## Table S1: Overview of Country Programs using Artificial Intelligence to Interpret Chest Radiographs

| Country    | Program goals                    | CAD used      | Screening approach                                  | Operators and readers          | Notes/References            |
|------------|----------------------------------|---------------|---|--------------------------------|-----------------------------|
| Bangladesh | Initial project goal was to      | Primarily     | In initial deployment for private sector            | All the images were taken      | 12                          |
|            | establish linkage between        | CAD4TB and    | engagement, people with presumptive TB (adults)     | by qualified radiographers     |                             |
|            | private providers and the TB     | later qXR and | were tested by CXR followed by Xpert. CAD read      | in the 3 centers. Expert       |                             |
|            | national program by providing    | Lunit were    | the films for evaluation purposes; it was not used  | radiologists re-read all films |                             |
|            | access to quality assured CXR    | used for      | in clinical decision making.                        | for a comparison               |                             |
|            | and Xpert testing to patients    | evaluations.  |   |                                |                             |
|            | referred by private providers    |               | In the second deployment people with                | In second deployment           |                             |
|            | in Dhaka.                        |               | presumptive TB and household contacts are tested    | qualified radiographers        |                             |
|            |                                  |               | by CXR and CAD. People with higher score than the   | perform X-rays. A subset of    |                             |
|            | A second implementation          |               | nationally adopted threshold value, or those with   | images (higher than            |                             |
|            | project used 14 mobile           |               | symptoms are referred for bacteriological testing   | threshold score but            |                             |
|            | systems thorugh a                |               | (Xpert/TruerNAT/Microscopy as available). We        | negative on bacteriological    |                             |
|            | collaboration with the NTP to    |               | expect to share preliminary findings at the union.  | testing) are sent for          |                             |
|            | increase TB case detection and   |               |   | radiologist interpretation     |                             |
|            | use in areas where X-ray         |               | Across the two initiatives more than 50,000 people  | and , reports are shared       |                             |
|            | facilities are not available.    |               | have been screened.                                 | with the patient.              |                             |
| India      | Engaging private informal        | qXR           | Private providers verbally screened individuals for | CXR conducted in private       |                             |
|            | providers for referrals of chest |               | TB. Abnormal CAD findings sent to a healthcare      | facilities with                |                             |
|            | X-ray. The program               |               | worker as text messages generated using the         | radiographers. All CXRs        |                             |
|            | compensated for CXR              |               | qTrack application, also developed by Qure.ai. All  | were read by radiologists      |                             |
|            | prescribed for TB screening by   |               | laboratory testing done at designated TB program    | as well as by the qXR AI       |                             |
|            | informal private providers to    |               | sites. Approximately 8300 people screened.          | software.                      |                             |
|            | encourage referrals. 8 private   |               |   |                                |                             |
|            | Xray facilities were engaged.    |               |   |                                |                             |
| Malawi     | PROSPECT Study. Individually     | CAD4TB        | PROSPECT. Adults with cough attending primary       | CXR conducted by study         | PROSPECT Study <sup>3</sup> |
|            | randomised trial in one urban    |               | care (HIV positive and negative) offered CXR with   | radiographer. Digital chest    |                             |
|            | primary healthcare centre        | qXR           | CAD4TBv5. X-rays done by radiographers. CAD         | X-rays were additionally       | SCALE Study <sup>4</sup>    |
|            |                                  |               | threshold of 45, with confirmation by sputum        | read remotely by a             |                             |
|            | SCALE study. Community           |               | Xpert.  | consultant radiologist, and    |                             |
|            | prevalence survey in urban       |               |   | participants with abnormal     |                             |

