HHS Public Access

Author manuscript

Lancet Digit Health. Author manuscript; available in PMC 2022 September 01.

Published in final edited form as:

Lancet Digit Health. 2021 September ; 3(9): e535–e536. doi:10.1016/S2589-7500(21)00142-4.

Can AI technologies close the diagnostic gap in tuberculosis?

Christine Tzelios,
Harvard Medical School, Boston, MA, USA

Ruvandhi R Nathavitharana
Division of Infectious Diseases, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA 02215, USA

In 2019, an estimated 10 million people developed tuberculosis, yet only 7·1 million cases were notified to tuberculosis programmes, underscoring the urgent need for improved early detection strategies.[1] Although WHO recommends rapid molecular tests as the initial diagnostic test for tuberculosis, their relatively high cost limits patient access and the screening throughput of chronically underfunded tuberculosis programmes.[2] Renewed interest in chest x-ray as a tuberculosis triage or screening test has been driven by prioritisation of active case-finding strategies.[2] Wider use of chest x-ray is facilitated by lower operating costs, improved image quality, and development of computer-aided detection (CAD) software that uses artificial intelligence (AI) algorithms to identify radiological abnormalities compatible with tuberculosis.[3]

In *The Lancet Digital Health*, Zhi Zhen Qin and colleagues independently evaluated five commercial AI algorithms as triage tests for active tuberculosis: CAD4TB (version 7), InferRead DR (version 2), Lunit INSIGHT CXR (version 4.9.0), JF CXR-1 (version 2), and qXR (version 3). This retrospective study used a database of 23 954 chest x-ray images, not previously used to train any AI algorithms, from individuals presenting or referred to three tuberculosis screening centres in Dhaka, Bangladesh.[4] Only two AI algorithms—qXR and CAD4TB—met WHO's Target Product Profile minimum criteria for triage tests, with specificities of at least 70% (74·3% [95% CI 73·3–74·9] for qXR, 72·9% [72·3–73·5] for CAD4TB) when sensitivity was set to 90%.[5] Above this sensitivity threshold, the receiver operating characteristic curves did not differ significantly between the five algorithms. However, at lower sensitivities, InferRead DR and JF CXR-1 generally performed worse than the other AI algorithms, with lower specificities; this corresponded to lower precision (ie, positive predictive value) being demonstrated in the precision–recall curves for these two algorithms. All algorithms performed worse in people older than 60 years or with a history of tuberculosis. Nonetheless, all algorithms achieved higher specificity than did human radiologists and reduced the number of Xpert MTB/RIF tests required by at least 50% while maintaining a sensitivity higher than 90%. Scaling up of CAD could thus expand screening throughput, particularly in settings where skilled radiologists are not readily available, and improve the cost-effectiveness of diagnostic algorithms by reducing the number of

rnathavi@bidmc.harvard.edu .

confirmatory molecular tests needed. A major strength of Qin and colleagues' analysis is that validation of CAD thresholds for the AI algorithms had not previously been done at the study site, since the need for site-specific CAD threshold validation might limit the ease of potential scale-up of these technologies in different contexts. However, the authors note quality assurance checks and local performance data remain essential to determine optimal threshold scores for use in different clinical settings. All AI algorithms allow users to vary test sensitivity and specificity by adjusting threshold scores to suit programmatic needs, but this leaves difficult decisions to implementers, despite guidance offered by WHO,[2] and could make future systematic comparisons of AI algorithm accuracy challenging.

In March, 2021, WHO recommended that CAD may be used instead of human readers for tuberculosis triage and screening for individuals aged 15 years or older.[2] Qin and colleagues' study focused almost exclusively on triage, since 98·4% of participants reported tuberculosis symptoms, which could improve AI algorithm performance since disease severity is likely to be higher. CAD can also be used as a screening test for seemingly healthy individuals, typically obtained through prevalence surveys or community-based campaigns in high-prevalence settings or among high-risk subpopulations. Despite being resource intensive, mass screening offers two key advantages. First, it enables detection of asymptomatic or subclinical tuberculosis. Half of all people with tuberculosis are asymptomatic but often still detectable on chest x-ray,[6] and identification of such patients early in their disease course could halt progression and transmission. Second, active screening promotes equity by extending diagnostic services to people who face structural, geographical, and financial barriers and often experience delays in obtaining care. Of note, chest x-ray is often not available at primary health centres,[7] so reducing costs and improving access is essential.

