-19 pandemic and beyond. On the one hand, the COVID-19 pandemic introduces implementation risks, such as lower service uptake due to lockdown and social distancing policies and higher risk of COVID-19 infection in health facilities. On the other hand, the pandemic presents opportunities for integrating COVID-19 and TB screening using Al solutions, as both COVID-19 and TB diseases may present similar signs and symptoms among patients. The rates of infection for both diseases are also similarly high in large urban and peri-urban areas. This presents an opportunity for the urgent promotion and adoption of CXR screening with Al-powered CAD, as well as for promoting operational effectiveness and efficiency of programmatic responses. One way to mitigate implementation risks related to COVID-19 is to consider other interventions that will reduce LTFU in other stages of TB diagnostics and care (i.e., PTLTFU and TLTFU) to improve TB diagnostic and treatment outcomes and optimize screening investments. Prioritizing areas with high population density and missing TB cases is another possible strategy for optimizing health outcome gains.

Mainstreaming CXR screening also requires the integration of its operating guidelines with the existing operating guidelines of the NTP, as well as of professional societies (e.g., Philippine College of Chest Physicians, Philippine College of Radiology). A prerequisite is the optimization of the local accuracy of the different CAD software algorithms. In addition, acceptability of AI-powered CAD results among

practitioners is critical for promoting local adoption and avoiding treatment delays or additional patient costs. The perceived credibility, relative advantage, and ease of use of AI-powered CAD, as well as its possible threat to the future practice of radiologists, can influence its acceptability among health care professionals. Studies on the acceptability of AI-powered CAD are limited.<sup>56</sup> As with other AI-powered health interventions, understanding the fundamental issues regarding its use, such as accuracy, ethical use, and data privacy, is critical for addressing possible apprehension among local users and stakeholders, and mitigating the challenges for AI technology adoption. It is important to consider findings of such assessments in formulating local guidelines for the use of AI-powered CAD for CXR screening and triage.<sup>57</sup> A recent review of literature suggests a clear understanding of how AI can help patients meet their health care needs can hasten the adoption of appropriate AI technologies.<sup>58</sup>

The financial sustainability and affordability of mainstreaming CXR screening, which vary with local government incomes and budgets, are important policy considerations and required inputs to the HTA process. <sup>22</sup> The study provides financial cost estimates for CXR screening installation and maintenance, including its annual capital and recurrent costs, for assessing the financial sustainability and affordability of the intervention. The availability of financial resources or budget in the implementing facility or local government unit(s) to adequately install and support the intervention over 10 years (the period of implementation) is critical. Finally, securing national government funding via the Philippines Universal Health Care Law (RA 11223) requires adherence to a comprehensive HTA process described in the DOH Methods Guide.<sup>59, 60</sup> The process has several component assessments, including those discussed above. Hastening the nomination process requires a sponsored nomination by the NTP or other DOH units as solicitation of external nominations at the DOH HTA unit has been delayed until 2022.

 <sup>&</sup>lt;sup>56</sup> For example, see Spiegel, J.M., Ehrlich, R., Yassi, A., Riera, F., Wilkinson, J., Lockhart, K., et al. (2021). Using artificial intelligence for high-volume identification of silicosis and tuberculosis: A bio-ethics approach. *Annals of Global Health, 87(1)*.
 <sup>57</sup> Schwalbe, N., and Wahl, B. (2020). Artificial intelligence and the future of global health. *The Lancet, 395(10236),* 1579-1586.
 <sup>58</sup> Lutfi, H., Glasauer, S., and Spittler, T. (2020). The health care benefits and impact of artificial intelligence applications on behaviour of health care users: a structured review of primary literature. *Journal of the International Society for Telemedicine and eHealth, 8,* e10-1.

<sup>&</sup>lt;sup>59</sup> According to the DOH HTA Unit, a health technology is the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures, and systems developed to solve a health problem and to improve quality of life. <sup>60</sup> According to the DOH HTA Unit, HTA is the systematic examination of the properties, effects, and impact of health technologies utilizing a multidisciplinary approach to evaluate the clinical, economic, organizational, social, and ethical implications of a health intervention or technology.