|          | Blantyre, Malawi prior to cluster randomised trial  |  | SCALE. randomly selected participants adults had<br>chest X-ray. All participants with TB symptoms or<br>abnormal CXR submitted two sputum samples<br>In total around 14,000 people screened   | findings identified were<br>recalled by telephone and<br>referred to the clinic or city<br>central hospital with<br>results.  |   |
|----------|---|--|--|---|---|
| Nigeria  | Active case finding in hard to<br>reach rural areas. Closing the<br>gap in TB case detection<br>especially among key<br>populations (nomadic<br>communities and internally<br>displaced persons) who have<br>been shown to have a higher<br>burden of TB in Nigeria   | qXR  | Symptom and CXR screening read onsite by CAD<br>and people with either CAD-abnormal (.30 or<br>above) or symptoms would be eligible for Xpert<br>testing.<br>About 10,000 people screened as part of active<br>case finding  | A team of 4 people<br>conducted the screening<br>camps including a trained<br>radiographer, screeners,<br>and a site coordinator. An<br>offsite radiologist read<br>abnormal CAD images for<br>potential clinical diagnosis.  | 5 |
| Pakistan | Massive active case finding for<br>TB program with over 50<br>mobile vans, part of a larger<br>Zero TB cities initiative which<br>began in Karachi- Sindh<br>(province) in 2017, and was<br>later scaled up nationally to<br>four other provinces (KPK,<br>Balochistan, Punjab and Gilgit<br>Baltistan) in the country. The<br>program focused on active<br>screening for TB in a variety of<br>settings such as hospitals,<br>community settings, factories,<br>mines and prisons. | Primarily<br>CAD4TB.<br>qXR was<br>used during<br>Covid-19 and<br>TB screening | A CAD4TB cut-off score of 70 was used to define<br>presumptive TB; people were then asked to submit<br>a sputum (spot) sample for Xpert MTB/RIF or Xpert<br>Ultra. Those with bacteriologically confirmed test,<br>as well as those that were heavily symptomatic<br>were linked to trained physicians at TB Basic<br>Management Units (BMUs) near their areas of<br>residence.<br>As part of this case finding program we conducted<br>over 1.5 million chest X-ray screens for TB between<br>2017-2021.<br>Covid-19 integrated screening was done an about<br>46,000 people in 2021. | The x-ray equipment and<br>associated software was<br>handled by trained<br>radiographers who were<br>adept at conducting these<br>x-rays as well as managing<br>the equipment and<br>associated accessories.<br>TB treating physicians at<br>treatment centers<br>conducted clinical<br>evaluation for<br>clinical diagnosis of Xpert<br>negative presumptive (if<br>required) and initiated<br>treatment. |   |