The limited sensitivity of symptom screening—the most commonly used tuberculosis screening test—is now well established.[2] Furthermore, a high proportion of patients who report symptoms do not receive follow-up tuberculosis testing.[8] Although digital chest x-ray with CAD holds great promise for triage and screening, it will only affect patient-important outcomes if results are linked to clinicians and acted upon promptly, with confirmatory testing for those with positive CAD results and follow-up evaluation for those with negative results but persistent symptoms. Tuberculosis care services can benefit from leveraging COVID-19 innovations, such as digital tools for education, referrals, and contact tracing, and platforms that facilitate sharing of real-time local and regional epidemiological data to direct public health responses.[9] Compared with non-specific biomarker tests such as C-reactive protein, chest x-ray can also help to diagnose conditions that cause similar symptoms, although this necessitates clear referral processes for non-tuberculosis pathologies.[10] Chest x-ray does not address the demand for rapid tests to detect extrapulmonary tuberculosis, but might pave the way for evaluation and scaling up of other technologies such as point-of-care ultrasound that could fill this gap.

Tuberculosis elimination depends on meaningful integration of modern biomedical solutions with innovative social and political strategies to alleviate poverty. More data are needed to understand the performance of CAD across a range of settings, particularly among asymptomatic populations and those with a history of tuberculosis. Nevertheless, the

sustainable scaling up of CAD and other AI technologies merits attention at the forefront of a broader rights-based approach to improving tuberculosis care.

Acknowledgments

We declare no competing interests. RRN is supported by a National Institutes of Health Career Development Award (NIAID K23 AI132648-04) and an American Society of Tropical Medicine and Hygiene Burroughs Wellcome Fellowship. CT is supported by an Infectious Diseases Society of America GERM Scholar Award.

References

1. WHO. Global tuberculosis report 2020. Geneva: World Health Organization, 2020.
2. WHO. WHO consolidated guidelines on tuberculosis. Module 2: screening—systematic screening for tuberculosis disease. Geneva: World Health Organization, 2021.
3. Harris M, Qi A, Jeagal L, et al. A systematic review of the diagnostic accuracy of artificial intelligence-based computer programs to analyze chest x-rays for pulmonary tuberculosis. PLoS One 2019; 14: e0221339. [PubMed: 31479448]
4. Qin ZZ, Ahmed S, Sarker MS, et al. Tuberculosis detection from chest x-rays for triaging in a high tuberculosis-burden setting: an evaluation of five artificial intelligence algorithms. Lancet Digital Health 2021; 3: e543–54. [PubMed: 34446265]
5. WHO. High-priority target product profiles for new tuberculosis diagnostics: report of a consensus meeting. Geneva: World Health Organization, 2014.
6. Frascella B, Richards AS, Sossen B, et al. Subclinical tuberculosis disease—a review and analysis of prevalence surveys to inform definitions, burden, associations and screening methodology. Clin Infect Dis 2020; published online 9 16. 10.1093/cid/ciaa1402.
7. Huddart S, MacLean E, Pai M. Location, location, location: tuberculosis services in highest burden countries. Lancet Glob Health 2016; 4: e907–08. [PubMed: 27855868]
8. Kweza PF, Van Schalkwyk C, Abraham N, Uys M, Claassens MM, Medina-Marino A. Estimating the magnitude of pulmonary tuberculosis patients missed by primary health care clinics in South Africa. Int J Tuberc Lung Dis 2018; 22: 264–72. [PubMed: 29471903]
9. Ruhwald M, Carmona S, Pai M. Learning from COVID-19 to reimagine tuberculosis diagnosis. Lancet Microbe 2021; 2: e169–70. [PubMed: 33778790]
10. Mungai BN, Joekes E, Masini E, et al. 'If not TB, what could it be?' Chest X-ray findings from the 2016 Kenya Tuberculosis Prevalence Survey. Thorax 2021; 76: 607–14. [PubMed: 33504563]