# ANNEX I: ESTIMATING INCREMENTAL COSTS OF MAINSTREAMING CXR SCREENING WITH EITHER AI-POWERED CAD OR HUMAN READERS

### A. Additional Investment Costs per Facility

<u>Table A.1.1</u> summarizes the additional costs for mainstreaming CXR screening in a facility with existing symptom-based screening activities. <u>Table 4.2</u> in Section 4.1 summarizes the annual investment costs required for each facility under SA2 (with AI-powered CAD) and SA3 (with human readers). SA2 entails a lower investment cost than SA3 over a period of 10 years (see <u>Table 4.2</u> in Section 4.1). All prices are expressed in 2021 prices and exclude taxes. This study used Microsoft Excel for all its computations. The following provides a detailed discussion of what each cost item entails and why it is critical to achieving the intervention's intended health impact.

Table A.I.I. Cost of mainstreaming CXR screening							
Cost Item	SA2: with Al-Powered CAD	SA3: with Human Readers	Data Sources				
I. Capital Cost							
Digital X-ray	Yes (I every 10 years)	Yes (1 every 10 years)	Stop I B				
CAD software	Yes (1 every 5 years)	No	TD ILLCC				
Laptop	Yes (1 every 5 years)	Yes (1 every 5 years)					
II. Recurrent Cost							
Human resources	Yes	Yes+					
Support and maintenance	Yes	Yes Yes					
Health promotion and	Yes	Yes Yes					
communications			sources				
Supplies, electricity, and	Yes	Yes					
contingencies							

+ Including cost of human readers/radiologists

### Capital Cost

The study considers the costs of an ultra-portable digital X-ray system (Delft), a laptop, and CAD4TB software (including installation and training) under SA2 (with AI-powered CAD).<sup>61</sup> While the digital X-ray will have an economic life of up to 10 years with proper maintenance, both the software and laptop require replacements every 5 years. SA3 (with human readers) excludes software cost. Equipment and software costs will include installation, staff training, and one year of support.

<sup>&</sup>lt;sup>61</sup> While the study relies on TB IHSS pilot study cost data, it considers other sources of information about prices. It considers an ultra-portable digital X-ray system instead of the system that TB IHSS used. For instance, according to Stop TB Partnership, Fujifilm's FDR Xair is available at USD 49,000 from the Global Drug Facility (GDF), while the Delft Imaging's Delft Light is available at USD 66,750. Possible CAD software packages are InferRead DR Chest from Infervision at USD 5,000 and CAD4TB from Delft Imaging at USD 16,700. These CAD software packages include one perpetual license and the required hardware, installation, training, and one-year support when procured via GDF.

### **Recurrent Cost**

Annual recurrent cost for mainstreaming CXR screening includes the cost of the required human resource complement, equipment maintenance, software support (SA2 only), social media and facility-based health education and promotion, communications, supplies, electricity, and contingencies.

### Human Resources

The additional HR are critical to support the screening of additional TB cases while reducing the CXR screening TAT. The study considers a compensation package based on the Philippine Salary Standardization Law V (effective January 2021) to cover 13 months of remuneration per year for the members of the CXR screening team, which includes screeners, a radiology technician, and radiologist(s). The study also allocates budget for salary increases starting in Year 2 of implementation. This budget increases every two years, allowing increases of up to 15 percent for all posts over a period of 10 years. It considers a step-wise increase in salary, or increase from one pay rate to the next higher rate within the established range for the position.