| Peru     | Prisons: TB screening program    | Prisons –  | Voluntary symptom and screening offered to all           | Women at prisons eligible       | 6 7<br>, |
|----------|----------------------------------|------------|--|---------------------------------|----------|
|          | to do active case finding in six | qXR        | women. A digital CXR was obtained for every              | for Ultra testing were also     |          |
|          | women's prisons                  |            | participant, regardless of symptoms. The findings        | evaluated by a physician for    |          |
|          |                                  |            | were analyzed using qXR software and classified as       | possible clinical diagnosis     |          |
|          | Community based active case      | Community- | normal or abnormal according to the                      | of TB and those diagnosed       |          |
|          | finding using mobile vans.       | based ACF  | manufacturer's default settings (0.5). Sputum            | with TB were referred to        |          |
|          |                                  | CAD4TB     | samples for Xpert testing were collected from            | the local health authority      |          |
|          |                                  |            | participants who had abnormal CXR, and normal            | for treatment initiation.       |          |
|          |                                  |            | CXR but with a productive cough lasting longer           |                                 |          |
|          |                                  |            | than 14 days or a history of HIV, and had either         | Physician at the mobile unit    |          |
|          |                                  |            | fever, weight loss, or night sweats.                     | can determine that there is     |          |
|          |                                  |            |  | evidence of TB based on         |          |
|          |                                  |            | The mobile units offer free chest radiography to         | clinical or radiologic criteria |          |
|          |                                  |            | anyone aged ≥4 years, regardless of symptoms.            | and recommend                   |          |
|          |                                  |            | Radiographs is scored by CAD4TB, with a score >50        | treatment.                      |          |
|          |                                  |            | classified as abnormal. Individuals with abnormal        |                                 |          |
|          |                                  |            | radiographs are given a clinical evaluation by the       | A doctor from the TB            |          |
|          |                                  |            | mobile unit physician who review the chest               | program at the local health     |          |
|          |                                  |            | radiograph obtained during screening.                    | facility confirms the           |          |
|          |                                  |            |  | diagnosis and initiates         |          |
|          |                                  |            |  | treatment.                      |          |
| S Africa | Vukuzazi Community-based         | CAD4TB     | In the field, any symptom, a CAD score $\geq$ 25, or any | Digital CXRs were also          | 8        |
|          | multi-disease screening and      |            | one able to undergo digital CXR (pregnant woman,         | interpreted by an expert        |          |
|          | biobanking study. Residents of   |            | infirmity that prevented climbing into the van)          | radiologist off-site for        |          |
|          | the Africa Health Research       |            | triggered sputum collection. Sputum was assessed         | assessment of                   |          |
|          | Institute demographic            |            | by Xpert Ultra and MGIT culture.                         | normal/abnormal and             |          |
|          | surveillance area in rural       |            |  | abnormality suggestive of       |          |
|          | KwaZulu-Natal were screened      |            | 18,041 adolescents and adult (>15 years of age)          | active TB.                      |          |
|          | for multiple conditions (HIV,    |            | were included.   | Radiologist-identified          |          |
|          | TB, hypertension, diabetes).     |            |  | abnormality that had been       |          |
|          | TB screening including WHO-4     |            |  | "missed" in the field,          |          |
|          | symptom screen and digital       |            |  | triggered attempt at            |          |
|          |                                  |            |  | sputum collection.              |          |

|         | chest x-ray interpreted in the field by CAD.   |   |   |  |  |
|---------|--|---|---|--|--|
| Vietnam | Multiple different projects and<br>pilot deployments was used to<br>inform this perspective piece.<br>Large focus on active case<br>finding with mobile vans but<br>also included facility-based<br>screening. | qXR primarily<br>in program<br>deployment.<br>DrAid<br>(VinBrain)<br>more<br>recently.<br>Several AI<br>software<br>including<br>Lunit Insight<br>as part of<br>different<br>evaluations. | Positioned the CAD software as a paired<br>read/interpretation with an on-site radiologist at<br>both community screening events and in health<br>facilities. Individuals with abnormal results on<br>either read (even when the CAD software and<br>radiologist findings are discordant) were eligible for<br>follow-on sputum testing with the Xpert MTB/RIF<br>assay.<br>Close to 20,000 screenings using the AI and human<br>reading in parallel as part of program deployment<br>were conducted. | CXR screening sites were<br>staffed with a radiographer<br>and radiologist as per<br>regulations in Vietnam,<br>who read all images before<br>or in parallel with the AI. AI<br>software was used for EQA<br>after the event when<br>parallel deployment was<br>not possible.<br>For evaluations of different<br>AI platforms, intermediate<br>and expert radiologists<br>were recruited as reference<br>standards | 9,10   |
| Zambia  | This was facility based active case finding project.   | CAD4TB  | The CAD threshold was set at <=60 Normal.<br>Patients with CAD >=61 received Xpert testing.<br>Presumptive TB was defined as any cough, fever,<br>night sweats or loss of weight among patients<br>presenting to the health facility.<br>Around 9,400 individuals were screened.  | Part of study procedure at<br>health facility with<br>radiographer. Radiologists<br>were not used as part of<br>the evaluations.   | First prospective<br>study to evaluate<br>CAD4TB. ZAMPACT<br>Project <sup>11</sup> , <sup>12</sup> |