Both SA2 and SA3 require two screeners and health education/promotion staff, preferably a nurse (salary grade [SG]-15) and a nurse assistant (SG-11). Aside from profiling cases, they will be responsible for implementing social media and facility-based campaigns about TB and CXR screening. They will be responsible for coordinating with hospital laboratory staff, referral diagnostic centers, and patients. These roles are critical for ensuring that the caseload and CXR TAT targets are met, and diagnostic TAT is not prolonged, to prevent PLTFU from increasing. Both SA2 and SA3 require one radiology technician to operate and ensure proper maintenance of the digital X-ray. This is to ensure that the digital X-ray will be at its best performance during CXR screening, preventing frequent suspension of services or delays, which may translate to lost opportunities for finding missing TB cases. SA2 requires at least one trained radiologist (SG-24) to confirm and certify CXR findings with Al-powered CAD and refer patients for diagnostic testing. SA3 requires at least two radiologists (1 SG-24, 1 SG-23) to read, interpret, and certify CXR findings. Having both radiologists is also necessary to achieve the target caseload and maintain short CXR TAT.

### Support and Maintenance

Since the procurement cost of equipment and software includes one-year support and maintenance, both SA2 and SA3 only consider an additional budget for support and maintenance starting Year 2 of implementation. This is crucial to ensuring that the equipment will last its intended useful life, and that the equipment will fully support the screening of all the target cases.

### Health Promotion and Communications

Both SA2 and SA3 include communication budget to support health promotion in-facility and via social media. This will also improve the communication between CXR screening staff and hospital laboratory staff, referral diagnostic centers, center for health development (CHD), provincial and city health offices

(PHO/CHO), and patients. TB IHSS experience suggests that health promotion via social media is effective in generating additional demand. It also highlights the need to maintain close coordination with hospital laboratory staff and referral diagnostic centers, as well as CHD and PHO/CHO, to trace missing patients. Without proper coordination, additional cases due to increased ICF activity may lead to an unexpected high laboratory workload, which may cause longer diagnostic TAT and higher loss to pretreatment loss to follow up (PLTFU).62 Strong collaboration and close coordination with the CHD of NCR, PHOs, and CHOs is required to identify rapid TB diagnostic laboratories for testing overflow samples, trace patients, and strengthen education and counselling about TB disease.<sup>63</sup> In addition, it is also important to fast-track laboratory results by email and instant messaging chat groups.

### Supplies, Electricity, and Contingencies

Lastly, both SA2 and SA3 include budget for screening and office supplies, electricity, and contingencies required to support expanded CXR screening in the facility.

# **B.** Other Costs

Since the study measures the health impacts based on the number of TB patients treated, it also considers the additional overhead costs for diagnostic and treatment under SA2 and SA3 using TB IHSS data and other relevant studies (Table A.I.2). Omitting these costs will overestimate the DALYs averted and other socioeconomic benefits generated by the intervention. As discussed in Annex 2, SA2 and SA3 are expected to generate the same number of cases and treatment outcomes. As such, both SA2 and SA3 entail the same additional diagnostic and treatment costs.

Table A.I.2. Other additional costs							
Cost Item	SA2: with Al-Powered CAD	SA3: with Human Readers	Data Sources				
Diagnostic Cost	Yes	Yes	TB IHSS, other				
Treatment Cost	Yes	Yes	studies				
Treatment Cost	Yes	Yes	studie				

+ including cost of human readers/radiologists.

### Diagnostic Cost

Diagnostic cost per year	=	Presumptive cases per year	x	Diagnostic cost per case
(PHP 4.9 million)		(3,339)		(PHP 1,479)

# Treatment Cost: All Cases Initiated to Treatment

Treatment cost per year	=	Cases initiated to	x	Treatment cost per case
(PHP 0.49 million)		treatment per year (239)		(PHP 2,040)

<sup>&</sup>lt;sup>62</sup> According to TB IHSS, the treatment initiation rate (50 percent in BatMC and ARMMC) is low or suboptimal due to the delay in diagnostic TAT (>1 month). The factors that contribute to this include: (i) overloaded laboratories in the hospitals in the initial period of the project; (ii) lack of communication among hospital laboratory staff, hospital management team, and project staff; and (iii) inability to trace patients due to incorrect phone numbers provided by them.

<sup>&</sup>lt;sup>63</sup> These interventions resulted in improvement in the timing of patients who initiated testing and treatment.

# ANNEX 2: ESTIMATING ADDITIONAL DEMAND AND TB CASES DIAGNOSED AND TREATED

The implementation of TB IHSS's innovative model for TB case finding in two large Philippine hospitals— BatMC and ARMMC—demonstrated that expanding and intensifying TB case finding by mainstreaming CXR screening affects both the demand for and supply of TB screening services (see Figure A.2.1). On the supply side, this intervention expands the capacity of facilities to screen more cases with greater accuracy. On the demand side, more patients are willing to avail themselves of the service, as it makes TB screening more accessible and affordable, both in terms of direct and indirect costs.



# Figure A.2.1. Health impact of mainstreaming CXR screening

How many additional cases, including patients and companions, can each additional CXR screening setup, with either AI-powered CAD or with human readers, screen, given additional capacity and demand for TB screening services? How many additional cases can be diagnosed and treated?

# A. Cases Screened per Year

A total of 12,277 cases were screened over 178 operating days (BatMC: 101 days; ARMMC: 77), yielding an average of 69 cases screened per day).

Average daily cases screened=Total cases/No. of operating days(BatMC + ARMMC: 69 per day)screened (12,277)(178)

If ICF activities can operate four days a week over 44 weeks each year, they can screen at least 12,139 cases per year. This is a conservative estimate based on observed utilization rather than maximum capacity or the optimal level of utilization. It considers 44 weeks only, instead of 52 weeks, to account for non-working holidays and weather disturbances.<sup>64</sup> It accounts for a day per week for system maintenance, which can be rescheduled to accommodate higher caseload as needed.

Cases screened per year	=	Ave. daily cases	х	No. of operating days per year
(12,139)		screened (69)		(176)

<sup>&</sup>lt;sup>64</sup> Based on TB IHSS experience, no ICF activities were held during non-working holidays or when there were weather disturbances. ICF activities were also held less frequently in the two hospitals during December.

### **B.** Presumptive **TB** Cases Diagnosed per Year

The number of expected cases to be screened (12,139) is multiplied by the average proportion of presumptive cases in the two hospitals (27.5 percent) to estimate the expected number of presumptive cases for further testing each year. The proportion of presumptive cases may vary across different facilities and regions. For instance, it was higher for ARMMC (30.3 percent) than in BatMC (24.9).

Presumptive TB cases	=	Cases screened	x	Presumptive TB cases, percent of screened
per year (3,339)		(12,139)		cases (BatMC + ARMMC: 27.5 percent)

# C. Additional TB Cases Diagnosed per Year

The new TB cases diagnosed are BCTB or CDTB TB cases.

Additional TB cases	=	Additional BCTB cases	+	Additional CDTB cases diagnosed
diagnosed per year (617)		diagnosed (138)		(479)

While all the additional BCTB cases among companions of patients (68) can be attributed to the intervention, only a fraction of the additional BCTB cases among patients should be counted (70 cases). The latter include BCTB cases that are presumptive by CXR screening only (60 cases) and 15 percent of those that are either presumptive by symptom screening only or by both symptom and CXR screening (52.0 percent of patients diagnosed with BCTB), which represents that additional demand generated by health promotion through social media. The assessment excludes around 55 cases, or 85 percent of BCTB cases that are presumptive by symptom screening, because these cases can be diagnosed by ICF without the intervention.

Additional BCTB	=	BCTB cases	+	BCTB cases	_	85 percent of BCTB cases
cases diagnosed per		diagnosed,		diagnosed,		presumptive by S/s, patients
year (138)		companion (68)		patients (125)		(55)

The number of BCTB cases diagnosed (68 patient companions; 125 patients) is estimated by multiplying the expected number of cases screened by the proportion of cases screened that are diagnosed as BCTB cases (1.6 percent of cases screened).

BCTB cases diagnosed	=	Cases	х	BCTB cases diagnosed, percent of cases screened
per year (patients: 125		screened		(patients: I percent; companions: 0.6 percent)
or companions: 68)		(12,139)		

Multiplying the total cases screened by the proportion of cases screened which are diagnosed as CDTB cases (3.9) equals the additional CDTB cases diagnosed due to the intervention (479).