## References

- Rahman MMTM, Codlin AJ, Rahman MMTM, Nahar A, Reja M, Islam T, et al. An evaluation of automated chest radiography reading software for tuberculosis screening among public- and private-sector patients. Eur Respir J [Internet]. 2017 May 21;49(5):1602159. Available from: http://dx.doi.org/10.1183/13993003.02159-2016
- 2. Qin ZZ, Barrett R, Ahmed S, Sarker MS, Paul K, Adel ASS, et al. Comparing different versions of computer-aided detection products when reading chest X-rays

for tuberculosis. PLOS Digit Heal [Internet]. 2022;1(6):e0000067. Available from: http://dx.doi.org/10.1371/journal.pdig.0000067

- 3. MacPherson P, Webb EL, Kamchedzera W, Joekes E, Mjoli G, Lalloo DG, et al. Computer-aided X-ray screening for tuberculosis and HIV testing among adults with cough in Malawi (the PROSPECT study): A randomised trial and cost-effectiveness analysis. Barnabas R V., editor. PLOS Med [Internet]. 2021 Sep 9;18(9):e1003752. Available from: http://dx.doi.org/10.1371/journal.pmed.1003752
- 4. Feasey HRA, Khundi M, Nzawa Soko R, Nightingale E, Burke RM, Henrion MYR, et al. Prevalence of bacteriologically-confirmed pulmonary tuberculosis in urban Blantyre, Malawi 2019–20: Substantial decline compared to 2013–14 national survey. PLOS Glob Public Heal [Internet]. 2023;3(10):e0001911. Available from: http://dx.doi.org/10.1371/journal.pgph.0001911
- 5. John S, Abdulkarim S, Usman S, Rahman MT, Creswell J. Comparing tuberculosis symptom screening to chest X-ray with artificial intelligence in an active case finding campaign in Northeast Nigeria. BMC Glob Public Heal [Internet]. 2023 Oct 6;1(1):17. Available from: https://doi.org/10.1186/s44263-023-00017-2
- 6. Chadha VK, Praseeja P. Active tuberculosis case finding in India The way forward. Indian J Tuberc [Internet]. 2019;66(1):170–7. Available from: https://doi.org/10.1016/j.ijtb.2018.05.014
- 7. Puma D, Geadas C, Calderon RI, Yuen CM, Jiménez J, Córdova M, et al. Active case-finding for TB among incarcerated women in Peru. Int J Tuberc Lung Dis. 2023;27(10):784–6.
- 8. Gunda R, Koole O, Gareta D, Olivier S, Surujdeen A, Smit T, et al. Cohort Profile: The Vukuzazi ('Wake Up and Know Yourself' in isiZulu) population science programme. Int J Epidemiol [Internet]. 2022 Jun 13;51(3):e131–42. Available from: https://academic.oup.com/ije/article/51/3/e131/6446138
- 9. Codlin AJ, Dao TP, Vo LNQ, Forse RJ, Van Truong V, Dang HM, et al. Independent evaluation of 12 artificial intelligence solutions for the detection of tuberculosis. Sci Rep [Internet]. 2021 Dec 13;11(1):23895. Available from: https://doi.org/10.1038/s41598-021-03265-0
- 10. Vo LNQ, Codlin A, Ngo TD, Dao TP, Dong TTT, Mo HTL, et al. Early Evaluation of an Ultra-Portable X-ray System for Tuberculosis Active Case Finding. Trop Med Infect Dis [Internet]. 2021 Sep 4;6(3):163. Available from: https://www.mdpi.com/2414-6366/6/3/163
- 11. Muyoyeta M, Moyo M, Kasese N, Ndhlovu M, Milimo D, Mwanza W, et al. Implementation research to inform the use of xpert MTB/RIF in primary health care facilities in high TB and HIV settings in resource constrained settings. PLoS One. 2015;10(6):1–18.
- 12. Muyoyeta M, Kasese NC, Milimo D, Mushanga I, Ndhlovu M, Kapata N, et al. Digital CXR with computer aided diagnosis versus symptom screen to define presumptive tuberculosis among household contacts and impact on tuberculosis diagnosis. BMC Infect Dis. 2017;17(1):1–8.