Additional CDTB cases=Cases screenedxCDTB cases diagnosed, percentage of<br/>cases screened (3.9 percent)diagnosed per year (478)(12,139)cases screened (3.9 percent)

### **D. Additional TB Cases Treated**

The additional TB cases treated are estimated by multiplying the number of additional TB cases diagnosed, notified, and enrolled (240) by the target TB success rate (50 percent of enrolled cases). This is a conservative target, as it is lower than the average 2020 treatment success rate in Batangas and Marikina (51.9 percent), as well as the national average treatment success rate (71.8 percent), and the regional averages in both CALABARZON (53.1 percent) and NCR (67.2 percent).<sup>65</sup>

Additional TB cases	=	Additional TB cases	х	Treatment success rate,
treated (120)		initiated to treatment (240)		percent of cases diagnosed
				(50)

The study estimates the number of additional TB cases initiated to treatment by multiplying the number of TB cases diagnosed and notified (617) by the treatment initiation rate in the two TB IHSS hospitals (38.8 percent).

Additional TB cases initiated	=	Additional TB cases diagnosed	х	Treatment initiation
to treatment (240)		and notified (617)		rate (38.8)

<u>Table A.2.2</u> summarizes the study's estimates using TB IHSS data. This exercise highlights the independent factors that can improve the intervention's health impact and, therefore, its cost-effectiveness: health service utilization and rates of treatment initiation and success. As these factors vary across regions, the intervention's cost-effectiveness will likewise vary. Specifically, for the same caseload, the intervention's cost-effectiveness is lower in areas with lower expected health care utilization and rates of treatment initiation and success; it is higher where those factors are higher.

<sup>&</sup>lt;sup>65</sup> According to the 2021 Philippine National TB Report, the treatment success rate among new TB cases in 2019 was 62.4 percent (N = 3,385 cases) in Marikina and 49.9 percent (N = 17,516 cases) in Batangas. National Tuberculosis Control Program, Department of Health, Philippines. (2021). *Philippine National Tuberculosis Report*.

Table A.2.1. Additional cases screened and TB cases diagnosed and treated								
ltem	SA2 (with Al- Powered CAD)	SA3 (Human Readers)						
Average cases screened per day	69.0	55.2						
Operating days per year	176.0	220.0						
Cases screened per year, projected	12,139.1	12,139.1						
Presumptive cases per year	3,339.1	3,339.1						
Presumptive cases per year, percentage of cases screened	27.5	27.51						
BCTB cases diagnosed	193.8	193.8						
Patient companions	68.2	68.2						
Patients	125.6	125.6						
Less: Patients, presumptive by S/s	55.5	55.5						
Cases diagnosed and notified due to intervention, projected	616.9	616.9						
BCTB cases	138.3	138.3						
CDTB cases	478.6	478.6						
TB cases initiated to treatment	239	239.5						
TB cases treated, projected	119.7	9.7						
TB cases treated, percentage of cases initiated to treatment	50.0	50.0						

SA2/SA3 = CXR screening for ICF.

# E. Additional Caseload for CXR Screening with Human Readers

TB IHSS data shows that CXR screening with AI-powered CAD can support up to over 100 cases per day. To provide the same services without prolonging the TAT, we assume that each radiologist will read up to four cases per hour, or 32 cases per 8-hour shift. Two radiologists will read up to 64 cases per day. Restricting the maximum number of cases screened per day to 64 cases per day implies a 21.3 percent reduction in average daily caseload, to around 54.3 cases per day. To mitigate this, SA3 will conduct CXR screening five days a week instead of only four days a week. System maintenance can be done for a few hours on days when caseloads are especially low. This will allow the CXR screening team to accommodate the same number of patients under SA2 and SA3. Both alternatives will have the same rates of case detection, treatment initiation, and treatment success.

# ANNEX 3: ESTIMATING DALYS AVERTED AND COST PER DALY

# A. DALYs Averted for Every TB Case Diagnosed and Treated

<u>Table A.3.1</u> summarizes the data used for estimating the DALYs for TB in the country. To get the average DALY per case detected and treated (1.7), the estimated DALY for TB (1.04 million years) is divided by the total number of TB cases in the country (0.60 million).

Table A.3.1. Data requirements for estimating additional DALYs averted							
Variable	Data Source						
National TB death rate	WHO (2020)						
Age-disaggregated population data	UNDESA (2019)						
Age-disaggregated national TB incidence	WHO (2020)						
Standard life expectancy at the age of death	UNDESA (2019)						
Disability weight factor	WHO (2020)						
Average duration of disease	Ragonnet et al. (2021), Tiemersma et al. (2011)						

# B. Additional DALYs Averted Due to Mainstreaming CXR Screening

To estimate the health impact of mainstreaming CXR screening in terms of DALYs averted (207.5), the estimated number of cases per year (119.7) is multiplied by the estimated DALYs averted per case treated (1.7).

DALYs averted per year	=	Cases treated per year	х	DALYs per TB case treated per
(207.5)		(119.7)		year (1.7)

# C. Cost per DALYs Averted

To estimate the cost per DALY averted or the ICER, the study applies a discount rate (3 and 7 percent) to both the annual costs and DALYs averted due to mainstreaming CXR screening over the project's economic life (10 years). Table A.3.2 summarizes the annual costs and DALYs averted due to mainstreaming CXR screening, both with AI-powered CAD (SA2) and with human readers (SA3). It shows the ICERs for both interventions (SA2 and SA3) at 3 percent and 7 percent discount rates.

Table A.3.2. Mainstreaming CXR screening: Costs, DALYs averted							
Year	SA2: with AI-F	owered CAD	SA3: with Human Readers				
	Project Costs (PHP million)	DALYs Averted	Project Costs (PHP million)	DALYs Averted			
2021	12.4	207.5	12.5	207.5			
2022	8.4	207.5	9.4	207.5			
2023	8.4	207.5	9.4	207.5			
2024	8.4	207.5	9.5	207.5			
2025	8.4	207.5	9.5	207.5			
2026	9.4	207.5	9.6	207.5			
2027	8.5	207.5	9.6	207.5			
2028	8.6	207.5	9.7	207.5			
2029	8.6	207.5	9.7	207.5			
2030	8.6	207.5	9.8	207.5			
Present Value at 3 percent	76.8	I,770	84.4	١,770			
Present Value at 6 percent	63.7	1,457	69.8	1,457			
ICER at 3 percent		43,376		47,667			
ICER at 7 percent		43,688		47,890			
GDP per capita		163,701		163,701			
GDP per capita x 3		491,104		491,104			

# ANNEX 4: DESCRIBING THE SOCIOECONOMIC BENEFITS OF MAINSTREAMING CXR SCREENING WITH EITHER AI-POWERED CAD OR HUMAN READERS IN PUBLIC HEALTH FACILITIES

As discussed in the main report (See Section 3), mainstreaming CXR screening generates socioeconomic benefits mainly through: (i) increased number of TB cases detected and treated, and (ii) reduced CXR screening TAT. The study quantifies the former by estimating the productivity losses averted due to early detection and treatment of TB, based on the estimates of DALYs averted from the study's CEA. The study also considers other socioeconomic benefits of mainstreaming CXR screening, including waiting and travel time savings due to shorter CXR TAT, and travel cost savings. While most of these indicators are best measured using primary data, given present physical mobility and time constraints, the study relies on available data from TB IHSS's pilot study in ARMMC and BatMC to describe the possible time and cost savings generated through the intervention, and the additional financial protection they can possibly bring.<sup>66</sup> It also uses supplemental data from Google Maps on travel time and distance to and from facilities, data from public fare matrices, data on income and employment from the Philippine Statistical Authority, data on minimum wages from the Department of Labor and Employment, and data on GDP per capita from the World Bank (see Table A.4.1).

Table A.4.1. Data requirements for estimating socioeconomic health impacts						
Indicator	Source of Data					
DALYs averted	CEA component of this study					
TB cases treated	CEA component of this study					
Roundtrip travel costs to and from the facility	TB IHSS data, public fare matrices					
Travel time to and from the facility	TB IHSS data, Google Maps					
Waiting time per visit (initial consult, symptom	Assumption					
screening, CXR screening, Xpert testing)						
GDP per capita	World Bank's World Development Indicators					
Minimum daily wage	Department of Labor and Employment (DOLE)					
Labor participation and employment rate	Philippine Statistical Authority					
Average household income	Family Income and Expenditure Survey					

# A. Time Savings

By improving the CXR TAT, SA2 and SA3 reduces the waiting time for each patient and their companions undergoing TB screening. Same-day release of CXR findings reduces the need for patients and their companions (e.g., family, guardians, or significant others) to travel to and from the facility and

<sup>&</sup>lt;sup>66</sup> Performing a comprehensive quantitative assessment of the socioeconomic benefits requires data from patient-exit surveys.

spend more for a second visit to the hospital to submit or receive CXR findings and submit a sputum sample. In addition to direct cost savings, waiting and travel time savings for patients and their companions due to faster CXR TAT implies less time away from productive activities, such as work or household chores, for both the patients and their companions.

#### Waiting And Travel Time Savings Due to CXR Screening TAT Reduction

As discussed in Section 3.4, same-day release of CXR findings eliminates the need for a second hospital visit to submit or receive CXR findings and submit a sputum sample. Since studies measuring patient waiting time are rare, this study assumes that, on average, each outpatient visit in a tertiary public hospital for TB screening and diagnostic takes around four hours from registration to receipt of prescription or endorsement slip. It estimates the total waiting time per case screened and diagnosed by multiplying 4 hours waiting time per visit by 1.85 to adjust for patients with companions, based on TB IHSS data (85 percent). As shown in Table A.4.2, reduction in CXR TAT saves around 7.4 hours per case screened and diagnosed. The same adjustment factor (1.85) is applied to average round trip travel time to estimate the average travel time savings per case. Using TB IHSS data on patients' *barangay* residence as reference point, the study contains the expected travel time to and from the hospital (i.e., roundtrip) from Google Maps. On average, a reduction in CXR TAT generates an average of 1 hour of travel time savings per case screened (see Table A.4.2).

Table A.4.2. Time savings and productivity losses averted due to CXR TAT reduction							
ltem	Batangas (BatMC)	Marikina (ARMMC)	Weighted Average	Source			
Travel time savings per case (hours)	0.5	1.5	1.0	Estimated			
Waiting time savings per case diagnosed (hours)	7.6	7.1	7.4	using TB IHSS data			
Minimum wage rate (PHP per day)	303.0	500.0	473.2	DOLE			
Labor force participation rate, 2019–20	62.8	59.0	61.1	Estimated			
Employment rate, 2019–20	91.1	91.1	91.1	using PSA data			
Productivity losses averted (PHP per case screened and diagnosed)	309.1	231.1	275.0	Author's estimate			

ARMMC data covers the period September 2019–March 2021. BatMC data covers the period August 2019–February 2020. DOLE = DOLE's National Wages and Productivity Commission. PSA = Philippine Statistics Authority.

### **B. Productivity Loss Averted**

Mainstreaming CXR Screening (SA2 or SA3) generates productivity losses averted due to early detection and treatment of TB and due to shorter CXR TAT.

#### Productivity Losses Averted Due to Early Diagnosis and Treatment

To estimate the economic value of the productivity losses averted due to early detection and treatment, the estimated number of DALYs averted per case treated (from the CEA) is multiplied by the average GDP per capita (PHP 163,701).

Productivity Loss Averted Per	=	DALYs averted per	х	Average annual GDP per
Case Treated (PHP 309,152)		case treated (1.9)		capita (PHP 163,701)

Productivity Losses Averted Due to CXR Screening Turnaround Time Reduction

This study estimates the economic value of time savings during TB screening in terms of productivity losses averted per case screened by multiplying the average travel and waiting time savings by the minimum wage rate per hour, labor force participation rate (2019–20) and employment rate (2019–20).

Productivity loss	=	Time	х	Minimum wage	х	Labor force	х	Employment
averted per case		savings		rate per hour		participation		rate
diagnosed		(8.3)		(PHP 59.15 per		rate		(91.1
(PHP 275.1)				hour)		(61.1 percent)		percent)

According to the Department of Labor and Employment's National Wages and Productivity Commission, the minimum daily wage rate in the non-agriculture sector is PHP 400 per day in CALABARZON and PHP 530 per day in NCR (Table A.4.3).<sup>67</sup> Based on the 2019 and 2020 Labor Force Survey of the Philippine Statistics Authority, the average labor force participation rates in CALABARZON and NCR were 62.8 percent and 59 percent, respectively, while their average employment rates in the same period were both 91.1 percent.<sup>68</sup>

# C. OOP Cost Savings

The study estimates how much travel cost each patient must spend to and from health facilities to seek TB-related health care treatments. Using TB IHSS data on patients' *barangay* residence as a reference point, the study obtains the expected travel distance to the hospital (i.e., roundtrip). Using this

<sup>&</sup>lt;sup>67</sup> Department of Labor and Employment's National Wages and Productivity Commission website. <u>https://nwpc.dole.gov.ph/</u> (accessed 27 September 2021)

<sup>&</sup>lt;sup>68</sup> According to the PSA, the labor force participation rates in CALABARZON and NCR were 61.7 percent and 57.5 percent, respectively, in 2020 and 64.0 percent and 60.5 percent, respectively, in 2019. The employment rates in CALABARZON and NCR were 88.4 percent and 88.3 percent, respectively, in 2020, and 93.8 percent and 94.0 percent, respectively, in 2019. Philippine Statistics Authority. (2021). Preliminary Results of the 2020 Annual Estimates of Labor Force Survey (LFS). Retrieved from: https://psa.gov.ph/statistics/survey/labor-and-employment/labor-force-

survey/title/2020%20Annual%20Preliminary%20Estimates%20of%20Labor%20Force%20Survey%20%28LFS%29

information, it then estimates the average travel fare using public fare matrices.<sup>69, 70, 71, 72</sup> Travel cost savings per case is equal to the estimated roundtrip travel cost multiplied by the patient-companion adjustment factor (1.85). Reducing CXR TAT generates an average of PHP 96 per case screened.

### **D. Financial Protection**

Finally, the study considers the financial protection gained or the potential reduction in patient catastrophic costs per case screened and TB case treated under SA2 and SA3. It estimates this by expressing the sum of direct cost savings (travel cost savings) and indirect cost savings (productivity losses averted due to CXR TAT reduction) as a proportion of household income. The average income per household is estimated based on the average annual income in 2018 in the national capital region and the CALABARZON region, according to the Family Income and Expenditure Survey. Note that the estimated financial protection gains in this study are underestimated, since they exclude productivity losses due to early diagnosis and treatment, which partly reflect screening outcomes.

<sup>&</sup>lt;sup>69</sup> Land Transportation Franchising and Regulatory Board. 2018 PUJ General Fare Guide. Retrieved from: https://ltfrb.gov.ph/wp-content/uploads/2020/08/PUJ-Fare-Guide-12.4.18.pdf

<sup>&</sup>lt;sup>70</sup> Japan International Cooperation Agency (JICA) and Department of Transportation and Communications (DOTC). (2019). The Project for Capacity Development on Transportation Planning and Database Management in the Republic of the Philippines, Travel Demand Forecasting, Manual Vol. 2. Retrieved from: https://openjicareport.jica.go.jp/pdf/12247649.pdf

<sup>&</sup>lt;sup>71</sup> Montenegro Shippling Lines website. Schedules and Fares. Retrieved from: http://montenegrolines.com.ph/

<sup>&</sup>lt;sup>72</sup> Supercat Ferry website and facebook page. Retrieved from: http://www.supercat.com.ph/ and

https://www.facebook.com/supercatfastferry

ANNEX 5: Cost-Utility Analysis of an Intensified Case Finding Strategy for Tuberculosis Using Artificial Intelligence-Powered Mobile Digital Chest X-ray in Two Tertiary Hospitals in the Philippines

